

SYNTHESIS AND BIOLOGICAL EVALUATION OF NOVEL ANTIMICROBIAL AGENTS FOR
THE CONTROL AND ERADICATION OF PATHOGENIC BACTERIAL BIOFILMS

by

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DEDICATION

I dedicate this dissertation to my grandmother, Jeana. For blazing the trail that led me to succeed in everything I have set my mind to.

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ABSTRACT

Multi-drug resistant (MDR) bacteria that possess the propensity to form biofilms have presented considerable challenges for the medical field in the treatment of chronic infections. Structure activity relationship (SAR) studies were conducted on novel 2-amino-5-nitrothiazole (ANT) derived antimicrobial agents against *Staphylococcus epidermidis* (ATCC 35984) and *Pseudomonas aeruginosa* (PAO1) via Minimum Inhibitory Concentration (MIC) assays and Minimum Biofilm Eradication Concentration (MBEC) assays, and the conclusions of these studies will be presented. In addition, N-trimethylsilyl-2-amino-5-nitrothiazole (*N*-TMS-ANT) was synthesized as a novel and highly efficient reagent for the direct synthesis of ANT derived antimicrobial agents. The preparative utility of this reagent will be described. Additionally, poly-substituted 2-aminoimidazoles have been shown to inhibit biofilm formation, disperse pre-formed biofilms and resensitize MDR bacterial strains to antibiotic treatment. Novel disubstituted 2-aminoimidazoles have been synthesized in excellent yields via an optimized route. Anti-biofilm results of these novel adjuvants against Methicillin-resistant *Staphylococcus aureus* (MRSA USA300 LAC) and a highly virulent strain of *Pseudomonas aeruginosa* (PA14) in Kirby-Bauer Disk Diffusion assays will be disclosed. Finally, the CDC Biofilm Reactor assay, a robust biofilm model, was utilized to further shed light on the activity of our lead adjuvants against MDR bacterial strains.

CHAPTER ONE

1. INTRODUCTION

1.1 Multi-Drug Resistant Biofilms

Multi-drug resistance (MDR) is an evolved property in bacteria that has been largely attributed to the frequent use of antibacterial agents in the medical setting. The evolution of resistance in bacteria can be broken down into several different mechanisms; efficient cellular efflux clearing in gram negative bacteria, production of enzymes which breakdown the pharmacophore, alterations to the target's binding site, and biofilm formation.¹⁻³ Of these defense mechanisms, this dissertation will focus on biofilm formation. Most bacteria can form biofilms, which possess significantly increased tolerance towards antimicrobial treatment compared to planktonic bacteria. Current literature estimates that this increased tolerance to antibiotic treatment displayed by bacterial biofilms is on the order of 1000 fold compared to planktonic bacteria.⁴ The formation of a biofilm occurs when free floating cells adhere to a surface, either biotic such as the lining of a cystic fibrosis patient's lungs or abiotic such as a medically implanted device. After attachment, the cells excrete extracellular polymeric substances (EPS) or what is commonly referred to as a matrix—composed of extracellular DNA, polysaccharides, and proteins. This matrix encases the bacteria to trap water and nutrients within the biofilm for prime growth conditions, while also keeping them protected from desiccation, host immune defenses, and antibiotic treatment.^{3, 5-11}

To further compound the challenge of resistant strains, biofilms have developed tolerance mechanisms which make them recalcitrant to treatment. Biofilms have several effective defense

mechanisms towards antimicrobial agents; protection from penetration via the matrix of EPS, utilization of alternative metabolisms, induction of stress responses and slowed or cessation of growth known as dormancy.^{6, 12-14} Bacteria within a biofilm are also able to communicate via quorum sensing and respond to stressors as a community accordingly.^{15, 16} Individual cells within the greater biofilm are not all going to be in the same physiological state and are going to be dependent on varying processes. Because of this, biofilms are a difficult problem from an engineering perspective, as their physical heterogeneity makes applying any assumptions very difficult.¹⁷

An early example in the literature of a biofilm's matrix preventing penetration of antibiotic treatment was documented in *Pseudomonas aeruginosa* biofilms by Nichols and colleagues. They found that the antibiotic tobramycin was binding to alginate and exopolysaccharides within the matrix, as tobramycin contains a positive charge and components within the matrix are negatively charged.^{9, 18} A surprising case of peripheral cells within a biofilm protecting the larger biofilm in a similar manner was detailed by Stewart and colleagues in which the enzyme responsible for breaking down hydrogen peroxide, catalase, was found to still be active within dead cells. Consequently, the treatment of the biofilm with hydrogen peroxide only resulted in thicker biofilms.¹⁹ During infection, bacteria in biofilms exhibit slow growth and a low metabolic state due to O₂ limitation imposed by intense O₂ consumption of metabolically active bacteria in the biofilm periphery. Due to these O₂ gradients throughout the infection, biofilms can be dependent on aerobic, microaerobic and anaerobic metabolism.²⁰ Bacteria deep within these biofilms reside dormant, often allowing them to survive exposure to antibiotics or other bactericidal agents and regenerate the biofilm, making them more likely to

achieve additional mechanisms of resistance. An infamous example is found in the antibiotic ciprofloxacin which is highly potent against planktonic bacteria as an inhibitor of DNA replication. However, in the case of dormant cells deep within a biofilm, this process is not occurring and therefore these persister cells survive its treatment, ultimately evolving resistance and proliferating.¹³ Another powerful mechanism of tolerance attributed to biofilms is quorum sensing. Quorum sensing is dependent on population density-- as bacteria produce small molecules for signaling, referred to as autoinducers, in high population densities the extracellular concentration is high enough that it is no longer favorable for these molecules to be exported out of the cell and the intracellular concentration therefore increases to a threshold point where these autoinducers are able to affect responses from the cell.^{15, 21, 22} Taking these complications into account, bacteria that have the propensity to form biofilms present a considerable challenge for the medical field in the treatment of chronic infections.²³

In the United States annually, it is estimated by the Center for Disease Control (CDC) that 2.8 million hospital-acquired infections occur, resulting in 35,000 deaths. The cost of treating these infections is estimated to be \$21–34 billion. Approximately 4 in 5 of these infections are a direct result of biofilms.²⁴ Current methods do not address the problem. Current antibiotics have serious side effects largely attributed to poor selectivity and often lead to development of further resistant strains, sometimes more rapidly than we can develop the antibiotic itself.²⁵ As evolution of resistance is foreseen for most new therapeutics, pharmaceutical entities are further disincentivized to develop new antibiotics as the use of such “drugs of last resort” is strictly controlled and there is therefore not a broad enough use of the drug for these companies to gain a profit. Due to this economic challenge, the development of

new antibiotics is an issue that has largely been left to the academic community.^{26, 27} There is a critical need for the development of drugs that are able to overcome these challenges and such development would have a substantial impact on the field of medicine.

1.2. Project Overview

This dissertation is a collection of works in which all were intended to explore structure activity relationships (SARs) for antibiotic compounds that were designed and synthesized by various inspirations. Since the first antibiotic use in 1941, the advent of Penicillin, resistance occurred almost immediately in a strain of *Staphylococcus aureus* that was characterized in 1942.²⁸ The concept of a biofilm is new to science compared to the long-standing history of developing new medicinal compounds for the betterment of society.^{1, 29} Due to this gap in innovation, the vast majority of current medicines on the market were not designed or developed with biofilms in mind.

We sought to address this by comparing traditional methods of biological screening of our compound libraries with those that are engineered to mimic biofilm conditions. In all our studies, we compared the lead compounds of the planktonic assays to that of the lead compounds of the biofilm assays. There was little to no overlap in which lead compounds against planktonic cultures were also active against their biofilm counterparts, something Danica Walsh also found in her studies in our group.³⁰⁻³² This lack of overlap highlights the need for studies that seek out leads specifically targeting biofilms to effectively identify successful future therapeutics, as it is estimated that roughly 80% of chronic infections are a direct result of biofilms.²³

We addressed this goal in three studies: The first focused on investigating SARs against biofilms and planktonic cultures of nitro-heteroaromatic drugs, known as thiazolides and

furans.³³ The benchmark therapeutic we compared the activities of our thiazolides against was nitazoxanide, and the benchmark therapeutic was nitrofurantoin and furazolidone for our furans. We found these drugs to be promising starting points, specifically nitazoxanide, in anti-biofilm activity due to their respective mode of action and the lack of known resistant strains that have evolved.³⁴ These therapeutics are most potent against anaerobic bacteria, as they target the metabolism of pyruvate, and are therefore interesting in respect to mature biofilms which exhibit anoxic regions where anaerobic metabolism is predominant. The second study is on the synthesis of a novel reagent for preparing the aforementioned nitro-drugs in higher yields.³⁵

In the third study, we sought to disrupt biofilm communication – quorum sensing. 2-aminoimidazoles have been found to be potent quorum sensing antagonists, causing biofilms to disperse back into planktonic phase bacteria. This renders them vulnerable to traditional antibiotics. They are therefore referred to as adjuvants, as they would be potent in combination with conventional treatments.

CHAPTER TWO

2. NOVEL NITRO-HETEROAROMATIC AGENTS FOR THE CONTROL AND ERADICATION OF
BIOFILM-FORMING BACTERIAContribution of Authors and Co-Authors

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Contributions: Prepared manuscript, performed compound synthesis and biological evaluation studies.

Co-Author: Gregory M. Durling

Contributions: Performed compound synthesis and biological evaluation studies.

Co-Author: Danica J. Walsh

Contributions: Performed compound synthesis and biological evaluation studies.

Co-Author: Tom Livinghouse

Contributions: Prepared manuscript, directed and conducted compound design and synthesis.

Co-Author: Philip S. Stewart

Contributions: Oversaw the biological evaluation studies and provided laboratory space for these.

Manuscript Information

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Antibacterial Resistance and Novel Strategies to Eradicate Bacterial Biofilms

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2.1 Abstract

The majority of bacteria naturally reside in accumulations called biofilms, which exhibit a substantially increased tolerance toward antimicrobials compared to free floating cells. The synthesis and biological activity of several new nitrothiazole, nitrobenzothiazole and nitrofurans containing antimicrobial agents for the eradication of biofilm-forming Gram-negative and Gram-positive pathogens is described. Nitazoxanide (NTZ), nitrofurantoin and furazolidone are commercial antimicrobials, which were used as models to show how structural modification improved activity toward planktonic bacteria and biofilms. Structure activity relationship (SAR) studies illustrate the ways in which improvements have been made on the aforementioned antimicrobial agents. It is of particular interest in this regard that the introduction of a chloro substituent at the 5-position of NTZ (analog **1b**) results in superb activity enhancement, as does the replacement of the 2-acetoxy substituent in the latter compound with a basic amine group (analog **7b**). It is also of importance that analog **4a**, which is a simple methacrylamide, displays noteworthy activity against both *S. epidermis* and *P. aeruginosa* biofilms.

2.2 Introduction

2.2.1 Biofilms in Nosocomial Infections

Frequent use of antibacterial agents in the medical setting has led to the emergence of multi-drug resistant bacteria. These bacteria have developed several different mechanisms of resistance – efficient cellular efflux clearing, alterations to the target binding site, and biofilm formation. Bacteria that have the propensity to form biofilms have presented a considerable challenge for the medical field in the treatment of nosocomial bacterial infections. Biofilms are

communities of bacteria that have adhered to a surface, either biotic or abiotic. Once attached, cells secrete extracellular polymeric substances (EPS) composed of extracellular DNA, polysaccharides and proteins. The EPS traps nutrients and water within the biofilm, allowing cells to mature under nutrient rich conditions while being protected from desiccation, host immune defenses and antimicrobial agents.^{5, 7, 36-38} As a consequence of these defense mechanisms, biofilms are associated with 3 out of 4 microbial infections in the body and are responsible for around 1.7 million hospital acquired infections per year,³⁷ resulting in nearly 100 thousand deaths annually in the United States.³⁸ Bacteria deep within these films reside dormant, often allowing them to survive exposure to antibiotics or other bactericidal agents and regenerate the biofilm, making them more likely to achieve additional mechanisms of resistance. In hospitals, where the use of antibacterial agents is frequent and resistant strains are emerging, life-threatening infections can occur when biofilms adhere to medical implants or more critical surfaces within the body, such as the urinary tract. Additionally, biofilms can disperse planktonic bacteria that adhere and form colonies distant from the original infection site. These infections persist after treatment with mainline antibiotics and present significant difficulties within hospitals throughout the world.

The Center for Disease Control (CDC) estimates that as many as 2.8 million nosocomial infections occur, leading to 35,000 deaths annually in the United States and as much as \$21-34 billion is spent to treat these infections. Biofilms are implicated in the majority nosocomial infections³⁹ therefore, development of drugs that are able to overcome this mechanism of resistance is of utmost importance and would have a profound impact in medicine.

2.2.2 Antimicrobial Design

Nitazoxanide is a broad-spectrum antiparasitic and broad-spectrum antiviral drug belonging to the thiazolide class. It is used as a first-line choice for the treatment of infections caused by *Cryptosporidium parvum* and *Giardia lamblia*.^{40, 41} When Nitazoxanide is metabolized, it is deacetylated to produce an active metabolite Tizoxanide.⁴² Thiazolides interfere with the pyruvate:ferredoxin oxidoreductase (PFOR) enzyme-dependent electron transfer reaction.⁴³ Nitazoxanide outcompetes the substrate pyruvate by targeting the vitamin co-factor thiamine pyrophosphate (TPP). Mechanistic studies suggest Nitazoxanide is biologically active as an anion and abstracts a proton from the TPP:pyruvate intermediate—which ultimately halts conversion of pyruvate to acetate, a key component for energy production. Docking studies have shown the nitro group is necessary for nitazoxanide's activity.⁴⁴ Nitazoxanide's mode of action holds promise of future drug development, as it does not interact with the PFOR enzyme directly and is therefore less likely to promote mutation-based drug resistant strains. PFOR is also a unique mechanism to the target group of pathogens and is not in humans, making it a prime candidate for therapeutics.⁴⁵⁻⁴⁷

Several analogues of nitazoxanide have been synthesized and studied previously but were evaluated exclusively toward planktonic cells of *Helicobacter pylori*, *Campylobacter jejuni*, *Clostridium difficile* as well as the protozoa *Giardia lamblia* and *Cryptosporidium parvum*. These analogues optimized nitazoxanide by replacing the nitro group with halogens as well as adding a number of other groups to the aromatic ring with fluoro, chloro, cyano, nitro and methoxy substituents.^{48, 49} In these studies, it was shown that 5-chloro and 5-methoxy substituents markedly increased activity. Although there has been very limited research

involving Nitazoxanide against biofilms, it has been shown to inhibit biofilm formation in *E. coli* and *S. epidermidis* and decrease cell viability of *C. difficile* biofilms.⁵⁰

Several nitazoxanide analogues herein were initially synthesized and biologically evaluated (Figure 2.1.). Structure activity relationship (SAR) studies are optimally conducted when direct comparisons can be made to a control molecule by introducing nominal changes, rather than altering many variables at once. With this goal in mind, substituents were introduced to the aryl ring to show how electron withdrawing groups (e.g., Cl) or electron donating groups (e.g., OCH₃) can impact activity. Alternatively, the location of the nitrothiazole carboxamide was shifted from the 2- to the 4-position relative to the acetoxy substituent.

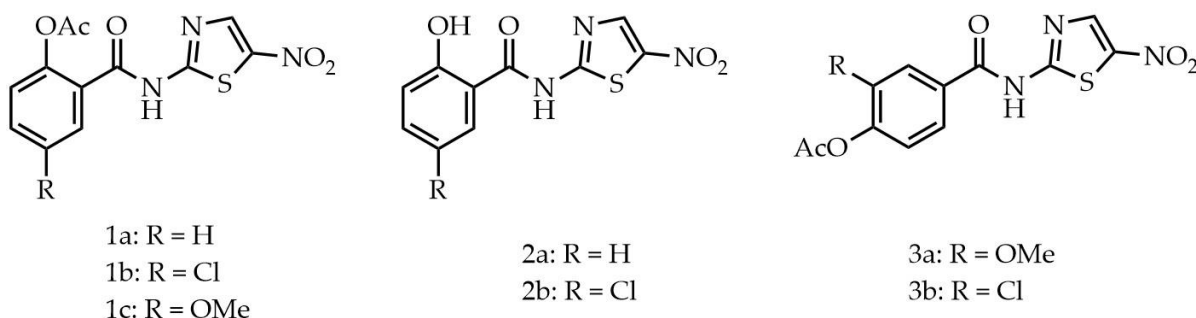


Figure 2.1. Nitazoxanide and initial analogs.

Further SAR analyses were conducted on the structurally simpler amides **4a-c** (Figure 2.2.). The methacrylamide present in **4a** could potentially serve as a 1,4-nucleophile acceptor whereas the chloroacetamide within **4c** could function as an alkylating agent. As a control example, the simple butyramide **4d** was selected for comparison. In addition, the “dual-warhead” candidate was synthesized. A previous study has described dramatically enhanced activities of Nitazoxanide analogues derived from 2-amino-6-nitrobenzothiazole.⁵¹ Therefore, **5a** was

prepared for a direct comparison to **4a** and the novel amide **5b** that also contains two nitro-heteroaromatic antimicrobial “warheads” was synthesized and evaluated.

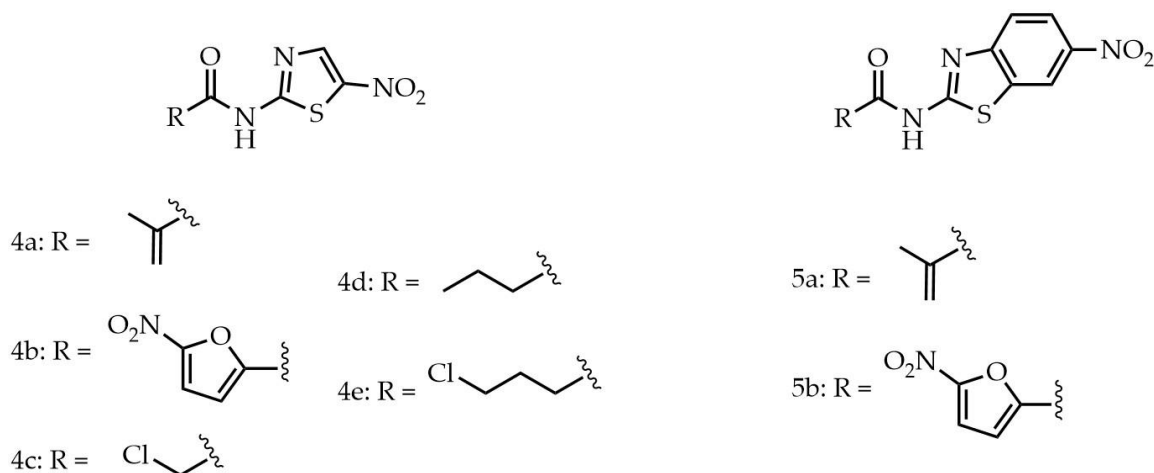


Figure 2.2. Second generation antimicrobials.

The acetoxy group is believed to be important for the activity of nitazoxanide (**1a**), since it can be hydrolyzed to the phenolic hydroxyl present in tizoxanide (**2a**) subsequent to cell penetration. As strategic alterations, anilines **7a,b** and acetanilides **6a,b** were synthesized and evaluated (Figure 2.3.). The synthesis of these analogs was readily achieved by the acylation of 2-amino-5-nitrothiazole with the appropriate isatoic anhydride in MeCN using Et₃N as the auxiliary base to provide **7a** and **7b** in 78% and 82% percent yield respectively. Simple acetylation (Ac₂O) then gave **6a** and **6b** (Scheme 2.1.).

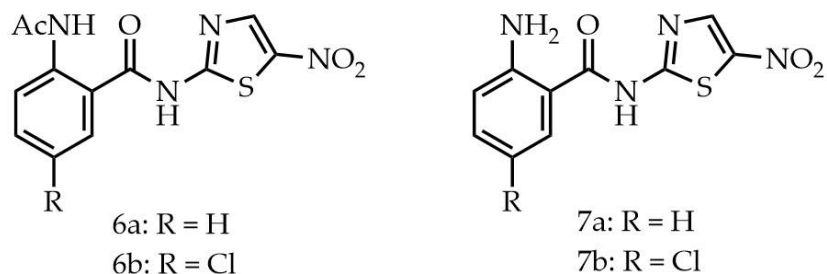
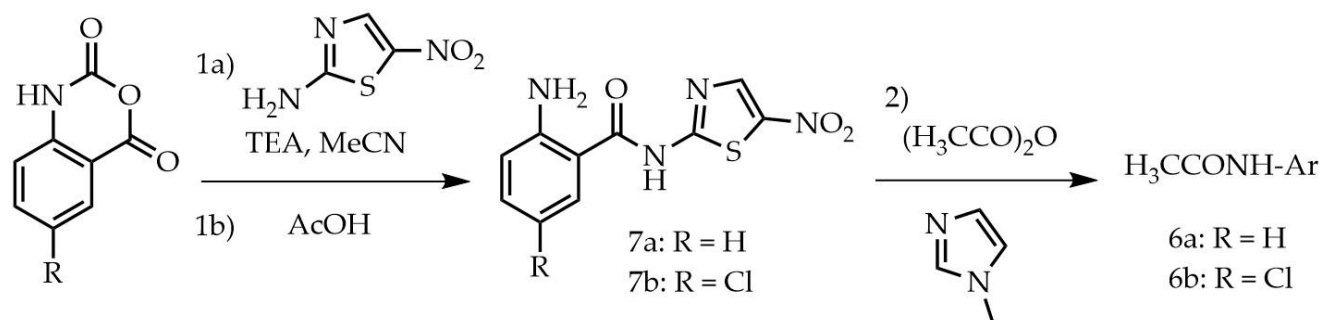


Figure 2.3. Aniline and acetanilide analogs.



Scheme 2.1. Synthesis of aniline and acetanilide analogs.

Other promising examples of drug models that include nitro functional groups are nitrofurantoin (**8a**) and furazolidone (**8b**). Both are Nitrofurans, which are a class of drugs that have been shown to be active against both Gram-positive and Gram-negative pathogens, with the ability to inhibit mRNA and therefore interfere with gene expression.⁵² Nitrofuranyl compounds have also been shown to be potent anti-tubercular agents⁵³⁻⁵⁵ and nitrofuranyl benzimidazoles have shown great potency against methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant *Enterococcus faecium*.⁵⁶ Nitrofurantoin is widely used to treat urinary tract infections. Mode of action studies show bacterial nitro reductases convert nitrofurantoin to electrophilic intermediates which attack ribosomal proteins, effectively halting protein synthesis.⁵⁷ Furazolidone is used to treat gastrointestinal infections and is a monoamine oxidase inhibitor.⁵⁸ The 4-nitrofurancarboxylic hydrazides **9a,b** and **10** were readily prepared by the condensation of 4-nitrofurancarbohydrazide with the appropriate acyl chloride (Figure 2.4.).

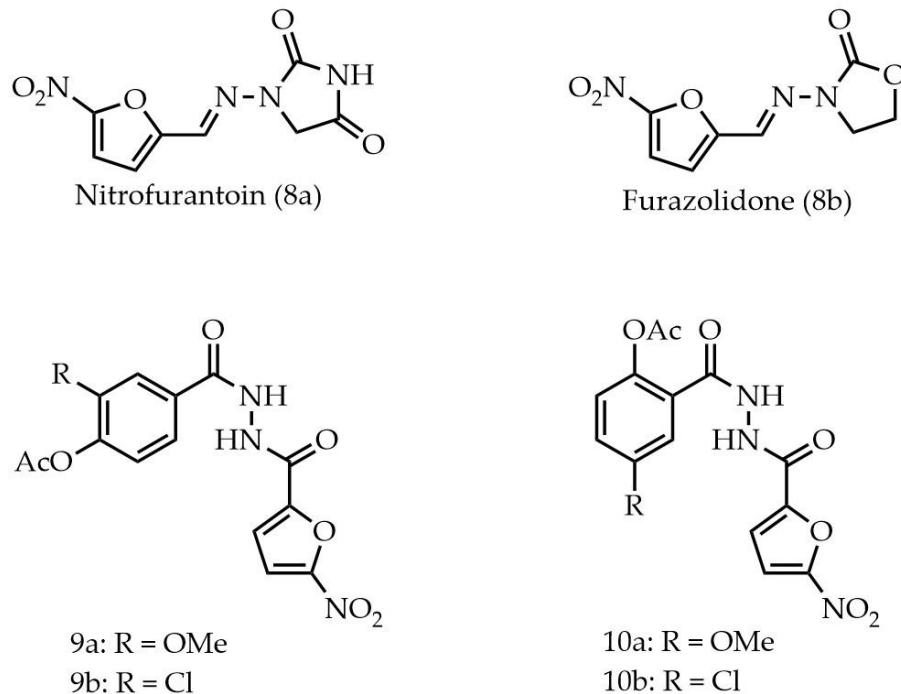


Figure 2.4. Nitrofuran analogs.

Investigation of these nitro-heteroaromatic analogs as potential therapeutic antibiotics for the treatment of nosocomial biofilm infections is described. The aim was to find potent compounds with high activity against biofilms for potential starting points in further pro-drug studies.

2.3 Results and Discussion

Biological evaluation of the commercial antimicrobials and their nitro-heteroaromatic analogs were conducted against *Staphylococcus epidermidis* and *Pseudomonas aeruginosa* in both the planktonic and biofilm states, via minimum inhibitory concentration (MIC) and minimum biofilm eradication concentration (MBEC) assays. The bacterium selected for this study were chosen based on comparison of Gram-negative and Gram-positive, as well as for their propensity to form biofilms. The Gram-negative bacterium selected for this study,

Pseudomonas aeruginosa, is opportunistic, exhibits multi-drug resistance, and has a pronounced propensity to form biofilms. The Gram-positive bacterium selected for this study, *Staphylococcus epidermidis*, has the ability to form biofilms and has been implicated in chronic urinary tract infections, as well as persistent infections on medical devices.³⁰⁻³² *Staphylococcus epidermidis* strain ATCC 35984 was chosen as a representative Gram-positive organism with well-documented biofilm-forming ability. Although the primary focus of this study is biofilm eradication, MIC results involving *S. epidermidis* and *P. aeruginosa* in the planktonic state will be presented initially as background material. These results are assembled in Table 2.1.

Table 2.1. Minimum inhibitory concentrations (MICs, in mM) of synthesized nitrothiazolyl and nitrofuranyl containing analogs compared to the market-available drugs nitazoxanide, Tizoxanide, nitrofurantoin, and furazolidone against nosocomial pathogens *Staphylococcus epidermidis* and *Pseudomonas aeruginosa*.

Compound	<i>S. epidermidis</i>	<i>P. aeruginosa</i>
Nitazoxanide (1a)	0.24	0.06
1b	0.019	1.9
1c	0.39	3.125
Tizoxanide (2a)	0.39	0.195
2b	3.9	7.8
3a	0.012	0.049
3b	0.006	0.195
4a	0.049	0.049
4c	0.012	0.39
4d	0.012	0.097
4e	0.098	3.125
5a	0.039	0.195
5b	<0.0015	0.098
6a	0.098	1.56
6b	0.78	1.56
7a	0.024	1.56
7b	0.003	0.78
Nitrofurantoin (8a)	0.049	0.098
Furazolidone (8b)	0.098	0.195

9a	0.39	0.78
9b	0.012	0.78
10a	0.0015	3.125
10b	0.006	0.195

Interestingly, nitazoxanide (**1a**) proved more active against both bacteria than its purported metabolite tizoxanide (**2a**). This contrast was even more substantial in the case of biofilms (vide infra). For the closely related analogs **1b** and **2b**, this trend was also observed with acetate **1b** being significantly more active toward *S. epidermidis*, but less so in the case of *P. aeruginosa*. For the positionally “inverted” acetate analog **3b**, comparatively excellent activity was observed against *S. epidermidis*, whereas **3a** was the most potent in the extended series toward *P. aeruginosa*.

For 2-amino-4-nitrothiazole (ANT) derivatives possessing potential nucleophile acceptors (e.g., **4a**, **4c** and **4e**) no activity improvement was observed compared to the simple butyramide for *S. epidermidis*, but methacrylamide **4a** showed substantial activity against *P. aeruginosa*. Importantly, the “dual-warhead” candidate **5b** derived from 2-amino-6-nitrobenzothiazole proved highly effective against *S. epidermidis* in accord with the observations of Gau et al.⁵¹ It is also significant that anilines **7a** and **7b** showed high activity toward *S. epidermidis* with **7b** being noteworthy in this regard. Acetylation of the basic nitrogen in these compounds to give **6a** and **6b** resulted in a loss of activity, in sharp contrast to the corresponding to phenol **2b** vs. acetate **1b** (vide supra). Within the 4-nitrofurran-2-carbohydrazide analog series excellent relative activities for **9b** and **10** were obtained against *S. epidermidis* with **10** also showing very good potency toward *P. aeruginosa*. It is of further interest that **10** corresponds structurally to **1b** in the “ANT” series, which proved outstanding in the MBEC studies that

follow. The unusual resilience of biofilm-mediated infections has been attributed to the retarded penetration of antimicrobial agents through binding to the robust EPS matrix, thereby hindering complete access throughout the biofilm.^{3, 7, 29, 59, 60} Another more important obstacle in treating biofilms is the dormancy of cells within the interior, due to low levels of nutrients and oxygen. This reduced activity cell state is less susceptible to conventional antibiotics, which work most effectively on actively dividing cells.^{6, 61} Biofilms are therefore often many times more robust than planktonic bacteria toward antimicrobial agents.

Table 2.2. Minimum biofilm eradication concentrations (MBECs, in mM) of synthesized nitrothiazolyl and nitrofuranyl containing analogs compared to the market-available drugs nitazoxanide, Tizoxanide, nitrofurantoin, and furazolidone against nosocomial pathogens *Staphylococcus epidermidis* and *Pseudomonas aeruginosa*.

Compound	<i>S. epidermidis</i>	<i>P. aeruginosa</i>
Nitazoxanide (1a)	50	3.125
1b	0.16	12.5
1c	1.56	25
Tizoxanide (2a)	>100	>100
2b	6.25	12.5
3a	1.56	25
3b	6.25	100
4a	1.56	3.125
4b	3.125	6.25
4c	3.125	50
4d	3.125	25
4e	12.5	50
5a	25	50
5b	3.125	25
6a	1.56	50
6b	1.56	25
7a	3.125	12.5
7b	0.39	3.125
Nitrofurantoin (8a)	3.125	12.5
Furazolidone (8b)	3.125	6.25
9a	3.125	12.5
9b	3.125	25

10a	12.5	25
10b	3.125	25

The MBEC results that were obtained for *Staphylococcus epidermidis* and *Pseudomonas aeruginosa* are compiled in Table 2.2. It should first be emphasized that, once again, the presumed phenolic metabolites **2a** and **2b** were less potent than the corresponding acetates **1a** and **1b**, and in the case of tizoxanide (**2a**) this was significant. Furthermore, all of the ANT analogs exhibited substantially improved activities against *S. epidermidis* than nitazoxanide (**1a**). For the biofilms of current interest, acetate **1b** and aniline **7b** were noteworthy in respect of their potencies. In contrast to the findings of Ballard,⁴⁸ the methoxy derivative **1c** was not particularly active. Methacrylamide **4a** also displayed high activity, and was comparable to **7b**, both being equipotent to nitazoxanide (**1a**) against *P. aeruginosa*. In contrast, the activities of the analogs derived from 2-amino-6-nitrobenzothiazole, **5a** and especially **5b**, were disappointing (see: MIC for **5b** above) and the ANT based “dual-warhead” analog **4b**. In the 4-nitrofur-2-carbohydrazide analog series, only **9a** showed potential promise compared to the commercial antimicrobials.

2.4 Materials and Methods

2.4.1 Chemistry

All chemical reagents and conventional antibiotics (**1a**, **8a**, **8b**) were purchased from commercial sources (TCI America, Portland, OR, USA and Sigma Aldrich, Burlington, NC, USA) and used as received without further purification. Solvents utilized in filtrations, transfers, and chromatography were certified ACS grade. HEPES buffer and DE broth were purchased from Sigma Aldrich. Thin-layer chromatography was performed on Silicycle Glass Backed TLC

Extra Hard Layer, 60 Å plates (thickness; 250µm, indicator; F-254) and visualization was accomplished with UV light (254 nm), and/or potassium permanganate. All synthesized compounds were characterized on a Bruker 500 MHz NMR Ascend Avance III HD (actively shielded) Spectrometer and a Bruker 600 MHz NMR Avance III NMR (actively shielded) Spectrometer. J values were depicted in hertz (Hz) and spin multiplicities were described as singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), and broad (b). Chemical shifts were reported in parts per million (δ), employing the solvent resonance as the internal standard.

2.4.2 Microbiology

P. aeruginosa (PA01) and *S. epidermidis* (35984) were acquired from American Type Culture Collection (ATCC). All bacteria were sub-cultured onto tryptic soy agar (TSA) plates and incubated at 37 °C, 150 rpm for 24 h. Overnight cultures were prepared by transferring single colonies from the plates into 25 mL tryptic soy broth (TSB) in Erlenmeyer flasks and incubating at 37 °C, 150 rpm for 16 h. Then, 10 µL of overnight cultures were transferred into 50 mL of TSB, vortexed, and standardized to 10^6 – 10^7 CFU/mL via absorbance readings at 600 nm.

The minimum inhibitory concentrations (MICs) of all compounds against *S. epidermidis* and *P. aeruginosa* were determined using a modified 96-well plate assay previously described by Walsh et al.³⁰⁻³² In short, Costar polystyrene 96-well plates were prepared with 150 µL of TSB and serial dilutions of the compound in dimethyl sulfoxide (DMSO). Both strains were cultured as described above in TSB and a replicator was used to inoculate each well. DMSO controls and blanks containing only TSB and inoculated cultures were also conducted. Plates were incubated at 37 °C for 24 h in static conditions. The optical density was taken at 600 nm via microplate

reader at 0 h and at 24 h, and the difference measured to determine the MIC. Experiments were done in biological triplicate with technical duplicates. The same starting and final concentrations of each compound was used for each replicate, and for this reason we conclude no standard error.

The minimum biofilm eradication concentrations (MBECs) of all compounds against *S. epidermidis* and *P. aeruginosa* were determined as previously described by Walsh et al.³⁰⁻³² and as follows. Costar polystyrene 96-well plates were prepared with 150 μ L of TSB. Both strains were cultured as described above in TSB and a replicator was used to inoculate each well. Plates were incubated at 37 °C for 24 h in static conditions. The planktonic phase cells and medium were gently removed and replaced with 150 μ L of TSB and tenfold dilutions of compound being evaluated in DMSO. The 96-well plates were incubated for an additional 24 h at 37 °C. Wells were thoroughly agitated to ensure the biofilm was broken up from the surface of the wells using pipettes before three tenfold dilutions of each sample were taken and drop plated on TSA plates. TSA plates were incubated for 24 h at 37 °C. The minimum biofilm eradication concentration (MBEC) was determined to be the lowest concentration at which no bacterial growth occurred. The same starting concentration of each compound was used for each replicate and the same final concentration was observed for each trial, for this reason there is no standard error. Experiments were performed in biological triplicate with technical duplicates.

2.5 Conclusions

2.5.1 Key Findings

Structure–activity relationship (SAR) studies were conducted using a panel of 22 amide derivatives of 2-amino-5-nitrothiazole, 2-amino-6-nitrobenzothiazole, and 4-nitrofur-2-carbazide against *Staphylococcus epidermidis* and *Pseudomonas aeruginosa* in both the

planktonic and biofilm states. Significantly for biofilms, the introduction of a chloro-substituent the 5-position of NTZ (analog **1b**) results in excellent activity enhancement, as does the replacement of the 2-acetoxy substituent in **1b** with a basic amine group (analog **7b**). It is also of importance that analog **4a**, which is a simple methacrylamide, displays noteworthy activity against both *S. epidermidis* and *P. aeruginosa* biofilms.

2.5.2 Future Research

Many of the analogs described in this study showed significant increases in potency toward the Gram-positive pathogen *Staphylococcus epidermidis* in the biofilm state. The utilization of these against other Gram-positive biofilms implicated in nosocomial infections (e.g., *Staphylococcus aureus*, *Streptococcus pneumoniae*, and *Enterococcus faecalis*) will be a topic for future disclosures from these laboratories. Future evaluation of intrinsic toxicity is also needed since it is possible that the analogs that we have described with enhanced antibacterial efficacy are so because their general toxicity has increased. Additional studies involving iminodiacetate pro-drug conjugates⁶ based on **1b**, **4a**, and **7b** will also be forthcoming.

2.6 Conflicts of Interest

The authors declare no conflict of interest.

2.7 Acknowledgements

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CHAPTER THREE

3. *N*-(TRIMETHYLSILYL)-2-AMINO-5-NITROTHIAZOLE; AN EFFICIENT REAGENT FOR THE
DIRECT SYNTHESIS OF 2-AMINO-5-NITROTHIAZOLE-BASED ANTIMICROBIAL AGENTS

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3.1 Abstract

Here we report the synthesis of a novel reagent designed to prepare 2-amino-5-nitrothiazole (ANT) amides and analogues in high yields. *N*-(Trimethylsilyl)-2-amino-5-nitrothiazole (*N*-(TMS)-ANT) was prepared in 99% yield via silylation of ANT using 1,1,1,3,3,3-hexameth-ylidisilazane (HMDS), trimethylsilyl chloride (TMSCl), and catalytic saccharin. *N*-(TMS)-ANT is a superb reagent for the preparation of ANT amides in excellent yields. Notably, cyclic anhydrides and base-sensitive acyl chlorides can be utilized with *N*-(TMS)-ANT to furnish ANT amides that are difficult to prepare by previously reported procedures.

3.2 Letter

Nitazoxanide (**3**, Figure 1), first synthesized by Rossignol and Cavier in 1975, is an orally bioavailable broad-spectrum antiparasitic and broad-spectrum antiviral drug that is the prototype for the thiazolide class of antimicrobials. It is a first-line treatment for *Cryptosporidium parvum* and *Giardia lamblia* infections. As an antiviral, it has shown efficacy for treating influenza, reducing shedding of the influenza virus, and holds promise as a broad-spectrum antiviral for respiratory infections.⁶² The pharmacophore responsible for its biological activity is derived from 2-amino-5-nitrothiazole (**2**).

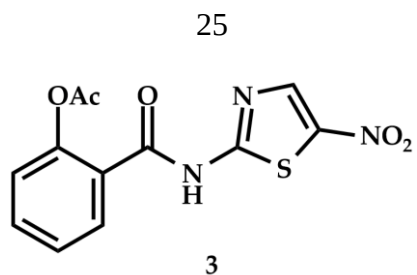
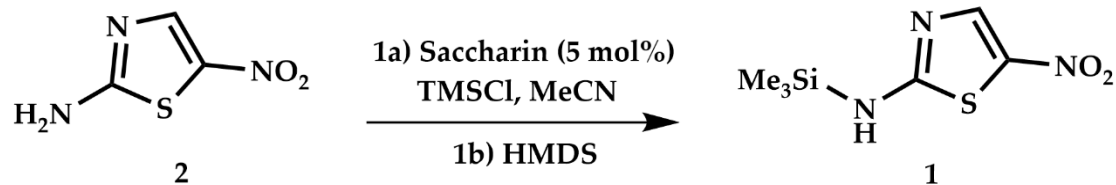


Figure 3.1. Nitazoxanide

In more recent years, ANT-based motifs have found applications in antibiofilm research, showing promising activity against *Escherichia coli*, *Staphylococcus epidermidis*, *Pseudomonas aeruginosa*, and *Clostridium difficile*.^{33, 40, 49, 50} Previously, most of the reported ANT-based amides were prepared via coupling of **2** with acyl chlorides in the presence of auxiliary bases. Standard procedures using ANT with Et₃N or K₂CO₃ as bases involve aqueous workups, which are capricious in that emulsions are often encountered, leading to variable yields (*vide infra*).^{33, 48} Subsequent purifications are also tedious, often requiring cautious column chromatography to obtain purified products. Since ANT derivatives have shown significant medicinal promise, an improved synthetic protocol for their synthesis was required.

Here we report the synthesis of *N*-(trimethylsilyl)-2-amino-5-nitrothiazole (**1**) (*N*-(TMS)-ANT), which efficiently couples with acyl chlorides, anhydrides, and other electrophiles directly in a 1:1 fashion. *N*-(TMS)-ANT (**1**) is efficiently prepared via silylation of ANT (**2**) using 1,1,1,3,3,3-hexamethyldisilazane (HMDS), trimethylsilyl chloride (TMSCl), and catalytic saccharin (Scheme 1).⁶³



Scheme 3.1. Synthesis of *N*-(trimethylsilyl)-2-amino-5-nitrothiazole (**1**).

The HMDS-derived byproduct NH_3 was found to be deleterious to the course of this reaction, so it was scavenged by the preliminary addition of TMSCl . In addition, in the absence of catalytic saccharin, *N*-silylation proceeded less efficiently. Using this procedure, the title compound **1** was obtained in near quantitative (99%) yield. The purification of commercial ANT was found crucial to the preparation of *N*-(TMS)-ANT (**1**) in high yield. Previously this was accomplished by recrystallization of ANT from large quantities of ethanol, which we found to be impractical, since dark impurities were difficult to remove using this solvent. Accordingly, we developed an alternative purification method involving decolorization with activated charcoal, filtration, and recrystallization from CH_3CN . Importantly, in the preparation of *N*-(TMS)-ANT (**1**), it was found critical to ensure that all reagents were anhydrous, since the presence of water led to incomplete silylation.

N-(TMS)-ANT (**1**) was subsequently treated with various electrophiles to provide the corresponding derivatives shown in Figure 3.2. The utilization of *N*-(TMS)-ANT (**1**) markedly improved the preparative efficiency leading to five previously reported antimicrobial agents (Figure 3.2.; **4**, **8**, **9**, **11**, **13**) from 87, 38, 86, 74, and 22 % to enhanced yields of 89, 86, 97, 98, and 93 %, respectively (Table 3.1.).

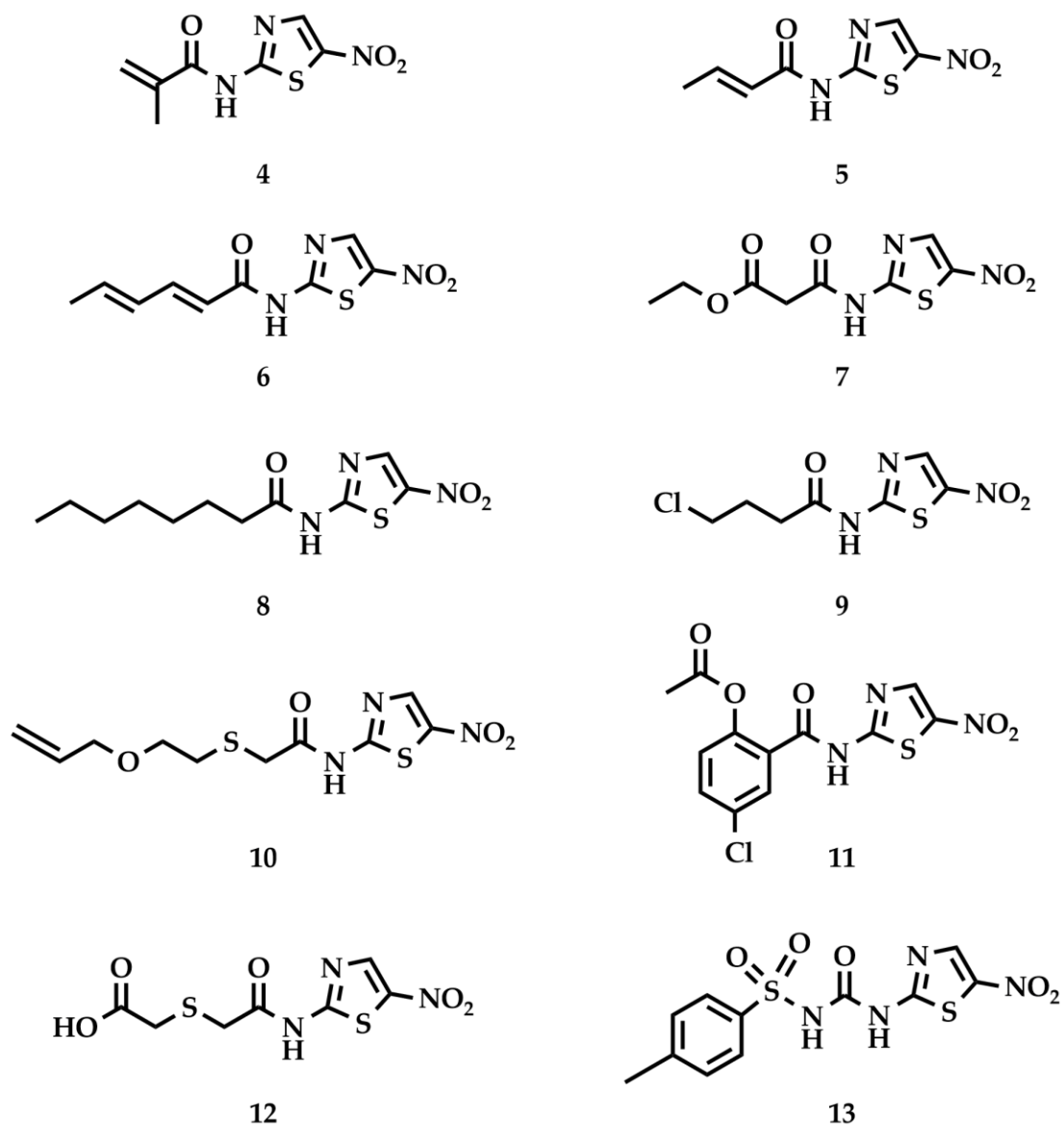


Figure 3.2. ANT derivatives prepared via coupling with *N*-(TMS)-ANT (**1**).

Table 3.1. Yields of Coupling Reactions Using *N*-(TMS)-ANT (**1**) Compared to those Previously Cited in the Literature.

Compound	Yield (%)	Literature Yield (%)
4 ^{a,c}	89	87 ³³
5 ^a	95	
6 ^a	85	
7 ^{a,b}	74	

8^a	86	38 ⁴⁸
9^a	97	86 ⁴⁹
10^{a,c}	79	
11^a	98	74 ³³
12^a	73	
13^a	93	22 ⁶⁴

^a Compounds selected based on functionality that prior SAR studies have shown to be important.

^b Extended *n*-alkyl and ester moieties are of interest (e.g., **7**) in antibiofilm applications.

^c Terminal alkenes (e.g., **4** and **10**) are also of interest, as they present the opportunity for union with larger molecular motifs via alkene cross-metathesis.

From a preparative standpoint, it is significant that ANT amides can also be accessed in high yield by simply adding the acyl chloride of interest to an acetonitrile solution of preformed *N*-(TMS)-ANT without filtration of the NH₄Cl byproduct (see Appendix A). Additional couplings using carboxylic anhydrides and a *N*-sulfonyl isocyanate expanded the library of available ANT compounds as well as the scope of electrophilic functionalization. It is of particular significance in a synthetic context that acyl chlorides corresponding to amides **5** and **6** undergo preliminary deconjugative deprotonation in the presence of Et₃N, leading to acyl-rearranged product mixtures. In addition, the use of Et₃N with the labile acyl chloride **7** under standard basic conditions resulted in its premature decomposition. Moreover, the reaction of cyclic anhydrides and sulfonyl isocyanates (corresponding to **12** and **13**) with **1** directly provides the corresponding TMS intermediates, which are converted into the desired products by simple passage through a pad of silica gel, thereby obviating inadequate aqueous-reliant purification methods.

N-(TMS)-ANT (**1**), a new reagent for the efficient, high yield synthesis of ANT derivatives has been efficiently prepared in excellent yield (See Notes below). Primary advantages associated with the use of **1** include its ability to cleanly amidate base labile acyl chlorides as well as cyclic anhydrides. Additional applications of **1** for the synthesis of other types of ANT containing antimicrobials will be the topic of future reports from this laboratory. Future studies will also include the biological evaluation of novel ANT-based antimicrobials for the control of biofilm-forming bacteria.

3.3 Conflicts of Interest

The authors declare no conflict of interest.

3.4 Acknowledgements

This research was funded by the National Institute of General Medical Sciences (NIGMS, grant number GM116949) and by an external donation from T.S.L. to the Montana State University (MSU) Foundation. Support for MSU's NMR Center and the 400 MHz NMR spectrometer used in this research has been provided by the National Science Foundation (Grant No. NSF-MRI: CHE-2018388) and MSU's Office of the Vice President for Research and Economic Development.

3.5 Notes

3.5.1 Preparation of *N*-(TMS)-ANT (**1**)

A 100 mL round-bottomed flask equipped with a magnetic stirring bar and a poly-seal cap was charged with 2-amino-5-nitrothiazole (3.625 g, 25.0 mmol), saccharin (0.169 g, 1.25 mmol), and anhydrous acetonitrile (25 mL). The reactant mixture was blanketed with argon and then trimethylsilyl chloride (1.05 g, 1.225 mL, 9.5 mmol) was added dropwise by syringe with stirring. After stirring for an additional 10 min at 23 °C, 1,1,1,3,3,3-hexamethyldisilazane (1.48 g, 1.91 mL, 9.17 mmol) was added dropwise by syringe. The reactant mixture was stirred for 1 h at 23 °C and then heated at 65 °C with stirring for an additional 1 h. The NH₄Cl precipitate was then filtered, with care being taken to avoid exposure to atmospheric moisture. The NH₄Cl was leached with anhydrous acetonitrile (5 mL), and the solvents were removed in vacuo. A 100 mL recovery flask was used for the final removal of trace solvents and subsequent sublimation under high vacuum (0.01 mmHg 60 °C) furnished the title compound **1** as a yellow/orange crystalline solid (5.4 g, 99%). ¹H NMR (CDCl₃, 500 MHz): δ 8.08 (1 H, s), 5.30 (1 H, s), 0.39 (9 H, s). ¹³C NMR (CDCl₃, 125 MHz): δ 169.7, 143.1, 29.9, 0.0. HRMS (ESI): m/z calcd for [C₆H₁₁N₃O₂SSi + H]⁺: 218.0414; found: 218.0425 (mass error Δm = 5 ppm).

3.5.2 Representative Amidation: Preparation of **5**

A 10 mL round-bottomed flask equipped with a magnetic stirring bar and polyseal cap was charged with *N*-(TMS)-ANT (217 mg, 1.0 mmol), anhydrous dichloromethane (3.0 mL), and blanketed with argon in succession. The mixture was stirred until homogeneous, then crotonoyl chloride (105 mg, 96 μL, 1.0 mmol) was subsequently added by gas-tight syringe, and the reactant mixture was allowed to stir at room temperature for 24 h. The solvent was then

removed in vacuo, and the residue was diluted with EtOAc (5 mL) and successively extracted with water (2×5 mL), saturated sodium bicarbonate (2×5 mL), and brine (2×5 mL). The organic layer was then passed through a pad of silica gel and removal of the solvent in vacuo provided the title compound (202 mg, 95%). ^1H NMR (DMSO- D_6 , 500 MHz): δ 13.13 (1 H, s), 8.65 (1 H, s), 7.10 (1 H, dq, $J = 7$ Hz), 6.26 (1 H, dq, $J = 7, 2$ Hz), 1.94 (3 H, dd, $J = 7, 2$ Hz). ^{13}C NMR (DMSO- D_6 , 125 MHz): δ 164.8, 162.5, 146.6, 143.3, 142.5, 123.0, 18.6. HRMS (ESI): m/z calcd for $[\text{C}_7\text{H}_7\text{N}_3\text{O}_3\text{S}]^+$: 213.0208; found: 213.0146 (mass error $\Delta m = 29$ ppm).

CHAPTER FOUR

4. NOVEL IMIDAZO[1,2-a]PYRIMIDINIUM TETRAFLUOROBORATE SALTS AND 2-AMINOIMIDAZOLES AS ADJUVANTS FOR THE TREATMENT OF MULTI-DRUG RESISTANT BIOFILMS

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Contributions: Performed biological evaluation studies and edited manuscript.

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Contributions: Collected confocal microscopy images, performed biological analysis and edited manuscript.

Co-Author: Tom Livinghouse

Contributions: Prepared manuscript, directed compound design and synthesis, and provided laboratory space for these.

Co-Author: Philip S. Stewart

Contributions: Oversaw the biological evaluation studies and provided laboratory space for these. Edited manuscript.

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Contributions: Oversaw CDC Biofilm Reactor studies and edited manuscript.

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4.1 Abstract

2-Aminoimidazoles have been reported to be potent adjuvants as they inhibit biofilm formation, disperse pre-formed biofilms and resensitize multi-drug resistant bacterial strains to antibiotic treatment. Novel disubstituted 2-aminoimidazoles have been synthesized in excellent yields via an optimized route. Anti-biofilm activities of these adjuvants against Methicillin-resistant *Staphylococcus aureus* (MRSA USA300 LAC) and a highly virulent strain of *Pseudomonas aeruginosa* (PA14) in Kirby-Bauer Disk Diffusion assays is reported herein. The CDC Biofilm Reactor assay, a robust biofilm model, was utilized to further elucidate the activity of lead agents against these MDR bacterial strains. Confocal microscopy images were collected to show the effect of these lead compounds against Methicillin-resistant *Staphylococcus aureus* (MRSA USA300 LAC) biofilms grown in the CDC Biofilm Reactor model.

4.2 Introduction

4.2.1. Multi-drug Resistant Biofilms

Multi-drug resistant (MDR) bacteria present a significant challenge in the medical field. One approach that is promising for addressing resistance is an adjuvant approach. Adjuvants have weak antibiotic activity on their own, but in combination with another antibiotic agent can lead to significant potentiation of activity. A classic example for antibiotic activity enhancement via an adjuvant is clavulanic acid. Clavulanic acid was isolated by Beechams in 1976 from *Streptomyces clavuligerus* and was found to be a powerful and irreversible inhibitor of most β -lactamases. The combination that is most known in clinical settings is Augmentin, which is a

combination of amoxicillin and clavulanic acid.⁶⁵ There are several advantages that arise from the utilization of adjuvants. These are; 1.) The primary drug can be given in a lower dose. 2.) Lower doses of the primary drug inherently leads to lower toxicity and fewer side effects. 3.) This can lead to a broader spectrum of activity. And 4.) Optimally designed combination therapies have the potential to slow resistance evolution.⁶⁶

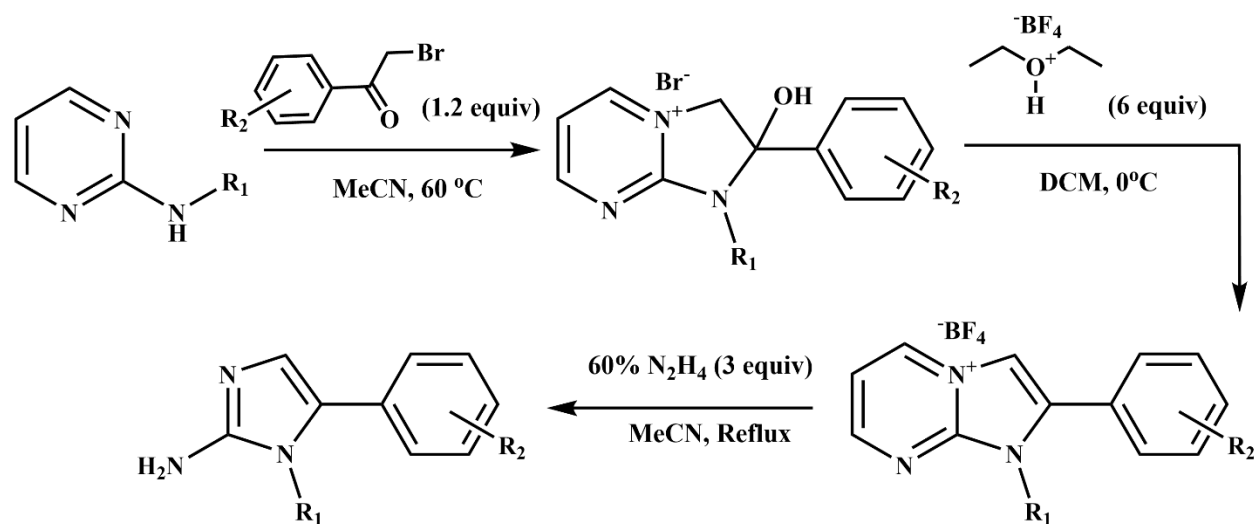
A powerful mechanism of resistance that most bacteria have evolved is the ability to accumulate into dense communities known as biofilms. Biofilms have several mechanisms of defense that make them more tolerant to antibiotic treatment than planktonic bacteria, literature has shown this increased tolerance to be on the order of 1000 fold.⁴ One powerful mechanism is quorum sensing, which is how bacteria can communicate.^{15, 16} There is a significant amount of literature suggesting quorum-sensing antagonism as a potential therapeutic strategy against pathogenic biofilms.^{16, 67-69} The chemical scaffold for which we propose to utilize in development of adjuvants are 2-aminoimidazoles. The 2-aminoimidazole (2-AI) pharmacophore is found in several marine alkaloids produced by deep-sea sponges. These natural products have been found to possess powerful antibiofilm activities and have served as the inspiration for synthetic analogs by many in the literature.⁷⁰⁻⁷⁵ While the mechanism of action has not been fully elucidated, there is evidence of 2-AIs acting as quorum sensing antagonists.⁷⁶⁻⁷⁸

There are two particularly active research groups who utilizing the 2-AI scaffold as small molecule adjuvants to target biofilms—Professor Hans P. Steenackers out of Leuven, Belgium in coordination with the University of Oxford and the University of Russia in Moscow and Professor Christian Melander at the University of Notre Dame. Professor Steenackers and collaborators have had success in the development of small molecule adjuvants that inhibit

biofilm formation without affecting planktonic cells. Their work is particularly notable against Gram-positive pathogens.⁷⁹ The mechanism of action for these adjuvants against *Salmonella Typhimurium* was published in a 2014 study, where they found that it reduces the transcription of CsgD and its regulon genes *csgB* and *adrA*.⁸⁰ CsgD is the LuxR-type master regulator of biofilm formation, *csgB* is involved in curli fimbriae production and *adrA* is involved in cellulose production.⁸¹ In 2016, Steenackers and colleagues reported the ability to fine-tune antibiofilm activity in poly-substituted 5-aryl-2-aminoimidazoles. This work shows the very important beginnings of SAR analysis for these adjuvants.⁸² In 2018 they also reported utilization of a 2-AI compound as an antibiofilm coating on titanium medical implants. They found that this covalently bound compound was able to inhibit the formation of *Staphylococcus aureus* biofilms without affecting the planktonic cells.⁸³ This work was continued and improved in an additional *in vivo* study in 2021.⁸⁴ Professor Melander and collaborators have had success in the development of small molecule adjuvants that broaden spectrum of activity in their library of antibiotics to Gram-negative species by crippling efflux pumps. In a 2017 study, they reported the success of three adjuvants to combat resistance to the antibiotic colistin.⁸⁵ In 2019, they also reported the utilization of two adjuvants that successfully expanded antibiotic spectrum of activity of macrolide and glycopeptide antibiotics from Gram-positive selectivity to inclusion of the Gram-negative bacterium *Acinetobacter baumannii*.⁸⁶ Their more interesting recent work has been centered around the dimerization of 2-AIs for dramatic increases in potency and success in resensitization studies.⁸⁷⁻⁹⁰

4.2.2. Antimicrobial Design and Synthesis

The synthesis of 2-aminoimidazoles had been previously reported but were capricious in execution. The route described by Babaev and Eycken in 2006 involves the formation of imidazo[1,2-*a*]pyrimidinium salts from 2-aminopyrimidines and α -bromoketones, followed by cleavage of the pyrimidine ring with hydrazine.⁹¹ While they chose to utilize microwave chemistry to form their salt intermediates, we instead chose to form the imidazo[1,2-*a*]pyrimidinium hydroxy bromide salts (**1.1-11.1**) by simply heating and subsequent dehydration using tetrafluoroboric acid diethyl etherate complex to provide the corresponding imidazo[1,2-*a*]pyrimidinium tetrafluoroborate salts (**1.2-11.2**) (Scheme 4.1.). We did, however, use the same conditions for the cleavage of the pyrimidine ring using excess hydrazine monohydrate⁹¹ to form the target 2-AIs (**1.3-11.3**).



Scheme 4.1. Novel synthesis of imidazo[1,2-*a*]pyrimidinium tetrafluoroborate salts and 2-aminoimidazoles.

We chose to synthesize *N*-1-alkyl-5-aryl-2-aminoimidazoles, as Steenackers had, due to their potency against Gram-positive pathogens. We first synthesized *n*-octyl derivatives at the *N*1

position, as he had reported those to be especially potent. The optimization of our synthesis was performed using derivatives **1a-1c**, **1e** and **1g** as a means of comparison and for biological evaluation as benchmarks. As Steenackers observed comparable activities with his imidazo[1,2-a]pyrimidinium perchlorate salts to the corresponding 2-AIs, but abandoned their further due to toxicity issues,⁹² we chose to evaluate our imidazo[1,2-a]pyrimidine tetrafluoroborate salts.

As 2-AIs are hypothesized to act as quorum sensing antagonists, we decided to incorporate sulfide linkers within our prospective adjuvants since this may lead to activity enhancements as has been observed with sulfide linkers in the case of acylated homoserine lactone autoinducers.⁹³⁻⁹⁸ To this end, we synthesized a sizeable library of imidazo[1,2-a]pyrimidine tetrafluoroborate salts (Figure 4.1. and 4.3.) and 2-aminoimidazoles (Figure 4.2. and 4.4.) with sulfide linkers.

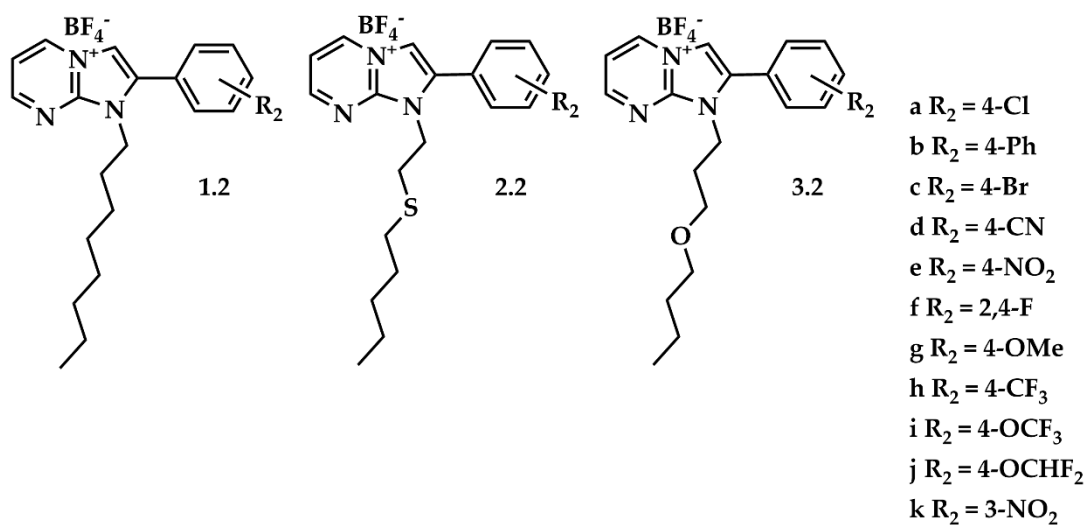


Figure 4.1. *N*1-alkyl-5-aryl imidazo[1,2-a]pyrimidinium tetrafluoroborate salt derivatives synthesized.

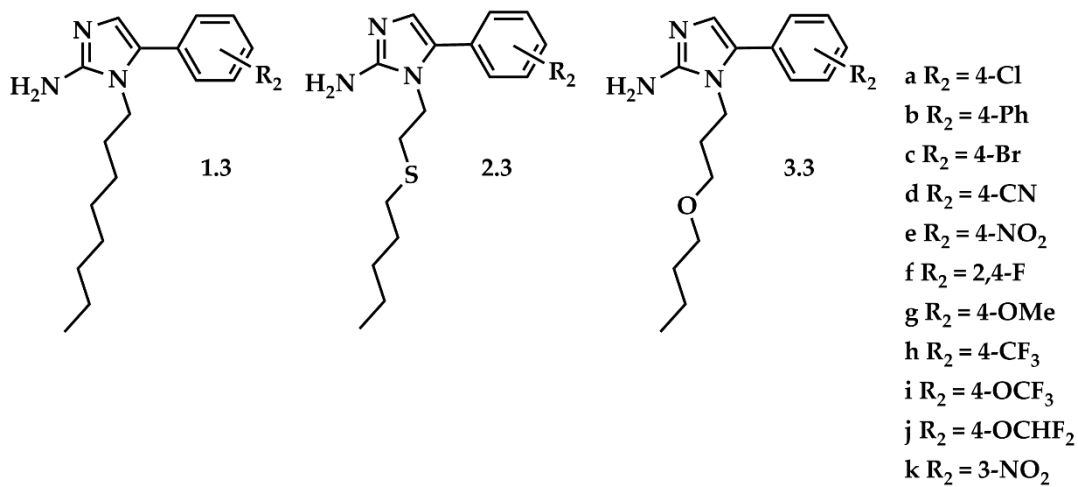


Figure 4.2. N1-alkyl-5-aryl 2-aminoimidazole derivatives synthesized.

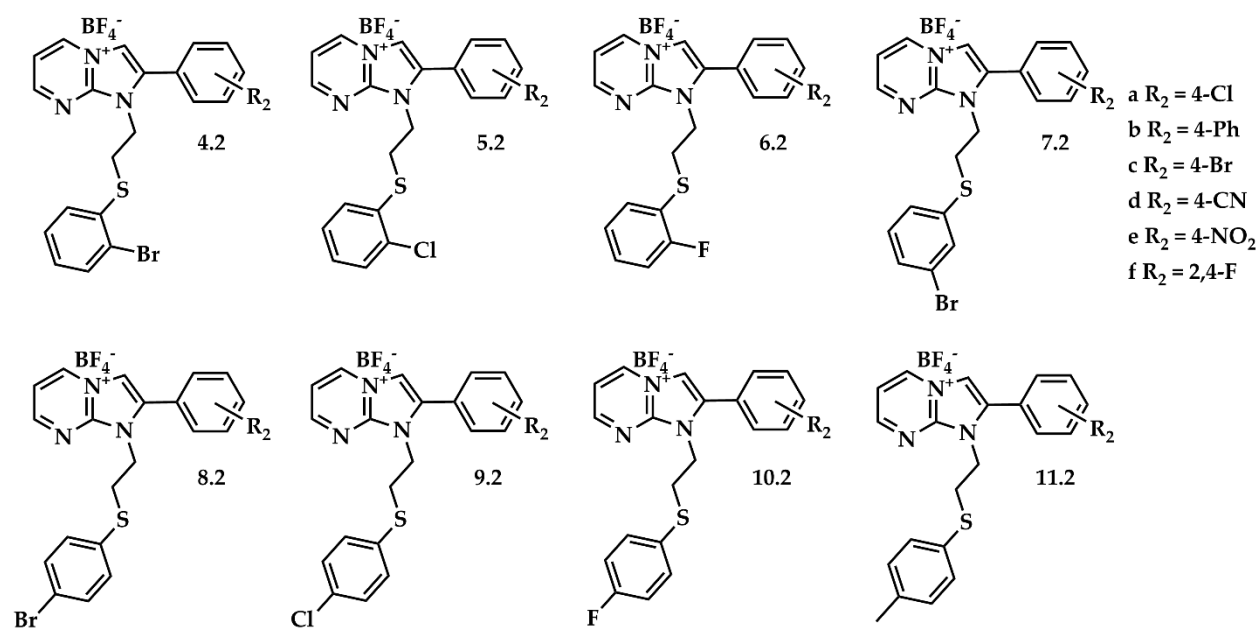


Figure 4.3. N1-aryl-5-aryl imidazo[1,2-a]pyrimidinium tetrafluoroborate salt derivatives synthesized.

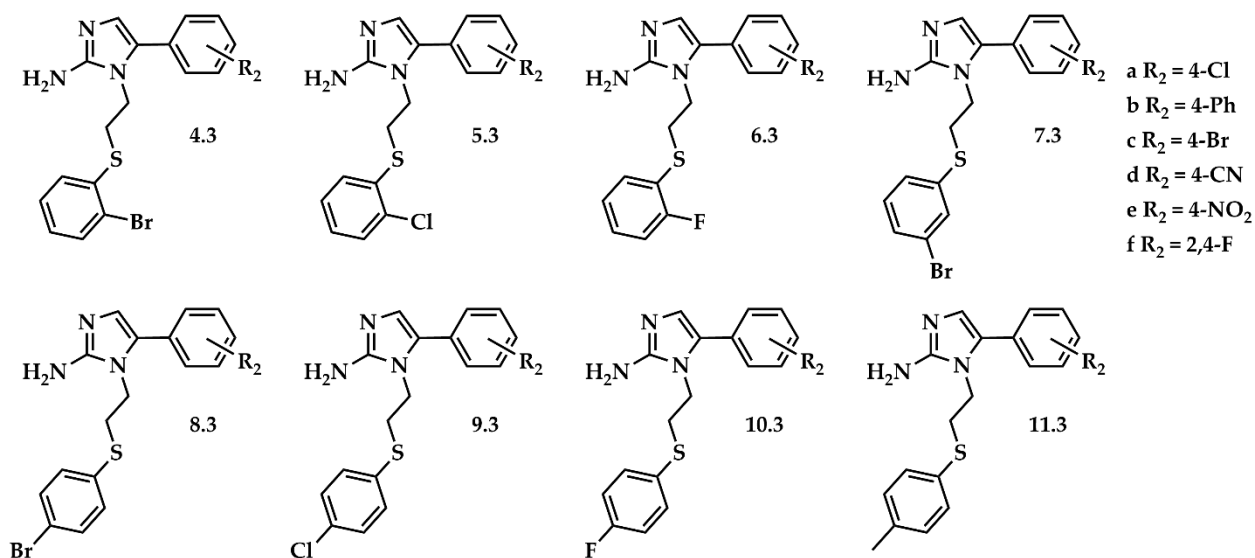


Figure 4.4. N1-aryl-5-aryl 2-aminoimidazole derivatives synthesized.

This library of prospective adjuvants was then screened for biological activities against methicillin-resistant *Staphylococcus aureus* (MRSA USA300 LAC) and multi-drug resistant *Pseudomonas aeruginosa* (PA14) in Kirby-Bauer Disk Diffusion (KBDD) assays in search of lead compounds. The lead compounds that were identified were then used against methicillin-resistant *Staphylococcus aureus* (MRSA USA300 LAC) in the CDC Biofilm Reactor model and imaged using confocal microscopy and LIVE/DEAD staining to further assess their activities. The aim of this study was to identify lead adjuvants for the synthesis of dimerized 2-AIs in future synergy and resensitization studies.

4.3 Methods

4.3.1 Chemistry

4.3.1.1. Research Materials All chemical reagents were purchased from commercial sources (TCI America, Portland, OR, USA, Ambeed, Arlington Heights, IL, USA and Sigma Aldrich, Burlington, NC, USA) and used as received without further purification, moisture sensitive reagents were distilled from CaH₂. Solvents utilized in filtrations, transfers, and chromatography were certified ACS grade. Thin-layer chromatography was performed on Silicycle Glass Backed TLC Extra Hard Layer, 60Å plates (thickness; 250 µm, indicator; F-254) and visualization was accomplished with UV light (254 nm), and/or potassium permanganate.

4.3.1.2. General Nucleophilic Aromatic Substitution for the Preparation 2-Aminopyrimidines (1-11) A 25 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with 2-chloropyrimidine (1.145 g, 10 mmol), the requisite amine (11 mmol), anhydrous, finely ground potassium carbonate (2.073 g, 15 mmol) and anhydrous MeCN (10 mL). The reaction mixture was allowed to stir at reflux overnight. After reflux the reaction was allowed to cool to room temperature. It was diluted with water (20 mL) and extracted with DCM (2 x 20 mL). The organic layer was purified by silica plug and removal of the solvent in vacuo provided the 2-aminopyrimidine.

4.3.1.2. General Bromination for the Preparation of α -Brominated Acetophenones (**a-m**)

A 15 mL round bottomed flask equipped with a magnetic stirring bar and poly cap was charged with the requisite acetophenone (5 mmol) and acetic acid (5 mL) and stirred at room temperature. A solution of bromine (0.799 g, 0.258 mL, 5 mmol) in acetic acid (2 mL) was prepared. A small portion of bromine in acetic acid solution (0.25 mL) was added and stirred at room temperature until the red color discharged (15-20 min). Then the remaining bromine in acetic acid solution was added dropwise with stirring (color should discharge immediately). The reaction was allowed to stir for an additional 1h at room temperature. A 50 mL round bottomed flask equipped with a magnetic stirring bar and ice water bath was charged with 25 mL of ice water and the reaction mixture was added dropwise. A solid precipitated out which was then filtered and washed with water (3 X 20 mL) to provide the α -brominated acetophenone.

4.3.1.5. General *N*-Alkylation Procedure for the Preparation of Imidazo[1,2-*a*]pyrimidinium Hydroxy Bromide Salts (**1.1-11.1**) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with the requisite aminopyrimidine (1 mmol), the requisite 2-bromoacetophenone (1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the imidazo[1,2-*a*]pyrimidinium hydroxy bromide salt as a white solid.

4.3.1.6. General Dehydration Procedure for the Preparation of Imidazo[1,2-a]pyrimidinium Tetrafluoroborate Salts (1.2-11.2) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with the requisite imidazo[1,2-a]pyrimidinium hydroxy bromide salt (1 mmol) and DCM (2 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.8 mL, 6 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to slowly return to room temperature as it stirred for 2-12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the imidazo[1,2-a]pyrimidinium tetrafluoroborate salt as a crystalline white solid.

4.3.1.7. General Hydrazinolysis Procedure for the Preparation of 2-Aminoimidazoles (1.3-11.3) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with the requisite imidazo[1,2-a]pyrimidinium tetrafluoroborate salt (1 mmol) and MeCN (3 mL). Hydrazine monohydrate (146 μ L, 3 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K_2CO_3 (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the 2-aminoimidazole as a crystalline yellow solid.

4.3.2. Microbiology

4.3.2.1. Strains and Media Growth for MIC and MBEC Assays Biological evaluation was conducted against *Pseudomonas aeruginosa* (PA14) and *Staphylococcus aureus* (MRSA USA300 LAC). Overnight cultures were prepared by transferring single colonies from the plates into 25 mL tryptic soy broth (TSB) in Erlenmeyer flasks and incubating at 37 °C, 150 rpm for 16 h. Then, 10 µL of overnight cultures were transferred into 50 mL of TSB, vortexed, and standardized to 10^5 – 10^6 CFU/mL via absorbance readings at 600 nm.

4.3.2.2. Minimum inhibitory concentration (MIC) Assays Polystyrene 96-well microtiter plates were inoculated with prepared standardized cultures of the strain at 10^5 – 10^6 CFU/mL with 150 µL of TSB and serial dilutions of the compound in TSB. TSB blanks, TSB controls, and DMSO controls without any added compound were also prepared. The optical density was taken at 600 nm via microplate reader at 0 h and plates were then covered, sealed with parafilm, and incubated at 37 °C for 24 h in static conditions. The optical density was again taken at 600 nm at 24 h, and the difference of that and 0 h was measured to determine the MIC. Experiments were done in biological triplicate with technical duplicates.

4.3.2.3. Minimum biofilm eradication concentration (MBEC) Assays Polystyrene 96-well microtiter plates were inoculated with prepared standardized cultures of the strain at 10^5 – 10^6 CFU/mL with 150 μ L of TSB. Plates were then covered, sealed with parafilm, and incubated at 37 °C for 24 h in static conditions. The medium was then gently discarded, and the plates washed with PBS buffer to remove any planktonic phase cells. Serial dilutions of the compound in 150 μ L of TSB and controls without any added compound were added to the wells. Plates were then covered, sealed with parafilm, and incubated again at 37 °C for 24 h in static conditions. Wells were then thoroughly agitated to ensure the biofilm was broken up from the surface of the wells using pipettes before 10 μ L aliquots in triplicate of each well were taken and drop plated on TSA plates. TSA plates were incubated at 37 °C for 24 h in static conditions. The lowest concentration at which no bacterial growth occurred was used to determine the MBEC. Experiments were performed in biological triplicates with technical duplicates.

4.3.2.4. Strains and Media Growth for Kirby-Bauer Assays Biological evaluation was conducted against *Pseudomonas aeruginosa* (PA14) and *Staphylococcus aureus* (MRSA USA300 LAC). Overnight cultures were prepared by transferring single colonies from the plates into 25 mL tryptic soy broth (TSB) in Erlenmeyer flasks and incubating at 37 °C, 150 rpm for 16 h. Then, 10 μ L of overnight cultures were transferred into 50 mL of TSB, vortexed, and standardized to 10^5 – 10^6 CFU/mL via absorbance readings at 600 nm for *Pseudomonas aeruginosa* (PA14). While 625 μ L of overnight cultures were transferred into 50 mL of TSB, vortexed, and standardized to 10^8 CFU/mL (0.5 McFarland Standard) via absorbance readings at 600 nm for *Staphylococcus aureus* (MRSA USA300 LAC).

4.3.2.5. Kirby-Bauer Disk Diffusion (KBDD) Assays Polystyrene petri dishes (100 mm x 15 mm) were prepped as Mueller-Hinton (MH) agar plates to a level of 4 mm. The MH agar plates were inoculated (200 μ L) with uniformity using a glass spreader. Once a confluent lawn of growth was attained, the plate was allowed to dry. Sterile 6 mm filter disks were impregnated with 20 μ L of antimicrobial working concentrations diluted in either DMSO or dH₂O. A 5-minute wait allowed for full absorption of the solutions. Within 15 minutes, impregnated antimicrobial disks were dispensed evenly (no less than 20 mm) from each other using sterile forceps. MH agar plates were incubated at 37 °C for 24 h under static conditions. Zones of inhibition were measured (in mm) and qualitative observations of the biofilm were recorded.

4.3.2.6. CDC Biofilm Reactor Assays Assays were adapted from ASTM method E2562-17 and ASTM method E2871-13. A CDC reactor containing 400 mL of 10% tryptic soy broth was inoculated with 4 mL of an overnight culture of MRSA USA300LAC. The biofilms were grown on polycarbonate coupons (12.7 mm in diameter and 3.8 mm thick) in batch phase at 37°C at 125 rpm for 24 h, and then under a continuous flow of 2.7 mL/min at 37°C at 125 rpm for 24 h. Coupons were removed and placed in 12 well plates with 3 mL of treatment in sterile PBS buffer in each well for each coupon. Coupons were left in treatments for 24 h at 37°C under static conditions. Coupons were then removed from the treatment wells and transferred to 50 mL conical tubes containing double strength DE broth (10 mL). To disaggregate the biofilms from the coupons, tubes were vortexed for 30 sec, sonicated for 30 sec, vortexed for 30 sec, sonicated for 30 sec and vortexed for 30 secs. Each tube was diluted ten-fold six times in sterile PBS Buffer, plated onto TSA and incubated at 37°C for 24 h before enumeration. All samples were done with technical duplicates within each assay and assays were evaluated in biological triplicate.

4.4 Results and Discussion

4.4.1. Chemistry

Novel 2-aminoimidazole agents were prepared across three distinct steps (Scheme 4.1.); first the *N*-alkylation of α -brominated acetophenones to provide the hydroxy salts, then dehydration using tetrafluoroboric acid diethyl etherate complex to provide the imidazo[1,2-*a*]pyrimidinium tetrafluoroborate salts, and ultimately hydrazinolysis of the pyrimidine ring using excess hydrazine to free pyrazole as a byproduct of the desired 2-aminoimidazole. Strengths of this synthesis include the use of facile conditions compared to the previous reported

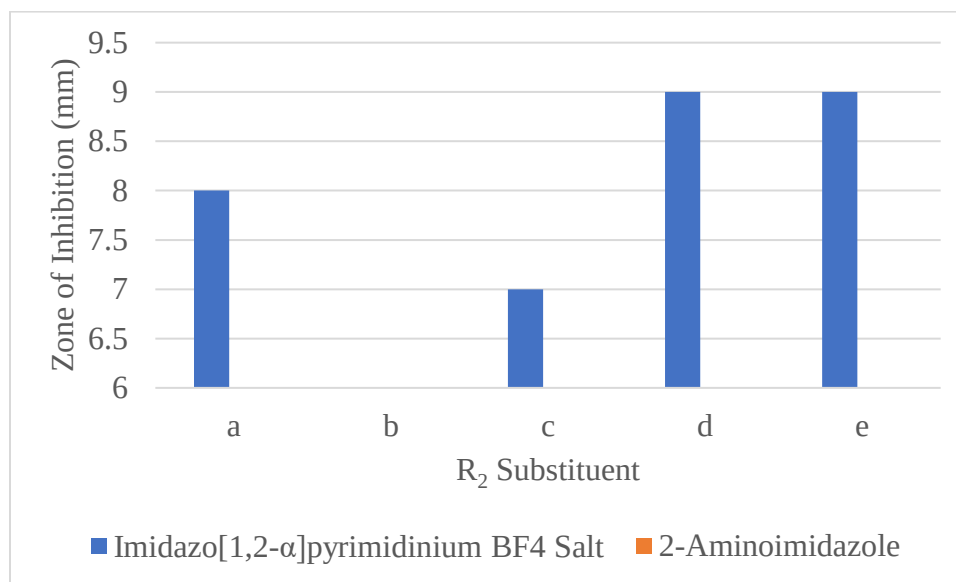
preparations, as well as simple byproducts which were easily removed without the need for column chromatography—a major reason our yields were respectable across three steps. In most cases, we found the limiting factor of our yields to be the *N*-alkylation step, especially for compounds with asymmetry as they were less likely to crystallize out as a solid (see Appendix A).

4.4.2. Microbiology

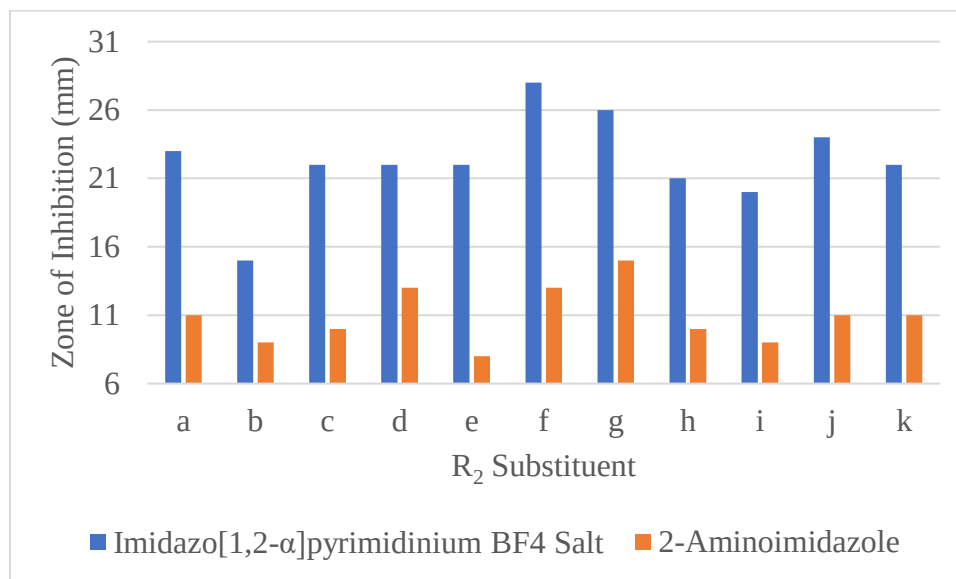
Initial bulk screening of all synthesized agents was done via Kirby-Bauer Disk Diffusion (KBDD) assays, as a means of rapid identification of lead agents. This initial screening was crucial for informing the design of more agents as the scope of this study was further explored. The first derivatives we synthesized were the *n*-octyl derivatives, based on Steenackers' successful lead agents (Graphs 4.1. and 4.2.), as a means of determining the best R₂ substituents to move forward with in our subsequent syntheses. It is important to note that derivatives (**1a**, **1b**, **1c**, **1e** and **1g**) were originally reported by Steenackers and served as benchmarks for us to beat in this study. All other compounds we report herein are novel.

We found our adjuvants to have minimal to no activity against *Pseudomonas aeruginosa* (PA14) in these assays, as shown in Graph 4.1. Due to this finding, we decided to move forward with biological screening against *Staphylococcus aureus* (MRSA USA300 LAC) for our library of adjuvants and paused our screening against PA14. The complete SAR analysis of our library against PA14 will be completed prior to the submission of this manuscript but will not be detailed in this dissertation beyond the *n*-octyl derivatives. All 2-aminoimidazoles in this series (**1.3a-1.3e**) displayed no activity (6 mm is the minimum for the zones of inhibition, as this is the diameter of the antibiotic disks). The precursor imidazo[1,2-*a*]pyrimidinium tetrafluoroborate

salts (**1.2a-1.2e**) possessed minimal activity (with the exception of **1.2b** which displayed no activity) but not to a degree we found worth investigating further for our preliminary assays.



Graph 4.1. KBDD assay results of *n*-octyl derivatives at 100 mM against PA14. Diameters of the zones of inhibition were measured in mm and averaged across biological triplicates.

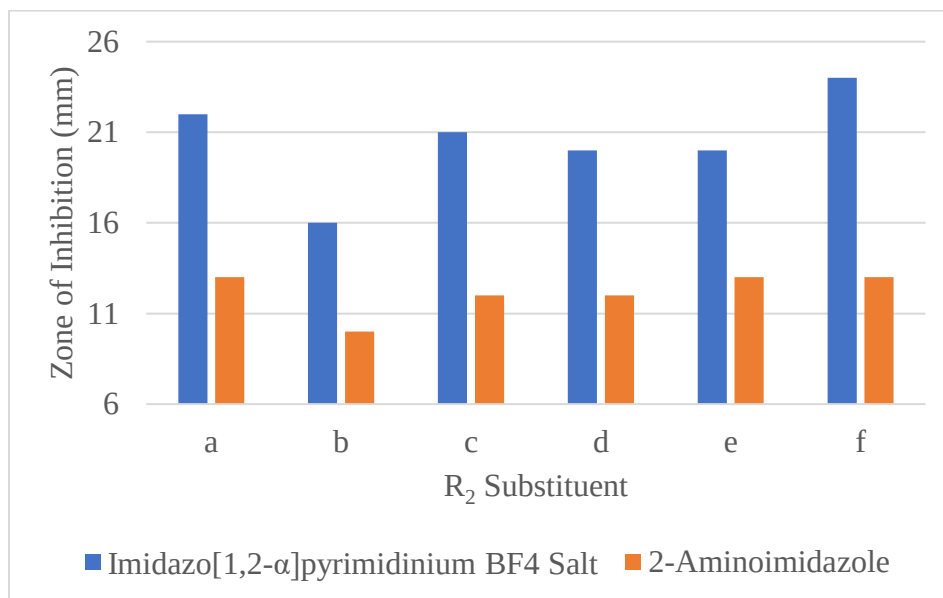


Graph 4.2. KBDD assay results of *n*-octyl derivatives at 100 mM against MRSA USA300 LAC. Diameters of the zones of inhibition were measured in mm and averaged across biological triplicates.

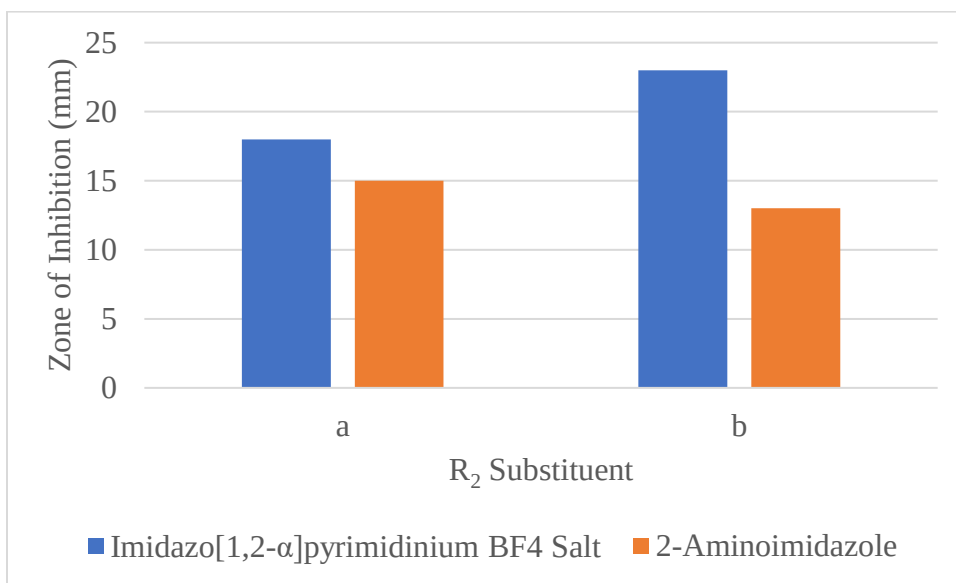
Based on Steenackers' prior observation that the imidazo[1,2-*a*]pyrimidinium precursors displayed comparable activity to that of the 2-aminoimidazoles, we decided to test our novel imidazo[1,2-*a*]pyrimidinium tetrafluoroborate salts. As is shown in Graph 4.1. and Graph 4.2., we found that in all cases of these *n*-octyl derivatives the precursor imidazo[1,2-*a*]pyrimidinium tetrafluoroborate salts vastly outperformed their corresponding 2-aminoimidazoles. The best of the benchmark salts originally reported by Steenackers was the 4-methoxy derivative (**1.2g**) at 26 mm, followed by the 4-chloro derivative (**1.2a**) at 23 mm, and the 4-bromo (**1.2c**) and 4-nitro (**1.2e**) both displayed zones of 22 mm. The least impressive of the benchmark salts was the biphenyl derivative (**1.2b**), with a zone of only 15 mm, making it the least active imidazo[1,2-*a*]pyrimidinium tetrafluoroborate salt in this series. The best R₂ substituent in the series turned out to be our 2,4-fluoro derivative (**1.2f**) for the salts, with a zone of 28 mm. Our second best of the salts in this series was the 4-difluoromethoxy derivative (**1.2j**), at 24 mm. Overall we found

our *n*-octyl salts to be impressive, with zones of inhibition of at least 20 mm. The best 2-aminoimidazole in this series was the benchmark 4-methoxy derivative (**1.3g**), its activity tied that of the biphenyl salt in this series. Our 4-cyano 2-AI derivative (**1.3d**) and 2,4-fluoro 2-AI (**1.3f**) tied for second best of the *n*-octyl 2-AIs.

The next set of compounds we synthesized with sulfide linkers within the *n*-octyl chain--with the sulfur in the third position (Graph 4.3.). As we saw with the *n*-octyl derivatives, again the imidazo[1,2-*a*]pyrimidinium tetrafluoroborate salts had much greater zones of inhibition than their corresponding 2-aminoimidazoles. The 2,4-fluoro derivative (**2.2f**) was again the leading R₂ substituent for the salts and it tied for best within the 2-aminoimidazoles of this series as well. It is difficult to ascertain whether the incorporation of the sulfide linker in the *n*-octyl chain improved activity overall, as the imidazo[1,2-*a*]pyrimidinium tetrafluoroborate salts in this series were not as active as the *n*-octyl salts but the 2-aminoimidazoles in this series were more active than the *n*-octyl 2-AIs.



Graph 4.3. KBDD assay results of n-ethyl-thiopentyl derivatives at 100 mM against MRSA USA300 LAC. Diameters of the zones of inhibition were measured in mm and averaged across biological triplicates.

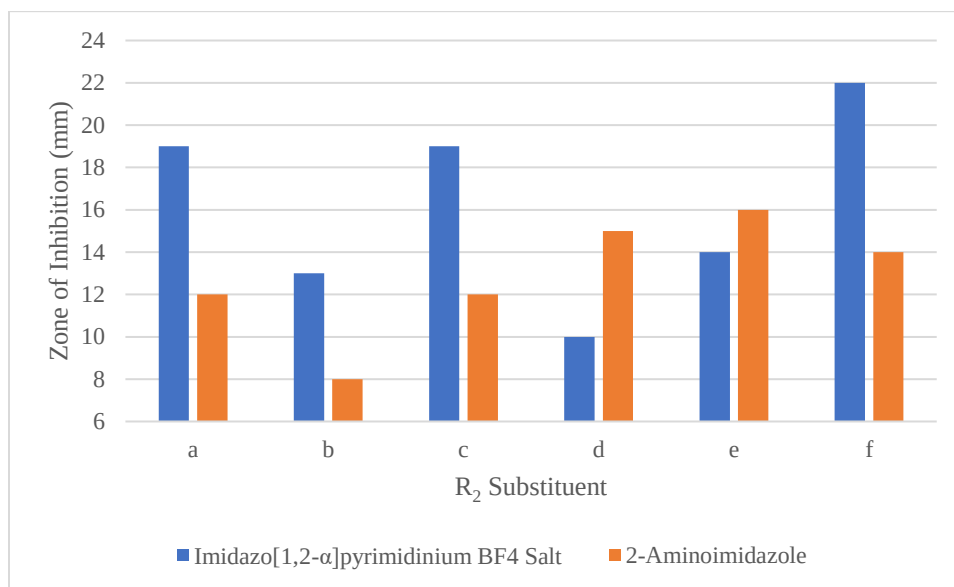


Graph 4.4. KBDD assay results of n-propyl-oxybutyl derivatives at 100 mM against MRSA USA300 LAC. Diameters of the zones of inhibition were measured in mm and averaged across biological triplicates.

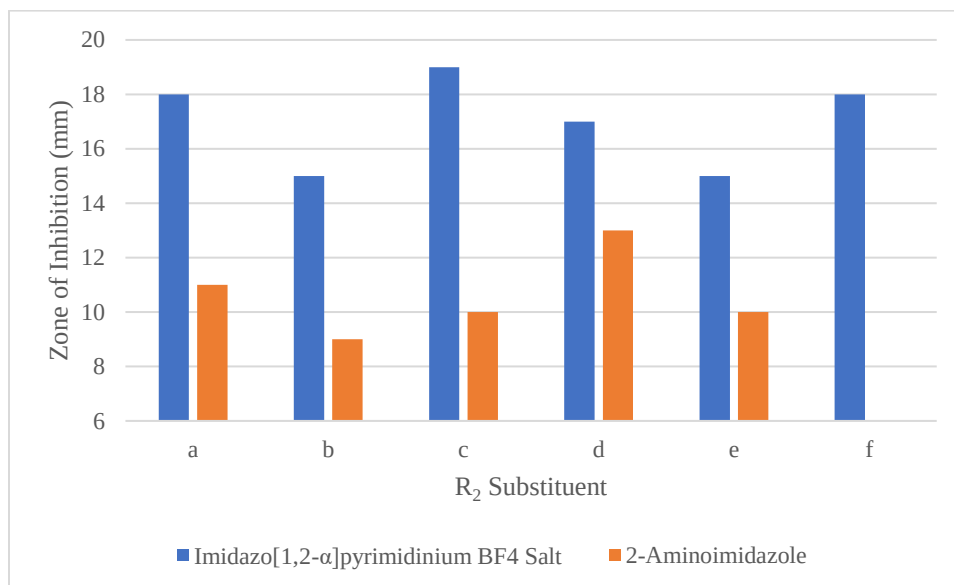
As a control, we synthesized derivatives with oxygen installed at the fourth position (Graph 4.4.) as a means of seeing if sulfur is really enhancing the activity or if the available lone pairs of electrons are somehow responsible for activity enhancement. The predominant SAR trend held in this series as well, as the 2-aminoimidazoles were not as active as the precursor salts. The 4-chloro salt derivative (**3.2a**) underperformed compared to its sulfide linker bearing counterpart (**2.2a**) shown in Graph 4.3., however the biphenyl salt derivative (**3.2b**) was especially active compared to its sulfide linker bearing counterpart (**2.2b**) and is a top contender overall of the salts in this study. Both 2-aminoimidazoles in this series were more active than the sulfide linker bearing counterparts. It would be interesting to expand this series with more R_2 substituents, such as the leading 2,4-fluoro, to see if the SAR trends hold for the 2-aminoimidazoles and to see if we can clarify the comparison of the salts to the sulfide linker bearing counterparts.

The first of our *N*1-aryl derivatives synthesized were the 2-Br series (**4.2a-f** and **4.3a-f**). The 2,4-fluoro derivative (**4.2f**) was again the best of the R_2 substituents in this series (Graph 4.5.). It is worth noting that two of the 2-aminoimidazoles in this series had higher activity than their corresponding imidazo[1,2-a]pyrimidinium tetrafluoroborate salt precursors. We then synthesized the 2-Cl series (**5.2a-f** and **5.3a-f**) and their activities (Graph 4.6.) were less impressive than the 2-Br series overall. An interesting difference was also shown in that the 4-bromo R_2 substituent outperformed the usual leading 2,4-fluoro, but it is again worth noting that the 2,4-fluoro 2-aminoimidazole in this series has yet to be synthesized or evaluated biologically. All imidazo[1,2-a]pyrimidinium tetrafluoroborate salts in this series had greater activity than their corresponding 2-aminoimidazoles. To continue comparison of halides, we synthesized the

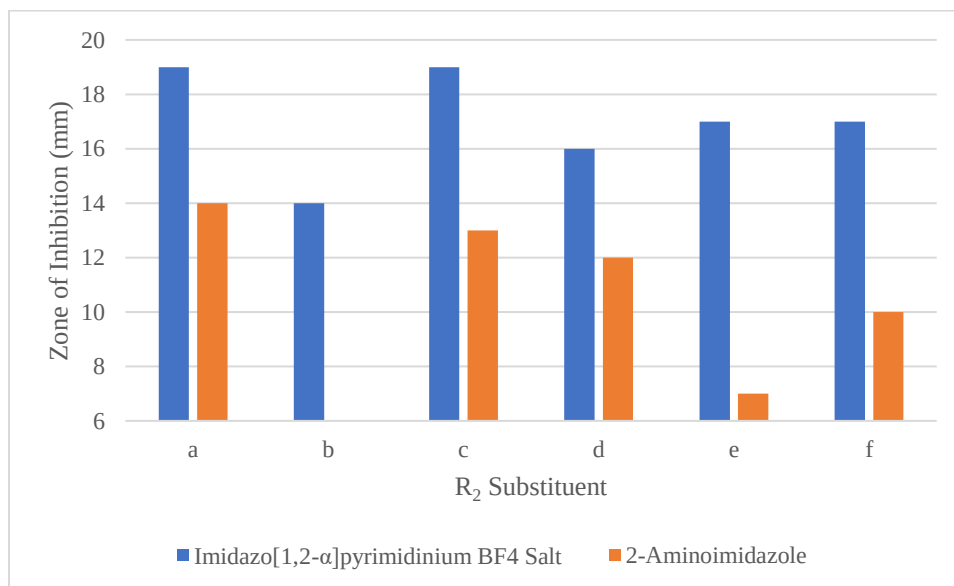
2-F series (**6.2a-f** and **6.3a-f**) and their activities (Graph 4.7.) were very similar to that of the 2-Cl series. It is worth noting that the biphenyl 2-aminoimidazole (**6.3b**) of this series has not been synthesized or biologically evaluated to date.



Graph 4.5. KBDD assay results of ethylthio-2-PhBr derivatives at 100 mM against MRSA USA300 LAC. Diameters of the zones of inhibition were measured in mm and averaged across biological triplicates.

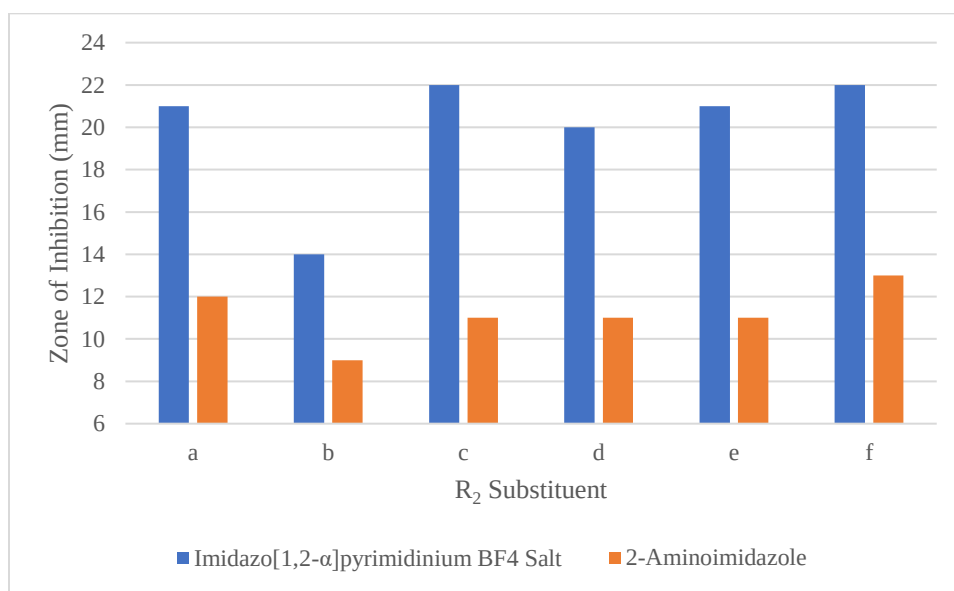


Graph 4.6. KBDD assay results of ethylthio-2-PhCl derivatives at 100 mM against MRSA USA300 LAC. Diameters of the zones of inhibition were measured in mm and averaged across biological triplicates.



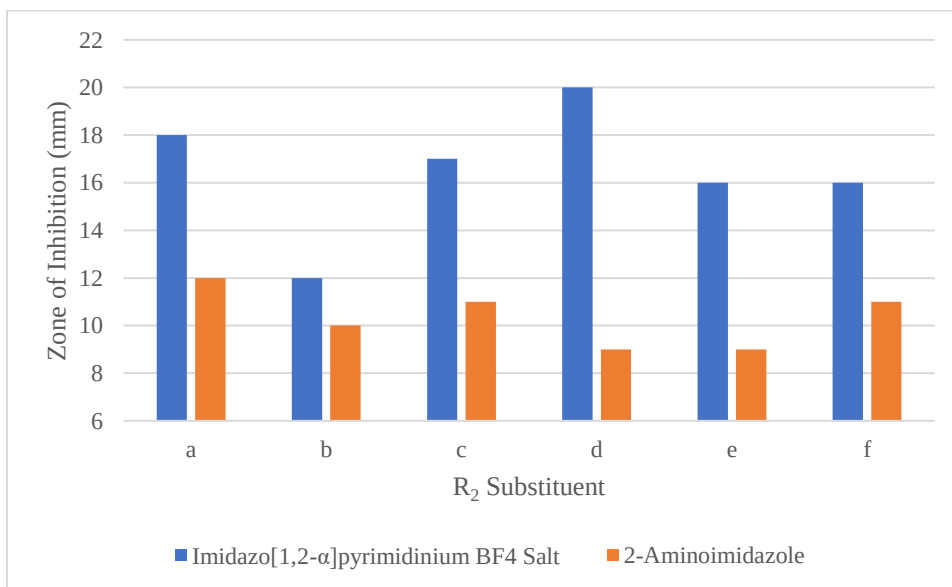
Graph 4.7. KBDD assay results of ethylthio-2-PhF derivatives at 100 mM against MRSA USA300 LAC. Diameters of the zones of inhibition were measured in mm and averaged across biological triplicates.

We then synthesized the 3-Br series (**7.2a-f** and **7.3a-f**) to see how activities would compare to the 2-Br series. The imidazo[1,2-a]pyrimidinium tetrafluoroborate salts in this series were all more active than the corresponding 2-aminoimidazoles (Graph 4.8.) and the best of the salts was a tie between the 4-bromo derivative (**7.2c**) and the 2,4-fluoro derivative (**7.2f**). The 4-chloro (**7.2a**) and 4-nitro (**7.2e**) came in as close seconds and the 4-cyano derivative (**7.2d**) was not far behind. This series overall proved to have significant activity against MRSA, with zones of inhibition of 20 mm or greater in all cases except the biphenyl derivative (**7.2b**) for the imidazo[1,2-a]pyrimidinium tetrafluoroborate salts, and would be a prime candidate to expand upon with other R₂ substituents. The best 2-aminoimidazole of this series was the 2,4-fluoro derivative (**7.3f**) but it is not a lead 2-aminoimidazole in this study overall.

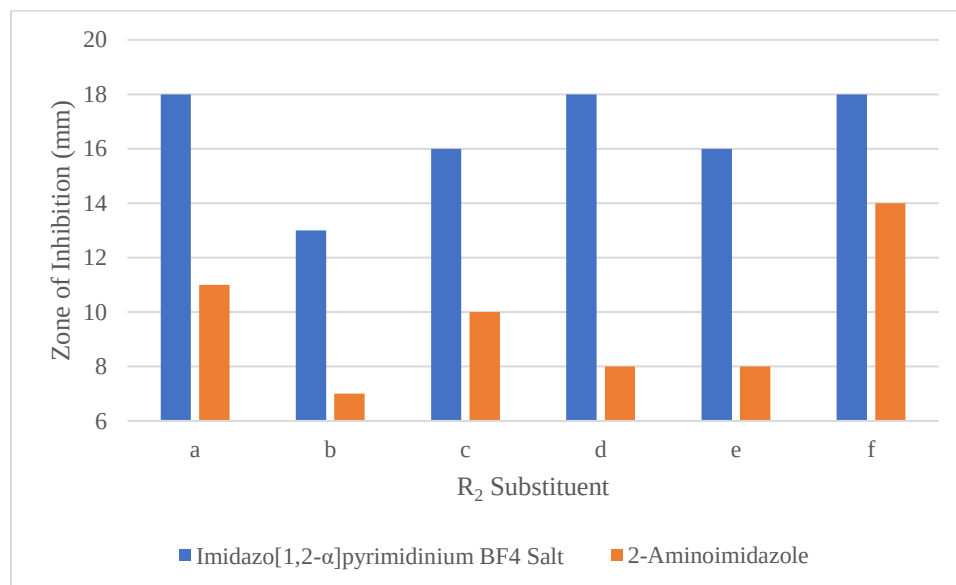


Graph 4.8. KBDD assay results of ethylthio-3-PhBr derivatives at 100 mM against MRSA USA300 LAC. Diameters of the zones of inhibition were measured in mm and averaged across biological triplicates.

The next logical derivatives to synthesize were the 4-Br series (**8.2a-f** and **8.3a-f**). The predominant trend continued, as the imidazo[1,2-a]pyrimidinium tetrafluoroborate salts displayed significantly higher activity than their respective 2-aminoimidazoles (Graph 4.9.). The R_2 substituents, however, did not follow the same SAR trends as the best of this series was the 4-cyano salt derivative (**8.2d**). To continue our aryl $N1$ derivatives, we chose to make the 4-Cl series (**9.2a-f** and **9.3a-f**) to compare to its respective 2-Cl series as well as the 4-Br series. Their general SARs (Graph 4.10.) continued to follow the overall trend that the imidazo[1,2-a]pyrimidinium tetrafluoroborate salts possessed much greater potency than their 2-aminoimidazole counterparts. Interestingly for this series, the 2,4-fluoro (**9.2f**), 4-chloro (**9.2a**), and 4-cyano (**9.2d**) all tied for the greatest activities of the salts. The best 2-aminoimidazole of this series was the 2,4-fluoro derivative (**9.3f**) but it is not a lead 2-aminoimidazole in this study overall.

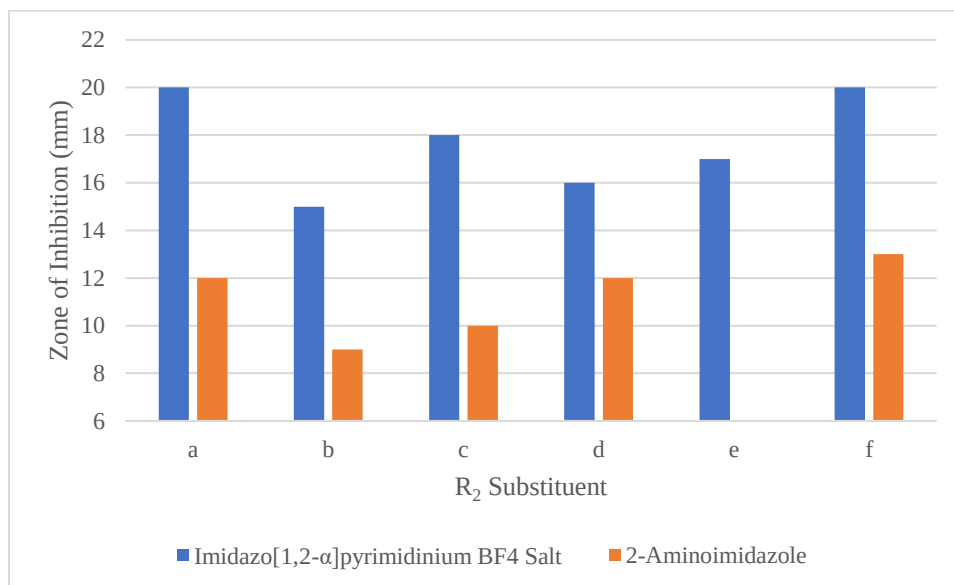


Graph 4.9. KBDD assay results of ethylthio-4-PhBr derivatives at 100 mM against MRSA USA300 LAC. Diameters of the zones of inhibition were measured in mm and averaged across biological triplicates.



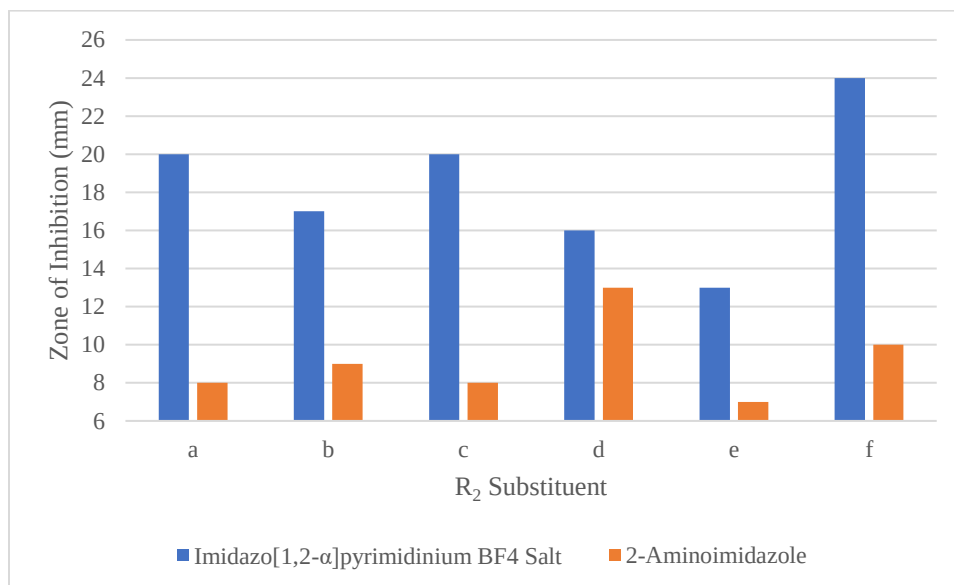
Graph 4.10. KBDD assay results of ethylthio-4-PhCl derivatives at 100 mM against MRSA USA300 LAC. Diameters of the zones of inhibition were measured in mm and averaged across biological triplicates.

We also synthesized the 4-F series (**10.2a-f** and **10.3a-f**) to round out our halide comparisons at the *para* position. Their activities (Graph 4.11.) also followed our overall SAR trend of the imidazo[1,2-a]pyrimidinium tetrafluoroborate salts being more potent overall than the 2-aminoimidazoles. The best of this series were the 4-chloro (**10.2a**) and 2,4-fluoro (**10.2f**), and these derivatives beat their 4-Cl counterparts with zones of inhibition at 20 mm as opposed to 18 mm. This series contains the 2-aminoimidazole with the poorest activity in our library, the 4-nitro derivative (**10.3e**), with no zone of inhibition shown. The best 2-aminoimidazole in this series was the 2,4-fluoro derivative (**10.3f**) but it is by no means a lead in this study overall.



Graph 4.11. KBDD assay results of ethylthio-4-PhF derivatives at 100 mM against MRSA USA300 LAC. Diameters of the zones of inhibition were measured in mm and averaged across biological triplicates.

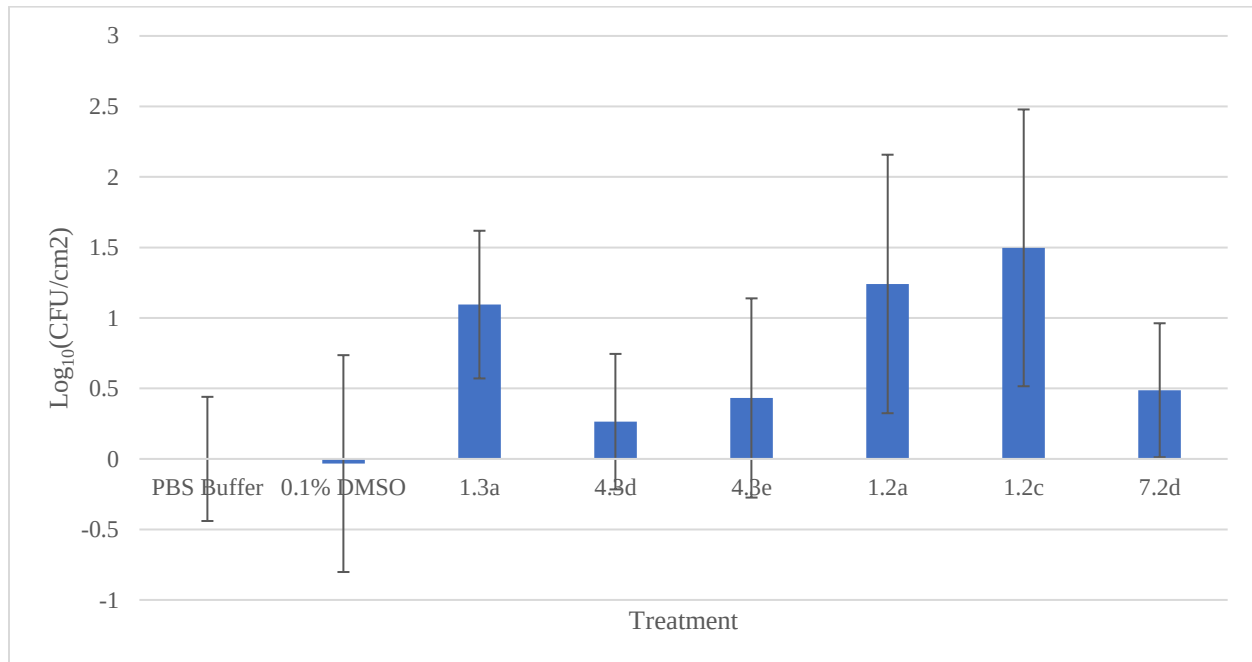
We completed our aryl *N*1 derivatives with the ethyl-thiotolyl series (**11.2a-f** and **11.3a-f**). We chose to synthesize this series as a means of comparing electronic effects, as the methyl group in the ethyl-thiotolyl series is electron donating whereas all the other aryl *N*1 derivatives we synthesized were electron withdrawing. As shown in Graph 4.12, the imidazo[1,2- α]pyrimidinium tetrafluoroborate salts of this series again beat all the 2-aminoimidazoles counterparts. The best salt derivative was the 2,4-fluoro (**11.2f**) and is one of our lead imidazo[1,2- α]pyrimidinium tetrafluoroborate salts overall. The activities of the 4-chloro (**11.2a**) and 4-bromo (**11.2c**) salt derivatives were also impressive, at 20 mm. The best 2-aminoimidazole of this series was the 4-cyano derivative (**11.3d**), but it is not a lead 2-AI overall.



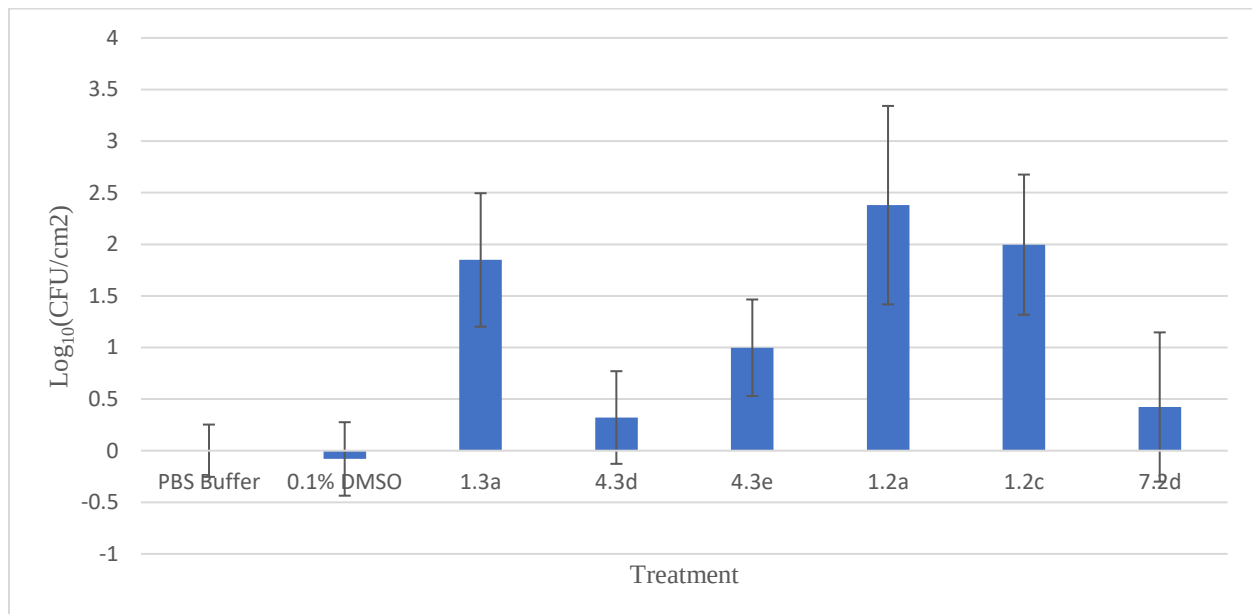
Graph 4.12. KBDD assay results of ethyl-thiotolyl derivatives at 100 mM against MRSA USA300 LAC. Diameters of the zones of inhibition were measured in mm and averaged across biological triplicates.

The evaluation of selected lead agent's ability to inhibit planktonic growth was done using MIC assays, as is standard practice. The evaluation of selected lead agent's ability to eradicate pre-formed biofilms was done using MBEC assays. Due to the breadth of our compound library in this study and the tedious nature of both of these microtiter dish assays, we chose to deprioritize them, as the KBDD assays and CDC Biofilm Reactor assays were of greater urgency. For this reason, this data will be included prior to publication of this manuscript but will not appear in this dissertation.

Finally, the CDC Biofilm Reactor assay, a robust biofilm model, was utilized to further elucidate the mechanism of action against MRSA USA300 LAC biofilms. Using this method, we quantified log₁₀ densities of the treated biofilms as well as the bulk fluid, and the log₁₀ reductions resulting from treatment (Graphs 4.13 and 4.14).



Graph 4.13. Log_{10} reductions of MRSA USA300 LAC biofilms grown in a CDC Biofilm Reactor. All antibiotic and adjuvant treatment concentrations were 100 μM . Error bars reflect standard deviation of the biofilm log densities across biological triplicates and technical duplicates.



Graph 4.14. Log_{10} reductions of MRSA USA300 LAC bulk fluid grown in a CDC Biofilm Reactor. All antibiotic and adjuvant treatment concentrations were 100 μM . Error bars reflect

standard deviation of the biofilm log densities across biological triplicates and technical duplicates.

The treatments shown in the initial CDC Biofilm Reactor analysis were chosen based on activities in KBDD assays and also to further quantify benchmark compound activities. The initial leads we chose to test were **4.3d** and **4.3e** for the 2-aminoimidazoles and **7.2d** for the imidazo[1,2-a]pyrimidinium tetrafluoroborate salts. The benchmark compounds we chose to test were **1.3a** for the 2-aminoimidazoles and **1.2a** and **1.2c** for the imidazo[1,2-a]pyrimidinium tetrafluoroborate salts. With these activities in hand, it is now imperative that we conduct more CDC Biofilm Reactor assays with the final lead adjuvants identified in this study prior to publication.

Confocal microscope imaging was also conducted to further analyze the reduction of biofilms on the coupons grown in these CDC Biofilm Reactor assays (Figures 4.5. and 4.6.). The agents chosen for these assays (**1.2a**, **1.2c**, **7.2d**, **1.3a**, **4.3d**, and **4.3e**) were important benchmarks for us to analyze, but we have now identified more impressive lead agents and will conduct these assays again with those agents (**1.2f**, **1.2g**, **1.2i**, **2.2f**, **11.2f** for the imidazo[1,2-a]pyrimidinium tetrafluoroborate salts and **1.3g**, **3.3a**, **4.3f**, **6.3a**, **9.3f** for the 2-aminoimidazoles) prior to publication of this work. One interesting observation to note in these confocal images, is the case of 2-aminoimidazole **4.3e** (Figure 4.6. panel D), as we observed what appears to be long red strings of cells, potentially indicating the compound was inhibiting cell division. It is worth noting that these are sample images and that further analysis of the confocal images taken will be conducted using the Odin software prior to final publication.

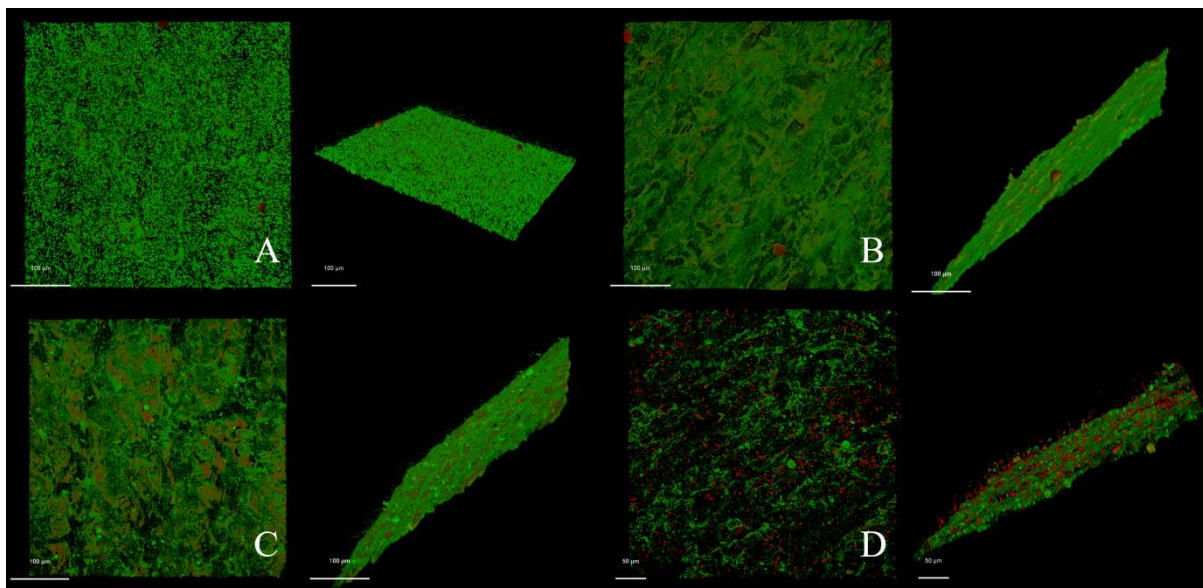


Figure 4.5. Confocal microscopy images of treated MRSA USA300 LAC biofilms grown in a CDC Biofilm Reactor model and stained with LIVE/DEAD. Images show A) Control treatment with 0.1% DMSO B) treatment with imidazo[1,2-a]pyridinium salt 1.2a at 100 μ M C) treatment with imidazo[1,2-a]pyridinium salt 1.2c at 100 μ M and D) treatment with imidazo[1,2-a]pyridinium salt 7.2d at 100 μ M.

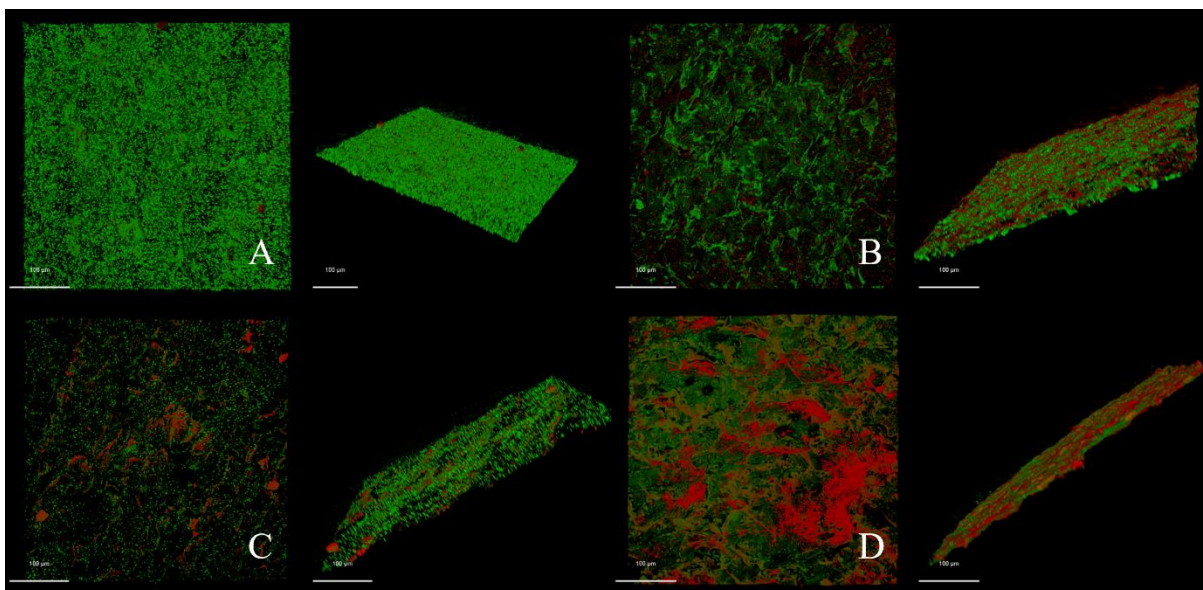


Figure 4.6. Confocal microscopy images of treated MRSA USA300 LAC biofilms grown in a CDC Biofilm Reactor model and stained with LIVE/DEAD. Images show A) Control treatment

with 0.1% DMSO B) treatment with 2-aminoimidazole 1.3a at 100 μ M C) treatment with 2-aminoimidazole 4.3d at 100 μ M and D) treatment with 2-aminoimidazole 4.3e at 100 μ M.

4.5 Conclusions

Novel 2-aminoimidazoles and imidazo[1,2-a]pyrimidinium tetrafluoroborate salts were synthesized in excellent yields via an optimized route. KBDD assays evaluated all compounds against *Staphylococcus aureus* MRSA USA300 LAC biofilms as an efficient means of bulk screening. The lead compounds identified in this study were then evaluated against *Staphylococcus aureus* MRSA USA300 LAC biofilms grown in the robust CDC Biofilm Reactor model and log reductions of biofilm density were found. Finally, these treated MRSA biofilms were imaged using confocal microscopy and LIVE/DEAD staining.

SAR analysis via KBDD assays in this study revealed the intermediate imidazo[1,2-a]pyrimidinium tetrafluoroborate salts to be much more potent than the target 2-aminoimidazoles in nearly every case. Preliminary CDC Biofilm Reactor assays support this overall trend as well. An important observation should be noted within the bulk fluid treatment data (Graph 4.14.); it appears that our adjuvants are also significantly reducing planktonic culture density as well as the biofilm density. This would suggest that our adjuvants have some antimicrobial activity, contrary to literature suggestion that these agents are merely dispersing the biofilms. This is also supported by our KBDD assays, as we saw clear zones of inhibition indicating bactericidal activity rather than semi-opaque, which would indicate bacteriostatic activity.

Before this work can be published, CDC Biofilm Reactor assays need to be ran using the final lead agents identified (**1.2f**, **1.2g**, **1.2i**, **2.2f**, **11.2f** for the imidazo[1,2-a]pyrimidinium tetrafluoroborate salts and **1.3g**, **3.3a**, **4.3f**, **6.3a**, **9.3f** for the 2-aminoimidazoles). We also plan to

collect confocal microscopy images of the treated biofilms from these assays. In depth analysis of the confocal images collected using the Imaris software will also be conducted prior to submission of this manuscript but will not be detailed within this dissertation.

The SAR analysis conducted in this study will be utilized in future work where we plan to dimerize both the lead 2-aminoimidazoles and the lead imidazo[1,2-a]pyrimidinium tetrafluoroborate salts. These novel dimers will be used in synergy and resensitization studies in a similar manner as has been done in the literature with great success.

4.6 Conflicts of Interest

The authors declare no conflicts of interest.

4.7 Acknowledgements

This research was funded through generous external donations from Professor Tom Livinghouse.

CHAPTER FIVE

5. CURRENT AND FUTURE STUDIES

5.1 Investigation of Anaerobic Metabolism of Pyruvate in Biofilm-Forming Bacteria as a Potential Target

We originally hypothesized that the novel nitro heteroaromatic agents we reported in Chapters 2 and 3 showed selectivity towards the Gram-positive organism *S. epidermidis* over the Gram-negative organism *P. aeruginosa* due to inherent differences between Gram-positive and Gram-negative organisms. However, we now hypothesize that the selectivity shown is due to differences in enzymes for anaerobic pyruvate metabolism. There are two types of enzymes responsible for anaerobic metabolism of pyruvate—pyruvate:ferredoxin oxidoreductase (PFOR) and pyruvate dehydrogenase (PDH).

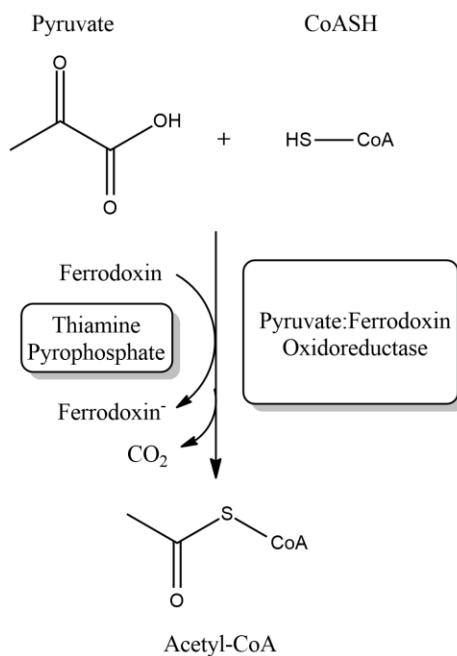
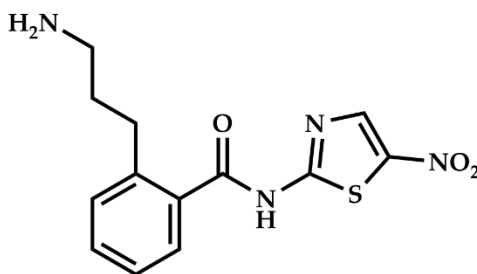


Figure 5.1. The anaerobic metabolism of pyruvate.

Nitazoxanide and the other analogues developed in its class target this metabolic pathway (Figure 5.1.) in anaerobic bacteria by outcompeting pyruvate for binding to the thiamine pyrophosphate (TPP) cofactor of PFOR in the active site.⁴⁶ *P. aeruginosa* has been shown to grow in anaerobic conditions within cystic fibrosis mucus.⁹⁹ However, its anaerobic metabolism is dependent on PDH^{100, 101} and consequently does not contain the target known to thiazolides. *S. epidermidis* does contain the PFOR enzyme, which is consistent with our observation of selectivity for it compared to *P. aeruginosa* in the prior published study.



1

Figure 5.2. Amixicile.

Amixicile (**1**) is an analogue of nitazoxanide, where the 2-acetoxy group was replaced with a propylamine to increase its solubility (Figure 5.2.). It was found to be a prime candidate for the treatment of *Clostridium difficile* infections and was less toxic than Nitazoxanide in murine models.^{47, 102-104} This analogue is very similar in structure to two analogues we synthesized in our last study (**7a** and **7b**) in that they have a free amine at the 2-position. One of these studies found amixicile to be effective in being selective towards anaerobic bacteria responsible for periodontal diseases, while the health-promoting aerobic bacteria were unharmed.¹⁰²

The literature shows that nitazoxanide and known analogues are effective against obligate anaerobes; however, there is much less known on how they affect facultative anaerobes or how they might affect anoxic regions within a biofilm. Rossignol and coworkers found in their study of screening nitazoxanide against various organisms that were both anaerobes and aerobes, that nitazoxanide demonstrated poor activity under aerobic conditions against members of the family *Enterobacteriaceae* and *Pseudomonas*, *Staphylococcus*, and *Enterococcus* species.⁴² However, their study showed an exception to this in *Staphylococcus aureus*, as did another study, where nitazoxanide was effective against the bacteria in aerobic conditions.¹⁰⁵ Studies have shown that biofilms exhibit oxygen gradients, and that Pyruvate fermentation occurs in the anoxic regions of the biofilm.^{12, 100, 101, 106} We are interested in evaluating the lead nitro heteroaromatic antimicrobials from Chapter 2 (Figure 5.3.) against biofilms of facultative anaerobes under an artificial anaerobic atmosphere to shed some light on this.

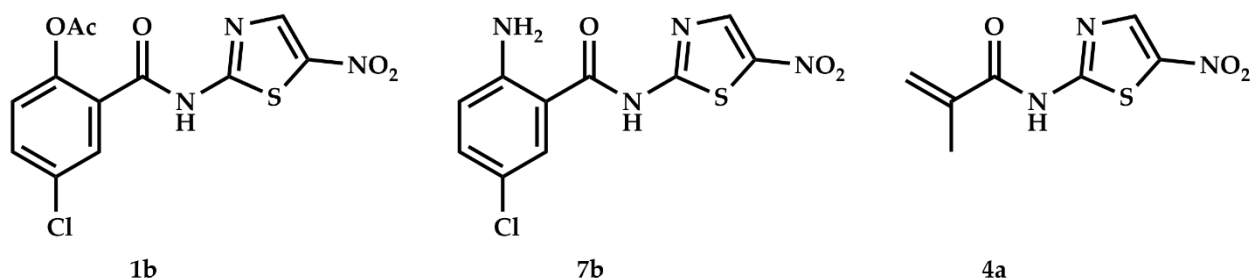


Figure 5.3. Lead compounds identified in Chapter 2.

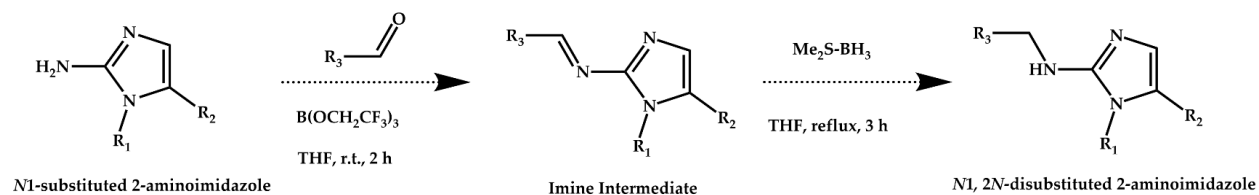
To test our evolving hypothesis, it would be imperative to compare aerobic and anaerobic conditions as well as strains that are both Gram-positive and Gram-negative, and either known to have a PFOR enzyme or not. Suitability of strains was determined by comparing genomic data of bacteria (*Clostridium difficile*, *Helicobacter pylori* and *Prevotella intermedia*) in which the

PFOR enzyme was successfully targeted by nitazoxanide or its analogues, to the PFOR enzyme of the proposed strains. We propose the following line up of strains to evaluate; *Streptococcus mutans* as the negative control Gram-positive bacterium that is known to utilize PDH, *Pseudomonas aeruginosa* (PAO1) as the negative control Gram-negative bacterium that is known to utilize PDH, *Staphylococcus aureus* as the model Gram-positive PFOR containing bacterium, and *Escherichia coli* (K-12) as the model Gram-negative PFOR containing bacterium.

Initial evaluation of the antimicrobials would include the following: 1) MIC determination via well plate procedures in standard aerobic conditions. 2) MIC determination via modified well plate procedures in anaerobic conditions. 3) MBEC determination via well plate procedures in standard aerobic conditions. 4) MBEC determination via modified well plate procedures in anaerobic conditions.

5.2 Poly-substituted 2-Aminoimidazoles and Imidazo[1,2-a]pyrimidinium Tetrafluoroborate Salts Library Expansion

Thus far our group has exclusively synthesized imidazo[1,2-a]pyrimidinium and 2-aminoimidazole derivatives with *N*1 and C5 substitution. We chose those positions based on Steenackers' work, as he showed this substitution pattern to be the most potent towards gram-positive pathogens^{82, 92, 107, 108} Steenackers also synthesized derivatives with 2*N* substitution, as he found those derivatives to be less toxic than those with *N*1 substitution.¹⁰⁹ For this reason, it would be imperative to synthesize 2-aminoimidazoles with 2*N* substituents. Amethyst Demeritte in our group has proposed to synthesize these using Sheppard's amidation reagent followed by reduction of the imine using BMS (Scheme 5.1) and this work will be published in her upcoming dissertation.



Scheme 5.1. Proposed synthesis of 2N-substituted 2-aminoimidazoles.

It has been established by Melander that changing the aryl substitution from the C5 to the C4 position led to higher activity against gram-negative pathogens *Acinetobacter baumannii* and *Pseudomonas aeruginosa*.⁸⁸ Minimal activity has been observed within our library of compounds against our gram-negative strain, *Pseudomonas aeruginosa* PA14. It is imperative that future work include this substitution pattern with our derivatives and see if we observe the same change in selectivity from gram-positive to gram-negative.

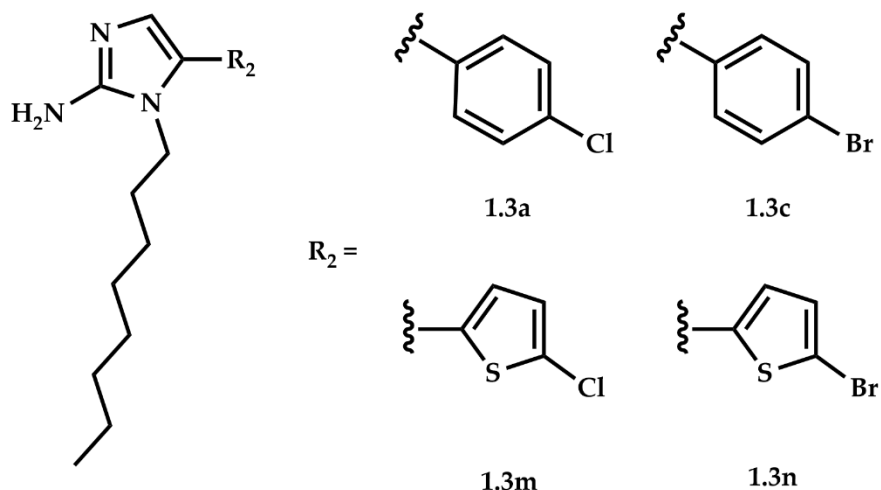


Figure 5.4. *n*-Octyl derivative comparison of phenyls and thiophenes as the C5 aromatic substituent installed.

An interesting possible expansion within our current array of aryl C5 substituents are thiophenes. Thiophenes possess unique biological properties and have been utilized in a wide

array of antimicrobial, antifungal and anticancer therapeutics. We synthesized two thiophene derivatives and found they possessed identical activity against MRSA USA300 LAC compared to their simple phenyl derivative counterparts (Figure 5.4.). Compounds **1.3a** and **1.3l** both had zones of inhibition of 11 mm and Compounds **1.3c** and **1.3m** both had zones of inhibition of 9 mm. One reason this work was not accomplished within this dissertation, was that the corresponding α -bromoketones were prone to degradation and needed to be prepared, purified and immediately utilized in the *N*-alkylation step. This tedious nature of thiophene derivative synthesis caused it to be of lesser priority than their phenyl counterparts.

We hypothesized in Chapter 4 that the incorporation of a sulfide linker within the *n*-octyl chain at the *N*1 position could enhance activity. We synthesized derivatives with a sulfide linker at the third position on this chain, but it would be interesting to see if there is a change in activity if this sulfide linker is moved further down the chain. To address this, several derivatives with a sulfide linker in the fourth position of the chain are currently being synthesized in our group.

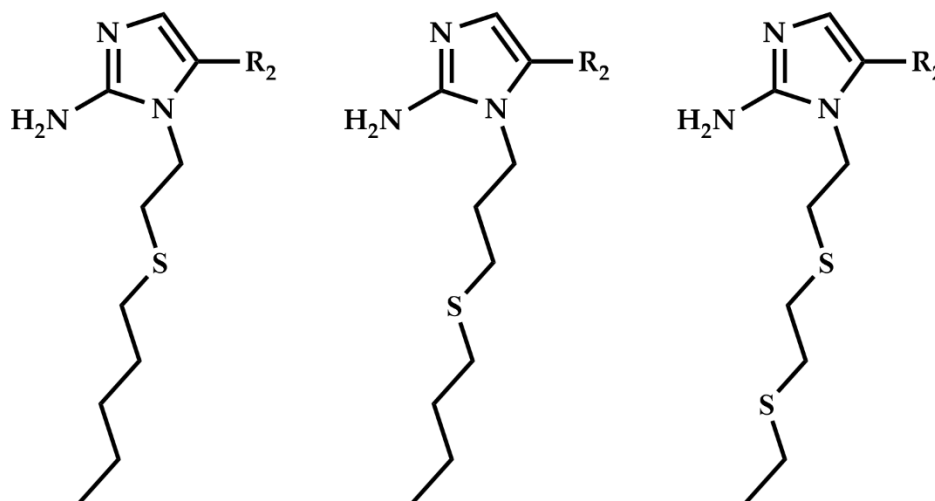
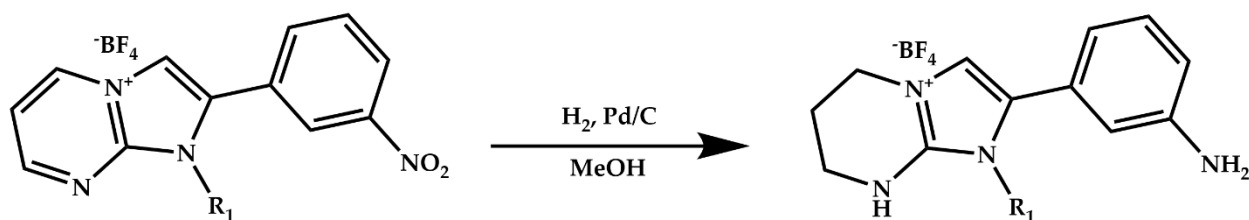


Figure 5.5. Sulfide linker derivative proposed expansion.

Along a similar line of interest, we plan to prepare binary sulfide analogs, with sulfide linkers in positions three and six. Initial synthesis of these derivatives in our group is underway (Figure 5.5.). These derivatives would further clarify any conclusions about the effects of incorporating a sulfide linker within our SAR analysis.

5.3 Tetrahydroimidizo[1,2-a]pyrimidinium tetrafluoroborate salts

Initial attempts in our laboratory to synthesize the precursor for dimerization—the meta substituted NH₂ derivative—via hydrogenation with palladium on carbon led to an unexpected discovery of a new series. We intended to simply reduce the meta-NO₂ group to the amine, as Melander and coworkers have done with their 2-aminoimidazole derivatives, as it is the precursor for their dimerized 2-aminoimidazoles.⁹⁰ We planned to use this strategy, but with our imidazo[1,2-a]pyrimidinium tetrafluoroborate salts. Instead, the pyrimidinium aromatic ring was reduced as well as the meta-NO₂ group, leading to a class of compounds (e.g., tetrahydroimidizo[1,2-a]pyrimidinium tetrafluoroborate salts, Scheme 5.2.).



Scheme 5.2. Synthesis of a novel tetrahydroimidizo[1,2-a]pyrimidinium tetrafluoroborate salt, where R₁ is *n*-octyl.

We have since expanded this series (altering both the aryl substituents as well as the N1 substituent) and prepared several of these new derivatives. We find these tetrahydroimidizo[1,2-a]pyrimidinium tetrafluoroborate salts to be interesting, as the 2N nitrogen in these quaternary

salts is now able to serve as a hydrogen bond donor, rather than the parent 2*N* nitrogen hydrogen bond acceptor. It is worth noting, that it is hypothesized that the parent imidazo[1,2-*a*]pyrimidinium derivatives are believed to be acting as pro-drugs in that the pyrimidinium ring is cleaved intracellularly to the 2-aminoimidazole, and this mechanism for cleavage is dependent on nucleophilic attack on the pyrimidinium ring. Therefore, it is possible that by breaking aromaticity, this hypothesized pro-drug activity may be neutered.

Isurika Wattegedara in our group has taken this project on and will be publishing this work in an upcoming manuscript and dissertation. Preliminary biological evaluation of their activity against MRSA USA300 LAC was conducted via KBDD assays and showed positive results, although the activities were slightly less than the parent imidazo[1,2-*a*]pyrimidinium tetrafluoroborate salts.

5.4 Novel Imidazo[1,2-*a*]pyrimidinium Dimers

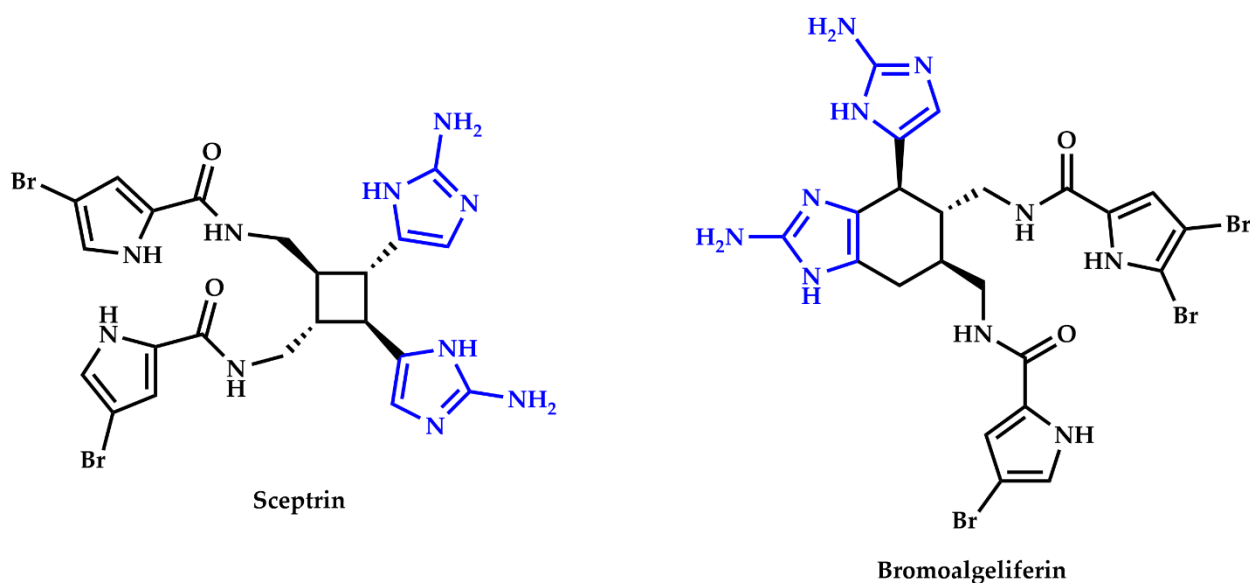
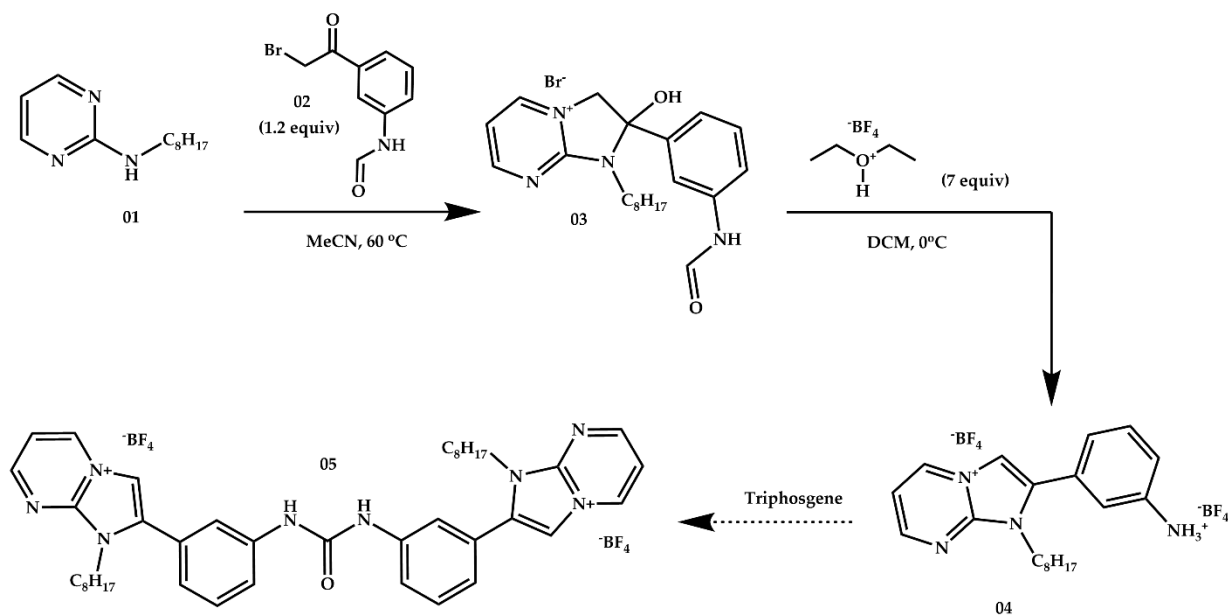


Figure 5.6. Inspiration from nature; structures of sponge-derived marine alkaloids that have been found to possess anti-biofilm properties. The 2-aminoimidazole motif is highlighted in blue.

The marine alkaloids produced in deep-sea sponges, such as Sceptrin and Bromoalgaliferin (Figure 5.6.), are the inspirations many have cited for their interest in development of 2-aminoimidazole derivatives.^{70, 72, 73, 110-115} What is noticeable in these potent natural products, is the presence of two 2-AI motifs. It is therefore of great interest to investigate dimerized 2-aminoimidazole derivatives, as both Steenackers' and Melander's groups have done.^{90, 116}

Since the established synthetic pathway to dimerized 2-aminoimidazoles was not suitable for our imidizo[1,2-a]pyrimidinium tetrafluoroborate salts, we designed a new route (Scheme 5.3). Since we needed to install an amine at the *meta* position of the C5-substituted aryl group, we chose a protecting group that would be benign in the initial alkylation step but would be deleted upon acidic treatment during the dehydration of the salt.



Scheme 5.3. Synthesis of imidizo[1,2-a]pyrimidinium tetrafluoroborate salt dimers, where R₁ is a varied alkyl substituent with sulfide linkers.

We therefore synthesized 3-formamidoacetophenone and brominated it using our usual conditions. The resulting acetophenone (**02**) was utilized in the usual *N*-alkylation to form the hydroxy salt (**03**) and dehydrated to form the bis(tetrafluoroborate) salt (**04**). We plan to dimerize the bis(tetrafluoroborate) salt to form **05** via the conditions described by Melander, using triphosgene, however we also believe that we can improve those conditions by replacing triphosgene with CDI.

Utilizing this synthetic pathway, we believe we could achieve significant activity enhancements as Melander has seen with his dimerized 2-aminoimidazoles.⁹⁰ These new dimers would be utilized in KBDD Synergism assays to screen for their potential use as adjuvants in combination with conventional antibiotics to resensitize resistant strains to treatment as Melander and coworkers has successfully done.⁹⁰

5.5 Synergy and Resensitization Studies

Since our 2-aminoimidazole and imidazo[1,2-*a*]pyrimidinium tetrafluoroborate salts are adjuvants, we need to evaluate their utility in combination with conventional antimicrobials. The

KBDD assay (Figure 5.7.) can be modified to screen for synergy between our adjuvants and traditional antibiotics.

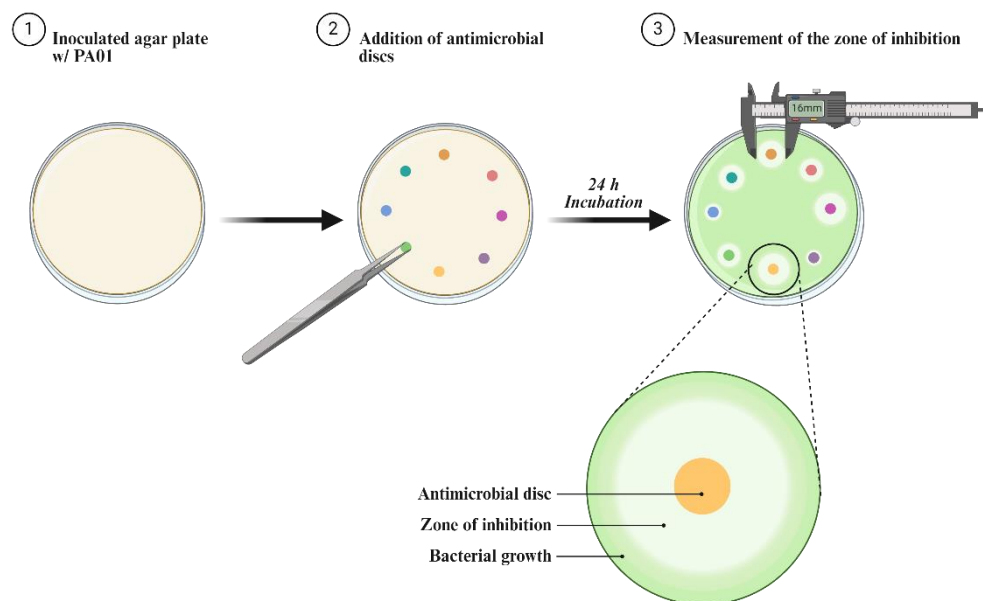


Figure 5.7. Illustration of a Kirby-Bauer disk diffusion assay created by Amethyst Demeritte using BioRender.com.

Antimicrobial loaded disks can be placed in close proximity on the agar to allow diffusion gradients to intersect. This assay would allow for efficient bulk screening for lead compounds which possess the desired synergistic effects (Figure 5.8.) and those lead adjuvant compounds could then be further evaluated in resensitization studies using the more robust CDC biofilm reactor assays.

KBDD assay results for the adjuvants in our library at 100 mM against MRSA USA300 LAC have been collected and are disclosed in Chapter 4. KBDD assay results of the selected antibiotics (vancomycin, novobiocin and tetracycline) at 100 mM for this study against MRSA USA300 LAC are as follows; 9, 12, and 16 mm respectively. With the separate activities in hand,

we are now ready to screen for synergism by using the KBDD synergism assays as described above (Figure 5.8.).

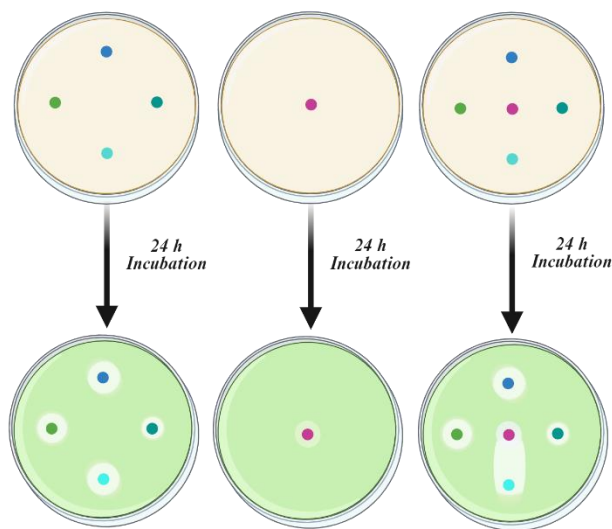
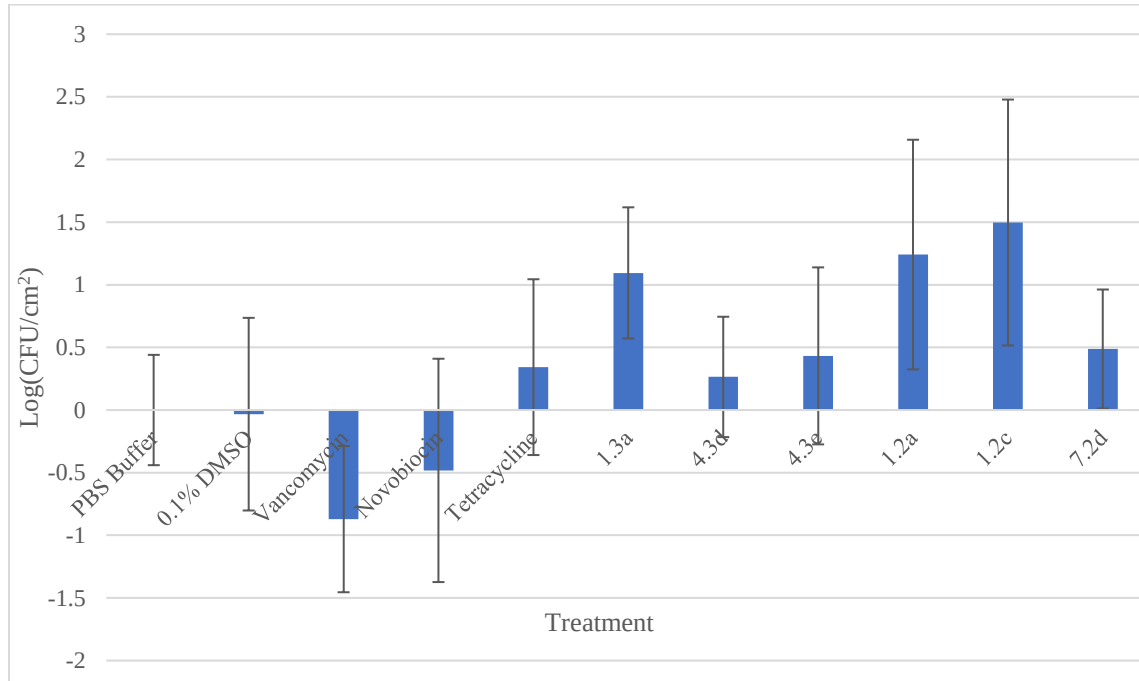


Figure 5.8. Illustration of a Kirby-Bauer disk diffusion synergism assay created using BioRender.com.

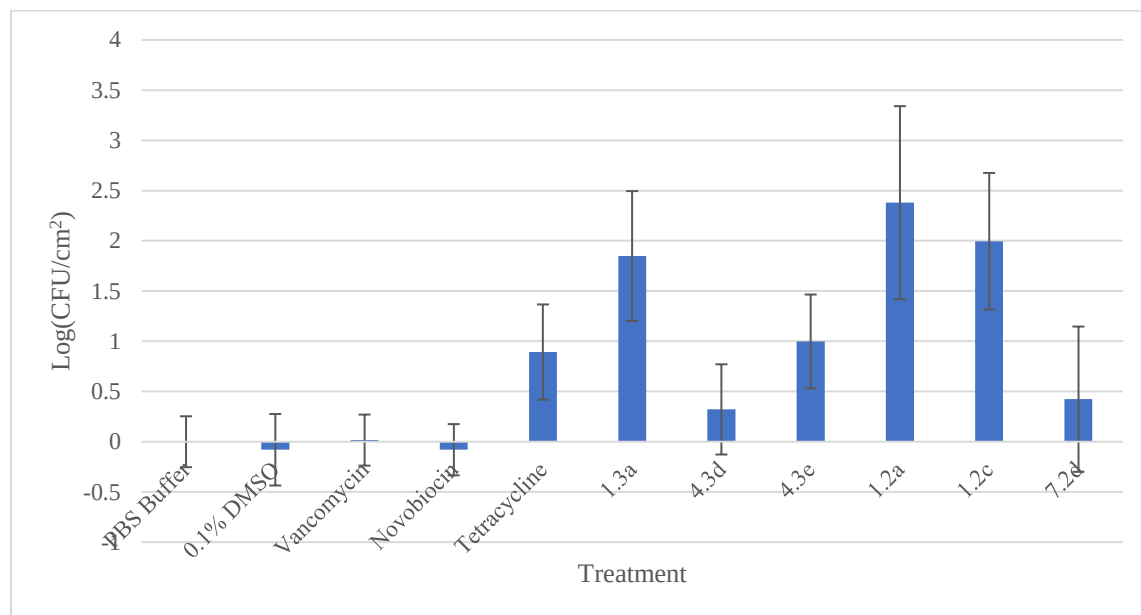
Resensitization studies would include treatment of biofilms with conventional antibiotics alone and treatment of biofilms with the adjuvants alone to establish their separate effects, followed by the treatment of biofilms with the adjuvant and antibiotic together to see any synergistic activity enhancements. As these would be done using the CDC biofilm reactor model, the biofilms could be stained and imaged using confocal microscopy for further analysis.

Preliminary results from the CDC Biofilm Reactor assays displayed in Graphs 5.1. and 5.2. show $\log_{10}$ reduction of the biofilms and bulk fluid samples upon treatment. Vancomycin and novobiocin treatments caused biofilm density to increase, while tetracycline was able to reduce the biofilm density. Vancomycin and novobiocin also failed to have much of any effect on the planktonic bacteria in the bulk fluid samples, but tetracycline managed to have an effect.

These results reinforce the findings of our KBDD assays, as we found vancomycin to have the least effect and tetracycline to be the leading antibiotic of the three in those as well.



Graph 5.1. Log reductions of MRSA USA300 LAC biofilms grown in a CDC Biofilm Reactor. All antibiotic and adjuvant treatment concentrations were 100 μ M. Error bars reflect standard deviation of the biofilm log densities across biological triplicates and technical duplicates.



Graph 5.2. Log reductions of MRSA USA300 LAC bulk fluid grown in a CDC Biofilm Reactor. All antibiotic and adjuvant treatment concentrations were 100 μ M. Error bars reflect standard deviation of the biofilm log densities across biological triplicates and technical duplicates.

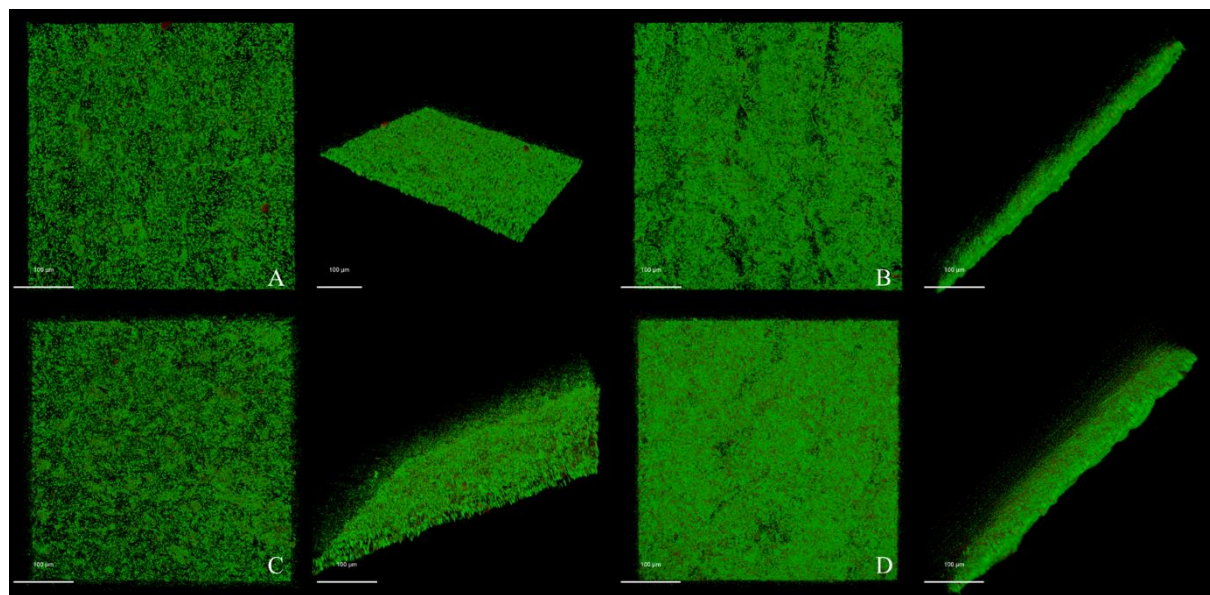


Figure 5.6. Confocal microscopy images of treated MRSA USA300 LAC biofilms grown in a CDC Biofilm Reactor model and stained with LIVE/DEAD. Images show A) Control treatment with 0.1% DMSO B) treatment with Novobiocin at 100 μ M C) treatment with Tetracycline at 100 μ M and D) treatment with Vancomycin at 100 μ M.

Treated biofilms grown in the CDC biofilm reactor were stained using LIVE/DEAD staining and imaged on the confocal microscope (Figure 5.6.). As is supported by the $\log_{10}$ reduction results collected from the CDC biofilm reactor assays, these conventional antibiotics had no substantial effects on the MRSA USA300LAC biofilms. With these initial results, we have established what these conventional antibiotics are capable of on their own. Our next step would be to treat using a combination of the adjuvants and antibiotics to look for synergistic activities.

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APPENDICES

APPENDIX A

EXPERIMENTALS

1A Chemical Synthesis Experiments

1.1A General Synthesis Methods

All chemical reagents and conventional antibiotics were purchased from commercial sources (TCI America, Portland, OR, USA and Sigma Aldrich, Burlington, NC, USA) and used as received without further purification, with the exception of the acyl chlorides which were distilled from CaH_2 and ANT, whose purification is detailed below. Solvents utilized in filtrations, transfers, and chromatography were certified ACS grade. Thin-layer chromatography was performed on Silicycle Glass Backed TLC Extra Hard Layer, 60 Å plates (thickness; 250 μm , indicator; F-254) and visualization was accomplished with UV light (254 nm), and/or potassium permanganate. All synthesized compounds were characterized on a Bruker 500 MHz NMR Ascend Avance III HD (actively shielded) Spectrometer and a Bruker 600 MHz NMR Avance III NMR (actively shielded) Spectrometer. J values were depicted in hertz (Hz) and spin multiplicities were described as singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), and broad (b). Chemical shifts were reported in parts per million (δ), employing the solvent resonance as the internal standard.

1.2A Preparation of molecules seen in Chapter 2

1.2.1A 2-Acetoxy-5-chloro-*N*-(5-nitrothiazol-2-yl)benzamide (**1b**) A 10 mL round-bottom flask equipped with a magnetic stirring bar and poly-cap was charged with 2-acetoxy-5-chlorobenzoic acid (0.215 g, 1 mmol) and 3 mL of DCM. A catalytic amount of DMF was added. To this stirred solution, oxalyl chloride (0.174 mL, 2 mmol) was added. The reactant mixture was loosely capped and stirred for 15 min at room temperature. The corrosive by products were removed in vacuo before 2-amino-5-nitrothiazole (0.145 g, 1 mmol) was added and the flask was equipped with an ice bath. Anhydrous DCM (4 mL) was added, followed by the dropwise addition of triethyl amine (0.167 mL, 1.2 mmol). The reactant mixture was allowed to return to room temperature as it stirred overnight. The solvent was then removed in vacuo, the product mixture was diluted with EtOAc (5 mL) and successively extracted with water (2 × 5 mL) and brine (2 × 5 mL) to provide the crude product. Recrystallization from EtOAc provided the title compound (253 mg, 74%). ¹H-NMR (D₆-DMSO, 500 MHz): δ 13.70 (1H, s), 8.72 (1H, s), 7.96 (1H, d, *J* = 3 Hz), 7.76 (1H, dd, *J* = 9, 3 Hz), 7.38 (1H, d, *J* = 9 Hz), 2.25 (3H, s). ¹³C-NMR (D₆-DMSO, 125 MHz) δ 169.3, 164.6, 162.1, 147.9, 142.9, 142.7, 133.6, 130.4, 130.1, 127.5, 125.9, 21.1.

1.2.2A 2-Acetoxy-5-methoxy-*N*-(5-nitrothiazol-2-yl)benzamide (1c) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly-cap was charged with 2-acetoxy-5-methoxybenzoic acid (0.210 g, 1 mmol) and 3 mL of DCM. A catalytic amount of DMF was added. To this stirred solution, oxalyl chloride (0.174 mL, 2 mmol) was added. The reactant mixture was loosely capped and stirred for 15 min at room temperature. The corrosive by products were removed in vacuo before 2-amino-5-nitrothiazole (0.145 g, 1 mmol) was added and the flask was equipped with an ice bath. Anhydrous DCM (4 mL) was added, followed by the dropwise addition of triethyl amine (0.167 mL, 1.2 mmol). The reactant mixture was allowed to return to room temperature as it stirred overnight. The solvent was then removed in vacuo, the product mixture was diluted with EtOAc (5 mL) and successively extracted with water (2 × 5 mL) to provide the crude product. Column chromatography using EtOAc:DCM (5:95) as the eluent (R_f: 0.24) provided the title compound (157 mg, 46%). ¹H NMR (*d*₆-DMSO, 500 MHz): δ 8.76 (1H, s), 7.48 (1H, s), 7.28 (1H, d, *J* = 1.4 Hz), 3.91 (3H, s), 2.28 (3H, s). ¹³C NMR (*d*₆-DMSO, 500 MHz) δ 169.7, 156.8, 143.1, 142.5, 125.0, 119.6, 114.7, 56.36, 21.1.

1.2.3A 2-Hydroxy-*N*-(5-nitrothiazol-2-yl)benzamide (**2a**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and a yellow poly cap was charged with nitazoxanide (154 mg, 0.5 mmol), THF (5 mL) and hydrazine acetate (69 mg, 0.75 mmol). The reactant mixture was stirred for 20 h at room temperature as the product slowly precipitated. The THF was removed in vacuo and the remaining solid was suspended in 1:1 MeOH-H₂O (5 mL). After stirring for 10 min at room temperature, the precipitate was collected by filtration and the filter cake was leached with 1:1 MeOH-H₂O (2 × 3 mL). Drying in vacuo provided tizoxanide (124 mg, 94%). ¹H NMR (*d*₆-DMSO, 500 MHz): δ 12.20 (s, 1H), 7.90 (1H, dd, *J* = 1.6, 7.9 Hz), 7.49 (1H, ddd, *J* = 1.6, 7.0, 8.4 Hz), 7.04 (1H d *J* = 8.2 Hz), 6.99 (1H, dd, *J* = 7.3, 7.7 Hz), 3.59 (1H m), 3.54 (1H, s). ¹³C NMR (*d*₆-DMSO, 500 MHz) δ 166.3, 162.4, 157.9, 143.0, 142.2, 135.4, 131.0, 120.2, 117.7, 117.2, 0.6.

1.2.4A 5-Chloro-2-hydroxy-*N*-(5-nitrothiazol-2-yl)benzamide (**2b**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and a yellow poly cap was charged with **1b** (171 mg, 0.5 mmol), THF (5 mL) and hydrazine acetate (69 mg, 0.75 mmol). The reactant mixture was stirred for 20 h at room temperature as the product slowly precipitated. The THF was removed in vacuo and the remaining solid was suspended in 1:1 MeOH-H₂O (5 mL). After stirring for 10 min at room temperature, the precipitate was collected by filtration and the filter cake was leached with 1:1 MeOH-H₂O (2 × 3 mL). Drying in vacuo provided the title compound (139 mg, 93%).

1.2.5A 2-Acetoxy-5-methoxy-*N*-(5-nitrothiazol-2-yl)benzamide (3a) A 10 mL round-bottom flask equipped with a magnetic stirring bar and poly-cap was charged with 4-acetoxy-3-methoxybenzoic acid (0.210 g, 1 mmol) and 3 mL of DCM. A catalytic amount of DMF was added. To this stirred solution, oxalyl chloride (0.174 mL, 2 mmol) was added. The reactant mixture was loosely capped and stirred for 15 min at room temperature. The corrosive by products were removed in vacuo before 2-amino-5-nitrothiazole (0.145 g, 1.0 mmol) was added and the flask was equipped with an ice bath. Anhydrous DCM (4 mL) was added, followed by the dropwise addition of triethyl amine (0.167 mL, 1.2 mmol). The reactant mixture was allowed to return to room temperature as it stirred overnight. The solvent was then removed in vacuo, the product mixture was diluted with EtOAc (5 mL) and successively extracted with water (2 × 5 mL) and brine (2 × 5 mL) to provide the crude product. Recrystallization from EtOAc provided the title compound (196 mg, 58%). ¹H NMR (D₆-DMSO, 300 MHz): δ 8.70 (1H, s) 7.87 (1H, s), 7.74 (1H, m), 7.28 (1H, d, *J* = 12.7 Hz). ¹³C NMR (D₆-DMSO, 500 MHz) δ 168.7, 151.4, 123.8, 122.1, 113.2, 56.7, 46.2, 20.9, 9.1, 1.6.

1.2.6A 4-Acetoxy-3-chloro-*N*-(5-nitrothiazol-2-yl)benzamide (**3b**) A 10 mL round-bottom flask equipped with a magnetic stirring bar and poly-cap was charged with 4-acetoxy-3-chlorobenzoic acid (0.215 g, 1 mmol) and 3 mL of DCM. A catalytic amount of DMF was added. To this stirred solution, oxalyl chloride (0.174 mL, 2 mmol) was added. The reactant mixture was loosely capped and stirred for 15 min at room temperature. The corrosive by products were removed in vacuo before 2-amino-5-nitrothiazole (0.145 g, 1.0 mmol) was added and the flask was equipped with an ice bath. Anhydrous DCM (4 mL) was added, followed by the dropwise addition of triethyl amine (0.167 mL, 1.2 mmol). The reactant mixture was allowed to return to room temperature as it stirred overnight. The solvent was then removed in vacuo, the product mixture was diluted with EtOAc (5 mL) and successively extracted with water (2 × 5 mL) and brine (2 × 5 mL) to provide the crude product. Recrystallization from EtOAc provided the title compound (215 mg, 63%). ¹H NMR (*d*₆-DMSO, 500 MHz): δ 13.69 (1H, s), 8.74 (1H, s), 8.37 (1H, d, *J* = 2.1 Hz), 8.14 (1H, dd, *J* = 2.1, 8.4 Hz), 7.57 (1H, d, *J* = 8.4 Hz), 2.39 (3H, s). ¹³C NMR (*d*₆-DMSO, 500 MHz) δ 168.5, 150.7, 143.0, 130.8, 129.5, 126.9, 125.2, 20.9.

1.2.7A N-(5-Nitrothiazol-2-yl)methacrylamide (4a) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly-cap was charged with 2-amino-6-nitrobenzothiazole (0.195 g, 1.00 mmol), THF (3 mL) and 1-methylimidazole (0.99 g, 1.2 mmol). The mixture was briefly warmed to dissolve the solid, whereupon it was cooled to 0 °C. Methacrylic anhydride (0.200 mL, 1.25 mmol) was then added with stirring and the reactant mixture was allowed to return to room temperature as it was stirred overnight. EtOAc (5 mL) was added and the mixture was successively extracted with water (2 × 5 mL) and brine (2 × 5 mL). Column chromatography using EtOAc:Hexanes (35:65) as the eluent (R_f: 0.22) provided the title compound (185 mg, 87%). ¹H NMR (*d*₆-DMSO, 500 MHz): δ 9.31 (1H, s), 8.35 (1H, s), 6.06 (1H, d, *J* = 0.52 Hz), 5.79 (1H, d, *J* = 1.53 Hz) 2.15 (3H, s). ¹³C NMR (*d*₆-DMSO, 500 MHz) δ 165.3, 160.9, 140.7, 137.2, 124.5, 18.1, 1.02.

1.2.8A 5-Nitro-*N*-(5-nitrothiazol-2-yl)furan-2-carboxamide (**4b**) A 25 mL round-bottomed flask equipped with a magnetic stirring bar and a reflux condensor was charged with 4-nitrofuran-2-carboxylic acid (157 mg, 1.00 mmol), 1,2-dichloroethane (10 mL) and DMF (20 mg). The mixture was stirred at room temperature as oxalyl chloride (254 mg, 2.0 mmol) was slowly added in a dropwise fashion, with stirring, as HCl, CO and CO₂ were evolved. After stirring for an additional 90 min at room temperature, the reactant mixture was concentrated in vacuo. The solid residue was dissolved in dry THF (10 mL) and transferred to a 50 mL flask, whereupon 2-amino-5-nitrothiazole (145 mg, 1.00 mmol) and 1-methylimidazole (99 mg, 1.2 mmol) were added with stirring at 0 °C. The resulting mixture was then stirred at room temperature for 24 h. Ethanol (25 mL) was added and the precipitate was collected by filtration, followed by leaching of the filter cake with ethanol (2 × 5 mL) and drying to provide the product (227 mg, 80%). ¹H NMR (*d*₆-DMSO, 500 MHz): δ 8.76 (1H, s), 7.88 (1H, d, *J* = 3.8 Hz), 7.84 (1H, d, *J* = 3.9 Hz). ¹³C NMR (*d*₆-DMSO, 500 MHz) δ 153.1, 142.4, 119.4, 113.7.

1.2.9A 2-Chloro-*N*-(5-nitrothiazol-2-yl)acetamide (**4c**) The title compound was prepared according to a literature procedure [35]. ¹H NMR (D₆-DMSO, 500 MHz): δ 13.45 (1H s), 8.66 (1H s), 4.51 (2H, s). ¹³C NMR (D₆-DMSO, 500 MHz) δ 167.3, 161.8, 143.1, 142.7, 42.8.

1.2.10A *N*-(5-nitrothiazol-2-yl)butyramide (**4d**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly-cap was charged with 2-amino-5-nitrothiazole (0.145 g, 1.00 mmol), THF (3 mL) and 1-methylimidazole (0.99 g, 1.2 mmol). The mixture was briefly warmed to dissolve the solid, whereupon it was cooled to 0 °C. Butyric anhydride (204.5 μ L, 1.25 mmol) was then added with stirring and the reactant mixture was stirred at room temperature overnight, then at 65 °C for 1.5 h. EtOAc (5 mL) was added and the mixture was successively extracted with water (2 $\times$ 3 mL) and brine (2 $\times$ 3 mL). Recrystallization from EtOAc provided the title compound (151 mg, 70%). ^1H NMR (d_6 -DMSO, 500 MHz): δ 13.09 (1H, s), 8.68 (1H, s), 2.58 (2H, m) 1.70 (2H, m) 0.97 (3H, t, J = 7.4 Hz). ^{13}C NMR (D_6 -DMSO, 500 MHz) δ 173.5, 162.2, 143.2, 142.1, 37.2, 18.3, 13.9.

1.2.11A 4-chloro-*N*-(5-nitrothiazol-2-yl)butyramide (**4e**) This compound was prepared similarly to **4d**. ^1H -NMR (D_6 -DMSO, 500 MHz): δ 8.63 (1H, s), 3.71 (2H, t, J = 6.5 Hz), 2.70 (2H, t, J = 7.3 Hz), 2.09 (2H, m). ^{13}C -NMR (D_6 -DMSO, 500 MHz) δ 172.7, 162.1, 143.1, 142.2, 45.1, 32.7, 27.5.

1.2.12A N-(6-Nitrobenzo[d]thiazol-2-yl)methacrylamide (5a) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly-cap was charged with 2-amino-6-nitrobenzothiazole (0.195 g, 1.00 mmol), THF (3 mL), and 1-methylimidazole (0.99 g, 1.2 mmol). The mixture was briefly warmed to dissolve the solid, whereupon it was cooled to 0 °C. Methacrylic anhydride (0.200 mL, 1.25 mmol) was then added with stirring and the reactant mixture was allowed to return to room temperature as it was stirred overnight and then at 65 °C for 1.5 h. EtOAc (5 mL) was added and the mixture was successively extracted with water (2 × 5 mL) and brine (2 × 5 mL). Column chromatography using EtOAc:Hexanes (35:65) as the eluent (R_f: 0.32) provided the title compound (176 mg, 67%). ¹H NMR (*d*₆-DMSO, 500 MHz): δ 13.83 (1H, s), 9.11 (1H, d, *J* = 2.0 Hz), 8.34 (1H, dd, *J* = 2.4, 8.9 Hz), 7.94 (1H, m), 7.92 (1H, m), 7.86 (1H, d, *J* = 3.9 Hz). ¹³C NMR (*d*₆-DMSO, 500 MHz) δ 153.1, 143.8, 122.6, 119.8, 119.2, 113.75.

1.2.13A 5-Nitro-*N*-(6-nitrobenzo[d]thiazol-2-yl)furan-2-carboxamide (5b) A 25 mL round-bottomed flask equipped with a magnetic stirring bar and a reflux condenser was charged with 4-nitrofuran-2-carboxylic acid (157 mg, 1.00 mmol), 1,2-dichloroethane (10 mL), and DMF (20 mg). The mixture was stirred at room temperature as oxalyl chloride (254 mg, 2.0 mmol) was slowly added in a dropwise fashion, with stirring, as HCl, CO and CO₂ were evolved. After stirring for an additional 90 min at room temperature, the reactant mixture was concentrated in vacuo. The solid residue was dissolved in dry THF (5 + 5 mL) and transferred to a 50 mL flask, whereupon 2-amino-6-nitrobenzothiazole (195 mg, 1.00 mmol) and 1-methylimidazole (99 mg, 1.2 mmol) were added with stirring at 0 °C. The resulting mixture was then stirred at room temperature for 24 h. Ethanol (25 mL) was added and the precipitate was collected by filtration, followed by leaching of the filter cake with ethanol (2 × 5 mL) and drying to provide the title compound (247 mg, 74%). ¹H NMR (*d*₆-DMSO, 500 MHz): δ 12.83 (1H, s), 9.09 (1H, d, *J* = 2.4 Hz), 8.31 (1H, dd, *J* = 2.4 8.9 Hz), 7.91(1H, d, *J* = 8.9 Hz), 6.22 (1H s), 5.83 (1H, d, *J* = 1.4 Hz), 2.02 (1H, s). ¹³C NMR (*d*₆-DMSO, 500 MHz) δ 125.2, 122.3, 120.9, 119.6, 18.7.

1.2.14A 2-Acetamido-*N*-(5-nitrothiazol-2-yl)benzamide (6a) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly-cap was charged with **7a** (1.00 mmol), DMAP (0.20 g) and dichloromethane (3 mL). Acetic anhydride (0.104 mL, 1.10 mmol) and triethylamine (0.160 mL, 1.15 mmol) were then sequentially added in a dropwise fashion with stirring. The reactant mixture was then stirred at room temperature overnight whereupon EtOAc (5 mL) was added and mixture was successively extracted with water (2 × 3 mL) and brine (2 × 3 mL) to provide the crude product. Column chromatography using EtOAc:DCM (25:75) as the eluent (R_f: 0.23) provided the title compound (273 mg, 89%). ¹H NMR (*d*₆-DMSO, 500 MHz): δ 13.48 (1H, s), 10.24 (1H, s), 8.69 (1H, s), 7.71 (2H, m), 7.57 (1H, ddd, *J* = 1.5, 6.8, 8.7 Hz), 7.26 (1H, ddd, *J* = 1.0, 7.4, 7.7 Hz), 2.03 (3H, s). ¹³C NMR (*d*₆-DMSO, 500 MHz) δ 168.8, 132.9, 129.6, 124.2, 24.2.

1.2.15A 2-Acetamido-5-chloro-*N*-(5-nitrothiazol-2-yl)benzamide (6b) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly-cap was charged with **7b** (1.00 mmol), DMAP (0.20 g), and dichloromethane (3 mL). Acetic anhydride (0.104 mL, 1.10 mmol) and triethylamine (0.160 mL, 1.15 mmol) were then sequentially added in a dropwise fashion with stirring. The reactant mixture was then stirred at room temperature overnight whereupon EtOAc (5 mL) was added and mixture was successively extracted with water (2 × 3 mL) and brine (2 × 3 mL) to provide the crude product. Column chromatography using EtOAc:DCM (25:75) as the eluent (R_f: 0.26) provided the title compound (224 mg, 66%). ¹H NMR (*d*₆-DMSO, 500 MHz): δ 13.57 (1H, s), 10.44 (1H, s), 8.69 (1H, s), 7.82 (1H, m), 7.79 (1H, m), 7.61 (1H, dd, *J* = 2.3, 8.7 Hz), 2.04 (3H, s). ¹³C-NMR (D₆-DMSO, 500 MHz) δ 168.9, 166.9, 142.8, 142.2, 136.2, 132.5, 129.3, 127.9, 126.6, 125.1, 118.5.

1.2.16A 2-Amino-*N*-(5-nitrothiazol-2-yl)benzamide (7a) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly-cap was charged with (ANT) 2-amino-5-nitrothiazole (0.145 g, 1.0 mmol) and isatoic anhydride (0.163 g, 1.0 mmol). Anhydrous acetonitrile (3 mL) was then added and the reactant mixture was blanketed with nitrogen. Dry triethylamine (0.212 g, 154 μ L, 2.1 mmol) was then added in one portion by gas-tight syringe, the poly-cap was tightly sealed, and the resulting mixture was vigorously stirred for 18 h. The reactant mixture was then quenched by the addition of acetic acid (0.120 g, 115 μ L, 2.0 mmol, caution, gas evolution) with stirring and diluted with EtOAc (5 mL). The mixture was then filtered through silica gel (3 g) and concentrated in vacuo to provide the crude product. Column chromatography using EtOAc:DCM (5:95) as the eluent (*R*_f: 0.27) provided the title compound (182 mg, 69%). ¹H NMR (*d*₆-DMSO, 500 MHz): δ 8.89 (2H s), 8.78 (1H, s), 8.69 (1H, S), 7.89 (1H, d, *J* = 8.1 Hz), 7.29 (1H, ddd, *J* = 1.3, 6.8, 7.1 Hz) 6.82 (1H, d, *J* = 8.3 Hz) 6.58 (1H, ddd, *J* = 0.82, 7.1, 7.9 Hz). ¹³C NMR (*d*₆-DMSO, 500 MHz) δ 115.17, 117.3, 129.8, 134.8, 151.9.

1.2.17A 2-Amido-5-chloro-*N*-(5-nitrothiazol-2-yl)benzamide (**7b**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly-cap was charged with (ANT) 2-amino-5-nitrothiazole (0.145 g, 1.0 mmol) and 5-chloroisatoic anhydride (0.198 g, 1.0 mmol). Anhydrous acetonitrile (4mL) was then added and the reactant mixture was blanketed with nitrogen. Dry triethylamine (0.212 g, 154 μ L, 2.1 mmol) was then added in one portion by gas-tight syringe, the poly-cap was tightly sealed, and the resulting mixture was vigorously stirred for 18 h. The reactant mixture was then quenched by the addition of acetic acid (0.120 g, 115 μ L, 2.0 mmol, caution, gas evolution) with stirring and diluted with EtOAc (5 mL). The mixture was then filtered through silica gel (3 g) and concentrated in vacuo to provide the crude product. Column chromatography using EtOAc:DCM (5:95) as the eluent (Rf: 0.35) provided the title compound (215 mg, 72%). ^1H NMR (d_6 -DMSO, 500 MHz): δ 8.89 (2H, s), 8.70 (1H, s), 7.91 (1H, dd, J = 2.3, 8.1 Hz), 7.29 (1H, m), 6.82 (1H, dd, J = 0.8, 8.5 Hz), 6.59 (1H, m). ^{13}C NMR (d_6 -DMSO, 500 MHz) δ 163.2, 151.9, 134.8, 129.8, 117.4, 115.2, 110.4.

1.2.18A 4-Acetoxy-3-methoxy-*N*-(5-nitrofuran-2-carbonyl)benzhydrazide (9a) A 10 mL round-bottom flask equipped with a magnetic stirring bar and poly-cap was charged with 4-acetoxy-3-methoxybenzoic acid (0.2102 g, 1 mmol) and 3 mL of DCM. A catalytic amount of DMF was added. To this stirred solution, oxalyl chloride (0.174 mL, 2 mmol) was added. The reaction mixture was loosely capped and stirred for 15 min at room temperature. The corrosive by products were removed in vacuo before 5-nitrofuran-2-carbohydrazide (0.171 g, 1.0 mmol) was added and the flask was equipped with an ice bath. Anhydrous DCM (3.5 mL) was added, followed by the dropwise addition of triethyl amine (0.167 mL, 1.2 mmol). The reaction mixture was allowed to return to room temperature as it stirred overnight. The solvent was then removed in vacuo, the product mixture was diluted with EtOAc (5 mL) and successively extracted with water and brine to provide the crude product. Column chromatography using EtOAc:Hexanes (30:70) as the eluent (*R*_f: 0.27) provided the title compound (143 mg, 52%). ¹H NMR (CDCl₃, 500 MHz): δ 11.08 (1H, s), 10.75 (1H, s), 7.86 (1H, d, *J* = 3.91 Hz), 7.68 (1H, d, *J* = 1.84 Hz) 7.62 (1H, d, *J* = 3.91 Hz) 7.60 (1H, dd, *J* = 1.9, 8.2 Hz), 7.32 (1H, d, *J* = 8.1 Hz), 3.92(3H, s), 2.35 (3H, S). ¹³C NMR (CDCl₃, 500 MHz) δ 167.6, 164.23, 155.14, 151.31, 150.2, 145.8, 141.6, 130.1, 122.4, 119.6, 115.9, 112.6, 111.1, 55.4, 19.7.

1.2.19A 4-Acetoxy-3-chloro-*N*-(2-(5-nitrofuran-2-carbonyl)benzhydrazide (**9b**) A 10 mL round-bottom flask equipped with a magnetic stirring bar and poly-cap was charged with 4-acetoxy-3-chlorobenzoic acid (0.215 g, 1 mmol) and 3 mL of DCM. A catalytic amount of DMF was added. To this stirred solution, oxalyl chloride (0.174 mL, 2 mmol) was added. The reaction mixture was loosely capped and stirred for 15 min at room temperature. The corrosive by products were removed in vacuo before 5-nitrofuran-2-carbohydrazide (0.171 g, 1.0 mmol) was added and the flask was equipped with an ice bath. Anhydrous DCM (4 mL) was added, followed by the dropwise addition of triethyl amine (0.167 mL, 1.2 mmol). The reaction mixture was allowed to return to room temperature as it stirred overnight. The solvent was then removed in vacuo. The product mixture was diluted with EtOAc (5 mL) and successively extracted with water and brine to provide the crude product. Column chromatography using EtOAc:Hexanes (80:20) as the eluent (R_f: 0.31) provided the crude product (132 mg, 49%). ¹H NMR (*d*₆-DMSO, 500 MHz): δ 11.05 (1H, s), 10.80 (1H, s), 8.08 (1H, d, *J* = 2.3 Hz), 7.91 (1H, dd, *J* = 2.5, 8.2 Hz), 7.78 (1H, d, *J* = 3.9 Hz), 7.55 (1H, d, *J* = 3.9 Hz), 7.50 (1H, d, *J* = 8.4 Hz), 2.36 (3H, s). ¹³C NMR (*d*₆-DMSO, 500 MHz) δ 173.3 169.0, 160.9, 154.6, 151.6, 136.5, 131.6, 25.6.

1.2.20A 2-Acetoxy-5-methoxy-*N*-(5-nitrofur-2-yl)benzhydrazide (**10a**) A 10 mL round-bottom flask equipped with a magnetic stirring bar and poly-cap was charged with 2-acetoxy-5-methoxybenzoic acid (0.210 g, 1 mmol) and 3 mL of DCM. A catalytic amount of DMF was added. To this stirred solution, oxalyl chloride (0.174 mL, 2 mmol) was added. The reaction mixture was loosely capped and stirred for 15 min at room temperature. The corrosive by products were removed in vacuo before 5-nitrofur-2-carbohydrazide (0.171 g, 1.0 mmol) was added and the flask was equipped with an ice bath. Anhydrous DCM (4 mL) was added, followed by the dropwise addition of triethyl amine (0.167 mL, 1.2 mmol). The reaction mixture was allowed to return to room temperature as it stirred overnight. The solvent was then removed in vacuo, the product mixture was diluted with EtOAc (5 mL) and successively extracted with water and brine to provide the crude product. Column chromatography using EtOAc:Hexanes (45:55) as the eluent (R_f: 0.32) provided the title compound (189 mg, 52%). ¹H NMR (D₆-DMSO, 500 MHz): 7.82 (1H, s), 7.33 (1H, m), 7.18 (1H, m), 7.08 (1H, m), 3.80 (3H, s), 1.94 (3H, s). ¹³C NMR (D₆-DMSO, 500 MHz): 169.0, 162.4, 156.7, 141.1, 140.9, 129.3, 124.3, 117.14, 116.8, 113.9, 102.8, 56.2, 56.1, 24.6, 21.0.

1.2.21A 2-Acetoxy-5-chloro-*N*-(5-nitrofur-2-carbonyl)benzhydrazide (**10b**) A 10 mL round-bottom flask equipped with a magnetic stirring bar and poly-cap was charged with 2-acetoxy-5-chlorobenzoic acid (0.215 g, 1 mmol) and 3 mL of DCM. A catalytic amount of DMF was added. To this stirred solution, oxalyl chloride (0.174 mL, 2 mmol) was added. The reaction mixture was loosely capped and stirred for 15 min at room temperature. The corrosive by products were removed in vacuo before 5-nitrofur-2-carbohydrazide (0.171 g, 1.0 mmol) was added and the flask was equipped with an ice bath. Anhydrous DCM (4 mL) was added, followed by the dropwise addition of triethyl amine (0.167 mL, 1.2 mmol). The reaction mixture was allowed to return to room temperature as it stirred overnight. The solvent was then removed in vacuo, the product mixture was diluted with EtOAc (5 mL) and successively extracted with water and brine to provide the crude product. Column chromatography using EtOAc:Hexanes (50:50) as the eluent (*R_f*: 0.28) provided the title compound (250 mg, 68%). ¹H NMR (*D*₆-DMSO, 500 MHz): δ 11.07 (1H, s), 10.59 (1H, s), 7.80 (1H, d, *J* = 3.9, 7.8 Hz), 7.69 (1H, dd, *J* = 2.6, 5.9 Hz), 7.67 (1H, dd, *J* = 2.4, 3.1 Hz), 7.55 (1H, d *J* = 3.9 Hz), 7.33 (1H, d, *J* = 8.5 Hz), 2.27 (3H, s), 3.41 (1H, s). ¹³C NMR (*d*₆-DMSO, 500 MHz) δ 169.3, 163.6, 155.9, 152.4, 147.6, 146.7, 132.4, 130.5, 129.2, 129.1, 126.3, 117.2, 113.7, 21.2.

1.3A Preparation of molecules seen in Chapter 3

1.3.1A Purification of 2-amino-5-nitrothiazole (**2**) A 100 mL round-bottomed flask was charged with 2-amino-5-nitrothiazole (1 g, 6.9 mmol), activated charcoal (0.25 g) and anhydrous acetonitrile (15 mL). The mixture was briefly brought to a light reflux with constant swirling before filtration via a glass fritted column using positive pressure. It was then concentrated in vacuo and any remaining acetonitrile was removed under high vacuum (0.01 mmHg).

1.3.2A *N*-(5-nitrothiazol-2-yl)methacrylamide (4) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(TMS)-ANT (**1**) (217 mg, 1.0 mmol), anhydrous acetonitrile (3.0 mL), and blanketed with argon in succession. The mixture was stirred until homogeneous. Methacryloyl chloride (105 mg, 98 μ L, 1.0 mmol) was subsequently added by gas-tight syringe and the reactant mixture was allowed to stir at room temperature for 12 h. The solvent was then removed in vacuo and the residue was diluted with EtOAc (5 mL) and successively extracted with water (2×5 mL), saturated sodium bicarbonate (2×5 mL), and brine (2×5 mL). Removal of the solvent in vacuo provided the title compound (190 mg, 89%). $^1\text{H-NMR}$ ($\text{D}_6\text{-DMSO}$, 500 MHz): δ 13.18 (1H, s), 8.69 (1H, s), 6.21 (1H, d, $J = 0.7$ Hz), 5.84 (1H, d, $J = 0.7$ Hz), 1.99 (3H, s). $^{13}\text{C-NMR}$ ($\text{D}_6\text{-DMSO}$, 125 MHz) δ 167.9, 162.9, 143.2, 142.4, 137.3, 125.7, 18.6.

1.3.3A (E)-N-(5-nitrothiazol-2-yl)but-2-enamide (5) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(TMS)-ANT (**1**) (217 mg, 1.0 mmol), anhydrous dichloromethane (3.0 mL), and blanketed with argon in succession. The mixture was stirred until homogeneous, then crotonoyl chloride (105 mg, 96 μ L, 1.0 mmol) was subsequently added by gas-tight syringe and the reactant mixture was allowed to stir at room temperature for 24 h. The solvent was then removed in vacuo and the residue was diluted with EtOAc (5 mL) and successively extracted with water (2 $\times$ 5 mL), saturated sodium bicarbonate (2 $\times$ 5 mL), and brine (2 $\times$ 5 mL). The organic layer was then passed through a pad of silica gel and removal of the solvent in vacuo provided the title compound (202 mg, 95%). ^1H -NMR (D_6 -DMSO, 500 MHz): δ 13.13 (1H, s), 8.65 (1H, s), 7.10 (1H, dq, J = 7 Hz), 6.26 (1H, dq, J = 7, 2 Hz), 1.94 (3H, dd, J = 7, 2 Hz). ^{13}C -NMR (D_6 -DMSO, 125 MHz) δ 164.8, 162.5, 146.6, 143.3, 142.5, 123.0, 18.6. HRMS Electrospray ionization (ESI) m/z calcd. for $[\text{C}_7\text{H}_7\text{N}_3\text{O}_3\text{S}]^+$: 213.0208, found: 213.0146 (mass error Δm = 29 ppm).

1.3.4A (2E,4E)-N-(5-nitrothiazol-2-yl)hexa-2,4-dienamide (6) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(TMS)-ANT (**1**) (217 mg, 1.0 mmol), anhydrous dichloromethane (3.0 mL), and blanketed with argon in succession. The mixture was stirred until homogeneous, then (2E,4E)-hexa-2,4-dienoyl chloride (131 mg, 1.0 mmol) was subsequently added by gas-tight syringe and the reactant mixture was allowed to stir at room temperature for 48 h. The solvent was then removed in vacuo and the residue was diluted with EtOAc (5 mL) and successively extracted with water (2 × 5 mL), saturated sodium bicarbonate (2 × 5 mL), and brine (2 × 5 mL). The organic layer was then passed through a pad of silica gel and removal of the solvent in vacuo provided the title compound (203 mg, 85%). ¹H-NMR (D₆-DMSO, 500 MHz): δ 13.19 (1H, s), 8.65 (1H, s), 7.42 (1H, dd, *J* = 15, 10 Hz), 6.39 (2H, m), 6.22 (1H, d, *J* = 15 Hz), 1.86 (3H, d, *J* = 5 Hz). ¹³C-NMR (D₆-DMSO, 125 MHz) δ 170.8, 165.4, 162.5, 146.0, 143.4, 142.5, 142.4, 130.2, 119.15, 60.2, 21.2, 19.1, 14.6. Note: A mixture of EE, EZ, ZE, and ZZ isomers are observed. The major isomer (EE) peaks are reported. HRMS Electrospray ionization (ESI) *m/z* calcd. for [C₉H₉N₃O₃S + H]⁺: 240.0438, found: 240.0422 (mass error Δ*m* = 7 ppm).

1.3.5A Ethyl-3-((5-nitrothiazol-2-yl)amino)-3-oxopropanoate (7) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(TMS)-ANT (**1**) (217 mg, 1.0 mmol), anhydrous dichloromethane (3.0 mL), and blanketed with argon in succession. The mixture was stirred until homogeneous, then ethyl 3-chloro-3-oxopropanoate (259 mg, 128 μ L, 1.0 mmol) was subsequently added by gas-tight syringe and the reactant mixture was allowed to stir at room temperature for 2 h. The solvent was then removed in vacuo and the residue was diluted with EtOAc (5 mL), saturated sodium bicarbonate (2×5 mL), and successively extracted with water (2×5 mL) and brine (2×5 mL). Removal of the solvent in vacuo provided the title compound (192 mg, 74%). $^1\text{H-NMR}$ (CDCl_3 , 500 MHz): δ 11.19 (1H, s), 8.36 (1H, s), 4.33 (2H, q, $J = 7$ Hz), 3.66 (2H, s), 1.37 (3H, t, $J = 7$ Hz). $^{13}\text{C-NMR}$ (CDCl_3 , 125 MHz): δ 168.7, 163.8, 159.9, 143.9, 140.8, 62.8, 39.7, 14.0. HRMS Electrospray ionization (ESI) m/z calcd. for $[\text{C}_8\text{H}_9\text{N}_3\text{O}_5\text{S}]^+$: 259.0263, found: 259.0204 (mass error $\Delta m = 23$ ppm).

1.3.6A *N*-(5-nitrothiazol-2-yl)octanamide (8) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(TMS)-ANT (**1**) (217 mg, 1.0 mmol), anhydrous acetonitrile (3.0 mL), and blanketed with argon in succession. The mixture was stirred until homogeneous, then octanoyl chloride (163 mg, 1.0 mmol) was subsequently added by gas-tight syringe and the reactant mixture was allowed to stir at room temperature for 12 h. The solvent was then removed in vacuo and the residue was diluted with EtOAc (5 mL), saturated sodium bicarbonate (2 × 5 mL), and successively extracted with water (2 × 5 mL), saturated sodium bicarbonate (2 × 5 mL), and brine (2 × 5 mL). Removal of the solvent in vacuo provided the title compound (233 mg, 86%). ¹H-NMR (CDCl₃, 500 MHz): δ 9.69 (1H, s), 8.32 (1H, s), 2.57 (2H, t, *J* = 7.5 Hz), 1.80 (2H, m), 1.43-1.29 (8H, CH envelope), 0.91 (3H, t, *J* = 7 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 171.3, 161.0, 143.6, 139.9, 36.3, 31.5, 29.0, 28.9, 24.8, 22.6, 14.0.

1.3.7A 4-chloro-*N*-(5-nitrothiazol-2-yl)butyramide (9) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(TMS)-ANT (**1**) (217 mg, 1.0 mmol), anhydrous dichloromethane (3.0 mL), and blanketed with argon in succession. The mixture was stirred until homogeneous, then cooled in an ice water bath. 4-chlorobutyryl chloride (155 mg, 123 μ L, 1.1 mmol) was then added by gas-tight syringe and the reactant mixture was allowed to stir at room temperature for 24 h. The reactant mixture was diluted with EtOAc (5 mL) and neutralized by the dropwise addition of saturated aqueous NaHCO₃ (1.2 mL) with vigorous stirring. The lower aqueous layer was removed by pipette and the organic phase was filtered through a small pad of silica gel. Removal of the solvent in vacuo provided the crude product. Column chromatography using EtOAc:Hexanes (40:60) as the eluent (R_f: 0.28) provided the title compound (243 mg, 97%). ¹H-NMR (D₆-DMSO, 500 MHz): δ 13.12 (1H, s), 8.63 (1H, s), 3.71 (2H, t, *J* = 6.5 Hz), 2.71 (2H, t, *J* = 7.3 Hz), 2.08 (2H, m). ¹³C-NMR (D₆-DMSO, 125 MHz) δ 172.7, 162.1, 143.2, 142.2, 45.1, 32.7, 27.5.

1.3.8A 2-((2-(allyloxy)ethyl)thio)-*N*-(5-nitrothiazol-2-yl)acetamide (**10**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(TMS)-ANT (**1**) (217 mg, 1.0 mmol), anhydrous dichloromethane (3.0 mL), and blanketed with argon in succession. The mixture was stirred until homogeneous, then 2-((2-(allyloxy)ethyl)thio)acetyl chloride (398 mg, 1.0 mmol) was subsequently added and the reactant mixture was allowed to stir at room temperature for 48 h. The solvent was then removed in vacuo and the residue was diluted with EtOAc (5 mL) and successively extracted with water (2 × 5 mL), saturated sodium bicarbonate (2 × 5 mL), and brine (2 × 5 mL). The organic layer was then passed through a pad of silica gel and removal of the solvent in vacuo provided the title compound (239 mg, 79%). ¹H-NMR (CDCl₃, 500 MHz): δ 11.00 (1H, s), 8.26 (1H, s), 5.86 (1H, ddt, *J* = 16.5, 11, 6 Hz), 5.23 (1H, ddt, *J* = 16.5, 3, 1.5 Hz), 5.16 (1H, ddt, *J* = 11, 3, 1.5 Hz), 4.07 (2H, dt, *J* = 6, 1.5 Hz), 3.70 (2H, t, *J* = 5 Hz), 3.52 (2H, s), 2.82 (2H, t, *J* = 5 Hz). ¹³C-NMR (CDCl₃, 125 MHz) δ 168.7, 161.0, 141.0, 133.6, 118.8, 72.4, 70.2, 36.9, 34.2. HRMS Electrospray ionization (ESI) *m/z* calcd. for [C₁₀H₁₃N₃O₄S₂ + H]⁺: 304.0421, found: 304.0440 (mass error Δ*m* = 6 ppm).

1.3.9A 2-acetoxy-5-chloro-*N*-(5-nitrothiazol-2-yl)benzamide (**11**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(TMS)-ANT (**1**) (217 mg, 1.0 mmol), anhydrous dichloromethane (3.0 mL), and blanketed with argon in succession. The mixture was stirred until homogeneous, then 2-acetoxy-5-chlorobenzoyl chloride (233 mg, 1.0 mmol) was subsequently added and the reactant mixture was allowed to stir at room temperature for 48 h. The solvent was then removed in vacuo and the residue was diluted with EtOAc (5 mL) and successively extracted with water (2 × 5 mL), saturated sodium bicarbonate (2 × 5 mL), and brine (2 × 5 mL). The organic layer was then passed through a pad of silica gel and removal of the solvent in vacuo provided the title compound (335 mg, 98%). ¹H-NMR (D₆-DMSO, 500 MHz): δ 13.70 (1H, s), 8.72 (1H, s), 7.96 (1H, d, *J* = 3 Hz), 7.76 (1H, dd, *J* = 9, 3 Hz), 7.38 (1H, d, *J* = 9 Hz), 2.25 (3H, s). ¹³C-NMR (D₆-DMSO, 125 MHz) δ 169.3, 164.6, 162.1, 147.9, 142.9, 142.7, 133.6, 130.4, 130.1, 127.5, 125.9, 21.1.

1.3.10A 2-((2-((5-nitrothiazol-2-yl)amino)-2-oxoethyl)thio)acetic acid (**12**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(TMS)-ANT (**1**) (217 mg, 1.0 mmol), anhydrous dichloromethane (3.0 mL), and blanketed with argon in succession. The mixture was stirred until homogeneous, then 1,4-oxathiane-2,6-dione (132 mg, 1.0 mmol) was subsequently added and the reactant mixture was allowed to stir at room temperature for 48 h. The reaction mixture was then quenched with MeOH (2 mL) and the solvent was removed in vacuo. The product mixture was then dissolved in DCM:THF (1:1.5, 5 mL) then passed through a pad of silica gel and removal of the solvent in vacuo provided the title compound (202 mg, 73%). ¹H-NMR (D₆-DMSO, 500 MHz): δ 13.08 (1H, s), 8.64 (1H, s), 3.61 (2H, s), 3.43 (2H, s). ¹³C-NMR (D₆-DMSO, 125 MHz) δ 171.2, 170.0, 162.1, 143.1, 142.5, 34.8, 34.2. HRMS Electrospray ionization (ESI) m/z calcd. for [C₇H₇N₃O₅S₂ + H]⁺: 277.9900, found: 277.9918 (mass error Δm = 6 ppm).

1.3.11A 4-methyl-*N*-((5-nitrothiazol-2-yl)carbamoyl)benzenesulfonamide (**13**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(TMS)-ANT (**1**) (217 mg, 1.0 mmol), anhydrous dichloromethane (3.0 mL), and blanketed with argon in succession. The mixture was stirred until homogeneous, then 4-methylbenzenesulfonyl isocyanate (198 mg, 153 μ L, 1.0 mmol) was subsequently added and the reactant mixture was allowed to stir at room temperature for 24 h. The solvent was then removed in vacuo and the product mixture was diluted with DCM (5 mL) and then passed through a pad of silica gel using 5-20% MeOH in DCM as the eluent and removal of the solvent in vacuo provided the title compound (318 mg, 93%). ^1H -NMR (D_6 -DMSO, 500 MHz): δ 11.46 (1H, s), 8.37 (1H, s), 7.70 (2H, d, J = 8 Hz), 7.23 (2H, d, J = 8 Hz), 2.33 (3H, s). ^{13}C -NMR (D_6 -DMSO, 125 MHz) δ 166.8, 156.2, 144.7, 142.7, 140.6, 140.2, 128.8, 127.3, 21.4.

1.4A Preparation of molecules seen in Chapter 4

1.4.1A 2-(4-chlorophenyl)-2-hydroxy-1-octyl-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (1.1a) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-octylpyrimidin-2-amine (0.207 g, 1 mmol), 2-bromo-1-(4-chlorophenyl)ethanone (0.280 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.372 g, 84%). ¹H-NMR (CDCl₃, 400 MHz): δ 8.97 (1H, d, *J* = 6.2 Hz), 8.83 (1H, dd, *J* = 4.7, 1.9 Hz), 7.71 (1H, s), 7.56 (2H, m), 7.45 (2H, m), 7.08 (1H, dd, *J* = 6.2, 4.7 Hz), 5.56 (1H, d, *J* = 15 Hz), 4.63 (1H, d, *J* = 15 Hz), 3.49 (1H, m), 3.35 (1H, m), 1.67 (1H, m), 1.51 (1H, m), 1.27 (2H, m) 1.24-1.10 (8H, CH envelope), 0.88 (3H, t, *J* = 7 Hz).

1.4.2A 2-([1,1'-biphenyl]-4-yl)-2-hydroxy-1-octyl-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (1.1b) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-octylpyrimidin-2-amine (0.207 g, 1 mmol), 1-([1,1'-biphenyl]-4-yl)-2-bromoethanone (0.330 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.378 g, 78%). ¹H-NMR (CDCl₃, 400 MHz): δ 9.11 (1H, dd, *J* = 6.3, 1.6 Hz), 8.80 (1H, dd, *J* = 4.6, 1.6 Hz), 7.67 (4H, app s), 7.61 (2H, d, *J* = 7.5 Hz), 7.57 (1H, s), 7.47 (2H, m), 7.39 (1H, m), 7.07 (1H, dd, *J* = 6.3, 4.6 Hz), 5.54 (1H, d, *J* = 14.5 Hz), 4.74 (1H, d, 14.5 Hz), 3.51 (1H, m), 3.38 (1H, m), 1.67 (1H, m), 1.53 (1H, m), 1.35-1.09 (10H, CH envelope), 0.83 (3H, t, *J* = 6.8 Hz).

1.4.3A 2-(4-bromophenyl)-2-hydroxy-1-octyl-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium bromide (**1.1c**) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-octylpyrimidin-2-amine (0.207 g, 1 mmol), 2-bromo-1-(4-bromophenyl)ethanone (0.334 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.428 g, 88%). ¹H-NMR (CDCl₃, 400 MHz): δ 9.07 (1H, m), 8.82 (1H, dd, *J* = 4.5, 1.9 Hz), 7.68 (1H, m), 7.61 (1H, d, *J* = 8.6 Hz), 7.51 (1H, d, *J* = 8.6 Hz), 7.08 (1H, dd, *J* = 6.3, 4.5 Hz), 5.55 (1H, d, *J* = 14.3 Hz), 4.65 (1H, d, *J* = 14.3 Hz), 3.48 (1H, m), 3.34 (1H, m), 1.66 (1H, m), 1.51 (1H, m), 1.26 (2H, m), 1.23-1.15 (8H, CH envelope), 0.88 (3H, t, *J* = 6.9 Hz).

1.4.4A 2-(4-cyanophenyl)-2-hydroxy-1-octyl-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium bromide (**1.1d**) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-octylpyrimidin-2-amine (0.207 g, 1 mmol), 4-(2-bromoacetyl)benzonitrile (0.269 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.319 g, 74%). ¹H-NMR (CDCl₃, 400 MHz): δ 9.10 (1H, m), 8.83 (1H, dd, *J* = 4.6, 1.9 Hz), 7.82 (1H, s), 7.77 (4H, app s), 7.09 (1H, dd, *J* = 6.2, 4.6 Hz), 5.62 (1H, d, *J* = 14.4 Hz), 4.64 (1H, d, *J* = 14.4 Hz), 3.48 (1H, m), 3.32 (1H, m), 1.64 (1H, m), 1.47 (1H, m), 1.30-1.11 (10H, CH envelope), 0.86 (3H, t, *J* = 6.9 Hz).

1.4.5A 2-hydroxy-2-(4-nitrophenyl)-1-octyl-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (1.1e) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-octylpyrimidin-2-amine (0.207 g, 1 mmol), 2-bromo-1-(4-nitrophenyl)ethanone (0.293 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.366 g, 81%). ¹H-NMR (CDCl₃, 400 MHz): δ 8.91 (1H, m), 8.53 (1H, m), 8.35 (2H, m), 8.20 (1H, s), 7.87 (2H, m), 5.69 (1H, d, *J* = 12 Hz), 4.56 (1H, d, *J* = 12 Hz), 3.55 (1H, m), 3.39 (1H, m), 1.29-1.15 (12H, CH envelope), 0.87 (3H, t, *J* = 6.5 Hz).

1.4.6A 2-(2,4-difluorophenyl)-2-hydroxy-1-octyl-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (1.1f) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-octylpyrimidin-2-amine (0.207 g, 1 mmol), 2-bromo-1-(2,4-difluorophenyl)ethanone (0.282 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.253 g, 57%). ¹H-NMR (CDCl₃, 400 MHz): δ 9.27 (1H, m), 8.80 (1H, dd, *J* = 5, 2.5 Hz), 7.99 (1H, dt, *J* = 8, 5 Hz), 7.72 (1H, s), 7.04 (2H, m), 6.87 (1H, ddd, *J* = 11.5, 8, 2.5 Hz), 5.55 (1H, dd, *J* = 16, 2.5 Hz), 4.78 (1H, dd, *J* = 16, 1 Hz), 3.47 (1H, m), 3.36 (1H, m), 1.58 (1H, m), 1.35 (1H, m), 1.25 (2H, m), 1.22-1.09 (8H, CH envelope), 0.87 (3H, t, *J* = 7 Hz).

1.4.7A 2-hydroxy-2-(4-methoxyphenyl)-1-octyl-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (1.1g) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-octylpyrimidin-2-amine (0.207 g, 1 mmol), 2-bromo-1-(4-methoxyphenyl)ethanone (0.275 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.248 g, 57%). ¹H-NMR (CDCl₃, 400 MHz): δ 8.80 (1H, dd, *J* = 6, 2 Hz), 7.44 (2H, m), 6.96 (1H, m), 6.87 (2H, m), 5.42 (1H, d, *J* = 16 Hz), 4.54 (1H, d, *J* = 16 Hz), 3.78 (3H, s), 3.39 (1H, m), 3.26 (1H, m), 1.59 (1H, m), 1.42 (1H, m), 1.25-1.04 (10H, CH envelope), 0.78 (3H, t, *J* = 6.9 Hz).

1.4.8A 2-hydroxy-1-octyl-2-(4-(trifluoromethyl)phenyl)-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (1.1h) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-octylpyrimidin-2-amine (0.207 g, 1 mmol), 2-bromo-1-(4-(trifluoromethyl)phenyl)ethanone (0.320 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.374 g, 79%). ¹H-NMR (CDCl₃, 400 MHz): δ 9.15 (1H, d, *J* = 6 Hz), 8.84 (1H, d, *J* = 2 Hz), 7.76 (5H, m), 7.11 (1H, t, *J* = 5 Hz), 5.60 (1H, d, *J* = 14 Hz), 4.70 (1H, d, *J* = 14 Hz), 3.51 (1H, m), 3.34 (1H, m), 1.67 (1H, m), 1.51 (1H, m), 1.27 (2H, m), 1.22-1.06 (8H, CH envelope), 0.87 (3H, t, *J* = 6.9 Hz).

1.4.9A 2-hydroxy-1-octyl-2-(4-(trifluoromethoxy)phenyl)-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (1.1i) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-octylpyrimidin-2-amine (0.207 g, 1 mmol), 2-bromo-1-(4-(trifluoromethoxy)phenyl)ethanone (0.340 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.375 g, 77%). ¹H-NMR (CDCl₃, 400 MHz): δ 9.30 (1H, dd, *J* = 6, 2 Hz), 8.81 (1H, dd, *J* = 6, 2 Hz), 7.68 (2H, d, *J* = 9 Hz), 7.56 (1H, s), 7.31 (2H, d, 8 Hz), 7.10 (1H, dd, *J* = 6, 4 Hz), 5.52 (1H, d, *J* = 15 Hz), 4.76 (1H, d, *J* = 15 Hz), 3.47 (1H, m), 3.33 (1H, m), 1.64 (1H, m), 1.47 (1H, m), 1.27 (2H, m), 1.23-1.08 (8H, CH envelope), 0.87 (3H, t, *J* = 7 Hz).

1.4.10A 2-(4-(difluoromethoxy)phenyl)-2-hydroxy-1-octyl-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (1.1j) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-octylpyrimidin-2-amine (0.155 g, 0.75 mmol), 2-bromo-1-(4-(difluoromethoxy)phenyl)ethanone (0.238 g, 0.9 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.258 g, 73%). ¹H-NMR (CDCl₃, 400 MHz): δ 9.20 (1H, app s), 8.81 (1H, dd, *J* = 4.5, 1.8 Hz), 7.64 (2H, d, *J* = 8.8 Hz), 7.57 (1H, s), 7.21 (2H, d, *J* = 8.8 Hz), 7.09 (1H, dd, *J* = 6.3, 4.5 Hz), 6.59 (1H, t, *J* = 73.3 Hz), 5.53 (1H, d, *J* = 14.5 Hz), 4.72 (1H, d, *J* = 14.5 Hz), 3.48 (1H, m), 3.34 (1H, m), 1.65 (1H, m), 1.49 (1H, m), 1.27 (2H, m), 1.23-1.10 (8H, CH envelope), 0.87 (3H, t, *J* = 6.9 Hz).

1.4.11A 2-hydroxy-2-(3-nitrophenyl)-1-octyl-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium bromide (**1.1k**) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-octylpyrimidin-2-amine (0.621 g, 3 mmol), 2-bromo-1-(3-nitrophenyl)ethanone (0.879 g, 3.6 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (1.242 g, 92%). ¹H-NMR (CDCl₃, 400 MHz): δ 9.03 (1H, dd, *J* = 4.7, 1.7 Hz), 8.79 (1H, dd, *J* = 4.7, 1.7 Hz), 8.36 (1H, t, *J* = 1.9 Hz), 8.25 (1H, dt, *J* = 8.2, 1.2 Hz), 7.99 (1H, dd, *J* = 7.8, 1.2 Hz), 7.84 (1H, s), 7.62 (1H, t, *J* = 8.2 Hz), 7.07 (1H, dd, *J* = 6.2, 4.7 Hz), 5.60 (1H, d, *J* = 14.4 Hz), 4.59 (1H, d, *J* = 14.4 Hz), 3.42 (1H, m), 3.27 (1H, m), 1.59 (1H, m), 1.42 (1H, m), 1.26-1.01 (12H, CH envelope), 0.78 (3H, t, *J* = 6.8 Hz).

1.4.12A 2-(3-formamidophenyl)-2-hydroxy-1-octyl-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium bromide (**1.1l**) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-octylpyrimidin-2-amine (0.153 g, 0.74 mmol), *N*-(3-(2-bromoacetyl)phenyl)formamide (0.216 g, 0.89 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.332 g, 99%). ¹H-NMR (CDCl₃, 400 MHz): δ 9.14 (1H, s), 8.83 (1H, m), 8.69 (1H, m), 8.29 (1H, s), 7.82 (1H, m), 7.25 (2H, m), 7.11 (1H, m), 6.96 (1H, m), 5.20 (1H, m), 4.78 (1H, m), 3.33 (1H, m), 3.18 (1H, m), 1.51 (1H, m), 1.36 (1H, m), 1.16 (2H, m), 1.13-0.89 (8H, CH envelope), 0.78 (3H, t, *J* = 6.8 Hz). Note: Presumed rotamer.

1.4.13A 2-(4-chlorophenyl)-2-hydroxy-1-(2-(pentylthio)ethyl)-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (2.1a) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-(pentylthio)ethyl)pyrimidin-2-amine (0.225 g, 1 mmol), 2-bromo-1-(4-chlorophenyl)ethanone (0.280 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.439 g, 96%). ¹H-NMR (CDCl₃, 400 MHz): δ 10.69 (1H, dd, *J* = 6.7, 1.7 Hz), 9.42 (1H, s), 8.96 (1H, dd, *J* = 4.4, 1.7 Hz), 7.58 (5H, m), 4.67 (2H, t, *J* = 6.9 Hz), 2.82 (2H, t, *J* = 6.9 Hz), 2.29 (2H, t, *J* = 7.3 Hz), 1.40 (2H, p, 6.9 Hz), 1.24 (4H, m), 0.87 (3H, t, *J* = 6.8 Hz).

1.4.14A 2-([1,1'-biphenyl]-4-yl)-2-hydroxy-1-(2-(pentylthio)ethyl)-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (2.1b) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-(pentylthio)ethyl)pyrimidin-2-amine (0.225 g, 1 mmol), 1-([1,1'-biphenyl]-4-yl)-2-bromoethanone (0.330 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.466 g, 93%). ¹H-NMR (CDCl₃, 400 MHz): δ 9.13 (1H, app s), 8.83 (1H, dd, *J* = 4.6, 1.9 Hz), 7.68 (5H, m), 7.61 (2H, m), 7.48 (2H, m), 7.40 (1H, m), 7.13 (1H, dd, *J* = 6.3, 4.7 Hz), 5.55 (1H, d, *J* = 14.4 Hz), 4.78 (1H, d, *J* = 14.4 Hz), 3.76 (1H, m), 3.58 (1H, m), 2.71 (2H, m), 2.40 (2H, m), 1.47 (2H, m), 1.26 (4H, m), 0.85 (3H, t, *J* = 6.9 Hz).

1.4.15A 2-(4-bromophenyl)-2-hydroxy-1-(2-(pentylthio)ethyl)-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (2.1c) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-(pentylthio)ethyl)pyrimidin-2-amine (0.225 g, 1 mmol), 2-bromo-1-(4-bromophenyl)ethanone (0.334 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.450 g, 93%). ¹H-NMR (CDCl₃, 400 MHz): δ 9.25 (1H, dd, *J* = 6.4, 1.9 Hz), 8.79 (1H, dd, *J* = 4.6, 2.0 Hz), 7.58 (3H, m), 7.51 (2H, d, *J* = 8.7 Hz), 7.11 (1H, dd, *J* = 6.3, 4.7 Hz), 5.48 (1H, d, *J* = 14.6 Hz), 4.72 (1H, d, *J* = 14.6 Hz), 3.68 (1H, m), 3.49 (1H, m), 2.64 (2H, t, *J* = 8.0 Hz), 2.37 (2H, m), 1.46 (2H, m), 1.27 (4H, m), 0.87 (3H, t, *J* = 6.9 Hz).

1.4.16A 2-(4-cyanophenyl)-2-hydroxy-1-(2-(pentylthio)ethyl)-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (2.1d) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-(pentylthio)ethyl)pyrimidin-2-amine (0.225 g, 1 mmol), 4-(2-bromoacetyl)benzonitrile (0.269 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.412 g, 92%). ¹H-NMR (CDCl₃, 400 MHz): δ 9.24 (1H, dd, *J* = 6.2, 1.5 Hz), 8.85 (1H, dd, *J* = 4.5, 1.8 Hz), 7.80 (5H, m), 7.16 (1H, dd, *J* = 6.2, 4.8 Hz), 5.58 (1H, d, *J* = 14.6 Hz), 4.71 (1H, d, *J* = 14.6 Hz), 3.71 (1H, m), 3.51 (1H, m), 2.67 (2H, m), 2.39 (2H, m), 1.48 (2H, m), 1.29 (4H, m), 0.89 (3H, t, *J* = 6.9 Hz).

1.4.17A 2-hydroxy-2-(4-nitrophenyl)-1-(2-(pentylthio)ethyl)-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (2.1e) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-(pentylthio)ethyl)pyrimidin-2-amine (0.225 g, 1 mmol), 2-bromo-1-(4-nitrophenyl)ethanone (0.293 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a pale yellow solid (0.423 g, 90%). ¹H-NMR (CDCl₃, 400 MHz): δ 8.90 (1H, dd, 4.6, 1 Hz), 8.71 (1H, app s), 8.34 (2H, d, *J* = 8.8 Hz), 8.19 (1H, s), 7.89 (2H, d, *J* = 8.8 Hz), 7.18 (1H, dd, *J* = 6, 4.6 Hz), 5.64 (1H, d, *J* = 14.1 Hz), 4.63 (1H, d, *J* = 14.1 Hz), 3.78 (1H, m), 3.59 (1H, m), 2.79 (1H, m), 2.66 (1H, m), 2.42 (2H, m), 1.49 (2H, m), 1.29 (4H, m), 0.89 (3H, t, *J* = 6.9 Hz).

1.4.18A 2-(2,4-difluorophenyl)-2-hydroxy-1-(2-(pentylthio)ethyl)-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (2.1f) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-(pentylthio)ethyl)pyrimidin-2-amine (0.225 g, 1 mmol), 2-bromo-1-(2,4-difluorophenyl)ethanone (0.282 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.288 g, 63%). ¹H-NMR (CDCl₃, 400 MHz): δ 9.14 (1H, d, *J* = 6.4 Hz), 8.81 (1H, dd, *J* = 4.6, 2.0 Hz), 7.98 (1H, dt, *J* = 9.1, 6.4 Hz), 7.87 (1H, s), 7.05 (2H, m), 6.88 (1H, ddd, *J* = 11.6, 8.3, 2.4 Hz), 5.56 (1H, dd, *J* = 14.3, 2.9 Hz), 4.76 (1H, dd, *J* = 14.3, 0.9 Hz), 3.67 (1H, m), 3.49 (1H, m), 2.75 (1H, m), 2.57 (1H, m), 2.39 (2H, m), 1.48 (2H, p, *J* = 7.3 Hz), 0.89 (3H, t, *J* = 6.9 Hz).

1.4.19A 1-(3-butoxypropyl)-2-(4-chlorophenyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (3.1a) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(3-butoxypropyl)pyrimidin-2-amine (0.209 g, 1 mmol), 2-bromo-1-(4-chlorophenyl)ethanone (0.280 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.375 g, 85%). ¹H-NMR (CDCl₃, 400 MHz): δ 9.04 (1H, dd, *J* = 6.4, 1.8 Hz), 8.81 (1H, dd, *J* = 4.6, 2.0 Hz), 7.63 (1H, s), 7.57 (2H, dt, *J* = 8.7, 2.5 Hz), 7.43 (2H, dt, *J* = 8.7, 2.6 Hz), 7.08 (1H, dd, *J* = 6.4, 4.6 Hz), 5.50 (1H, d, *J* = 14.4 Hz), 4.67 (1H, d, *J* = 14.4 Hz), 3.68 (1H, m), 3.39 (3H, m), 3.29 (2H, td, *J* = 6.6, 1.3 Hz), 1.96 (1H, m), 1.86 (1H, m), 1.44 (2H, p, *J* = 7.0 Hz), 1.28 (2H, sx, *J* = 7.3 Hz), 0.88 (3H, t, *J* = 7.3 Hz).

1.4.20A 2-([1,1'-biphenyl]-4-yl)-1-(3-butoxypropyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (3.1b) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(3-(butylthio)propyl)pyrimidin-2-amine (0.225 g, 1 mmol), 1-([1,1'-biphenyl]-4-yl)-2-bromoethanone (0.330 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.417 g, 86%). ¹H-NMR (CDCl₃, 400 MHz): δ 9.04 (1H, app s), 8.82 (1H, dd, *J* = 4.5, 1.9 Hz), 7.68 (4H, m), 7.61 (3H, m), 7.48 (2H, m), 7.39 (1H, m), 7.09 (1H, dd, *J* = 6.3, 4.7 Hz), 5.53 (1H, d, *J* = 14.3 Hz), 4.75 (1H, d, *J* = 14.3 Hz), 3.74 (1H, m), 3.44 (3H, m), 3.29 (2H, t, *J* = 6.5 Hz), 1.97 (2H, m), 1.45 (2H, p, *J* = 6.8 Hz), 1.28 (2H, sx, 7.4 Hz), 0.86 (3H, t, *J* = 7.3 Hz).

1.4.21A 1-(2-((2-bromophenyl)thio)ethyl)-2-(4-chlorophenyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (4.1a) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-((2-bromophenyl)thio)ethyl)pyrimidin-2-amine (0.310 g, 1 mmol), 2-bromo-1-(4-chlorophenyl)ethanone (0.280 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.533 g, 98%). ¹H-NMR (CDCl₃, 400 MHz): δ 9.11 (1H, d, *J* = 5.4 Hz), 8.85 (1H, dd, *J* = 4.5, 1.8 Hz), 7.84 (1H, s), 7.52 (3H, m), 7.39 (2H, d, *J* = 8.6 Hz), 7.16 (3H, m), 7.01 (1H, m), 5.54 (1H, d, *J* = 14.4 Hz), 4.69 (1H, d, *J* = 14.4 Hz), 3.75 (1H, m), 3.53 (1H, m), 3.26 (2H, t, *J* = 8.0 Hz).

1.4.22A 2-([1,1'-biphenyl]-4-yl)-1-(2-((2-bromophenyl)thio)ethyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (4.1b) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-((2-bromophenyl)thio)ethyl)pyrimidin-2-amine (0.310 g, 1 mmol), 1-([1,1'-biphenyl]-4-yl)-2-bromoethanone (0.330 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.352 g, 99%). ¹H-NMR (CDCl₃, 400 MHz): δ 9.07 (1H, dd, *J* = 6.4, 1.8 Hz), 8.87 (1H, dd, *J* = 4.6, 1.8 Hz), 7.87 (1H, s), 7.66 (4H, m), 7.59 (2H, m), 7.44 (4H, m), 7.16 (3H, m), 6.95 (1H, m), 5.57 (1H, d, *J* = 14.4 Hz), 4.76 (1H, d, *J* = 14.4 Hz), 3.84 (1H, m), 3.59 (1H, m), 3.31 (2H, t, *J* = 8.1 Hz).

1.4.23A 2-(4-bromophenyl)-1-(2-((2-bromophenyl)thio)ethyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (4.1c) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-((2-bromophenyl)thio)ethyl)pyrimidin-2-amine (0.310 g, 1 mmol), 2-bromo-1-(4-bromophenyl)ethanone (0.334 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.283 g, 96%). ¹H-NMR (CDCl₃, 400 MHz): δ 8.90 (1H, d, *J* = 5.4 Hz), 8.87 (1H, dd, *J* = 4.4, 1.4 Hz), 7.96 (1H, s), 7.51 (5H, m), 7.17 (3H, m), 7.02 (1H, m), 5.55 (1H, d, *J* = 14.3 Hz), 4.63 (1H, d, *J* = 14.3 Hz), 3.78 (1H, m), 3.55 (1H, m), 3.28 (2H, m).

1.4.24A 1-(2-((2-bromophenyl)thio)ethyl)-2-(4-cyanophenyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (4.1d) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-((2-bromophenyl)thio)ethyl)pyrimidin-2-amine (0.310 g, 1 mmol), 4-(2-bromoacetyl)benzonitrile (0.269 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.517 g, 97%). ¹H-NMR (CDCl₃, 400 MHz): δ 8.91 (1H, m), 8.52 (1H, m), 8.34 (1H, s), 7.72 (4H, m), 7.52 (2H, m), 7.18 (2H, m), 7.00 (1H, s), 5.59 (1H, d, *J* = 14.1 Hz), 4.57 (1H, d, *J* = 14.1 Hz), 3.80 (1H, m), 3.60 (1H, m), 3.39 (1H, m), 3.24 (1H, m).

1.4.25A 1-(2-((2-bromophenyl)thio)ethyl)-2-hydroxy-2-(4-nitrophenyl)-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (4.1e) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-((2-bromophenyl)thio)ethyl)pyrimidin-2-amine (0.310 g, 1 mmol), 2-bromo-1-(4-nitrophenyl)ethanone (0.293 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.365 g, 94%). ¹H-NMR (CDCl₃, 400 MHz): δ 8.93 (1H, m), 8.48 (1H, s), 8.42 (1H, m), 8.23 (2H, d, *J* = 8.9 Hz), 7.83 (2H, d, *J* = 8.9 Hz), 7.49 (1H, m), 7.19 (3H, m), 5.61 (1H, d, *J* = 13.8 Hz), 4.60 (1H, d, *J* = 13.8 Hz), 3.81 (1H, m), 3.64 (1H, m), 3.42 (1H, m), 3.26 (1H, m).

1.4.26A 1-(2-((2-bromophenyl)thio)ethyl)-2-(2,4-difluorophenyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (4.1f) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-((2-bromophenyl)thio)ethyl)pyrimidin-2-amine (0.310 g, 1 mmol), 2-bromo-1-(2,4-difluorophenyl)ethanone (0.282 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.520 g, 95%). ¹H-NMR (CDCl₃, 400 MHz): δ 9.28 (1H, d, *J* = 5.9 Hz), 8.85 (1H, dd, *J* = 4.6, 1.9 Hz), 7.91 (2H, m), 7.49 (1H, d, *J* = 7.9 Hz), 7.21 (2H, d, *J* = 4.1 Hz), 7.13 (1H, dd, *J* = 6.3, 4.6 Hz), 6.99 (2H, m), 6.85 (1H, ddd, *J* = 11.5, 8.2, 2.4 Hz), 5.55 (1H, dd, *J* = 14.4, 2.6 Hz), 4.78 (1H, d, *J* = 14.4 Hz), 3.73 (1H, m), 3.48 (1H, m), 3.30 (1H, m), 3.17 (1H, m).

1.4.27A 2-(4-chlorophenyl)-1-(2-((2-chlorophenyl)thio)ethyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (5.1a) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-((2-chlorophenyl)thio)ethyl)pyrimidin-2-amine (0.266 g, 1 mmol), 2-bromo-1-(4-chlorophenyl)ethanone (0.280 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.483 g, 97%). ¹H-NMR (CDCl₃, 400 MHz): δ 9.28 (1H, d, *J* = 5.9 Hz), 8.84 (1H, dd, *J* = 4.6, 1.9 Hz), 7.91 (2H, m), 7.49 (1H, d, *J* = 7.9 Hz), 7.21 (2H, d, *J* = 4.1 Hz), 7.13 (1H, dd, *J* = 6.3, 4.7 Hz), 6.99 (2H, m), 6.85 (1H, ddd, *J* = 11.5, 8.2, 2.4 Hz), 5.55 (1H, dd, *J* = 14.4, 2.6 Hz), 4.78 (1H, d, *J* = 14.4 Hz), 3.72 (1H, m), 3.48 (1H, m), 3.30 (1H, m), 3.17 (1H, m).

1.4.28A 2-([1,1'-biphenyl]-4-yl)-1-(2-((2-chlorophenyl)thio)ethyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (5.1b) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-((2-chlorophenyl)thio)ethyl)pyrimidin-2-amine (0.266 g, 1 mmol), 1-([1,1'-biphenyl]-4-yl)-2-bromoethanone (0.330 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.510 g, 94%). ¹H-NMR (CDCl₃, 400 MHz): δ 9.20 (1H, dd, *J* = 6.3, 1.7 Hz), 8.87 (1H, dd, *J* = 4.6, 1.9 Hz), 7.81 (1H, s), 7.67 (4H, m), 7.60 (2H, m), 7.49 (2H, t, 7.1 Hz), 7.42 (1H, m), 7.28 (1H, m), 7.18 (2H, m), 7.11 (1H, td, 7.4, 1.4 Hz), 7.04 (1H, td, 7.6, 1.6 Hz), 5.57 (1H, d, *J* = 14.5 Hz), 4.80 (1H, d, *J* = 14.5 Hz), 3.83 (1H, m), 3.59 (1H, m), 3.31 (2H, t, *J* = 8.1 Hz).

1.4.29A 2-(4-bromophenyl)-1-(2-((2-chlorophenyl)thio)ethyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (5.1c) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-((2-chlorophenyl)thio)ethyl)pyrimidin-2-amine (0.266 g, 1 mmol), 2-bromo-1-(4-bromophenyl)ethanone (0.334 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.542 g, 99%). ¹H-NMR (CDCl₃, 400 MHz): δ 8.86 (1H, d, *J* = 4.9 Hz), 7.99 (1H, s), 7.55 (2H, dt, *J* = 8.7, 1.9 Hz), 7.48 (2H, dt, *J* = 8.7, 2.3 Hz), 7.33 (1H, dd, *J* = 7.6, 1.0 Hz), 7.14 (4H, m), 5.55 (1H, d, *J* = 14.3 Hz), 4.63 (1H, d, *J* = 14.3 Hz), 3.76 (1H, m), 3.55 (1H, m), 3.28 (2H, m).

1.4.30A 1-(2-((2-chlorophenyl)thio)ethyl)-2-(4-cyanophenyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (5.1d) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-((2-chlorophenyl)thio)ethyl)pyrimidin-2-amine (0.266 g, 1 mmol), 4-(2-bromoacetyl)benzonitrile (0.269 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.455 g, 93%). ¹H-NMR (CD₃CN, 400 MHz): δ 8.94 (1H, dd, *J* = 4.7, 2.0 Hz), 8.45 (1H, dd, *J* = 6.35 Hz), 7.81 (5H, m), 7.38 (1H, m), 7.21 (4H, m), 5.05 (1H, d, *J* = 14.6 Hz), 4.70 (1H, d, *J* = 14.6 Hz), 3.64 (1H, m), 3.44 (1H, m), 3.23 (2H, m).

1.4.31A 1-(2-((2-chlorophenyl)thio)ethyl)-2-hydroxy-2-(4-nitrophenyl)-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (5.1e) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-((2-chlorophenyl)thio)ethyl)pyrimidin-2-amine (0.266 g, 1 mmol), 2-bromo-1-(4-nitrophenyl)ethanone (0.293 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.500 g, 98%). ¹H-NMR (CD₃CN, 400 MHz): δ 8.95 (1H, dd, *J* = 4.6, 1.7 Hz), 8.47 (1H, dd, *J* = 6.4, 1.7 Hz), 8.22 (2H, d, *J* = 8.9 Hz), 8.01 (1H, s), 7.92 (2H, d, *J* = 8.9 Hz), 7.34 (1H, dd, *J* = 7.9, 1.2 Hz), 7.24 (3H, m), 7.14 (1H, td, *J* = 7.8, 1.6 Hz), 5.09 (1H, d, *J* = 14.6 Hz), 4.74 (1H, d, *J* = 14.6 Hz), 3.66 (1H, m), 3.48 (1H, m), 3.25 (2H, m).

1.4.32A 1-(2-((2-chlorophenyl)thio)ethyl)-2-(2,4-difluorophenyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (5.1f) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-((2-chlorophenyl)thio)ethyl)pyrimidin-2-amine (0.266 g, 1 mmol), 2-bromo-1-(2,4-difluorophenyl)ethanone (0.282 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.431 g, 86%). ¹H-NMR (CDCl₃, 400 MHz): δ 9.17 (1H, app s), 8.84 (1H, dd, *J* = 4.6, 2.0 Hz), 7.98 (1H, s), 7.92 (1H, dd, *J* = 9.1, 6.4 Hz), 7.32 (1H, dd, *J* = 7.8, 1.5 Hz), 7.24 (1H, dd, *J* = 7.8, 1.6 Hz), 7.17 (1H, td, *J* = 7.4, 1.5 Hz), 7.11 (2H, m), 6.98 (1H, ddd, *J* = 11.5, 9.0, 2.5 Hz), 6.85 (1H, ddd, *J* = 11.7, 8.3, 2.5 Hz), 5.57 (1H, dd, *J* = 14.3, 3.0 Hz), 4.77 (1H, d, *J* = 14.3 Hz), 3.72 (1H, m), 3.49 (1H, m), 3.31 (1H, m), 3.18 (1H, m).

1.4.33A 2-(4-chlorophenyl)-1-(2-((2-fluorophenyl)thio)ethyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (6.1a) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-((2-fluorophenyl)thio)ethyl)pyrimidin-2-amine (0.249 g, 1 mmol), 2-bromo-1-(4-chlorophenyl)ethanone (0.280 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.409 g, 85%). ¹H-NMR (CDCl₃, 400 MHz): δ 10.58 (1H, d, *J* = 5.0 Hz), 9.29 (1H, s), 8.91 (1H, d, *J* = 3.7 Hz), 7.56 (1H, dd, *J* = 6.6, 4.5 Hz), 7.46 (4H, q, *J* = 8.5 Hz), 7.26 (1H, m), 7.08 (1H, m), 6.98 (2H, m), 4.68 (2H, t, *J* = 7.0 Hz), 3.29 (2H, t, *J* = 7.3 Hz).

1.4.34A 2-([1,1'-biphenyl]-4-yl)-1-(2-((2-fluorophenyl)thio)ethyl)-2-hydroxy-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium bromide (6.1b) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-((2-fluorophenyl)thio)ethyl)pyrimidin-2-amine (0.249 g, 1 mmol), 1-([1,1'-biphenyl]-4-yl)-2-bromoethanone (0.330 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.492 g, 94%). ¹H-NMR (CDCl₃, 400 MHz): δ 9.16 (1H, dd, *J* = 6.2, 1.7 Hz), 8.82 (1H, dd, *J* = 4.6, 2.0 Hz), 7.72 (1H, s), 7.61 (6H, m), 7.48 (2H, m), 7.41 (1H, m), 7.24 (1H, td, *J* = 7.9, 1.6 Hz), 7.13 (2H, m), 6.96 (2H, m), 5.53 (1H, d, *J* = 14.4 Hz), 4.78 (1H, d, *J* = 14.4 Hz), 3.76 (1H, m), 3.56 (1H, m), 3.18 (2H, m).

1.4.35A 2-(4-bromophenyl)-1-(2-((2-fluorophenyl)thio)ethyl)-2-hydroxy-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium bromide (6.1c) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-((2-fluorophenyl)thio)ethyl)pyrimidin-2-amine (0.249 g, 1 mmol), 2-bromo-1-(4-bromophenyl)ethanone (0.334 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.423 g, 80%). ¹H-NMR (CDCl₃, 400 MHz): δ 10.51 (1H, d, *J* = 6.9 Hz), 9.24 (1H, s), 8.91 (1H, dd, *J* = 4.2, 1.2 Hz), 7.59 (3H, m), 7.41 (2H, d, *J* = 8.3 Hz), 7.25 (1H, m), 7.07 (1H, td, *J* = 7.5, 1.6 Hz), 6.98 (2H, m), 4.67 (2H, t, *J* = 7.6 Hz), 3.28 (2H, t, *J* = 7.1 Hz).

1.4.36A 2-(4-cyanophenyl)-1-(2-((2-fluorophenyl)thio)ethyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (6.1d) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-((2-fluorophenyl)thio)ethyl)pyrimidin-2-amine (0.249 g, 1 mmol), 4-(2-bromoacetyl)benzonitrile (0.269 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.428 g, 90%). ¹H-NMR (CDCl₃, 400 MHz): δ 9.19 (1H, d, *J* = 5.8 Hz), 8.85 (1H, d, *J* = 4.3 Hz), 7.88 (1H, s), 7.71 (4H, dd, *J* = 13.9, 8.7 Hz), 7.23 (2H, m), 7.17 (1H, m), 7.03 (2H, m), 5.56 (1H, d, *J* = 14.1 Hz), 4.71 (1H, d, *J* = 14.1 Hz), 3.69 (1H, m), 3.49 (1H, m), 3.14 (2H, t, *J* = 7.9 Hz).

1.4.37A 1-(2-((2-fluorophenyl)thio)ethyl)-2-hydroxy-2-(4-nitrophenyl)-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (6.1e) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-((2-fluorophenyl)thio)ethyl)pyrimidin-2-amine (0.249 g, 1 mmol), 2-bromo-1-(4-nitrophenyl)ethanone (0.293 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.468 g, 95%). ¹H-NMR (CD₃CN, 400 MHz): δ 8.91 (1H, dd, *J* = 4.6, 1.7 Hz), 8.45 (1H, dd, *J* = 6.4, 1.7 Hz), 8.22 (2H, d, *J* = 9.0 Hz), 8.06 (1H, s), 7.89 (2H, d, *J* = 9.0 Hz), 7.31 (1H, td, *J* = 7.7, 1.2 Hz), 7.23 (2H, m), 7.07 (2H, m), 5.08 (1H, d, *J* = 14.5 Hz), 4.71 (1H, d, *J* = 14.5 Hz), 3.60 (1H, m), 3.42 (1H, m), 3.22 (1H, m), 3.08 (1H, m).

1.4.38A 2-(2,4-difluorophenyl)-1-(2-((2-fluorophenyl)thio)ethyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (6.1f) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-((2-fluorophenyl)thio)ethyl)pyrimidin-2-amine (0.249 g, 1 mmol), 2-bromo-1-(2,4-difluorophenyl)ethanone (0.282 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.432 g, 89%). ¹H-NMR (CDCl₃, 400 MHz): δ 9.26 (1H, d, *J* = 6.1 Hz), 8.80 (1H, d, *J* = 4.0 Hz), 7.85 (2H, m), 7.29 (1H, m), 7.21 (1H, dd, *J* = 13.1, 7.0 Hz), 7.10 (1H, t, *J* = 5.4 Hz), 7.04 (1H, t, *J* = 7.4 Hz), 6.97 (2H, m), 6.84 (1H, m), 5.53 (1H, dd, *J* = 14.4, 1.9 Hz), 4.76 (1H, d, *J* = 14.4 Hz), 3.64 (1H, m), 3.47 (1H, m), 3.21 (1H, m), 3.01 (1H, m).

1.4.39A 1-(2-((3-bromophenyl)thio)ethyl)-2-(4-chlorophenyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (7.1a) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-((3-bromophenyl)thio)ethyl)pyrimidin-2-amine (0.310 g, 1 mmol), 2-bromo-1-(4-chlorophenyl)ethanone (0.280 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.449 g, 83%). ¹H-NMR (CDCl₃, 400 MHz): δ 8.98 (1H, dd, *J* = 6.3, 1.8 Hz), 8.92 (1H, dd, *J* = 4.6, 1.9 Hz), 7.93 (1H, s), 7.53 (3H, m), 7.42 (2H, d, *J* = 8.6 Hz), 7.29 (1H, dt, *J* = 5.7, 3.4 Hz), 7.15 (1H, dd, *J* = 6.2, 4.8 Hz), 7.12 (1H, m), 7.09 (1H, m), 5.56 (1H, d, *J* = 14.3 Hz), 4.63 (1H, d, *J* = 14.2 Hz), 3.77 (1H, m), 3.45 (1H, m), 3.25 (2H, m).

1.4.40A 2-([1,1'-biphenyl]-4-yl)-1-(2-((3-bromophenyl)thio)ethyl)-2-hydroxy-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium bromide (**7.1b**) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-((3-bromophenyl)thio)ethyl)pyrimidin-2-amine (0.310 g, 1 mmol), 1-([1,1'-biphenyl]-4-yl)-2-bromoethanone (0.330 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.519 g, 89%). ¹H-NMR (CDCl₃, 400 MHz): δ 9.28 (1H, dd, *J* = 6.4, 2.0 Hz), 8.90 (1H, dd, *J* = 6.6, 2.6 Hz), 7.75 (1H, s), 7.65 (4H, app s), 7.59 (2H, dt, *J* = 7.1, 1.6 Hz), 7.55 (1H, t, *J* = 1.8 Hz), 7.47 (2H, t, *J* = 7.4 Hz), 7.39 (1H, tt, *J* = 9.5, 1.3 Hz), 7.24 (1H, dddd, *J* = 7.8, 2.9, 0.5, 0.4 Hz), 7.17 (1H, dd, *J* = 11.0, 1.7 Hz), 7.10 (1H, dt, *J* = 8.1, 2.8 Hz), 7.03 (1H, t, *J* = 7.8 Hz), 5.56 (1H, d, *J* = 14.6 Hz), 4.79 (1H, d, *J* = 14.5 Hz), 3.80 (1H, m), 3.49 (1H, m), 3.27 (2H, m).

1.4.41A 2-(4-bromophenyl)-1-(2-((3-bromophenyl)thio)ethyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (7.1c) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-((3-bromophenyl)thio)ethyl)pyrimidin-2-amine (0.310 g, 1 mmol), 2-bromo-1-(4-bromophenyl)ethanone (0.334 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.513 g, 87%). ¹H-NMR (CDCl₃, 400 MHz): δ 8.99 (1H, dd, *J* = 6.3, 1.9 Hz), 8.92 (1H, dd, *J* = 4.6, 2.0 Hz), 7.92 (1H, s), 7.58 (2H, d, *J* = 8.2 Hz), 7.53 (1H, d, *J* = 2.0 Hz), 7.47 (2H, d, *J* = 8.7 Hz), 7.29 (1H, dt, *J* = 8.9, 3.9 Hz), 7.15 (1H, dd, *J* = 11.0, 1.6 Hz), 7.09 (2H, m), 5.56 (1H, d, *J* = 14.3 Hz), 4.63 (1H, d, *J* = 14.3 Hz), 3.78 (1H, m), 3.43 (1H, m), 3.25 (2H, m).

1.4.42A 1-(2-((3-bromophenyl)thio)ethyl)-2-(4-cyanophenyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (7.1d) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-((3-bromophenyl)thio)ethyl)pyrimidin-2-amine (0.310 g, 1 mmol), 4-(2-bromoacetyl)benzonitrile (0.269 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a pale yellow solid (0.457 g, 86%). ¹H-NMR (CD₃CN, 400 MHz): δ 8.97 (1H, dd, *J* = 4.4, 1.8 Hz), 8.45 (1H, dd, *J* = 6.3, 1.8 Hz), 7.91 (1H, s), 7.82 (4H, q, *J* = 7.9 Hz), 7.53 (1H, s), 7.36 (1H, dt, *J* = 6.8, 2.9 Hz), 7.20 (3H, m), 5.06 (1H, d, *J* = 14.5 Hz), 4.67 (1H, d, *J* = 14.5 Hz), 3.65 (1H, m), 3.38 (1H, m), 3.25 (1H, m), 3.15 (1H, m).

1.4.43A 1-(2-((3-bromophenyl)thio)ethyl)-2-hydroxy-2-(4-nitrophenyl)-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (7.1e) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-((3-bromophenyl)thio)ethyl)pyrimidin-2-amine (0.310 g, 1 mmol), 2-bromo-1-(4-nitrophenyl)ethanone (0.293 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a pale yellow solid (0.513 g, 87%). ¹H-NMR (CD₃CN, 400 MHz): δ 8.98 (1H, dd, *J* = 3.0, 1.8 Hz), 8.47 (1H, dd, *J* = 4.9, 1.8 Hz), 8.26 (2H, d, *J* = 8.9 Hz), 7.91 (2H, d, *J* = 8.9 Hz), 7.67 (1H, s), 7.51 (1H, s), 7.33 (1H, m), 7.25 (1H, dd, *J* = 4.9, 1.8 Hz), 7.17 (2H, m), 5.06 (1H, d, *J* = 14.5 Hz), 4.71 (1H, d, *J* = 14.5 Hz), 3.66 (1H, m), 3.41 (1H, m), 3.25 (1H, m), 3.16 (1H, m).

1.4.44A 1-(2-((3-bromophenyl)thio)ethyl)-2-(2,4-difluorophenyl)-2-hydroxy-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium bromide (7.1f) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-((3-bromophenyl)thio)ethyl)pyrimidin-2-amine (0.310 g, 1 mmol), 2-bromo-1-(2,4-difluorophenyl)ethanone (0.282 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.496 g, 91%). ¹H-NMR (CDCl₃, 400 MHz): δ 9.09 (1H, app s), 8.90 (1H, dd, *J* = 4.6, 1.9 Hz), 8.01 (1H, d, *J* = 1.8 Hz), 7.96 (1H, tt, *J* = 9.3, 9.1 Hz), 7.51 (1H, t, *J* = 1.7 Hz), 7.29 (1H, dt, *J* = 6.2, 3.1 Hz), 7.11 (3H, m), 7.03 (1H, tt, *J* = 9.4 8.3 Hz), 6.85 (1H, ddd, *J* = 11.9, 8.3, 5.8 Hz), 5.58 (1H, dd, *J* = 14.3, 2.7 Hz), 4.75 (1H, d, *J* = 14.2 Hz), 3.73 (1H, m), 3.39 (1H, m), 3.28 (1H, m), 3.17 (1H, m).

1.4.45A 1-(2-((4-bromophenyl)thio)ethyl)-2-(4-chlorophenyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (8.1a) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-((4-bromophenyl)thio)ethyl)pyrimidin-2-amine (0.310 g, 1 mmol), 2-bromo-1-(4-chlorophenyl)ethanone (0.280 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a tan solid (0.523 g, 96%). ¹H-NMR (CDCl₃, 400 MHz): δ 9.21 (1H, d, *J* = 5.8 Hz), 8.82 (1H, d, *J* = 3.2 Hz), 7.75 (1H, s), 7.50 (2H, d, *J* = 8.6 Hz), 7.41 (2H, d, *J* = 8.6 Hz), 7.35 (2H, d, *J* = 8.3 Hz), 7.13 (1H, dd, *J* = 6.1, 4.9 Hz), 7.07 (2H, d, *J* = 8.5 Hz), 5.51 (1H, d, *J* = 14.5 Hz), 4.69 (1H, d, *J* = 14.5 Hz), 3.70 (1H, m), 3.42 (1H, m), 3.17 (2H, m).

1.4.46A 2-([1,1'-biphenyl]-4-yl)-1-(2-((4-bromophenyl)thio)ethyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (8.1b) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-((4-bromophenyl)thio)ethyl)pyrimidin-2-amine (0.310 g, 1 mmol), 1-([1,1'-biphenyl]-4-yl)-2-bromoethanone (0.330 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a yellow solid (0.530 g, 91%). ¹H-NMR (CDCl₃, 400 MHz): δ 9.13 (1H, app s), 8.83 (1H, d, *J* = 3.0 Hz), 7.76 (1H, s), 7.61 (5H, m), 7.47 (2H, t, *J* = 7.5 Hz), 7.39 (2H, t, *J* = 7.2 Hz), 7.29 (2H, m), 7.15 (1H, dd, *J* = 6.3, 4.9 Hz), 7.04 (2H, d, *J* = 8.4 Hz), 5.54 (1H, d, *J* = 14.5 Hz), 4.74 (1H, d, *J* = 14.5 Hz), 3.77 (1H, m), 3.49 (1H, m), 3.21 (2H, m).

1.4.47A 2-(4-bromophenyl)-1-(2-((4-bromophenyl)thio)ethyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (8.1c) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-((4-bromophenyl)thio)ethyl)pyrimidin-2-amine (0.310 g, 1 mmol), 2-bromo-1-(4-bromophenyl)ethanone (0.334 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a tan solid (0.571 g, 97%). ¹H-NMR (CDCl₃, 400 MHz): δ 9.18 (1H, d, *J* = 6.2 Hz), 8.83 (1H, dd, *J* = 4.6, 2.0 Hz), 7.77 (1H, s), 7.57 (2H, d, *J* = 8.9 Hz), 7.44 (2H, d, *J* = 8.4 Hz), 7.36 (2H, d, *J* = 8.4 Hz), 7.13 (1H, dd, *J* = 6.3, 4.7 Hz), 7.07 (2H, dt, *J* = 9.3, 2.7 Hz), 5.51 (1H, d, *J* = 14.5 Hz), 4.68 (1H, d, *J* = 14.5 Hz), 3.70 (1H, m), 3.43 (1H, m), 3.17 (2H, m).

1.4.48A 1-(2-((4-bromophenyl)thio)ethyl)-2-(4-cyanophenyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (8.1d) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-((4-bromophenyl)thio)ethyl)pyrimidin-2-amine (0.310 g, 1 mmol), 4-(2-bromoacetyl)benzonitrile (0.269 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a yellow solid (0.447 g, 97%). ¹H-NMR (CDCl₃, 400 MHz): δ 9.01 (1H, app s), 8.88 (1H, dd, *J* = 4.7, 1.7 Hz), 8.09 (1H, s), 7.73 (4H, q, *J* = 9.5 Hz), 7.38 (2H, d, *J* = 9.1 Hz), 7.17 (1H, dd, *J* = 6.4, 4.7 Hz), 7.13 (2H, d, *J* = 8.7 Hz), 5.61 (1H, d, *J* = 14.5 Hz), 4.62 (1H d, *J* = 14.5 Hz), 3.77 (1H, m), 3.40 (1H, m), 3.23 (2H, m).

1.4.49A 1-(2-((4-bromophenyl)thio)ethyl)-2-hydroxy-2-(4-nitrophenyl)-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (**8.1e**) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-((4-bromophenyl)thio)ethyl)pyrimidin-2-amine (0.310 g, 1 mmol), 2-bromo-1-(4-nitrophenyl)ethanone (0.293 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a yellow solid (0.525 g, 95%). ¹H-NMR (CD₃CN, 400 MHz): δ 8.94 (1H, m), 8.46 (1H, m), 8.24 (2H, d, *J* = 8.7 Hz), 7.89 (2H, d, *J* = 8.7 Hz), 7.80 (1H, s), 7.39 (2H, d, *J* = 8.4 Hz), 7.24 (1H, m), 7.15 (2H, d, *J* = 8.4 Hz), 5.06 (1H, d, *J* = 14.5 Hz), 4.71 (1H, d, *J* = 14.5 Hz), 3.63 (1H, m), 3.39 (1H, m), 3.23 (1H, m), 3.11 (1H, m).

1.4.50A 1-(2-((4-bromophenyl)thio)ethyl)-2-(2,4-difluorophenyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (**8.1f**) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-((4-bromophenyl)thio)ethyl)pyrimidin-2-amine (0.310 g, 1 mmol), 2-bromo-1-(2,4-difluorophenyl)ethanone (0.282 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a tan solid (0.479 g, 88%). ¹H-NMR (CDCl₃, 400 MHz): δ 9.27 (1H, dd, *J* = 6.4, 1.9 Hz), 8.84 (1H, dd, *J* = 4.3, 2.0 Hz), 7.88 (1H, m), 7.85 (1H, s), 7.44 (1H, m), 7.37 (2H, d, *J* = 8.5 Hz), 7.15 (1H, dd, *J* = 6.4, 4.7 Hz), 7.11 (2H, d, *J* = 8.6 Hz), 7.02 (1H, m), 6.86 (1H, m), 5.56 (1H, dd, *J* = 14.5, 2.6 Hz), 4.78 (1H, d, *J* = 14.5 Hz), 3.69 (1H, m), 3.40 (1H, m), 3.25 (1H, m), 3.08 (1H, m).

1.4.51A 2-(4-chlorophenyl)-1-(2-((4-chlorophenyl)thio)ethyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (9.1a) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-((4-chlorophenyl)thio)ethyl)pyrimidin-2-amine (0.266 g, 1 mmol), 2-bromo-1-(4-chlorophenyl)ethanone (0.280 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.469 g, 94%). ¹H-NMR (D₆-DMSO, 400 MHz): δ 9.10 (1H, dd, *J* = 4.7, 1.8 Hz), 8.93 (1H, dd, *J* = 6.3, 1.7 Hz), 8.04 (1H, s), 7.79 (2H, d, *J* = 8.6 Hz), 7.57 (2H, d, *J* = 8.6 Hz), 7.41 (1H, dd, *J* = 6.3, 4.7 Hz), 7.33 (2H, d, *J* = 8.5 Hz), 7.13 (2H, d, *J* = 8.5 Hz), 4.86 (2H, q, *J* = 10.5 Hz), 3.47 (1H, m), 3.32 (1H, m), 3.16 (1H, m), 2.96 (1H, m).

1.4.52A 2-([1,1'-biphenyl]-4-yl)-1-(2-((4-chlorophenyl)thio)ethyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (9.1b) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-((4-chlorophenyl)thio)ethyl)pyrimidin-2-amine (0.266 g, 1 mmol), 1-([1,1'-biphenyl]-4-yl)-2-bromoethanone (0.330 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.518 g, 96%). ¹H-NMR (D₆-DMSO, 400 MHz): δ 9.11 (1H, dd, *J* = 4.7, 1.7 Hz), 8.95 (1H, dd, *J* = 6.3, 1.4 Hz), 8.00 (1H, s), 7.84 (4H, q, *J* = 9.2 Hz), 7.75 (2H, d, *J* = 7.4 Hz), 7.52 (2H, t, *J* = 7.6 Hz), 7.42 (2H, m), 7.25 (2H, d, *J* = 7.4 Hz), 7.11 (2H, d, *J* = 8.5 Hz), 4.91 (2H, app s), 3.54 (1H, m), 3.38 (1H, m), 3.17 (1H, m), 3.01 (1H, m).

1.4.53A 2-(4-bromophenyl)-1-(2-((4-chlorophenyl)thio)ethyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (9.1c) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-((4-chlorophenyl)thio)ethyl)pyrimidin-2-amine (0.266 g, 1 mmol), 2-bromo-1-(4-bromophenyl)ethanone (0.334 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.509 g, 94%). ¹H-NMR (D₆-DMSO, 400 MHz): δ 9.10 (1H, dd, *J* = 4.7, 1.8 Hz), 8.92 (1H, dd, *J* = 6.3, 1.6 Hz), 8.02 (1H, s), 7.71 (4H, app s), 7.41 (1H, dd, *J* = 6.3, 4.7 Hz), 7.33 (2H, d, *J* = 8.5 Hz), 7.12 (2H, d, *J* = 8.5 Hz), 4.86 (2H, q, *J* = 10.0 Hz), 3.46 (1H, m), 3.35 (1H, m), 3.15 (1H, m), 2.97 (1H, m).

1.4.54A 1-(2-((4-chlorophenyl)thio)ethyl)-2-(4-cyanophenyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (9.1d) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-((4-chlorophenyl)thio)ethyl)pyrimidin-2-amine (0.266 g, 1 mmol), 4-(2-bromoacetyl)benzonitrile (0.269 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.435 g, 89%). ¹H-NMR (D₆-DMSO, 400 MHz): δ 9.12 (1H, m), 8.94 (1H, m), 8.16 (1H, s), 7.97 (4H, m), 7.43 (1H, t, *J* = 5.4 Hz), 7.34 (2H, d, *J* = 8.4 Hz), 7.17 (2H, d, *J* = 8.4 Hz), 4.88 (2H, q, *J* = 13.2 Hz), 3.49 (1H, m), 3.30 (1H, m), 3.15 (1H, m), 2.98 (1H, m).

1.4.55A 1-(2-((4-chlorophenyl)thio)ethyl)-2-hydroxy-2-(4-nitrophenyl)-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (9.1e) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-((4-chlorophenyl)thio)ethyl)pyrimidin-2-amine (0.266 g, 1 mmol), 2-bromo-1-(4-nitrophenyl)ethanone (0.293 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a yellow solid (0.472 g, 93%). ¹H-NMR (CD₃CN, 400 MHz): δ 8.94 (1H, m), 8.45 (1H, m), 8.24 (2H, d, *J* = 8.2 Hz), 7.89 (2H, d, *J* = 8.9 Hz), 7.87 (1H, s), 7.23 (5H, m), 5.06 (1H, d, *J* = 14.7 Hz), 4.70 (1H, d, *J* = 14.7 Hz), 3.62 (1H, m), 3.40 (1H, m), 3.23 (1H, m), 3.10 (1H, m).

1.4.56A 1-(2-((4-chlorophenyl)thio)ethyl)-2-(2,4-difluorophenyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (9.1f) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-((4-chlorophenyl)thio)ethyl)pyrimidin-2-amine (0.266 g, 1 mmol), 2-bromo-1-(2,4-difluorophenyl)ethanone (0.282 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.377 g, 75%). ¹H-NMR (CDCl₃, 400 MHz): δ 9.29 (1H, app s), 8.83 (1H, dd, *J* = 6.5, 2.6 Hz), 7.88 (2H, m), 7.23 (2H, d, *J* = 8.7 Hz), 7.17 (2H, d, *J* = 8.7 Hz), 7.12 (1H, dd, *J* = 6.2, 4.5 Hz), 7.01 (1H, m), 6.86 (1H, m), 5.56 (1H, dd, *J* = 14.4, 2.5 Hz), 4.78 (1H, d, *J* = 14.8 Hz), 3.68 (1H, m), 3.40 (1H, m), 3.26 (1H, m), 3.07 (1H, m).

1.4.57A 2-(4-chlorophenyl)-1-(2-((4-fluorophenyl)thio)ethyl)-2-hydroxy-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium bromide (10.1a) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-((4-fluorophenyl)thio)ethyl)pyrimidin-2-amine (0.249 g, 1 mmol), 2-bromo-1-(4-chlorophenyl)ethanone (0.280 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.460 g, 95%). ¹H-NMR (D₆-DMSO, 400 MHz): δ 9.08 (1H, dd, *J* = 4.7, 1.9 Hz), 8.93 (1H, m), 8.01 (1H, s), 7.77 (2H, d, *J* = 8.6 Hz), 7.55 (2H, d, *J* = 8.6 Hz), 7.40 (1H, dd, *J* = 6.3, 4.7 Hz), 7.20 (2H, m), 7.12 (2H, m), 4.86 (2H, q, *J* = 9.3 Hz), 3.45 (1H, m), 3.31 (1H, m), 3.11 (1H, m), 2.90 (1H, m).

1.4.58A 2-([1,1'-biphenyl]-4-yl)-1-(2-((4-fluorophenyl)thio)ethyl)-2-hydroxy-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium bromide (10.1b) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-((4-fluorophenyl)thio)ethyl)pyrimidin-2-amine (0.249 g, 1 mmol), 1-([1,1'-biphenyl]-4-yl)-2-bromoethanone (0.330 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.523 g, 99%). ¹H-NMR (CDCl₃, 400 MHz): δ 9.15 (1H, d, *J* = 5.8 Hz), 8.81 (1H, dd, *J* = 4.6, 2.0 Hz), 7.73 (1H, s), 7.61 (6H, m), 7.49 (2H, t, *J* = 7.5 Hz), 7.42 (1H, q, *J* = 9.3 Hz), 7.20 (2H, m), 7.13 (1H, dd, *J* = 11.0, 1.6 Hz), 6.89 (2H, m), 7.41 (1H, m), 7.19 (2H, m), 7.13 (1H, dd, *J* = 11.0, 1.6 Hz), 6.89 (2H, t, *J* = 8.7 Hz), 5.53 (1H, d, *J* = 14.5 Hz), 4.75 (1H, d, *J* = 14.5 Hz), 3.74 (1H, m), 3.49 (1H, m), 3.16 (2H, m).

1.4.59A 2-(4-bromophenyl)-1-(2-((4-fluorophenyl)thio)ethyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (10.1c) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-((4-fluorophenyl)thio)ethyl)pyrimidin-2-amine (0.249 g, 1 mmol), 2-bromo-1-(4-bromophenyl)ethanone (0.334 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.504 g, 96%). ¹H-NMR (CDCl₃, 400 MHz): δ 8.83 (2H, m), 7.90 (1H, s), 7.56 (2H, d, *J* = 8.6 Hz), 7.43 (2H, d, *J* = 8.6 Hz), 7.22 (2H, dd, *J* = 8.8, 5.2 Hz), 7.12 (1H, dd, *J* = 11.0, 1.6 Hz), 6.95 (2H, t, *J* = 8.7 Hz), 5.53 (1H, d, *J* = 14.2 Hz), 4.59 (1H, d, *J* = 14.2 Hz), 3.71 (1H, m), 3.46 (1H, m), 3.13 (2H, m).

1.4.60A 2-(4-cyanophenyl)-1-(2-((4-fluorophenyl)thio)ethyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (10.1d) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-((4-fluorophenyl)thio)ethyl)pyrimidin-2-amine (0.249 g, 1 mmol), 4-(2-bromoacetyl)benzonitrile (0.269 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.454 g, 96%). ¹H-NMR (CD₃CN, 400 MHz): δ 8.91 (1H, dd, *J* = 4.7, 1.8 Hz), 8.43 (1H, dd, *J* = 6.3, 1.7 Hz), 7.97 (1H, s), 7.79 (4H, m), 7.27 (1H, dd, *J* = 6.3, 4.7 Hz), 7.03 (2H, t, *J* = 8.8 Hz), 5.05 (1H, d, *J* = 14.5 Hz), 4.66 (1H, d, *J* = 14.5 Hz), 3.57 (1H, m), 3.36 (1H, m), 3.18 (1H, m), 3.02 (1H, m).

1.4.61A 1-(2-((4-fluorophenyl)thio)ethyl)-2-hydroxy-2-(4-nitrophenyl)-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (10.1e) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-((4-fluorophenyl)thio)ethyl)pyrimidin-2-amine (0.249 g, 1 mmol), 2-bromo-1-(4-nitrophenyl)ethanone (0.293 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.470 g, 95%). ¹H-NMR (D₆-DMSO, 400 MHz): δ 9.11 (1H, m), 8.95 (1H, dd, *J* = 6.3, 1.7 Hz), 8.30 (2H, d, *J* = 8.7 Hz), 8.21 (1H, s), 8.02 (2H, d, *J* = 8.7 Hz), 7.43 (1H, m), 7.24 (2H, m), 7.10 (2H, t, *J* = 8.7 Hz), 4.90 (2H, q, *J* = 12.0 Hz), 3.46 (1H, m), 3.32 (1H, m), 3.13 (1H, m), 2.93 (1H, m).

1.4.62A 2-(2,4-difluorophenyl)-1-(2-((4-fluorophenyl)thio)ethyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (10.1f) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-((4-fluorophenyl)thio)ethyl)pyrimidin-2-amine (0.249 g, 1 mmol), 2-bromo-1-(2,4-difluorophenyl)ethanone (0.282 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.438 g, 90%). ¹H-NMR (CDCl₃, 400 MHz): δ 9.04 (1H, d, *J* = 6.1 Hz), 8.80 (1H, dd, *J* = 6.1, 2.8 Hz), 7.94 (1H, s), 7.85 (1H, dt, *J* = 9.1, 6.5 Hz), 7.23 (2H, dd, *J* = 8.8, 5.3 Hz), 7.08 (1H, dd, *J* = 6.3, 4.6 Hz), 6.96 (3H, m), 6.84 (1H, ddd, *J* = 11.8, 8.3, 2.4 Hz), 5.53 (1H, dd, *J* = 14.2, 2.6 Hz), 4.72 (1H, d, *J* = 14.5 Hz), 3.65 (1H, m), 3.40 (1H, m), 3.19 (1H, m), 2.99 (1H, m).

1.4.63A 2-(4-chlorophenyl)-2-hydroxy-1-(2-(*p*-tolylthio)ethyl)-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium bromide (**11.1a**) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-(*p*-tolylthio)ethyl)pyrimidin-2-amine (0.245 g, 1 mmol), 2-bromo-1-(4-chlorophenyl)ethanone (0.280 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.445 g, 93%). ¹H-NMR (CDCl₃, 400 MHz): δ 9.11 (1H, app s), 8.81 (1H, dd, *J* = 6.3, 2.7 Hz), 7.72 (1H, s), 7.49 (2H, d, *J* = 8.6 Hz), 7.37 (2H, d, *J* = 8.6 Hz), 7.11 (1H, dd, *J* = 11.1, 1.6 Hz), 7.05 (4H, q, *J* = 12.2 Hz), 5.50 (1H, d, *J* = 14.5 Hz), 4.67 (1H, d, *J* = 14.4 Hz), 3.68 (1H, m), 3.47 (1H, m), 3.10 (2H, m), 2.32 (3H, s).

1.4.64A 2-([1,1'-biphenyl]-4-yl)-2-hydroxy-1-(2-(*p*-tolylthio)ethyl)-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium bromide (**11.1b**) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-(*p*-tolylthio)ethyl)pyrimidin-2-amine (0.245 g, 1 mmol), 1-([1,1'-biphenyl]-4-yl)-2-bromoethanone (0.330 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.462 g, 89%). ¹H-NMR (CDCl₃, 400 MHz): δ 8.99 (1H, d, *J* = 6.2 Hz), 8.83 (1H, dd, *J* = 6.2, 2.6 Hz), 7.77 (1H, s), 7.61 (6H, m), 7.48 (2H, t, *J* = 7.5 Hz), 7.41 (1H, tt, *J* = 9.4, 7.2 Hz), 7.13 (1H, dd, *J* = 11.0, 1.7 Hz), 7.09 (2H, d, *J* = 8.3 Hz), 6.98 (2H, d, *J* = 8.3 Hz), 5.55 (1H, d, *J* = 14.4 Hz), 4.73 (1H, d, *J* = 14.3 Hz), 3.77 (1H, m), 3.56 (1H, m), 3.15 (2H, m), 2.25 (3H, s).

1.4.65A 2-(4-bromophenyl)-2-hydroxy-1-(2-(*p*-tolylthio)ethyl)-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium bromide (**11.1c**) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-(*p*-tolylthio)ethyl)pyrimidin-2-amine (0.245 g, 1 mmol), 2-bromo-1-(4-bromophenyl)ethanone (0.334 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.498 g, 95%). ¹H-NMR (CDCl₃, 400 MHz): δ 9.13 (1H, d, *J* = 6.2 Hz), 8.82 (1H, dd, *J* = 6.5, 6.2 Hz), 7.72 (1H, s), 7.54 (2H, d, *J* = 8.3 Hz), 7.43 (2H, d, *J* = 8.3 Hz), 7.11 (1H, dd, *J* = 6.3, 4.7 Hz), 7.06 (4H, q, *J* = 9.2 Hz), 5.50 (1H, d, *J* = 14.5 Hz), 4.68 (1H, d, *J* = 14.5 Hz), 3.68 (1H, m), 3.47 (1H, m), 3.10 (2H, m), 2.33 (3H, s).

1.4.66A 2-(4-cyanophenyl)-2-hydroxy-1-(2-(*p*-tolylthio)ethyl)-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium bromide (**11.1d**) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-(*p*-tolylthio)ethyl)pyrimidin-2-amine (0.245 g, 1 mmol), 4-(2-bromoacetyl)benzonitrile (0.269 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.392 g, 84%). ¹H-NMR (D₆-DMSO, 400 MHz): δ 9.10 (1H, dd, *J* = 4.7, 1.7 Hz), 8.95 (1H, dd, *J* = 6.3, 1.7 Hz), 8.14 (1H, s), 7.95 (4H, m), 7.42 (1H, dd, *J* = 6.3, 4.7 Hz), 7.07 (2H, d, *J* = 8.2 Hz), 7.00 (2H, d, *J* = 8.2 Hz), 4.88 (2H, q, *J* = 12.9 Hz), 3.43 (1H, m), 3.30 (1H, m), 3.11 (1H, m), 2.87 (1H, m), 2.29 (3H, s).

1.4.67A 2-hydroxy-2-(4-nitrophenyl)-1-(2-(*p*-tolylthio)ethyl)-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium bromide (**11.1e**) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-(*p*-tolylthio)ethyl)pyrimidin-2-amine (0.245 g, 1 mmol), 2-bromo-1-(4-nitrophenyl)ethanone (0.293 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a yellow solid (0.466 g, 95%). ¹H-NMR (D₆-DMSO, 400 MHz): δ 9.11 (1H, m), 8.97 (1H, m), 8.30 (2H, d, *J* = 7.6 Hz), 8.21 (1H, s), 8.02 (2H, d, *J* = 7.6 Hz), 7.43 (1H, m), 7.02 (4H, app s), 4.92 (2H, q, *J* = 13.3 Hz), 3.44 (1H, m), 3.32 (1H, m), 3.13 (1H, m), 2.91 (1H, m), 2.24 (3H, s).

1.4.68A 2-(2,4-difluorophenyl)-2-hydroxy-1-(2-(*p*-tolylthio)ethyl)-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium bromide (**11.1f**) A 5 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with *N*-(2-(*p*-tolylthio)ethyl)pyrimidin-2-amine (0.245 g, 1 mmol), 2-bromo-1-(2,4-difluorophenyl)ethanone (0.282 g, 1.2 mmol) and anhydrous MeCN (1 mL). The reaction mixture was allowed to stir at 60 °C for 2h. The product mixture was then diluted with ether (5 mL), filtered with ether (15 mL) and dried to provide the hydroxy salt as a white solid (0.339 g, 71%). ¹H-NMR (D₆-DMSO, 400 MHz): δ 9.10 (1H, dd, *J* = 4.7, 1.9 Hz), 8.95 (1H, dd, *J* = 6.3, 1.9 Hz), 8.21 (1H, s), 7.80 (1H, m), 7.41 (2H, m), 7.24 (1H, td, *J* = 8.5, 2.4 Hz), 7.10 (2H, d, *J* = 8.2 Hz), 7.04 (2H, d, *J* = 8.2 Hz), 5.00 (1H, d, *J* = 15.2 Hz), 4.88 (1H, d, *J* = 15.2 Hz), 3.52 (1H, m), 3.35 (1H, m), 3.13 (1H, m), 2.86 (1H, m), 2.28 (3H, s).

1.4.69A 2-(4-chlorophenyl)-1-octyl-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate

(1.2a) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **1.1a** (0.339 g, 0.77 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.62 mL, 4.6 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the imidazo[1,2-*a*]pyrimidinium salt as a crystalline white solid (0.327 g, 99%). ¹H-NMR (CDCl₃, 500 MHz): δ 9.32 (1H, d, *J* = 6.7 Hz), 8.92 (1H, dd, *J* = 4.5, 1.8 Hz), 8.33 (1H, s), 7.56 (5H, m), 4.45 (2H, t, *J* = 7.4 Hz), 1.74 (2H, p, *J* = 6.7 Hz), 1.28-1.19 (10H, CH envelope), 0.87 (3H, t, *J* = 7.1 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 156.84, 142.46, 138.82, 137.92, 136.93, 131.07, 129.94, 123.31, 114.60, 112.36, 44.86, 31.62, 29.07, 28.89, 28.66, 26.32, 22.55, 14.04.

1.4.70A 2-([1,1'-biphenyl]-4-yl)-1-octyl-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium

tetrafluoroborate (**1.2b**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **1.1b** (0.229 g, 0.48 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.38 mL, 2.88 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was maintained at 0 °C for 2 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the crude imidazo[1,2-*a*]pyrimidinium salt as a crystalline white solid. The crude product was dissolved in DCM (10mL) and loaded onto a thin pad of silica gel. Impurities were removed using 1% MeOH/DCM before using 10%MeOH/DCM to elute the purified product (0.200 g, 88%). ¹H-NMR (CDCl₃, 500 MHz): δ 9.43 (1H, dd, *J* = 6.8, 1.5 Hz), 8.93 (1H, dd, *J* = 4.5, 1.7 Hz), 8.43 (1H, s), 7.79 (2H, d, *J* = 8.3 Hz), 7.66 (4H, m), 7.58 (1H, dd, *J* = 6.8, 4.5 Hz), 7.50 (2H, t, *J* = 7.2 Hz), 7.43 (1H, tt, *J* = 9.3, 7.4 Hz), 4.52 (2H, t, *J* = 7.9 Hz), 1.80 (2H, p, *J* = 7.3 Hz), 1.27-1.18 (10H, CH envelope), 0.83 (3H, t, *J* = 7.1 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 156.53, 144.24, 142.41, 139.35, 138.93, 138.06, 130.06, 129.12, 128.43, 128.19, 127.21, 123.43, 114.57, 112.20, 44.96, 31.63, 29.16, 28.91, 28.69, 26.34, 22.55, 14.02.

1.4.71A 2-(4-bromophenyl)-1-octyl-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate

(1.2c) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **1.1c** (0.374 g, 0.77 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.63 mL, 4.62 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was maintained at 0 °C for 2 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the crude imidazo[1,2-*a*]pyrimidinium salt as a crystalline white solid. The crude product was dissolved in DCM (10mL) and loaded onto a thin pad of silica gel. Impurities were removed using 1% MeOH/DCM before using 10%MeOH/DCM to elute the purified product (0.447 g, 94%). ¹H-NMR (CDCl₃, 500 MHz): δ 9.33 (1H, dd, *J* = 6.7, 1.3 Hz), 8.92 (1H, dd, *J* = 4.1, 1.6 Hz), 8.34 (1H, s), 7.72 (2H, d, *J* = 8.4 Hz), 7.56 (1H, dd, *J* = 7.0, 4.6 Hz), 7.49 (2H, d, *J* = 8.4 Hz), 4.45 (2H, t, *J* = 8.1 Hz), 1.74 (2H, p, *J* = 7.4 Hz), 1.28-1.18 (10H, CH envelope), 0.87 (3H, t, *J* = 7.1 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 156.84, 142.47, 138.87, 137.00, 132.93, 131.21, 126.27, 123.76, 114.61, 112.35, 44.89, 31.62, 29.09, 28.89, 28.66, 26.31, 22.55, 14.05.

1.4.72A 2-(4-cyanophenyl)-1-octyl-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate

(1.2d) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **1.1d** (0.194 g, 0.45 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.36 mL, 2.7 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the imidazo[1,2-*a*]pyrimidinium salt as a crystalline white solid (0.157 g, 83%). ¹H-NMR (CDCl₃, 500 MHz): δ 9.34 (1H, d, *J* = 5.4 Hz), 8.96 (1H, d, *J* = 4.3 Hz), 8.45 (1H, s), 7.89 (2H, d, *J* = 8.1 Hz), 7.79 (2H, d, *J* = 8.1 Hz), 7.60 (1H, dd, *J* = 6.7, 4.5 Hz), 4.47 (2H, t, *J* = 7.3 Hz), 1.75 (2H, p, *J* = 7.2 Hz), 1.28-1.18 (10H, CH envelope), 0.87 (3H, t, *J* = 7.1 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 157.33, 142.68, 139.07, 135.98, 133.21, 130.57, 129.40, 117.49, 115.38, 114.78, 113.19, 45.13, 31.60, 29.17, 28.88, 28.67, 26.33, 22.54, 14.03.

1.4.73A 2-(4-nitrophenyl)-1-octyl-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate

(1.2e) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **1.1e** (0.356 g, 0.79 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.63 mL, 4.7 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the imidazo[1,2-*a*]pyrimidinium salt as a crystalline tan solid (0.333 g, 96%). ¹H-NMR (CDCl₃, 500 MHz): δ 9.31 (1H, d, *J* = 6.1 Hz), 8.96 (1H, d, *J* = 2.8 Hz), 8.43 (3H, m), 7.87 (2H, d, *J* = 8.8 Hz), 7.61 (1H, dd, *J* = 6.9, 4.4 Hz), 4.48 (2H, t, *J* = 7.8 Hz), 1.74 (2H, p, *J* = 7.1 Hz), 1.26-1.18 (10H, CH envelope), 0.85 (3H, t, *J* = 7.1 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 157.46, 149.41, 142.75, 139.01, 135.58, 131.24, 131.10, 124.58, 114.82, 113.28, 45.15, 31.59, 29.17, 28.88, 28.68, 26.35, 22.53, 14.01.

1.4.74A 2-(2,4-difluorophenyl)-1-octyl-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium

tetrafluoroborate (**1.2f**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **1.1f** (0.119 g, 0.27 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.22 mL, 1.6 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the imidazo[1,2-*a*]pyrimidinium salt as a crystalline tan solid (0.112 g, 96%). ¹H-NMR (CDCl₃, 500 MHz): δ 9.34 (1H, dd, *J* = 6.8, 1.7 Hz), 8.97 (1H, dd, *J* = 4.4, 1.7 Hz), 8.35 (1H, s), 7.70 (1H, tt, *J* = 8.3, 6.2 Hz), 7.64 (1H, dd, *J* = 6.8, 4.4 Hz), 7.14 (1H, td, *J* = 8.2, 2.3 Hz), 7.07 (1H, m), 4.35 (2H, t, *J* = 7.7 Hz), 1.73 (2H, p, *J* = 7.3 Hz), 1.27-1.17 (10H, CH envelope), 0.86 (3H, t, *J* = 7.1 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 165.23 (dd, *J* = 256.6, 11.5 Hz), 160.49 (dd, *J* = 253.2, 12.5 Hz), 157.31, 142.47, 138.98, 134.44 (dd, *J* = 10.0, 2.6 Hz), 131.71, 114.73, 113.83, 113.36 (dd, *J* = 21.7, 3.5 Hz), 109.15 (dd, *J* = 14.9, 3.0 Hz), 105.05 (t, *J* = 26.4 Hz), 45.39, 31.61, 28.85, 28.74, 28.63, 26.31, 22.54, 14.03. ¹⁹F-NMR (CDCl₃, 470 MHz): δ -101.98, -107.55, -151.99.

1.4.75A 2-(4-methoxyphenyl)-1-octyl-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium

tetrafluoroborate (1.2g) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **1.1g** (0.248 g, 0.57 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.46 mL, 3.42 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the imidazo[1,2-*a*]pyrimidinium salt as a crystalline tan solid (0.232 g, 96 %). ¹H-NMR (CDCl₃, 500 MHz): δ 9.35 (1H, d, *J* = 6.1 Hz), 8.90 (1H, d, *J* = 3.6 Hz), 8.29 (1H, s), 7.57 (1H, dd, *J* = 6.5, 4.7 Hz), 7.52 (2H, d, *J* = 8.6 Hz), 7.08 (2H, d, *J* = 8.6 Hz), 4.46 (2H, t, *J* = 7.9 Hz), 3.91 (3H, s), 1.77 (2H, p, *J* = 7.6 Hz), 1.28-1.19 (10H, CH envelope), 0.86 (3H, t, *J* = 7.1 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 161.91, 156.30, 142.23, 138.71, 138.29, 131.17, 116.61, 115.12, 114.56, 111.69, 55.55, 44.78, 31.64, 29.08, 28.90, 28.69, 26.34, 22.55, 14.05.

1.4.76A 2-(4-trifluoromethylphenyl)-1-octyl-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**1.2h**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **1.1h** (0.374 g, 0.79 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.63 mL, 4.74 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the imidazo[1,2-*a*]pyrimidinium salt as a crystalline white solid (0.325 g, 89%). ¹H-NMR (CDCl₃, 500 MHz): δ 9.31 (1H, d, *J* = 6.7 Hz), 8.93 (1H, d, *J* = 3.3 Hz), 8.38 (1H, s), 7.84 (2H, d, *J* = 8.1 Hz), 7.78 (2H, d, *J* = 8.1 Hz), 7.57 (1H, dd, *J* = 6.4, 4.4 Hz), 4.46 (2H, t, *J* = 8.1 Hz), 1.75 (2H, p, *J* = 6.8 Hz), 1.26-1.16 (10H, CH envelope), 0.86 (3H, t, *J* = 7.1 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 157.15, 142.60, 138.91, 136.44, 133.30 (q, *J* = 33.3 Hz), 130.39, 128.65, 126.51, 124.52 (t, *J* = 273.0 Hz), 114.70, 112.82, 44.98, 31.59, 29.10, 28.86, 28.64, 26.30, 22.52, 14.00. ¹⁹F-NMR (CDCl₃, 470 MHz): δ -63.11, -152.37.

1.4.77A 2-(4-trifluoromethoxyphenyl)-1-octyl-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (1.2i) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **1.1i** (0.375 g, 0.77 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.62 mL, 4.6 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the imidazo[1,2-*a*]pyrimidinium salt as a crystalline white solid (0.320 g, 87%). ¹H-NMR (CDCl₃, 500 MHz): δ 9.31 (1H, dd, *J* = 6.8, 1.7 Hz), 8.92 (1H, dd, *J* = 4.4, 1.7 Hz), 8.34 (1H, s), 7.68 (2H, d, *J* = 8.3 Hz), 7.56 (1H, dd, *J* = 6.8, 4.4 Hz), 7.42 (2H, d, *J* = 8.3 Hz), 4.44 (2H, t, *J* = 7.9 Hz), 1.75 (2H, p, *J* = 7.0 Hz), 1.27-1.17 (10H, CH envelope), 0.85 (3H, t, *J* = 7.1 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 156.91, 151.34, 142.47, 138.84, 136.65, 131.69, 123.40, 121.64, 121.36 (q, *J* = 256.5), 114.62, 112.54, 44.88, 31.59, 29.09, 28.87, 28.65, 26.31, 22.52, 14.00. ¹⁹F-NMR (CDCl₃, 470 MHz): δ -57.71, -152.40.

1.4.78A 2-(4-difluoromethoxyphenyl)-1-octyl-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**1.2j**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **1.1j** (0.258 g, 0.55 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.44 mL, 3.3 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the imidazo[1,2-*a*]pyrimidinium salt as a crystalline white solid (0.206 g, 81%). ¹H-NMR (CDCl₃, 500 MHz): δ 9.34 (1H, m), 8.93 (1H, m), 8.35 (1H, s), 7.63 (2H, m), 7.56 (1H, m), 7.33 (2H, m), 6.65 (1H, t, *J* = 73.7 Hz), 4.46 (2H, t, *J* = 7.3 Hz), 1.76 (2H, p, *J* = 6.9 Hz), 1.27-1.18 (10H, CH envelope), 0.86 (3H, t, *J* = 7.0 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 156.75, 153.25, 142.40, 138.82, 137.10, 131.57, 121.67, 120.28, 115.32 (t, *J* = 262.4 Hz), 114.57, 112.38, 44.88, 31.61, 29.12, 28.89, 28.67, 26.33, 22.53, 14.02. ¹⁹F-NMR (CDCl₃, 470 MHz): δ -81.82, -81.98, -152.29.

1.4.79A 2-(3-nitrophenyl)-1-octyl-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate

(1.2k) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **1.1k** (1.242 g, 2.75 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (2.2 mL, 16.5 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the imidazo[1,2-*a*]pyrimidinium salt as an amber oil that slowly crystallized (1.037 g, 86%). ¹H-NMR (CDCl₃, 500 MHz): δ 9.29 (1H, dd, *J* = 6.8, 1.6 Hz), 8.96 (1H, dd, *J* = 4.4, 1.6 Hz), 8.45 (2H, m), 8.42 (1H, s), 8.06 (1H, d, *J* = 8.0 Hz), 7.82 (1H, m), 7.62 (1H, dd, *J* = 6.8, 4.4 Hz), 4.46 (2H, t, *J* = 7.5 Hz), 1.79 (2H, p, *J* = 7.2 Hz), 1.27-1.18 (10H, CH envelope), 0.85 (3H, t, *J* = 7.1 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 157.50, 148.47, 142.68, 138.95, 136.23, 135.41, 131.11, 126.71, 125.89, 124.40, 114.88, 113.21, 45.11, 31.59, 29.22, 28.88, 28.68, 26.37, 22.53, 14.02.

1.4.80A 2-(4-chlorophenyl)-1-(2-(pentylthio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (2.2a) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **2.1a** (0.410 g, 0.89 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.71 mL, 5.34 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the imidazo[1,2-*a*]pyrimidinium salt as a crystalline yellow-orange solid (0.351 g, 88%). ¹H-NMR (CDCl₃, 500 MHz): δ 9.17 (1H, m), 8.89 (1H, dd, *J* = 4.4, 1.8 Hz), 8.18 (1H, m), 7.55 (5H, m), 4.62 (2H, t, *J* = 7.2 Hz), 2.79 (2H, t, *J* = 7.2 Hz), 2.29 (2H, t, *J* = 7.4 Hz), 1.39 (2H, p, *J* = 7.1 Hz), 1.25 (4H, m), 0.87 (3H, t, *J* = 7.1 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 157.20, 142.74, 138.48, 138.43, 137.81, 137.77, 136.88, 131.36, 129.82, 123.36, 114.85, 112.03, 43.80, 31.83, 30.88, 30.19, 28.91, 22.21, 13.94.

1.4.81A 2-([1,1'-biphenyl]-4-yl)-1-(2-(pentylthio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**2.2b**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **2.1b** (0.454 g, 0.91 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.73 mL, 5.5 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the imidazo[1,2-*a*]pyrimidinium salt as a crystalline tan solid (0.410 g, 92%). ¹H-NMR (CDCl₃, 500 MHz): δ 9.37 (1H, dd, *J* = 6.7, 1.8 Hz), 8.93 (1H, dd, *J* = 4.4, 1.8 Hz), 8.36 (1H, s), 7.78 (2H, d, *J* = 8.3 Hz), 7.69 (2H, d, *J* = 8.3 Hz), 7.63 (2H, d, *J* = 8.3 Hz), 7.57 (1H, dd, *J* = 6.8, 4.6 Hz), 7.50 (2H, t, *J* = 7.2 Hz), 7.44 (1H, m), 4.72 (2H, t, *J* = 7.4 Hz), 2.85 (2H, t, *J* = 7.6 Hz), 2.33 (2H, t, *J* = 7.3 Hz), 1.42 (2H, p, *J* = 6.8 Hz), 1.23 (4H, m), 0.82 (3H, t, *J* = 6.5 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 156.70, 144.29, 142.72, 139.26, 138.84, 138.06, 130.24, 129.14, 128.46, 128.18, 127.18, 123.30, 114.76, 112.11, 43.91, 31.89, 30.88, 30.32, 28.92, 22.19, 13.88.

1.4.86A 2-(4-bromophenyl)-1-(2-(pentylthio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (2.2c) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **2.1c** (0.299 g, 0.59 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.47 mL, 3.54 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was maintained at 0 °C for 2 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the crude imidazo[1,2-*a*]pyrimidinium salt as a crystalline yellow-orange solid. The crude product was dissolved in DCM (10mL) and loaded onto a thin pad of silica gel. Impurities were removed using 1% MeOH/DCM before using 10%MeOH/DCM to elute the purified product (0.294 g, 99%).

1.4.87A 2-(4-cyanophenyl)-1-(2-(pentylthio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (2.2d) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **2.1d** (0.394 g, 0.88 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.7 mL, 5.28 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the imidazo[1,2-*a*]pyrimidinium salt as a crystalline amber solid (0.306 g, 79%). ¹H-NMR (CDCl₃, 500 MHz): δ 9.30 (1H, dd, *J* = 6.8, 1.7 Hz), 8.96 (1H, dd, *J* = 4.4, 1.7 Hz), 8.38 (1H, s), 7.88 (2H, d, *J* = 8.3 Hz), 7.82 (2H, d, *J* = 8.3 Hz), 7.59 (1H, dd, *J* = 6.8, 4.2 Hz), 4.66 (2H, t, *J* = 7.0 Hz), 2.84 (2H, t, *J* = 7.0 Hz), 2.31 (2H, t, *J* = 7.6 Hz), 1.42 (2H, p, *J* = 7.0 Hz), 1.25 (4H, m), 0.88 (3H, t, *J* = 7.0 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 157.48, 142.94, 138.92, 136.22, 133.16, 130.87, 129.30, 117.47, 115.36, 114.98, 112.94, 44.14, 32.02, 30.84, 30.38, 28.87, 22.20, 13.92.

1.4.88A 2-(4-nitrophenyl)-1-(2-(pentylthio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (2.2e) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **2.1e** (0.423 g, 0.9 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.72 mL, 5.4 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was maintained at 0 °C for 2 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the crude imidazo[1,2-*a*]pyrimidinium salt as a crystalline red solid. The crude product was dissolved in DCM (10mL) and loaded onto a thin pad of silica gel. Impurities were removed using 1% MeOH/DCM before using 10%MeOH/DCM to elute the purified product (0.389 g, 94%). ¹H-NMR (CDCl₃, 500 MHz): δ 9.29 (1H, dd, *J* = 6.9, 1.6 Hz), 8.96 (1H, dd, *J* = 4.0, 1.6 Hz), 8.41 (3H, m), 7.89 (2H, d, *J* = 8.4 Hz), 7.60 (1H, dd, *J* = 6.8, 4.4 Hz), 4.66 (2H, t, *J* = 7.4 Hz), 1.41 (2H, p, *J* = 7.4 Hz), 1.23 (4H, m), 0.85 (3H, t, *J* = 6.9 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 157.54, 149.46, 142.99, 138.96, 135.91, 131.37, 131.01, 124.57, 115.00, 113.11, 44.22, 32.06, 30.83, 30.41, 28.88, 22.18, 13.88.

1.4.89A 2-(2,4-difluorophenyl)-1-(2-(pentylthio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (2.2f) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **2.1f** (0.290 g, 0.63 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.5 mL, 3.8 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was maintained at 0 °C for 2 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the crude imidazo[1,2-*a*]pyrimidinium salt as a crystalline red solid. The crude product was dissolved in DCM (10mL) and loaded onto a thin pad of silica gel. Impurities were removed using 1% MeOH/DCM before using 10%MeOH/DCM to elute the purified product (0.244 g, 86%). ¹H-NMR (CDCl₃, 500 MHz): δ 9.28 91H, d, *J* = 6.0 Hz), 8.98 (1H, dd, *J* = 4.3, 1.2 Hz), 8.30 (1H, s), 7.73 (1H, t, *J* = 7.3 Hz), 7.67 (1H, dd, *J* = 6.7, 4.6 Hz), 7.12 (1H, m), 7.05 (1H, m), 4.52 (2H, t, *J* = 7.7 Hz), 2.82 (2H, t, *J* = 6.8 Hz), 2.34 (2H, t, *J* = 7.2 Hz), 1.43 (2H, p, *J* = 6.8 Hz), 1.26 (4H, m), 0.87 (3H, t, *J* = 6.7 Hz).). ¹³C-NMR (CDCl₃, 125 MHz): δ 165.19 (dd, *J* = 256.4, 11.8 Hz), 160.51 (dd, *J* = 253.4, 12.5 Hz), 157.77, 142.75, 138.79, 134.52 (dd, *J* = 9.9, 2.5 Hz), 131.37, 115.07, 113.65, 113.27 (dd, *J* = 21.8, 3.4 Hz), 109.15 (dd, *J* = 14.7, 3.7 Hz), 105.04 (t, *J* = 26.0 Hz), 44.43, 31.88, 30.86, 30.02, 28.95, 22.19, 13.90.

1.4.90A 2-(4-chlorophenyl)-1-(3-butoxypropyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (3.2a) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **3.1a** (0.375 g, 0.85 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.68 mL, 5.1 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the imidazo[1,2-*a*]pyrimidinium salt as a crystalline salmon-pink solid (0.340 g, 93%). ¹H-NMR (CDCl₃, 500 MHz): δ 9.32 (1H, dd, *J* = 6.8, 1.6 Hz), 8.92 (1H, dd, *J* = 4.3, 1.6 Hz), 8.33 (1H, s), 7.57 (5H, m), 4.62 (2H, t, *J* = 7.2 Hz), 3.35 (2H, t, *J* = 5.4 Hz), 3.18 (2H, t, *J* = 6.6 Hz), 2.05 (2H, p, *J* = 6.1 Hz), 1.33 (2H, p, *J* = 6.6 Hz), 1.22 (2H, sx, *J* = 7.7 Hz), 0.88 (3H, t, *J* = 7.3 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 156.72, 142.70, 138.75, 137.86, 137.22, 131.13, 129.88, 123.27, 114.58, 112.22, 70.86, 66.96, 42.84, 31.64, 29.18, 19.23, 13.89.

1.4.91A 2-([1,1'-biphenyl]-4-yl)-1-(3-butoxypropyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**3.2b**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **3.1b** (0.417 g, 0.86 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.69 mL, 5.2 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the imidazo[1,2-*a*]pyrimidinium salt as a crystalline yellow solid (0.404 g, 99%). ¹H-NMR (CDCl₃, 500 MHz): δ 9.42 (1H, d, *J* = 6.1 Hz), 8.93 (1H, dd, *J* = 4.3, 1.4 Hz), 8.43 (1H, s), 7.79 (2H, d, *J* = 8.2 Hz), 7.70 (2H, d, *J* = 8.2 Hz), 7.64 (2H, d, *J* = 7.7 Hz), 7.58 (1H, dd, *J* = 6.7, 4.4 Hz), 7.50 (2H, t, *J* = 7.6 Hz), 7.43 (1H, m), 4.70 (2H, t, *J* = 7.2 Hz), 3.38 (2H, t, *J* = 5.4 Hz), 3.19 (2H, t, *J* = 6.6 Hz), 2.10 (2H, p, *J* = 6.6 Hz), 1.33 (2H, p, *J* = 8.1 Hz), 1.21 (2H, sx, *J* = 7.7 Hz), 0.83 (3H, t, *J* = 7.3 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 156.38, 144.19, 142.67, 139.39, 138.85, 138.32, 130.11, 129.11, 128.39, 128.17, 127.19, 123.41, 114.53, 112.08, 70.86, 67.06, 42.97, 31.63, 29.25, 19.21, 13.86.

1.4.94A 1-(2-((2-bromophenyl)thio)ethyl)-2-(4-chlorophenyl)-1*H*-imidazo[1,2-
a]pyrimidin-4-ium tetrafluoroborate (**4.2a**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **4.1a** (0.264 g, 0.49 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.39 mL, 2.9 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the imidazo[1,2-
a]pyrimidinium salt as a crystalline white solid (0.221 g, 85%). ¹H-NMR (D₆-DMSO, 500 MHz): δ 9.44 (1H, d, *J* = 6.4 Hz), 9.21 (1H, d, *J* = 4.1 Hz), 8.58 (1H, s), 7.87 (1H, t, *J* = 4.9 Hz), 7.63 (4H, m), 7.56 (1H, d, *J* = 7.7 Hz), 7.29 (1H, t, *J* = 7.5 Hz), 7.19 (1H, d, *J* = 7.5 Hz), 7.14 (1H, t, *J* = 7.4 Hz), 4.73 (2H, t, *J* = 6.0 Hz), 3.44 (2H, t, *J* = 6.0 Hz). ¹³C-NMR (D₆-DMSO, 125 MHz): δ 158.48, 143.24, 139.11, 136.61, 136.33, 135.61, 133.44, 131.86, 129.85, 128.59, 127.53, 127.42, 124.15, 122.56, 115.38, 111.98, 42.71, 30.02.

1.4.95A 2-([1,1'-biphenyl]-4-yl)-1-(2-((2-bromophenyl)thio)ethyl)-1*H*-imidazo[1,2-
a]pyrimidin-4-ium tetrafluoroborate (**4.2b**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **4.1b** (0.557 g, 0.95 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.76 mL, 5.7 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the imidazo[1,2-
a]pyrimidinium salt as a crystalline white solid (0.503 g, 92%). ¹H-NMR (CDCl₃, 500 MHz): δ 9.39 (1H, d, *J* = 6.1 Hz), 8.90 (1H, d, *J* = 3.9 Hz), 8.35 (1H, s), 7.69 (2H, d, *J* = 8.4 Hz), 7.61 (4H, m), 7.55 (1H, dd, *J* = 6.1, 3.9 Hz), 7.52 (2H, t, *J* = 7.2 Hz), 7.46 (2H, m), 7.10 (1H, td, *J* = 7.9, 1.1 Hz), 7.06 (1H, m), 6.99 (1H, td, *J* = 7.5, 1.6 Hz), 4.78 (2H, t, *J* = 7.1 Hz), 3.38 (2H, t, *J* = 7.1 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 159.70, 144.26, 142.69, 139.28, 138.95, 138.18, 134.27, 133.48, 130.17, 129.49, 129.16, 128.49, 128.19, 128.02, 127.18, 125.09, 122.81, 114.78, 112.25, 43.56, 31.10.

1.4.96A 2-(4-bromophenyl)-1-(2-((2-bromophenyl)thio)ethyl)-1*H*-imidazo[1,2-
a]pyrimidin-4-ium tetrafluoroborate (**4.2c**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **4.1c** (0.283 g, 0.48 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.39 mL, 2.9 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the imidazo[1,2-
a]pyrimidinium salt as a crystalline white solid (0.235 g, 85%). ¹H-NMR (D₆-DMSO, 500 MHz): δ 9.42 (1H, dd, *J* = 6.7, 1.8 Hz), 9.18 (1H, dd, *J* = 4.4, 1.8 Hz), 8.56 (1H, s), 7.84 (1H, dd, *J* = 6.7, 4.4 Hz), 7.71 (2H, m), 7.55 (3H, m), 7.26 (1H, m), 7.16 (1H, m), 7.12 (1H, m), 4.71 (2H, t, *J* = 6.5 Hz), 3.42 (2H, t, *J* = 6.5 Hz). ¹³C-NMR (D₆-DMSO, 125 MHz): δ 158.48, 143.26, 139.10, 136.68, 135.60, 133.46, 132.77, 132.01, 128.59, 127.52, 127.40, 125.18, 124.52, 122.55, 115.38, 111.92, 42.69, 30.02.

1.4.97A 1-(2-((2-bromophenyl)thio)ethyl)-2-(4-cyanophenyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**4.2d**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **4.1d** (0.517 g, 0.97 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.78 mL, 5.8 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the crude imidazo[1,2-*a*]pyrimidinium salt as a crystalline white solid. The crude product was dissolved in DCM (10mL) and loaded onto a thin pad of silica gel. Impurities were removed using 1% MeOH/DCM before using 10%MeOH/DCM to elute the purified product (0.458 g, 91%). ¹H-NMR (D₆-DMSO, 500 MHz): δ 9.48 (1H, dd, *J* = 6.7, 1.6 Hz), 9.24 (1H, dd, *J* = 4.4, 1.6 Hz), 8.67 (1H, s), 7.97 (2H, d, *J* = 8.5 Hz), 7.89 (1H, dd, *J* = 6.7, 4.5 Hz), 7.83 (2H, d, *J* = 8.5 Hz), 7.54 (1H, dd, *J* = 8.1, 0.8 Hz), 7.30 (1H, td, *J* = 7.4, 0.9 Hz), 7.21 (1H, dd, *J* = 7.9, 1.0 Hz), 7.13 (1H, td, *J* = 7.0, 1.0 Hz), 4.78 (2H, t, *J* = 6.3 Hz), 3.45 (2H, t, *J* = 6.3 Hz). ¹³C-NMR (D₆-DMSO, 125 MHz): δ 158.85, 143.42, 139.29, 136.17, 135.77, 133.42, 133.34, 130.88, 129.88, 128.62, 127.36, 127.11, 122.32, 118.53, 115.49, 113.67, 112.49, 42.58, 29.99.

1.4.98A 1-(2-((2-bromophenyl)thio)ethyl)-2-(4-nitrophenyl)-1*H*-imidazo[1,2-
a]pyrimidin-4-ium tetrafluoroborate (**4.2e**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **4.1e** (0.360 g, 0.65 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.52 mL, 3.9 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the crude imidazo[1,2-a]pyrimidinium salt as a crystalline white solid. The crude product was dissolved in DCM (10mL) and loaded onto a thin pad of silica gel. Impurities were removed using 1% MeOH/DCM before using 10%MeOH/DCM to elute the purified product (0.357 g, 100%).

1.4.99A 1-((2-bromophenyl)thio)ethyl)-2-(2,4-difluorophenyl)-1*H*-imidazo[1,2-
a]pyrimidin-4-ium tetrafluoroborate (**4.2f**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **4.1f** (0.520 g, 0.95 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.76 mL, 5.7 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the crude imidazo[1,2-a]pyrimidinium salt as a crystalline white solid. The crude product was dissolved in DCM (10mL) and loaded onto a thin pad of silica gel. Impurities were removed using 1% MeOH/DCM before using 10%MeOH/DCM to elute the purified product (0.495 g, 98%). ¹H-NMR (D₆-DMSO, 500 MHz): δ 9.47 (1H, d, *J* = 6.5 Hz), 9.23 (1H, d, *J* = 4.1 Hz), 8.64 (1H, s), 7.88 (1H, dd, *J* = 6.5, 4.4 Hz), 7.70 (1H, q, *J* = 6.6 Hz), 7.57 (1H, d, *J* = 7.9 Hz), 7.51 (1H, td, *J* = 10.4, 1.8 Hz), 7.30 (1H, m), 7.24 (2H, m), 7.13 (1H, t, *J* = 7.5 Hz), 4.67 (2H, t, *J* = 6.3 Hz), 3.46 (2H, t, *J* = 6.3 Hz). ¹³C-NMR (D₆-DMSO, 125 MHz): δ 164.40 (dd, *J* = 253.4, 11.5 Hz), 160.25 (dd, *J* = 251.5, 13.4 Hz), 158.79, 143.31, 139.23, 135.77, 134.15 (dd, *J* = 10.4, 2.0 Hz), 133.39, 130.76, 128.61, 127.40, 127.07, 122.35, 115.41, 113.53, 113.30 (dd, *J* = 22.4, 3.2 Hz), 109.84 (dd, *J* = 14.4, 3.6 Hz), 105.74 (t, *J* = 25.9 Hz), 42.74, 29.99. ¹⁹F-NMR (D₆-DMSO, 470 MHz): δ -104.59, -107.73, -148.30.

1.4.100A 2-(4-chlorophenyl)-1-(2-((2-chlorophenyl)thio)ethyl)-1*H*-imidazo[1,2-
a]pyrimidin-4-ium tetrafluoroborate (5.2a) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **5.1a** (0.484 g, 0.97 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.78 mL, 5.82 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the imidazo[1,2-a]pyrimidinium salt as a crystalline white solid (0.395 g, 83%). ¹H-NMR (D₆-DMSO, 500 MHz): δ 9.43 (1H, d, *J* = 6.7 Hz), 9.21 (1H, d, *J* = 4.4 Hz), 8.57 (1H, s), 7.86 (1H, dd, *J* = 6.2, 4.6 Hz), 7.65 (2H, d, *J* = 8.3 Hz), 7.60 (2H, d, *J* = 8.3 Hz), 7.40 (1H, m), 7.22 (3H, m), 4.73 (2H, t, *J* = 6.5 Hz), 3.45 (2H, t, *J* = 6.5 Hz). ¹³C-NMR (D₆-DMSO, 125 MHz): δ 158.48, 143.31, 139.10, 136.59, 136.35, 133.58, 132.16, 131.85, 130.21, 129.84, 128.08, 127.75, 127.46, 124.17, 115.38, 111.98, 42.84, 29.59.

1.4.101A 2-([1,1'-biphenyl]-4-yl)-1-(2-((2-chlorophenyl)thio)ethyl)-1*H*-imidazo[1,2-
a]pyrimidin-4-ium tetrafluoroborate (**5.2b**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **5.1b** (0.510 g, 0.94 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.75 mL, 5.6 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the imidazo[1,2-
a]pyrimidinium salt as a crystalline white solid (0.483 g, 97%). ¹H-NMR (CDCl₃, 500 MHz): δ 9.34 (1H, dd, *J* = 6.7, 1.4 Hz), 8.88 (1H, dd, *J* = 4.4, 1.7 Hz), 8.32 (1H, s), 7.68 (2H, d, *J* = 7.8 Hz), 7.59 (4H, t, *J* = 8.6 Hz), 7.52 (3H, m), 7.45 (1H, m), 7.05 (3H, m), 4.76 (2H, t, *J* = 7.2 Hz), 3.37 (2H, t, *J* = 7.6 Hz). (CDCl₃, 125 MHz): δ 156.65, 144.61, 144.36, 139.32, 138.88, 138.26, 134.96, 132.15, 130.17, 130.13, 130.06, 129.16, 128.49, 128.24, 128.18, 127.30, 127.18, 122.83, 114.75, 112.19, 43.76, 30.74.

1.4.102A 2-(4-bromophenyl)-1-(2-((2-chlorophenyl)thio)ethyl)-1*H*-imidazo[1,2-
a]pyrimidin-4-ium tetrafluoroborate (5.2c) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **5.1c** (0.543 g, 1 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.8 mL, 6 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the imidazo[1,2-
a]pyrimidinium salt as a crystalline white solid (0.300 g, 56%). ¹H-NMR (D₆-DMSO, 500 MHz): δ 9.44 (1H, dd, *J* = 6.7, 1.7 Hz), 9.21 (1H, dd, *J* = 4.5, 1.7 Hz), 8.58 (1H, s), 7.87 (1H, dd, *J* = 6.7, 4.5 Hz), 7.74 (2H, d, *J* = 8.2 Hz), 7.58 (2H, d, *J* = 8.2 Hz), 7.42 (1H, m), 7.23 (3H, m), 4.73 (2H, t, *J* = 6.5 Hz), 3.45 (2H, t, *J* = 6.5 Hz). ¹³C-NMR (D₆-DMSO, 125 MHz): δ 158.48, 143.25, 139.10, 136.67, 133.57, 132.76, 132.15, 131.99, 130.23, 128.08, 127.73, 127.46, 125.21, 124.53, 115.38, 111.93, 42.83, 29.59.

1.4.103A 1-(2-((2-chlorophenyl)thio)ethyl)-2-(4-cyanophenyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (5.2d) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **5.1d** (0.411 g, 0.84 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.67 mL, 5 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the crude imidazo[1,2-*a*]pyrimidinium salt as a crystalline white solid. The crude product was dissolved in DCM (10mL) and loaded onto a thin pad of silica gel. Impurities were removed using 1% MeOH/DCM before using 10%MeOH/DCM to elute the purified product (0.386 g, 96%). ¹H-NMR (D₆-DMSO, 500 MHz): δ 9.48 (1H, d, *J* = 6.7 Hz), 9.24 (1H, dd, *J* = 4.4, 1.5 Hz), 8.67 (1H, s), 7.97 (2H, d, *J* = 8.1 Hz), 7.89 (1H, dd, *J* = 6.7, 4.5 Hz), 7.82 (2H, d, *J* = 8.1 Hz), 7.38 (1H, d, *J* = 7.5 Hz), 7.22 (3H, m), 4.77 (2H, t, *J* = 6.3 Hz), 3.46 (2H, t, *J* = 6.3 Hz).

1.4.104A 1-(2-((2-chlorophenyl)thio)ethyl)-2-(4-nitrophenyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (5.2e) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **5.1e** (0.500 g, 0.98 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.78 mL, 5.88 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the imidazo[1,2-*a*]pyrimidinium salt as a crystalline yellow solid (0.450 g, 92%). ¹H-NMR (D₆-DMSO, 500 MHz): δ 9.48 (1H, d, *J* = 5.9 Hz), 9.25 (1H, d, *J* = 4.4 Hz), 8.72 (1H, s), 8.28 (2H, d, *J* = 8.0 Hz), 7.90 (3H, d, *J* = 7.8 Hz), 7.25 (3H, m), 7.12 (1H, m), 4.81 (2H, app s). ¹³C-NMR (D₆-DMSO, 125 MHz): δ 158.96, 148.68, 143.51, 139.32, 135.84, 133.76, 131.73, 131.51, 129.91, 128.08, 127.22, 127.06, 124.52, 115.55, 112.63, 42.49, 29.50.

1.4.105A 1-(2-((2-chlorophenyl)thio)ethyl)-2-(2,4-difluorophenyl)-1*H*-imidazo[1,2-
a]pyrimidin-4-ium tetrafluoroborate (5.2f) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **5.1f** (0.431 g, 0.86 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.69 mL, 5.2 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the imidazo[1,2-
a]pyrimidinium salt as a crystalline white solid (0.398 g, 95%). ¹H-NMR (D₆-DMSO, 500 MHz): δ 9.45 (1H, dd, *J* = 6.7, 1.7 Hz), 9.22 (1H, dd, *J* = 4.4, 1.7 Hz), 8.62 (1H, s), 7.87 (1H, dd, *J* = 6.7, 4.4 Hz), 7.68 (1H, m), 7.49 (1H, td, *J* = 9.8, 2.4 Hz), 7.40 (1H, dd, *J* = 8.2, 0.8 Hz), 7.22 (4H, m), 4.65 (2H, t, *J* = 6.4 Hz). ¹³C-NMR (D₆-DMSO, 125 MHz): δ 164.44 (dd, *J* = 253.4, 18.3 Hz), 160.37 (dd, *J* = 262.5, 25.1 Hz), 158.78, 143.30, 139.22, 134.12 (dd, *J* = 10.3, 1.9 Hz), 133.73, 131.97, 130.77, 130.15, 128.09, 127.32 (d, *J* = 1.7 Hz), 115.41, 113.52, 113.27 (dd, *J* = 22.2, 3.1 Hz), 109.86 (dd, *J* = 14.3, 3.3 Hz), 105.70 (t, *J* = 26.5 Hz), 42.83, 29.51. ¹⁹F-NMR (D₆-DMSO, 470 MHz): δ -104.58, -107.86, -148.29.

1.4.106A 2-(4-chlorophenyl)-1-(2-((2-fluorophenyl)thio)ethyl)-1*H*-imidazo[1,2-
a]pyrimidin-4-ium tetrafluoroborate (**6.2a**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **6.1a** (0.409 g, 0.85 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.68 mL, 5.1 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the crude imidazo[1,2-a]pyrimidinium salt as a crystalline white solid. The crude product was dissolved in DCM (10mL) and loaded onto a thin pad of silica gel. Impurities were removed using 1% MeOH/DCM before using 10%MeOH/DCM to elute the purified product (0.356 g, 89%). ¹H-NMR (D₆-DMSO, 500 MHz): δ 9.41 (1H, dd, *J* = 6.7, 1.7 Hz), 9.20 (1H, dd, *J* = 4.4, 1.7 Hz), 8.55 (1H, s), 7.85 (1H, dd, *J* = 6.7, 4.4 Hz), 7.67 (4H, app s), 7.31 (1H, m), 7.18 (2H, m), 7.08 (1H, td, *J* = 7.6, 1.2 Hz), 4.70 (2H, t, *J* = 6.7 Hz), 3.38 (2H, t, *J* = 6.7 Hz). ¹³C-NMR (D₆-DMSO, 125 MHz): δ 161.50, 159.55, 158.45, 143.23, 139.03, 136.45 (d, *J* = 7.8 Hz), 131.86, 131.02, 129.94, 129.27 (d, *J* = 7.7 Hz), 125.40 (d, *J* = 4.1 Hz), 124.21, 120.88 (d, *J* = 17.3 Hz), 116.28, 116.10, 115.37, 112.06, 43.83, 30.35. ¹⁹F-NMR (D₆-DMSO, 470 MHz): δ -110.14, -148.29.

1.4.107A 2-([1,1'-biphenyl]-4-yl)-1-(2-((2-fluorophenyl)thio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**6.2b**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **6.1b** (0.492 g, 0.94 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.75 mL, 5.64 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the imidazo[1,2-*a*]pyrimidinium salt as a crystalline white solid (0.122 g, 25%). ¹H-NMR (D₆-DMSO, 500 MHz): δ 9.43 (1H, dd, *J* = 6.7, 1.6 Hz), 9.20 (1H, dd, *J* = 4.3, 1.6 Hz), 8.63 (1H, s), 8.01 (2H, d, *J* = 8.0 Hz), 7.84 (3H, m), 7.26 (1H, m), 7.18 (1H, m), 7.11 (1H, m), 7.06 (1H, m), 4.70 (2H, t, *J* = 6.5 Hz), 3.36 (2H, t, *J* = 6.5 Hz). ¹³C-NMR (D₆-DMSO, 125 MHz): δ 158.84, 143.37, 139.23, 135.93, 133.56, 130.92, 130.67, 129.96, 129.07 (d, *J* = 8.2 Hz), 125.44 (d, *J* = 3.3 Hz), 121.06, 120.93, 118.52, 116.21, 116.04, 115.50, 113.90, 112.66, 43.79, 30.25. ¹⁹F-NMR (D₆-DMSO, 470 MHz): δ -110.28, -148.30.

1.4.108A 2-(4-bromophenyl)-1-(2-((2-fluorophenyl)thio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (6.2c) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **6.1c** (0.423 g, 0.8 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.64 mL, 4.8 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the crude imidazo[1,2-*a*]pyrimidinium salt as a crystalline white solid. The crude product was dissolved in DCM (10mL) and loaded onto a thin pad of silica gel. Impurities were removed using 1% MeOH/DCM before using 10%MeOH/DCM to elute the purified product (0.366 g, 89%). ¹H-NMR (D₆-DMSO, 500 MHz): δ 9.39 (1H, dd, *J* = 6.7, 1.0 Hz), 9.19 (1H, dd, *J* = 4.4, 1.0 Hz), 8.54 (1H, s), 7.84 (1H, dd, *J* = 6.7, 4.4 Hz), 7.79 (2H, d, *J* = 8.3 Hz), 7.59 (2H, d, *J* = 8.3 Hz), 7.30 (1H, m), 7.16 (2H, m), 7.07 (1H, t, *J* = 7.6 Hz), 4.68 (2H, t, *J* = 6.6 Hz). ¹³C-NMR (D₆-DMSO, 125 MHz): δ 161.48, 159.56, 158.44, 143.20, 139.02, 136.50, 132.86, 132.01, 131.00, 129.22 (d, *J* = 7.7 Hz), 125.36 (dd, *J* = 9.9, 3.6 Hz), 124.57, 120.86 (d, *J* = 17.2 Hz), 116.20 (d, *J* = 22.3 Hz), 115.37, 112.00, 43.82, 30.35. ¹⁹F-NMR (D₆-DMSO, 470 MHz): δ -110.13, -148.29.

1.4.109A 2-(4-cyanophenyl)-1-(2-((2-fluorophenyl)thio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**6.2d**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **6.1d** (0.428 g, 0.9 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.72 mL, 5.4 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the crude imidazo[1,2-*a*]pyrimidinium salt as a crystalline white solid. The crude product was dissolved in DCM (10mL) and loaded onto a thin pad of silica gel. Impurities were removed using 1% MeOH/DCM before using 10%MeOH/DCM to elute the purified product (0.395 g, 95%). ¹H-NMR (D₆-DMSO, 500 MHz): δ 9.41 (1H, dd, *J* = 6.7, 1.7 Hz), 9.20 (1H, dd, *J* = 4.4, 1.7 Hz), 8.55 (1H, s), 7.85 (1H, dd, *J* = 6.7, 4.4 Hz), 7.67 (4H, app s), 7.31 (1H, m), 7.18 (2H, m), 7.08 (1H, td, *J* = 7.6, 1.2 Hz), 4.70 (2H, t, *J* = 6.7 Hz), 3.38 (2H, t, *J* = 6.7 Hz). ¹³C-NMR (D₆-DMSO, 125 MHz): δ 161.50, 159.55, 158.45, 143.23, 139.03, 136.47 (d, *J* = 8.0 Hz), 131.86, 131.02, 129.94, 129.27 (d, *J* = 8.1 Hz), 125.40 (d, *J* = 3.6 Hz), 124.21, 120.87 (d, *J* = 17.5 Hz), 116.20 (d, *J* = 21.4 Hz), 115.37, 112.06, 43.83, 30.35. ¹⁹F-NMR (D₆-DMSO, 470 MHz): δ -110.14, -148.30.

1.4.110A 1-(2-((2-fluorophenyl)thio)ethyl)-2-(4-nitrophenyl)-1*H*-imidazo[1,2-
a]pyrimidin-4-ium tetrafluoroborate (**6.2e**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **6.1e** (0.525 g, 0.95 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.76 mL, 5.7 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the imidazo[1,2-
a]pyrimidinium salt as a crystalline tan solid (0.286 g, 60%). ¹H-NMR (D₆-DMSO, 500 MHz): δ 9.45 (1H, dd, *J* = 6.7, 1.7 Hz), 9.24 (1H, dd, *J* = 4.4, 1.7 Hz), 8.68 (1H, s), 8.35 (2H, d, *J* = 8.7 Hz), 7.93 (2H, d, *J* = 8.7 Hz), 7.88 (1H, dd, *J* = 6.7, 4.4 Hz), 7.21 (2H, m), 7.06 (2H, m), 4.75 (2H, t, *J* = 6.4 Hz), 3.40 (2H, t, *J* = 6.4 Hz). ¹³C-NMR (D₆-DMSO, 125 MHz): δ 160.13 (d, *J* = 242.6 Hz), 158.95, 148.98, 143.46, 139.26, 135.61, 131.73, 131.57, 130.46, 128.88 (d, *J* = 8.2 Hz), 125.41 (d, *J* = 3.3 Hz), 124.67, 121.06 9d, *J* = 16.5 Hz), 115.97 (d, *J* = 20.8 Hz), 115.54, 112.81, 43.61, 30.17. ¹⁹F-NMR (D₆-DMSO, 470 MHz): δ -110.33, -148.30.

1.4.111A 2-(2,4-difluorophenyl)-1-(2-((2-fluorophenyl)thio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**6.2f**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **6.1f** (0.432 g, 0.89 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.712 mL, 5.34 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the crude imidazo[1,2-*a*]pyrimidinium salt as a crystalline white solid. The crude product was dissolved in DCM (10mL) and loaded onto a thin pad of silica gel. Impurities were removed using 1% MeOH/DCM before using 10%MeOH/DCM to elute the purified product (0.392 g, 93%). ¹H-NMR (D₆-DMSO, 500 MHz): δ 9.44 (1H, dd, *J* = 6.7, 1.7 Hz), 9.22 (1H, dd, *J* = 4.4, 1.7 Hz), 8.62 (1H, s), 7.86 (1H, dd, *J* = 6.7, 4.4 Hz), 7.71 (1H, q, *J* = 8.4 Hz), 7.55 (1H, td, *J* = 10.6, 2.2 Hz), 7.28 (3H, m), 7.16 (1H, t, *J* = 9.6 Hz), 7.10 (1H, t, *J* = 7.6 Hz), 4.59 (2H, t, *J* = 6.6 Hz), 3.40 (2H, t, *J* = 6.6 Hz). ¹³C-NMR (D₆-DMSO, 125 MHz): δ 161.42 (d, *J* = 14.0 Hz), 159.40 (d, *J* = 10.2 Hz), 158.77, 145.77, 143.25, 139.19, 134.24 (dd, *J* = 13.9, 4.1 Hz), 130.59 (d, *J* = 15.7 Hz), 129.08 (d, *J* = 8.5 Hz), 125.43 (d, *J* = 3.0 Hz), 121.03 (d, *J* = 17.6 Hz), 116.18 (d, *J* = 23.2 Hz), 115.39, 113.61, 113.35 (d, *J* = 21.6, 3.5 Hz), 109.86 (dd, *J* = 15.4, 4.2 Hz), 105.77 (t, *J* = 25.2 Hz), 43.73, 30.14. ¹⁹F-NMR (D₆-DMSO, 470 MHz): δ -104.38, -108.11, -110.43, -148.29.

1.4.112A 1-(2-((3-bromophenyl)thio)ethyl)-2-(4-chlorophenyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (7.2a) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **7.1a** (0.449 g, 0.83 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.66 mL, 4.98 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the imidazo[1,2-*a*]pyrimidinium salt as a crystalline white solid (0.353 g, 66%). ¹H-NMR (D₆-DMSO, 500 MHz): δ 9.38 (1H, m), 9.18 (1H, m), 8.53 (1H, m), 7.82 (1H, m), 7.66 (4H, m), 7.33 (2H, m), 7.10 (2H, m), 4.67 (2H, t, *J* = 5.4 Hz), 3.42 (2H, t, *J* = 5.4 Hz). ¹³C-NMR (D₆-DMSO, 125 MHz): δ 158.42, 143.18, 139.02, 137.05, 136.56, 136.49, 131.95, 131.24, 130.47, 129.99, 129.48, 127.53, 124.25, 122.68, 115.42, 112.00, 43.83, 30.86.

1.4.113A 2-([1,1'-biphenyl]-4-yl)-1-(2-((3-bromophenyl)thio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (7.2b) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **7.1b** (0.519 g, 0.89 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.71 mL, 5.34 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the imidazo[1,2-*a*]pyrimidinium salt as a crystalline white solid (0.488 g, 95%). ¹H-NMR (D₆-DMSO, 500 MHz): δ 9.39 (1H, dd, *J* = 6.7, 1.7 Hz), 9.19 (1H, dd, *J* = 4.4, 1.7 Hz), 8.55 (1H, s), 7.90 (2H, d, *J* = 8.3 Hz), 7.83 (1H, dd, *J* = 6.7, 4.4 Hz), 7.77 (4H, m), 7.56 (2H, t, *J* = 7.6 Hz), 7.47 (1H, m), 7.39 (1H, m), 7.30 (1H, m), 7.11 (2H, m), 4.75 (2H, t, *J* = 6.6 Hz), 3.48 (2H, t, *J* = 6.6 Hz).

1.4.114A 2-(4-bromophenyl)-1-(2-((3-bromophenyl)thio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (7.2c) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **7.1c** (0.513 g, 0.87 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.7 mL, 5.22 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the crude imidazo[1,2-*a*]pyrimidinium salt as a crystalline white solid. The crude product was dissolved in DCM (10mL) and loaded onto a thin pad of silica gel. Impurities were removed using 1% MeOH/DCM before using 10%MeOH/DCM to elute the purified product (0.452 g, 90%). ¹H-NMR (D₆-DMSO, 500 MHz): δ 9.41 (1H, dd, *J* = 6.7, 1.6 Hz), 9.22 (1H, dd, *J* = 4.4, 1.6 Hz), 8.56 (1H, s), 7.86 (1H, dd, *J* = 6.7, 4.4 Hz), 7.83 (2H, d, *J* = 8.5 Hz), 7.63 (2H, d, *J* = 8.5 Hz), 7.38 (2H, m), 7.18 (1H, t, *J* = 7.9 Hz), 7.10 (1H, d, *J* = 7.9 Hz), 4.71 (2H, t, *J* = 6.5 Hz), 3.46 (2H, t, *J* = 6.5 Hz). ¹³C-NMR (D₆-DMSO, 125 MHz): δ 158.43, 143.19, 139.02, 137.05, 136.64, 132.91, 132.10, 131.24, 130.45, 129.48, 127.53, 125.36, 124.60, 122.69, 115.43, 111.95, 43.85, 30.86.

1.4.115A 1-(2-((3-bromophenyl)thio)ethyl)-2-(4-cyanophenyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (7.2d) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **7.1d** (0.457 g, 0.86 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.69 mL, 5.16 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the imidazo[1,2-*a*]pyrimidinium salt as a crystalline white solid (0.407 g, 90%). ¹H-NMR (CDCl₃, 500 MHz): δ 9.18 (1H, dd, *J* = 6.8, 1.6 Hz), 8.94 (1H, dd, *J* = 4.4, 1.6 Hz), 8.26 (1H, s), 7.78 (2H, d, *J* = 8.7 Hz), 7.70 (2H, d, *J* = 8.7 Hz), 7.54 (1H, dd, *J* = 6.8, 4.4 Hz), 7.32 (1H, dt, *J* = 8.0, 0.9 Hz), 7.22 (1H, s), 7.07 (1H, t, *J* = 7.8 Hz), 7.01 (1H, dt, *J* = 8.0, 1.2 Hz), 4.66 (2H, t, *J* = 7.0 Hz), 3.34 (2H, t, *J* = 7.0 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 157.47, 142.77, 138.83, 136.28, 135.45, 133.10, 132.00, 130.69, 130.64, 130.37, 128.80, 128.26, 123.01, 117.45, 115.38, 115.00, 112.85, 44.25, 31.83.

1.4.116A 1-(2-((3-bromophenyl)thio)ethyl)-2-(4-nitrophenyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (7.2e) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **7.1e** (0.516 g, 0.93 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.74 mL, 5.58 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the imidazo[1,2-*a*]pyrimidinium salt as a crystalline orange solid (0.400 g, 79%). ¹H-NMR (D₆-DMSO, 500 MHz): δ 9.45 (1H, dd, *J* = 6.7, 1.7 Hz), 9.25 (1H, dd, *J* = 4.5, 1.7 Hz), 8.69 (1H, s), 8.38 (2H, d, *J* = 8.5 Hz), 7.94 (2H, d, *J* = 8.5 Hz), 7.88 (1H, dd, *J* = 6.7, 4.5 Hz), 7.30 (1H, dt, *J* = 7.4, 1.5 Hz), 7.22 (1H, s), 7.13 (2H, m), 4.75 (2H, t, *J* = 6.3 Hz), 3.46 (2H, t, *J* = 6.3 Hz). ¹³C-NMR (D₆-DMSO, 125 MHz): δ 158.93, 148.93, 143.45, 139.26, 137.12, 135.78, 131.82, 131.64, 131.20, 129.97, 129.23, 127.09, 124.72, 122.63, 115.59, 112.76, 43.55, 30.71.

1.4.117A 1-(2-((3-bromophenyl)thio)ethyl)-2-(2,4-difluorophenyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (7.2f) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **7.1f** (0.496 g, 0.91 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.73 mL, 5.5 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the crude imidazo[1,2-*a*]pyrimidinium salt as a crystalline white solid. The crude product was dissolved in DCM (10mL) and loaded onto a thin pad of silica gel. Impurities were removed using 1% MeOH/DCM before using 10%MeOH/DCM to elute the purified product (0.432 g, 89%). ¹H-NMR (D₆-DMSO, 500 MHz): δ 9.44 (1H, dd, *J* = 6.7, 1.6 Hz), 9.24 (1H, dd, *J* = 4.4, 1.6 Hz), 8.62 (1H, s), 7.87 (1H, dd, *J* = 6.7, 4.4 Hz), 7.75 (1H, m), 7.57 (1H, td, *J* = 10.6, 2.6 Hz), 7.35 (3H, m), 7.19 (1H, t, *J* = 7.7 Hz), 7.15 (1H, d, *J* = 7.9 Hz), 4.61 (2H, t, *J* = 6.4 Hz), 3.47 (2H, t, *J* = 6.4 Hz). ¹³C-NMR (D₆-DMSO, 125 MHz): δ 164.61 (dd, *J* = 252.9, 10.7 Hz), 160.40 (dd, *J* = 251.8, 13.4 Hz), 158.73, 143.22, 139.16, 137.12, 134.38 (dd, *J* = 10.5, 2.2 Hz), 131.28, 130.78, 130.12, 129.35, 127.15, 122.68, 115.44, 113.54, 113.45 (dd, *J* = 22.0, 3.3 Hz), 109.94 (dd, *J* = 14.5, 3.7 Hz), 105.80 (t, *J* = 26.0 Hz), 43.73, 30.69. ¹⁹F-NMR (D₆-DMSO, 470 MHz): δ -104.11, -108.15, -148.30.

1.4.118A 1-(2-((4-bromophenyl)thio)ethyl)-2-(4-chlorophenyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**8.2a**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **8.1a** (0.522 g, 0.96 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.77 mL, 5.76 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the imidazo[1,2-*a*]pyrimidinium salt as a crystalline white solid (0.437 g, 86%). ¹H-NMR (D₆-DMSO, 500 MHz): δ 9.38 (1H, m), 9.18 (1H, m), 8.53 (1H, m), 7.83 (1H, m), 7.66 (4H, m), 7.37 (2H, m), 7.03 (2H, m), 4.64 (2H, m). ¹³C-NMR (D₆-DMSO, 125 MHz): δ 158.44, 143.14, 139.01, 136.51, 133.72, 132.20, 132.01, 130.67, 129.97, 124.25, 119.77, 115.36, 112.02, 43.69, 30.96.

1.4.119A 2-([1,1'-biphenyl]-4-yl)-1-(2-((4-bromophenyl)thio)ethyl)-1*H*-imidazo[1,2-
a]pyrimidin-4-ium tetrafluoroborate (**8.2b**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **8.1b** (0.486 g, 0.83 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.66 mL, 5 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the imidazo[1,2-
a]pyrimidinium salt as a crystalline white solid (0.431 g, 90%). ¹H-NMR (D₆-DMSO, 500 MHz): δ 9.42 (1H, dd, *J* = 6.7, 1.7 Hz), 9.21 (1H, dd, *J* = 4.4, 1.7 Hz), 8.58 (1H, s), 7.92 (2H, d, *J* = 8.7 Hz), 7.86 (1H, dd, *J* = 6.7, 4.4 Hz), 7.82 (2H, d, *J* = 7.3 Hz), 7.76 (2H, d, *J* = 8.2 Hz), 7.60 (2H, t, *J* = 7.7 Hz), 7.51 (1H, t, *J* = 7.3 Hz), 7.36 (2H, d, *J* = 8.5 Hz), 7.08 (2H, d, *J* = 8.5 Hz), 4.73 (2H, t, *J* = 6.7 Hz), 3.46 (2H, t, *J* = 6.7 Hz). ¹³C-NMR (D₆-DMSO, 125 MHz): δ 158.22, 143.20, 142.98, 139.29, 138.94, 137.39, 133.76, 132.21, 130.81, 130.72, 129.66, 128.84, 128.84, 128.02, 127.45, 124.41, 119.78, 115.33, 111.78, 43.97, 31.06.

1.4.120A 2-(4-bromophenyl)-1-(2-((4-bromophenyl)thio)ethyl)-1*H*-imidazo[1,2-
a]pyrimidin-4-ium tetrafluoroborate (**8.2c**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **8.1c** (0.571 g, 0.97 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.78 mL, 5.82 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the imidazo[1,2-a]pyrimidinium salt as a crystalline white solid (0.471 g, 82%). ¹H-NMR (D₆-DMSO, 500 MHz): δ 9.40 (1H, dd, *J* = 6.7, 1.7 Hz), 9.20 (1H, dd, *J* = 4.5, 1.7 Hz), 8.55 (1H, s), 7.85 (1H, dd, *J* = 6.7, 4.5 Hz), 7.81 (2H, d, *J* = 8.4 Hz), 7.60 (2H, d, *J* = 8.4 Hz), 7.40 (2H, d, *J* = 8.4 Hz), 7.04 (2H, d, *J* = 8.4 Hz), 4.65 (2H, t, *J* = 6.6 Hz), 3.40 (2H, t, *J* = 6.6 Hz). ¹³C-NMR (D₆-DMSO, 125 MHz): δ 158.45, 143.16, 139.01, 136.60, 133.73, 132.90, 132.21, 132.17, 130.63, 125.33, 124.63, 119.76, 115.36, 111.97, 43.69, 30.95.

1.4.121A 1-(2-((4-bromophenyl)thio)ethyl)-2-(4-cyanophenyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**8.2d**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **8.1d** (0.518 g, 0.97 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.78 mL, 5.82 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the imidazo[1,2-*a*]pyrimidinium salt as a crystalline tan solid (0.328 g, 65%). ¹H-NMR (D₆-DMSO, 500 MHz): δ 9.44 (1H, dd, *J* = 6.7, 1.6 Hz), 9.24 (1H, dd, *J* = 4.4, 1.6 Hz), 8.64 (1H, s), 8.07 (2H, d, *J* = 8.3 Hz), 7.87 (3H, m), 7.40 (2H, d, *J* = 8.7 Hz), 7.05 (2H, d, *J* = 8.3 Hz), 4.70 (2h, t, *J* = 6.4 Hz), 3.43 (2H, t, *J* = 6.4 Hz). ¹³C-NMR (D₆-DMSO, 125 MHz): δ 158.84, 143.39, 139.22, 136.07, 133.75, 133.62, 132.19, 131.06, 130.48, 130.03, 119.71, 118.56, 115.65, 113.93, 112.64, 43.71, 30.90.

1.4.122A 1-(2-((4-bromophenyl)thio)ethyl)-2-(4-nitrophenyl)-1*H*-imidazo[1,2-
a]pyrimidin-4-ium tetrafluoroborate (**8.2e**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **8.1e** (0.525 g, 0.95 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.76 mL, 5.7 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the imidazo[1,2-
a]pyrimidinium salt as a crystalline tan solid (0.446 g, 86%). ¹H-NMR (D₆-DMSO, 500 MHz): δ 9.46 (1H, dd, *J* = 6.7, 1.7 Hz), 9.25 (1H, dd, *J* = 4.5, 1.7 Hz), 8.69 (1H, s), 8.38 (2H, d, *J* = 8.8 Hz), 7.94 (2H, d, *J* = 8.8 Hz), 7.89 (2H, d, *J* = 6.7, 4.5 Hz), 7.35 (2H, d, *J* = 8.6 Hz), 7.04 (2H, d, *J* = 8.6 Hz), 4.73 (2H, t, *J* = 6.4 Hz), 3.44 (2H, t, *J* = 6.4 Hz). ¹³C-NMR (D₆-DMSO, 125 MHz): δ 158.94, 148.97, 143.41, 139.24, 135.74, 133.78, 132.10, 131.70, 130.25, 124.75, 119.50, 115.54, 79.44, 43.49, 30.77.

1.4.123A 1-(2-((4-bromophenyl)thio)ethyl)-2-(2,4-difluorophenyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**8.2f**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **8.1f** (0.479 g, 0.88 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.7 mL, 5.3 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the crude imidazo[1,2-*a*]pyrimidinium salt as a crystalline yellow solid. The crude product was dissolved in DCM (10mL) and loaded onto a thin pad of silica gel. Impurities were removed using 1% MeOH/DCM before using 10%MeOH/DCM to elute the purified product (0.372 g, 79%). ¹H-NMR (D₆-DMSO, 500 MHz): δ 9.44 (1H, dd, *J* = 6.6, 1.3 Hz), 9.23 (1H, dd, *J* = 4.4, 1.3 Hz), 8.61 (1H, s), 7.87 (1H, dd, *J* = 6.6, 4.4 Hz), 7.73 (1H, q, *J* = 6.5 Hz), 7.58 (1H, td, *J* = 10.4, 2.0 Hz), 7.42 (2H, d, *J* = 8.4 Hz), 7.34 (1H, td, *J* = 8.8, 2.0 Hz), 7.09 (2H, d, *J* = 8.4 Hz), 4.58 (2H, t, *J* = 6.4 Hz), 3.43 (2H, t, *J* = 6.4 Hz). ¹³C-NMR (D₆-DMSO, 125 MHz): δ 164.66 (dd, *J* = 252.0, 13.0 Hz), 160.37 (dd, *J* = 250.2, 13.0 Hz), 158.77, 143.20, 139.16, 134.40 (d, *J* = 9.4 Hz), 133.78, 132.22, 130.69, 130.43, 119.66, 115.38, 113.58, 113.43 (dd, *J* = 21.5, 2.9 Hz), 109.89 (dd, *J* = 14.1, 3.5 Hz), 105.84 (t, *J* = 25.3 Hz), 43.70, 30.87. ¹⁹F-NMR (D₆-DMSO, 470 MHz): δ -104.30, -108.08, -148.30.

1.4.124A 2-(4-chlorophenyl)-1-(2-((4-chlorophenyl)thio)ethyl)-1*H*-imidazo[1,2-
a]pyrimidin-4-ium tetrafluoroborate (**9.2a**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **9.1a** (0.469 g, 0.94 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.75 mL, 5.6 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the imidazo[1,2-
a]pyrimidinium salt as a crystalline white solid (0.365 g, 80%). ¹H-NMR (D₆-DMSO, 500 MHz): δ 9.41 (1H, dd, *J* = 6.7, 1.7 Hz), 9.21 (1H, dd, *J* = 4.4, 1.7 Hz), 8.56 (1H, s), 7.86 (1H, dd, *J* = 6.7, 4.4 Hz), 7.68 (4H, app s), 7.28 (2H, d, *J* = 8.4 Hz), 7.13 (2H, d, *J* = 8.4 Hz), 4.67 (2H, t, *J* = 6.6 Hz), 3.41 (2H, t, *J* = 6.6 Hz). ¹³C-NMR (D₆-DMSO, 125 MHz): δ 158.45, 143.15, 139.01, 136.50, 133.16, 132.01, 131.51, 130.50, 129.97, 129.32, 124.26, 115.36, 112.03, 43.72, 31.11.

1.4.125A 2-([1,1'-biphenyl]-4-yl)-1-(2-((4-chlorophenyl)thio)ethyl)-1*H*-imidazo[1,2-
a]pyrimidin-4-ium tetrafluoroborate (**9.2b**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **9.1b** (0.518 g, 0.96 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.77 mL, 5.8 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the imidazo[1,2-
a]pyrimidinium salt as a crystalline white solid (0.462 g, 91%). ¹H-NMR (D₆-DMSO, 500 MHz): δ 9.42 (1H, dd, *J* = 6.7, 1.7 Hz), 9.21 (1H, dd, *J* = 4.4, 1.7 Hz), 8.58 (1H, s), 7.92 (2H, d, *J* = 8.4 Hz), 7.86 (1H, dd, *J* = 6.7, 4.4 Hz), 7.82 (2H, d, *J* = 7.6 Hz), 7.76 (2H, d, *J* = 8.4 Hz), 7.60 (2H, t, *J* = 7.7 Hz), 7.51 (1H, t, *J* = 7.6 Hz), 7.24 (2H, d, *J* = 8.6 Hz), 7.15 (2H, d, *J* = 8.6 Hz), 4.73 (2H, t, *J* = 6.7 Hz), 3.46 (2H, t, *J* = 6.7 Hz). ¹³C-NMR (D₆-DMSO, 125 MHz): δ 158.22, 143.20, 142.96, 139.21, 138.94, 137.38, 133.18, 131.51, 130.71, 130.65, 129.65, 129.33, 128.84, 128.02, 127.43, 124.37, 115.32, 111.78, 43.95, 31.22.

1.4.126A 2-(4-bromophenyl)-1-(2-((4-chlorophenyl)thio)ethyl)-1*H*-imidazo[1,2-
a]pyrimidin-4-ium tetrafluoroborate (**9.2c**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **9.1c** (0.509 g, 0.94 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.75 mL, 5.6 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the imidazo[1,2-
a]pyrimidinium salt as a crystalline white solid (0.463 g, 87%). ¹H-NMR (D₆-DMSO, 500 MHz): δ 9.40 (1H, dd, *J* = 6.7, 1.6 Hz), 9.20 (1H, dd, *J* = 4.4, 1.6 Hz), 8.55 (1H, s), 7.85 (1H, dd, *J* = 6.7, 4.4 Hz), 7.81 (2H, d, *J* = 8.3 Hz), 7.60 (2H, d, *J* = 8.3 Hz), 7.28 (2H, d, *J* = 8.1 Hz), 7.11 (2H, d, *J* = 8.1 Hz), 4.66 (2H, t, *J* = 6.6 Hz), 3.40 (2H, t, *J* = 6.6 Hz). ¹³C-NMR (D₆-DMSO, 125 MHz): δ 158.45, 143.16, 139.01, 136.59, 133.16, 132.90, 132.16, 131.50, 130.46, 129.33, 125.33, 124.63, 115.37, 111.97, 43.71, 31.11.

1.4.127A 1-(2-((4-chlorophenyl)thio)ethyl)-2-(4-cyanophenyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**9.2d**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **9.1d** (0.435 g, 0.89 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.71 mL, 5.3 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the imidazo[1,2-*a*]pyrimidinium salt as a crystalline yellow solid (0.122 g, 29%). ¹H-NMR (D₆-DMSO, 500 MHz): δ 9.41 (1H, m), 9.21 (1H, m), 8.61 (1H, m), 8.04 (2H, m), 7.84 (3H, m), 7.25 (2H, m), 7.08 (2H, m), 4.68 (2H, m), 3.39 (2H, m). ¹³C-NMR (D₆-DMSO, 125 MHz): δ 158.83, 143.31, 139.19, 136.13, 133.62, 133.18, 131.46, 131.05, 130.30, 129.99, 129.31, 118.45, 115.49, 113.97, 112.64, 43.71, 31.04.

1.4.128A 1-(2-((4-chlorophenyl)thio)ethyl)-2-(4-nitrophenyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**9.2e**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **9.1e** (0.472 g, 0.93 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.74 mL, 5.58 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the imidazo[1,2-*a*]pyrimidinium salt as a crystalline yellow solid (0.237 g, 51%). ¹H-NMR (D₆-DMSO, 500 MHz): δ 9.46 (1H, dd, *J* = 6.7, 1.6 Hz), 9.25 (1H, dd, *J* = 4.4, 1.6 Hz), 8.69 (1H, s), 8.38 (2H, d, *J* = 8.4 Hz), 7.94 (2H, d, *J* = 8.4 Hz), 7.89 (1H, dd, *J* = 6.7, 4.4 Hz), 7.23 (2H, d, *J* = 8.6 Hz), 7.11 (2H, d, *J* = 8.6 Hz), 4.73 (2H, t, *J* = 6.4 Hz), 3.44 (2H, t, *J* = 6.4 Hz). ¹³C-NMR (D₆-DMSO, 125 MHz): δ 158.94, 148.98, 143.50, 139.24, 135.71, 133.23, 131.70, 131.29, 130.09, 129.22, 124.75, 115.53, 112.77, 43.53, 30.93.

1.4.129A 1-(2-((4-chlorophenyl)thio)ethyl)-2-(2,4-difluorophenyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**9.2f**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **9.1f** (0.377 g, 0.75 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.6 mL, 4.5 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the imidazo[1,2-*a*]pyrimidinium salt as a crystalline white solid (0.316 g, 86%). ¹H-NMR (D₆-DMSO, 500 MHz): δ 9.43 (1H, dd, *J* = 6.8, 1.6 Hz), 9.22 (1H, dd, *J* = 4.4, 1.6 Hz), 8.61 (1H, s), 7.86 (1H, dd, *J* = 6.8, 4.4 Hz), 7.73 (1H, m), 7.58 (1H, td, *J* = 10.1, 2.3 Hz), 7.34 (1H, td, *J* = 8.6, 2.3 Hz), 7.29 (2H, d, *J* = 8.6 Hz), 7.16 (2H, d, *J* = 8.6 Hz), 4.58 (2H, t, *J* = 6.5 Hz), 3.42 (2H, t, *J* = 6.5 Hz). ¹³C-NMR (D₆-DMSO, 125 MHz): δ 158.77, 143.21, 139.17, 134.41 (d, *J* = 11.0 Hz), 133.22, 131.42, 130.68, 130.26, 129.34, 115.38, 113.43 (dd, *J* = 21.8, 3.1 Hz), 109.89 (dt, *J* = 14.8, 2.7 Hz), 105.86 (t, *J* = 26.6 Hz), 43.73, 31.03. ¹⁹F-NMR (D₆-DMSO, 470 MHz): δ -104.37, -108.08, -148.29.

1.4.130A 2-(4-chlorophenyl)-1-(2-((4-fluorophenyl)thio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**10.2a**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **10.1a** (0.460 g, 0.95 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.76 mL, 5.7 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the crude imidazo[1,2-*a*]pyrimidinium salt as a crystalline white solid. The crude product was dissolved in DCM (10mL) and loaded onto a thin pad of silica gel. Impurities were removed using 1% MeOH/DCM before using 10%MeOH/DCM to elute the purified product (0.394 g, 88%). ¹H-NMR (D₆-DMSO, 500 MHz): δ 9.39 (1H, dd, *J* = 6.7, 1.6 Hz), 9.19 (1H, dd, *J* = 4.4, 1.6 Hz), 8.53 (1H, s), 7.84 (1H, dd, *J* = 6.7, 4.4 Hz), 7.68 (4H, app s), 7.16 (2H, m), 7.08 (2H, m), 4.65 (2H, t, *J* = 6.7 Hz). ¹³C-NMR (D₆-DMSO, 125 MHz): δ 158.43, 143.15, 139.00, 136.50, 136.47 (d, *J* = 12.5 Hz), 132.03, 131.97, 130.00, 129.41 (d, *J* = 2.9 Hz), 124.27, 116.50 (d, *J* = 24.1 Hz), 115.36, 112.05, 49.07, 44.03, 32.07. ¹⁹F-NMR (D₆-DMSO, 470 MHz): δ -115.10, -148.30.

1.4.131A 2-([1,1'-biphenyl]-4-yl)-1-(2-((4-fluorophenyl)thio)ethyl)-1*H*-imidazo[1,2-
a]pyrimidin-4-ium tetrafluoroborate (**10.2b**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **10.1b** (0.524 g, 1 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.8 mL, 6 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the imidazo[1,2-a]pyrimidinium salt as a crystalline white solid (0.463 g, 90%). ¹H-NMR (D₆-DMSO, 500 MHz): δ 9.41 (1H, dd, *J* = 6.7, 1.7 Hz), 9.20 (1H, dd, *J* = 4.3, 1.7 Hz), 8.57 (1H, s), 7.93 (2H, d, *J* = 8.3 Hz), 7.85 (1H, dd, *J* = 6.7, 4.3 Hz), 7.82 (2H, d, *J* = 7.9 Hz), 7.77 (2H, d, *J* = 8.3 Hz), 7.60 (2H, t, *J* = 7.6 Hz), 7.51 (1H, t, *J* = 7.3 Hz), 7.20 (2H, m), 7.04 (2H, t, *J* = 8.8 Hz), 4.72 (2H, t, *J* = 6.7 Hz), 3.41 (2H, t, *J* = 6.7 Hz). ¹³C-NMR (D₆-DMSO, 125 MHz): δ 158.20, 143.19, 142.95, 139.21, 138.91, 137.30, 132.20 (d, *J* = 8.4 Hz), 130.68, 129.66, 129.38, 128.85, 128.04, 127.39, 124.38, 116.58, 116.41, 115.31, 111.80, 44.24, 33.20. ¹⁹F-NMR (D₆-DMSO, 470 MHz): δ -115.07, -148.30.

1.4.132A 2-(4-bromophenyl)-1-(2-((4-fluorophenyl)thio)ethyl)-1*H*-imidazo[1,2-
a]pyrimidin-4-ium tetrafluoroborate (**10.2c**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **10.1c** (0.504 g, 0.96 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.77 mL, 5.8 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the imidazo[1,2-
a]pyrimidinium salt as a crystalline white solid (0.389 g, 79%). ¹H-NMR (D₆-DMSO, 500 MHz): δ 9.40 (1H, dd, *J* = 6.6, 1.5 Hz), 9.20 (1H, dd, *J* = 4.4, 1.5 Hz), 8.54 (1H, s), 7.84 (3H, m), 7.61 (2H, d, *J* = 8.4 Hz), 7.17 (2H, m), 7.08 (2H, t, *J* = 8.7 Hz), 4.65 (2H, t, *J* = 6.7 Hz). ¹³C-NMR (D₆-DMSO, 125 MHz): δ 161.52 (d, *J* = 244.2 Hz), 158.43, 143.16, 139.00, 136.49, 132.92, 132.12, 131.98 (d, *J* = 8.2 Hz), 129.38 (d, *J* = 3.3 Hz), 125.33, 124.63, 116.50 (d, *J* = 22.0 Hz), 115.36, 111.99, 44.02, 32.06. ¹⁹F-NMR (D₆-DMSO, 470 MHz): δ -115.05, -148.30.

1.4.133A 2-(4-cyanophenyl)-1-(2-((4-fluorophenyl)thio)ethyl)-1*H*-imidazo[1,2-
a]pyrimidin-4-ium tetrafluoroborate (**10.2d**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **10.1d** (0.454 g, 0.96 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.77 mL, 5.8 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the imidazo[1,2-
a]pyrimidinium salt as a crystalline white solid (0.310 g, 70%). ¹H-NMR (D₆-DMSO, 500 MHz): δ 9.43 (1H, m), 9.23 (1H, m), 8.63 (1H, s), 8.09 (2H, d, *J* = 8.3 Hz), 7.87 (3H, m), 7.16 (2H, m), 7.08 (2H, t, *J* = 8.8 Hz), 4.69 (2H, t, *J* = 6.5 Hz), 3.36 (2H, t, *J* = 6.5 Hz). ¹³C-NMR (D₆-DMSO, 125 MHz): δ 161.49 (d, *J* = 244.6 Hz), 158.82, 143.33, 139.18, 135.91, 133.66, 131.75 (d, *J* = 8.1 Hz), 131.03, 130.00, 129.41 (d, *J* = 2.9 Hz), 118.50, 116.52 (d, *J* = 22.0 Hz), 115.49, 113.93, 112.68, 44.06, 31.98. ¹⁹F-NMR (D₆-DMSO, 470 MHz): δ -115.23, -148.30.

1.4.134A 1-(2-((4-fluorophenyl)thio)ethyl)-2-(4-nitrophenyl)-1*H*-imidazo[1,2-
a]pyrimidin-4-ium tetrafluoroborate (**10.2e**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **10.1e** (0.525 g, 0.95 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.76 mL, 5.7 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the imidazo[1,2-
a]pyrimidinium salt as a crystalline white solid (0.400 g, 87%). ¹H-NMR (D₆-DMSO, 500 MHz): δ 9.44 (1H, dd, *J* = 6.7, 1.7 Hz), 9.23 (1H, dd, *J* = 4.4, 1.7 Hz), 8.67 (1H, s), 8.65 (2H, d, *J* = 8.6 Hz), 7.94 (2H, d, *J* = 8.6 Hz), 7.87 (1H, dd, *J* = 6.7, 4.4 Hz), 7.15 (2H, m), 7.03 (2H, t, *J* = 8.8 Hz), 4.71 (2H, t, *J* = 6.6 Hz), 3.36 (2H, t, *J* = 6.6 Hz). ¹³C-NMR (D₆-DMSO, 125 MHz): δ 162.41, 160.46, 158.93, 149.08, 143.41, 139.21, 135.56, 131.67 (t, *J* = 8.2 Hz), 129.42 (d, *J* = 2.7 Hz), 124.79, 116.52, 116.34, 115.53, 112.84, 43.93, 31.92. ¹⁹F-NMR (D₆-DMSO, 470 MHz): δ -115.42, -148.30.

1.4.135A 2-(2,4-difluorophenyl)-1-(2-((4-fluorophenyl)thio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**10.2f**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **10.1f** (0.438 g, 0.9 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.72 mL, 5.4 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the crude imidazo[1,2-*a*]pyrimidinium salt as a crystalline white solid. The crude product was dissolved in DCM (10mL) and loaded onto a thin pad of silica gel. Impurities were removed using 1% MeOH/DCM before using 10%MeOH/DCM to elute the purified product (0.241 g, 57%). ¹H-NMR (D₆-DMSO, 500 MHz): δ 9.43 (1H, dd, *J* = 6.7, 1.7 Hz), 9.22 (1H, dd, *J* = 4.4, 1.7 Hz), 8.61 (1H, s), 7.86 (1H, dd, *J* = 6.7, 4.4 Hz), 7.74 (1H, m), 7.60 (1H, td, *J* = 10.2, 2.6 Hz), 7.36 (1H, td, *J* = 8.7, 2.4 Hz), 7.21 (2H, m), 7.10 (2H, t, *J* = 8.8 Hz), 4.55 (2H, t, *J* = 6.7 Hz), 3.37 (2H, t, *J* = 6.7 Hz). ¹³C-NMR (D₆-DMSO, 125 MHz): δ 162.52, 160.54, 158.76, 143.21, 139.16, 134.43 (d, *J* = 10.5 Hz), 131.79 (d, *J* = 8.7 Hz), 130.59, 129.43 (d, *J* = 3.6 Hz), 116.63, 116.45, 115.37, 113.62, 113.46 (dd, *J* = 22.0, 5.0 Hz), 109.89 (dd, *J* = 13.8, 3.1 Hz), 105.87 (t, *J* = 26.3 Hz), 44.00, 32.00. ¹⁹F-NMR (D₆-DMSO, 470 MHz): δ -104.43, -108.07, -115.37, -148.30.

1.4.136A 2-(4-chlorophenyl)-1-(2-(*p*-tolylthio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**11.2a**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **11.1a** (0.420 g, 0.88 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.7 mL, 5.28 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the crude imidazo[1,2-*a*]pyrimidinium salt as a crystalline tan solid. The crude product was dissolved in DCM (10mL) and loaded onto a thin pad of silica gel. Impurities were removed using 1% MeOH/DCM before using 10%MeOH/DCM to elute the purified product (0.385 g, 94%). ¹H-NMR (D₆-DMSO, 500 MHz): δ 9.34 (1H, d, *J* = 6.6 Hz), 9.16 (1H, d, *J* = 4.1 Hz), 8.49 (1H, s), 7.81 (1H, dd, *J* = 6.6, 4.1 Hz), 7.66 (4H, app s), 6.98 (4H, m), 4.62 (2H, t, *J* = 6.6 Hz), 3.31 (2H, t, *J* = 6.6 Hz), 2.27 (3H, s). ¹³C-NMR (D₆-DMSO, 125 MHz): δ 158.36, 143.10, 138.94, 136.71, 136.49, 136.41, 131.98, 130.11, 130.06, 129.99, 129.83, 124.27, 115.30, 112.84, 44.32, 31.75, 21.02.

1.4.137A 2-([1,1'-biphenyl]-4-yl)-1-(2-(*p*-tolylthio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**11.2b**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **11.1b** (0.423 g, 0.81mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.65 mL, 4.86 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the imidazo[1,2-*a*]pyrimidinium salt as a crystalline tan solid (0.369 g, 89%).

1.4.138A 2-(4-bromophenyl)-1-(2-(*p*-tolylthio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**11.2c**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **12.1c** (0.476 g, 0.91 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.73 mL, 5.46 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the imidazo[1,2-*a*]pyrimidinium salt as a crystalline tan solid (0.426 g, 91%). ¹H-NMR (D₆-DMSO, 500 MHz): δ 9.34 (1H, dd, *J* = 6.7, 1.2 Hz), 9.16 (1H, dd, *J* = 4.4, 1.2 Hz), 8.49 (1H, s), 7.80 (3H, m), 7.58 (2H, d, *J* = 8.2 Hz), 6.98 (4H, m), 4.61 (2H, t, *J* = 6.7 Hz), 3.31 (2H, t, *J* = 6.7 Hz), 2.28 (3H, s). ¹³C-NMR (D₆-DMSO, 125 MHz): δ 158.36, 143.11, 138.94, 136.69, 136.49, 132.91, 132.13, 130.11, 130.07, 129.79, 125.32, 124.63, 115.30, 111.98, 44.30, 31.73, 21.06.

1.4.139A 2-(4-cyanophenyl)-1-(2-(*p*-tolylthio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**11.2d**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **11.1d** (0.432 g, 0.92 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.74 mL, 5.52 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the crude imidazo[1,2-*a*]pyrimidinium salt as a crystalline tan solid. The crude product was dissolved in DCM (10mL) and loaded onto a thin pad of silica gel. Impurities were removed using 1% MeOH/DCM before using 10%MeOH/DCM to elute the purified product (0.164 g, 39%). ¹H-NMR (D₆-DMSO, 500 MHz): δ 9.41 (1H, dd, *J* = 6.7, 1.6 Hz), 9.22 (1H, dd, *J* = 4.4, 1.6 Hz), 8.61 (1H, s), 8.07 (2H, d, *J* = 8.3 Hz), 7.86 (3H, m), 7.02 (2H, d, *J* = 8.6 Hz), 6.96 (2H, d, *J* = 8.6 Hz), 4.68 (2H, t, *J* = 6.6 Hz), 3.35 (2H, t, *J* = 6.6 Hz), 2.31 (3H, s). ¹³C-NMR (D₆-DMSO, 125 MHz): δ 158.75, 143.27, 139.14, 136.59, 135.94, 133.63, 131.03, 130.15, 130.04, 129.98, 129.57, 118.58, 115.43, 113.86, 112.63, 44.25, 31.65, 20.99.

1.4.140A 2-(4-nitrophenyl)-1-(2-(*p*-tolylthio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**11.2e**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **11.1e** (0.466 g, 0.95 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.76 mL, 5.7 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the crude imidazo[1,2-*a*]pyrimidinium salt as a crystalline tan solid. The crude product was dissolved in DCM (10mL) and loaded onto a thin pad of silica gel. Impurities were removed using 1% MeOH/DCM before using 10%MeOH/DCM to elute the purified product (0.268 g, 59%). ¹H-NMR (D₆-DMSO, 500 MHz): δ 9.42 (1H, dd, *J* = 6.7, 1.6 Hz), 9.23 (1H, dd, *J* = 4.3, 1.6 Hz), 8.65 (1H, s), 8.38 (2H, d, *J* = 8.7 Hz), 7.92 (2H, d, *J* = 8.7 Hz), 7.87 (1H, dd, *J* = 6.7, 4.3 Hz), 6.96 (4H, app s), 4.71 (2H, t, *J* = 6.5 Hz), 2.24 (3H, s). ¹³C-NMR (D₆-DMSO, 125 MHz): δ 158.98, 152.95, 149.08, 139.23, 136.41, 135.61, 131.74, 131.66, 130.22, 129.95, 129.35, 124.76, 115.54, 112.77, 44.11, 31.51, 20.86.

1.4.141A 2-(2,4-difluorophenyl)-1-(2-(*p*-tolylthio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**11.2f**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and poly seal cap was charged with **11.1f** (0.339 g, 0.71 mmol) and DCM (3 mL). The flask was then equipped with an ice bath and tetra fluoroboric acid diethyl ether complex (0.57 mL, 4.3 mmol) was added via disposable glass pipette with vigorous stirring. The reaction was allowed to warm to room temperature and stirred for 12 h before quenching via the addition of saturated aqueous sodium tetrafluoroborate (2 mL). The organic layer was extracted with DCM (3 x 2 mL) and the solvent was removed in vacuo to provide the imidazo[1,2-*a*]pyrimidinium salt as a crystalline tan solid (0.329 g, 99%). ¹H-NMR (D₆-DMSO, 500 MHz): δ 9.40 (1H, dd, *J* = 6.7, 1.4 Hz), 9.21 (1H, dd, *J* = 4.3, 1.4 Hz), 8.59 (1H, s), 7.85 (1H, dd, *J* = 6.7, 4.3 Hz), 7.74 (1H, q, *J* = 6.6 Hz), 7.60 (1H, td, *J* = 10.8, 2.3 Hz), 7.36 (1H, td, *J* = 8.4, 2.1 Hz), 7.02 (4H, app s), 4.54 (2H, t, *J* = 6.6 Hz), 3.34 (2H, t, *J* = 6.6 Hz), 2.29 (3H, s). ¹³C-NMR (D₆-DMSO, 125 MHz): δ 164.72 (dd, *J* = 251.3, 14.3 Hz), 160.43 (dd, *J* = 250.6, 14.3 Hz), 158.70, 143.16, 139.11, 136.66, 134.43 (d, *J* = 10.6 Hz), 130.62, 130.14, 130.09, 129.68, 115.32, 113.60, 113.46 (dd, *J* = 22.1, 3.5 Hz), 109.88 (dd, *J* = 14.0, 4.3 Hz), 105.85 (t, *J* = 25.6 Hz), 44.30, 31.75, 20.94. ¹⁹F-NMR (D₆-DMSO, 470 MHz): δ -104.44, -108.12, -148.30.

1.4.142A 5-(4-chlorophenyl)-1-octyl-1*H*-imidazol-2-amine (**1.3a**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **1.2a** (0.802 g, 1.87 mmol) and MeCN (3 mL). Hydrazine monohydrate (273 μ L, 5.6 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the 2-aminoimidazole as a yellow crystalline solid (0.535 g, 94%). ¹H-NMR (CDCl₃, 500 MHz): δ 7.38 (2H, d, *J* = 8.5 Hz), 7.26 (2H, d, *J* = 8.5 Hz), 6.68 (1H, s), 4.05 (2H, s), 3.74 (2H, t, *J* = 7.8 Hz), 1.58 (2H, p, *J* = 7.2 Hz), 1.27 (2H, p, *J* = 6.6 Hz), 1.22-1.11 (8H, CH envelope), 0.87 (3H, t, *J* = 7.1 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 148.86, 133.25, 129.51, 129.46, 128.92, 128.44, 123.53, 43.24, 31.69, 29.63, 29.05, 28.95, 26.49, 22.60, 14.07.

1.4.143A 5-([1,1'-biphenyl]-4-yl)-1-octyl-1H-imidazol-2-amine (**1.3b**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **1.2b** (0.335 g, 0.78 mmol) and MeCN (3 mL). Hydrazine monohydrate (114 μ L, 2.34 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the 2-aminoimidazole as a tan crystalline solid (0.236 g, 87%). ¹H-NMR (CDCl₃, 500 MHz): δ 7.64 (4H, m), 7.47 (2H, t, J = 7.4 Hz), 7.41 (2H, d, J = 8.4 Hz), 7.37 (1H, tt, J = 7.4, 2.3 Hz), 6.74 (1H, s), 4.00 (2H, s), 3.81 (2H, t, J = 7.6 Hz), 1.65 (2H, p, J = 7.2 Hz), 1.29-1.16 (10H, CH envelope), 0.85 (3H, t, J = 7.1 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 148.78, 140.53, 139.94, 130.06, 129.36, 128.85, 128.51, 127.42, 127.35, 126.97, 123.59, 43.32, 31.71, 29.74, 29.09, 28.99, 26.55, 22.60, 14.06.

1.4.144A 5-(4-bromophenyl)-1-octyl-1*H*-imidazol-2-amine (**1.3c**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **1.2c** (1.66 g, 3.5 mmol) and MeCN (3 mL). Hydrazine monohydrate (510 μ L, 10.5 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the 2-aminoimidazole as a yellow crystalline solid (1.22 g, 99%). ¹H-NMR (CDCl₃, 500 MHz): δ 7.53 (2H, m), 7.19 (2H, m), 6.68 (1H, s), 4.04 (2H, s), 3.74 (2H, t, *J* = 7.6 Hz), 1.58 (2H, p, *J* = 7.2 Hz), 1.32-1.16 (10H, CH envelope), 0.87 (3H, t, *J* = 7.1 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 148.95, 131.87, 129.99, 129.70, 128.45, 123.64, 121.29, 43.26, 31.69, 29.64, 29.06, 28.95, 26.49, 22.60, 14.08.

1.4.145A 4-(2-amino-1-octyl-1*H*-imidazol-5-yl)benzonitrile (**1.3d**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **1.2d** (0.311 g, 0.74 mmol) and MeCN (3 mL). Hydrazine monohydrate (114 μ L, 2.34 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the 2-aminoimidazole as a yellow crystalline solid (0.217 g, 99%). ¹H-NMR (CDCl₃, 500 MHz): δ 7.68 (2H, d, *J* = 8.5 Hz), 7.42 (2H, d, *J* = 8.5 Hz), 6.82 (1H, s), 4.09 (2H, s), 3.79 (2H, t, *J* = 7.6 Hz), 1.61 (2H, p, *J* = 7.2 Hz), 1.28-1.18 (10H, CH envelope), 0.87 (3H, t, *J* = 7.1 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 150.28, 135.65, 132.63, 127.95, 127.42, 126.01, 118.88, 110.09, 43.69, 31.67, 29.64, 29.05, 28.95, 26.50, 22.59, 14.07.

1.4.146A 5-(4-nitrophenyl)-1-octyl-1*H*-imidazol-2-amine (**1.3e**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **1.2e** (0.333 g, 0.76 mmol) and MeCN (3 mL). Hydrazine monohydrate (112 μ L, 2.3 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the 2-aminoimidazole as a yellow crystalline solid (0.236 g, 87%). ¹H-NMR (CDCl₃, 500 MHz): δ 8.27 (2H, d, *J* = 8.8 Hz), 7.47 (2H, d, *J* = 8.8 Hz), 6.88 (1H, s), 4.41 (2H, s), 3.84 (2H, t, *J* = 7.7 Hz), 1.64 (2H, p, *J* = 6.8 Hz), 1.27-1.17 (10H, CH envelope), 0.86 (3H, t, *J* = 7.1 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 150.68, 146.22, 137.35, 129.36, 127.17, 125.96, 124.36, 43.85, 31.67, 29.57, 29.05, 28.96, 26.50, 22.58, 14.05.

1.4.147A 5-(2,4-difluorophenyl)-1-octyl-1*H*-imidazol-2-amine (**1.3f**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **1.2f** (0.237 g, 0.55 mmol) and MeCN (3 mL). Hydrazine monohydrate (80 μ L, 1.65 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the 2-aminoimidazole as a yellow crystalline solid (0.131 g, 77%). ¹H-NMR (CDCl₃, 500 MHz): δ 7.28 (1H, m), 6.93 (2H, m), 6.66 (1H, s), 4.25 (2H, s), 3.63 (2H, t, J = 7.5 Hz), 1.52 (2H, p, J = 7.0 Hz), 1.33-1.08 (10H, CH envelope), 0.86 (3H, t, J = 7.2 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 162.95 (dd, J = 250.6, 11.6 Hz), 160.23 (dd, J = 249.6, 12.0 Hz), 148.64, 133.01 (dd, J = 9.2, 3.6 Hz), 124.07, 122.03, 114.94 (dd, J = 15.4, 3.4 Hz), 111.65 (dd, J = 21.2, 3.7 Hz), 104.35 (t, J = 25.9 Hz), 43.38 (d, J = 2.8 Hz), 31.67, 29.21, 29.00, 28.90, 26.48, 22.57, 14.05. ¹⁹F-NMR (CDCl₃, 470 MHz): δ -108.62, -109.34.

1.4.148A 5-(4-methoxyphenyl)-1-octyl-1*H*-imidazol-2-amine (1.3g) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **1.2g** (0.232 g, 0.55 mmol) and MeCN (3 mL). Hydrazine monohydrate (52 μ L, 1.64 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the crude 2-aminoimidazole as a yellow crystalline solid. Impurities were removed using 1% MeOH/DCM before using 10%MeOH/DCM to elute the purified product (0.107 g, 65%). ¹H-NMR (CDCl₃, 500 MHz): δ 7.24 (2H, d, J = 8.5 Hz), 6.94 (2H, d, J = 8.5 Hz), 6.59 (1H, s), 4.36 (2H, s), 3.84 (3H, s), 3.70 (2H, t, J = 7.6 Hz), 1.56 (2H, p, J = 6.7 Hz), 1.31-1.13 (10H, CH envelope), 0.86 (3H, t, J = 7.1 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 159.37, 147.79, 130.21, 129.35, 122.71, 120.50, 114.14, 55.33, 43.04, 31.70, 29.46, 29.04, 28.93, 26.48, 22.59, 14.07.

1.4.149A 1-octyl-5-(4-(trifluoromethyl)phenyl)-1*H*-imidazol-2-amine (**1.3h**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **1.2h** (0.118 g, 0.25 mmol) and MeCN (3 mL). Hydrazine monohydrate (36 μ L, 0.75 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the crude 2-aminoimidazole as a yellow crystalline solid. Impurities were removed using 1% MeOH/DCM before using 10%MeOH/DCM to elute the purified product (0.078 g, 96%). ¹H-NMR (CDCl₃, 500 MHz): δ 7.66 (2H, d, *J* = 7.9 Hz), 7.44 (2H, d, *J* = 7.9 Hz), 6.77 (1H, s), 4.02 (2H, s), 3.79 (2H, t, *J* = 7.7 Hz), 1.61 (2H, p, *J* = 7.0 Hz), 1.28-1.18 (10H, CH envelope), 0.87 (3H, t, *J* = 7.1 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 149.55, 134.70, 129.41, 129.08, 128.83, 128.33, 127.76, 125.73 (q, *J* = 3.6 Hz), 125.25, 124.95, 43.47, 31.67, 29.66, 29.04, 28.94, 26.48, 22.57, 14.03. ¹⁹F-NMR (CDCl₃, 470 MHz): δ -62.50.

1.4.150A 1-octyl-5-(4-(trifluoromethoxy)phenyl)-1*H*-imidazol-2-amine (**1.3i**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **1.2i** (0.204 g, 0.43 mmol) and MeCN (3 mL). Hydrazine monohydrate (63 μ L, 1.29 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the 2-aminoimidazole as a yellow crystalline solid (0.147 g, 96%). ¹H-NMR (CDCl₃, 500 MHz): δ 7.35 (2H, d, J = 8.7 Hz), 7.25 (2H, d, J = 8.7 Hz), 6.69 (1H, s), 3.99 (2H, s), 3.74 (2H, t, J = 7.1 Hz), 1.59 (2H, p, J = 7.0 Hz), 1.28-1.18 (10H, CH envelope), 0.87 (3H, t, J = 7.1 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 148.94, 148.37, 129.91, 129.54, 128.25, 124.02, 121.20, 120.50 (q, J = 257.1 Hz), 43.24, 31.66, 29.66, 29.03, 28.93, 26.49, 22.57, 14.03. ¹⁹F-NMR (CDCl₃, 470 MHz): δ -57.84.

1.4.151A 5-(4-(difluoromethoxy)phenyl)-1-octyl-1*H*-imidazol-2-amine (**1.3j**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **1.2J** (0.108 g, 0.23 mmol) and MeCN (3 mL). Hydrazine monohydrate (34 μ L, 0.69 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the 2-aminoimidazole as a yellow crystalline solid (0.068 g, 88%). ¹H-NMR (CDCl₃, 500 MHz): δ 7.32 (2H, d, J = 8.7 Hz), 7.17 (2H, d, J = 8.7 Hz), 6.67 (1H, s), 6.55 (1H, t, J = 73.6 Hz), 3.94 (2H, s), 3.73 (2H, t, J = 7.6 Hz), 1.58 (2H, p, J = 7.1 Hz), 1.28-1.18 (10H, CH envelope), 0.87 (3H, t, J = 7.1 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 150.35, 148.67, 129.78, 128.51, 128.47, 123.65, 119.80, 115.82 (t, J = 260.3 Hz), 43.20, 31.68, 29.69, 29.05, 28.96, 26.51, 22.58, 14.05. ¹⁹F-NMR (CDCl₃, 470 MHz): δ -80.78, -80.94.

1.4.152A 5-(3-nitrophenyl)-1-octyl-1*H*-imidazol-2-amine (**1.3k**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **1.2k** (0.116 g, 0.26 mmol) and MeCN (3 mL). Hydrazine monohydrate (38 μ L, 0.78 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the 2-aminoimidazole as a yellow crystalline solid (0.083 g, 99%). ¹H-NMR (CDCl₃, 500 MHz): δ 8.16 (2H, m), 7.66 (1H, m), 7.57 (1H, t, J = 7.9 Hz), 6.81 (1H, s), 4.05 (2H, s), 3.79 (2H, t, J = 7.6 Hz), 1.63 (2H, p, J = 7.5 Hz), 1.26-1.16 (10H, CH envelope), 0.85 (3H, t, J = 7.1 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 149.80, 148.57, 133.45, 132.81, 129.79, 127.28, 125.42, 121.94, 121.65, 43.59, 31.66, 29.74, 29.03, 28.96, 26.52, 22.57, 14.04.

1.4.153A 5-(4-chlorophenyl)-1-(2-(pentylthio)ethyl)-1*H*-imidazol-2-amine (2.3a) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **2.2a** (256 mg, 0.57 mmol) and MeCN (3 mL). Hydrazine monohydrate (83 μ L, 1.71 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the 2-aminoimidazole as a yellow crystalline solid (0.177 g, 96%). ¹H-NMR (CDCl₃, 500 MHz): δ 7.54 (1H, m), 7.39 (1H, m), 7.26 (1H, m), 7.21 (1H, m), 6.70 (1H, d, J = 3.2 Hz), 4.30 (2H, s), 3.99 (2H, t, J = 6.8 Hz), 2.64 (2H, td, J = 6.8, 0.9 Hz), 2.32 (2H, t, J = 7.5 Hz), 1.45 (2H, p, J = 7.3 Hz), 1.28 (4H, m), 0.89 (3H, td, J = 7.0, 1.9 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 149.38, 131.98, 129.95, 129.71, 129.03, 128.17, 123.97, 43.64, 32.36, 31.71, 30.92, 29.19, 22.25, 13.97.

1.4.154A 5-([1,1'-biphenyl]-4-yl)-1-(2-(pentylthio)ethyl)-1*H*-imidazol-2-amine (**2.3b**) A

10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **2.2b** (0.46 g, 0.93 mmol) and MeCN (3 mL). Hydrazine monohydrate (136 μ L, 2.79 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the 2-aminoimidazole as a yellow crystalline solid (0.283 g, 83%). ¹H-NMR (CDCl₃, 500 MHz): δ 7.64 (4H, m), 7.47 (2H, t, *J* = 7.7 Hz), 7.41 (2H, d, *J* = 8.3 Hz), 7.38 (1H, tt, *J* = 7.4, 1.1 Hz), 6.75 (1H, s), 4.25 (2H, s), 4.06 (2H, t, *J* = 6.9 Hz), 2.70 (2H, t, *J* = 6.9 Hz), 2.35 (2H, t, *J* = 7.5 Hz), 1.46 (2H, p, *J* = 7.1 Hz), 1.27 (4H, m), 0.85 (3H, t, *J* = 7.0 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 149.22, 140.40, 140.31, 129.72, 129.04, 128.88, 128.76, 127.52, 127.44, 126.98, 124.03, 43.76, 32.34, 31.81, 30.93, 29.22, 22.25, 13.93.

1.4.155A 5-(4-bromophenyl)-1-(2-(pentylthio)ethyl)-1*H*-imidazol-2-amine (2.3c) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **2.2c** (234 mg, 0.48 mmol) and MeCN (3 mL). Hydrazine monohydrate (70 μ L, 1.44 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the 2-aminoimidazole as a yellow crystalline solid (0.157 g, 89%). ¹H-NMR (CDCl₃, 500 MHz): δ 7.39 (2H, d, *J* = 8.6 Hz), 7.27 (2H, d, *J* = 8.6 Hz), 6.70 (1H, s), 4.26 (2H, s), 3.99 (2H, t, *J* = 6.9 Hz), 2.64 (2H, t, *J* = 6.9 Hz), 2.33 (2H, t, *J* = 7.4 Hz), 1.45 (2H, p, *J* = 7.2 Hz), 1.28 (4H, m), 0.89 (3H, t, *J* = 7.1 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 149.32, 133.59, 129.24, 129.02, 128.16, 124.15, 43.64, 32.36, 31.72, 30.91, 29.19, 22.25, 13.95.

1.4.156A 4-(2-amino-1-(2-(pentylthio)ethyl)-1*H*-imidazol-5-yl)benzonitrile (**2.3d**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **2.2d** (364 mg, 0.83 mmol) and MeCN (3 mL). Hydrazine monohydrate (121 μ L, 2.49 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the 2-aminoimidazole as a yellow crystalline solid (0.231 g, 89%). ¹H-NMR (CDCl₃, 500 MHz): δ 7.69 (2H, d, *J* = 8.4 Hz), 7.43 (2H, d, *J* = 8.4 Hz), 6.84 (1H, s), 4.39 (2H, s), 4.05 (2H, t, *J* = 6.7 Hz), 2.71 (2H, t, *J* = 6.7 Hz), 2.36 (2H, t, *J* = 7.4 Hz), 1.47 (2H, p, *J* = 7.4 Hz), 1.28 (4H, m), 0.89 (3H, t, *J* = 6.7 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 150.78, 135.33, 132.70, 127.78, 127.64, 126.30, 118.73, 110.42, 44.01, 32.47, 31.78, 30.89, 29.13, 22.24, 13.95.

1.4.157A 5-(4-nitrophenyl)-1-(2-(pentylthio)ethyl)-1*H*-imidazol-2-amine (**2.3e**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **2.2e** (0.371 g, 0.81 mmol) and MeCN (3 mL). Hydrazine monohydrate (117 μ L, 2.4 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the crude 2-aminoimidazole as a yellow crystalline solid. Impurities were removed using 1% MeOH/DCM before using 10%MeOH/DCM to elute the purified product (0.265 g, 98%). ¹H-NMR (CDCl₃, 500 MHz): δ 8.28 (2H, d, *J* = 8.4 Hz), 7.50 (2H, d, *J* = 8.4 Hz), 6.90 (1H, s), 4.84 (2H, s), 4.11 (2H, t, *J* = 6.6 Hz), 2.74 (2H, t, *J* = 6.7 Hz), 2.36 (2H, t, *J* = 7.4 Hz), 1.46 (2H, p, *J* = 7.1 Hz), 1.27 (4H, m), 0.87 (3H, t, *J* = 6.8 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 150.90, 146.53, 136.74, 127.63, 127.53, 125.16, 124.41, 44.11, 32.51, 31.64, 30.89, 29.12, 22.24, 13.93.

1.4.158A 5-(2,4-difluorophenyl)-1-(2-(pentylthio)ethyl)-1H-imidazol-2-amine (2.3f) A

10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **2.2f** (0.381 g, 0.85 mmol) and MeCN (3 mL). Hydrazine monohydrate (124 μ L, 2.55 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the crude 2-aminoimidazole as a yellow crystalline solid. Impurities were removed using 1% MeOH/DCM before using 10%MeOH/DCM to elute the purified product (0.073 g, 26%). ¹H-NMR (CDCl₃, 500 MHz): δ 7.31 (1H, m), 6.95 (2H, m), 6.69 (1H, s), 4.51 (2H, s), 3.89 (2H, t, *J* = 6.8 Hz), 2.63 (2H, t, *J* = 6.8 Hz), 2.32 (2H, t, *J* = 7.4 Hz), 1.46 (2H, p, *J* = 7.2 Hz), 1.29 (4H, m), 0.90 (3H, m). ¹³C-NMR (CDCl₃, 125 MHz): δ 163.10 (dd, *J* = 251.1, 12.1 Hz), 160.30 (dd, *J* = 249.3, 12.1 Hz), 149.22, 133.37 (dd, *J* = 9.2, 3.6 Hz), 124.77, 121.77, 114.65 (dd, *J* = 15.8, 3.8 Hz), 111.79 (dd, *J* = 21.4, 3.6 Hz), 104.41 (t, *J* = 25.7 Hz), 43.82, 32.36, 31.47, 30.90, 29.19, 22.23, 13.93.

1.4.159A 1-(3-butoxypropyl)-5-(4-chlorophenyl)-1*H*-imidazol-2-amine (**3.3a**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **3.2a** (0.093 g, 0.22 mmol) and MeCN (3 mL). Hydrazine monohydrate (20 μ L, 0.66 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the crude 2-aminoimidazole as a yellow crystalline solid. Impurities were removed using 1% MeOH/DCM before using 10% MeOH/DCM to elute the purified product (0.066 g, 97%).

1.4.160A 5-([1,1'-biphenyl]-4-yl)-1-(3-butoxypropyl)-1*H*-imidazol-2-amine (**3.3b**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **3.2b** (0.250 g, 0.53 mmol) and MeCN (3 mL). Hydrazine monohydrate (77 μ L, 1.59 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the 2-aminoimidazole as a yellow crystalline solid (0.159 g, 86%). ¹H-NMR (CDCl₃, 500 MHz): δ 7.62 (4H, m), 7.44 (4H, m), 7.36 (1H, m), 6.74 (1H, s), 4.44 (2H, s), 3.98 (2H, t, *J* = 6.5 Hz), 3.38 (2H, t, *J* = 6.7 Hz), 3.33 (2H, t, *J* = 5.5 Hz), 1.82 (2H, p, *J* = 5.8 Hz), 1.53 (2H, p, *J* = 7.4 Hz), 1.35 (2H, sx, *J* = 7.5 Hz), 0.91 (3H, t, *J* = 7.4 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 149.96, 140.53, 139.91, 130.10, 128.85, 128.52, 128.47, 127.41, 127.33, 126.96, 123.95, 70.83, 66.27, 39.26, 31.80, 29.96, 19.37, 13.92.

1.4.161A 1-(2-((2-bromophenyl)thio)ethyl)-5-(4-chlorophenyl)-1*H*-imidazol-2-amine

(4.3a) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **4.2a** (0.325 g, 0.61 mmol) and MeCN (3 mL). Hydrazine monohydrate (89 μ L, 1.83mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the 2-aminoimidazole as a yellow crystalline solid (0.191 g, 77%). ¹H-NMR (CDCl₃, 500 MHz): δ 7.53 (1H, m), 7.31 (2H, m), 7.17 (2H, m), 7.12 (1H, m), 7.06 (1H, m), 6.97 (1H, m), 6.65 (1H, s), 4.14 (2H, s), 3.98 (2H, t, *J* = 7.5 Hz), 3.08 (2H, t, *J* = 7.5 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 148.90, 135.14, 133.69, 133.47, 129.76, 129.21, 129.07, 128.81, 128.02, 127.92, 127.83, 124.91, 123.94, 42.39, 31.89.

1.4.162A 5-([1,1'-biphenyl]-4-yl)-1-(2-((2-bromophenyl)thio)ethyl)-1*H*-imidazol-2-amine (**4.3b**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **4.2b** (0.218 g, 0.38 mmol) and MeCN (3 mL). Hydrazine monohydrate (53 μ L, 1.1 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the 2-aminoimidazole as a yellow crystalline solid (0.141 g, 82%). ¹H-NMR (CDCl₃, 500 MHz): δ 7.62 (4H, m), 7.50 (3H, m), 7.40 (1H, m), 7.35 (2H, d, *J* = 8.3 Hz), 7.05 (1H, m), 6.98 (2H, m), 6.73 (1H, s), 4.32 (2H, s), 4.09 (2H, t, *J* = 7.5 Hz), 3.10 (2H, t, *J* = 7.5 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 148.70, 140.58, 140.32, 135.32, 133.39, 129.07, 129.00, 128.96, 128.93, 128.78, 127.93, 127.84, 127.63, 127.58, 127.55, 127.08, 127.00, 124.56, 123.01, 42.51, 31.76.

1.4.163A 5-(4-bromophenyl)-1-(2-((2-bromophenyl)thio)ethyl)-1*H*-imidazol-2-amine (**4.3c**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **4.2c** (0.421 g, 0.73 mmol) and MeCN (3 mL). Hydrazine monohydrate (107 μ L, 2.2 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the 2-aminoimidazole as a yellow crystalline solid (0.175 g, 53%).

1.4.164A 4-(2-amino-1-(2-((2-bromophenyl)thio)ethyl)-1*H*-imidazol-5-yl)benzonitrile

(4.3d) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **4.2d** (0.419 g, 0.8 mmol) and MeCN (3 mL). Hydrazine monohydrate (117 μ L, 2.4 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the 2-aminoimidazole as a yellow crystalline solid (0.208 g, 65%).

1.4.165A 1-(2-((2-bromophenyl)thio)ethyl)-5-(4-nitrophenyl)-1*H*-imidazol-2-amine

(4.3e) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **4.2e** (0.456 g, 0.84 mmol) and MeCN (3 mL). Hydrazine monohydrate (122 μ L, 2.52 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the 2-aminoimidazole as a yellow crystalline solid (0.235 g, 67%).

1.4.166A 1-(2-((2-bromophenyl)thio)ethyl)-5-(2,4-difluorophenyl)-1*H*-imidazol-2-amine

(4.3f) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **4.2f** (0.191 g, 0.36 mmol) and MeCN (3 mL). Hydrazine monohydrate (52 μ L, 1.08 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the crude 2-aminoimidazole as a yellow crystalline solid. Impurities were removed using 1% MeOH/DCM before using 10%MeOH/DCM to elute the purified product (0.096 g, 65%). ¹H-NMR (CDCl₃, 500 MHz): δ 7.54 (1H, dd, J = 7.7, 0.9 Hz), 7.24 (1H, m), 7.16 (1H, td, J = 7.7, 1.2 Hz), 7.06 (2H, m), 6.91 (1H, td, J = 8.1, 2.2 Hz), 6.84 (1H, td, J = 9.3, 2.5 Hz), 6.66 (1H, s), 4.15 (2H, s), 3.90 (2H, t, J = 7.4 Hz), 3.04 (2H, t, J = 7.4 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 148.67, 135.32, 133.46, 133.25 (dd, J = 9.1, 3.6 Hz), 129.10, 127.87, 127.77, 124.89, 121.89, 111.90 (dd, J = 20.9, 3.8 Hz), 104.40 (t, J = 26.1 Hz), 42.57 (d, J = 3.3 Hz), 31.84. ¹⁹F-NMR (D₆-DMSO, 470 MHz): δ -108.47, -108.69.

1.4.167A 5-(4-chlorophenyl)-1-(2-((2-chlorophenyl)thio)ethyl)-1*H*-imidazol-2-amine

(5.3a) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **5.2a** (0.386 g, 0.79 mmol) and MeCN (3 mL). Hydrazine monohydrate (117 μ L, 2.4 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the crude 2-aminoimidazole as a yellow crystalline solid. Impurities were removed using 1% MeOH/DCM before using 10%MeOH/DCM to elute the purified product (0.289 g, 99%). ¹H-NMR (CDCl₃, 500 MHz): δ 7.36 (1H, m), 7.31 (2H, m), 7.16 (3H, m), 7.09 (1H, m), 7.01 (1H, m), 6.65 (1H, s), 4.31 (2H, s), 3.98 (2H, t, *J* = 7.5 Hz), 3.02 (2H, t, *J* = 7.5 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 148.86, 134.80, 133.77, 133.02, 130.18, 129.76, 129.74, 129.07, 128.66, 128.03, 127.84, 127.30, 123.48, 42.50, 31.52.

1.4.168A 5-([1,1'-biphenyl]-4-yl)-1-(2-((2-chlorophenyl)thio)ethyl)-1*H*-imidazol-2-amine (5.3b) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **5.2b** (0.373 g, 0.70 mmol) and MeCN (3 mL). Hydrazine monohydrate (102 μ L, 2.1 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the crude 2-aminoimidazole as a yellow crystalline solid. Impurities were removed using 1% MeOH/DCM before using 10%MeOH/DCM to elute the purified product (0.270 g, 96%). ¹H-NMR (CDCl₃, 500 MHz): δ 7.62 (4H, m), 7.49 (2H, t, *J* = 7.7 Hz), 7.40 (1H, t, *J* = 7.3 Hz), 7.34 (3H, t, *J* = 8.0 Hz), 7.07 (1H, m), 7.03 (2H, m), 6.72 (1H, s), 4.34 (2H, s), 4.08 (2H, t, *J* = 7.5 Hz), 3.10 (2H, t, *J* = 7.5 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 148.69, 140.58, 140.32, 134.51, 133.26, 130.09, 129.32, 129.00, 128.95, 128.92, 128.90, 127.62, 127.58, 127.53, 127.30, 126.99, 122.92, 42.66, 31.46.

1.4.169A 5-(4-bromophenyl)-1-(2-((2-chlorophenyl)thio)ethyl)-1*H*-imidazol-2-amine

(5.3c) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **5.2c** (0.205 g, 0.38 mmol) and MeCN (3 mL). Hydrazine monohydrate (55 μ L, 1.14 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the crude 2-aminoimidazole as a yellow crystalline solid. Impurities were removed using 1% MeOH/DCM before using 10%MeOH/DCM to elute the purified product (0.150 g, 97%). ¹H-NMR (CDCl₃, 500 MHz): δ 7.47 (2H, d, J = 8.5 Hz), 7.37 (1H, dd, J = 7.9, 1.2 Hz), 7.18 (1H, td, J = 7.7, 1.5 Hz), 7.11 (3H, m), 7.04 (1H, m), 6.67 (1H, s), 4.14 (2H, s), 3.98 (2H, t, J = 7.5 Hz), 3.03 (2H, t, J = 7.5 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 148.86, 134.87, 132.97, 132.03, 130.20, 129.98, 129.83, 129.19, 128.08, 127.90, 127.33, 123.75, 121.87, 42.56, 31.59.

1.4.170A 4-(2-amino-1-(2-((2-chlorophenyl)thio)ethyl)-1*H*-imidazol-5-yl)benzonitrile

(5.3d) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **5.2d** (0.165 g, 0.34 mmol) and MeCN (3 mL). Hydrazine monohydrate (50 μ L, 1.02 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the crude 2-aminoimidazole as a yellow crystalline solid. Impurities were removed using 1% MeOH/DCM before using 10%MeOH/DCM to elute the purified product (0.072 g, 60%). ¹H-NMR (CDCl₃, 500 MHz): δ 7.61 (2H, d, *J* = 8.3 Hz), 7.40 (1H, d, *J* = 8.0 Hz), 7.33 (2H, d, *J* = 8.3 Hz), 7.23 (1H, td, *J* = 6.8, 2.0 Hz), 7.15 (2H, m), 6.81 (1H, s), 4.27 (2H, s), 4.06 (2H, t, *J* = 7.4 Hz), 3.10 (2H, t, *J* = 7.4 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 150.21, 135.31, 134.90, 132.74, 132.62, 130.51, 130.29, 128.27, 127.71, 127.67, 127.31, 125.97, 118.69, 110.50, 42.86, 31.79.

1.4.171A 1-(2-((2-chlorophenyl)thio)ethyl)-5-(4-nitrophenyl)-1*H*-imidazol-2-amine

(5.3e) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **5.2e** (0.232 g, 0.47 mmol) and MeCN (3 mL). Hydrazine monohydrate (68 μ L, 1.4 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the 2-aminoimidazole as a yellow crystalline solid (0.088 g, 50%). ¹H-NMR (CDCl₃, 500 MHz): δ 8.16 (2H, d, *J* = 8.8 Hz), 7.35 (3H, m), 7.18 (2H, m), 7.12 (1H, m), 6.86 (1H, s), 4.18 (2H, s), 4.07 (2H, t, *J* = 7.4 Hz), 3.10 (2H, t, *J* = 7.4 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 150.59, 146.31, 136.91, 135.56, 132.62, 130.86, 130.28, 128.38, 127.42, 127.33, 127.30, 127.03, 124.28, 42.97, 31.92.

1.4.173A 5-(4-chlorophenyl)-1-(2-((2-fluorophenyl)thio)ethyl)-1*H*-imidazol-2-amine

(6.3a) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **6.2a** (0.085 g, 0.18 mmol) and MeCN (3 mL). Hydrazine monohydrate (26 μ L, 0.54 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the crude 2-aminoimidazole as a yellow crystalline solid. Impurities were removed using 1% MeOH/DCM before using 10%MeOH/DCM to elute the purified product (0.060 g, 96%).

1.4.175A 5-(4-bromophenyl)-1-(2-((2-fluorophenyl)thio)ethyl)-1*H*-imidazol-2-amine

(6.3c) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **6.2c** (0.100 g, 0.19 mmol) and MeCN (3 mL). Hydrazine monohydrate (28 μ L, 0.57 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the crude 2-aminoimidazole as a yellow crystalline solid. Impurities were removed using 1% MeOH/DCM before using 10%MeOH/DCM to elute the purified product (0.074 g, 99%). ¹H-NMR (CDCl₃, 500 MHz): δ 7.44 (2H, d, J = 8.2 Hz), 7.29 (1H, m), 7.17 (1H, td, J = 7.7, 1.5 Hz), 7.07 (2H, d, J = 8.2 Hz), 7.03 (2H, m), 6.64 (1H, s), 4.17 (2H, s), 3.95 (2H, t, J = 7.5 Hz), 2.98 (2H, t, J = 7.5 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 161.79 (d, J = 246.0 Hz), 148.91, 133.10, 131.96, 129.84, 129.66 (d, J = 8.0 Hz), 129.18, 128.00, 124.74 (d, J = 3.9 Hz), 123.59, 121.77, 120.61 (d, J = 17.4 Hz), 116.10 (d, J = 22.5 Hz), 43.04, 32.60 (d, J = 2.6 Hz). ¹⁹F-NMR (CDCl₃, 470 MHz): δ -108.51, -149.68.

1.4.176A 4-(2-amino-1-(2-((2-fluorophenyl)thio)ethyl)-1H-imidazol-5-yl)benzonitrile

(6.3d) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **6.2d** (0.393 g, 0.85 mmol) and MeCN (3 mL). Hydrazine monohydrate (124 μ L, 2.55 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the crude 2-aminoimidazole as a yellow crystalline solid. Impurities were removed using 1% MeOH/DCM before using 10%MeOH/DCM to elute the purified product (0.187 g, 65%). ¹H-NMR (CDCl₃, 500 MHz): δ 7.59 (2H, m), 7.31 (3H, m), 7.25 (1H, m), 7.07 (2H, m), 6.79 (1H, s), 4.20 (2H, s), 4.02 (2H, t, J = 7.4 Hz), 3.05 (2H, t, J = 7.4 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 162.93, 160.97, 150.35, 135.03, 133.55, 132.59, 129.98 (d, J = 8.4 Hz), 127.52, 126.28, 124.77 (d, J = 3.8 Hz), 120.43 (d, J = 17.4 Hz), 118.74, 116.15 (d, J = 22.7 Hz), 110.35, 43.44, 32.76 (d, J = 2.6 Hz). ¹⁹F-NMR (CDCl₃, 470 MHz): δ -108.24.

1.4.177A 1-(2-((2-fluorophenyl)thio)ethyl)-5-(4-nitrophenyl)-1*H*-imidazol-2-amine

(6.3e) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **6.2e** (0.192 g, 0.40 mmol) and MeCN (3 mL). Hydrazine monohydrate (58 μ L, 1.2 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the crude 2-aminoimidazole as a yellow crystalline solid. Impurities were removed using 1% MeOH/DCM before using 10%MeOH/DCM to elute the purified product (0.092 g, 64%). ¹H-NMR (CDCl₃, 500 MHz): δ 8.15 (2H, d, J = 8.7 Hz), 7.33 (2H, d, J = 8.7 Hz), 7.27 (2H, m), 7.03 (2H, m), 6.83 (1H, s), 4.39 (2H, s), 4.05 (2H, t, J = 7.4 Hz), 3.05 (2H, t, J = 7.4 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 161.98 (d, J = 246.2 Hz), 150.64, 146.32, 136.73, 133.69, 130.06 (d, J = 22.5 Hz), 127.31, 127.25, 126.25, 124.77 (d, J = 3.7 Hz), 124.27, 120.31 (d, J = 17.9 Hz), 116.14 (d, J = 22.5 Hz), 43.51, 32.73 (d, J = 3.0 Hz). ¹⁹F-NMR (CDCl₃, 470 MHz): δ -108.17.

1.4.179A 1-(2-((3-bromophenyl)thio)ethyl)-5-(4-chlorophenyl)-1*H*-imidazol-2-amine

(7.3a) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **7.2a** (0.171 g, 0.32 mmol) and MeCN (3 mL). Hydrazine monohydrate (47 μ L, 0.96 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the 2-aminoimidazole as a yellow crystalline solid (0.130 g, 99%). ¹H-NMR (CDCl₃, 500 MHz): δ 7.34 (4H, m), 7.17 (2H, d, *J* = 8.4 Hz), 7.08 (1H, m), 7.03 (1H, m), 6.65 (1H, s), 4.06 (2H, s), 3.99 (2H, t, *J* = 7.3 Hz), 2.99 (2H, t, *J* = 7.3 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 148.85, 136.54, 133.70, 132.17, 130.48, 129.97, 129.57, 129.11, 128.83, 128.07, 127.99, 124.16, 123.02, 42.81, 32.94.

1.4.180A 5-([1,1'-biphenyl]-4-yl)-1-(2-((3-bromophenyl)thio)ethyl)-1*H*-imidazol-2-amine (7.3b) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **7.2b** (0.368 g, 0.64 mmol) and MeCN (3 mL). Hydrazine monohydrate (93 μ L, 1.92 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the crude 2-aminoimidazole as a yellow crystalline solid. Impurities were removed using 1% MeOH/DCM before using 10%MeOH/DCM to elute the purified product (0.288 g, 99%). ¹H-NMR (CDCl₃, 500 MHz): δ 7.62 (4H, m), 7.48 (2H, t, *J* = 7.7 Hz), 7.38 (2H, m), 7.32 (2H, d, *J* = 8.2 Hz), 7.27 (1H, m), 7.02 (2H, m), 6.70 (1H, s), 4.38 (2H, s), 4.09 (2H, t, *J* = 7.2 Hz), 3.07 (2H, t, *J* = 7.2 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 148.72, 140.57, 140.27, 136.69, 132.03, 129.81, 128.92, 128.76, 127.79, 127.62, 127.53, 126.99, 122.98, 122.76, 42.91, 32.82.

1.4.181A 5-(4-bromophenyl)-1-(2-((3-bromophenyl)thio)ethyl)-1H-imidazol-2-amine

(7.3c) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **7.2c** (0.201 g, 0.35 mmol) and MeCN (3 mL). Hydrazine monohydrate (51 μ L, 1.05 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the crude 2-aminoimidazole as a yellow crystalline solid. Impurities were removed using 1% MeOH/DCM before using 10% MeOH/DCM to elute the purified product (0.110 g, 69%). ¹H-NMR (CDCl₃, 500 MHz): δ 7.48 (2H, d, J = 8.4 Hz), 7.34 (2H, d, J = 7.1 Hz), 7.08 (3H, m), 7.02 (1H, d, J = 7.4 Hz), 6.65 (1H, s), 4.22 (2H, s), 4.00 (2H, t, J = 7.2 Hz), 2.99 (2H, t, J = 7.2 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 148.82, 136.46, 132.18, 132.09, 130.52, 130.00, 129.86, 129.01, 128.11, 128.00, 123.35, 123.02, 122.00, 42.81, 32.87.

1.4.182A 4-(2-amino-1-(2-((3-bromophenyl)thio)ethyl)-1*H*-imidazol-5-yl)benzonitrile

(7.3d) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **7.2d** (0.417 g, 0.8 mmol) and MeCN (3 mL). Hydrazine monohydrate (116 μ L, 2.4 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the crude 2-aminoimidazole as a yellow crystalline solid. Impurities were removed using 1% MeOH/DCM before using 10%MeOH/DCM to elute the purified product (0.317 g, 99%). ¹H-NMR (CDCl₃, 500 MHz): δ 7.62 (2H, d, *J* = 8.2 Hz), 7.37 (1H, m), 7.32 (3H, m), 7.10 (2H, m), 6.79 (1H, s), 4.17 (2H, s), 4.05 (2H, t, *J* = 7.1 Hz), 3.04 (2H, t, *J* = 7.1 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 150.26, 136.31, 134.97, 132.69, 132.35, 130.50, 130.21, 128.41, 127.56, 126.41, 123.09, 118.71, 110.56, 43.14, 33.05.

1.4.183A 1-(2-((3-bromophenyl)thio)ethyl)-5-(4-nitrophenyl)-1*H*-imidazol-2-amine

(7.3e) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **7.2e** (0.296 g, 0.54 mmol) and MeCN (3 mL). Hydrazine monohydrate (79 μ L, 1.63 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the crude 2-aminoimidazole as a yellow crystalline solid. Impurities were removed using 1% MeOH/DCM before using 10%MeOH/DCM to elute the purified product (0.210 g, 93%). ¹H-NMR (CDCl₃, 500 MHz): δ 8.19 (2H, d, J = 8.4 Hz), 7.34 (4H, m), 7.10 (2H, m), 6.84 (1H, s), 4.21 (2H, s), 4.08 (2H, t, J = 7.1 Hz), 3.05 (2H, t, J = 7.1 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 150.61, 146.35, 136.85, 136.21, 132.41, 130.49, 130.26, 128.54, 127.41, 127.25, 127.03, 124.37, 123.10, 43.21, 33.09.

1.4.184A 1-(2-((3-bromophenyl)thio)ethyl)-5-(2,4-difluorophenyl)-1*H*-imidazol-2-amine

(7.3f) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **7.2f** (0.145 g, 0.27 mmol) and MeCN (3 mL). Hydrazine monohydrate (47 μ L, 0.81 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the crude 2-aminoimidazole as a yellow crystalline solid. Impurities were removed using 1% MeOH/DCM before using 10%MeOH/DCM to elute the purified product (0.081 g, 73%). ¹H-NMR (CDCl₃, 500 MHz): δ 7.34 (2H, m), 7.21 (1H, m), 7.09 (2H, m), 6.92 (1H, td, *J* = 8.2, 2.5 Hz), 6.86 (1H, td, *J* = 9.4, 2.5 Hz), 6.65 (1H, s), 4.16 (2H, s), 3.88 (2H, t, *J* = 7.2 Hz), 3.02 (2H, t, *J* = 7.2 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 160.06 (dd, *J* = 251.4, 13.5 Hz), 148.67, 136.63, 134.75, 133.12 (dd, *J* = 10.0, 4.5 Hz), 132.14, 130.43, 129.95, 128.84, 124.77, 123.02, 122.01, 111.93 (dd, *J* = 21.1, 3.8 Hz), 104.47 (t, *J* = 25.4 Hz), 42.98 (d, *J* = 3.4 Hz), 32.78. ¹⁹F-NMR (CDCl₃, 470 MHz): δ -108.54.

1.4.185A 1-(2-((4-bromophenyl)thio)ethyl)-5-(4-chlorophenyl)-1*H*-imidazol-2-amine

(8.3a) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **8.2a** (0.248 g, 0.47 mmol) and MeCN (3 mL). Hydrazine monohydrate (68 μ L, 1.4 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the crude 2-aminoimidazole as a yellow crystalline solid. Impurities were removed using 1% MeOH/DCM before using 10%MeOH/DCM to elute the purified product (0.137 g, 71%).

1.4.186A 5-([1,1'-biphenyl]-4-yl)-1-(2-((4-bromophenyl)thio)ethyl)-1*H*-imidazol-2-

amine (8.3b) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **8.2b** (0.431 g, 0.75 mmol) and MeCN (3 mL). Hydrazine monohydrate (109 μ L, 2.25 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the 2-aminoimidazole as a yellow crystalline solid (0.252 g, 75%). ¹H-NMR (CDCl₃, 500 MHz): δ 7.65 (2H, m), 7.60 (2H, d, *J* = 8.0 Hz), 7.49 (2H, t, *J* = 7.7 Hz), 7.39 (1H, tt, *J* = 6.6, 1.1 Hz), 7.30 (4H, dd, *J* = 8.3, 6.3 Hz), 7.00 (2H, d, *J* = 8.5 Hz), 6.72 (1H, s), 4.08 (2H, s), 4.03 (2H, t, *J* = 7.4 Hz), 3.03 (2H, t, *J* = 7.4 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 148.76, 140.46, 140.22, 133.45, 132.22, 131.10, 129.71, 129.28, 128.97, 128.74, 127.63, 127.49, 127.05, 123.86, 120.74, 42.86, 32.90.

1.4.187A 5-(4-bromophenyl)-1-(2-((4-bromophenyl)thio)ethyl)-1*H*-imidazol-2-amine

(8.3c) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **8.2c** (0.261 g, 0.45 mmol) and MeCN (3 mL). Hydrazine monohydrate (131 μ L, 2.7 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the 2-aminoimidazole as a yellow crystalline solid (0.174 g, 85%). ¹H-NMR (CDCl₃, 500 MHz): δ 7.50 (2H, d, *J* = 7.9 Hz), 7.37 (2H, d, *J* = 7.9 Hz), 7.10 (2H, d, *J* = 7.3 Hz), 7.00 (2H, d, *J* = 7.3 Hz), 6.67 (1H, s), 4.24 (2H, s), 3.98 (2H, t, *J* = 7.3 Hz), 2.98 (2H, t, *J* = 7.3 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 148.99, 133.26, 132.27, 132.04, 131.32, 130.96, 129.88, 129.22, 128.01, 121.87, 120.99, 42.72, 32.99.

1.4.188A 4-(2-amino-1-(2-((4-bromophenyl)thio)ethyl)-1*H*-imidazol-5-yl)benzonitrile

(8.3d) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **8.2d** (0.444 g, 0.85 mmol) and MeCN (3 mL). Hydrazine monohydrate (124 μ L, 2.55 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the 2-aminoimidazole as a yellow crystalline solid (0.292 g, 86%). ¹H-NMR (CDCl₃, 500 MHz): δ 7.63 (2H, d, *J* = 8.5 Hz), 7.39 (2H, d, *J* = 8.5 Hz), 7.31 (2H, d, *J* = 8.5 Hz), 7.09 (2H, d, *J* = 8.5 Hz), 6.80 (1H, s), 4.24 (2H, s), 4.04 (2H, t, *J* = 7.2 Hz), 3.04 (2H, t, *J* = 7.2 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 150.31, 134.93, 133.05, 132.66, 132.33, 132.01, 131.88, 127.54, 126.20, 121.42, 118.60, 110.55, 43.10, 33.44.

1.4.189A 1-(2-((4-bromophenyl)thio)ethyl)-5-(4-nitrophenyl)-1*H*-imidazol-2-amine

(8.3e) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **8.2e** (0.239 g, 0.44 mmol) and MeCN (3 mL). Hydrazine monohydrate (63 μ L, 1.3 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the 2-aminoimidazole as a yellow crystalline solid (0.121 g, 66%).

1.4.190A 1-(2-((4-bromophenyl)thio)ethyl)-5-(2,4-difluorophenyl)-1*H*-imidazol-2-amine

(8.3f) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **8.2f** (0.376 g, 0.70 mmol) and MeCN (3 mL). Hydrazine monohydrate (102 μ L, 2.1 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the 2-aminoimidazole as a yellow crystalline solid (0.266 g, 93%). ¹H-NMR (CDCl₃, 500 MHz): δ 7.36 (2H, d, *J* = 8.5 Hz), 7.21 (1H, m), 7.05 (2H, d, *J* = 8.5 Hz), 6.93 (1H, m), 6.86 (1H, m), 6.67 (1H, s), 4.07 (2H, s), 3.85 (2H, t, *J* = 7.4 Hz), 2.95 (2H, t, *J* = 7.4 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 163.08 (dd, *J* = 252.2, 11.0 Hz), 160.06 (dd, *J* = 249.6, 12.3 Hz), 148.79, 133.39, 133.11 (dd, *J* = 9.0, 4.6 Hz), 132.22, 131.50, 125.33, 121.87, 121.00, 114.49 (d, *J* = 20.0 Hz), 111.83 (dd, *J* = 19.9, 3.7 Hz), 104.42 (t, *J* = 25.8 Hz), 42.90 (d, *J* = 2.7 Hz), 33.08.

1.4.191A 5-(4-chlorophenyl)-1-(2-((4-chlorophenyl)thio)ethyl)-1*H*-imidazol-2-amine

(9.3a) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **9.2a** (0.284 g, 0.58 mmol) and MeCN (3 mL). Hydrazine monohydrate (85 μ L, 1.74 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the 2-aminoimidazole as a yellow crystalline solid (0.210 g, 99%). ¹H-NMR (CDCl₃, 500 MHz): δ 7.33 (2H, d, *J* = 8.4 Hz), 7.21 (2H, d, *J* = 8.5 Hz), 7.15 (2H, d, *J* = 8.4 Hz), 7.08 (2H, d, *J* = 8.5 Hz), 6.66 (1H, s), 4.02 (2H, s), 3.96 (2H, t, *J* = 7.3 Hz), 2.96 (2H, t, *J* = 7.3 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 148.87, 133.70, 133.19, 132.59, 131.28, 129.60, 129.34, 129.05, 128.93, 128.03, 124.26, 42.78, 33.34.

1.4.192A 5-([1,1'-biphenyl]-4-yl)-1-(2-((4-chlorophenyl)thio)ethyl)-1*H*-imidazol-2-amine (**9.3b**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **9.2b** (0.336 g, 0.63 mmol) and MeCN (3 mL). Hydrazine monohydrate (92 μ L, 1.9 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the 2-aminoimidazole as a yellow crystalline solid (0.223 g, 87%). ¹H-NMR (CDCl₃, 500 MHz): δ 7.63 (2H, d, *J* = 8.2 Hz), 7.59 (2H, d, *J* = 8.2 Hz), 7.48 (2H, t, *J* = 7.7 Hz), 7.38 (1H, tt, *J* = 7.4, 1.0 Hz), 7.30 (2H, d, *J* = 8.2 Hz), 7.15 (2H, d, *J* = 8.4 Hz), 7.07 (2H, d, *J* = 8.4 Hz), 6.71 (1H, s), 4.00 (4H, m), 3.02 (2H, t, *J* = 7.4 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 148.76, 140.39, 140.25, 132.92, 132.77, 131.07, 129.40, 129.31, 128.95, 128.69, 127.61, 127.46, 127.02, 124.17, 42.90, 33.21.

1.4.193A 5-(4-bromophenyl)-1-(2-((4-chlorophenyl)thio)ethyl)-1H-imidazol-2-amine

(9.3c) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **9.2c** (0.299 g, 0.56 mmol) and MeCN (3 mL). Hydrazine monohydrate (82 μ L, 1.68 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the crude 2-aminoimidazole as a yellow crystalline solid. Impurities were removed using 1% MeOH/DCM before using 10%MeOH/DCM to elute the purified product (0.171 g, 75%). ¹H-NMR (CDCl₃, 500 MHz): δ 7.49 (2H, d, J = 8.4 Hz), 7.21 (2H, d, J = 8.5 Hz), 7.08 (4H, m), 6.66 (1H, s), 4.15 (2H, s), 3.97 (2H, t, J = 7.3 Hz), 2.97 (2H, t, J = 7.3 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 148.97, 133.21, 132.54, 132.04, 131.26, 129.89, 129.36, 129.18, 128.06, 123.62, 121.90, 42.78, 33.27.

1.4.194A 4-(2-amino-1-(2-((4-chlorophenyl)thio)ethyl)-1*H*-imidazol-5-yl)benzonitrile

(9.3d) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **9.2d** (0.076 g, 0.16 mmol) and MeCN (3 mL). Hydrazine monohydrate (23 μ L, 0.48 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the crude 2-aminoimidazole as a yellow crystalline solid. Impurities were removed using 1% MeOH/DCM before using 10%MeOH/DCM to elute the purified product (0.054 g, 95%). ¹H-NMR (CDCl₃, 500 MHz): δ 7.62 (2H, d, *J* = 8.5 Hz), 7.29 (2H, d, *J* = 8.5 Hz), 7.23 (2H, d, *J* = 8.2 Hz), 7.15 (2H, d, *J* = 8.2 Hz), 6.79 (1H, s), 4.09 (2H, s), 4.02 (2H, t, *J* = 7.2 Hz), 3.01 (2H, t, *J* = 7.2 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 150.34, 135.07, 133.59, 132.65, 132.37, 131.78, 129.41, 127.62, 127.52, 126.51, 118.67, 110.50, 43.15, 33.70.

1.4.195A 1-(2-((4-chlorophenyl)thio)ethyl)-5-(4-nitrophenyl)-1*H*-imidazol-2-amine

(9.3e) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **9.2e** (0.152 g, 0.3 mmol) and MeCN (3 mL). Hydrazine monohydrate (44 μ L, 0.91 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the 2-aminoimidazole as a yellow crystalline solid (0.107 g, 96%). ¹H-NMR (CDCl₃, 500 MHz): δ 8.19 (2H, d, *J* = 8.7 Hz), 7.34 (2H, d, *J* = 8.7 Hz), 7.21 (2H, d, *J* = 8.5 Hz), 7.15 (2H, d, *J* = 8.5 Hz), 6.85 (1H, s), 4.13 (2H, s), 4.05 (2H, t, *J* = 7.2 Hz), 3.04 (2H, t, *J* = 7.2 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 150.67, 146.31, 136.94, 133.64, 132.30, 131.81, 129.41, 127.36, 127.27, 127.19, 124.33, 43.27, 33.72.

1.4.196A 1-(2-((4-chlorophenyl)thio)ethyl)-5-(2,4-difluorophenyl)-1*H*-imidazol-2-amine

(9.3f) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **9.2f** (0.209 g, 0.43 mmol) and MeCN (3 mL). Hydrazine monohydrate (62 μ L, 1.28 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the 2-aminoimidazole as a yellow crystalline solid (0.140 g, 89%). ¹H-NMR (CDCl₃, 500 MHz): δ 7.18 (3H, m), 7.11 (2H, d, *J* = 8.4 Hz), 6.92 (1H, td, *J* = 8.2, 2.5 Hz), 6.84 (1H, td, *J* = 9.6, 2.5 Hz), 6.65 (1H, s), 4.00 (2H, s), 3.83 (2H, t, *J* = 7.4 Hz), 2.97 (2H, t, *J* = 7.4 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 163.02 (dd, *J* = 247.0, 12.1 Hz), 160.05 (dd, *J* = 242.2, 12.7 Hz), 148.74, 133.18, 133.12 (dd, *J* = 9.5, 4.0 Hz), 132.69, 132.23, 131.41, 129.30, 125.37, 121.88, 114.49 (dd, *J* = 15.9, 4.1 Hz), 111.82 (dd, *J* = 21.1, 3.7 Hz), 104.40 (t, *J* = 25.8 Hz), 42.94 (d, *J* = 3.0 Hz), 33.31.

1.4.197A 5-(4-chlorophenyl)-1-(2-((4-fluorophenyl)thio)ethyl)-1*H*-imidazol-2-amine

(10.3a) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **10.2a** (0.103 g, 0.36 mmol) and MeCN (3 mL). Hydrazine monohydrate (52 μ L, 1.08 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the 2-aminoimidazole as a yellow crystalline solid (0.083 g, 66%). ¹H-NMR (CDCl₃, 500 MHz): δ 7.32 (2H, d, J = 8.5 Hz), 7.17 (2H, m), 7.13 (2H, d, J = 8.5 Hz), 6.95 (2H, m), 6.64 (1H, s), 4.20 (2H, s), 3.95 (2H, t, J = 7.3 Hz), 2.94 (2H, t, J = 7.3 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 163.24, 161.27, 148.83, 133.83, 133.04 (d, J = 8.2 Hz), 129.66, 129.05, 128.95, 128.62, 128.01, 123.11, 116.37 (d, J = 22.0 Hz), 42.87, 34.27.

1.4.198A 5-([1,1'-biphenyl]-4-yl)-1-(2-((4-fluorophenyl)thio)ethyl)-1*H*-imidazol-2-amine

(10.3b) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **10.2b** (0.343 g, 0.67 mmol) and MeCN (3 mL). Hydrazine monohydrate (98 μ L, 2.01 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the 2-aminoimidazole as a yellow crystalline solid (0.245 g, 94%). ¹H-NMR (CDCl₃, 500 MHz): δ 7.63 (2H, d, J = 7.4 Hz), 7.58 (2H, d, J = 8.2 Hz), 7.49 (2H, t, J = 7.6 Hz), 7.39 (1H, t, J = 7.3 Hz), 7.29 (2H, d, J = 8.2 Hz), 7.20 (2H, dd, J = 8.6, 5.2 Hz), 6.92 (2H, t, J = 8.6 Hz), 6.71 (1H, s), 4.02 (2H, t, J = 7.6 Hz), 4.00 (2H, s), 3.01 (2H, t, J = 7.6 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 163.13, 161.16, 148.77, 140.30 (d, J = 2.6 Hz), 132.93 (d, J = 8.2 Hz), 129.44, 129.22 (d, J = 3.4 Hz), 128.94, 128.63, 127.59, 127.42, 126.96, 124.11, 116.42, 116.24, 43.01, 34.38.

1.4.199A 5-(4-bromophenyl)-1-(2-((4-fluorophenyl)thio)ethyl)-1*H*-imidazol-2-amine

(10.3c) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **10.2c** (0.292 g, 0.57 mmol) and MeCN (3 mL). Hydrazine monohydrate (83 μ L, 1.71 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the crude 2-aminoimidazole as a yellow crystalline solid. Impurities were removed using 1% MeOH/DCM before using 10%MeOH/DCM to elute the purified product (0.196 g, 88%). ¹H-NMR (CDCl₃, 500 MHz): δ 7.47 (2H, d, *J* = 8.3 Hz), 7.17 (2H, d, *J* = 8.7, 5.2 Hz), 7.07 (2H, d, *J* = 8.3 Hz), 6.96 (2H, t, *J* = 8.6 Hz), 6.66 (1H, s), 3.97 (2H, s), 3.94 (2H, t, *J* = 7.3 Hz), 2.92 (2H, t, *J* = 7.3 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 148.93, 133.03 (d, *J* = 8.2 Hz), 131.96, 129.80, 129.46, 129.06 (d, *J* = 3.2 Hz), 128.06, 124.34, 121.65, 116.38 (d, *J* = 21.9 Hz), 42.91, 34.39.

1.4.200A 4-(2-amino-1-(2-((4-fluorophenyl)thio)ethyl)-1*H*-imidazol-5-yl)benzonitrile

(10.3d) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **10.2d** (0.156 g, 0.34 mmol) and MeCN (3 mL). Hydrazine monohydrate (49 μ L, 1.01 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the 2-aminoimidazole as a yellow crystalline solid (0.102 g, 89%). ¹H-NMR (CDCl₃, 500 MHz): δ 7.59 (2H, d, *J* = 8.2 Hz), 7.27 (2H, d, *J* = 8.2 Hz), 7.23 (2H, dd, *J* = 8.7, 5.2 Hz), 6.96 (2H, t, *J* = 8.5 Hz), 6.77 (1H, s), 4.14 (2H, s), 3.99 (2H, t, *J* = 7.2 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 163.38, 161.40, 150.37, 135.08, 133.45 (d, *J* = 8.2 Hz), 132.62, 128.91 (d, *J* = 3.5 Hz), 127.49, 126.45, 118.63, 116.45 (d, *J* = 21.9 Hz), 110.41, 43.28, 34.63.

1.4.201A 1-(2-((4-fluorophenyl)thio)ethyl)-5-(4-nitrophenyl)-1*H*-imidazol-2-amine

(10.3e) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **10.2e** (0.315 g, 0.65 mmol) and MeCN (3 mL). Hydrazine monohydrate (95 μ L, 1.96 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the crude 2-aminoimidazole as a yellow crystalline solid. Impurities were removed using 1% MeOH/DCM before using 10%MeOH/DCM to elute the purified product (0.126 g, 54%). ¹H-NMR (CDCl₃, 500 MHz): δ 8.21 (2H, d, *J* = 8.9 Hz), 7.36 (2H, d, *J* = 8.9 Hz), 7.26 (2H, m), 6.98 (2H, t, *J* = 8.6 Hz), 6.86 (1H, s), 4.52 (2H, s), 4.08 (2H, t, *J* = 7.1 Hz), 3.04 (2H, t, *J* = 7.1 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 161.50, 150.57, 146.49, 136.57, 133.48 (d, *J* = 8.0 Hz), 128.82, 127.44, 127.30, 125.76, 124.32, 116.47 (d, *J* = 21.9 Hz), 43.38, 34.56.

1.4.202A 5-(2,4-difluorophenyl)-1-(2-((4-fluorophenyl)thio)ethyl)-1H-imidazol-2-amine

(10.3f) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **10.2f** (0.069 g, 0.15 mmol) and MeCN (3 mL). Hydrazine monohydrate (21 μ L, 0.44 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the 2-aminoimidazole as a yellow crystalline solid (0.051 g, 97%). ¹H-NMR (CDCl₃, 500 MHz): δ 7.20 (3H, m), 6.96 (2H, t, *J* = 8.6 Hz), 6.91 (1H, td, *J* = 8.3, 2.4 Hz), 6.84 (1H, td, *J* = 9.2, 2.5 Hz), 6.66 (1H, s), 3.99 (2H, s), 3.84 (2H, t, *J* = 7.3 Hz), 2.95 (2H, t, *J* = 7.3 Hz). ¹³C-NMR (CDCl₃, 125 MHz): δ 148.73, 133.18, 133.11, 125.34, 121.85, 116.40, 116.23, 111.69, 104.37, 43.03, 34.32.

1.4.203A 5-(4-chlorophenyl)-1-(2-(*p*-tolylthio)ethyl)-1H-imidazol-2-amine (**11.3a**)

A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **11.2a** (0.39 mmol) and MeCN (3 mL). Hydrazine monohydrate (57 μ L, 1.17 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the 2-aminoimidazole as a yellow crystalline solid (0.135 g, 99%). ¹H-NMR (CDCl₃, 500 MHz): δ 7.28 (2H, d, *J* = 8.4 Hz), 7.12 (4H, m), 7.06 (2H, d, *J* = 8.0 Hz), 6.65 (1H, s), 3.99 (2H, s), 3.92 (2H, t, *J* = 7.5 Hz), 2.95 (2H, t, *J* = 7.5 Hz), 2.35 (3H, s). ¹³C-NMR (CDCl₃, 125 MHz): δ 148.97, 137.47, 133.44, 130.87, 130.21, 130.03, 129.55, 129.00, 128.95, 128.01, 124.14, 42.86, 33.81, 21.07.

1.4.204A 5-([1,1'-biphenyl]-4-yl)-1-(2-(*p*-tolylthio)ethyl)-1*H*-imidazol-2-amine (**11.3b**)

A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **11.2b** (0.460 g, 0.93 mmol) and MeCN (3 mL). Hydrazine monohydrate (136 μ L, 2.79 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the 2-aminoimidazole as a yellow crystalline solid (0.212 g, 66%). ¹H-NMR (CDCl₃, 500 MHz): δ 7.63 (2H, d, *J* = 7.3 Hz), 7.57 (2H, d, *J* = 8.1 Hz), 7.48 (2H, t, *J* = 7.7 Hz), 7.39 (1H, m), 7.31 (2H, d, *J* = 8.0 Hz), 7.13 (2H, d, *J* = 8.1 Hz), 7.02 (2H, d, *J* = 8.2 Hz), 6.72 (1H, s), 4.01 (4H, m), 3.02 (2H, t, *J* = 7.4 Hz), 2.25 (3H, s). ¹³C-NMR (CDCl₃, 125 MHz): δ 148.89, 140.42, 140.21, 137.17, 130.56, 130.45, 130.01, 129.46, 128.90, 128.67, 127.53, 127.41, 126.97, 123.87, 42.98, 33.73, 20.95.

1.4.205A 5-(4-bromophenyl)-1-(2-(*p*-tolylthio)ethyl)-1*H*-imidazol-2-amine (**11.3c**) A 10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **11.2c** (0.202 g, 0.39 mmol) and MeCN (3 mL). Hydrazine monohydrate (57 μ L, 1.17 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the 2-aminoimidazole as a yellow crystalline solid (0.134 g, 88%). ¹H-NMR (CDCl₃, 500 MHz): δ 7.44 (2H, d, *J* = 8.5 Hz), 7.11 (2H, d, *J* = 7.8 Hz), 7.07 (4H, m), 6.66 (1H, s), 4.01 (2H, s), 3.92 (2H, t, *J* = 7.5 Hz), 2.95 (2H, t, *J* = 7.5 Hz), 2.36 (3H, s). ¹³C-NMR (CDCl₃, 125 MHz): δ 149.05, 137.47, 131.91, 130.86, 130.19, 130.05, 129.78, 129.45, 128.03, 124.12, 121.54, 42.87, 33.78, 21.10.

1.4.208A 5-(2,4-difluorophenyl)-1-(2-(*p*-tolylthio)ethyl)-1*H*-imidazol-2-amine (**11.3f**) A

10 mL round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **11.2f** (0.123 g, 0.26 mmol) and MeCN (3 mL). Hydrazine monohydrate (38 μ L, 0.78 mmol) was added via gas tight syringe and the reaction mixture was allowed to stir at reflux for 2.5 h. The solvent was then removed in vacuo, the residue was diluted in EtOAc (10 mL) and washed with 10% aq K₂CO₃ (3 x 5 mL) and saturated brine (2 x 5 mL). The solvent was removed in vacuo to yield the 2-aminoimidazole as a yellow crystalline solid (0.071 g, 79%). ¹H-NMR (CDCl₃, 500 MHz): δ 7.20 (1H, m), 7.13 (2H, d, *J* = 8.1 Hz), 7.07 (2H, d, *J* = 8.1 Hz), 6.90 (1H, td, *J* = 8.3, 2.5 Hz), 6.82 (1H, m), 6.66 (1H, s), 3.99 (2H, s), 3.82 (2H, t, *J* = 7.6 Hz), 2.95 (2H, t, *J* = 7.6 Hz), 2.35 (3H, s). ¹³C-NMR (CDCl₃, 125 MHz): δ 148.80, 137.37, 133.11 (dd, *J* = 9.5, 4.1 Hz), 130.86, 130.32, 129.97, 125.20, 121.75, 111.67 (dd, *J* = 21.0, 3.7 Hz), 104.34 (t, *J* = 25.9 Hz), 42.98 (d, *J* = 3.0 Hz), 33.69, 21.01.

2A Biological Evaluation Experiments

2.1A General Preparation of Bacterial Cultures

Biological evaluation was conducted against *Pseudomonas aeruginosa* (PA14) and *Staphylococcus aureus* (USA300 LAC). Overnight cultures were prepared by transferring single colonies from the plates into 25 mL tryptic soy broth (TSB) in Erlenmeyer flasks and incubating at 37 °C, 150 rpm for 16 h. Then, 10 μ L of overnight cultures were transferred into 50 mL of TSB, vortexed, and standardized to 10⁵–10⁶ CFU/mL via absorbance readings at 600 nm for *Pseudomonas aeruginosa* (PA14). While 625 μ L of overnight cultures were transferred into 50 mL of TSB, vortexed, and standardized to 10⁸ CFU/mL (0.5 McFarland Standard) via absorbance readings at 600 nm for *Staphylococcus aureus* (USA300 LAC).

2.2A Minimum Inhibitory Concentration (MIC) Assays

Polystyrene 96-well microtiter plates were inoculated with prepared standardized cultures of the strain at 10^5 – 10^6 CFU/mL with 150 μ L of TSB and serial dilutions of the compound in TSB. TSB blanks, TSB controls, and DMSO controls without any added compound were also prepared. The optical density was taken at 600 nm via microplate reader at 0 h and plates were then covered, sealed with parafilm, and incubated at 37 °C for 24 h in static conditions. The optical density was again taken at 600 nm at 24 h, and the difference of that and 0 h was measured to determine the MIC. Experiments were done in biological triplicate with technical duplicates.

2.3A Minimum Biofilm Eradication Concentration (MBEC) Assays

Polystyrene 96-well microtiter plates were inoculated with prepared standardized cultures of the strain at 10^5 – 10^6 CFU/mL with 150 μ L of TSB. Plates were then covered, sealed with parafilm, and incubated at 37 °C for 24 h in static conditions. The medium was then gently discarded, and the plates washed with PBS buffer to remove any planktonic phase cells. Serial dilutions of the compound in 150 μ L of TSB and controls without any added compound were added to the wells. Plates were then covered, sealed with parafilm, and incubated again at 37 °C for 24 h in static conditions. Wells were then thoroughly agitated to ensure the biofilm was broken up from the surface of the wells using pipettes before 10 μ L aliquots in triplicate of each well were taken and drop plated on TSA plates. TSA plates were incubated at 37 °C for 24 h in static conditions. The lowest concentration at which no bacterial growth occurred was used to determine the MBEC. Experiments were performed in biological triplicates with technical duplicates.

2.4A Kirby-Bauer Disk-Diffusion Assays

Polystyrene petri dishes (100 mm x 15 mm) were prepped as Mueller-Hinton (MH) agar plates to a level of 4 mm. The MH agar plates were inoculated (200 μ L) with uniformity using a glass spreader. Once a confluent lawn of growth was attained, the plate was allowed to dry. Sterile 6 mm filter disks were impregnated with 20 μ L of antimicrobial working concentrations diluted in either DMSO or dH₂O. A 5-minute wait allowed for full absorption of the solutions. Within 15 minutes, impregnated antimicrobial disks were dispensed evenly (no less than 20 mm) from each other using sterile forceps. MH agar plates were incubated at 37 °C for 24 h under static conditions. Zones of inhibition were measured (in mm) and qualitative observations of the biofilm were recorded.

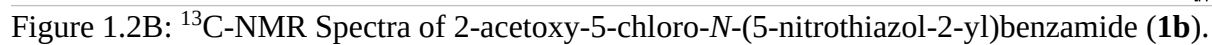
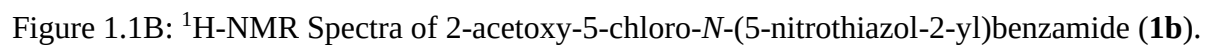
2.5A CDC Biofilm Reactor Assays

Assays were adapted from ASTM method E2562-17 and ASTM method E2871-13. A CDC reactor containing 400 mL of 10% tryptic soy broth was inoculated with 4 mL of an overnight culture of MRSA USA300LAC. The biofilms were grown on polycarbonate coupons (12.7 mm in diameter and 3.8 mm thick) in batch phase at 37°C at 125 rpm for 24 h, and then under a continuous flow of 2.7 mL/min at 37°C at 125 rpm for 24 h. Coupons were removed and placed in 12 well plates with 3 mL of treatment in sterile PBS buffer in each well for each coupon. Coupons were left in treatments for 24 h at 37°C under static conditions. Coupons were then removed from the treatment wells and transferred to 50 mL conical tubes containing double strength DE broth (10 mL). To disaggregate the biofilms from the coupons, tubes were vortexed for 30 sec, sonicated for 30 sec, vortexed for 30 sec, sonicated for 30 sec and vortexed for 30 secs. Each tube was diluted ten-fold six times in sterile PBS Buffer, plated onto TSA and

incubated at 37°C for 24 h before enumeration. All samples were done with technical duplicates within each assay and assays were evaluated in biological triplicate.

APPENDIX B

SPECTRAL DATA



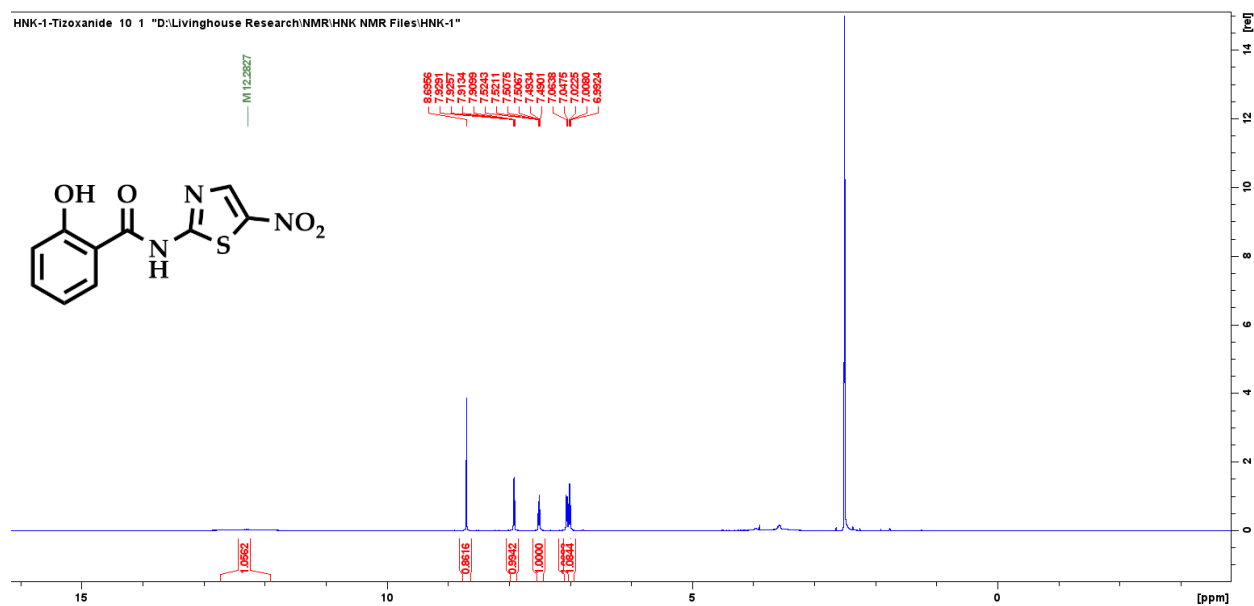


Figure 1.3B: ^1H NMR Spectra of 2-Hydroxy-*N*-(5-nitrothiazol-2-yl)benzamide (2a).

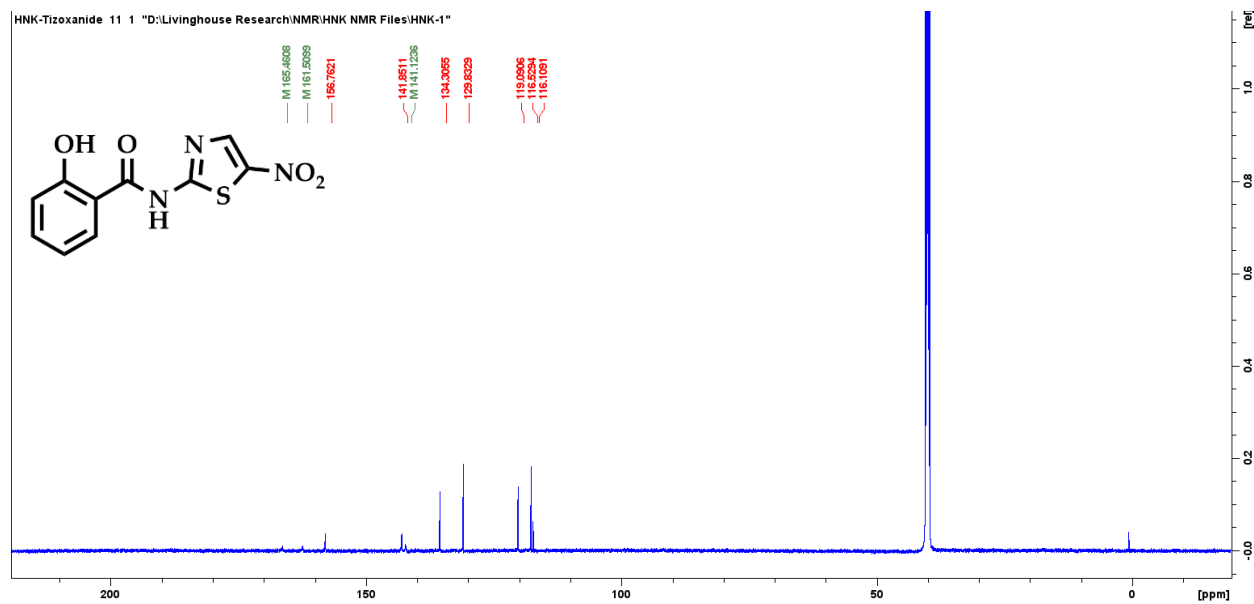


Figure 1.4B: ^{13}C NMR Spectra of 2-Hydroxy-*N*-(5-nitrothiazol-2-yl)benzamide (2a).

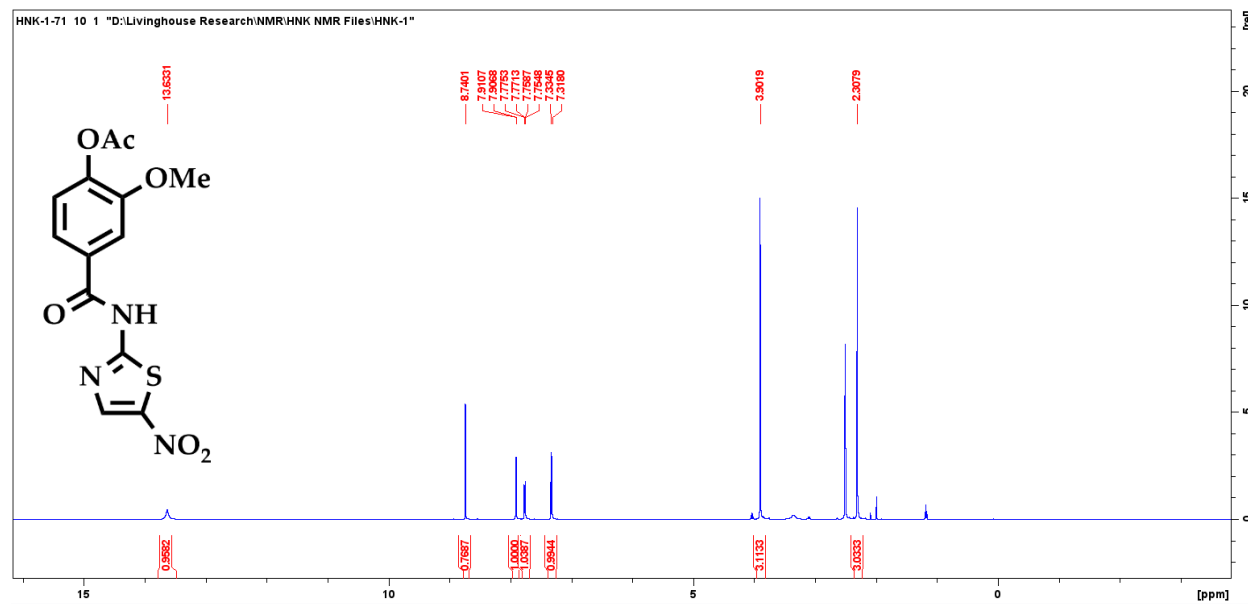


Figure 1.5B: ¹H NMR Spectra of 2-Acetoxy-5-methoxy-*N*-(5-nitrothiazol-2-yl)benzamide (**3a**).

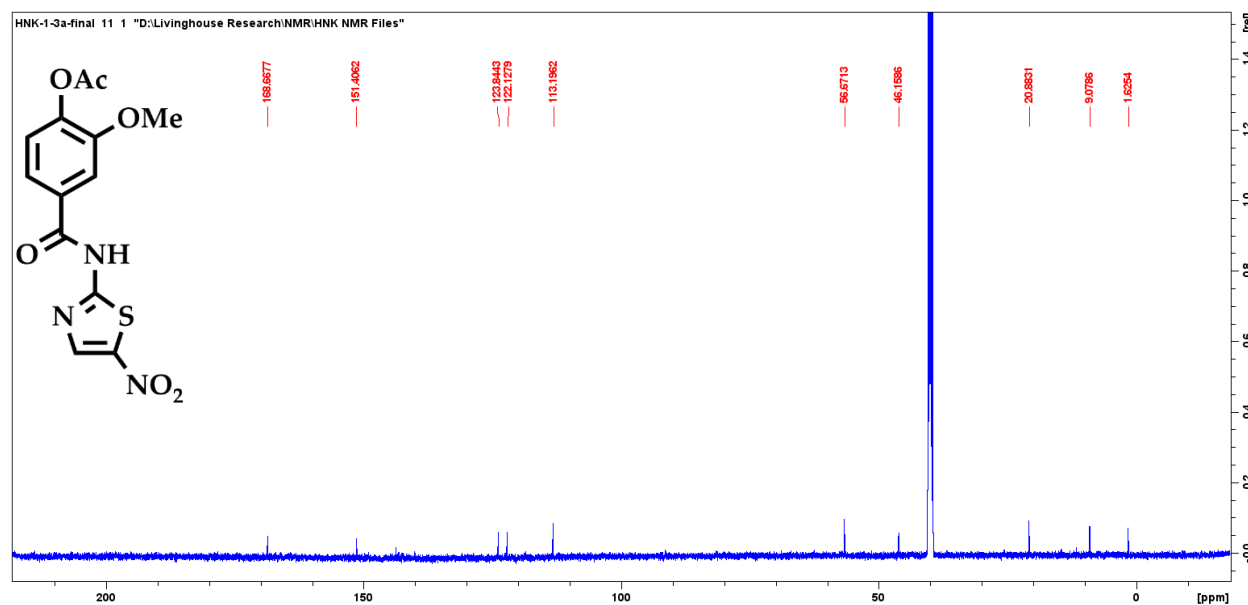


Figure 1.6B: ¹³C NMR Spectra of 2-Acetoxy-5-methoxy-*N*-(5-nitrothiazol-2-yl)benzamide (**3a**).

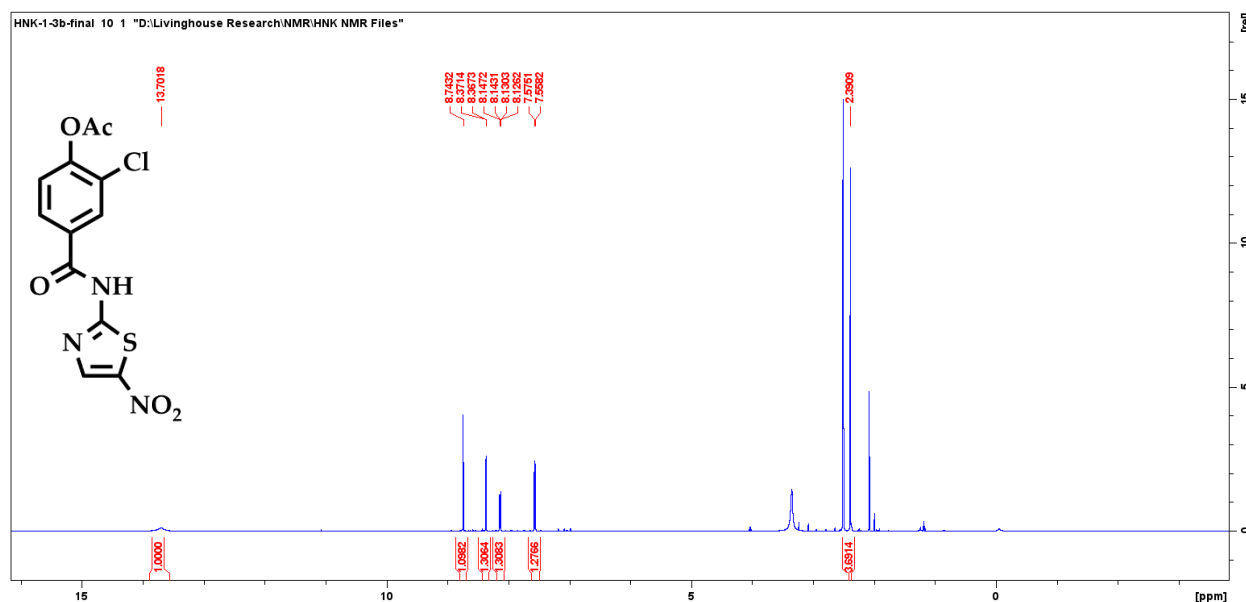


Figure 1.7B: ¹H NMR Spectra of 4-Acetoxy-3-Chloro-*N*-(5-nitrothiazol-2-yl)benzamide (**3b**).

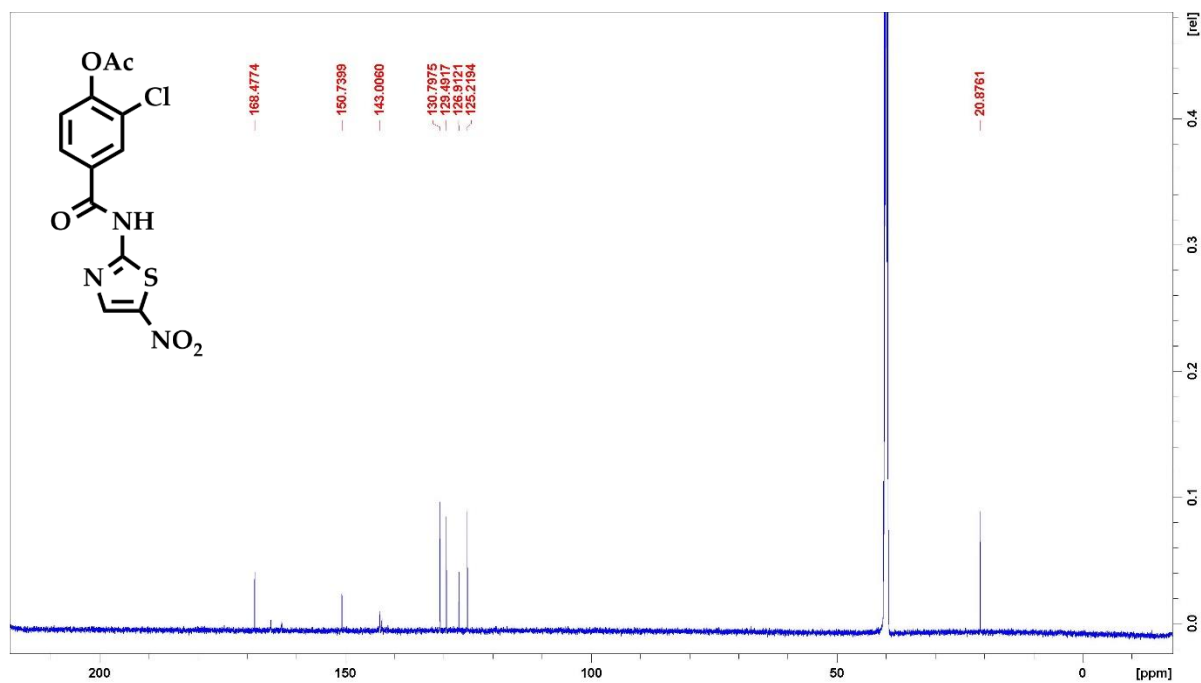


Figure 1.8B: ¹³C NMR Spectra of 4-Acetoxy-3-Chloro-*N*-(5-nitrothiazol-2-yl)benzamide (**3b**).

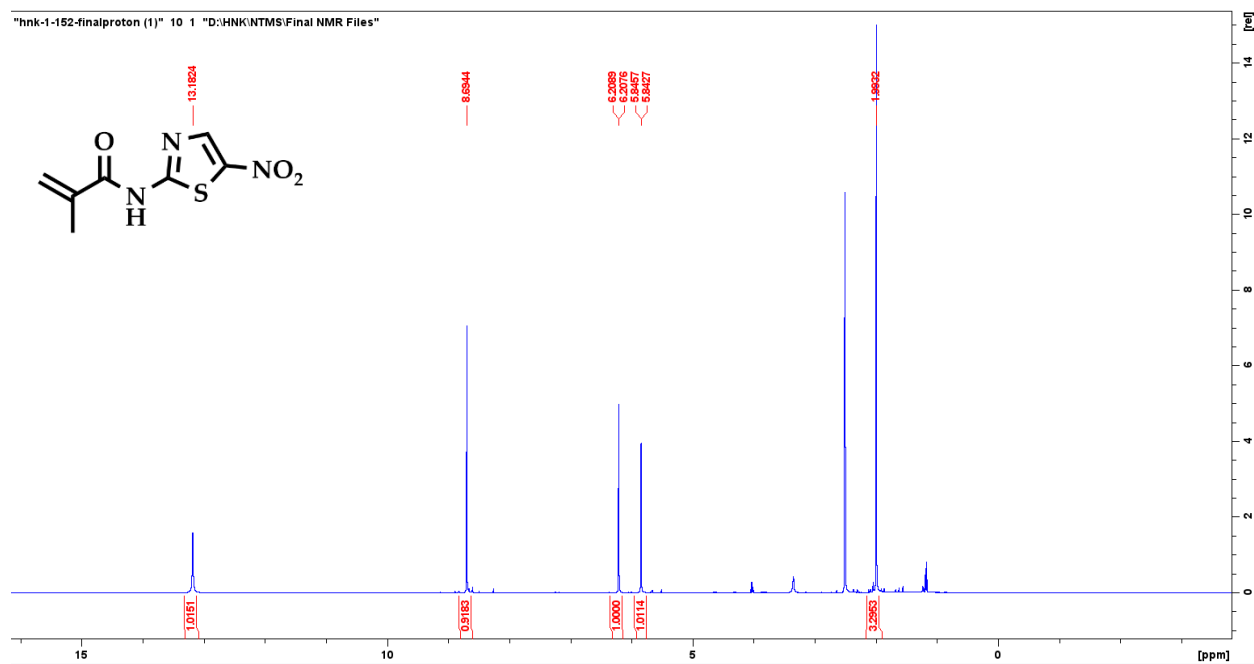


Figure 1.9B: ^1H -NMR Spectra of *N*-(5-nitrothiazol-2-yl)methacrylamide (**4a**).

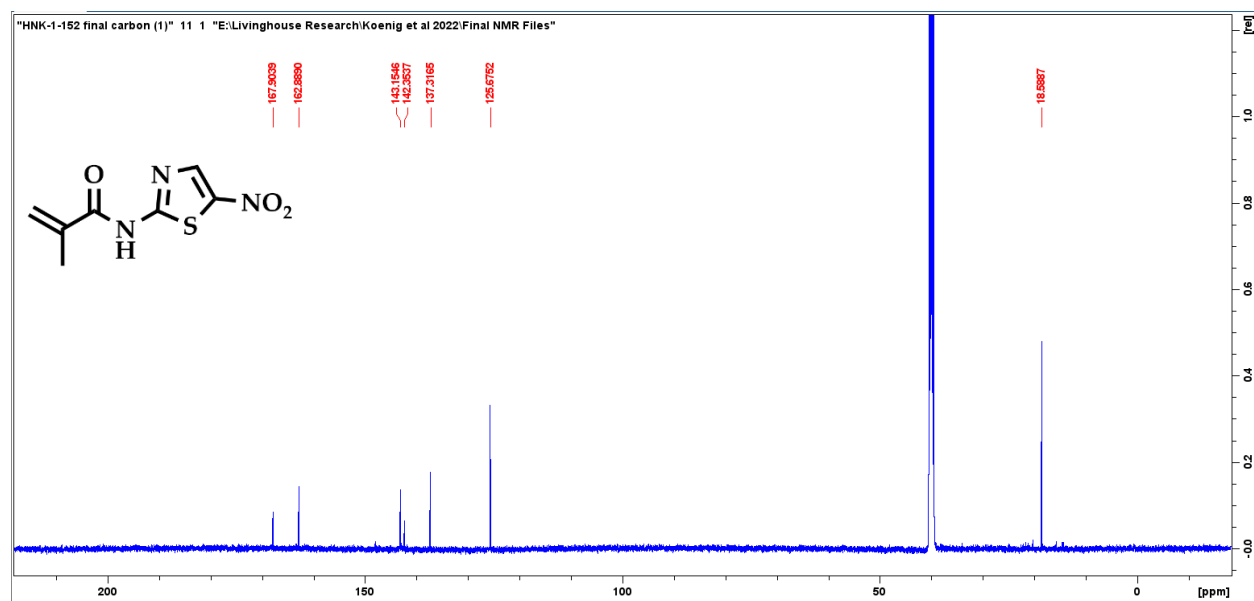


Figure 1.10B: ^{13}C -NMR Spectra of *N*-(5-nitrothiazol-2-yl)methacrylamide (**4a**).

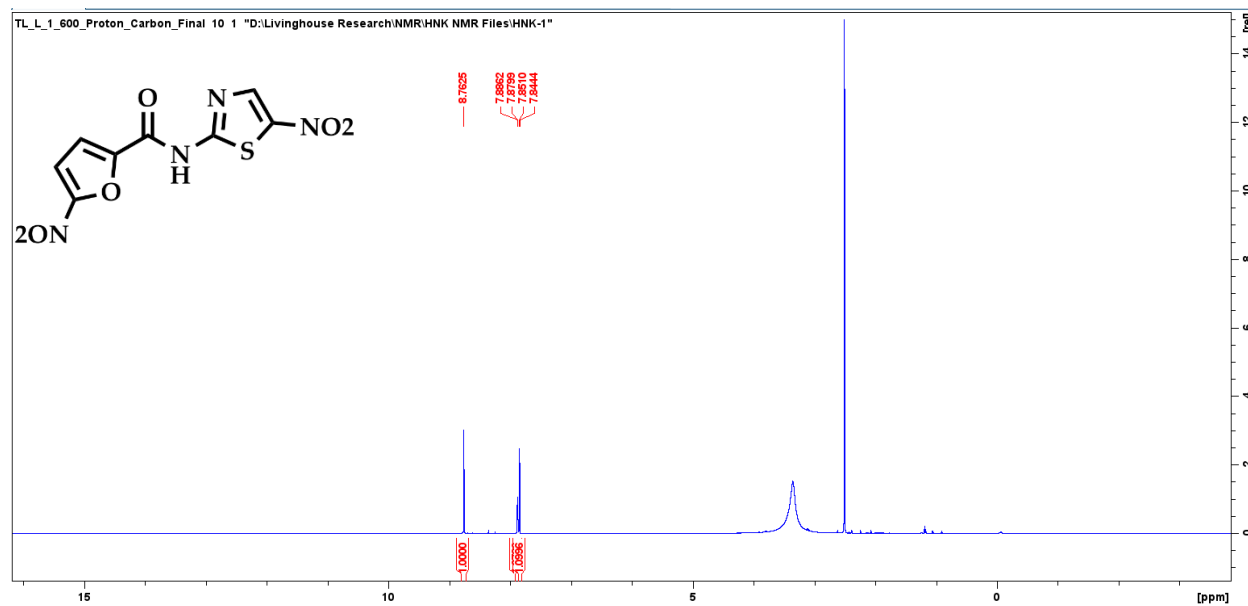


Figure 1.11B: ^1H NMR Spectra of 5-Nitro-*N*-(5-nitrothiazol-2-yl)furan-2-carboxamide (**4b**).

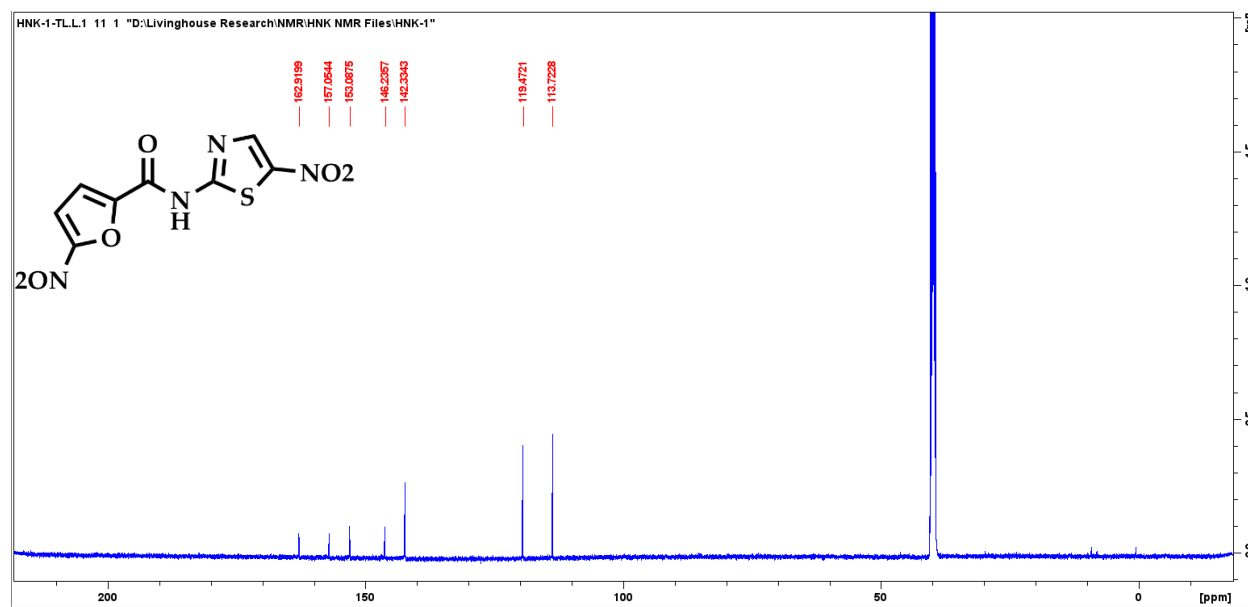
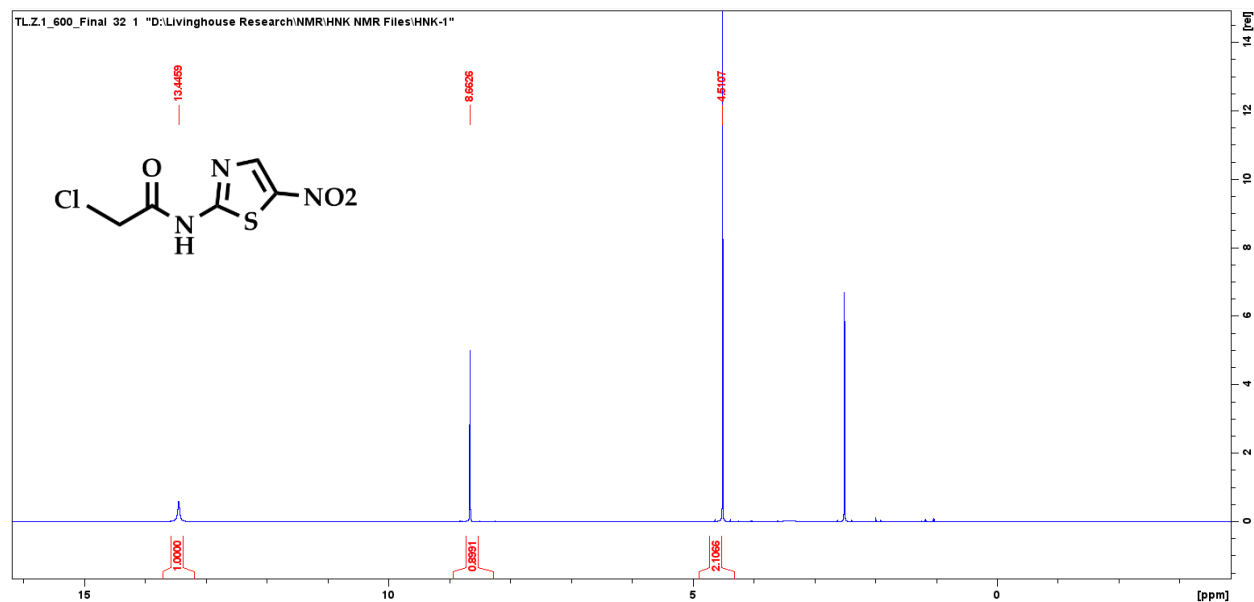
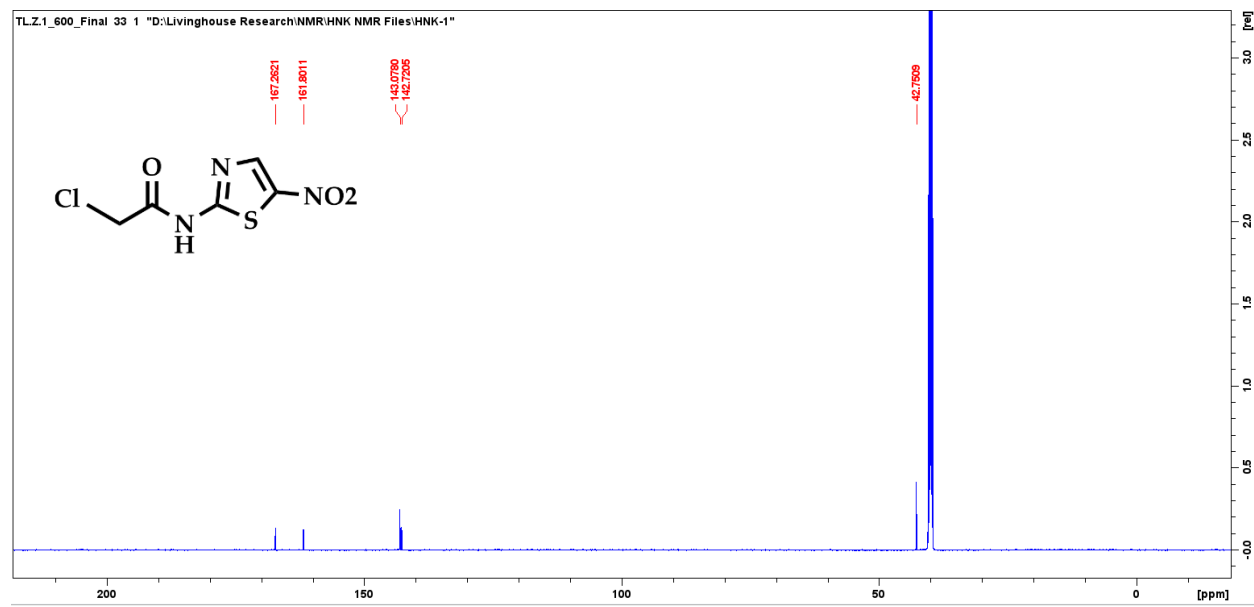


Figure 1.12B: ^{13}C NMR Spectra of 5-Nitro-*N*-(5-nitrothiazol-2-yl)furan-2-carboxamide (**4b**).

Figure 1.13B: ^1H NMR Spectra of 2-Chloro-*N*-(5-nitrothiazol-2-yl)acetamide (**4c**).Figure 1.14B: ^{13}C NMR Spectra of 2-Chloro-*N*-(5-nitrothiazol-2-yl)acetamide (**4c**).

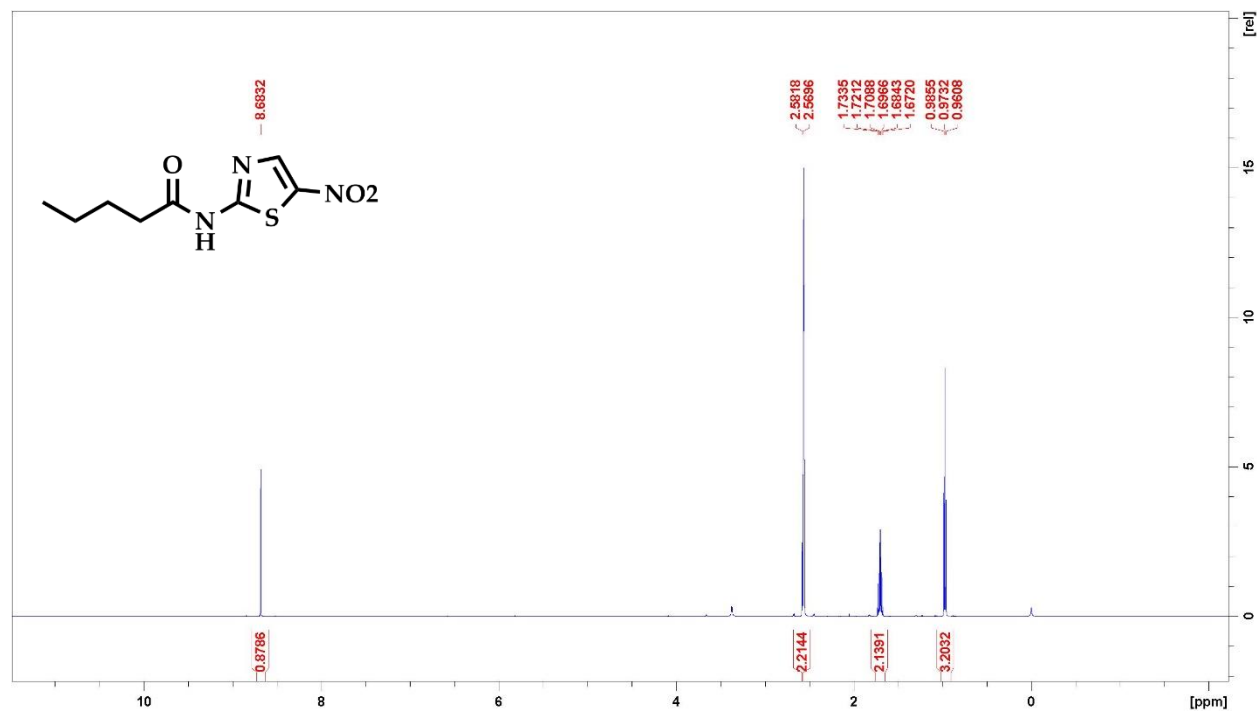


Figure 1.15B: ¹H NMR Spectra of *N*-(5-Nitrothiazol-2-yl)butyramide (**4d**).

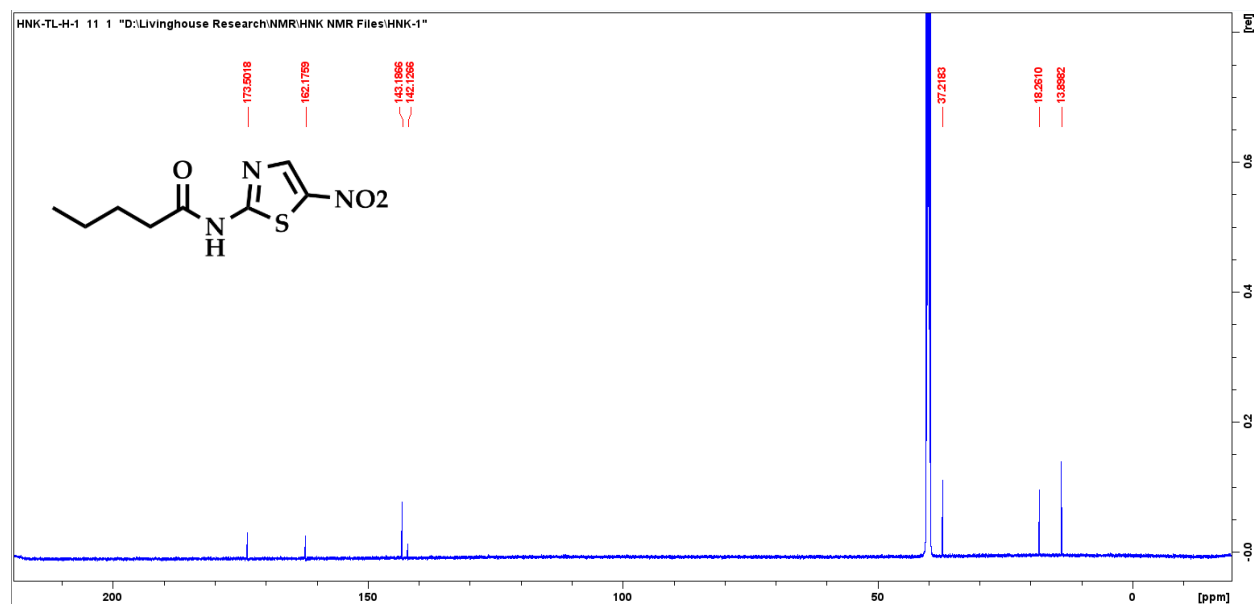
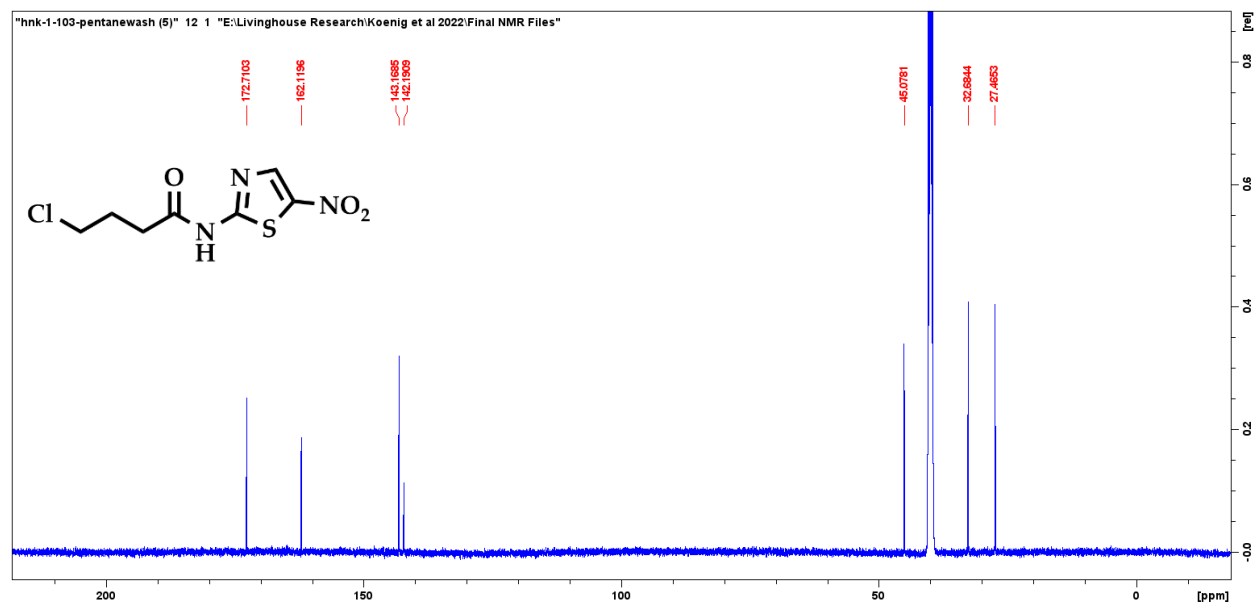
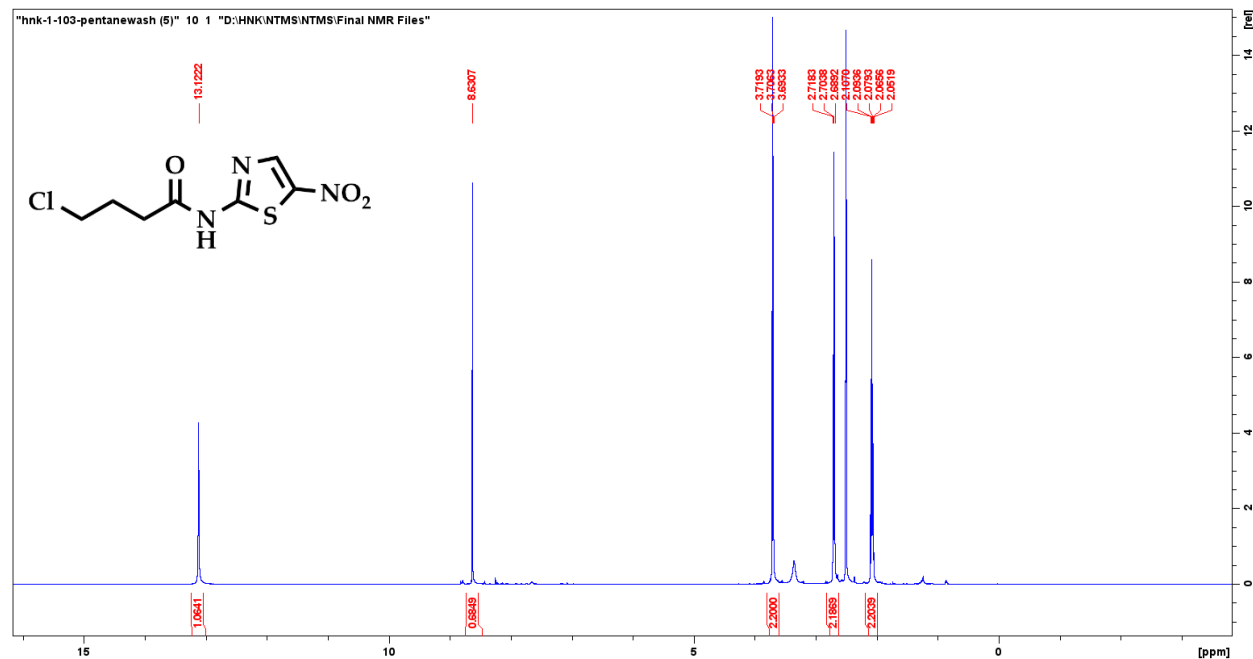


Figure 1.16B: ¹³C NMR Spectra of *N*-(5-Nitrothiazol-2-yl)butyramide (**4d**).

Figure 1.17B: ¹H-NMR Spectra of 4-chloro-*N*-(5-nitrothiazol-2-yl)butyramide (**4e**).Figure 1.18B: ¹³C-NMR Spectra of 4-chloro-*N*-(5-nitrothiazol-2-yl)butyramide (**4e**).

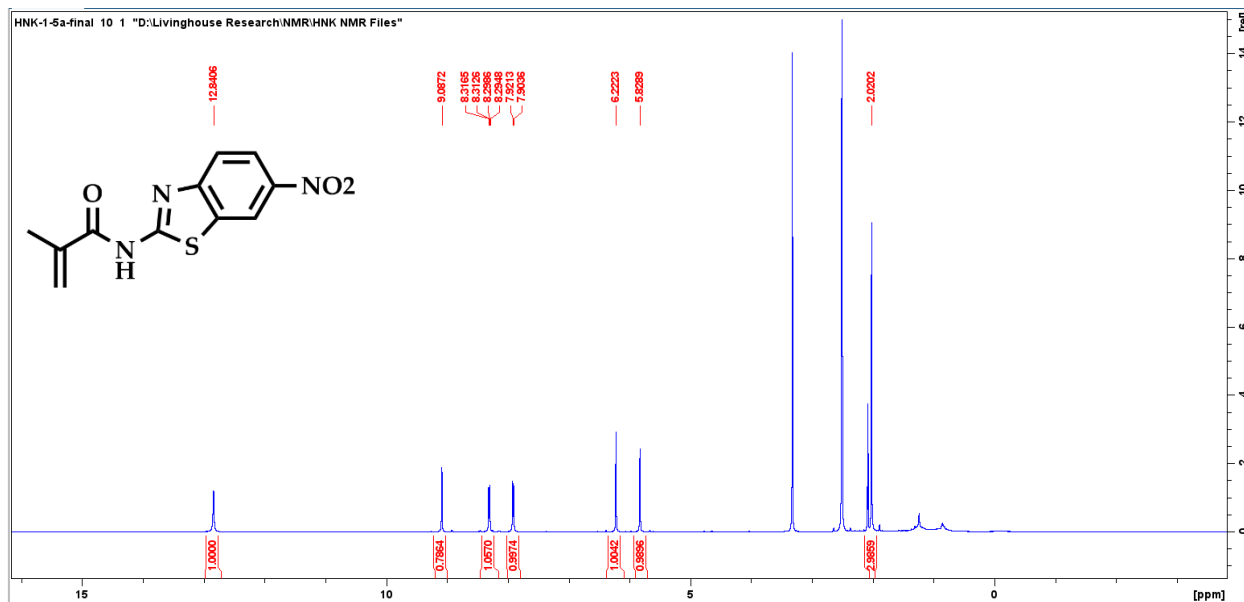


Figure 1.19B: ^1H -NMR Spectra of *N*-(6-Nitrobenzo[d]thiazol-2-yl)methacrylamide (5a).

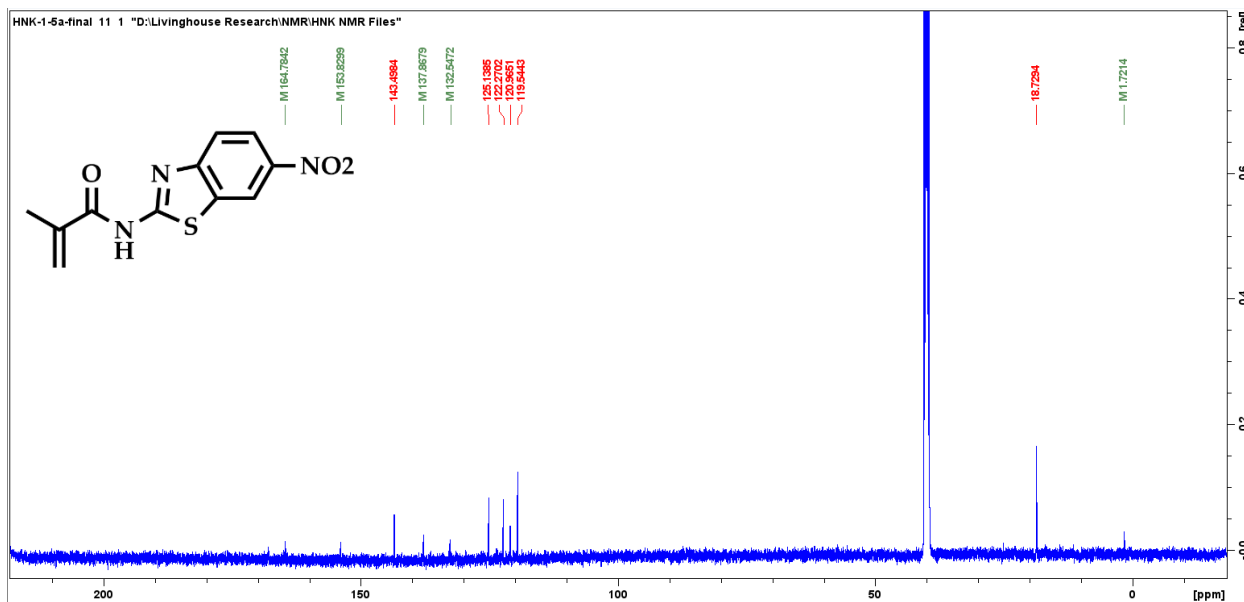


Figure 1.20B: ^{13}C -NMR Spectra of *N*-(6-Nitrobenzo[d]thiazol-2-yl)methacrylamide (5a).

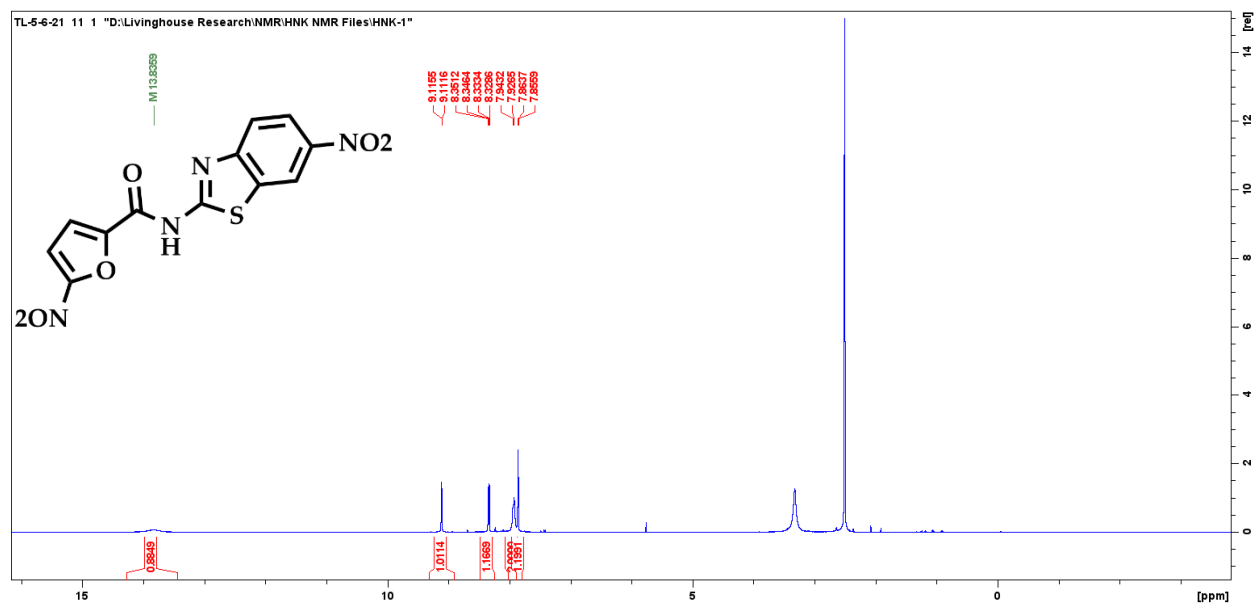


Figure 1.21B: ^1H NMR Spectra of 5-Nitro-N-(6-nitrobenzo[d]thiazol-2-yl)furan-2-carboxamide (5b).

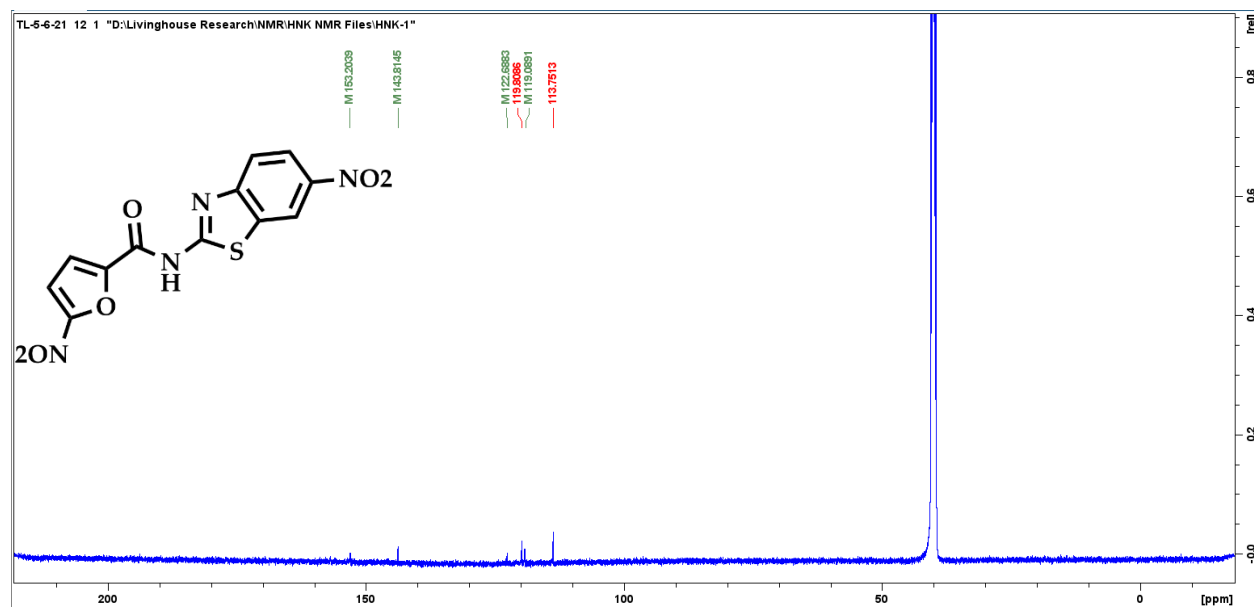


Figure 1.22B: ^{13}C NMR Spectra of 5-Nitro-N-(6-nitrobenzo[d]thiazol-2-yl)furan-2-carboxamide (5b).

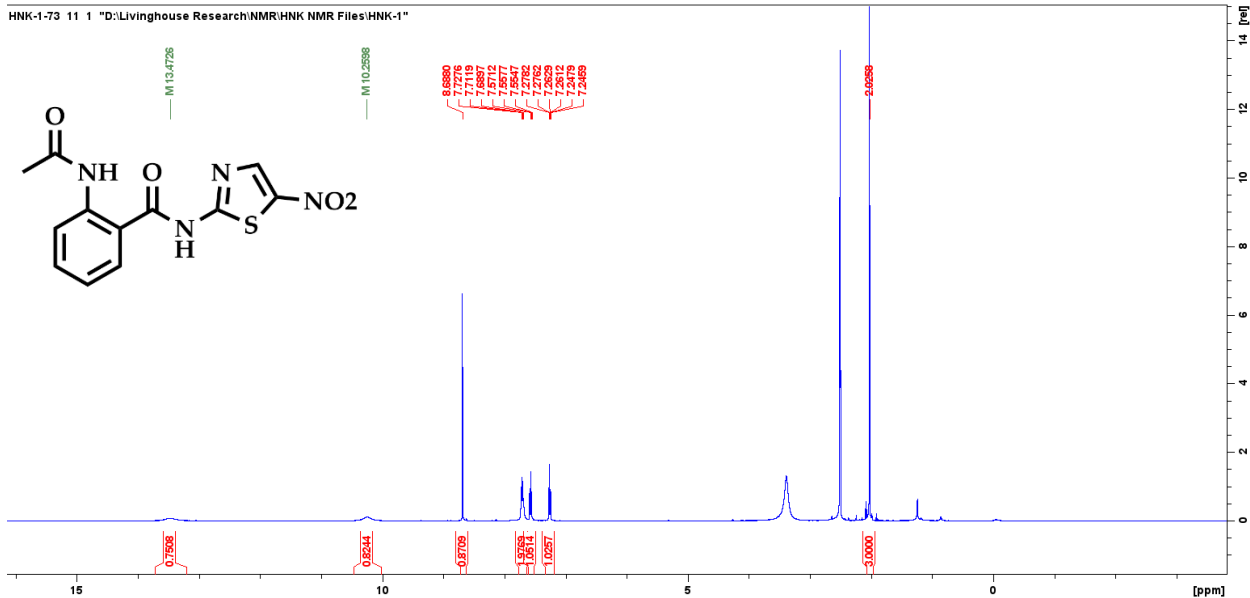


Figure 1.23B: ^1H NMR Spectra of 2-Acetamido-*N*-(5-nitrothiazol-2-yl)benzamide (**6a**).

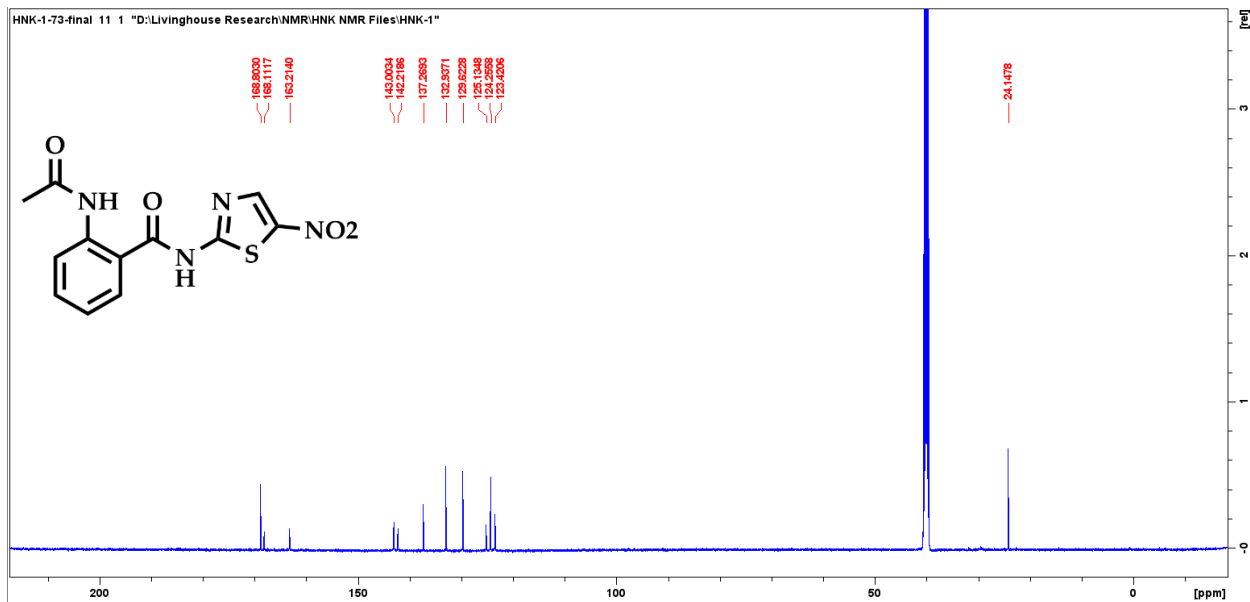


Figure 1.24B: ^{13}C NMR Spectra of 2-Acetamido-*N*-(5-nitrothiazol-2-yl)benzamide (**6a**).

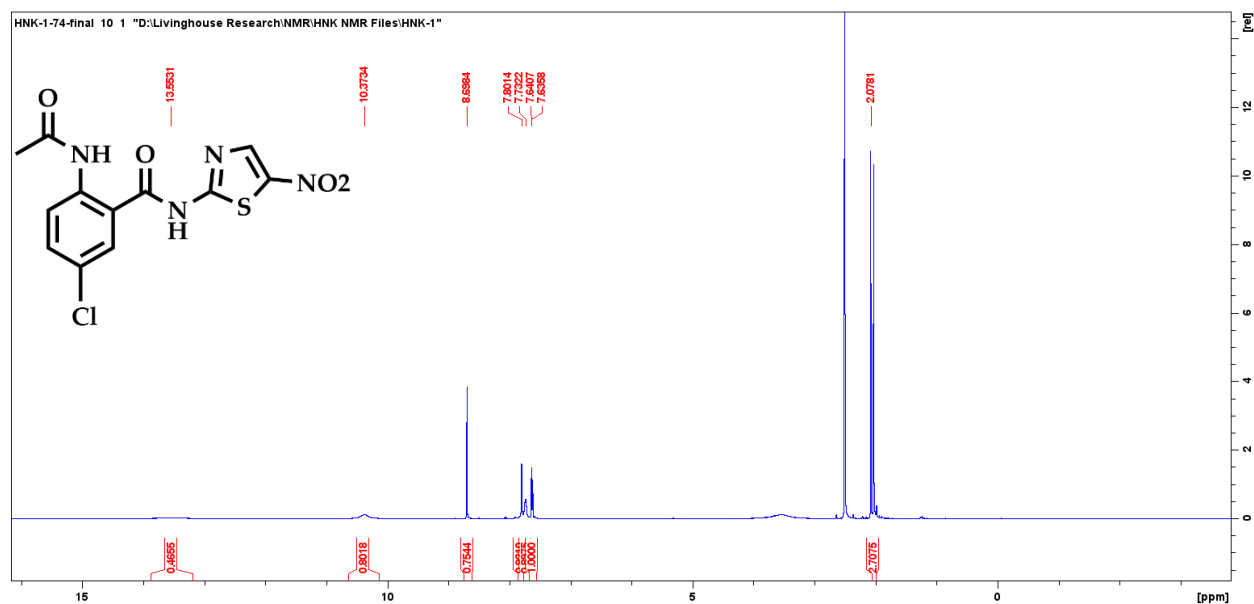


Figure 1.25B: ¹H NMR Spectra of 2-Acetamido-5-chloro-*N*-(5-nitrothiazol-2-yl)benzamide (**6b**).

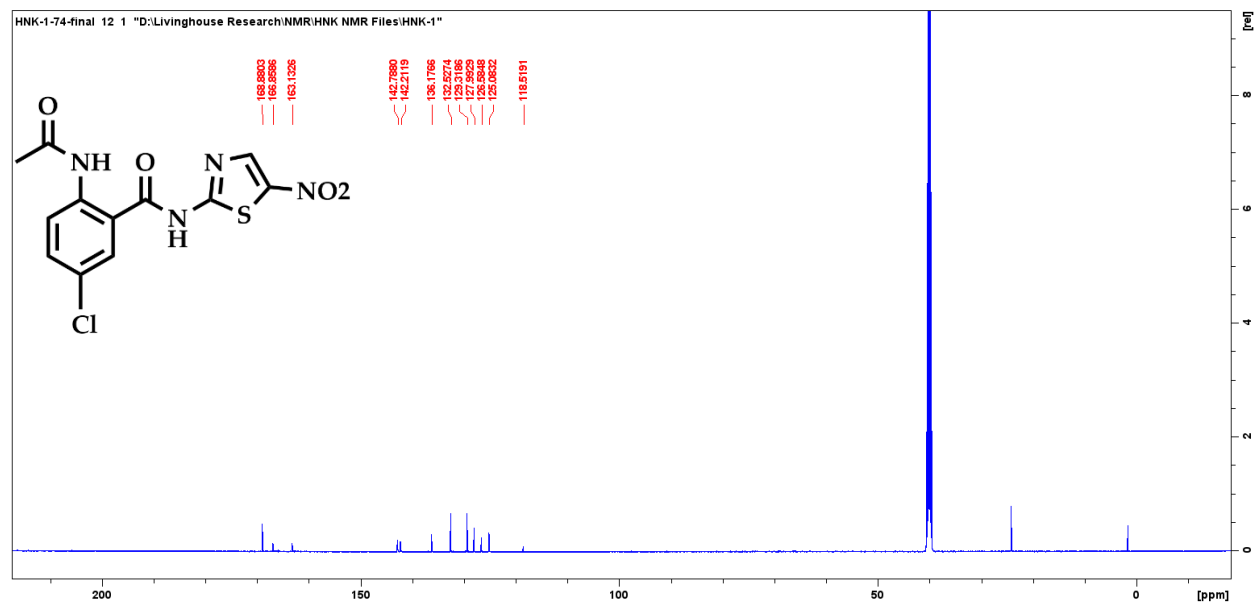


Figure 1.26B: ¹³C NMR Spectra of 2-Acetamido-5-chloro-*N*-(5-nitrothiazol-2-yl)benzamide (**6b**).

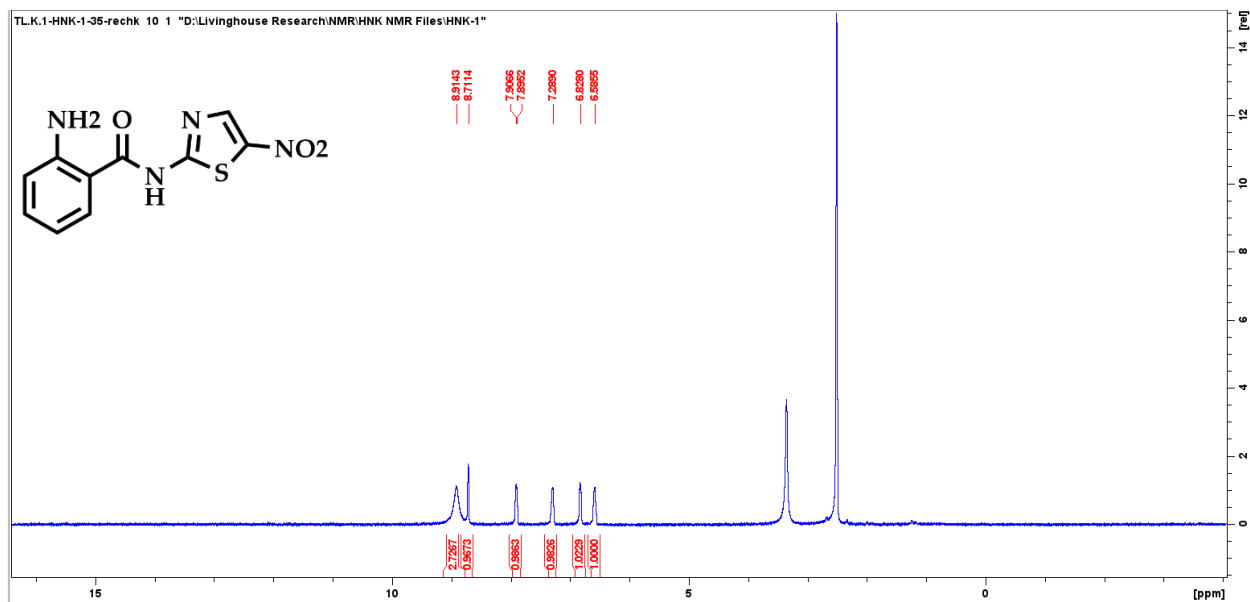


Figure 1.27B: ^1H NMR Spectra of 2-Amino-*N*-(5-nitrothiazol-2-yl)benzamide (7a).

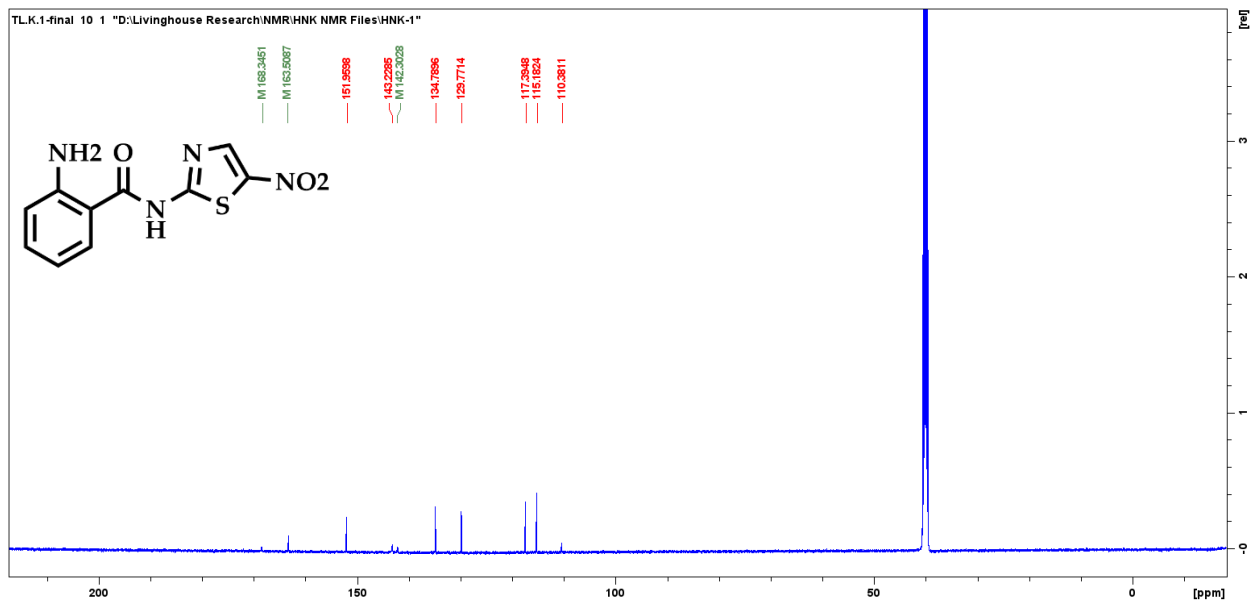


Figure 1.28B: ^{13}C NMR Spectra of 2-Amino-*N*-(5-nitrothiazol-2-yl)benzamide (7a).

TL-HNK_C 13 1 "D:\Livinghouse Research\NMR\HNK NMR Files\HNK-1"

Nc1ccc(Cl)cc1C(=O)Nc2nc([N+](=O)[O-])cs2

163.2469
151.5382
134.7882
129.7640
117.5795
115.1697
110.4004

200 150 100 50 0 [ppm]

The image displays a ¹³C NMR spectrum of 2-chloro-N-(4-nitrothiazol-2-yl)-3-aminobenzamide. The chemical structure is shown in the top left corner. The spectrum features several peaks in the aromatic region, with the following chemical shifts (ppm) labeled above the baseline: 163.2469, 151.5382, 134.7882, 129.7640, 117.5795, 115.1697, and 110.4004. A large, sharp peak is visible at approximately 38 ppm, likely corresponding to the solvent DMSO-d₆. The x-axis is labeled from 200 to 0 ppm.

Figure 1.30B: ^{13}C NMR Spectra of 2-Amido-5-chloro-*N*-(5-nitrothiazol-2-yl)benzamide (**7b**).

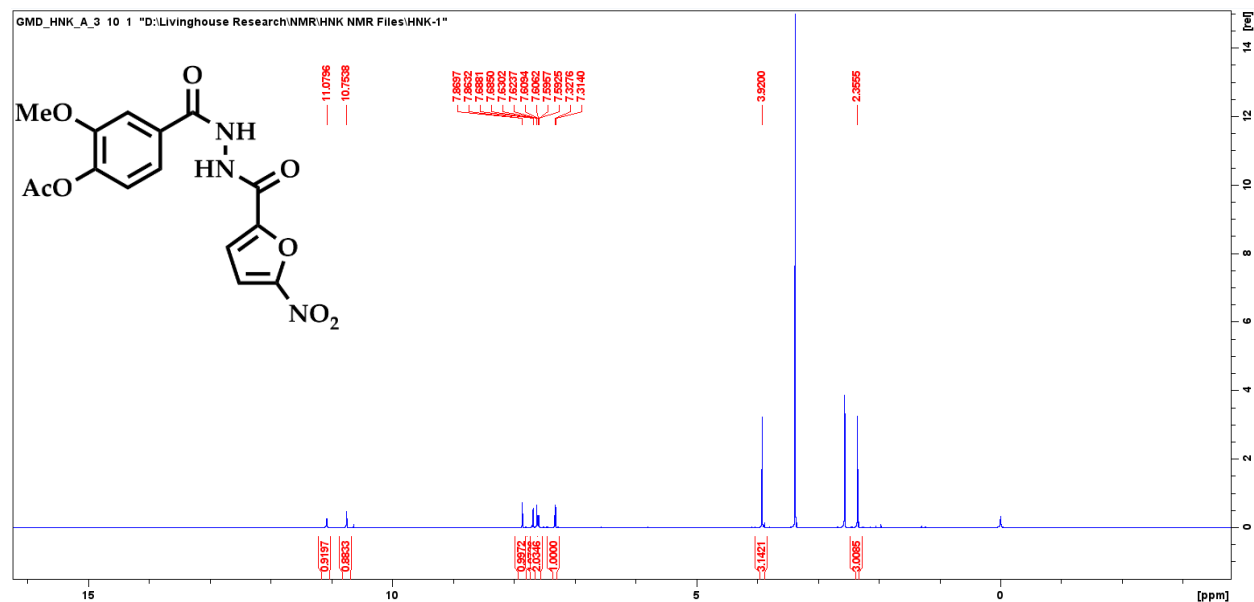


Figure 1.31B: ¹H NMR Spectra of 4-Acetoxy-3-methoxy-*N*-(5-nitrofuran-2-carbonyl)benzhydrazide (**9a**).

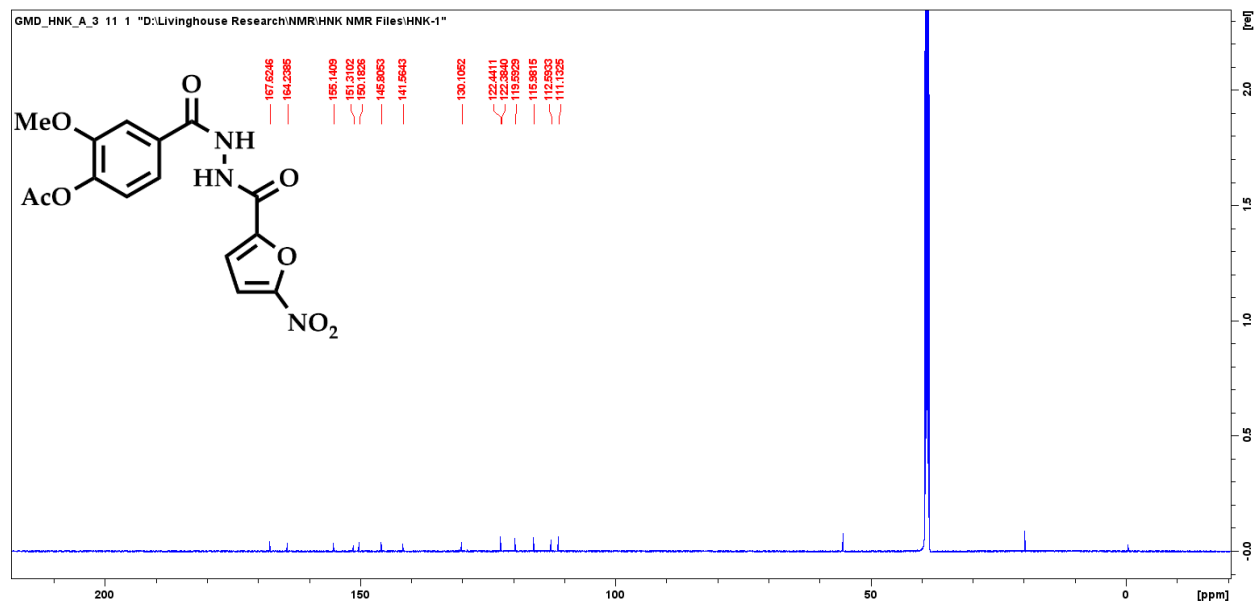


Figure 1.32B: ¹³C NMR Spectra of 4-Acetoxy-3-methoxy-*N*-(5-nitrofuran-2-carbonyl)benzhydrazide (**9a**).

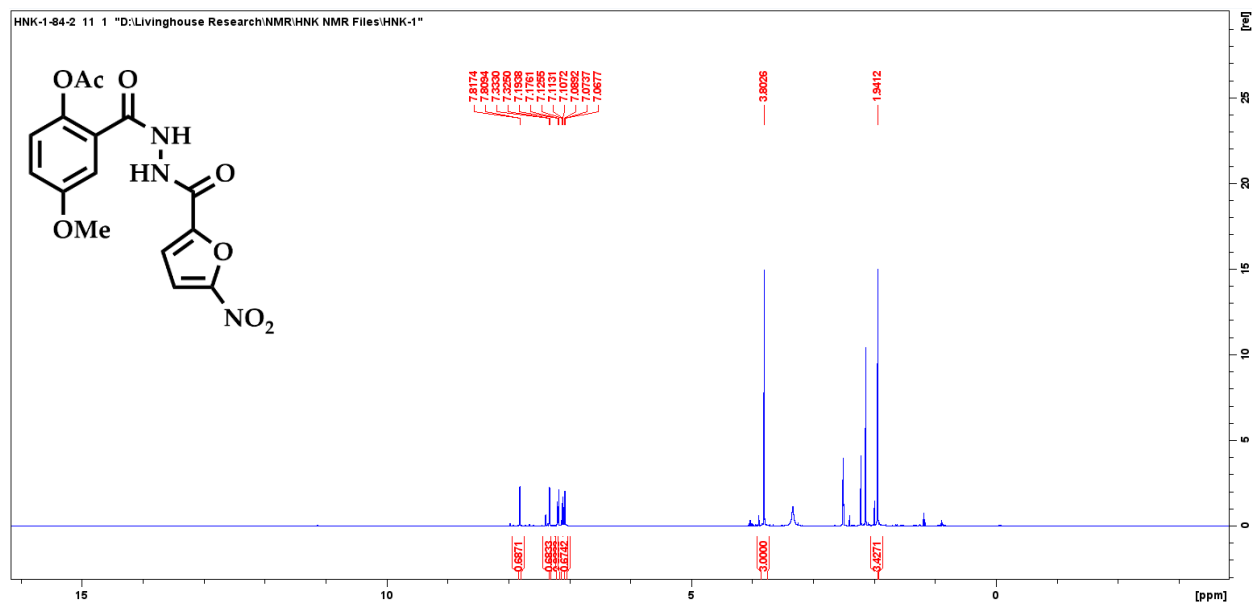


Figure 1.33B: ¹H NMR Spectra of 2-Acetoxy-5-methoxy-N-(5-nitrofuran-2-carbonyl)benzhydrazide (**10a**).

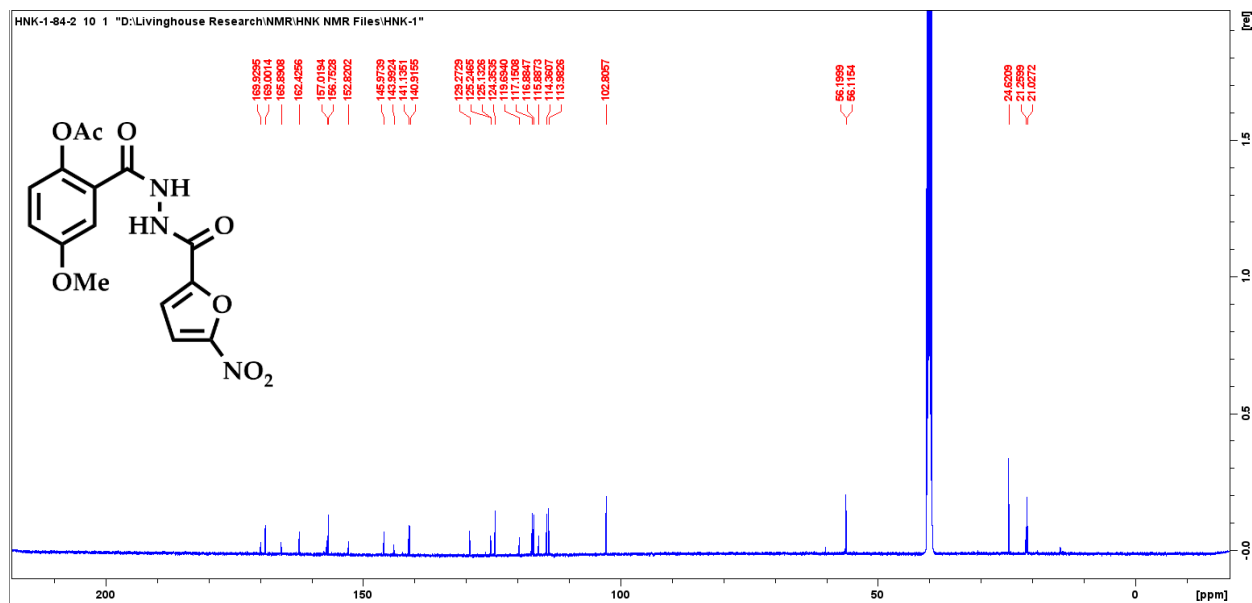


Figure 1.34B: ¹³C NMR Spectra of 2-Acetoxy-5-methoxy-N-(5-nitrofuran-2-carbonyl)benzhydrazide (**10a**).

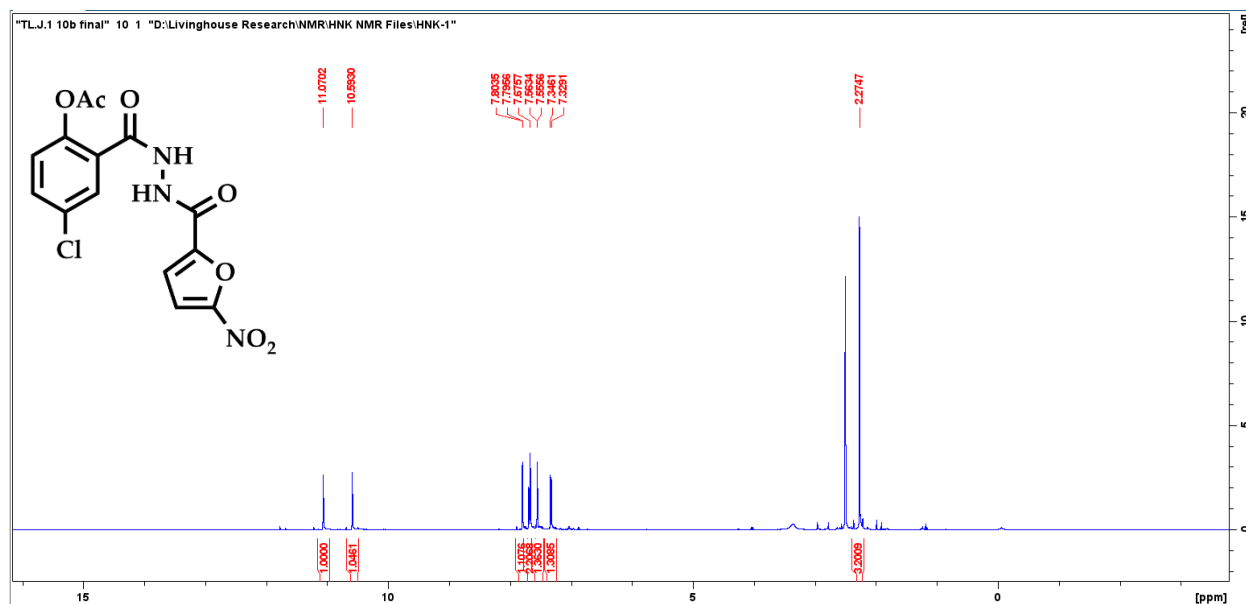


Figure 1.35B: ^1H NMR Spectra of 2-Acetoxy-5-chloro-*N*-(5-nitrofuran-2-carbonyl)benzhydrazide (**10b**).

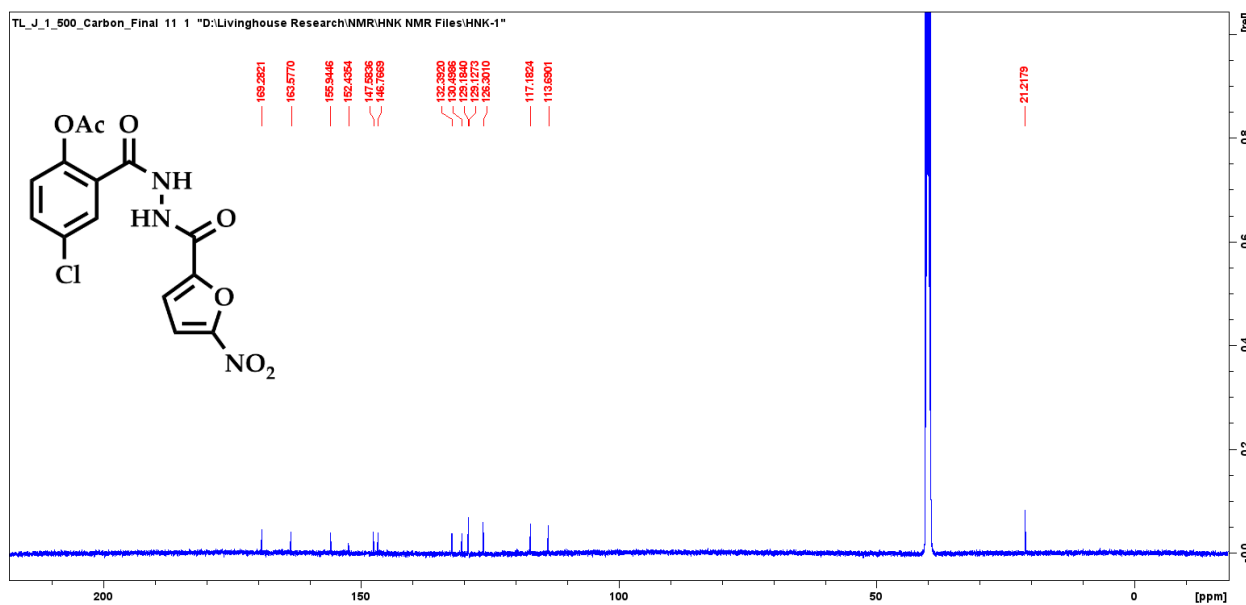
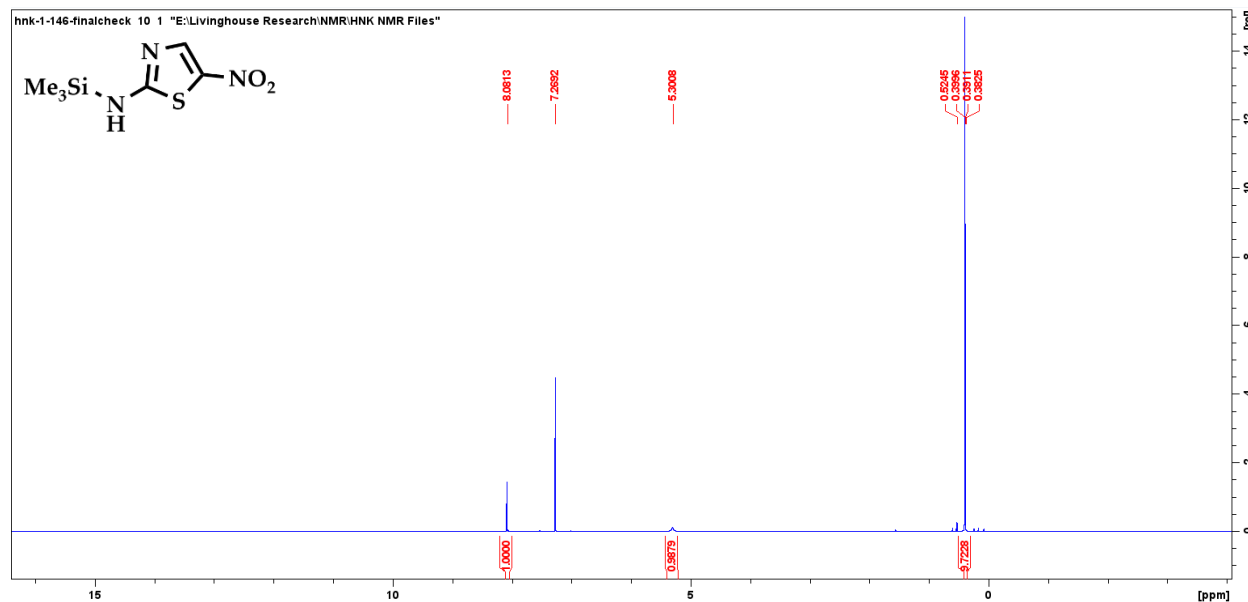
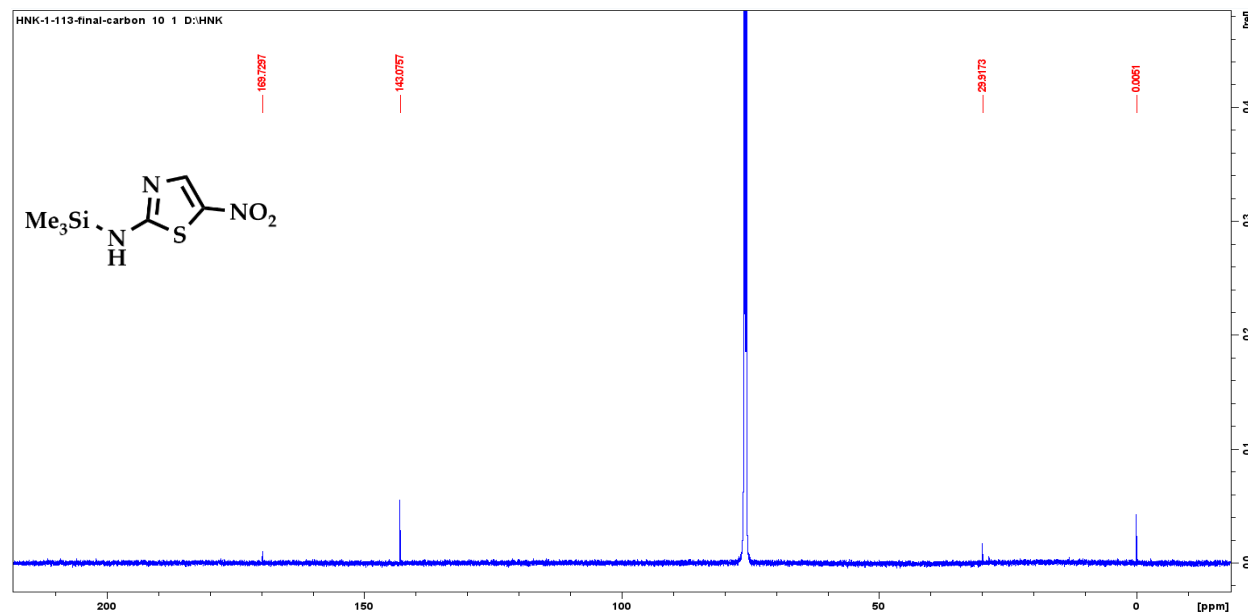


Figure 1.36B: ^{13}C NMR Spectra of 2-Acetoxy-5-chloro-*N*-(5-nitrofuran-2-carbonyl)benzhydrazide (**10b**).

2B Characterization of Compounds Synthesized in Chapter 3Figure 2.1B: ^1H -NMR Spectra of *N*-(trimethylsilyl)-2-amino-5-nitrothiazole (**1**).Figure 2.2B: ^{13}C -NMR Spectra of *N*-(trimethylsilyl)-2-amino-5-nitrothiazole (**1**).

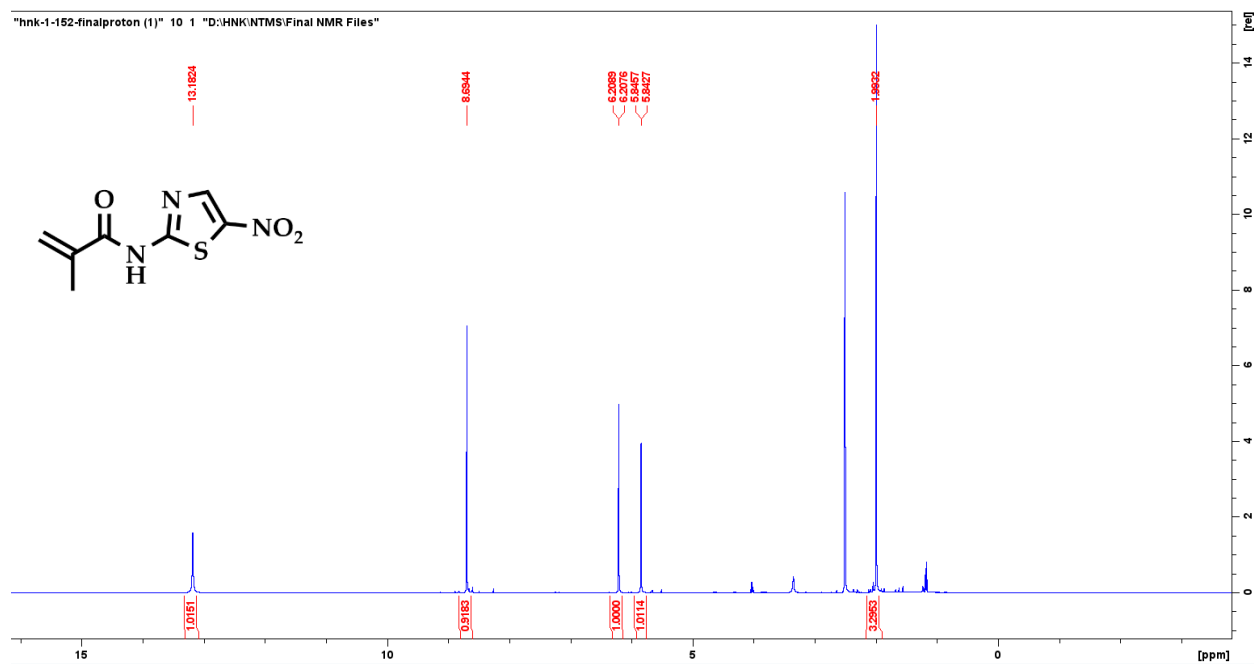


Figure 2.3B: ^1H -NMR Spectra of *N*-(5-nitrothiazol-2-yl)methacrylamide (**4**).

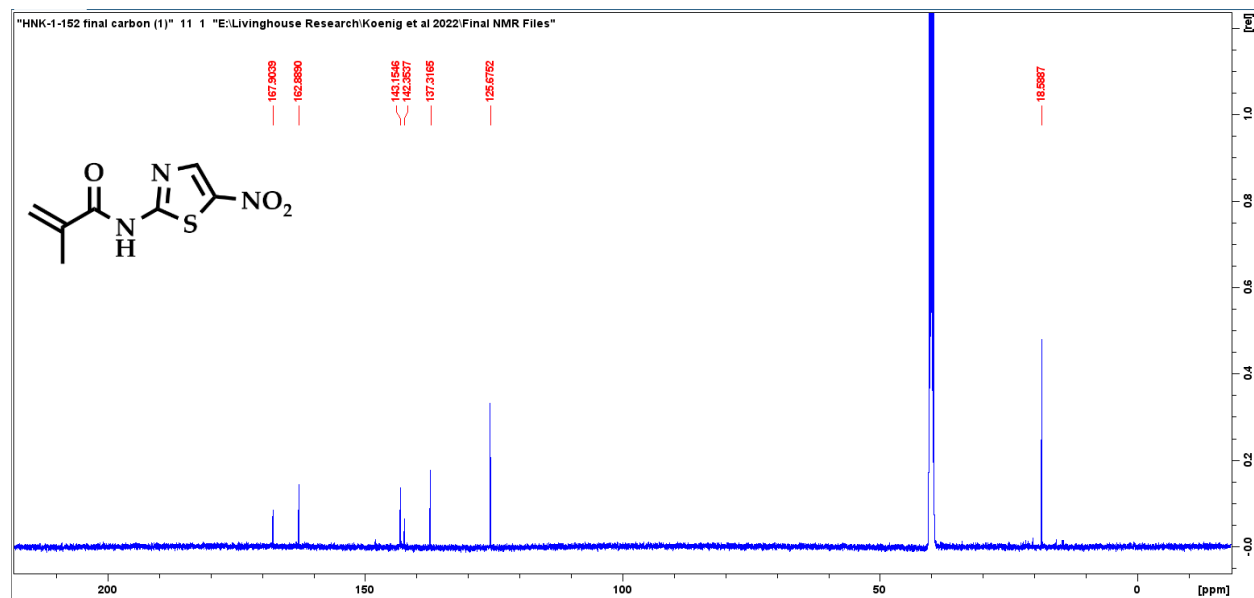


Figure 2.4B: ^{13}C -NMR Spectra of *N*-(5-nitrothiazol-2-yl)methacrylamide (**4**).

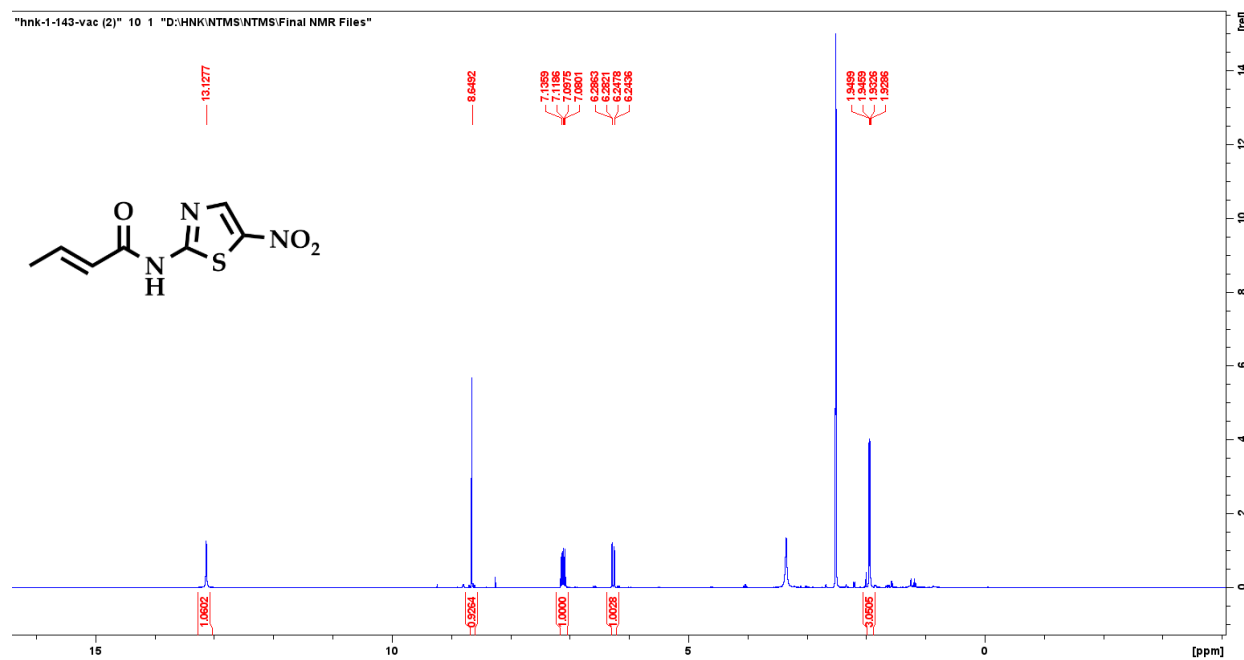


Figure 2.5B: ^1H -NMR Spectra of (E)-N-(5-nitrothiazol-2-yl)but-2-enamide (5).

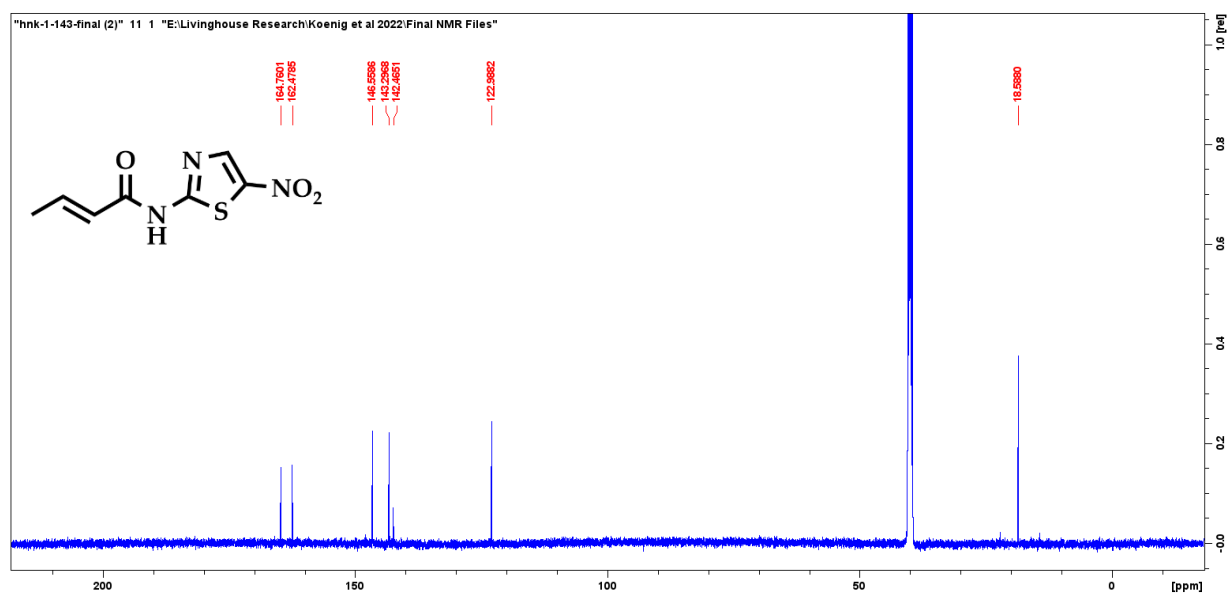


Figure 2.6B: ^{13}C -NMR Spectra of (E)-N-(5-nitrothiazol-2-yl)but-2-enamide (5).

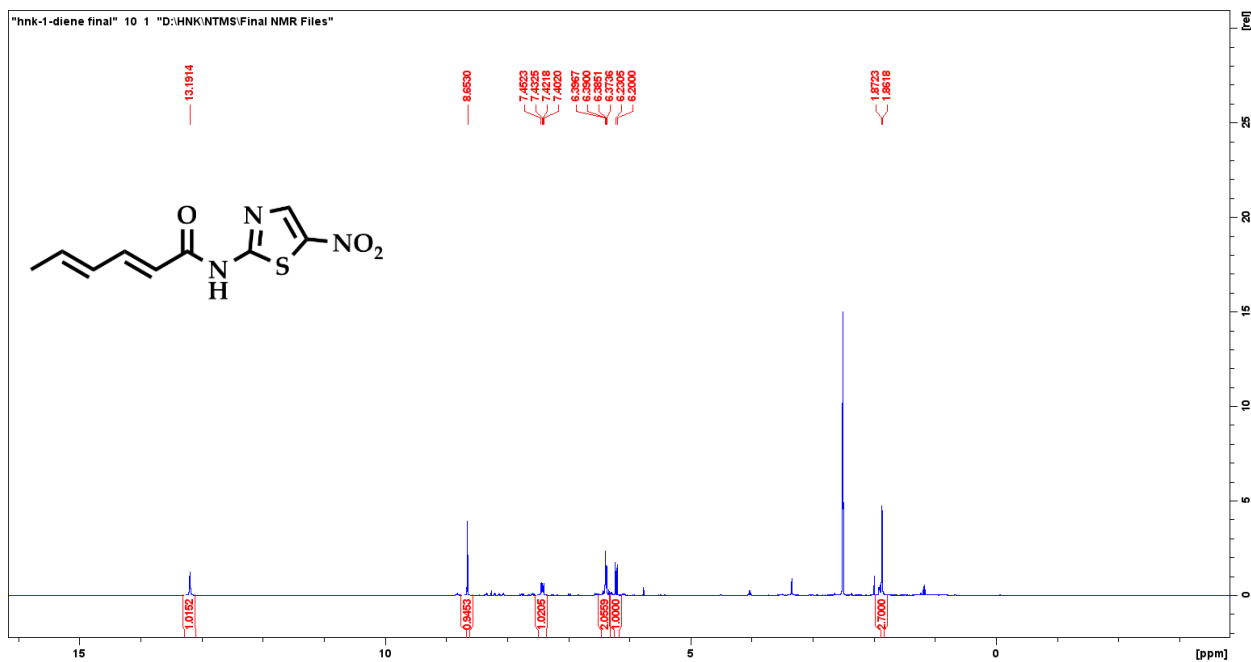


Figure 2.7B: ^1H -NMR Spectra of (2E,4E)-N-(5-nitrothiazol-2-yl)hexa-2,4-dienamide (6).

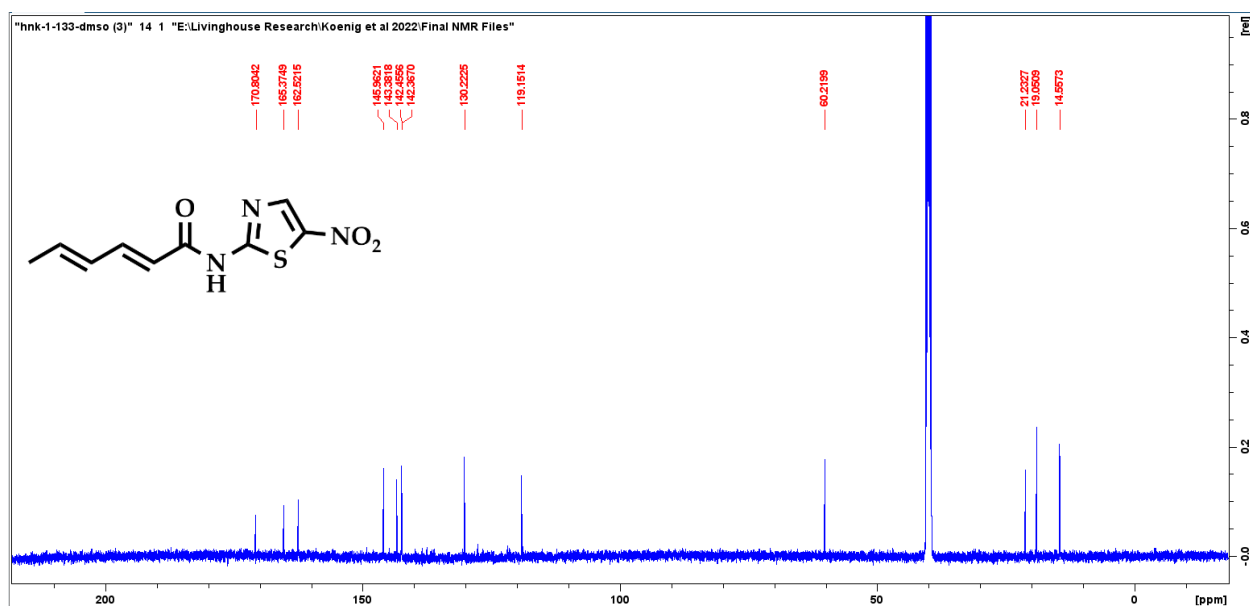


Figure 2.8B: ^{13}C -NMR Spectra of (2E,4E)-N-(5-nitrothiazol-2-yl)hexa-2,4-dienamide (6).

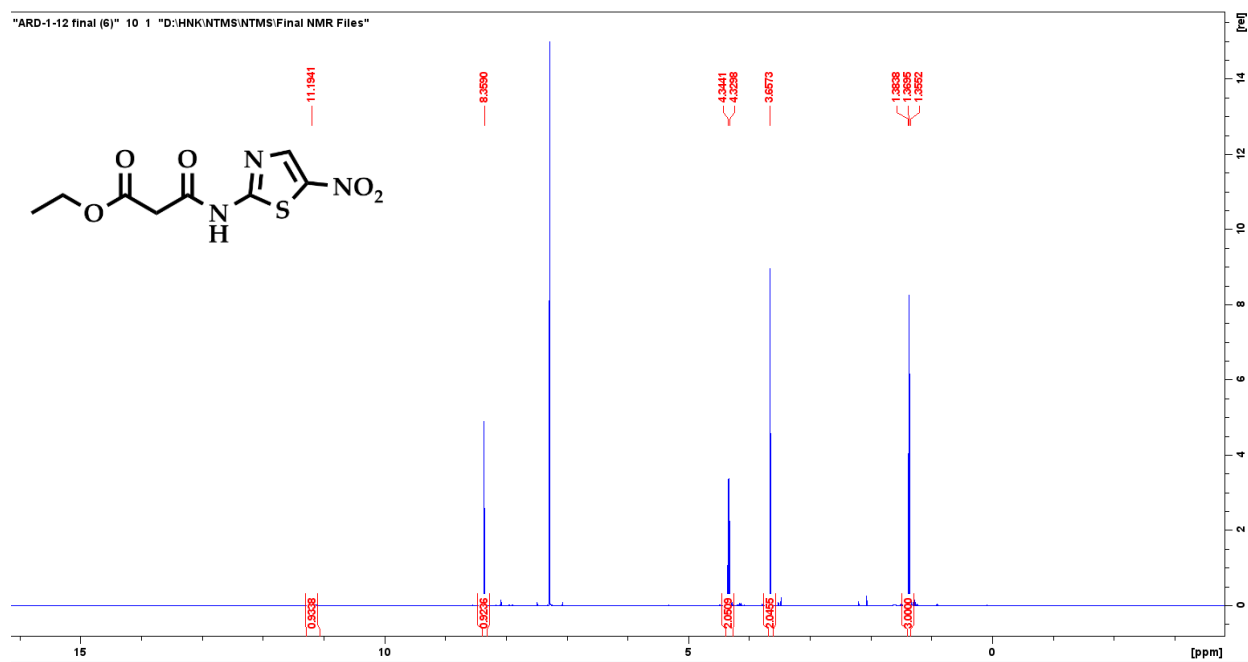


Figure 2.9B: ¹H-NMR Spectra of ethyl 3-((5-nitrothiazol-2-yl)amino)-3-oxopropanoate (7).

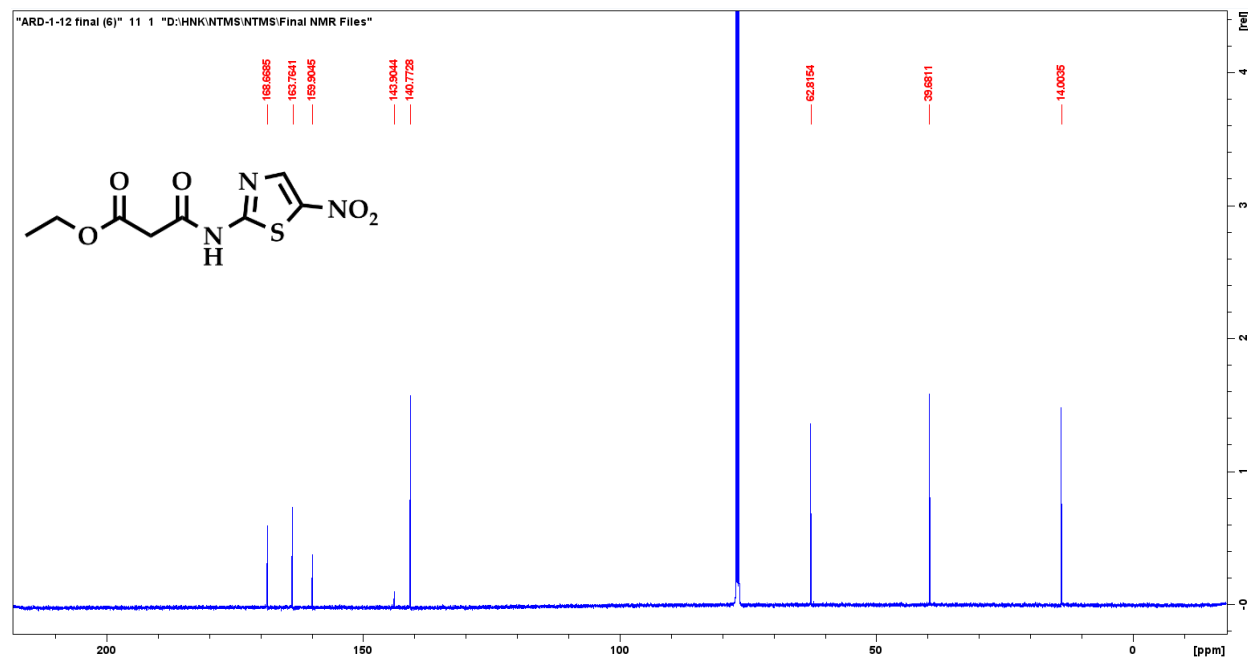


Figure 2.10B: ¹³C-NMR Spectra of ethyl 3-((5-nitrothiazol-2-yl)amino)-3-oxopropanoate (7).

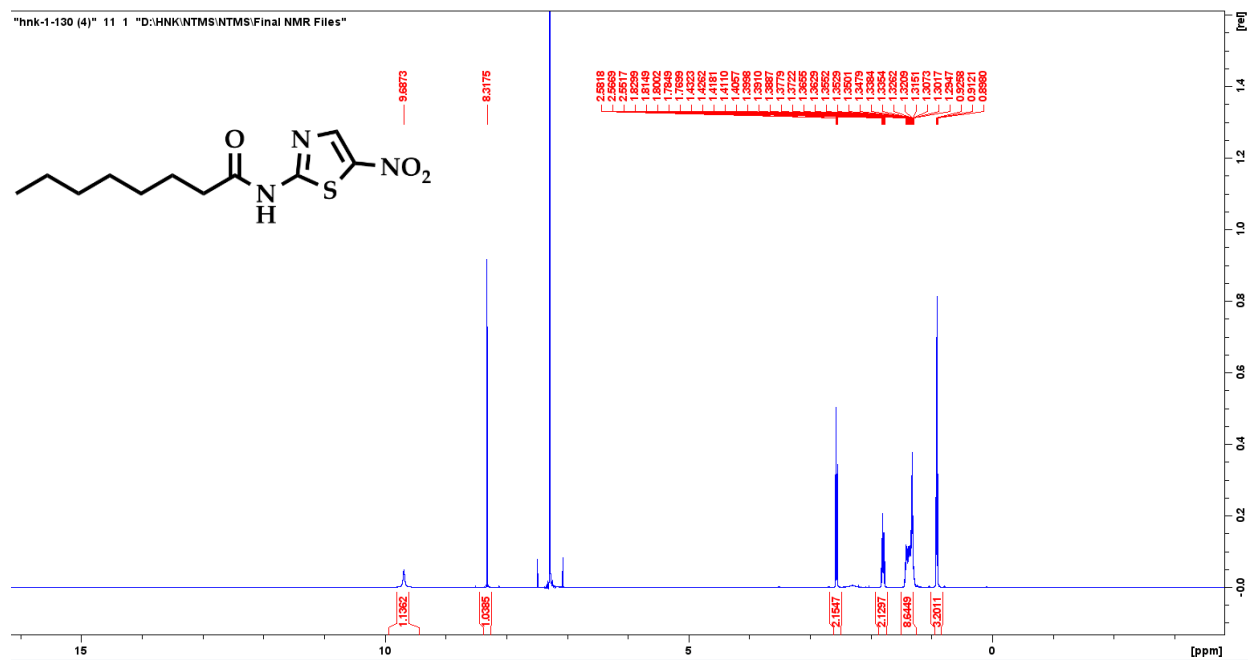


Figure 2.11B: ^1H -NMR Spectra of *N*-(5-nitrothiazol-2-yl)octanamide (**8**).

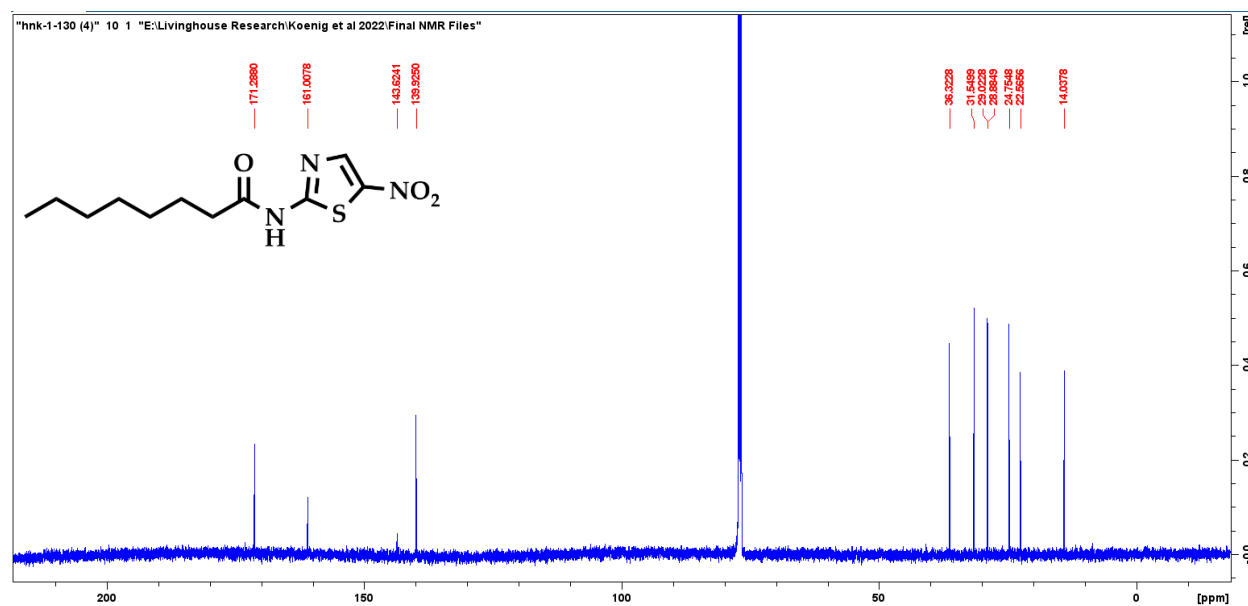


Figure 2.12B: ^{13}C -NMR Spectra of *N*-(5-nitrothiazol-2-yl)octanamide (**8**).

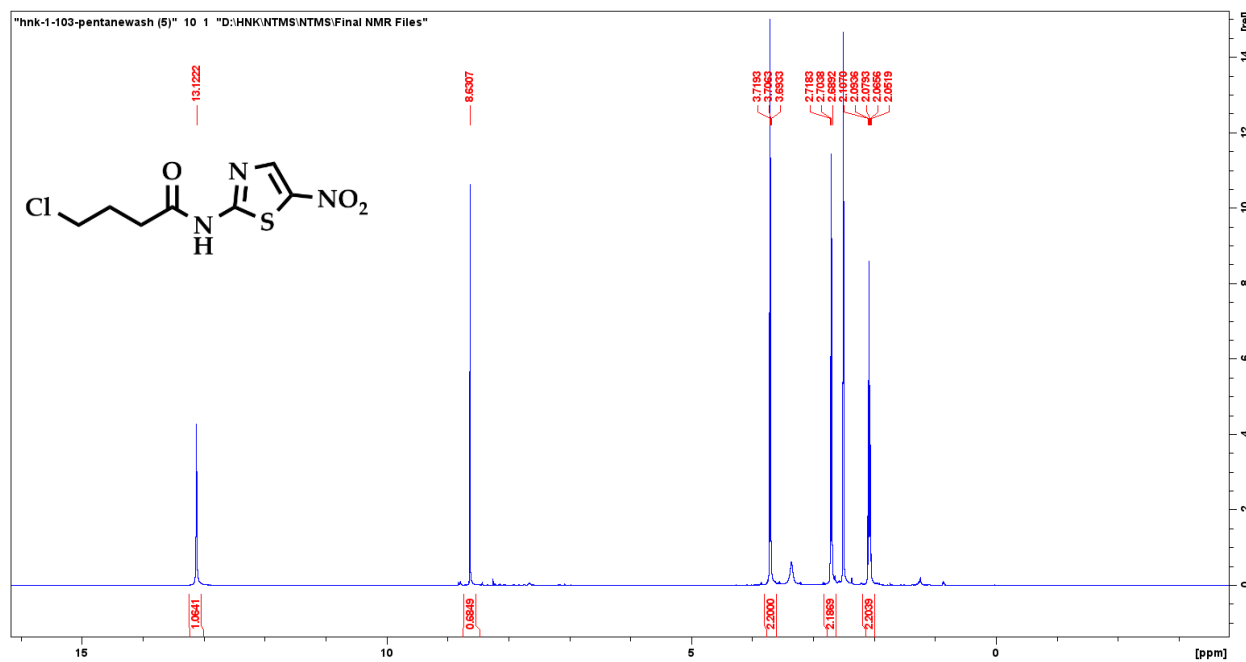


Figure 2.13B: ^1H -NMR Spectra of 4-chloro-*N*-(5-nitrothiazol-2-yl)butyramide (9).

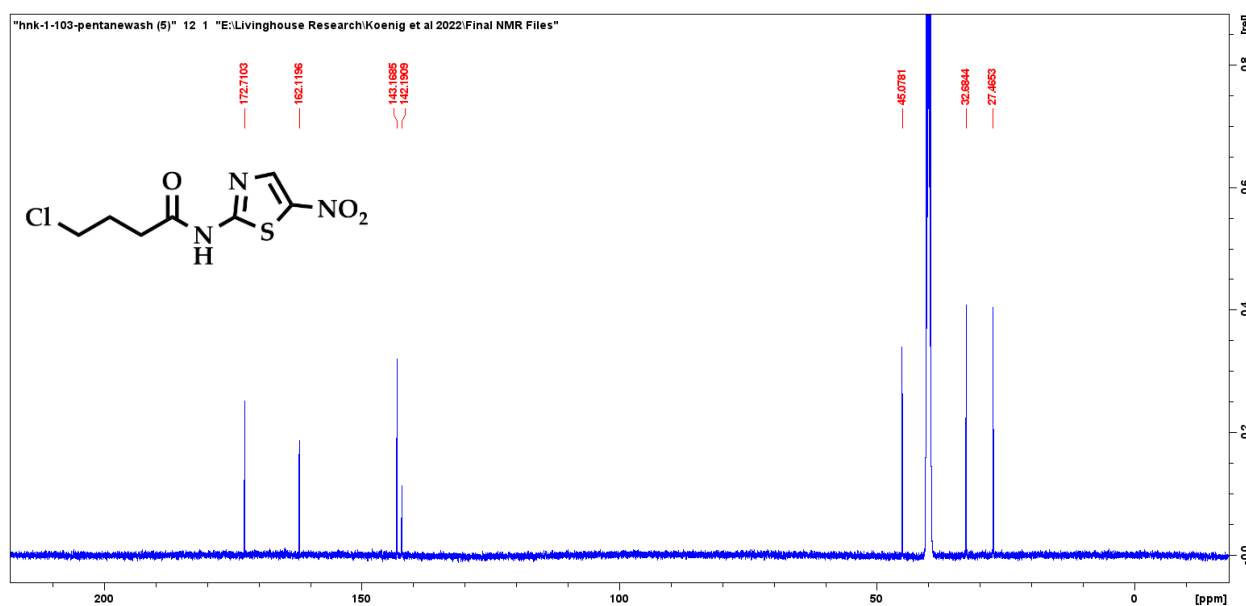


Figure 2.14B: ^{13}C -NMR Spectra of 4-chloro-*N*-(5-nitrothiazol-2-yl)butyramide (9).

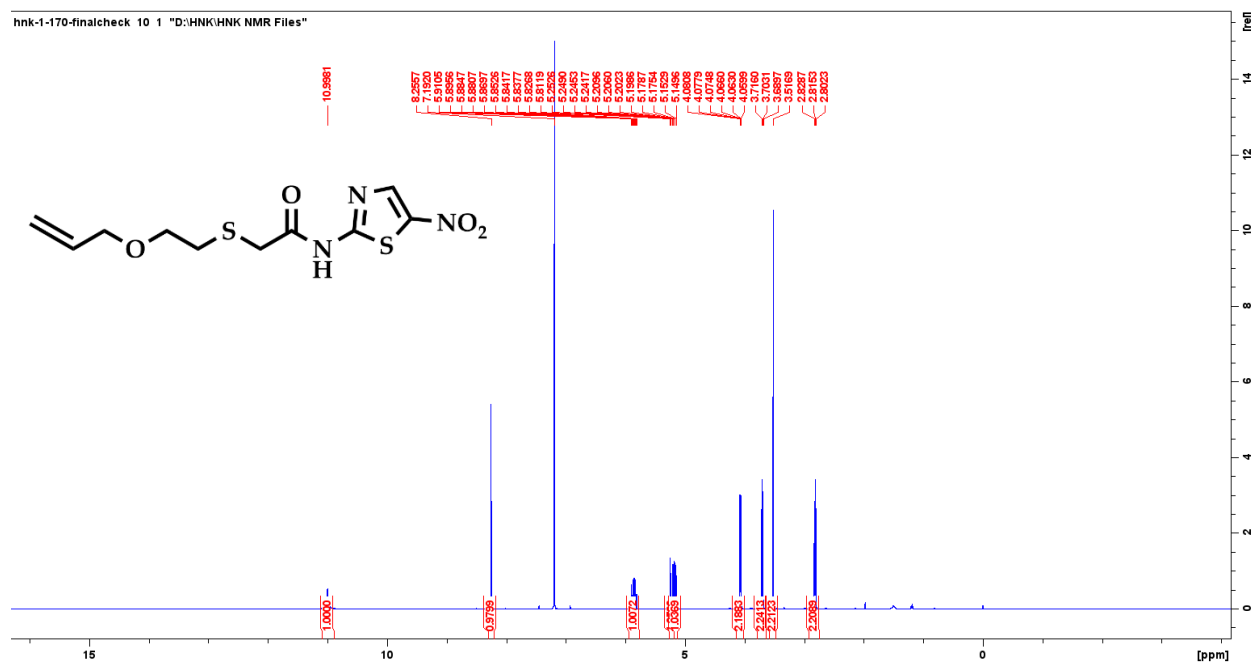


Figure 2.15B: ^1H -NMR Spectra of 2-((2-(allyloxy)ethyl)thio)-*N*-(5-nitrothiazol-2-yl)acetamide (10).

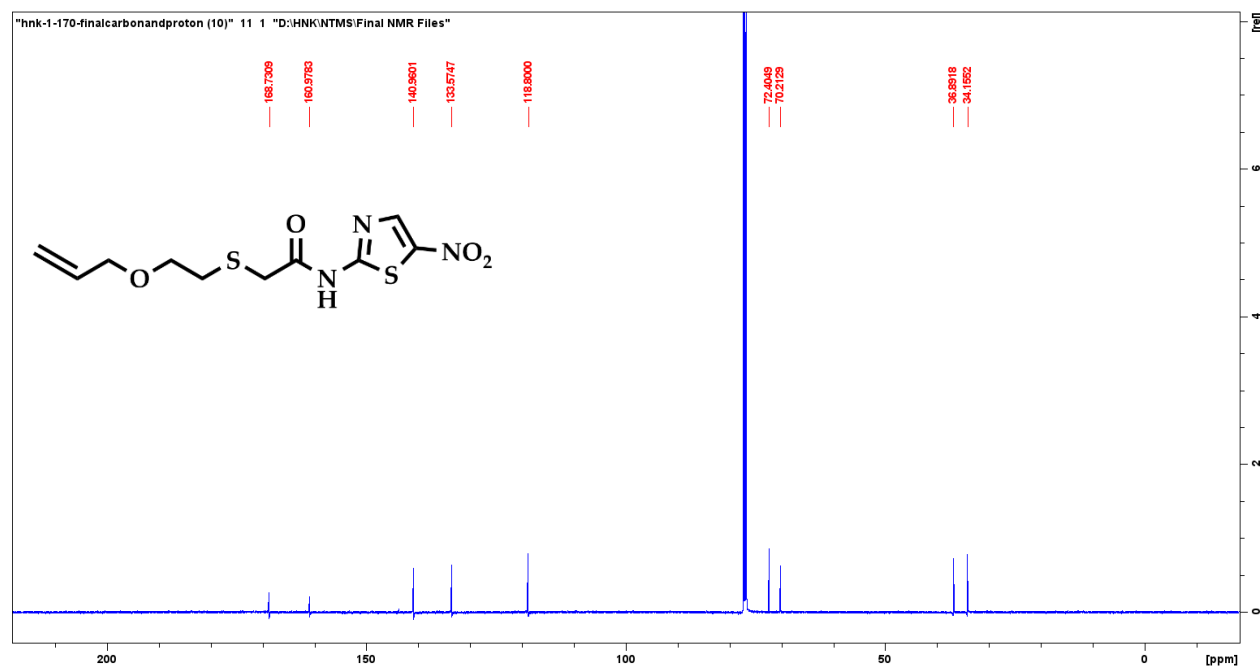


Figure 2.16B: ^{13}C -NMR Spectra of 2-((2-(allyloxy)ethyl)thio)-*N*-(5-nitrothiazol-2-yl)acetamide (10).

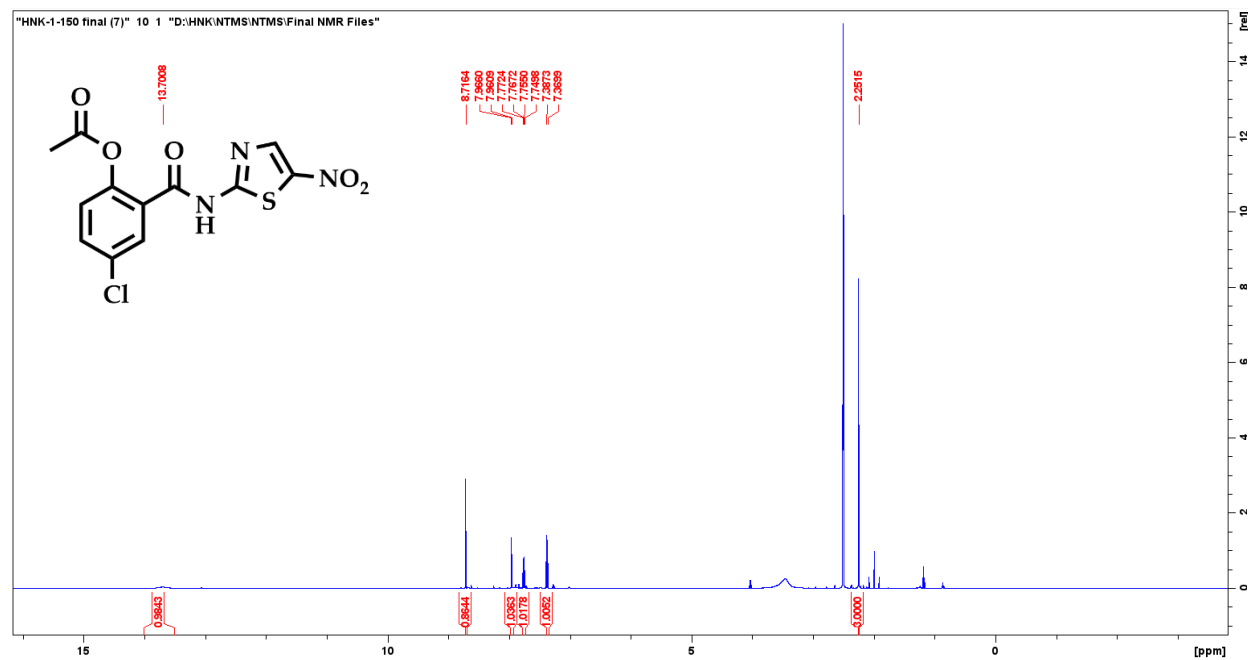


Figure 2.17B: ^1H -NMR Spectra of 2-acetoxy-5-chloro-*N*-(5-nitrothiazol-2-yl)benzamide (**11**).

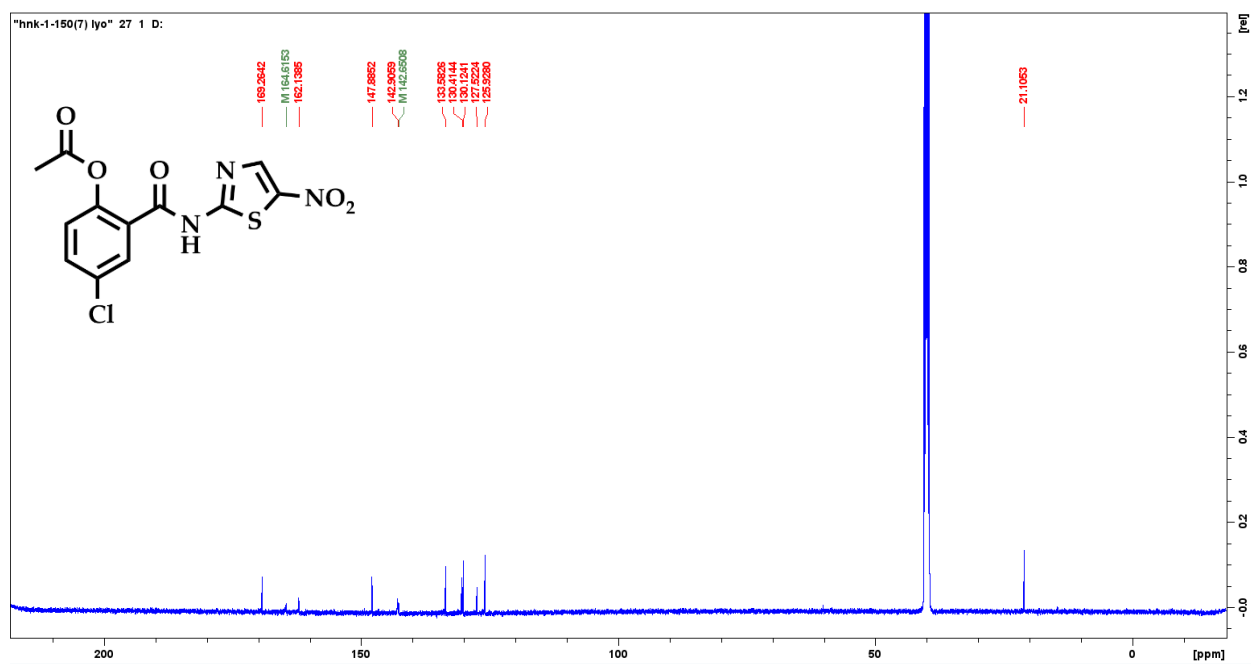


Figure 2.18B: ^{13}C -NMR Spectra of 2-acetoxy-5-chloro-*N*-(5-nitrothiazol-2-yl)benzamide (**11**).

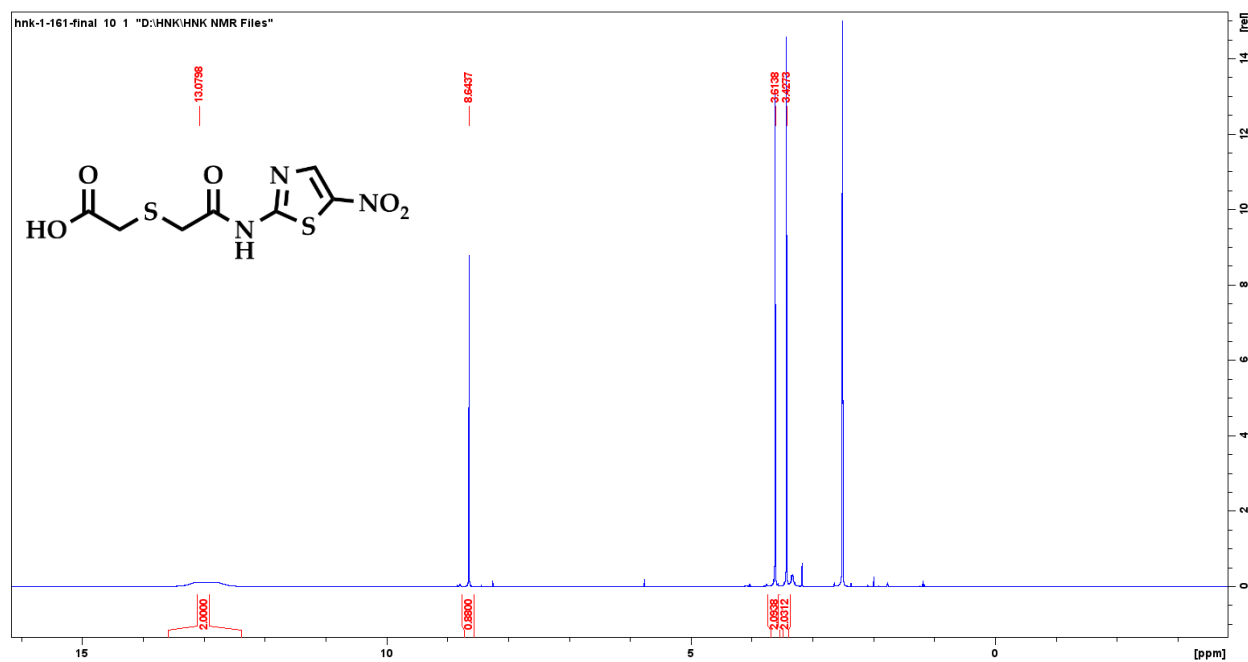


Figure 2.19B: ^1H -NMR Spectra of 2-((2-((5-nitrothiazol-2-yl)amino)-2-oxoethyl)thio)acetic acid (12).

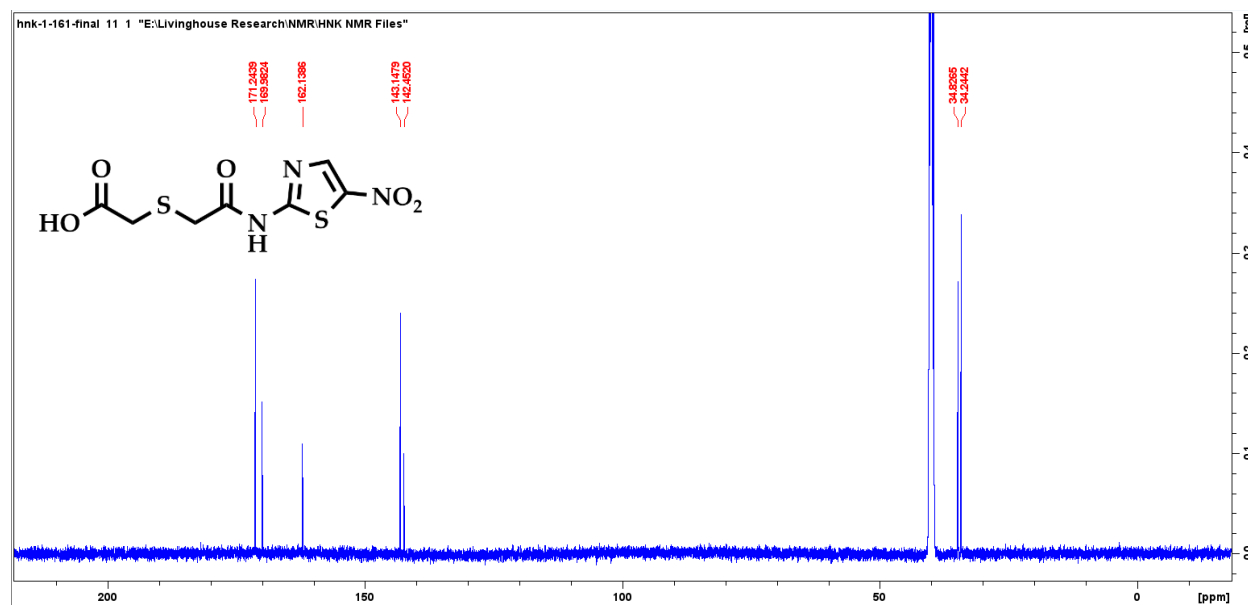


Figure 2.20B: ^{13}C -NMR Spectra of 2-((2-((5-nitrothiazol-2-yl)amino)-2-oxoethyl)thio)acetic acid (12).

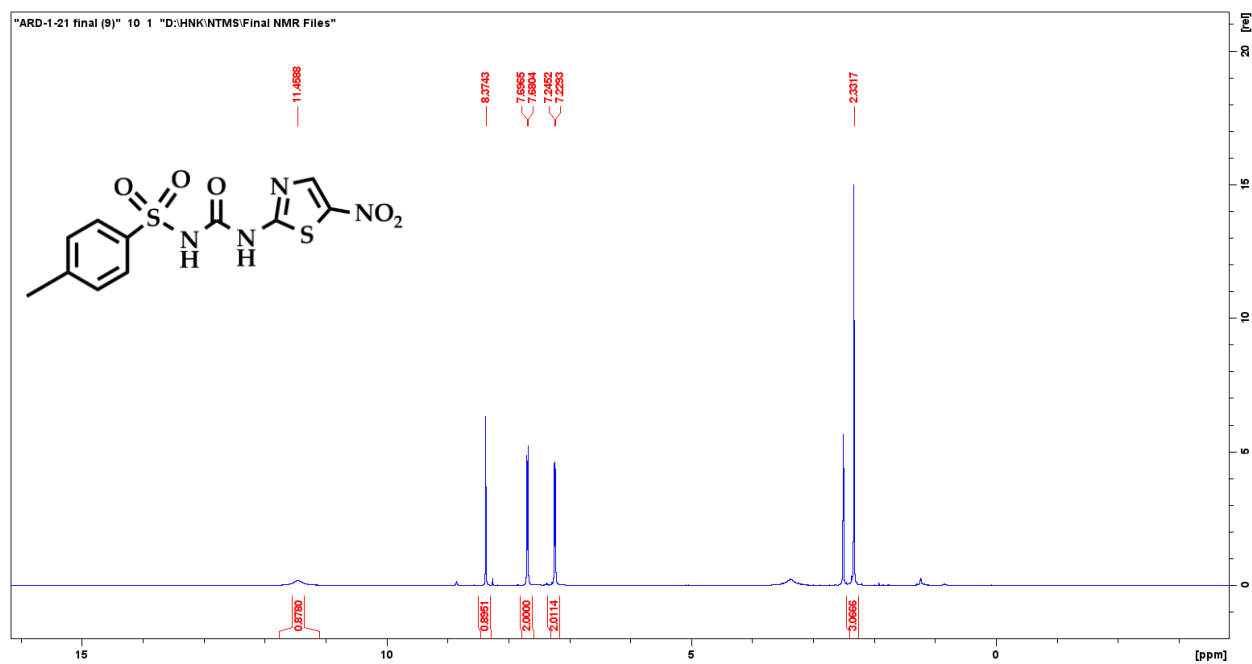


Figure 2.21B: ^1H -NMR Spectra of 4-methyl-N-((5-nitrothiazol-2-yl)carbamoyl)benzenesulfonamide (**13**).

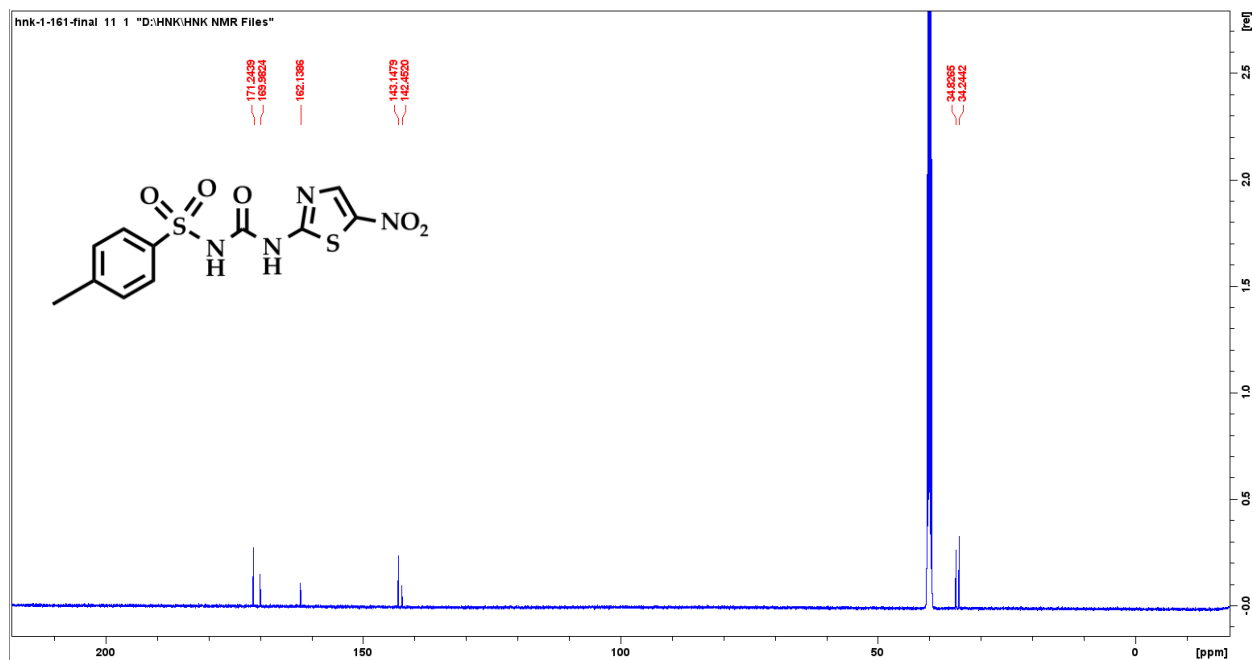


Figure 2.22B: ^{13}C -NMR Spectra of 4-methyl-N-((5-nitrothiazol-2-yl)carbamoyl)benzenesulfonamide (**13**).

3B Characterization of Compounds Synthesized in Chapter 4

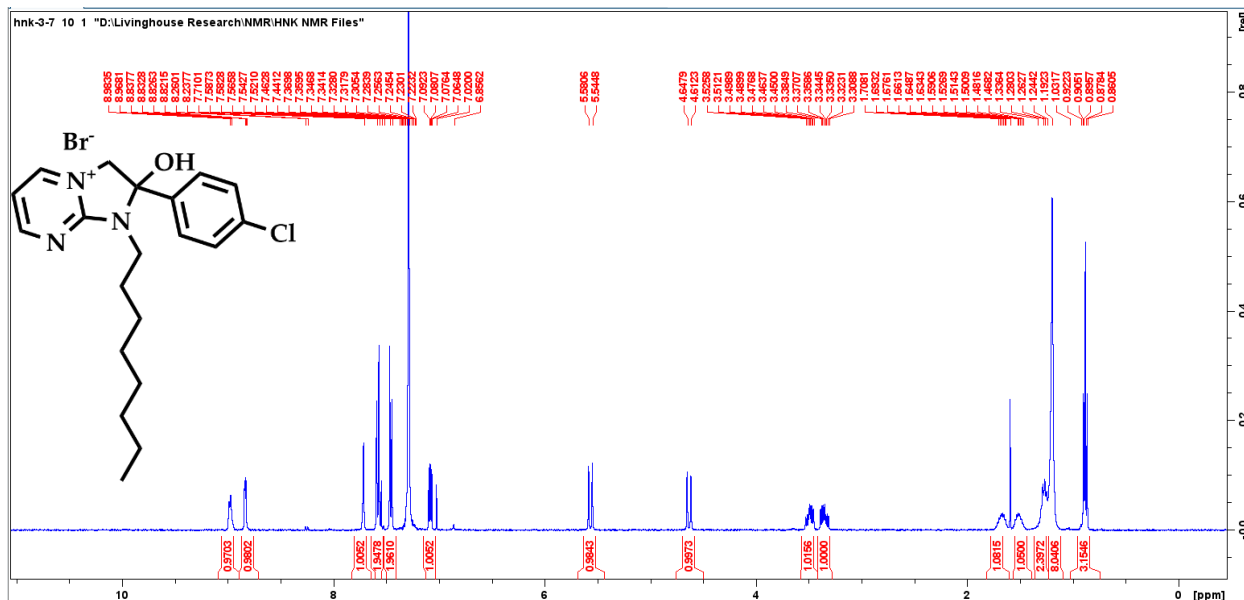


Figure 3.1B: ¹H-NMR Spectra of 2-(4-chlorophenyl)-2-hydroxy-1-octyl-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (**1.1a**).

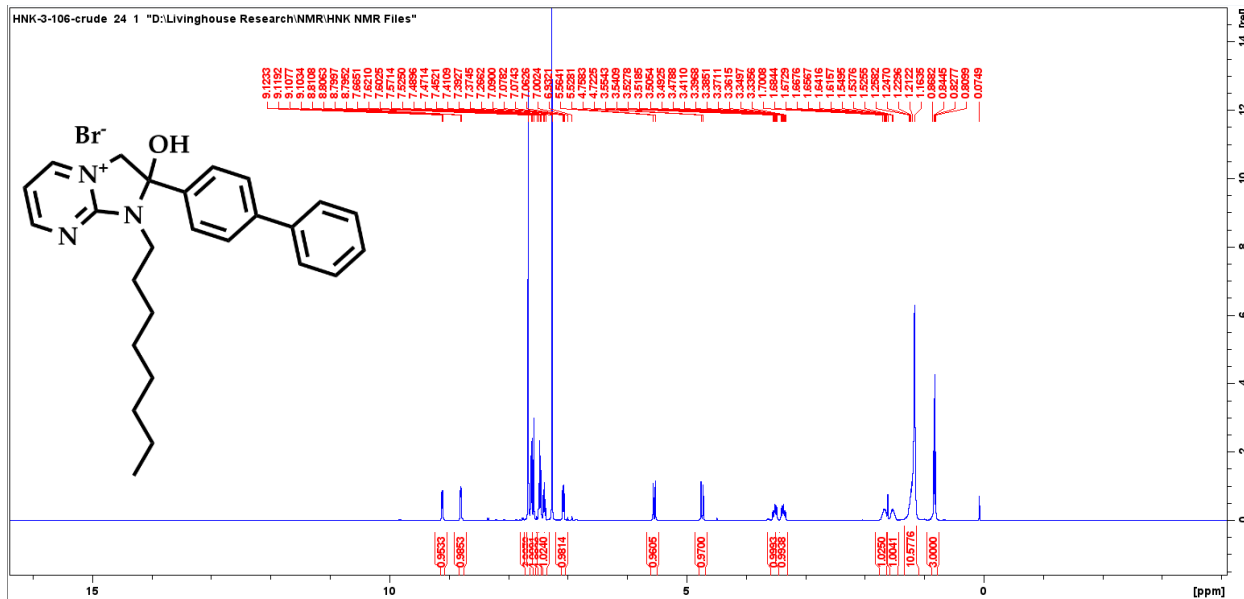


Figure 3.2B: ¹H-NMR Spectra of 2-([1,1'-biphenyl]-4-yl)-2-hydroxy-1-octyl-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (**1.1b**).

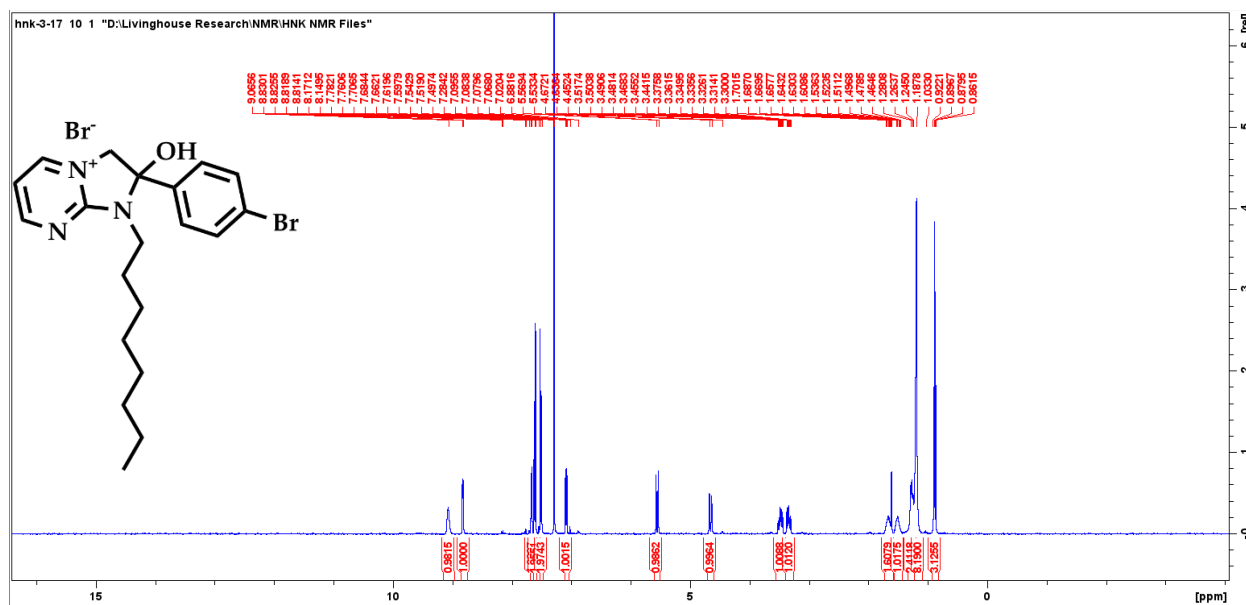


Figure 3.3B: ^1H -NMR Spectra of 2-(4-bromophenyl)-2-hydroxy-1-octyl-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (**1.1c**).

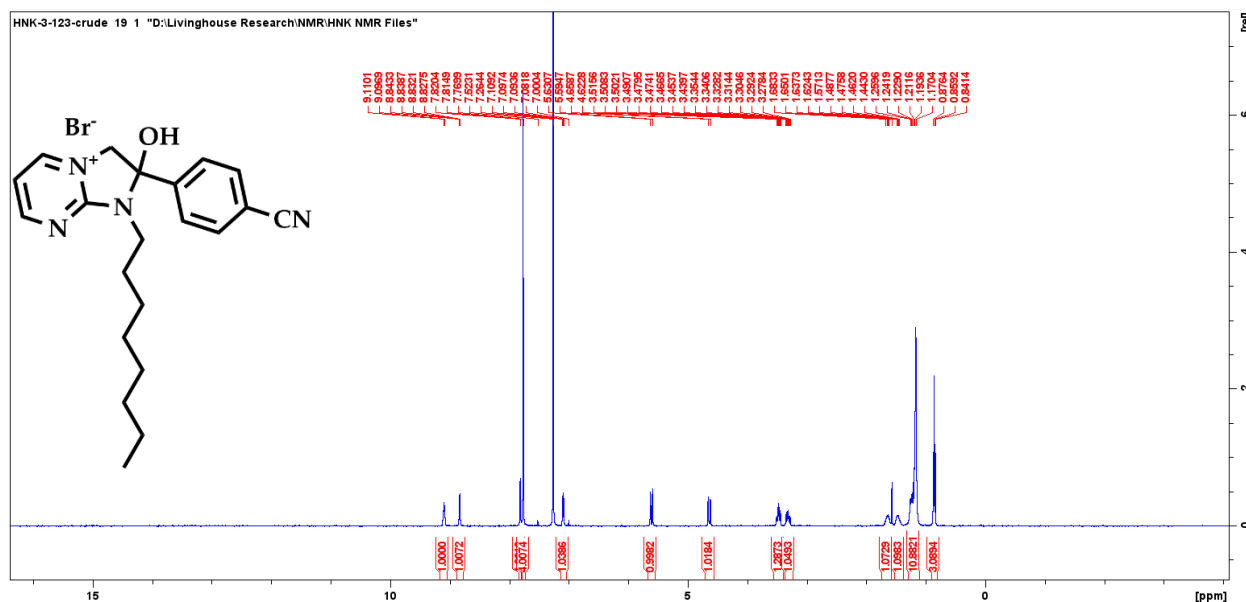


Figure 3.4B: ^1H -NMR Spectra of 2-(4-cyanophenyl)-2-hydroxy-1-octyl-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (**1.1d**).

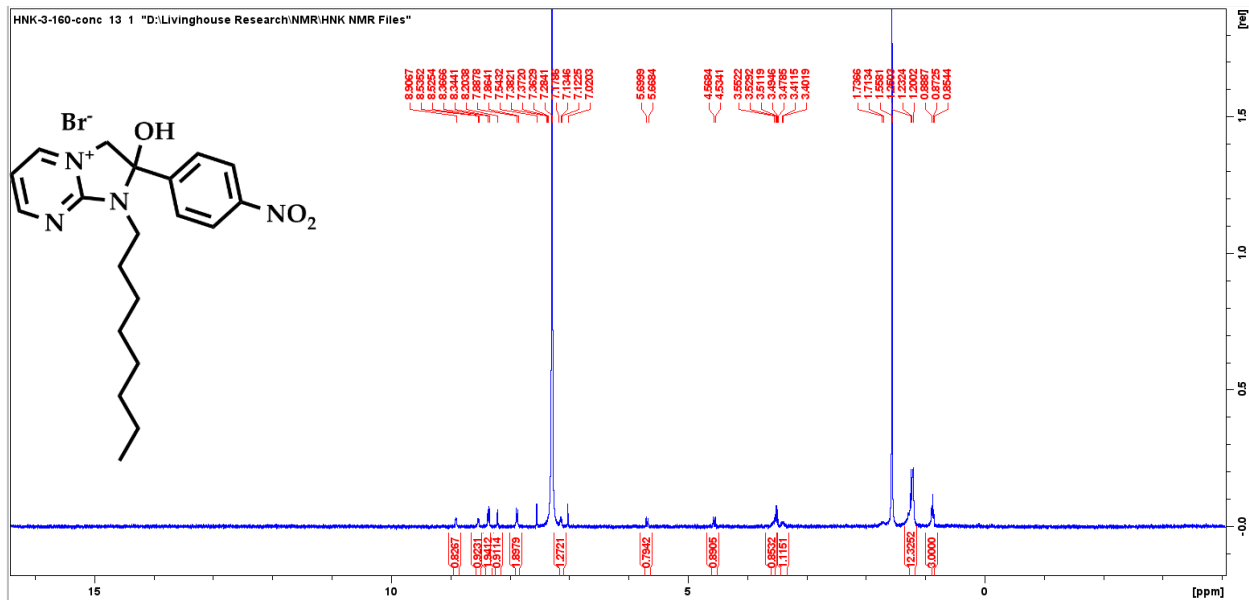


Figure 3.5B: ¹H-NMR Spectra of 2-hydroxy-2-(4-nitrophenyl)-1-octyl-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium bromide (**1.1e**).

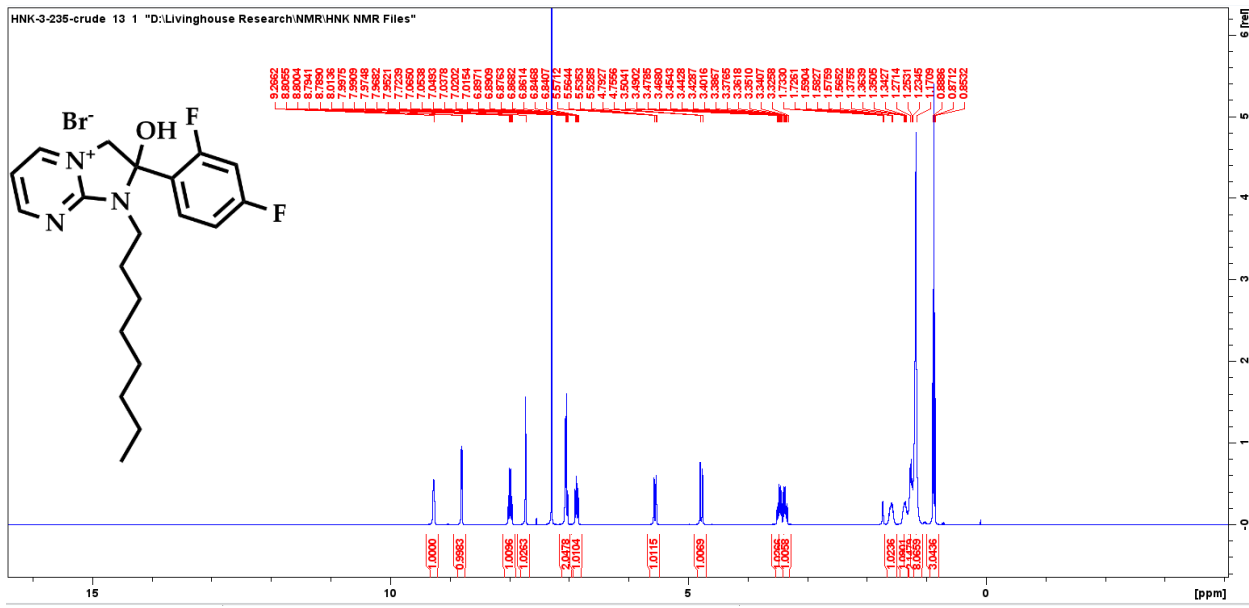


Figure 3.6B: ¹H-NMR Spectra of 2-(2,4-difluorophenyl)-2-hydroxy-1-octyl-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium bromide (**1.1f**).

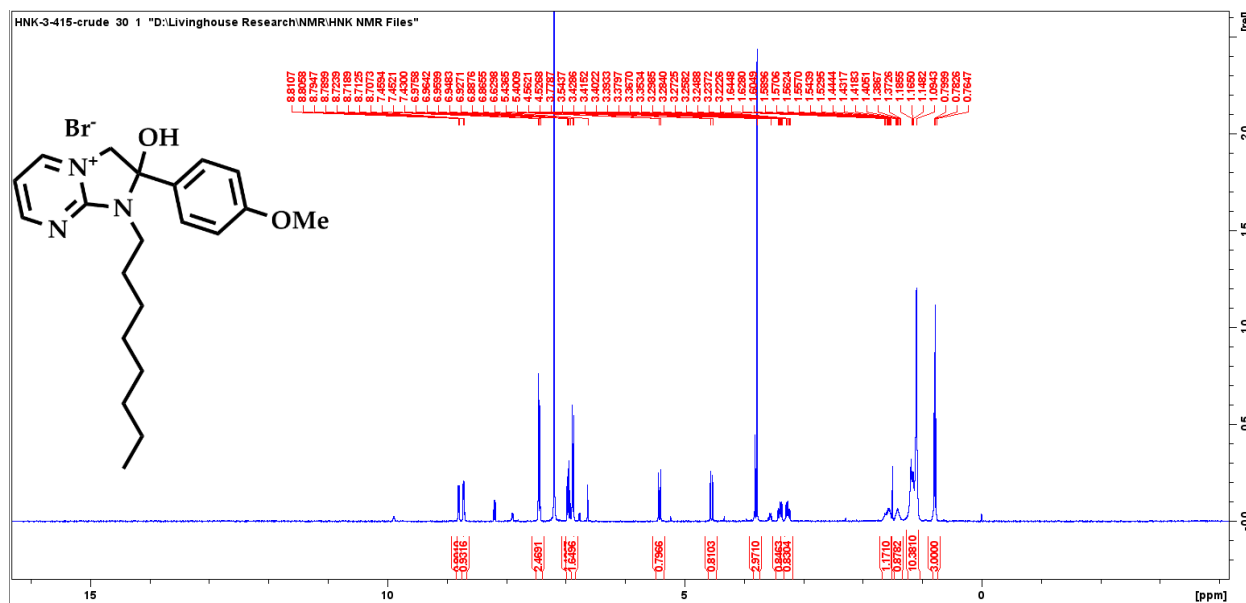


Figure 3.7B: ¹H-NMR Spectra of 2-hydroxy-2-(4-methoxyphenyl)-1-octyl-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (**1.1g**).

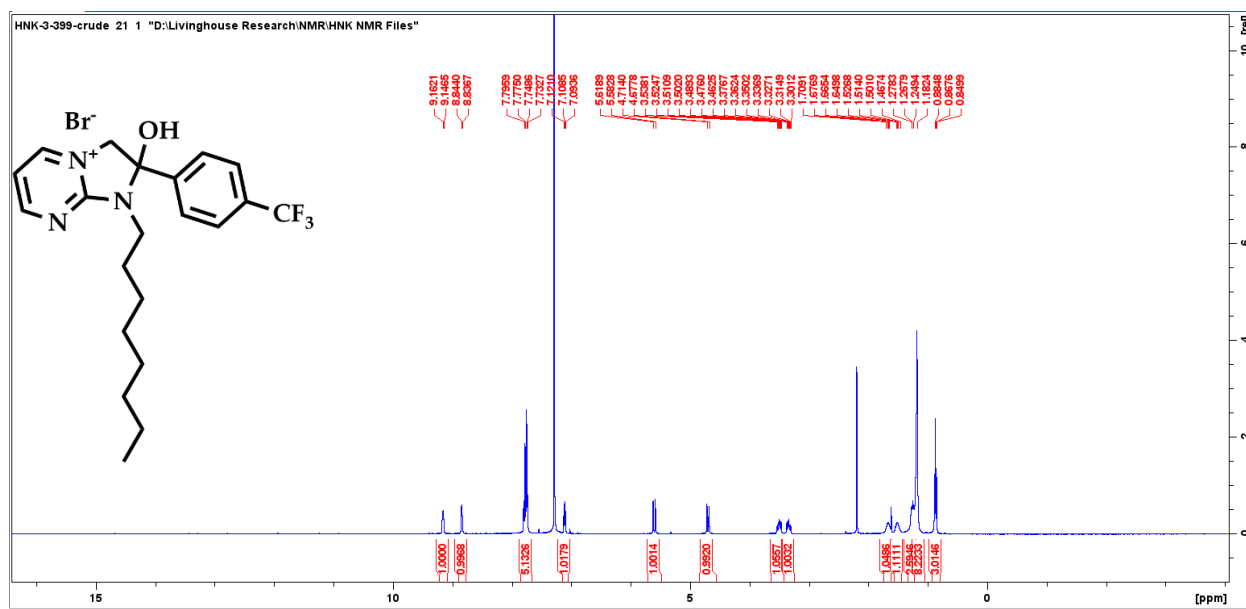


Figure 3.8B: ¹H-NMR Spectra of 2-hydroxy-1-octyl-2-(4-(trifluoromethyl)phenyl)-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium bromide (**1.1h**).

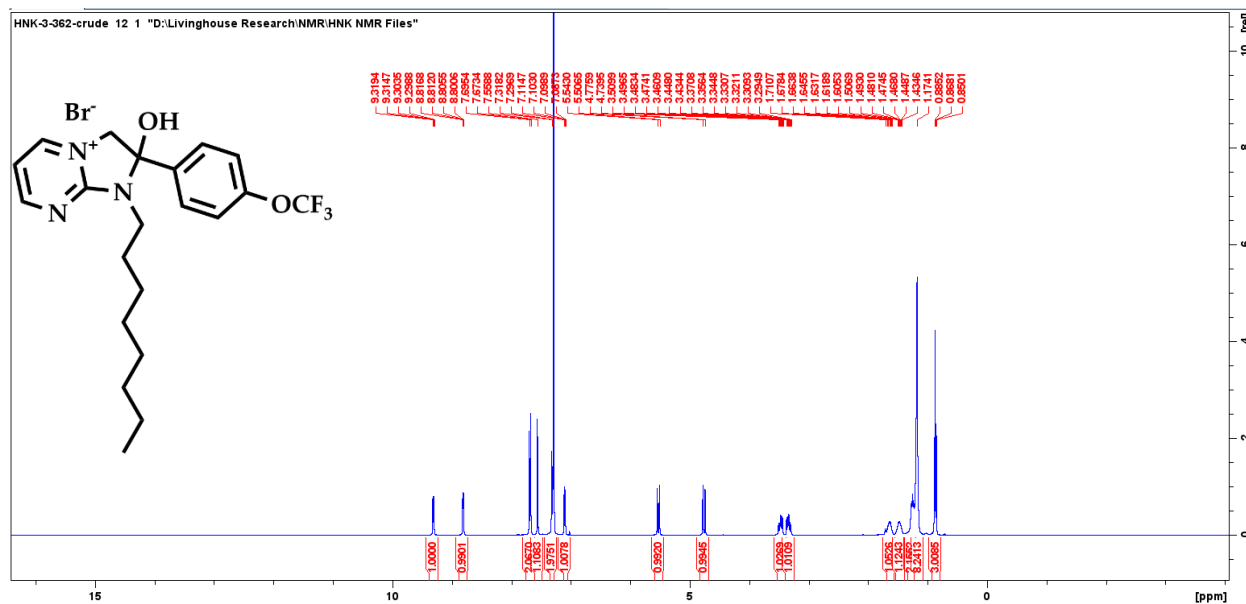


Figure 3.9B: ¹H-NMR Spectra of 2-hydroxy-1-octyl-2-(4-(trifluoromethoxy)phenyl)-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium bromide (**1.1i**).

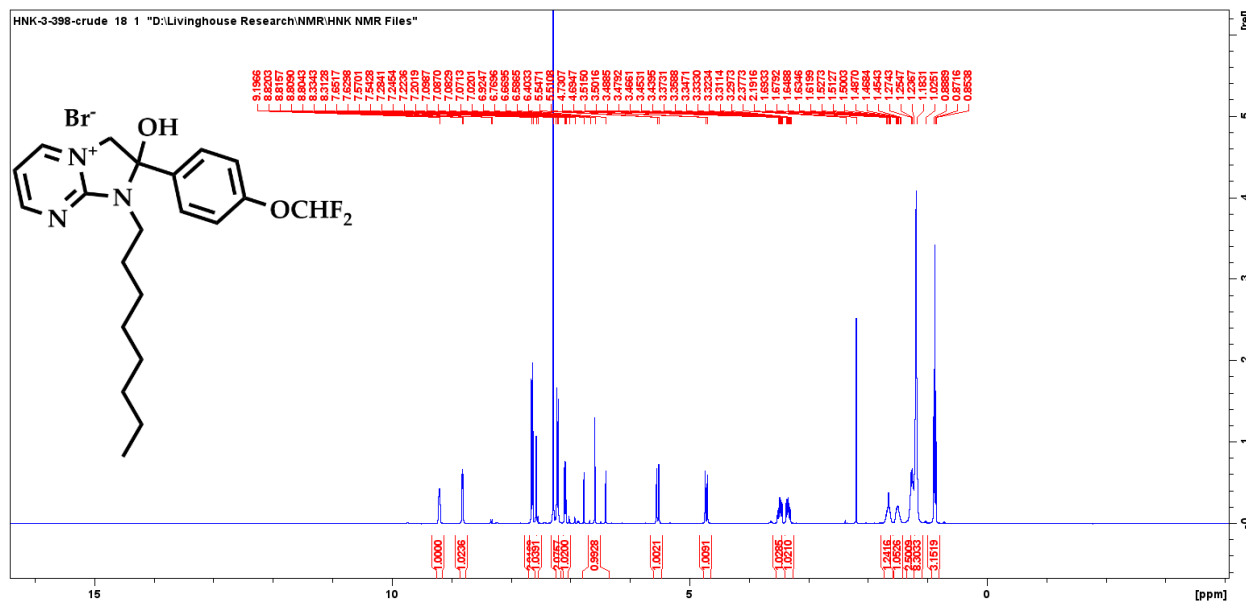


Figure 3.10B: ¹H-NMR Spectra of 2-(4-(difluoromethoxy)phenyl)-2-hydroxy-1-octyl-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium bromide (**1.1j**).

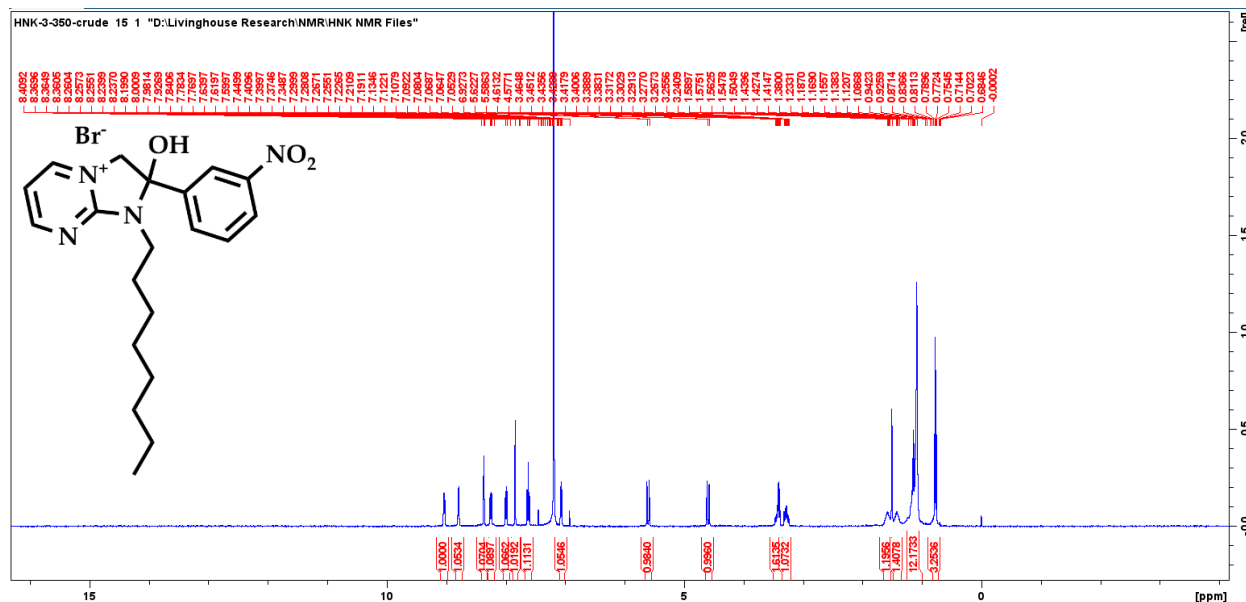
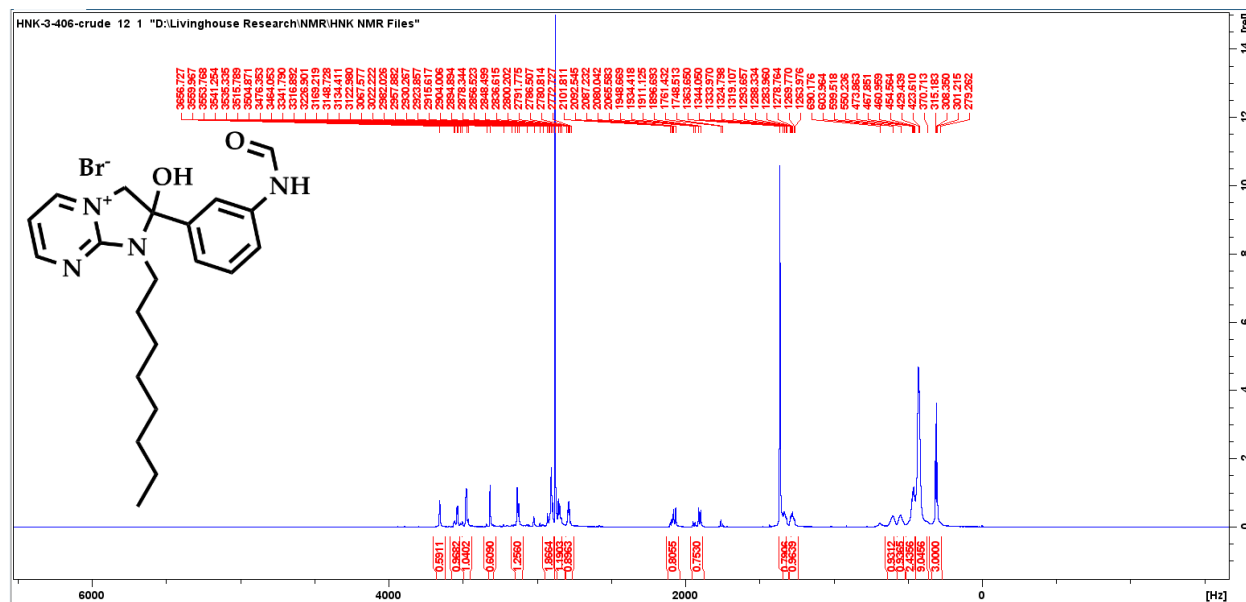


Figure 3.11B: ¹H-NMR Spectra of 2-hydroxy-2-(3-nitrophenyl)-1-octyl-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (**1.1k**).



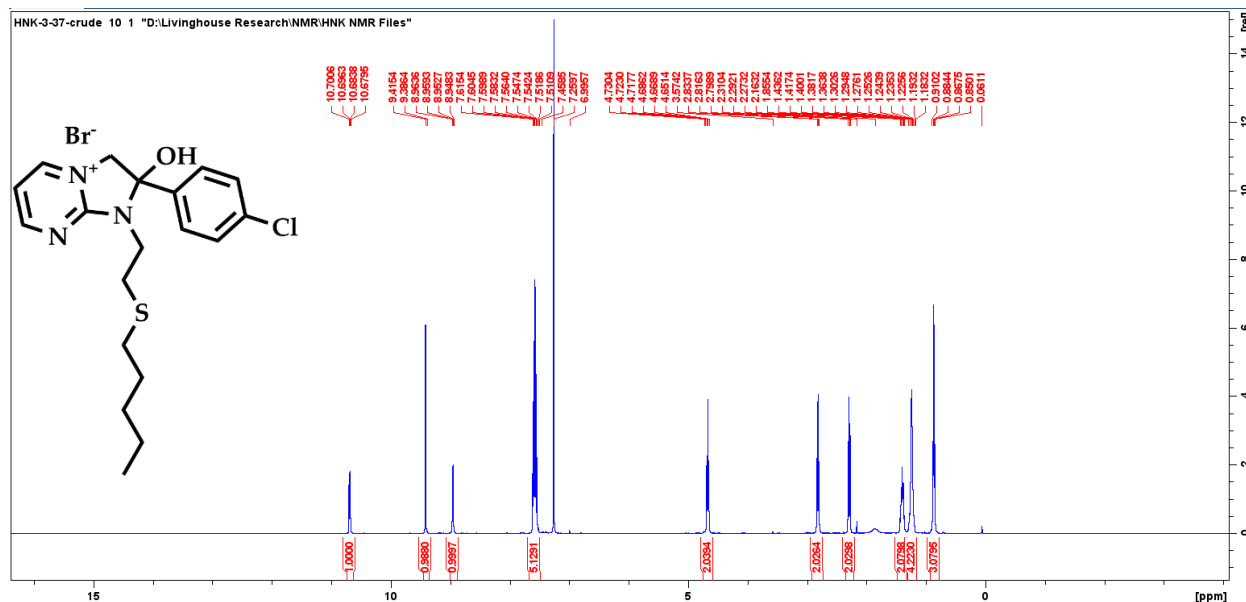


Figure 3.13B: ^1H -NMR Spectra of 2-(4-chlorophenyl)-2-hydroxy-1-(2-(pentylthio)ethyl)-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (2.1a).

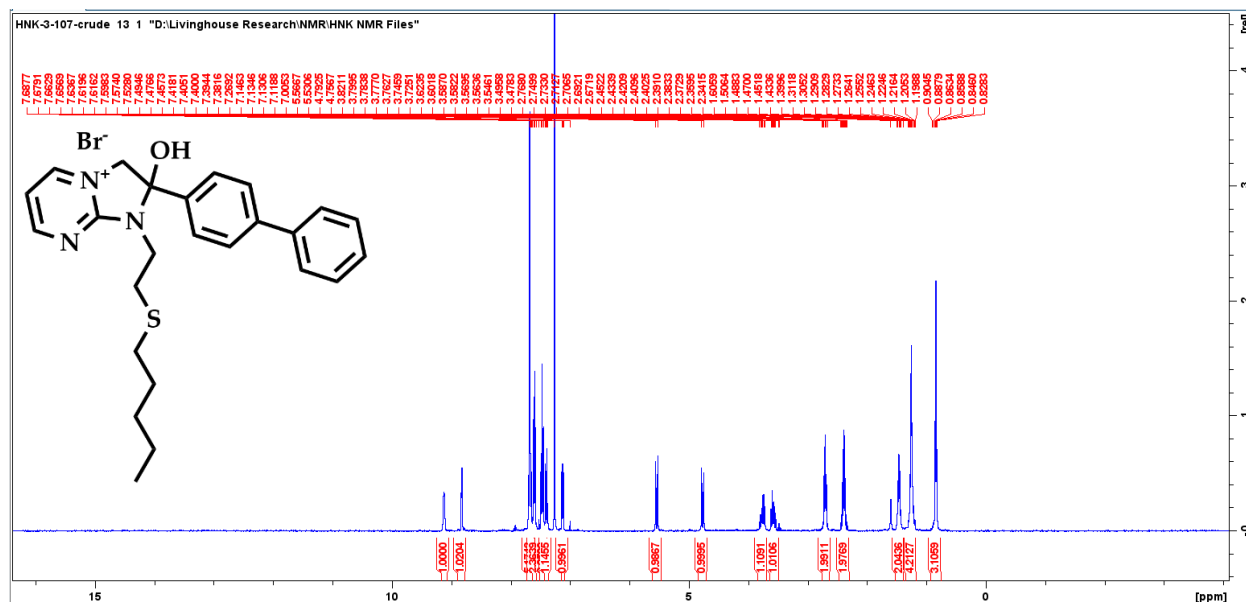


Figure 3.14B: ^1H -NMR Spectra of 2-([1,1'-biphenyl]-4-yl)-2-hydroxy-1-(2-(pentylthio)ethyl)-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (2.1b).

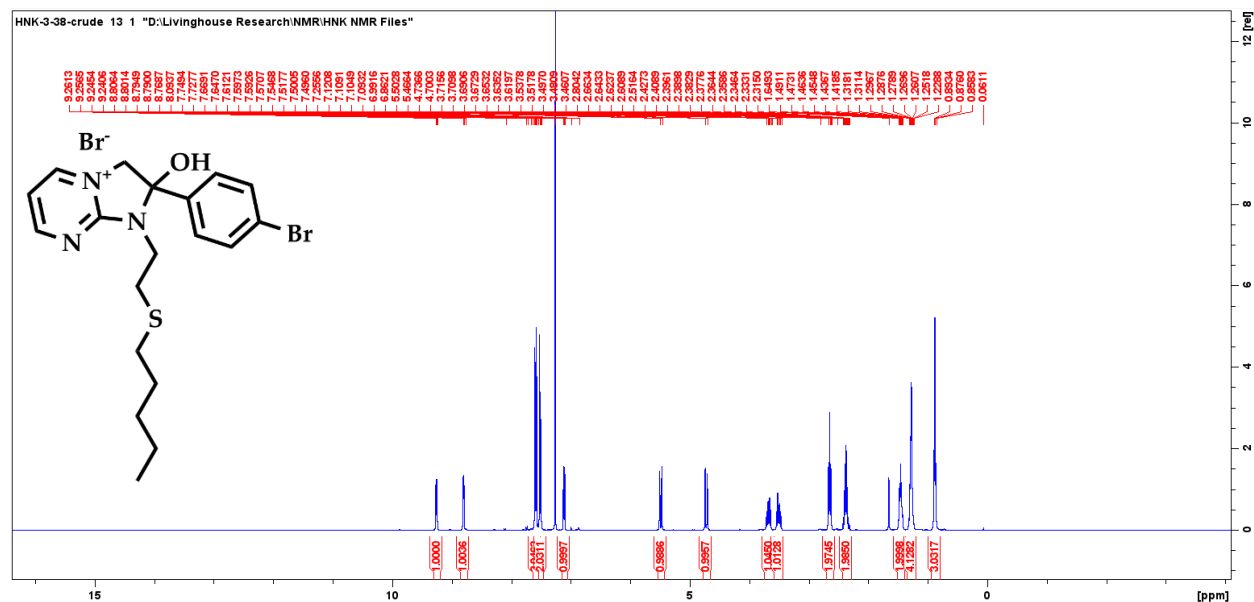


Figure 3.15B: ¹H-NMR Spectra of 2-(4-bromophenyl)-2-hydroxy-1-(2-(pentylthio)ethyl)-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium bromide (**2.1c**).

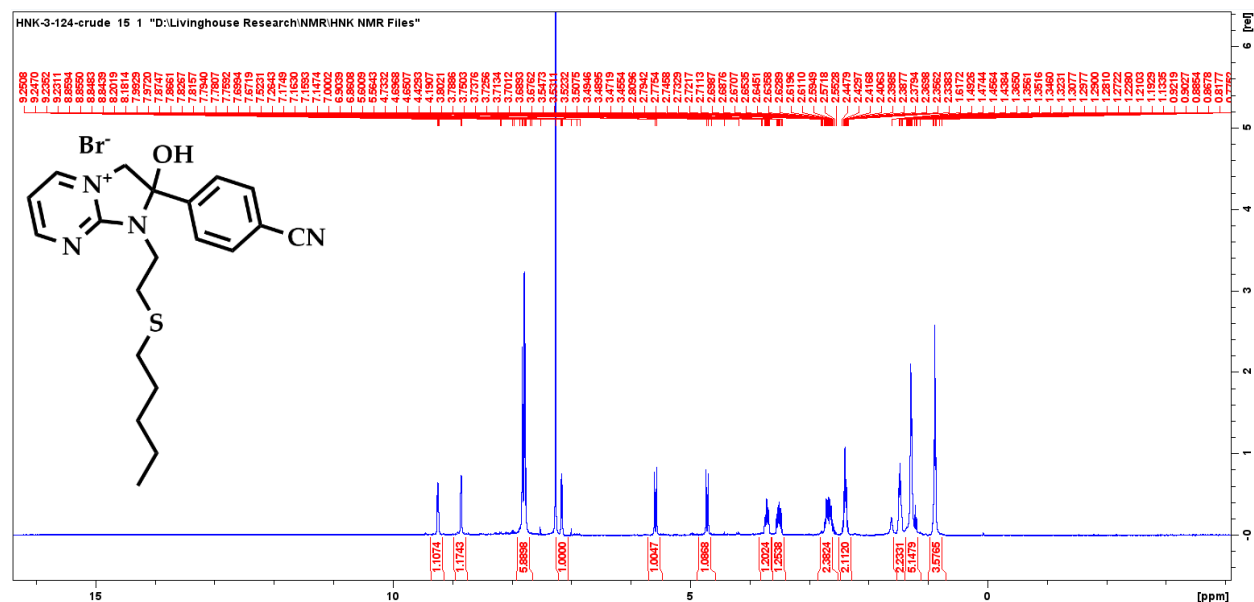


Figure 3.16B: ¹H-NMR Spectra of 2-(4-cyanophenyl)-2-hydroxy-1-(2-(pentylthio)ethyl)-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium bromide (**2.1d**).

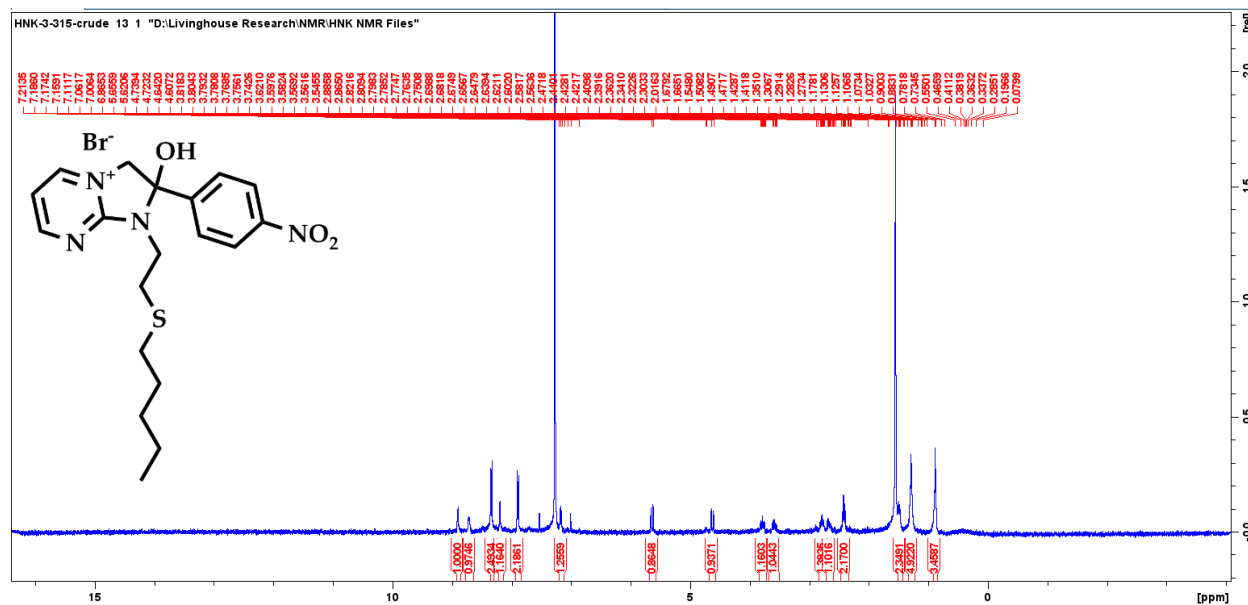


Figure 3.17B: ¹H-NMR Spectra of 2-hydroxy-2-(4-nitrophenyl)-1-(2-(pentylthio)ethyl)-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (2.1e).

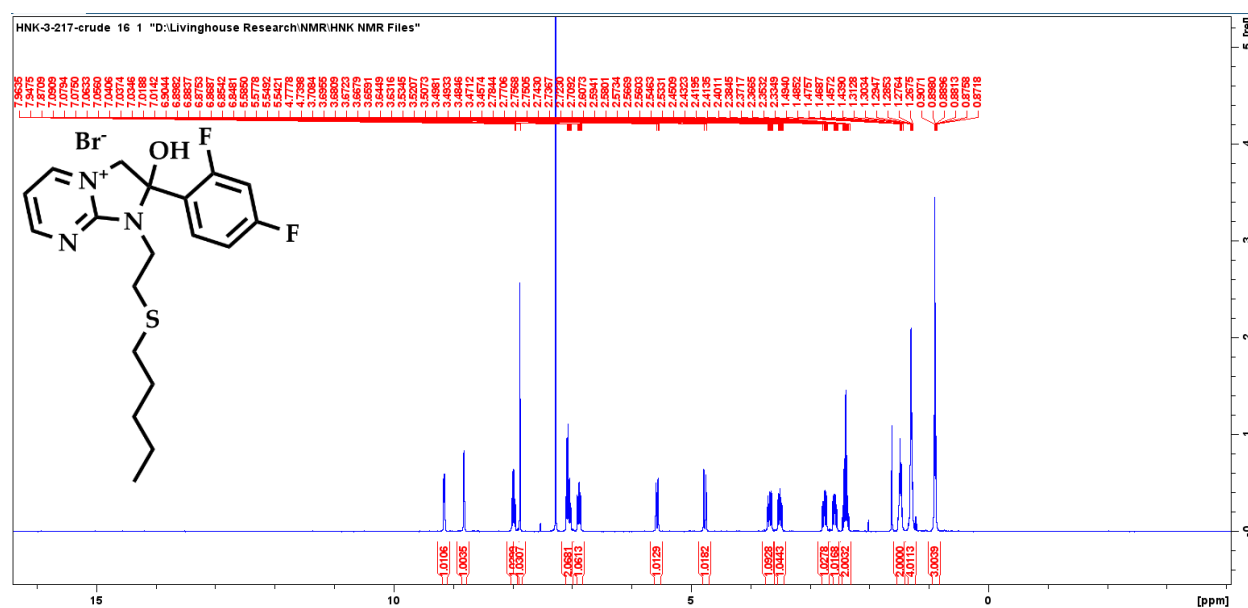


Figure 3.18B: ¹H-NMR Spectra of 2-(2,4-difluorophenyl)-2-hydroxy-1-(2-(pentylthio)ethyl)-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (2.1f).

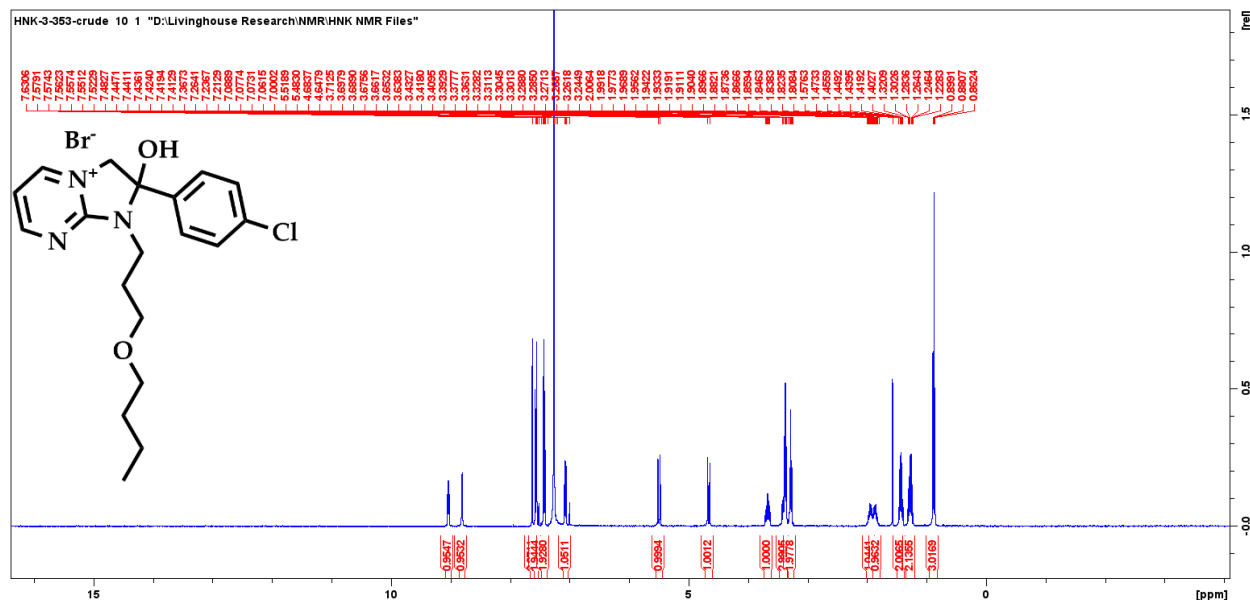


Figure 3.19B: ^1H -NMR Spectra of 1-(3-butoxypropyl)-2-(4-chlorophenyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (**3.1a**).

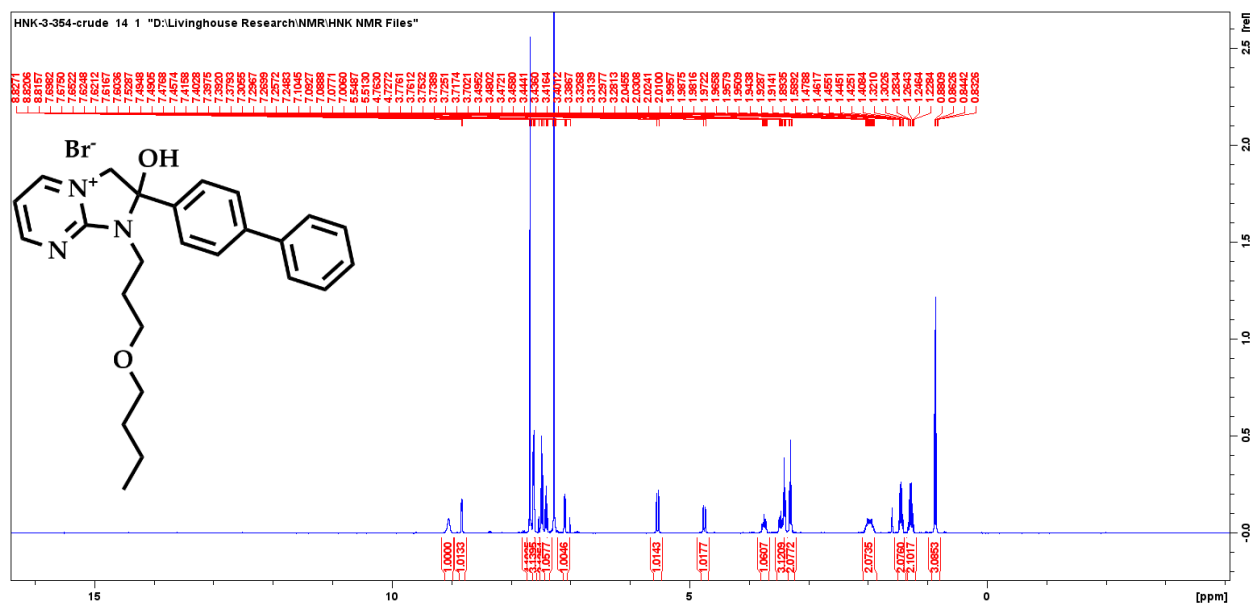


Figure 3.20B: ^1H -NMR Spectra of 2-([1,1'-biphenyl]-4-yl)-1-(3-butoxypropyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (**3.1b**).

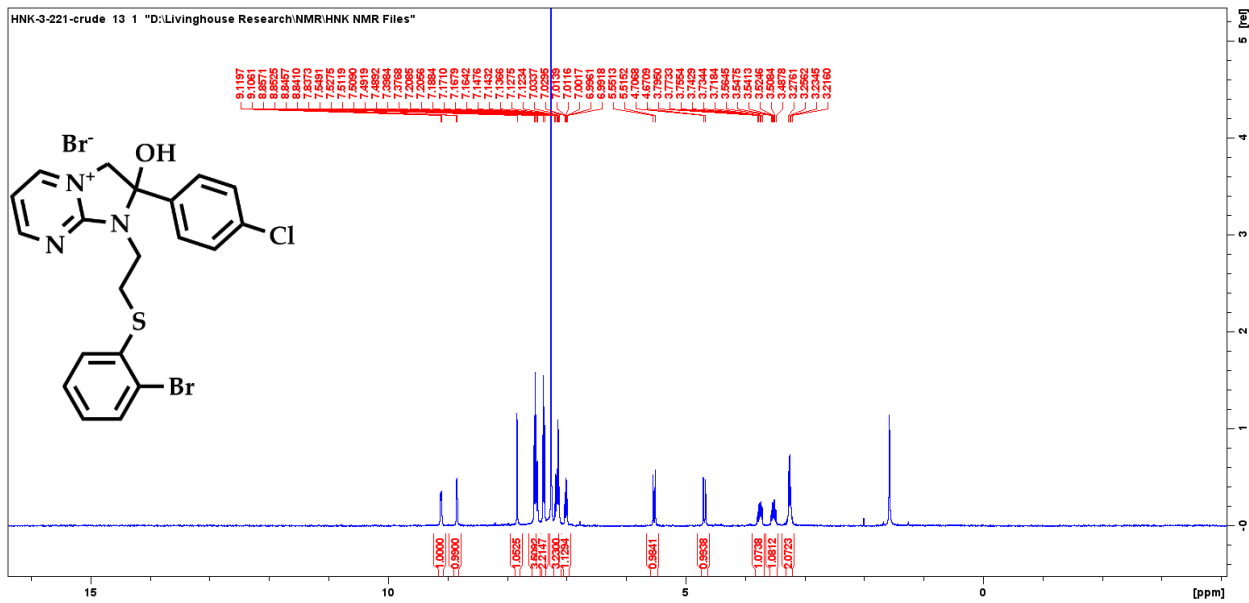


Figure 3.21B: ¹H-NMR Spectra of 1-(2-((2-bromophenyl)thio)ethyl)-2-(4-chlorophenyl)-2-hydroxy-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium bromide (**4.1a**).

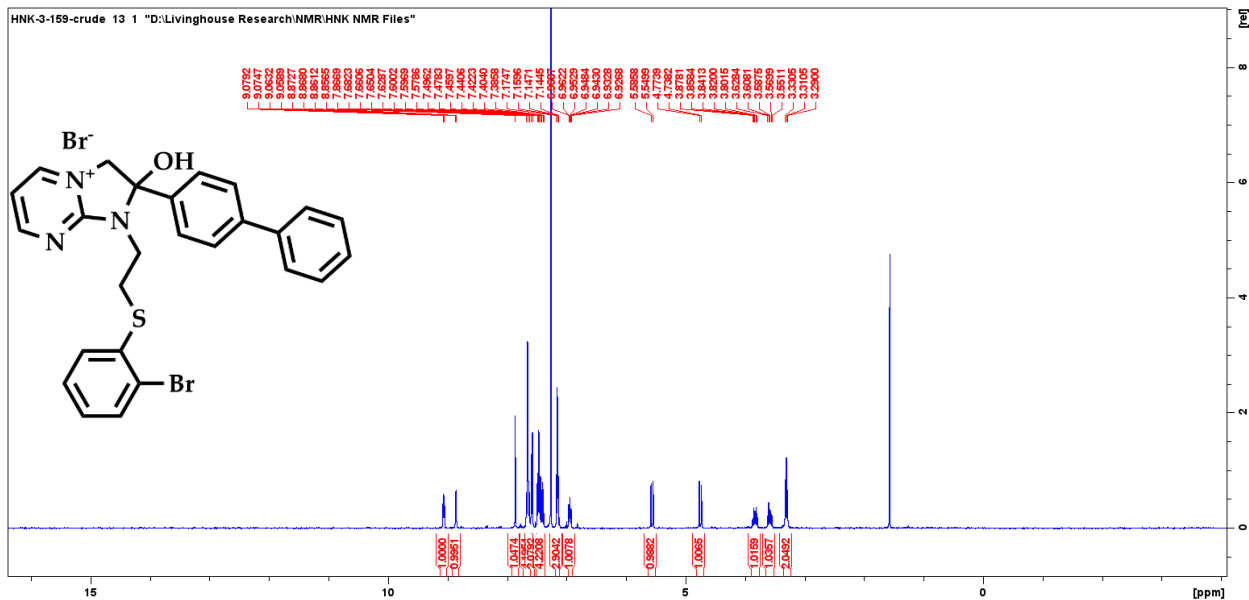


Figure 3.22B: ¹H-NMR Spectra of 2-([1,1'-biphenyl]-4-yl)-1-(2-((2-bromophenyl)thio)ethyl)-2-hydroxy-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium bromide (**4.1b**).

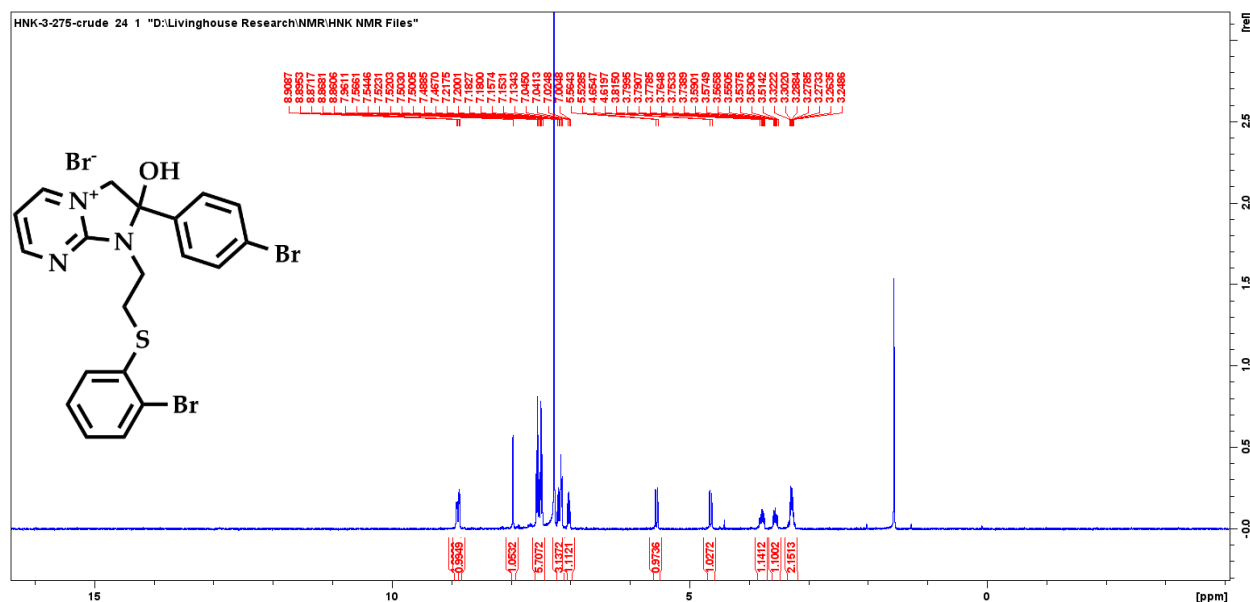


Figure 3.23B: ^1H -NMR Spectra of 2-(4-bromophenyl)-1-(2-((2-bromophenyl)thio)ethyl)-2-hydroxy-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium bromide (**4.1c**).

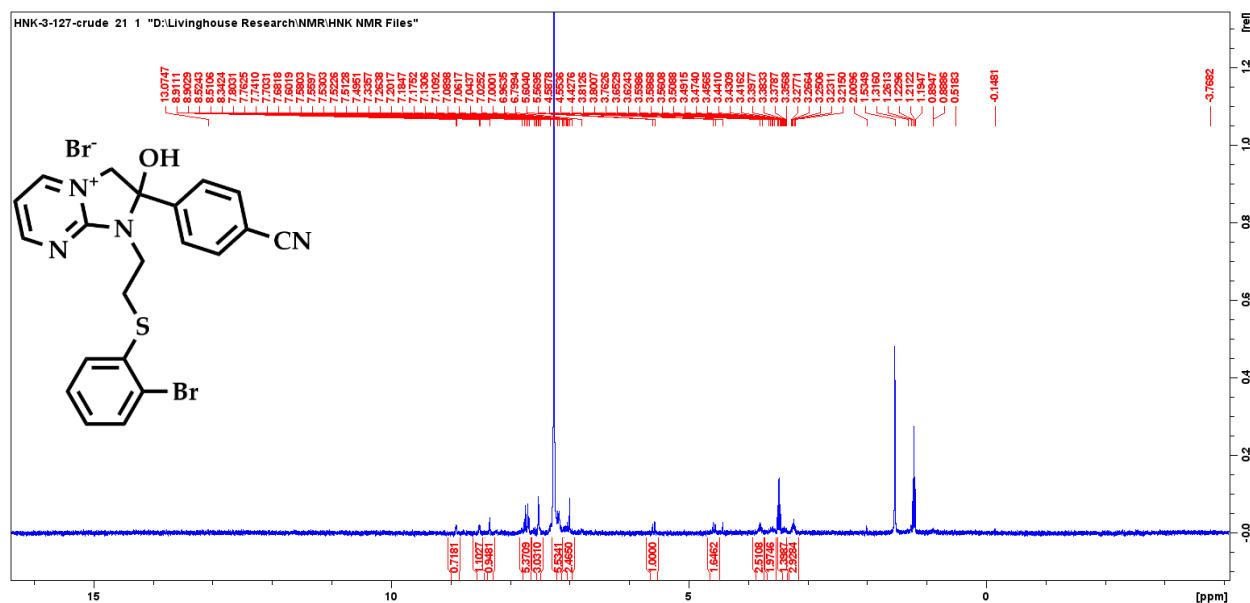


Figure 3.24B: ^1H -NMR Spectra of 1-(2-((2-bromophenyl)thio)ethyl)-2-(4-cyanophenyl)-2-hydroxy-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium bromide (**4.1d**).

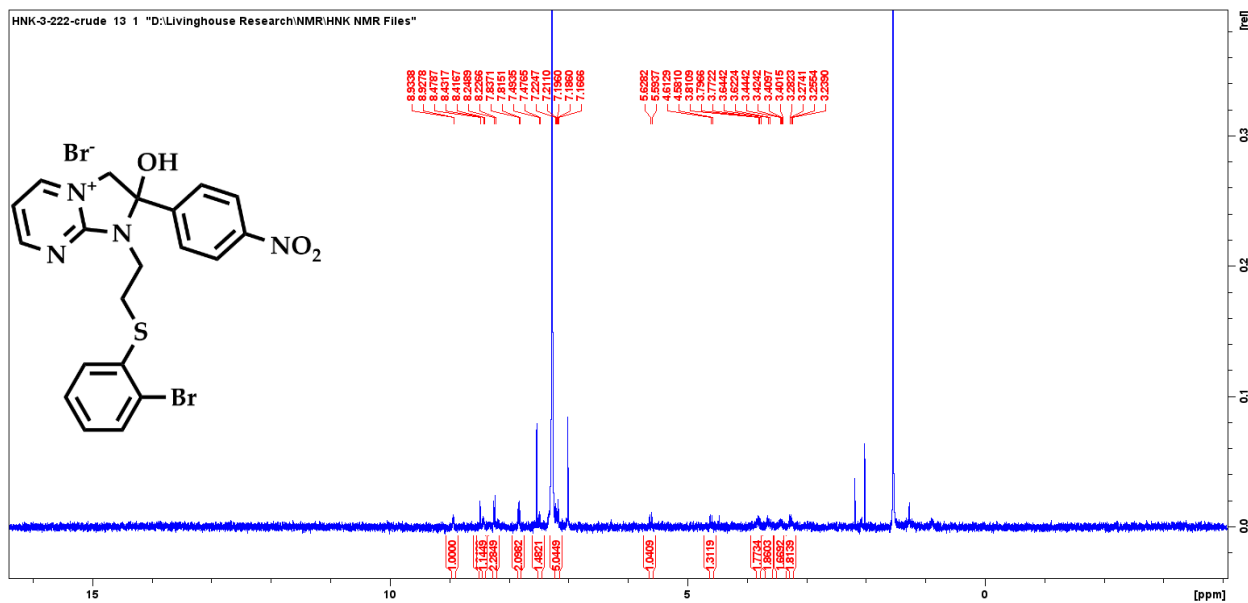


Figure 3.25B: ^1H -NMR Spectra of 1-(2-((2-bromophenyl)thio)ethyl)-2-(4-nitrophenyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (**4.1e**).

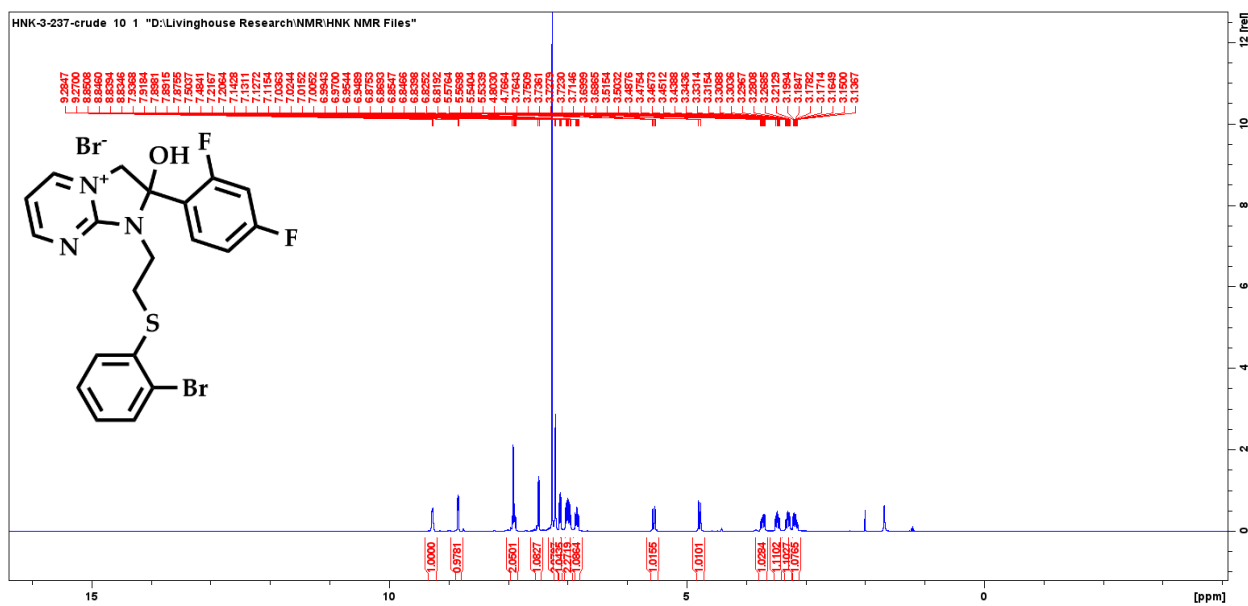


Figure 3.26B: ^1H -NMR Spectra of 1-(2-((2-bromophenyl)thio)ethyl)-2-(2,4-difluorophenyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (**4.1f**).

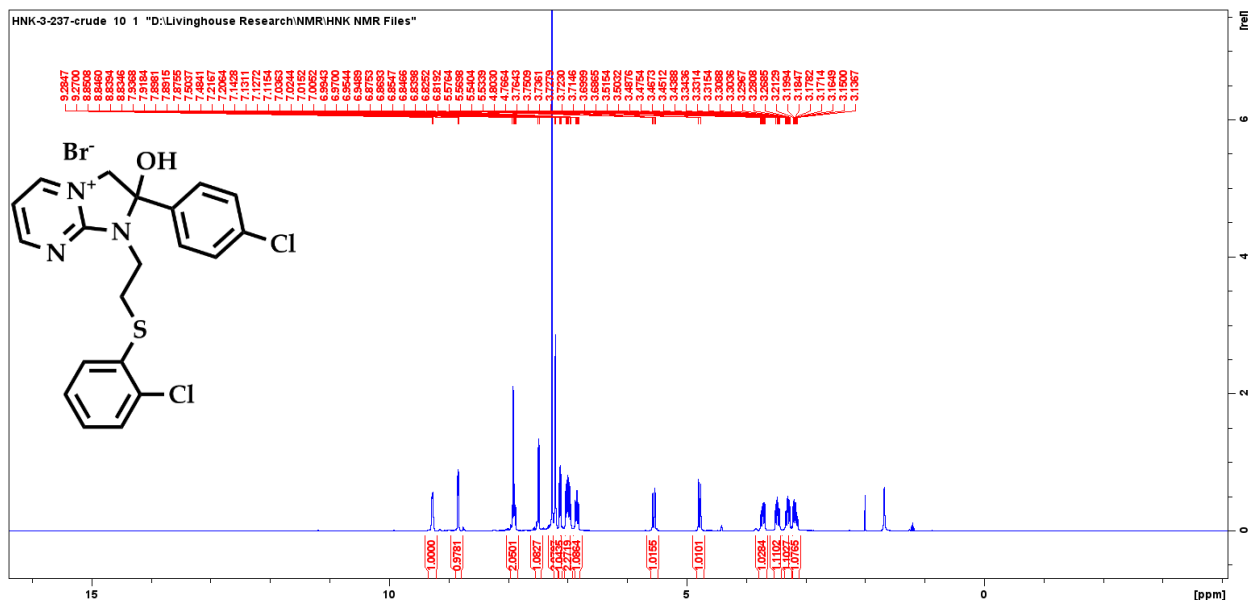


Figure 3.27B: ^1H -NMR Spectra of 2-(4-chlorophenyl)-1-(2-((2-chlorophenyl)thio)ethyl)-2-hydroxy-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium bromide (**5.1a**).

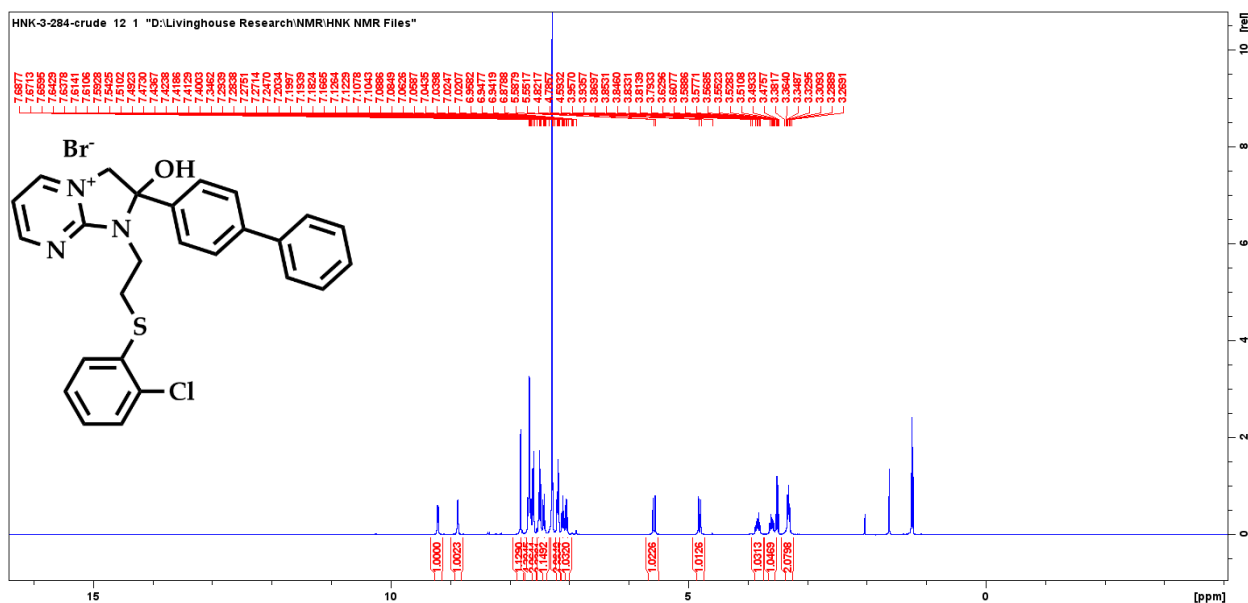


Figure 3.28B: ^1H -NMR Spectra of 2-([1,1'-biphenyl]-4-yl)-1-(2-((2-chlorophenyl)thio)ethyl)-2-hydroxy-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium bromide (**5.1b**).

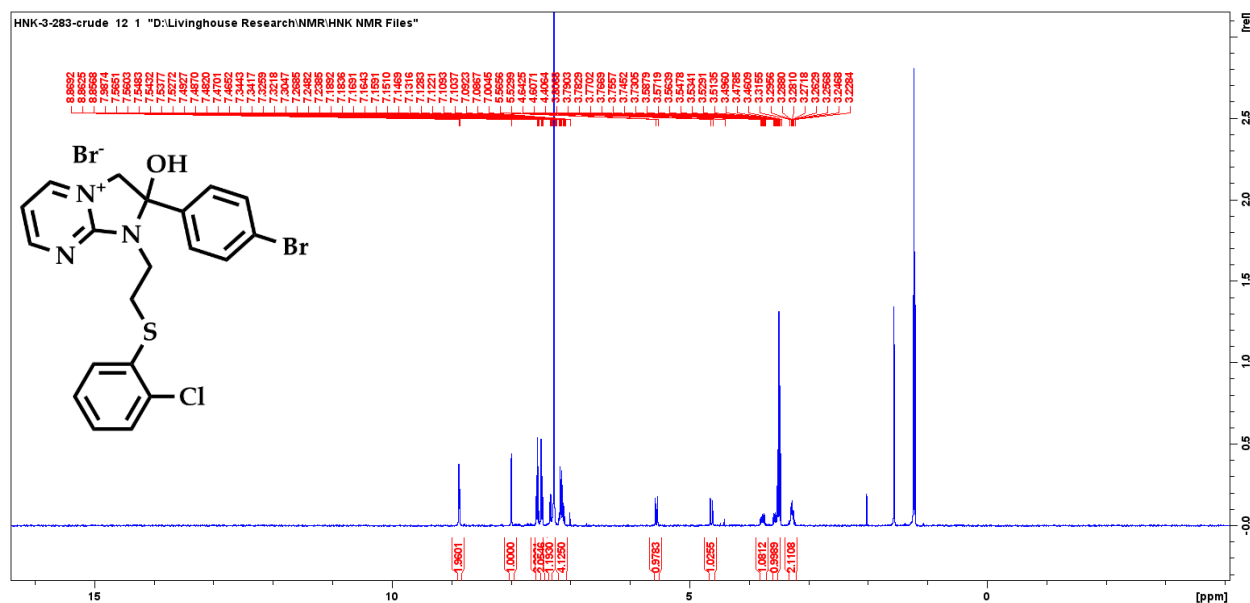


Figure 3.29B: ^1H -NMR Spectra of 2-(4-bromophenyl)-1-(2-((2-chlorophenyl)thio)ethyl)-2-hydroxy-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium bromide (**5.1c**).

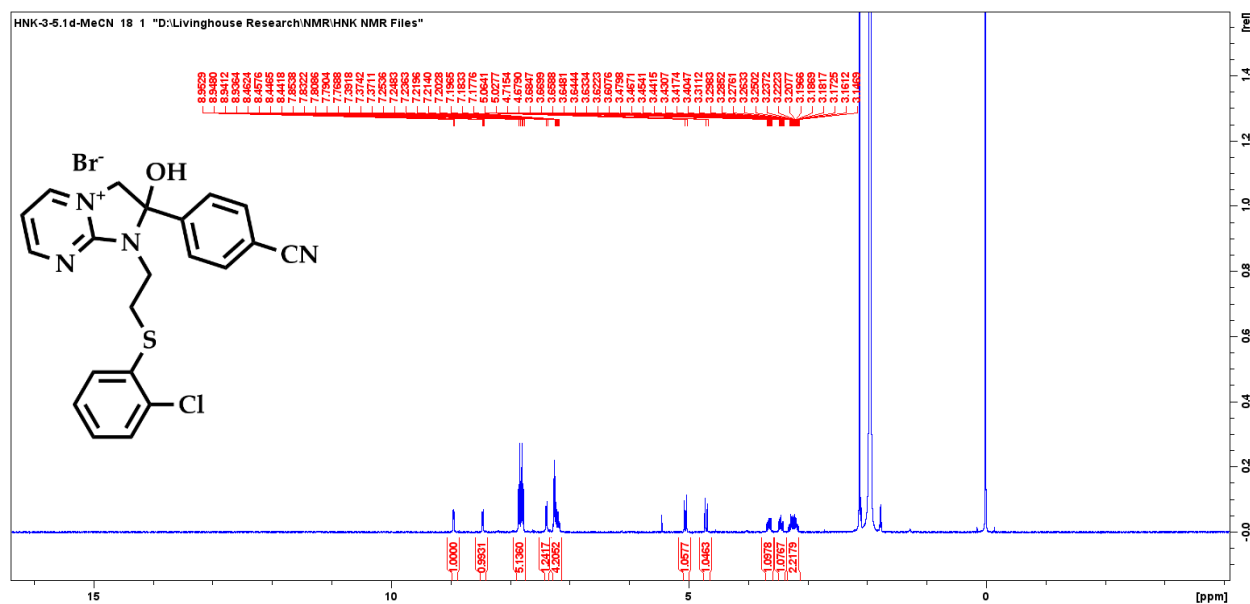


Figure 3.30B: ^1H -NMR Spectra of 1-(2-((2-chlorophenyl)thio)ethyl)-2-(4-cyanophenyl)-2-hydroxy-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium bromide (**5.1d**).

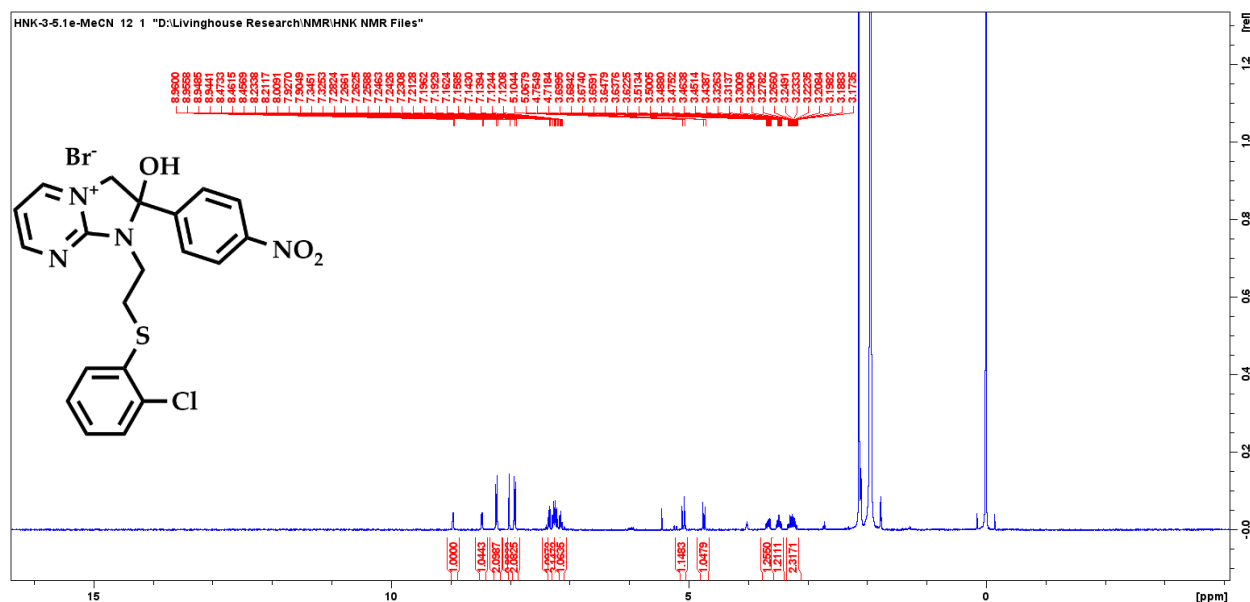


Figure 3.31B: ¹H-NMR Spectra of 1-(2-((2-chlorophenyl)thio)ethyl)-2-(4-nitrophenyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (5.1e).

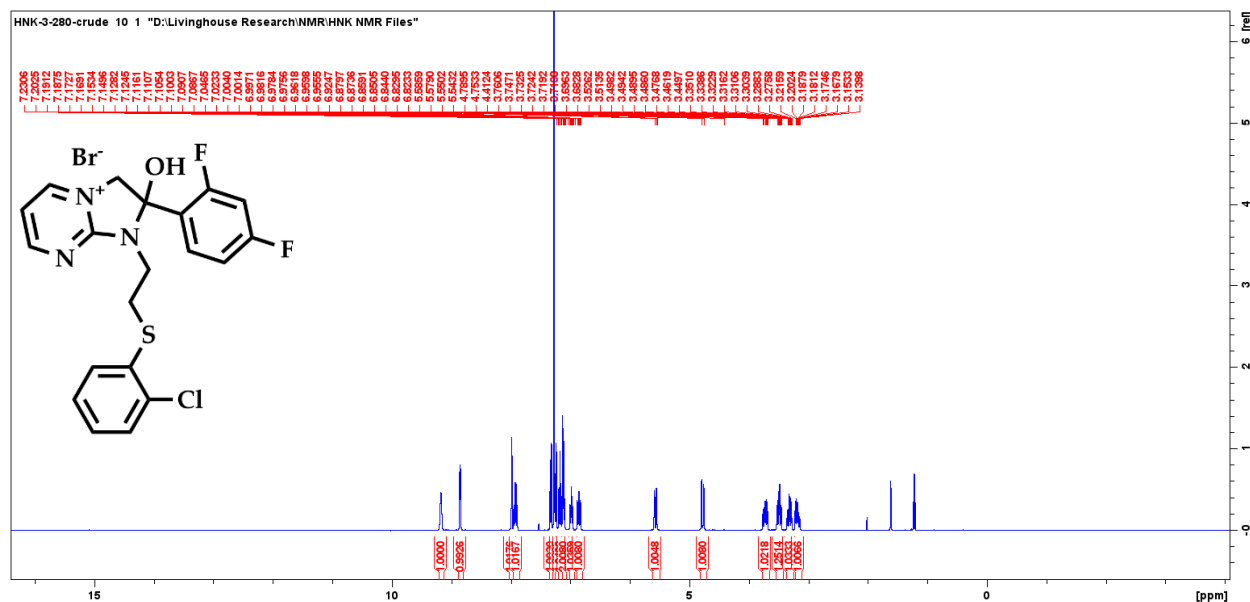


Figure 3.32B: ¹H-NMR Spectra of 1-(2-((2-chlorophenyl)thio)ethyl)-2-(2,4-difluorophenyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (5.1f).

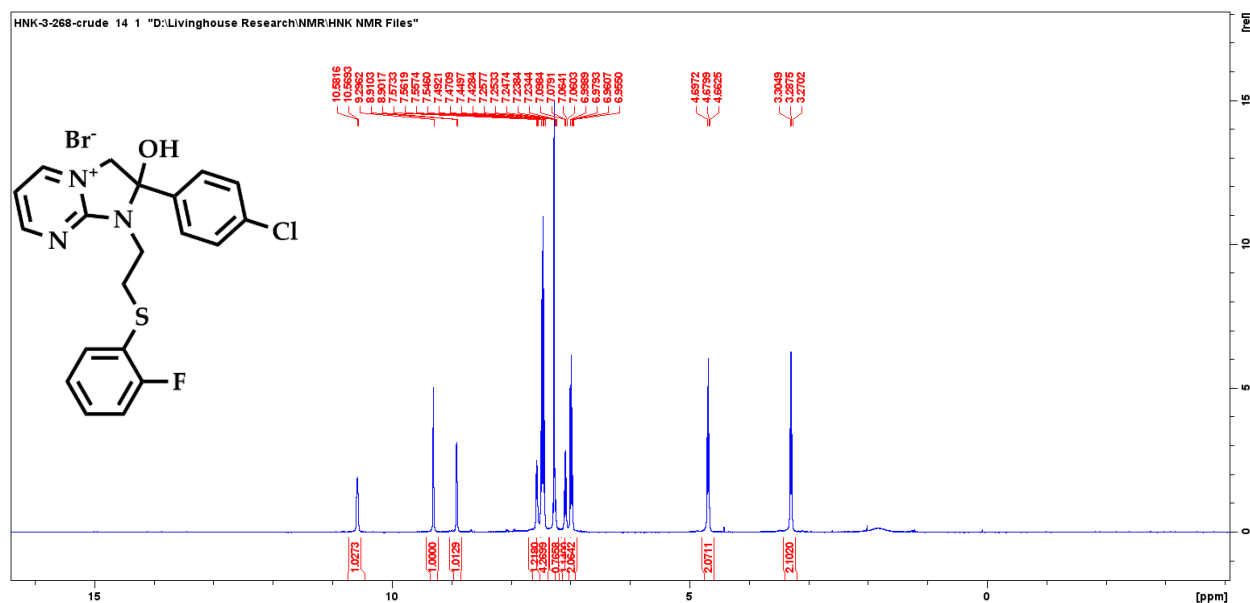


Figure 3.33B: ¹H-NMR Spectra of 2-(4-chlorophenyl)-1-(2-((2-fluorophenyl)thio)ethyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (**6.1a**).

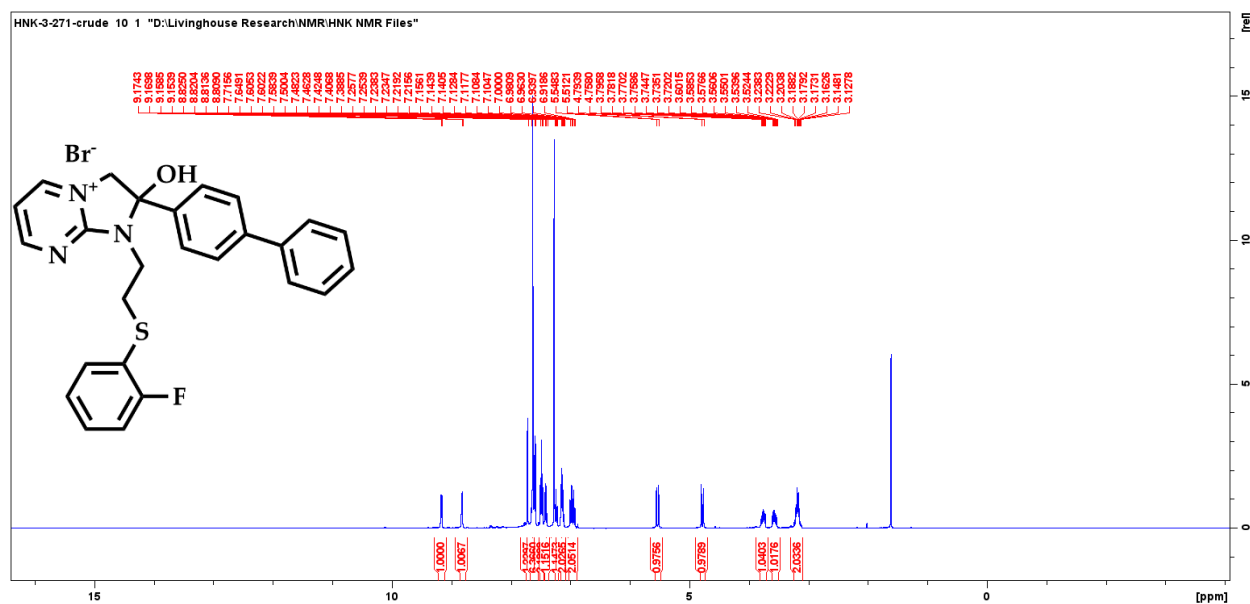


Figure 3.34B: ¹H-NMR Spectra of 2-([1,1'-biphenyl]-4-yl)-1-(2-((2-fluorophenyl)thio)ethyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (**6.1b**).

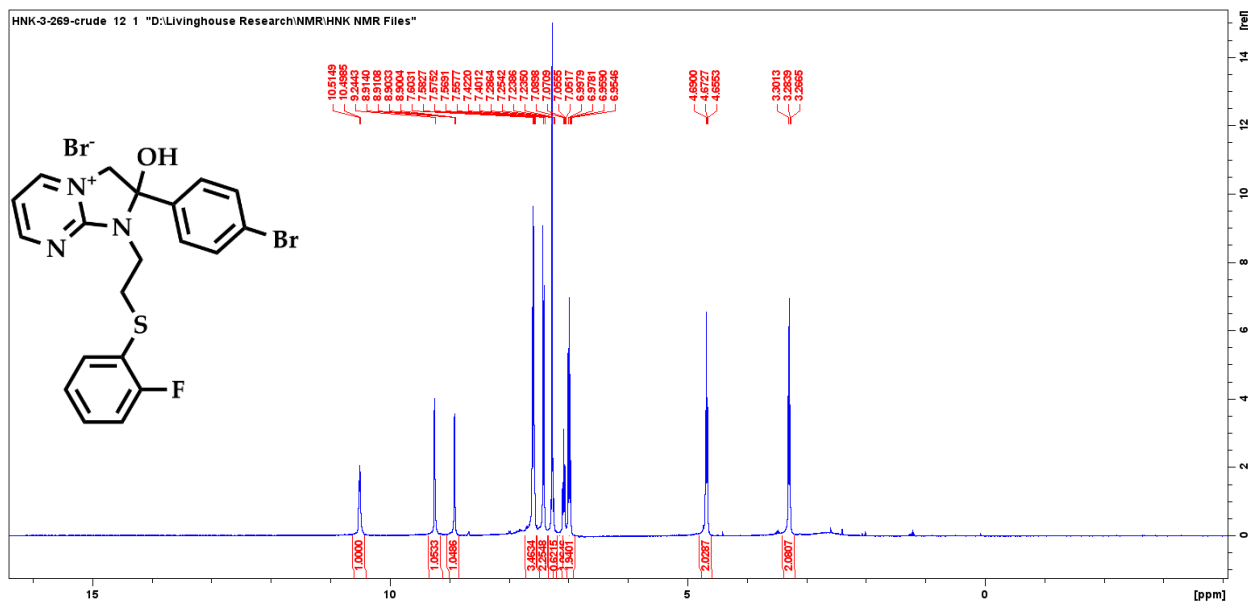


Figure 3.35B: ^1H -NMR Spectra of 2-(4-bromophenyl)-1-(2-((2-fluorophenyl)thio)ethyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (**6.1c**).

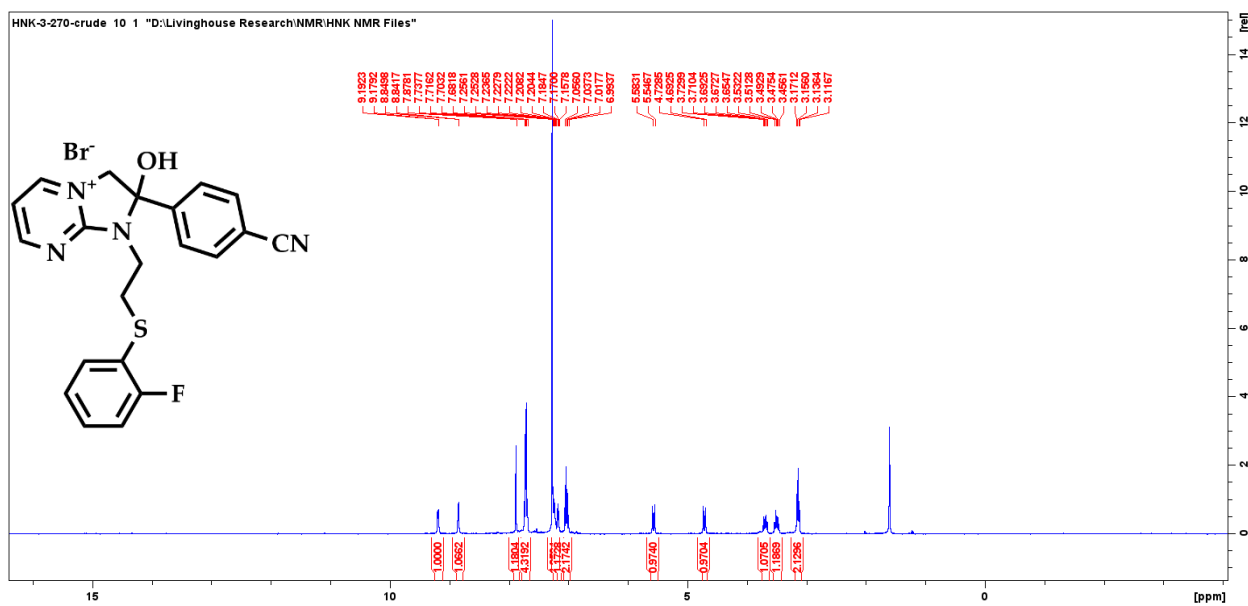


Figure 3.36B: ^1H -NMR Spectra of 2-(4-cyanophenyl)-1-(2-((2-fluorophenyl)thio)ethyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (**6.1d**).

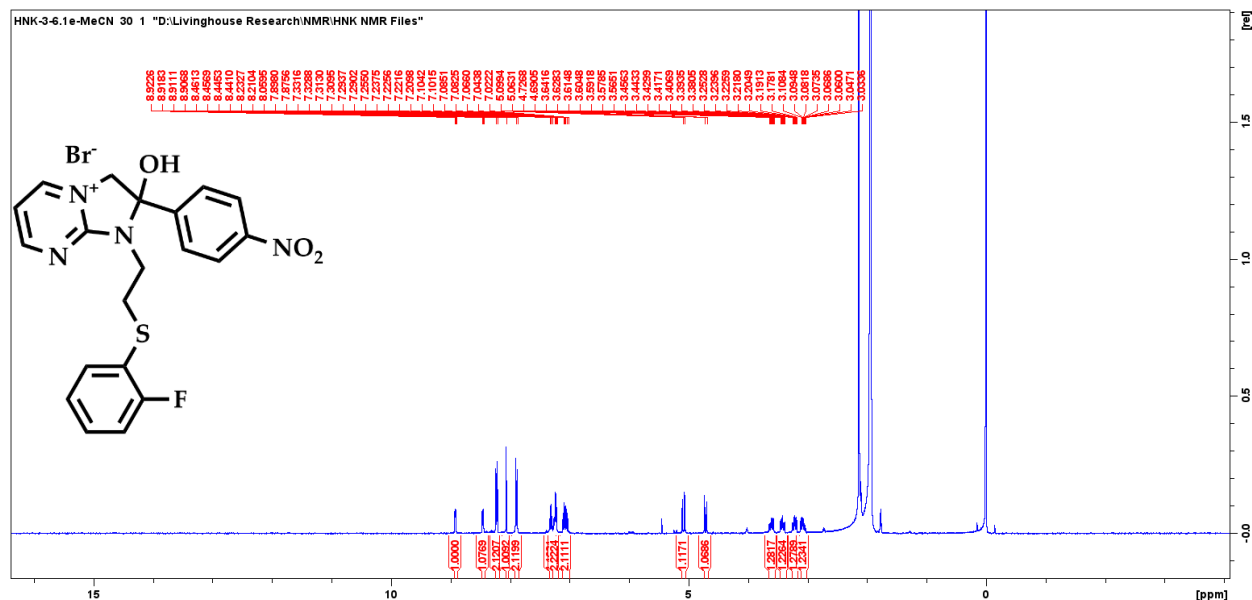


Figure 3.37B: ¹H-NMR Spectra of 2-(4-nitrophenyl)-1-(2-((2-fluorophenyl)thio)ethyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (**6.1e**).

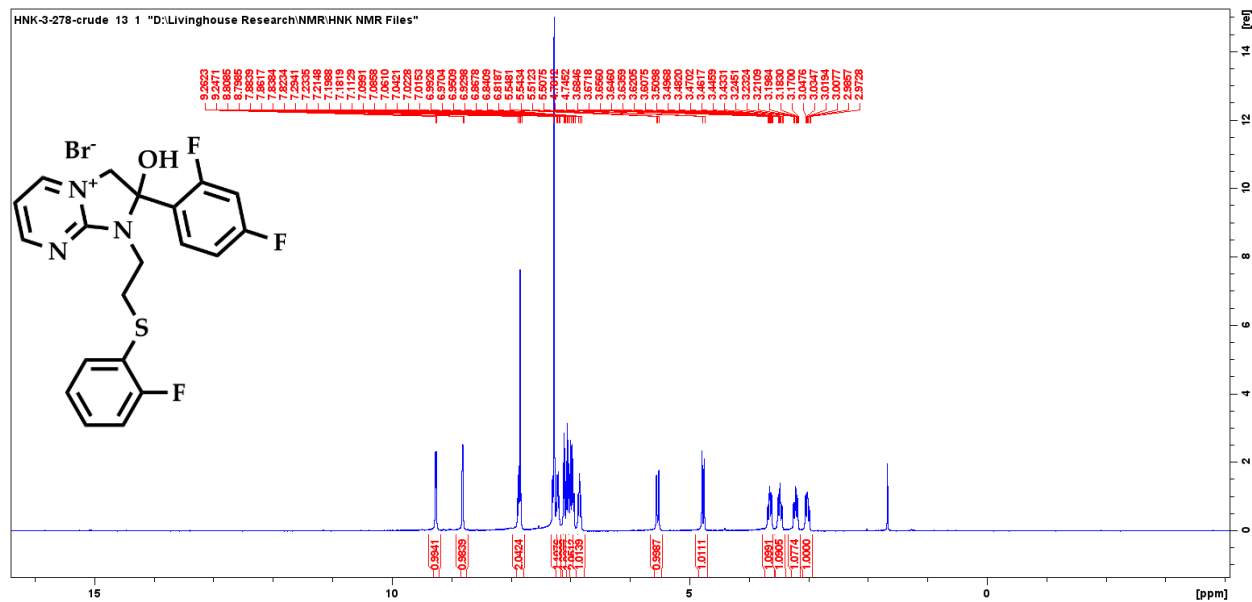


Figure 3.38B: ¹H-NMR Spectra of 2-(2,4-difluorophenyl)-1-(2-((2-fluorophenyl)thio)ethyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (**6.1f**).

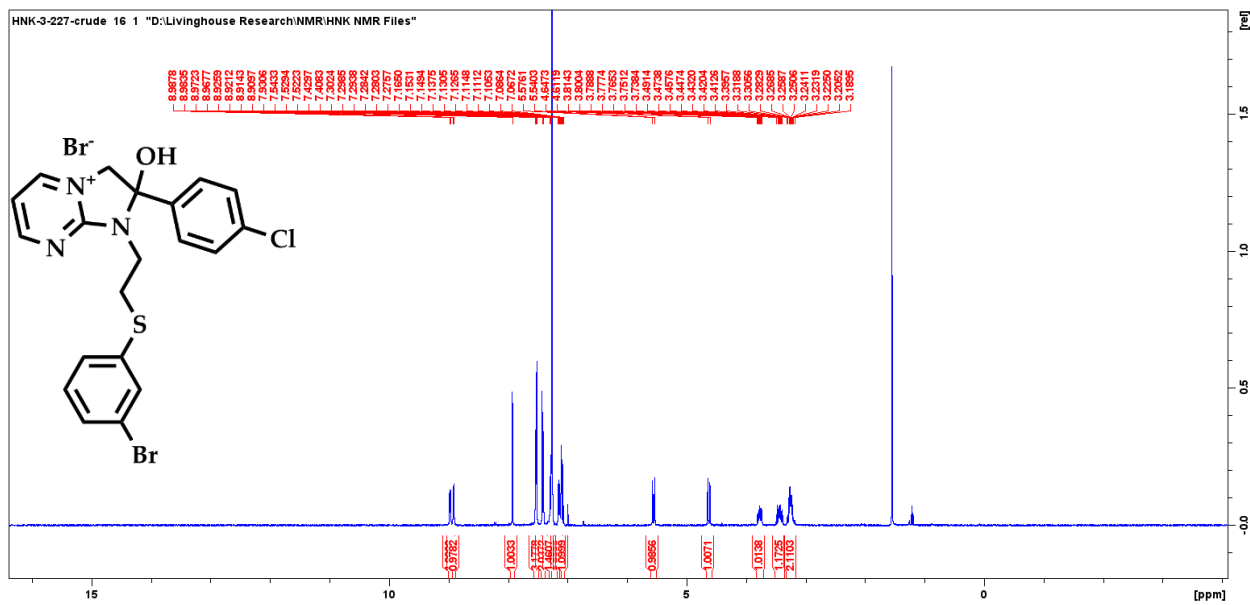


Figure 3.39B: ¹H-NMR Spectra of 1-(2-((3-bromophenyl)thio)ethyl)-2-(4-chlorophenyl)-2-hydroxy-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium bromide (**7.1a**).

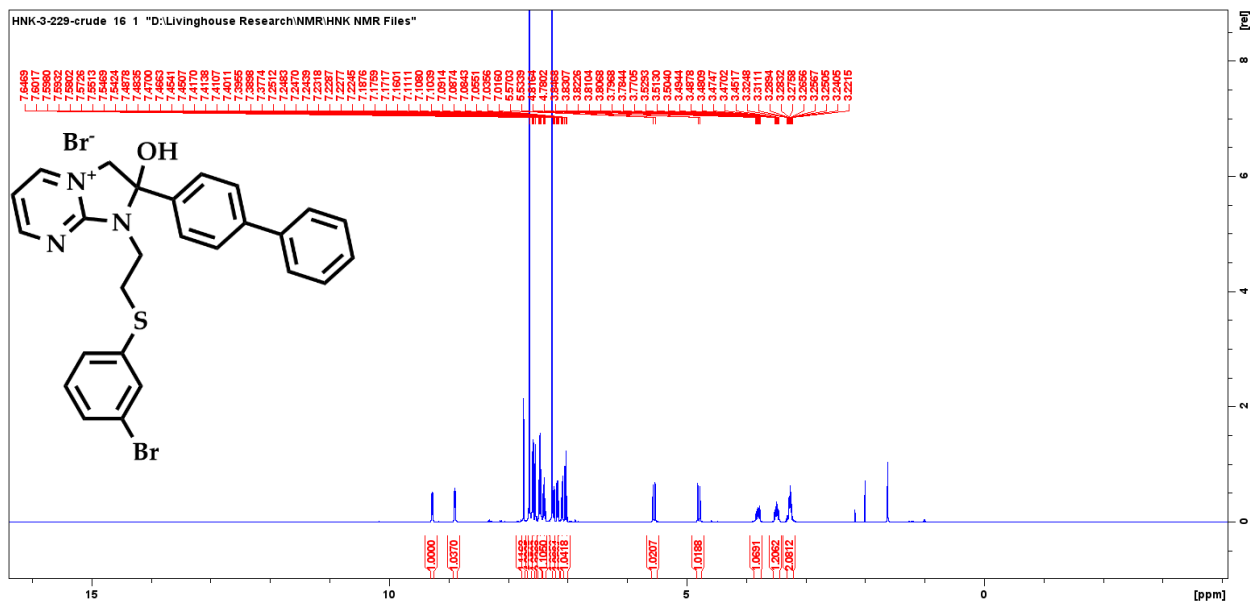


Figure 3.40B: ¹H-NMR Spectra of 2-([1,1'-biphenyl]-4-yl)-1-(2-((3-bromophenyl)thio)ethyl)-2-hydroxy-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium bromide (**7.1b**).

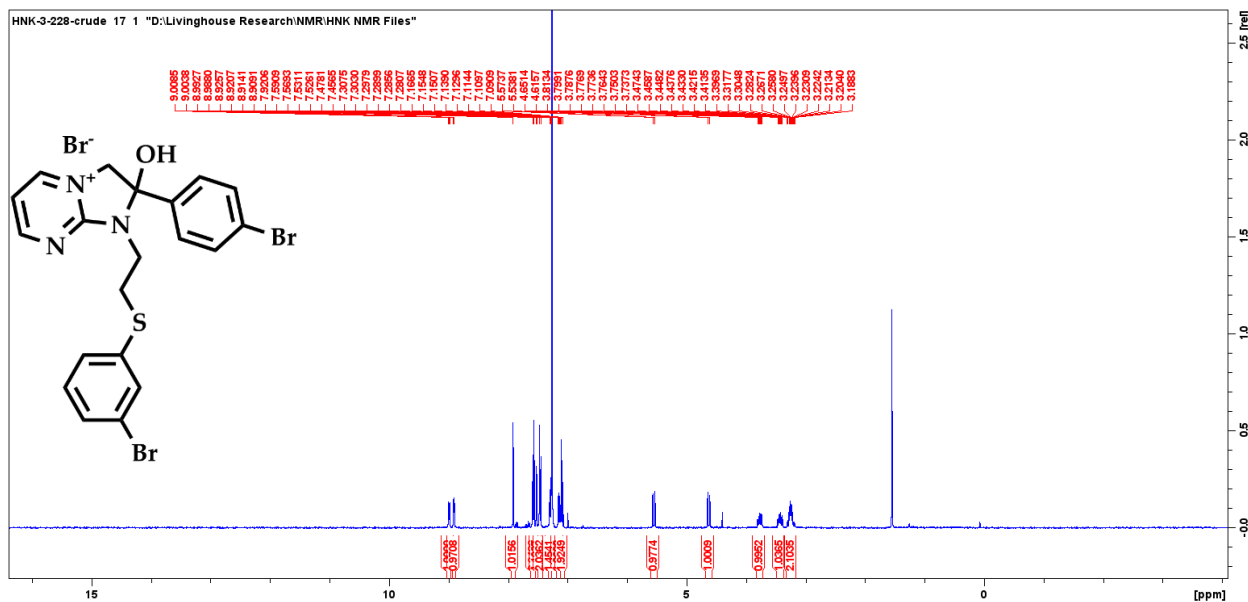


Figure 3.41B: ¹H-NMR Spectra of 2-(4-bromophenyl)-1-(2-((3-bromophenyl)thio)ethyl)-2-hydroxy-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium bromide (**7.1c**).

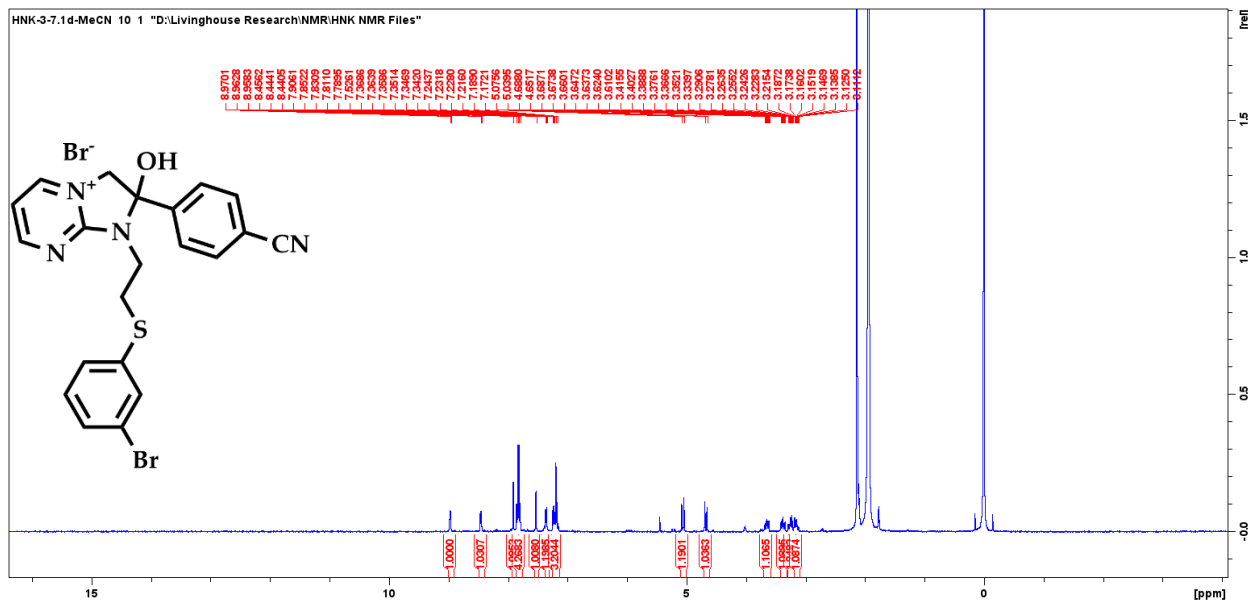


Figure 3.42B: ^1H -NMR Spectra of 2-(4-cyanophenyl)-1-(2-((3-bromophenyl)thio)ethyl)-2-hydroxy-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium bromide (**7.1d**).

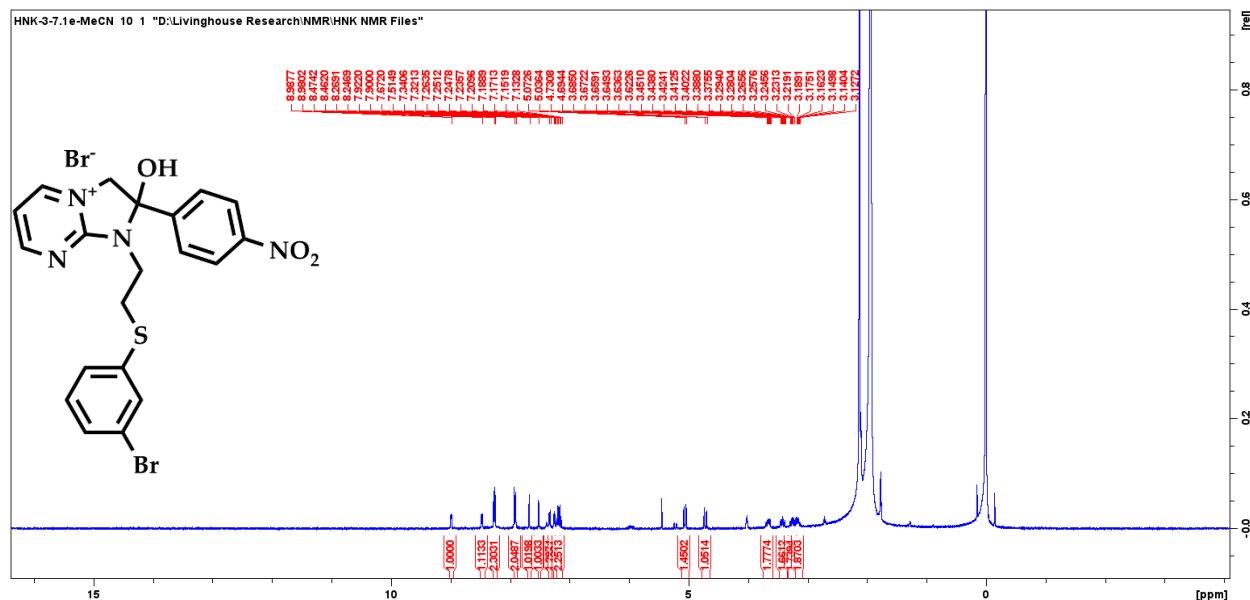


Figure 3.43B: ^1H -NMR Spectra of 2-(4-nitrophenyl)-1-(2-((3-bromophenyl)thio)ethyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (7.1e).

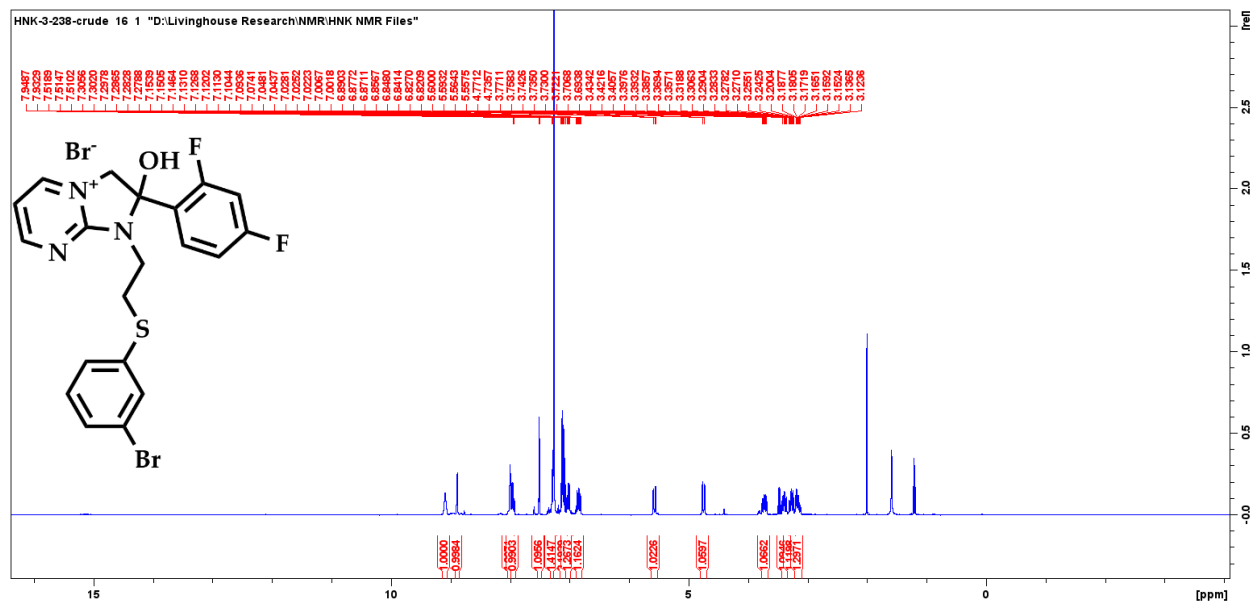


Figure 3.44B: ^1H -NMR Spectra of 1-(2-((3-bromophenyl)thio)ethyl)-2-(2,4-difluorophenyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (7.1f).

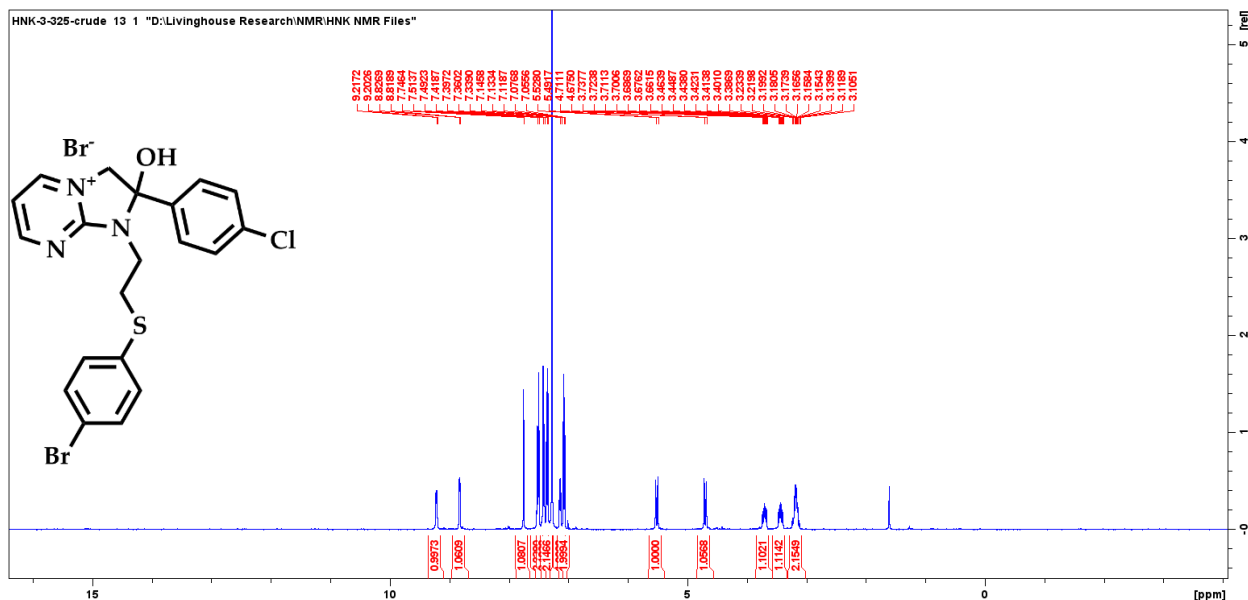


Figure 3.45B: ^1H -NMR Spectra of 1-(2-((4-bromophenyl)thio)ethyl)-2-(4-chlorophenyl)-2-hydroxy-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium bromide (**8.1a**).

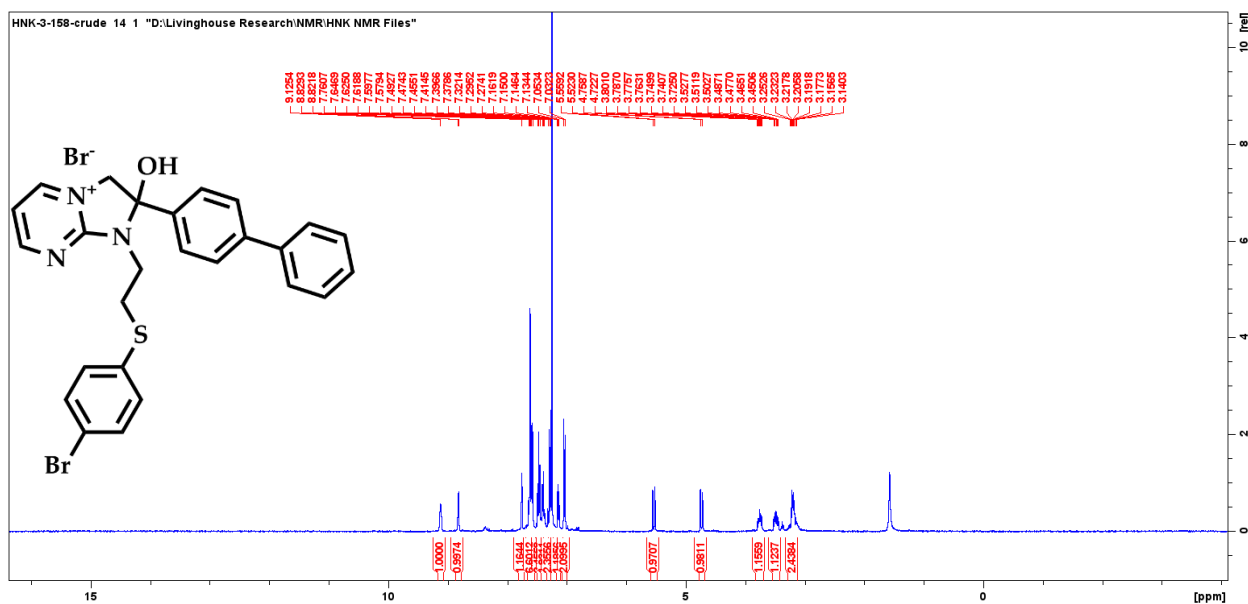


Figure 3.46B: ^1H -NMR Spectra of 2-([1,1'-biphenyl]-4-yl)-1-(2-((4-bromophenyl)thio)ethyl)-2-hydroxy-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium bromide (**8.1b**).

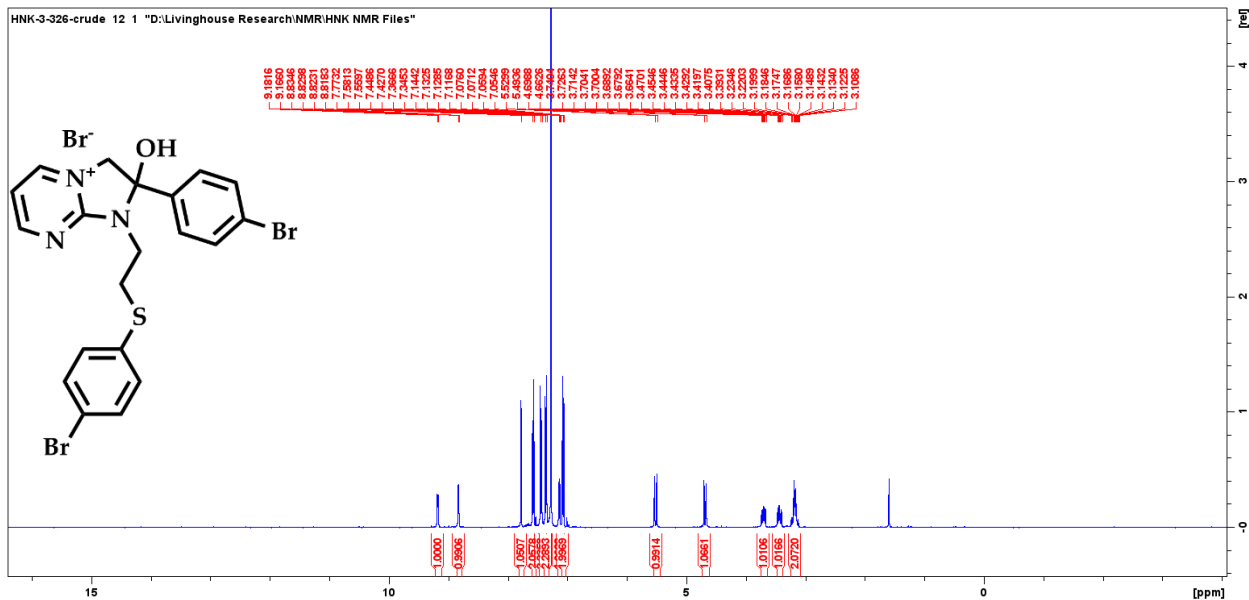


Figure 3.47B: ^1H -NMR Spectra of 2-(4-bromophenyl)-1-(2-((4-bromophenyl)thio)ethyl)-2-hydroxy-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium bromide (**8.1c**).

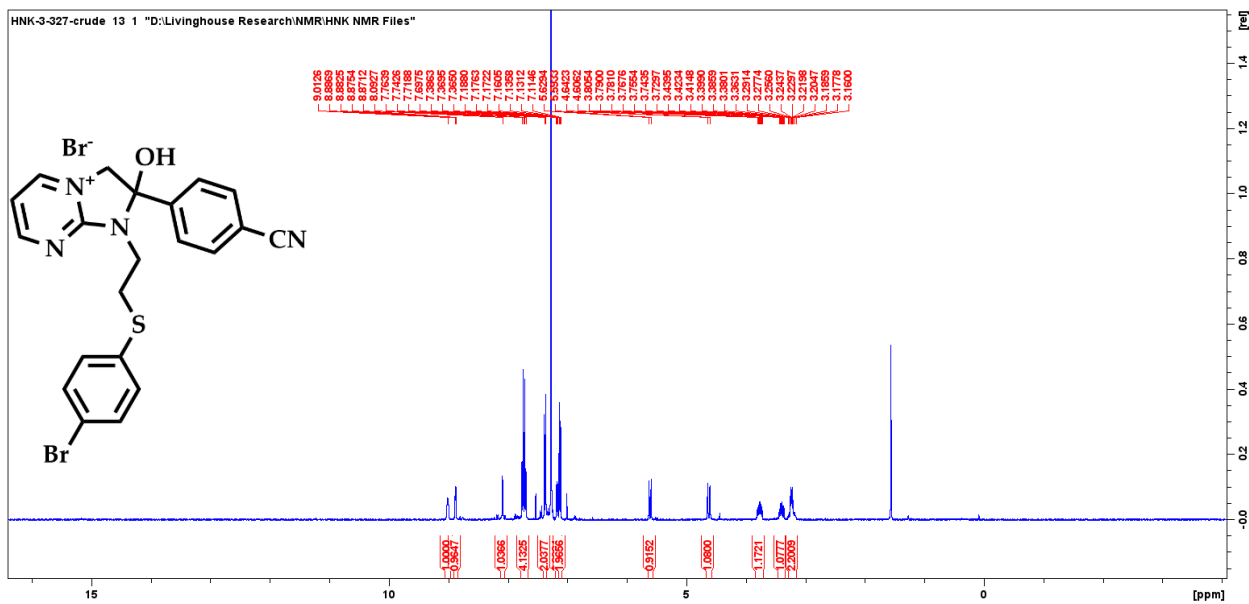


Figure 3.48B: ¹H-NMR Spectra of 1-(2-((4-bromophenyl)thio)ethyl)-2-(4-cyanophenyl)-2-hydroxy-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium bromide (**8.1d**).

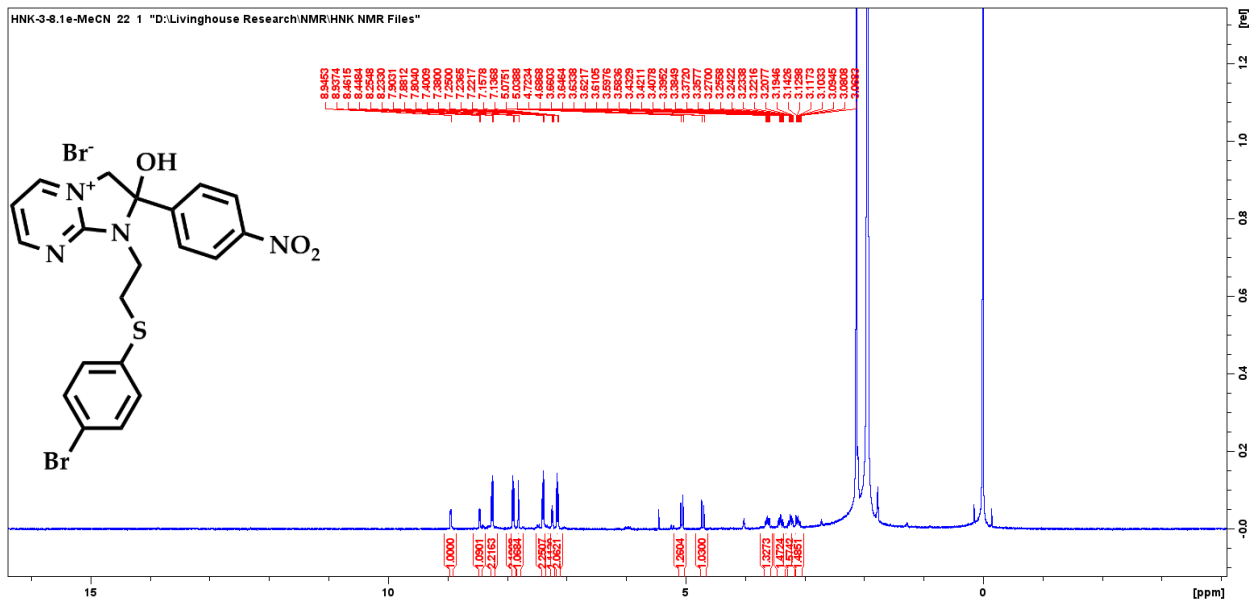


Figure 3.49B: ¹H-NMR Spectra of 1-(2-((4-bromophenyl)thio)ethyl)-2-(4-nitrophenyl)-2-hydroxy-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium bromide (**8.1d**).

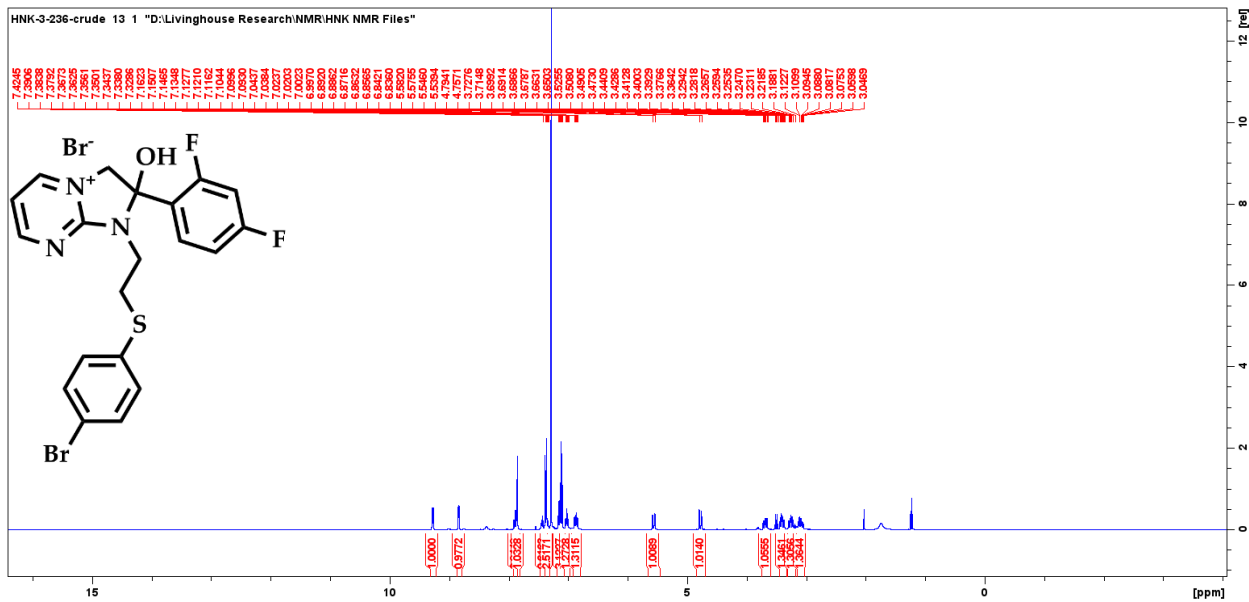


Figure 3.50B: ¹H-NMR Spectra of 1-(2-((4-bromophenyl)thio)ethyl)-2-(2,4-difluorophenyl)-2-hydroxy-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium bromide (**8.1.f**).

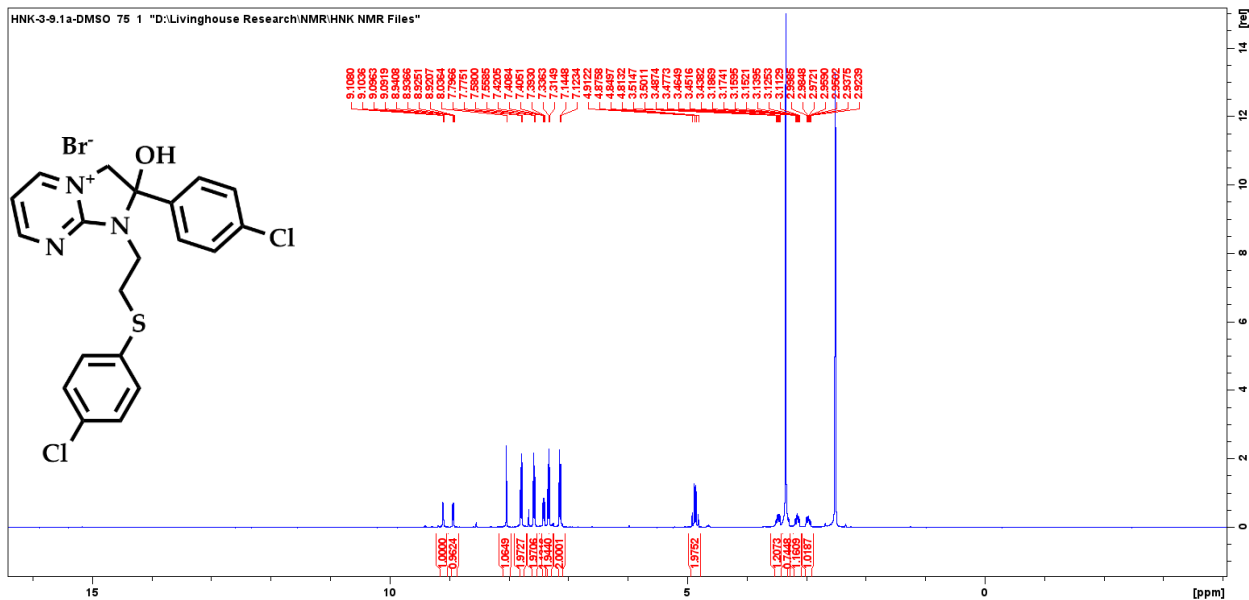


Figure 3.51B: ¹H-NMR Spectra of 1-(2-((4-chlorophenyl)thio)ethyl)-2-(4-chlorophenyl)-2-hydroxy-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium bromide (**9.1a**).

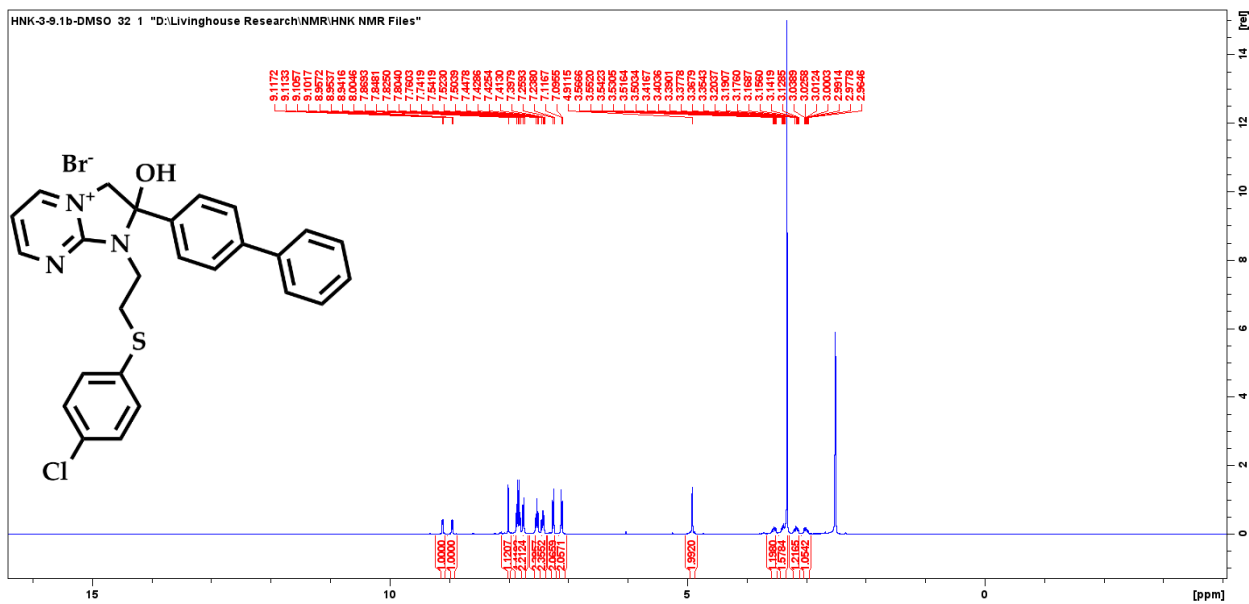


Figure 3.52B: ¹H-NMR Spectra of 2-([1,1'-biphenyl]-4-yl)-1-(2-((4-chlorophenyl)thio)ethyl)-2-hydroxy-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium bromide (**9.1b**).

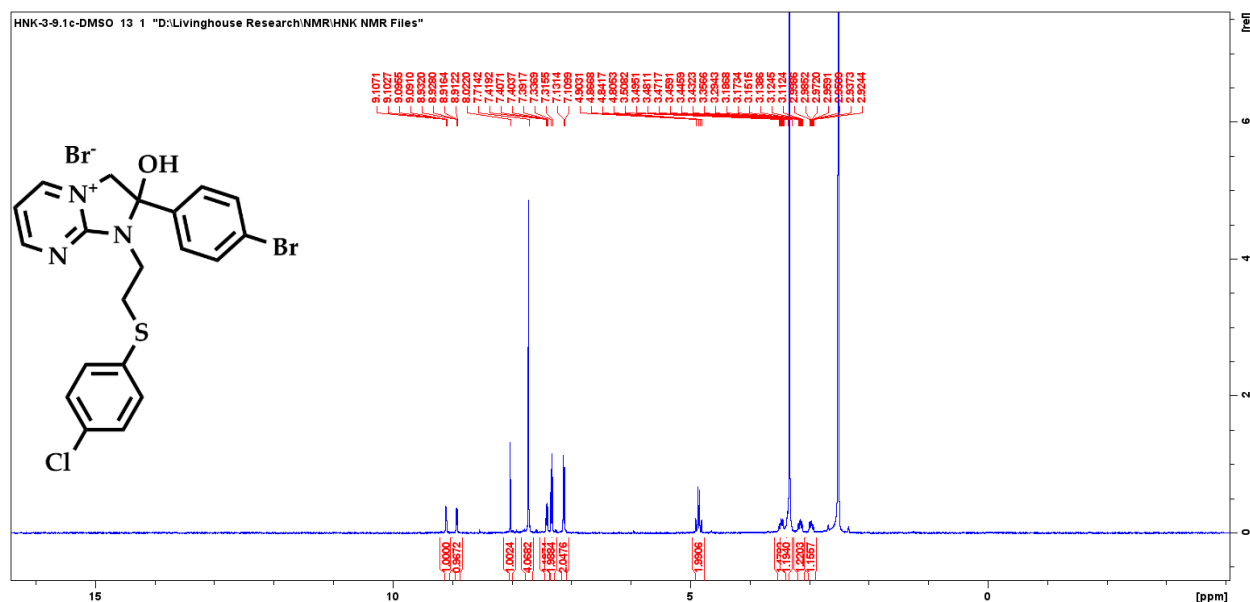


Figure 3.53B: ^1H -NMR Spectra of 1-(2-((4-chlorophenyl)thio)ethyl)-2-(4-bromophenyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (**9.1c**).

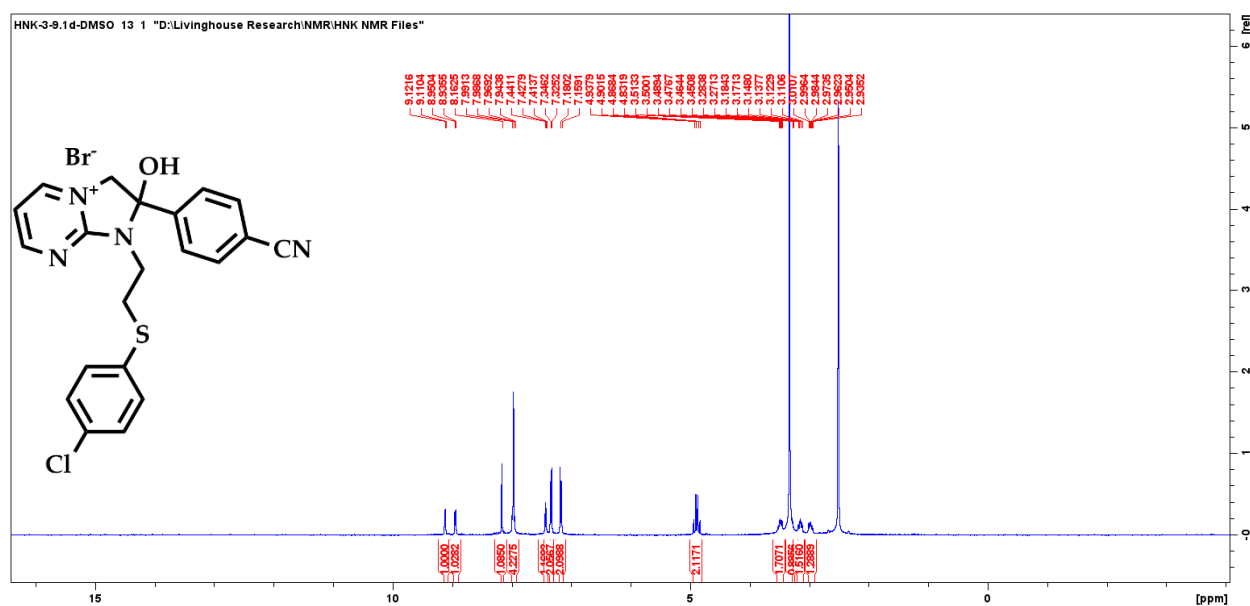


Figure 3.54B: ^1H -NMR Spectra of 1-(2-((4-chlorophenyl)thio)ethyl)-2-(4-cyanophenyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (**9.1d**).

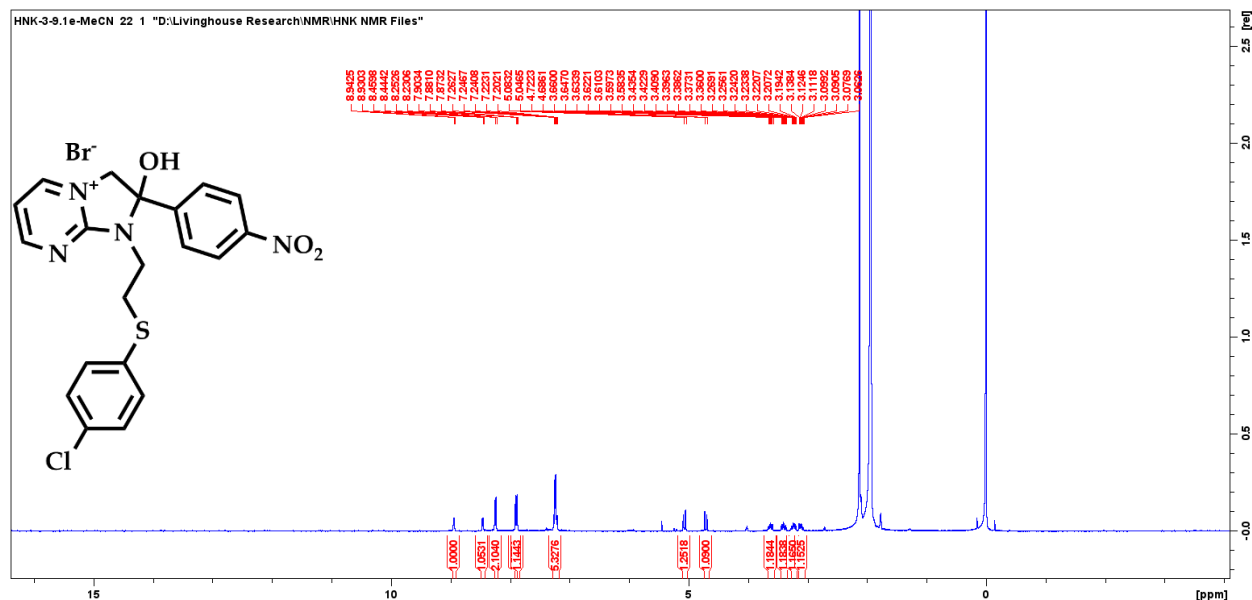


Figure 3.55B: ¹H-NMR Spectra of 1-(2-((4-chlorophenyl)thio)ethyl)-2-(4-nitrophenyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (**9.1e**).

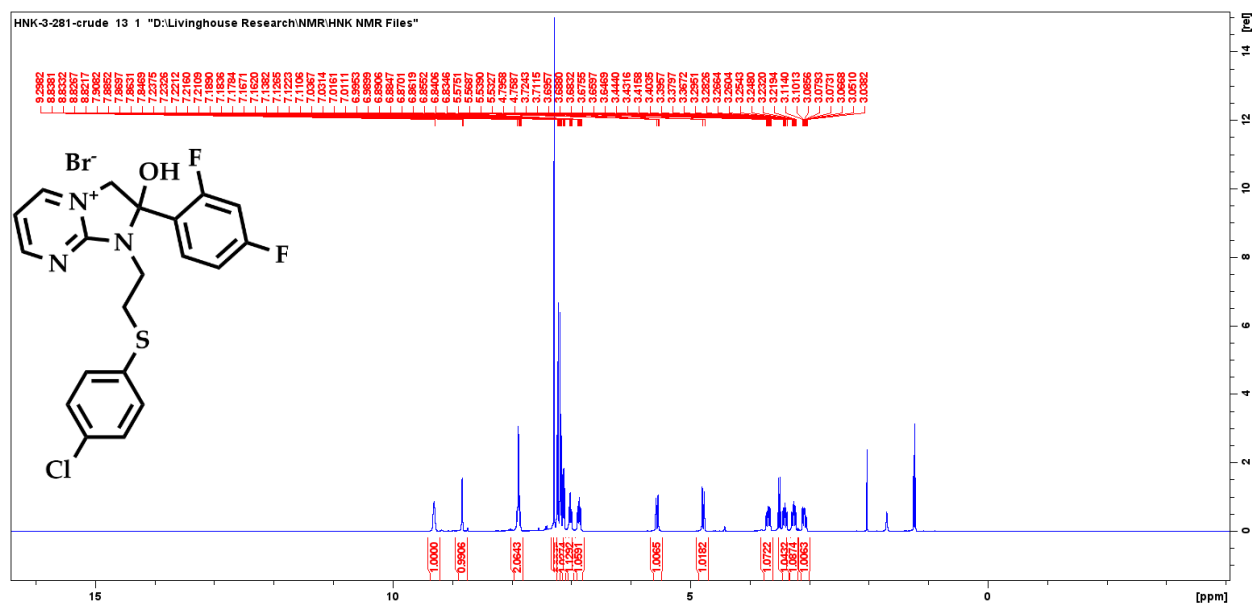


Figure 3.56B: ¹H-NMR Spectra of 1-(2-((4-chlorophenyl)thio)ethyl)-2-(2,4-difluorophenyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (**9.1f**).

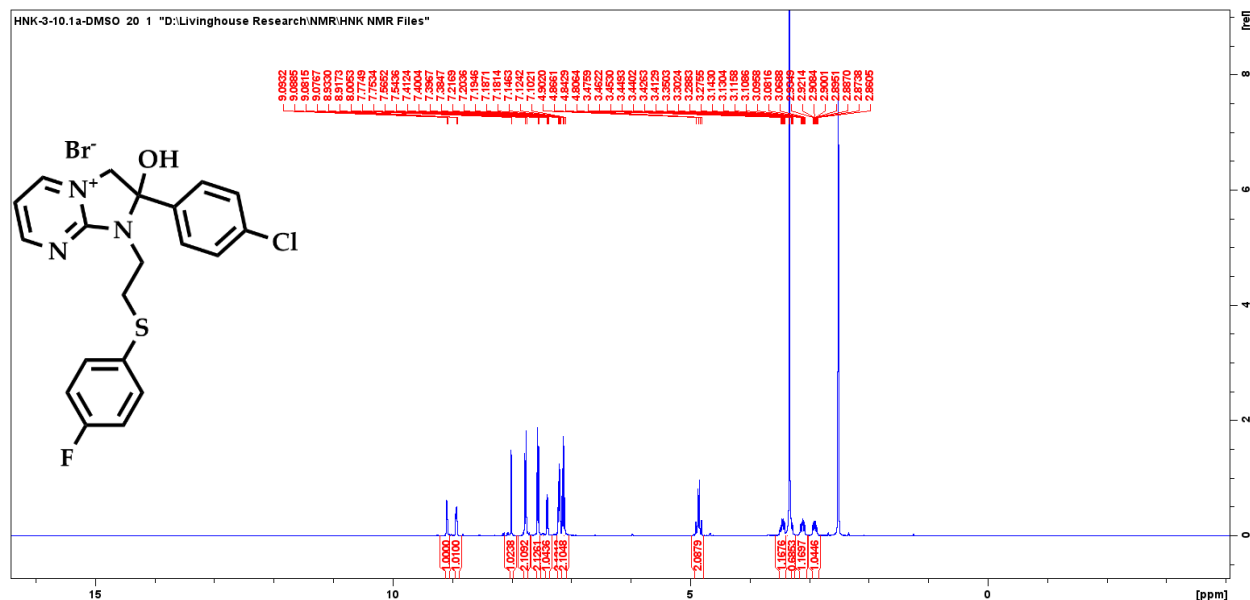


Figure 3.57B: ¹H-NMR Spectra of 2-(4-chlorophenyl)-1-(2-((4-fluorophenyl)thio)ethyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (**10.1a**).

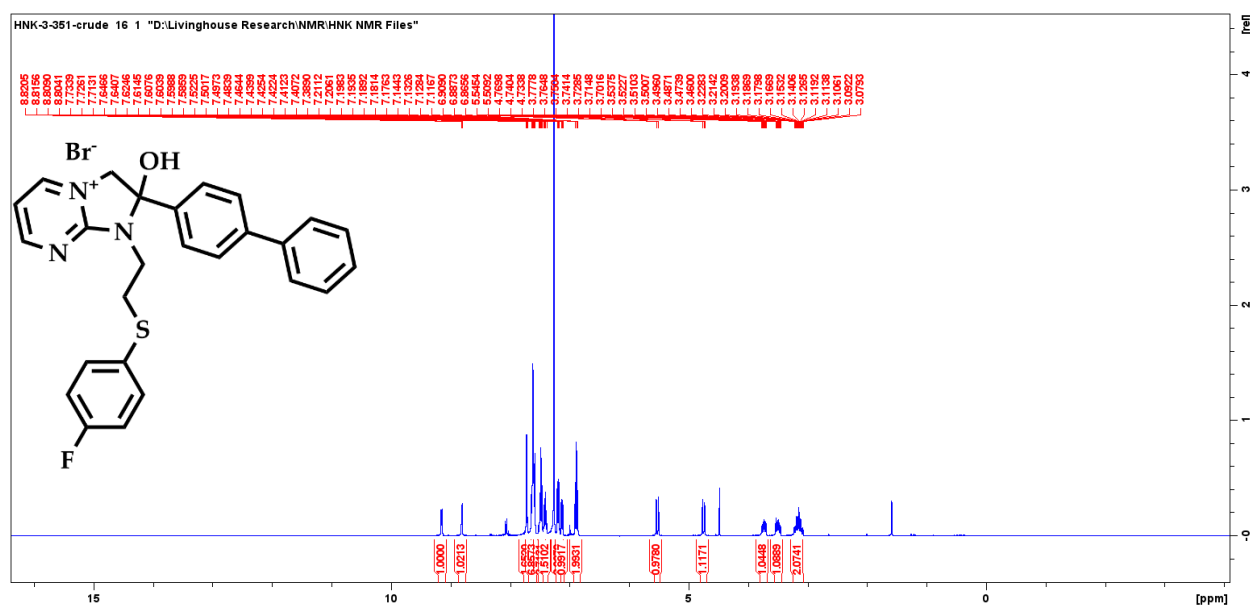


Figure 3.58B: ¹H-NMR Spectra of 2-([1,1'-biphenyl]-4-yl)-1-(2-((4-fluorophenyl)thio)ethyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (**10.1b**).

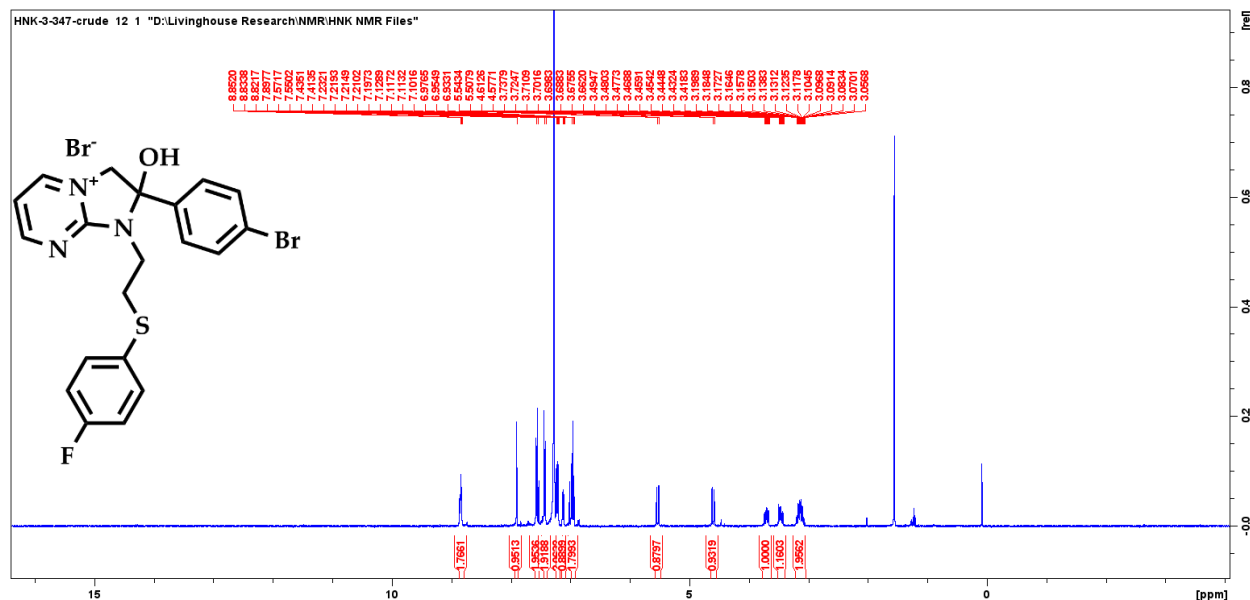


Figure 3.59B: ^1H -NMR Spectra of 2-(4-bromophenyl)-1-(2-((4-fluorophenyl)thio)ethyl)-2-hydroxy-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium bromide (**10.1c**).

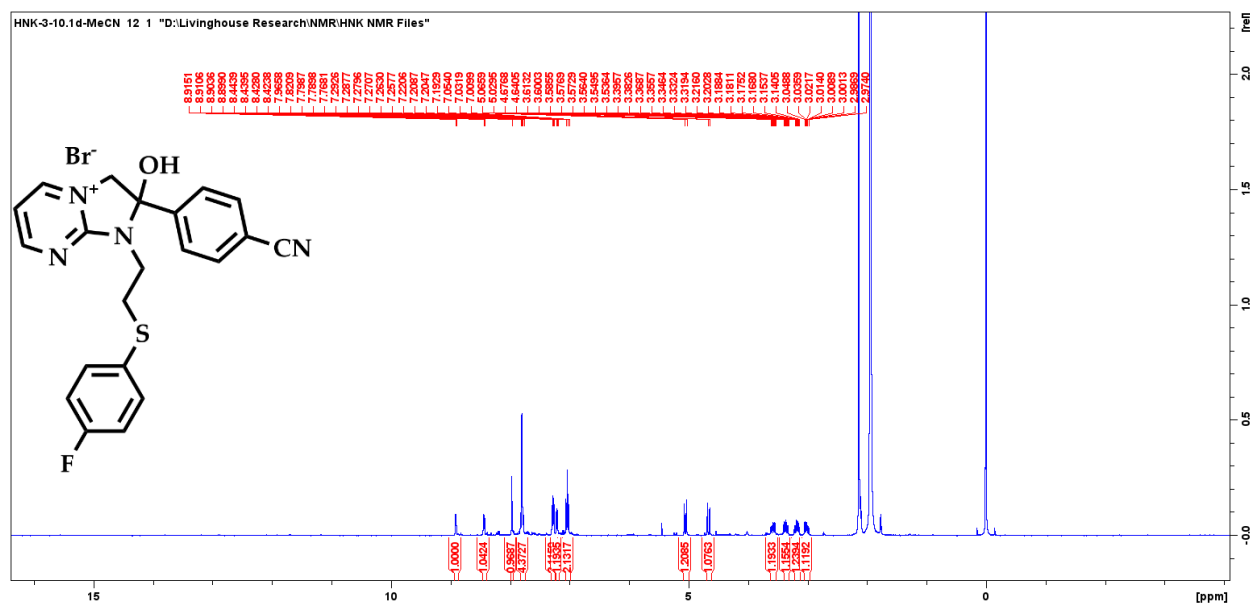


Figure 3.60B: ^1H -NMR Spectra of 2-(4-cyanophenyl)-1-(2-((4-fluorophenyl)thio)ethyl)-2-hydroxy-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium bromide (**10.1d**).

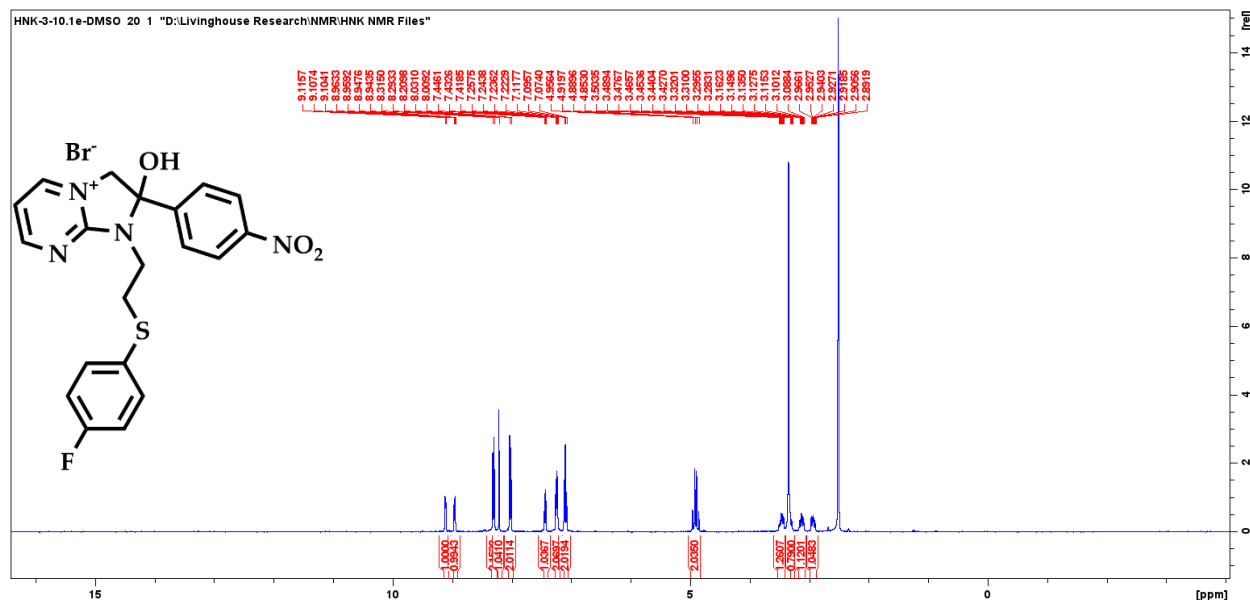


Figure 3.61B: ¹H-NMR Spectra of 2-(4-cyanophenyl)-1-(2-((4-fluorophenyl)thio)ethyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (**10.1e**).

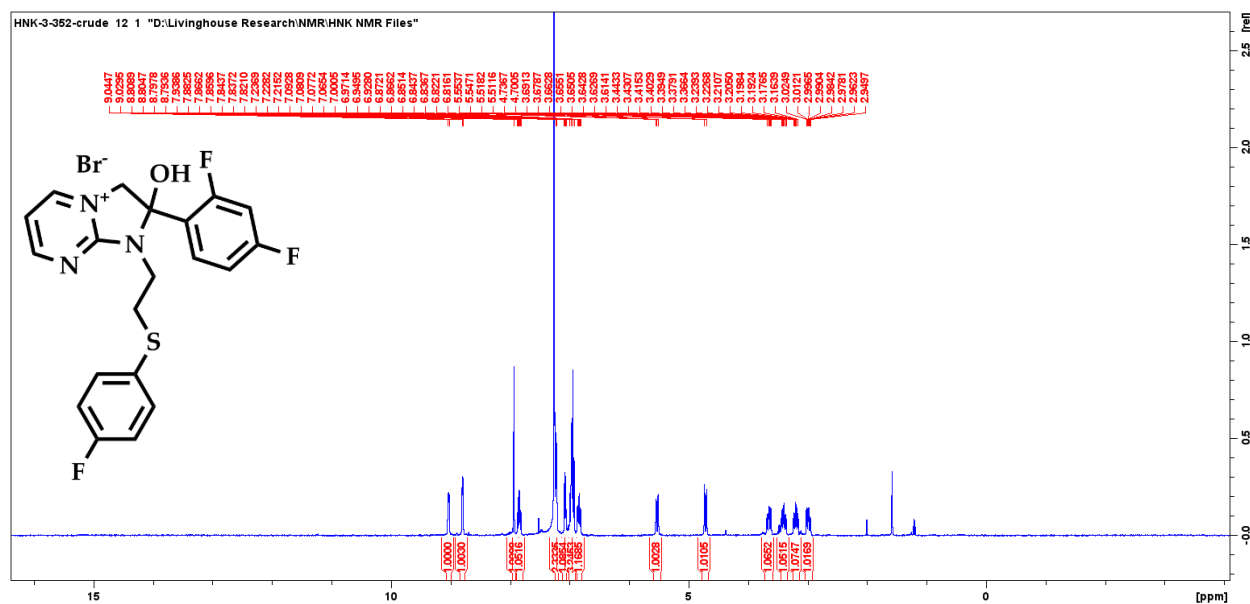


Figure 3.62B: ¹H-NMR Spectra of 2-(2,4-difluorophenyl)-1-(2-((4-fluorophenyl)thio)ethyl)-2-hydroxy-2,3-dihydro-1H-imidazo[1,2-a]pyrimidin-4-ium bromide (**10.1f**).

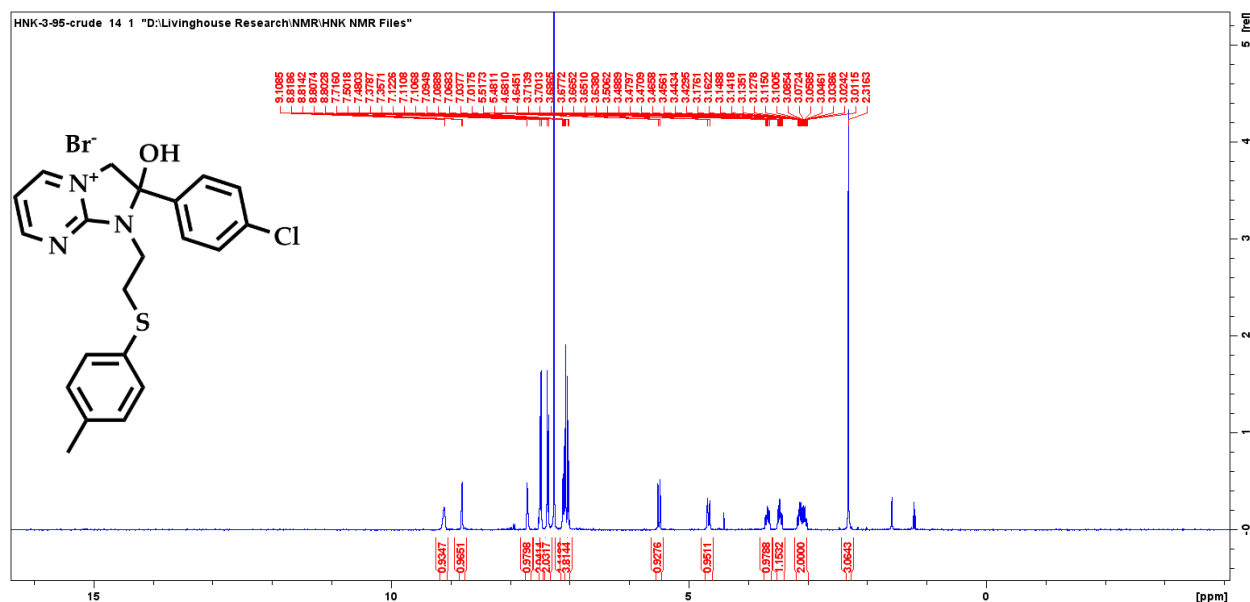


Figure 3.63B: ^1H -NMR Spectra of 2-(4-chlorophenyl)-2-hydroxy-1-(2-(*p*-tolylthio)ethyl)-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium bromide (**11.1a**).

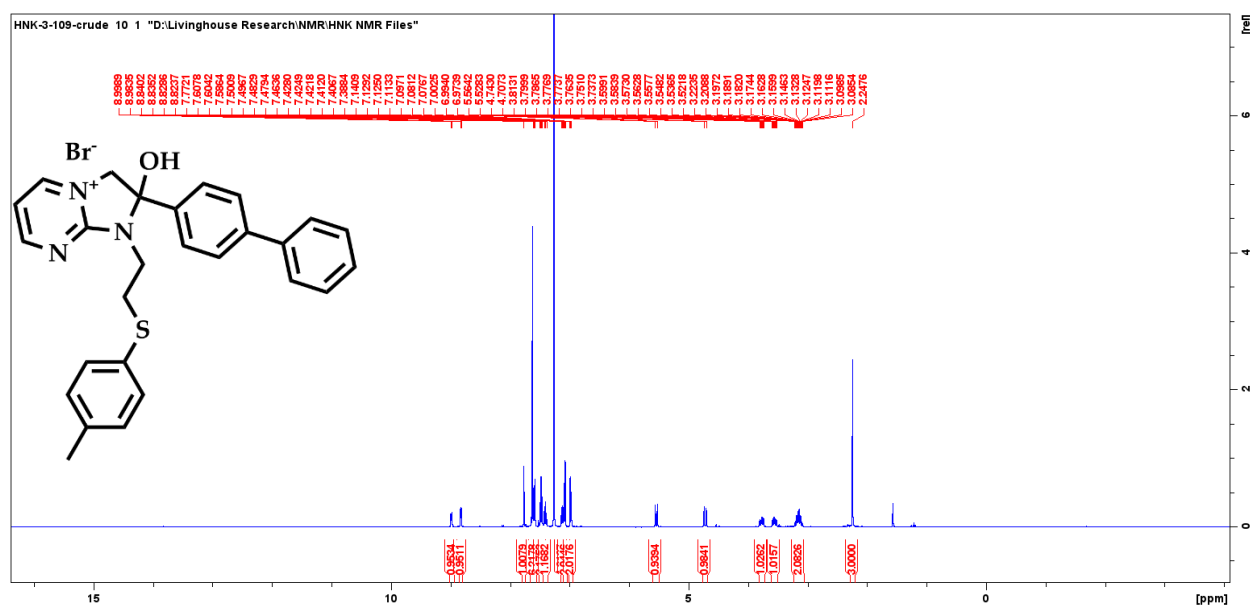


Figure 3.64B: ^1H -NMR Spectra of 2-([1,1'-biphenyl]-4-yl)-2-hydroxy-1-(2-(*p*-tolylthio)ethyl)-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium bromide (**11.1b**).

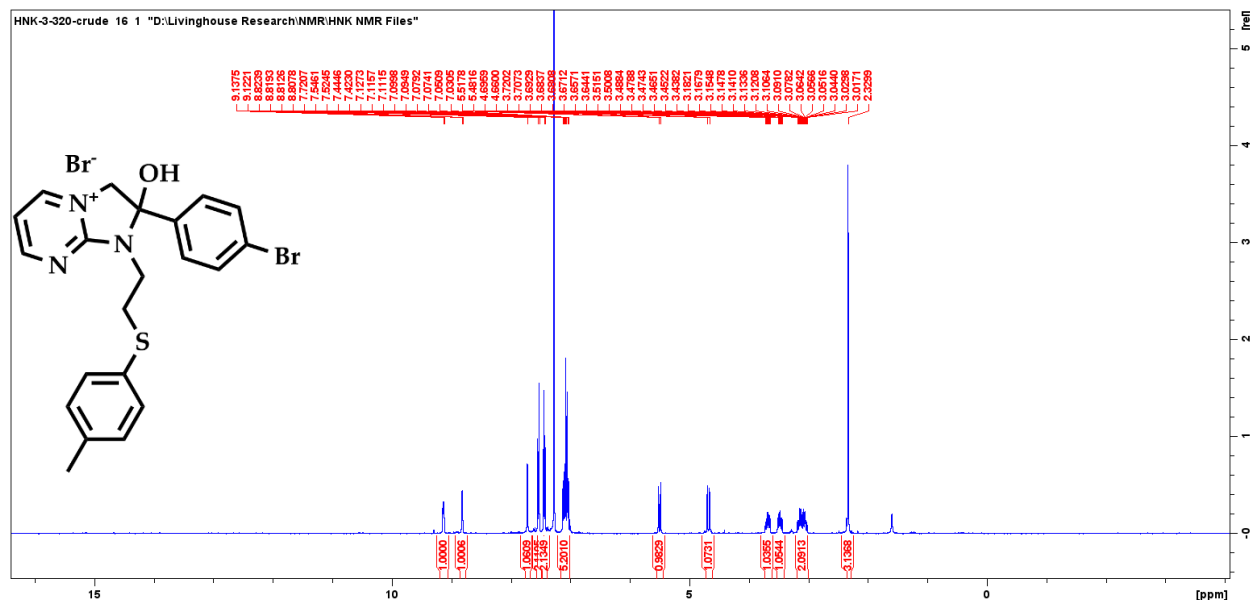


Figure 3.65B: ^1H -NMR Spectra of 2-(4-bromophenyl)-2-hydroxy-1-(2-(*p*-tolylthio)ethyl)-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium bromide (**11.1c**).

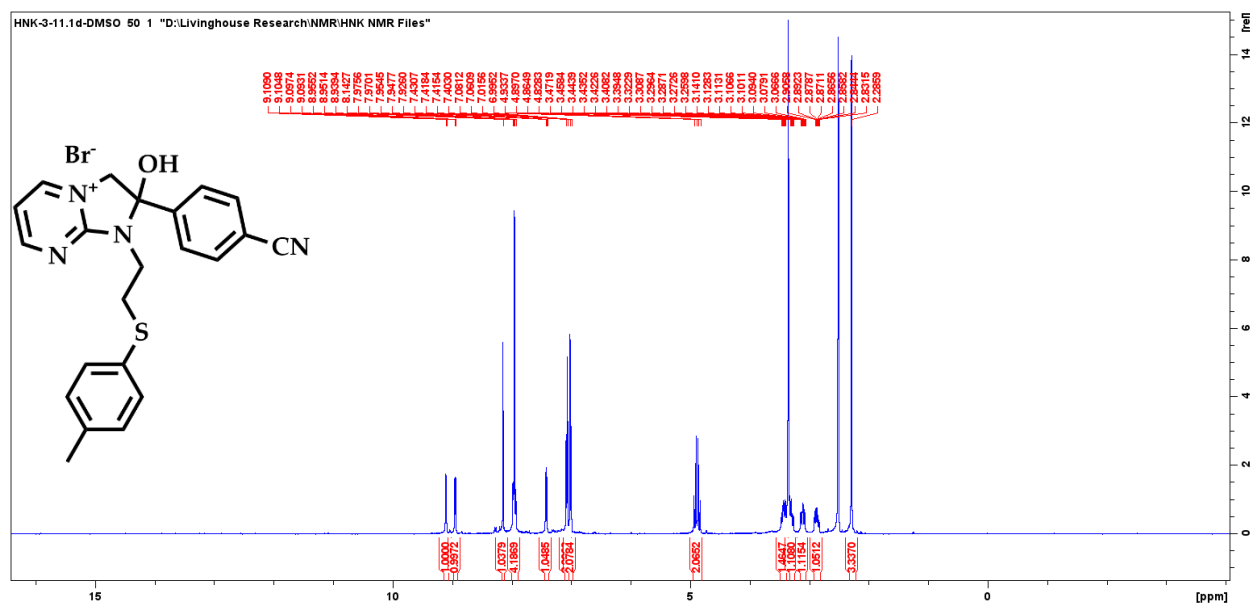


Figure 3.66B: ^1H -NMR Spectra of 2-(4-cyanophenyl)-2-hydroxy-1-(2-(*p*-tolylthio)ethyl)-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium bromide (**11.1d**).

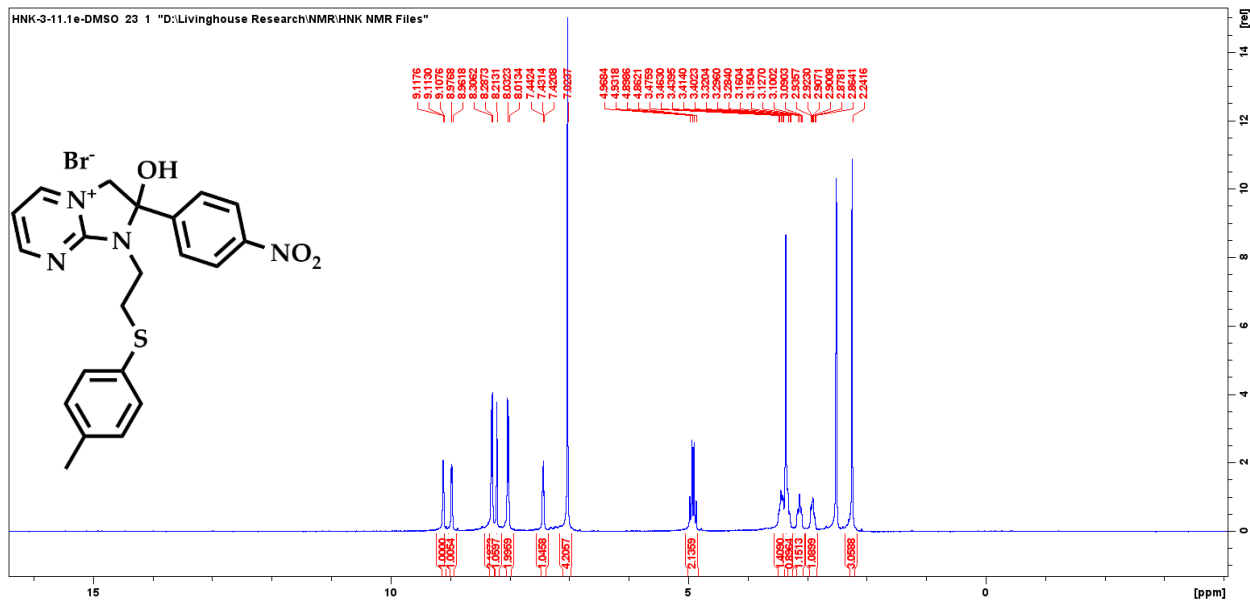


Figure 3.67B: ¹H-NMR Spectra of 2-(4-nitrophenyl)-2-hydroxy-1-(2-(*p*-tolylthio)ethyl)-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium bromide (**11.1e**).

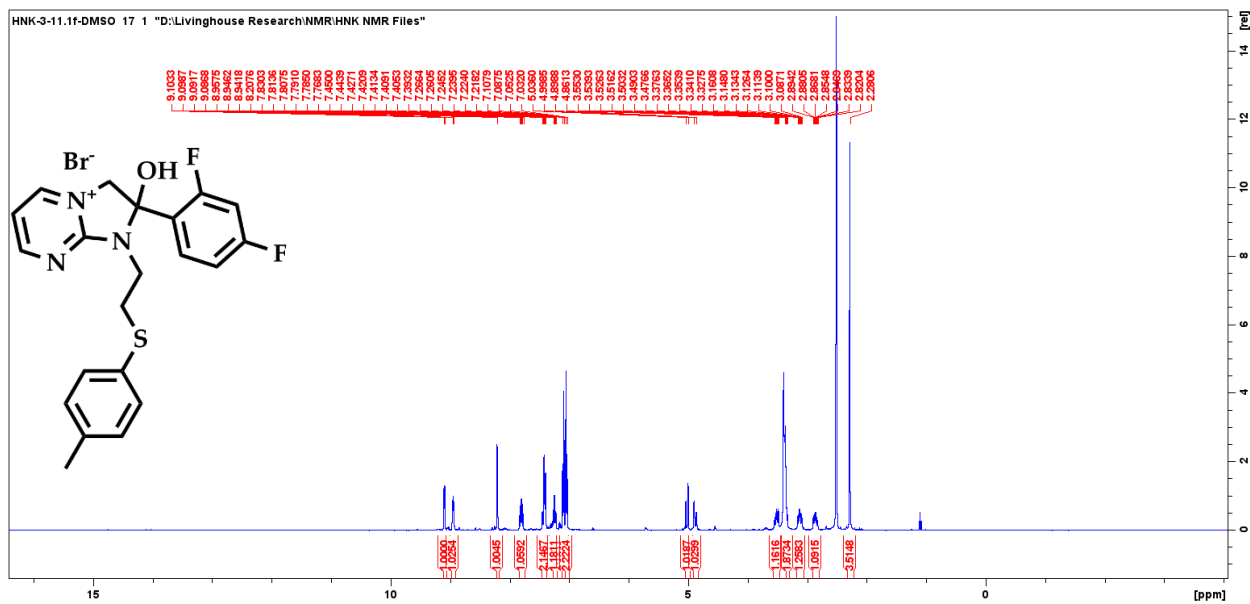


Figure 3.68B: ¹H-NMR Spectra of 2-(2,4-difluorophenyl)-2-hydroxy-1-(2-(*p*-tolylthio)ethyl)-2,3-dihydro-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium bromide (**11.1f**).

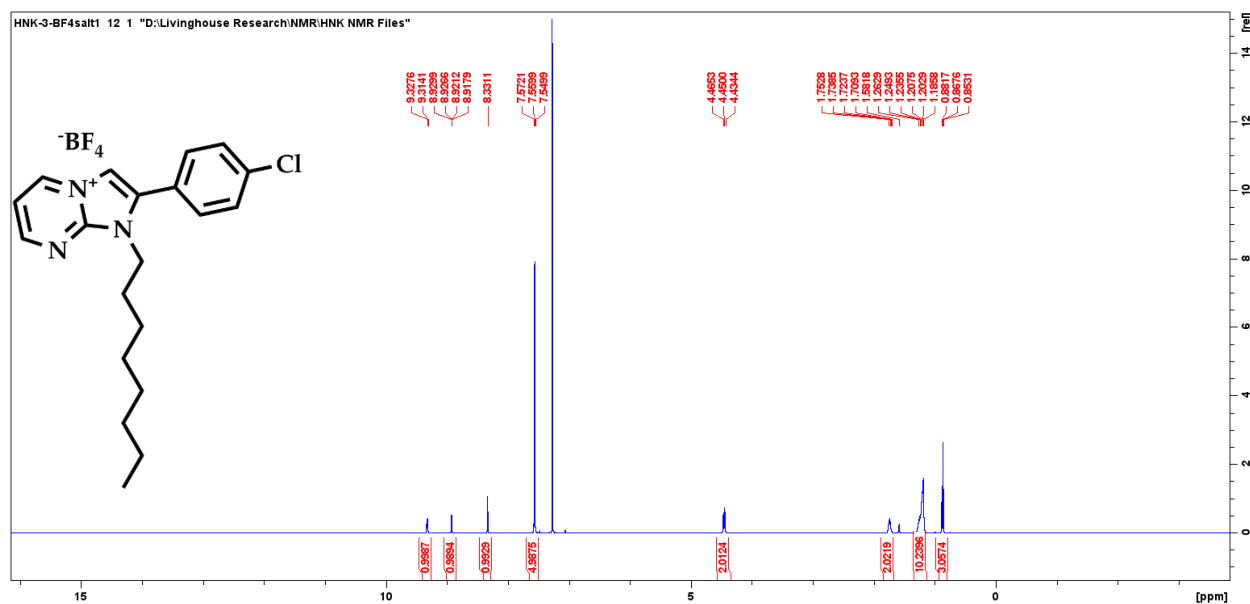


Figure 3.69B: ^1H -NMR Spectra of 2-(4-chlorophenyl)-1-octyl-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**1.2a**).

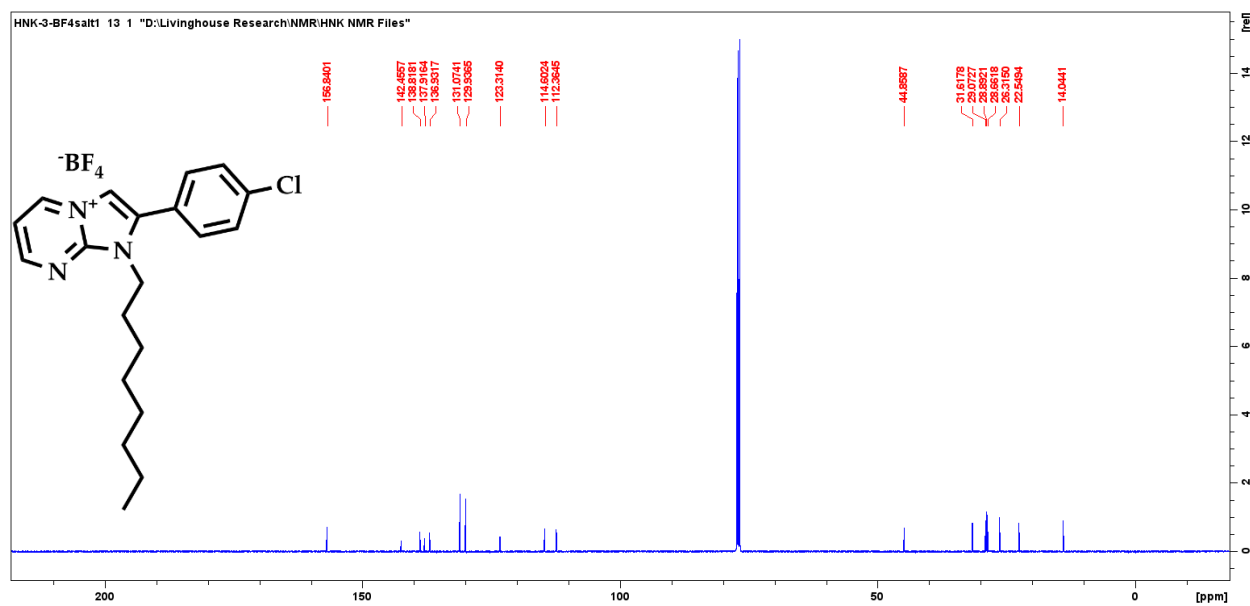


Figure 3.70B: ^{13}C -NMR Spectra of 2-(4-chlorophenyl)-1-octyl-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**1.2a**).

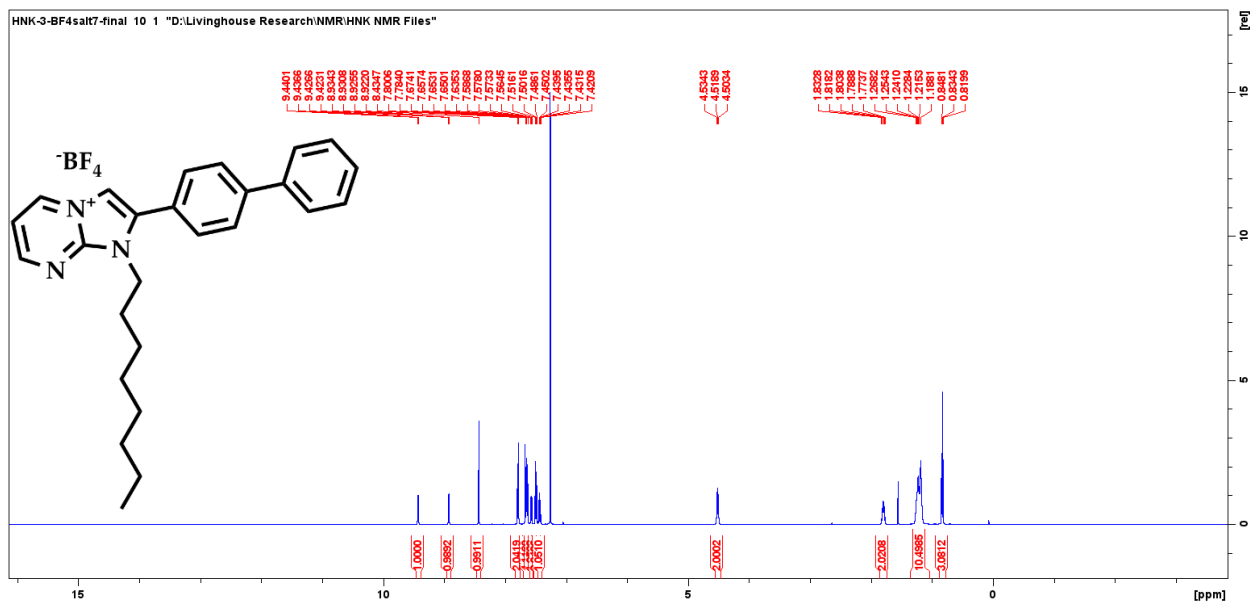


Figure 3.71B: ¹H-NMR Spectra of 2-([1,1'-biphenyl]-4-yl)-1-octyl-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**1.2b**).

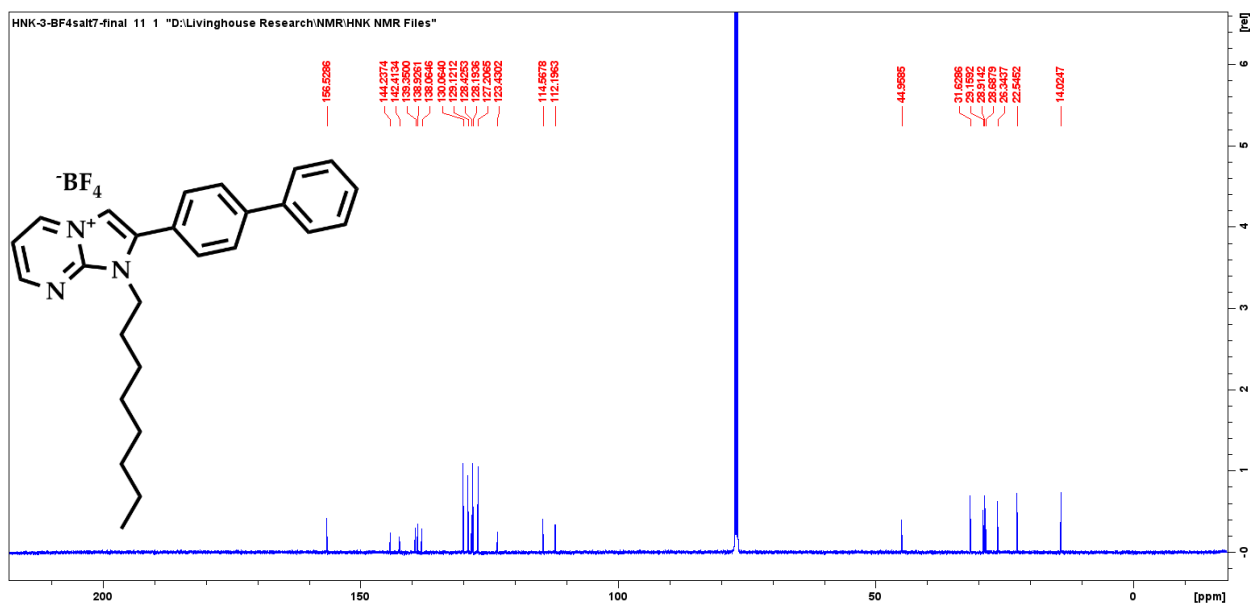


Figure 3.72B: ^{13}C -NMR Spectra of 2-([1,1'-biphenyl]-4-yl)-1-octyl-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**1.2b**).

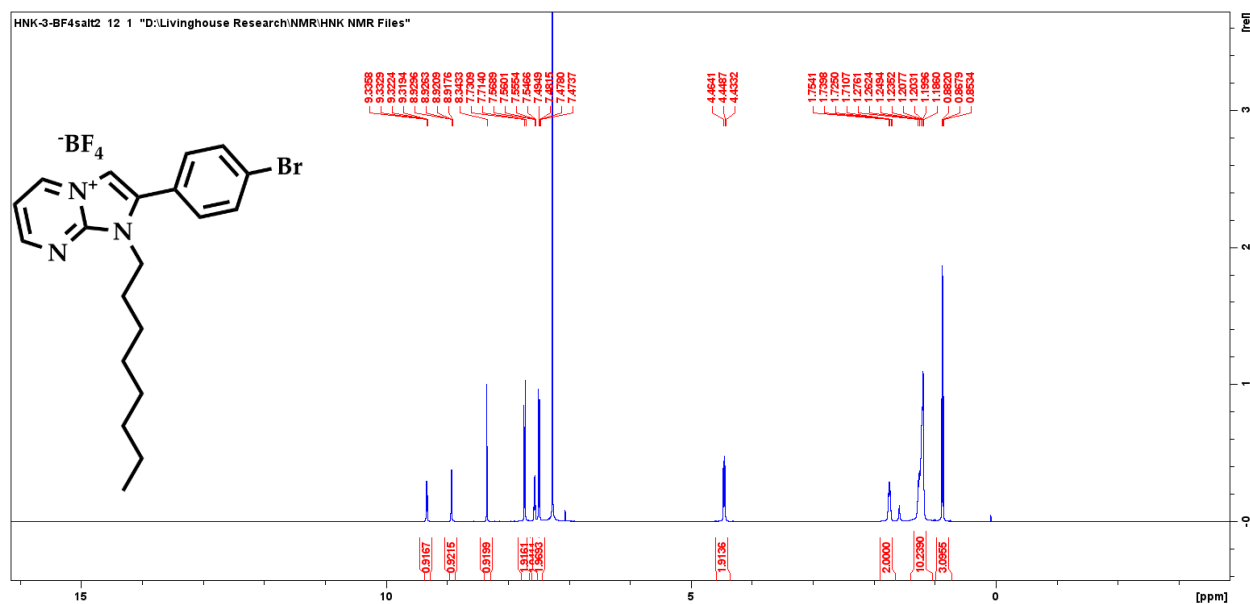


Figure 3.73B: ^1H -NMR Spectra of 2-(4-bromophenyl)-1-octyl-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**1.2c**).

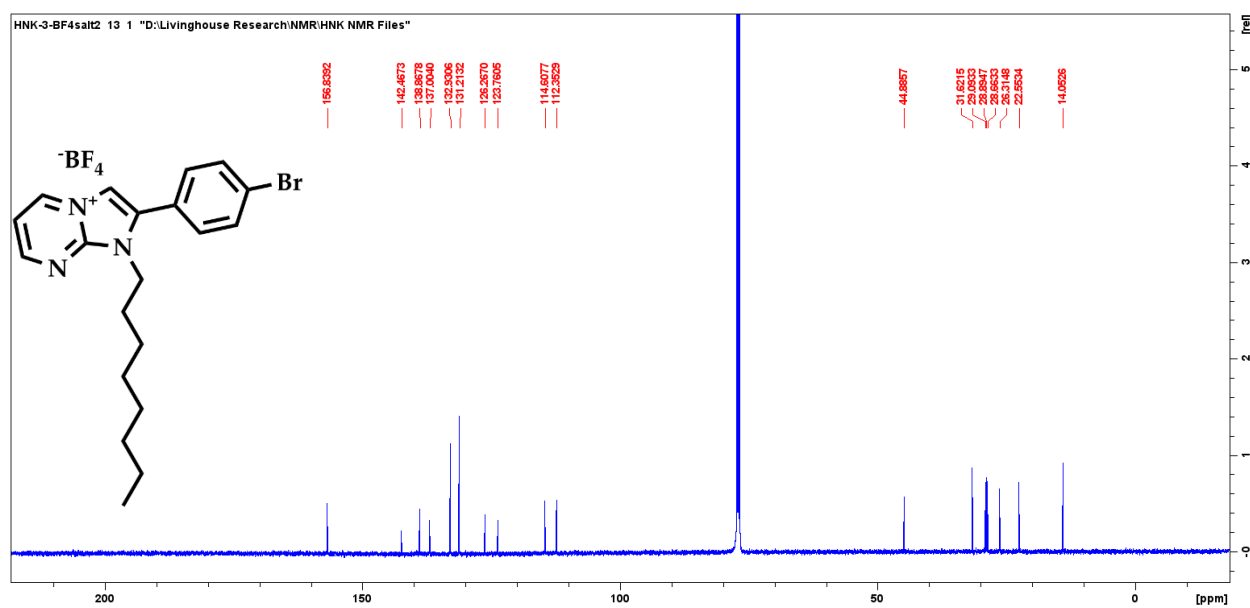


Figure 3.74B: ^{13}C -NMR Spectra of 2-(4-bromophenyl)-1-octyl-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**1.2c**).

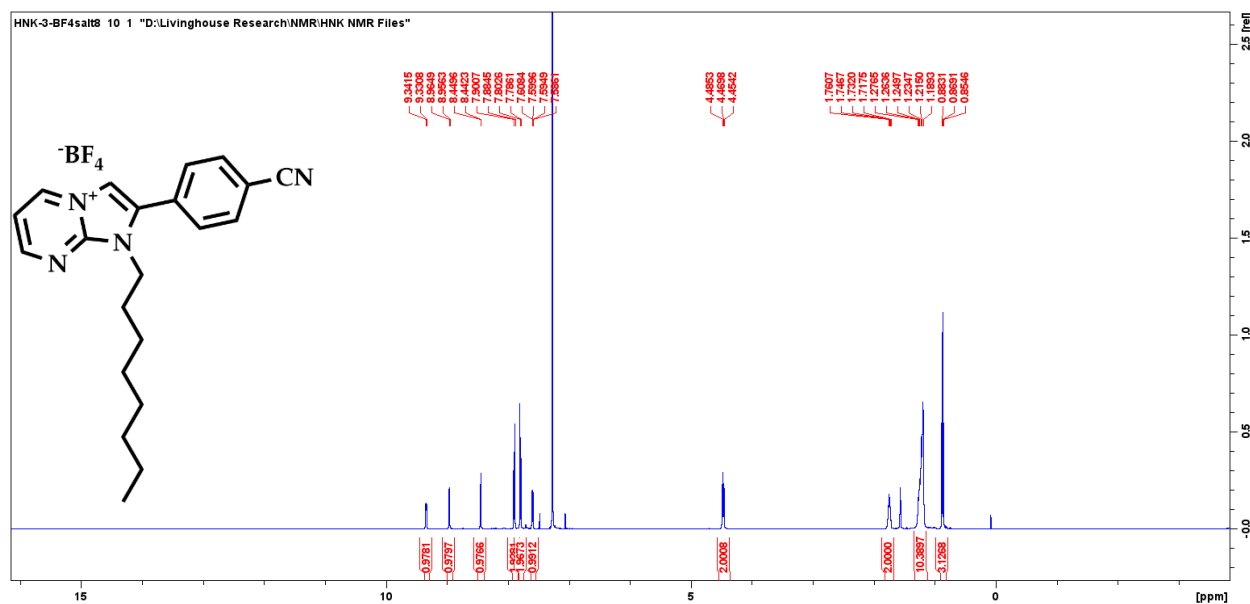


Figure 3.75B: ^1H -NMR Spectra of 2-(4-cyanophenyl)-1-octyl-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (**1.2d**).

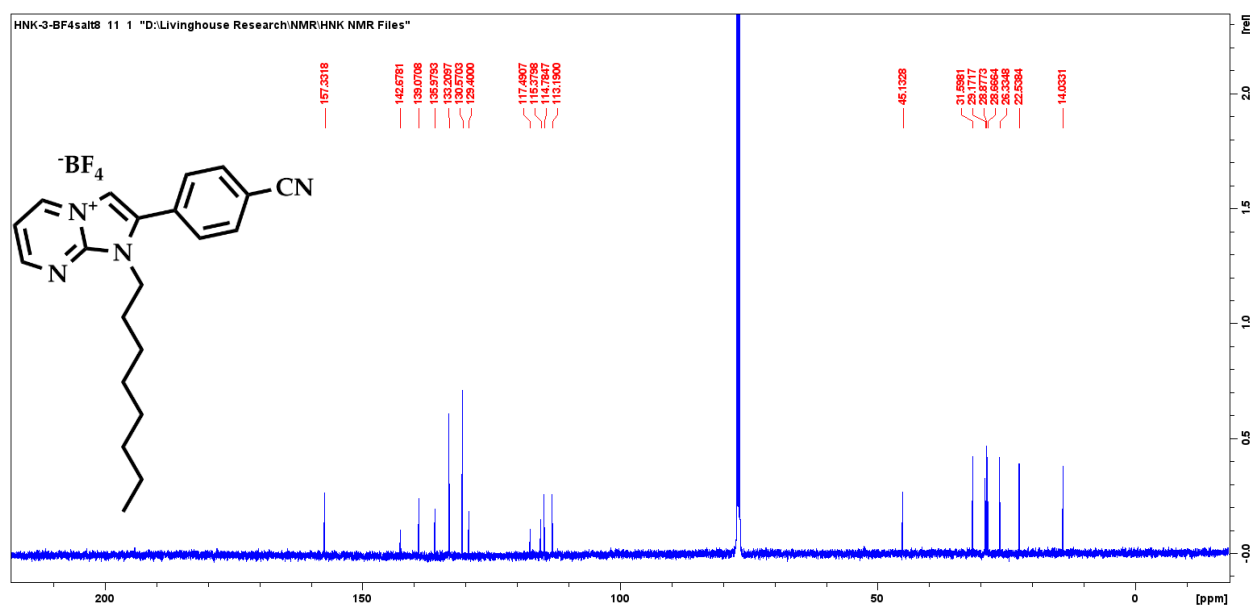


Figure 3.76B: ^{13}C -NMR Spectra of 2-(4-cyanophenyl)-1-octyl-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (**1.2d**).

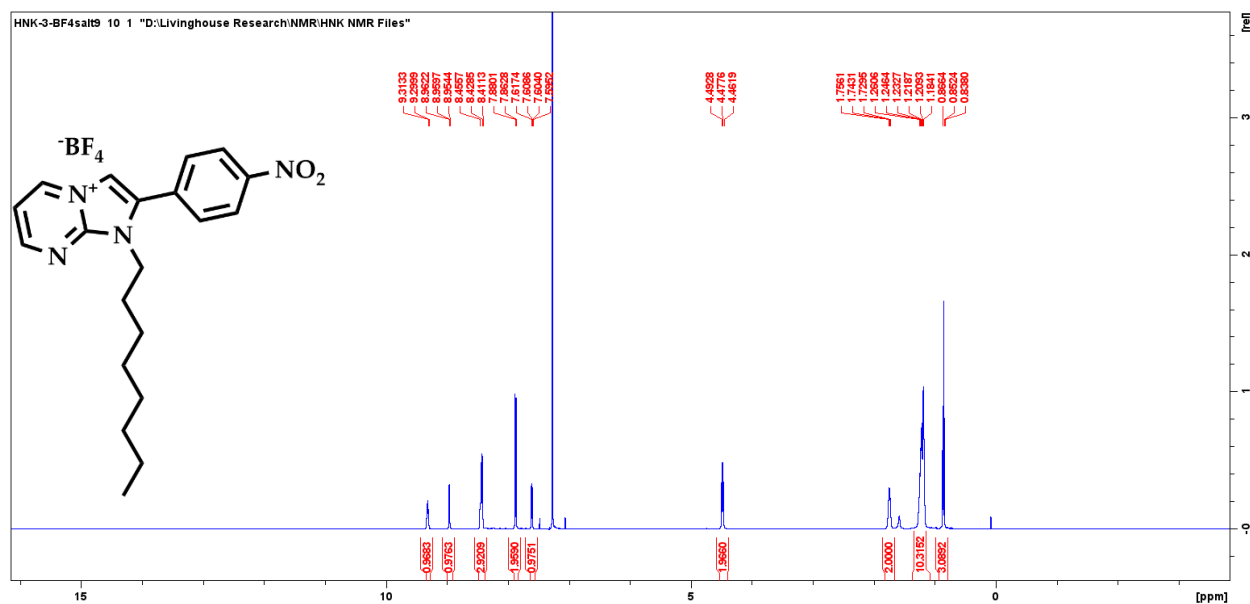


Figure 3.77B: ^1H -NMR Spectra of 2-(4-nitrophenyl)-1-octyl-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**1.2e**).

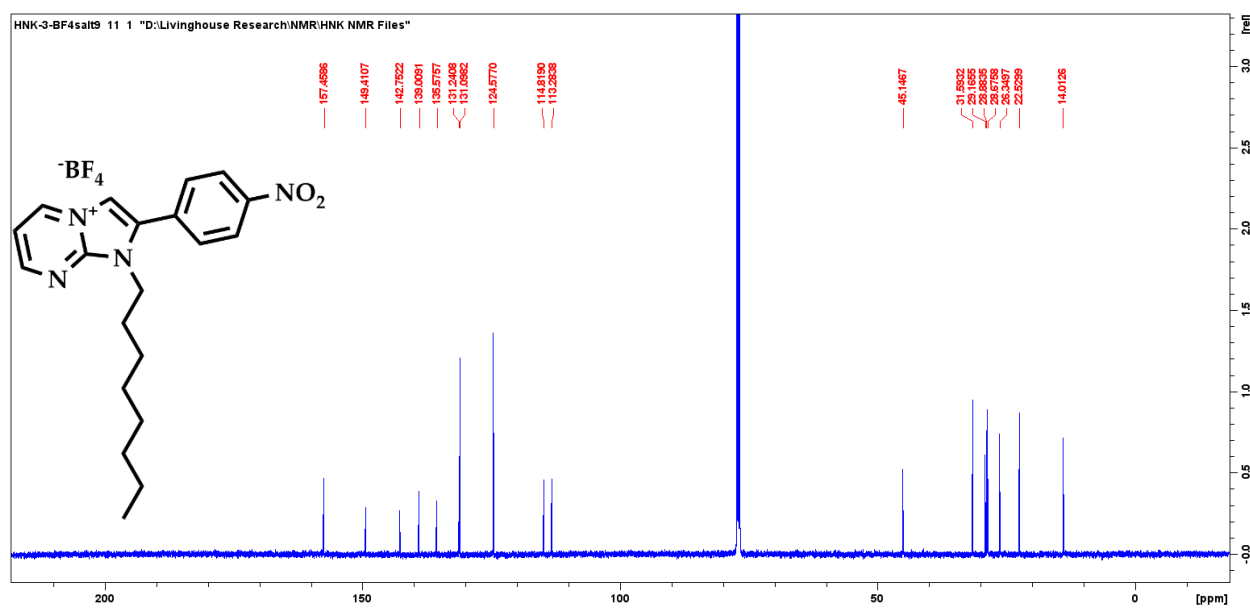


Figure 3.78B: ^{13}C -NMR Spectra of 2-(4-nitrophenyl)-1-octyl-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**1.2e**).

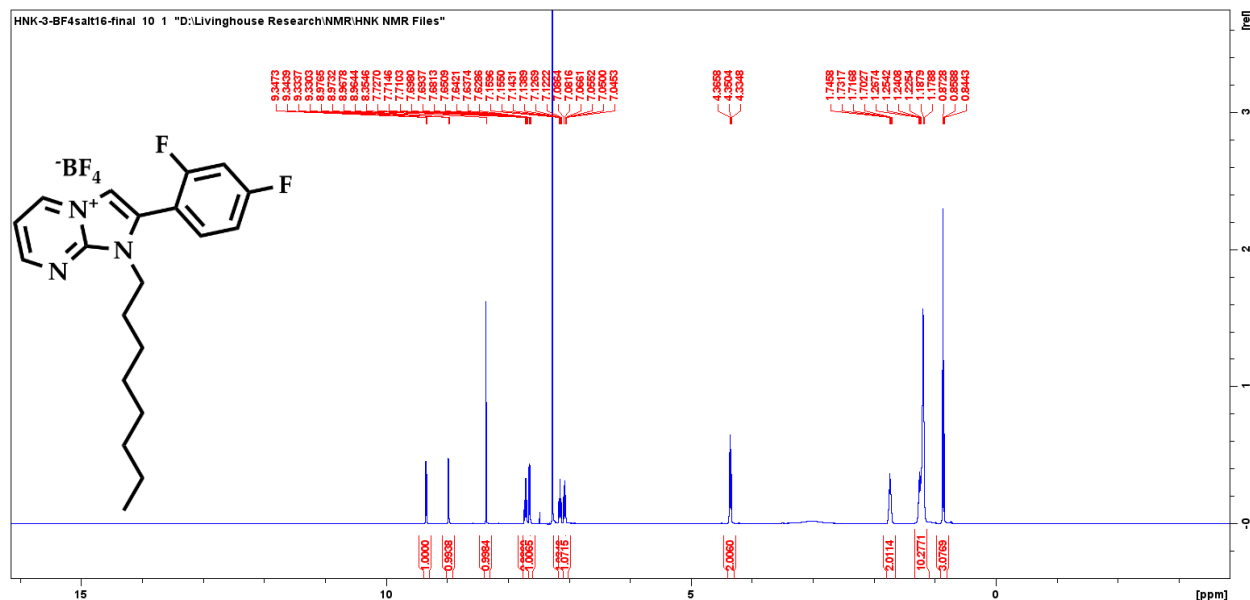


Figure 3.79B: ^1H -NMR Spectra 2-(2,4-difluorophenyl)-1-octyl-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**1.2f**).

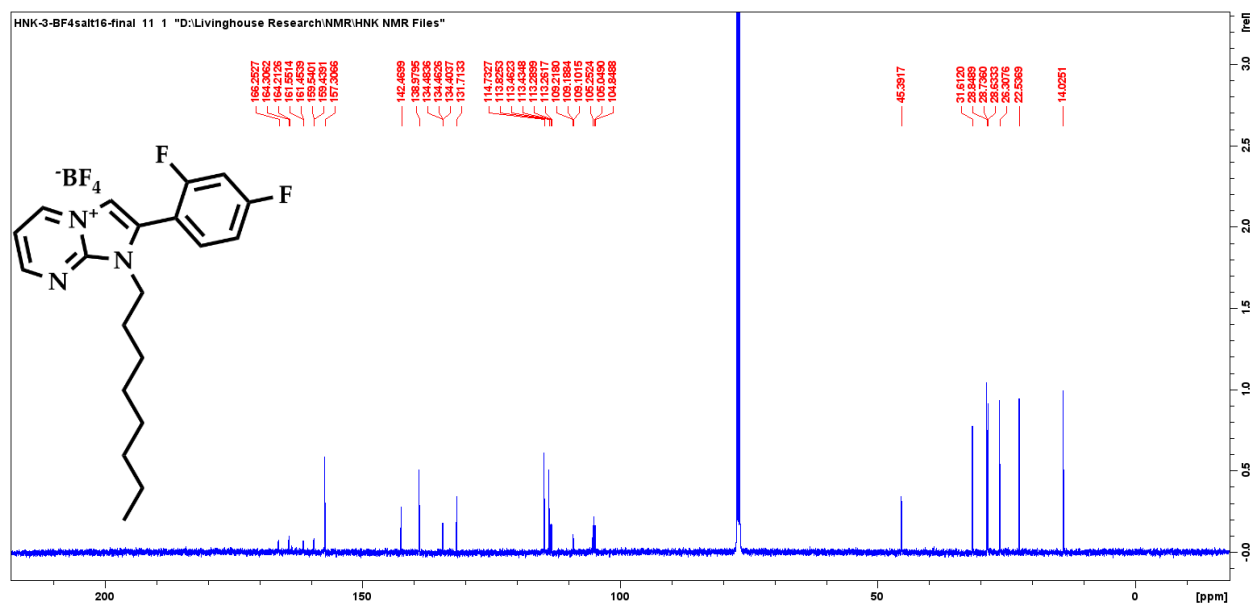


Figure 3.80B: ^{13}C -NMR Spectra of 2-(2,4-difluorophenyl)-1-octyl-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**1.2f**).

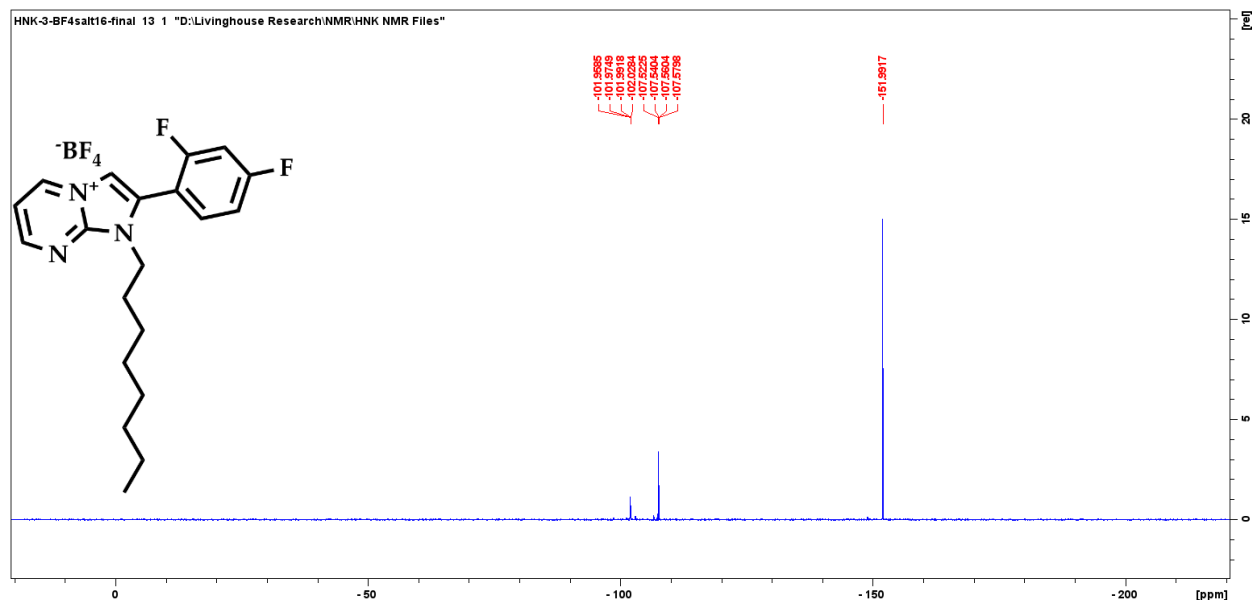


Figure 3.81B: ^{19}F -NMR Spectra of 2-(2,4-difluorophenyl)-1-octyl-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**1.2f**).

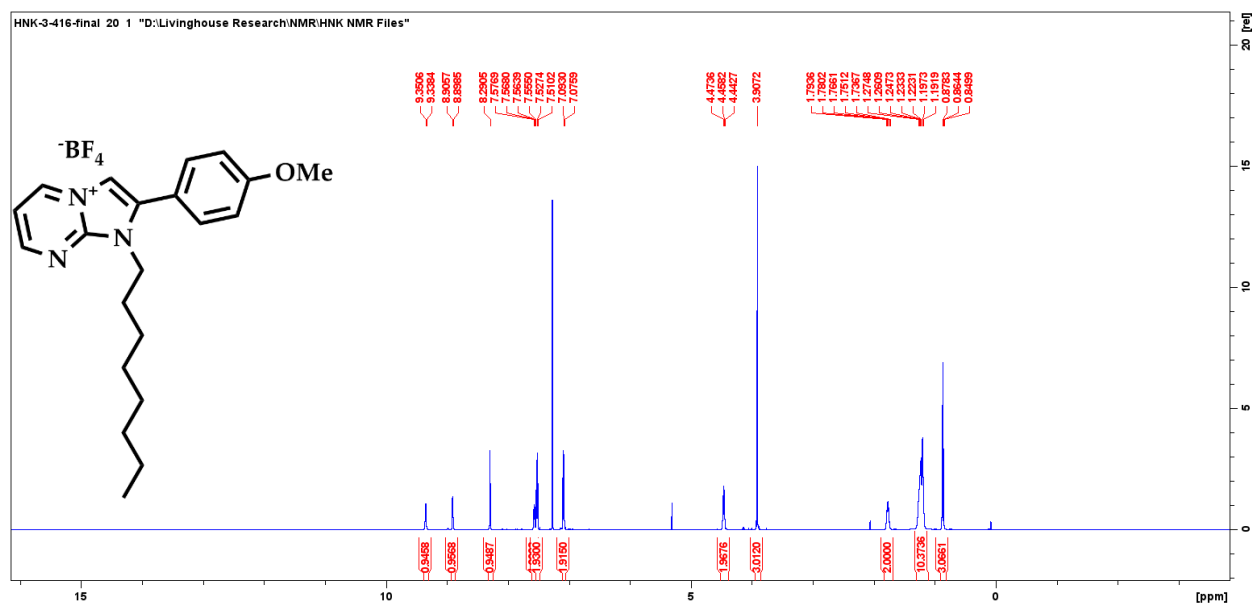


Figure 3.82B: ^1H -NMR Spectra of 2-(4-methoxyphenyl)-1-octyl-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**1.2g**).

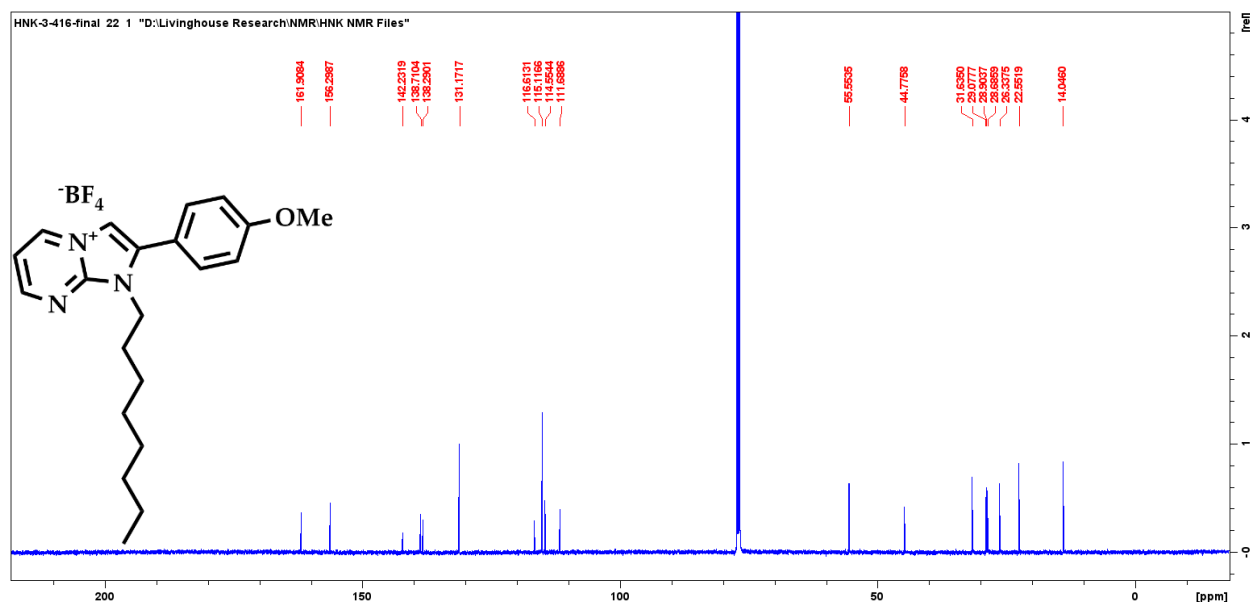


Figure 3.83B: ¹³C-NMR Spectra of 2-(4-methoxyphenyl)-1-octyl-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**1.2g**).

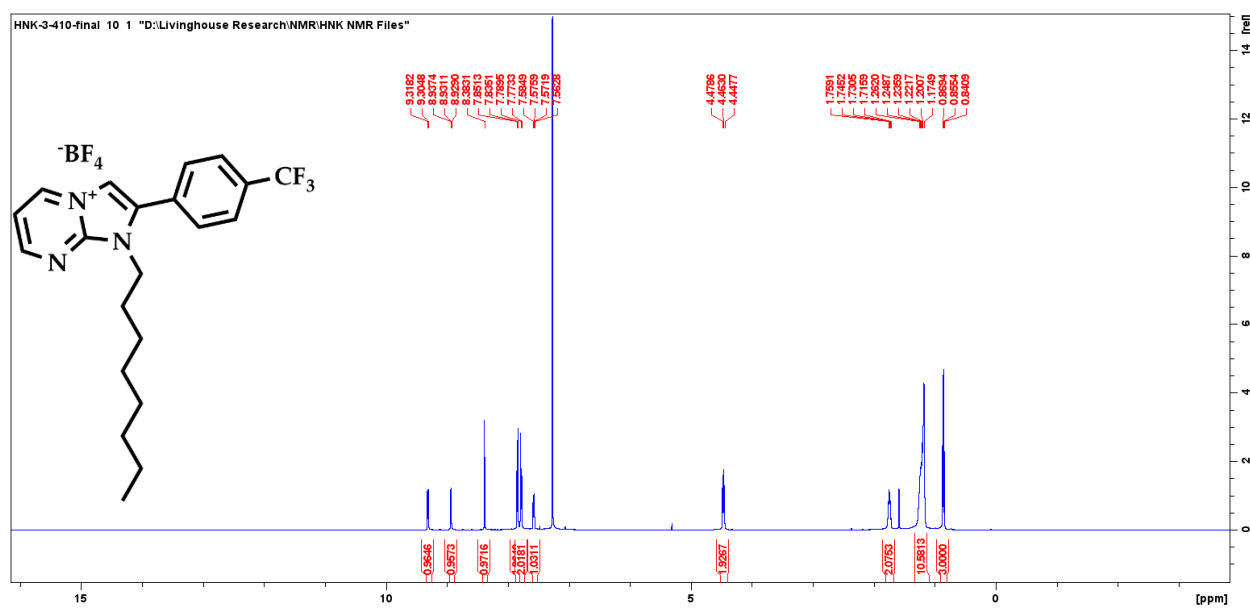


Figure 3.84B: ¹H-NMR Spectra of 2-(4-trifluoromethylphenyl)-1-octyl-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**1.2h**).

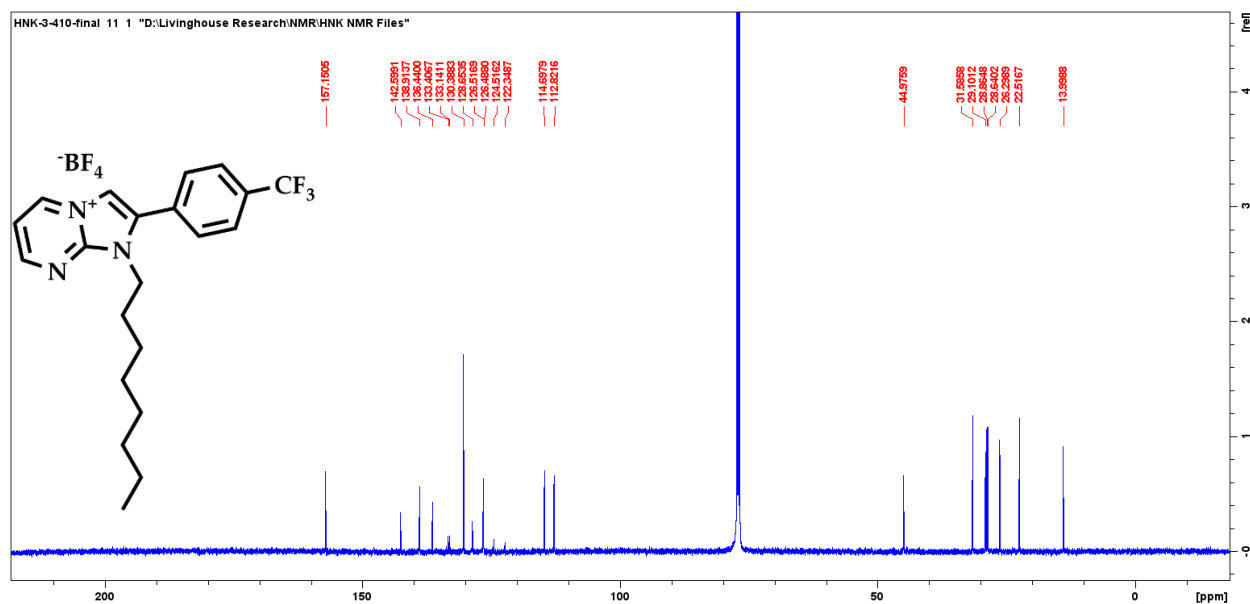


Figure 3.85B: ^{13}C -NMR Spectra of 2-(4-trifluoromethylphenyl)-1-octyl-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**1.2h**).

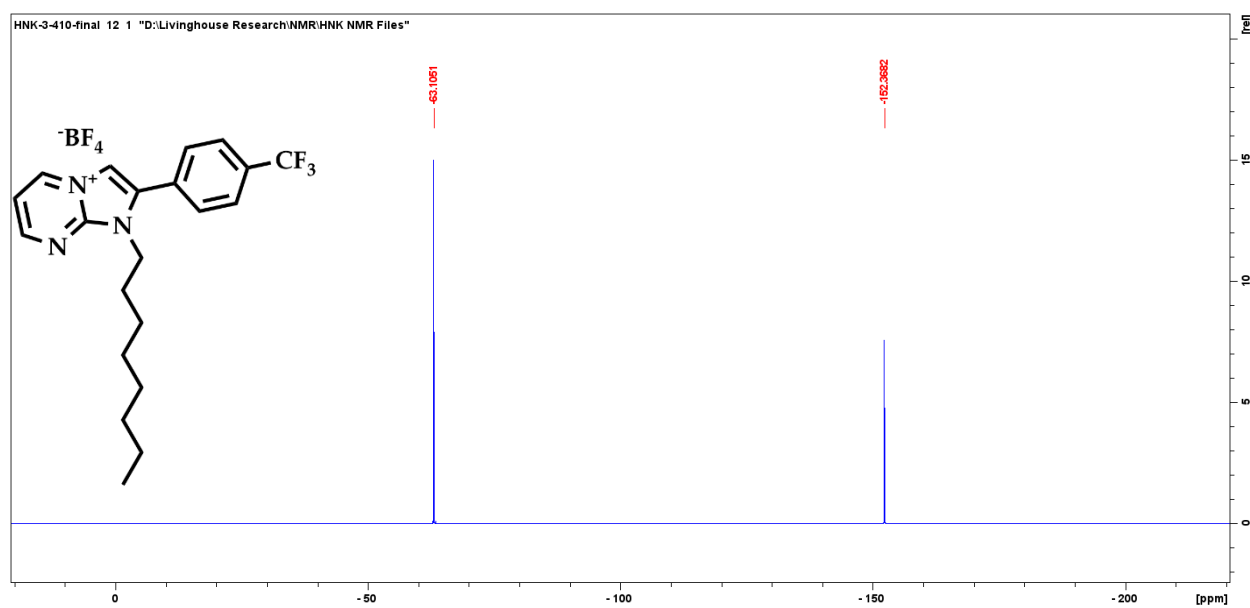


Figure 3.86B: ^{19}F -NMR Spectra of 2-(4-trifluoromethylphenyl)-1-octyl-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**1.2h**).

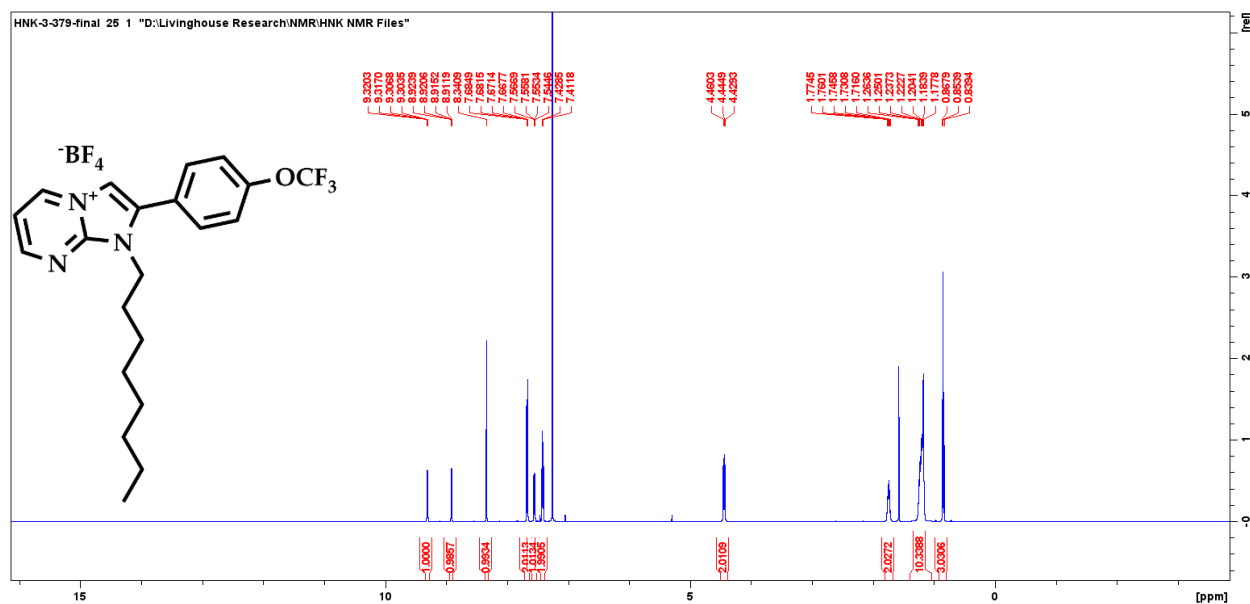


Figure 3.87B: ^1H -NMR Spectra of 2-(4-trifluoromethoxyphenyl)-1-octyl-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**1.2i**).

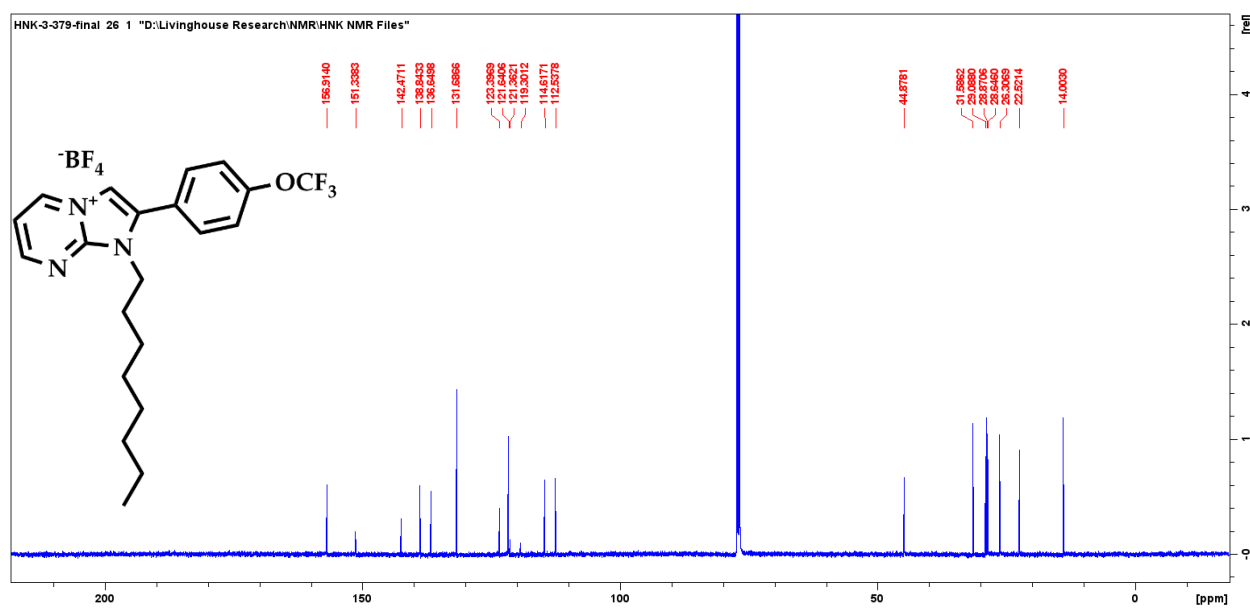


Figure 3.88B: ^{13}C -NMR Spectra of 2-(4-trifluoromethoxyphenyl)-1-octyl-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**1.2i**).

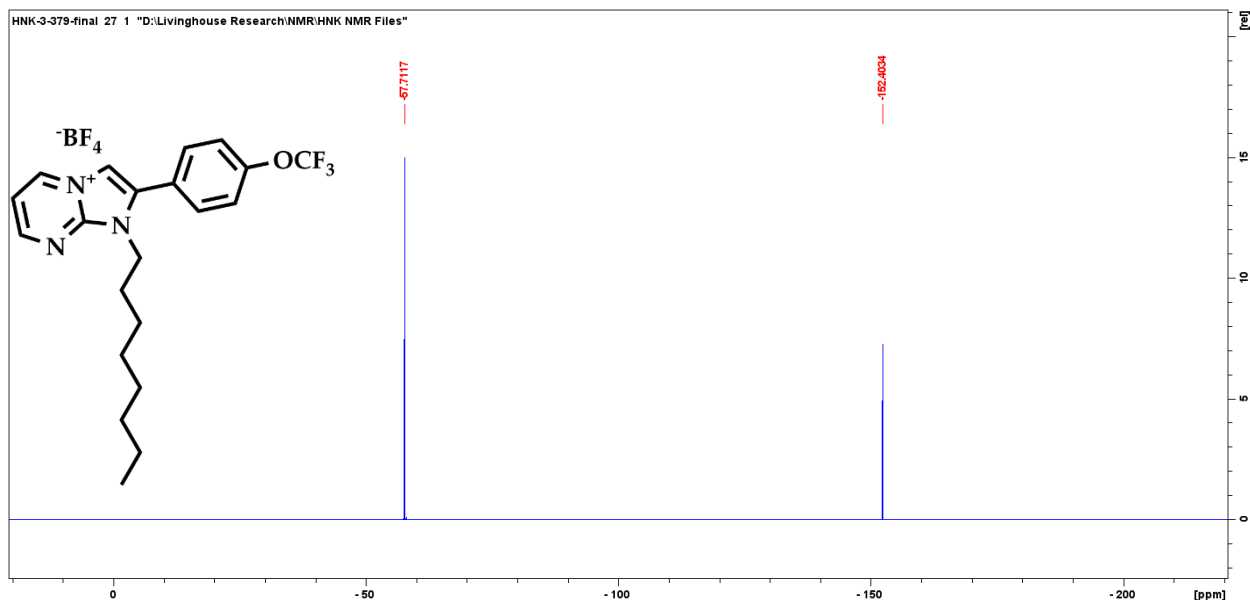


Figure 3.89B: ^{19}F -NMR Spectra of 2-(4-trifluoromethoxyphenyl)-1-octyl-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**1.2i**).

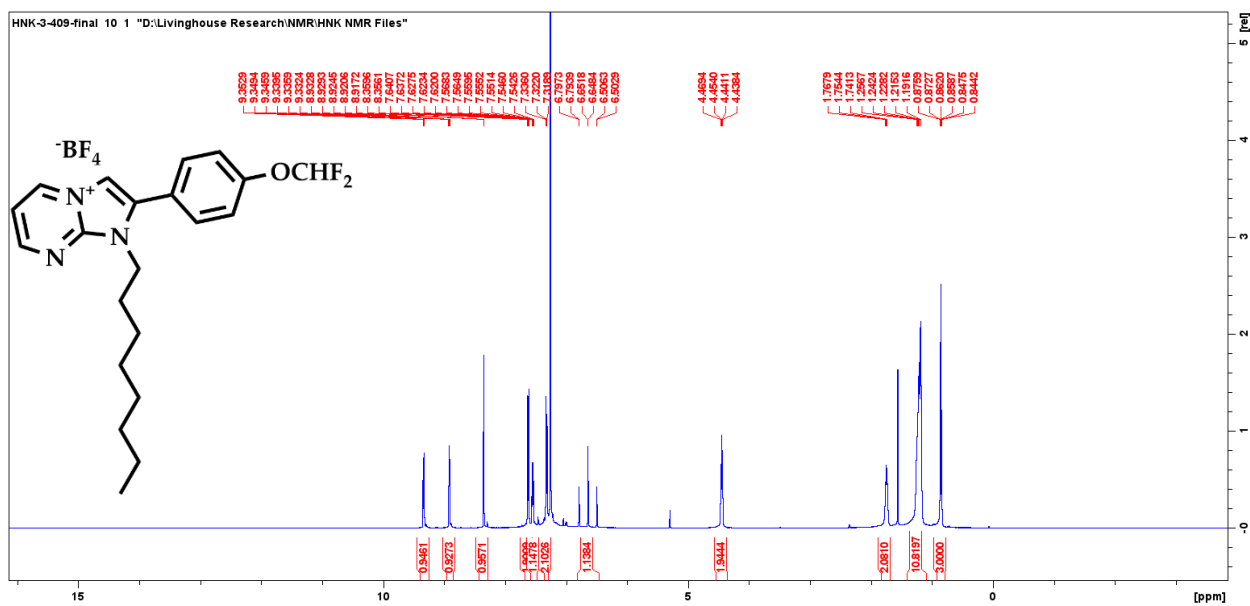


Figure 3.90B: ^1H -NMR Spectra of 2-(4-difluoromethoxyphenyl)-1-octyl-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**1.2j**).

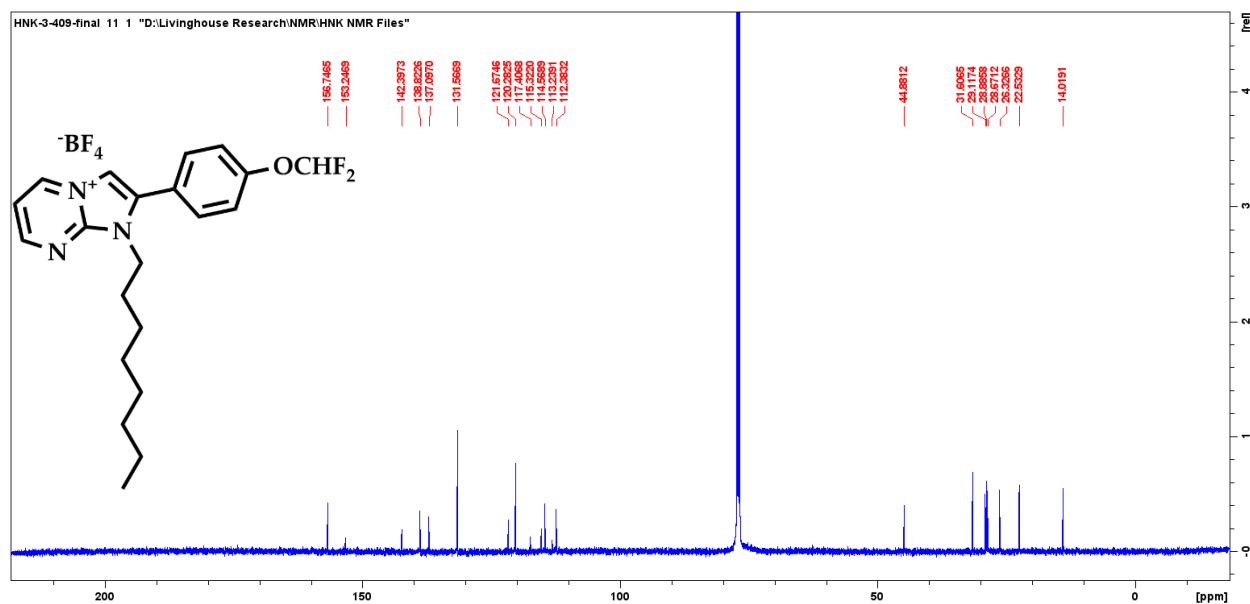


Figure 3.91B: ^{13}C -NMR Spectra of 2-(4-difluoromethoxyphenyl)-1-octyl-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**1.2j**).

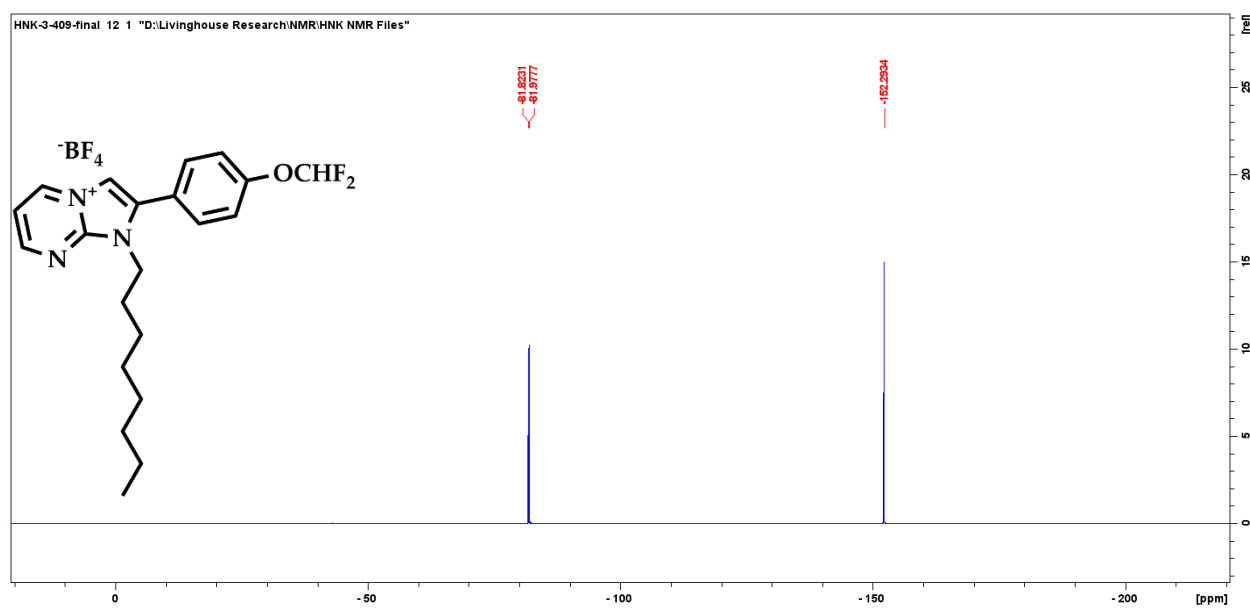


Figure 3.92B: ^{19}F -NMR Spectra of 2-(4-difluoromethoxyphenyl)-1-octyl-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**1.2j**).

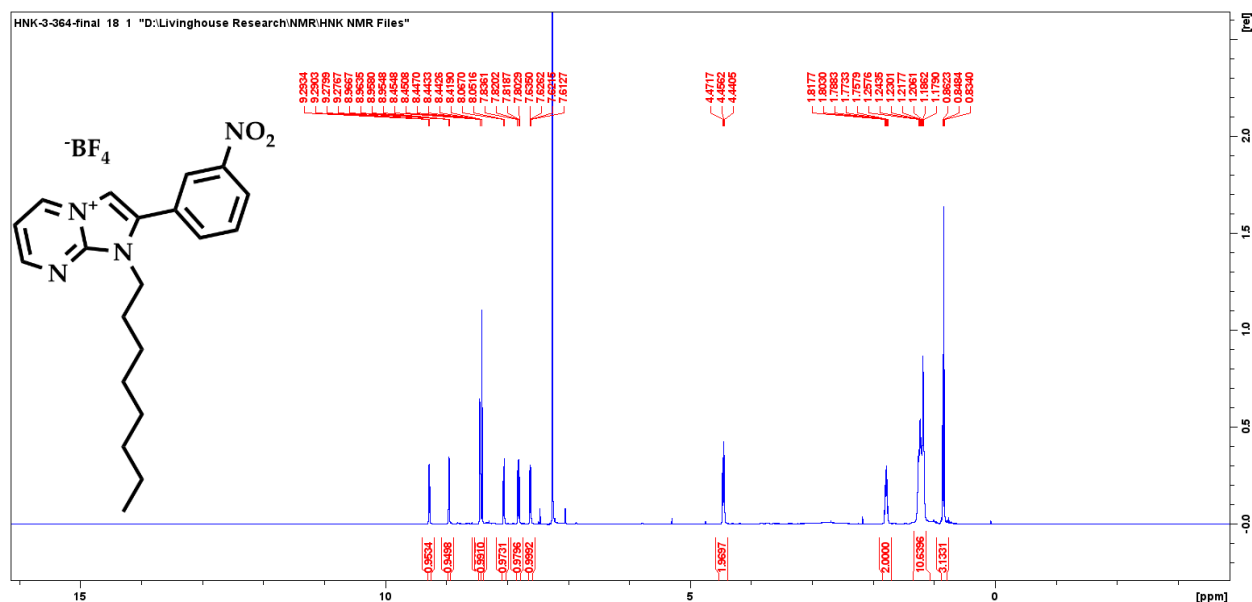


Figure 3.93B: ^1H -NMR Spectra of 2-(3-nitrophenyl)-1-octyl-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**1.2k**).

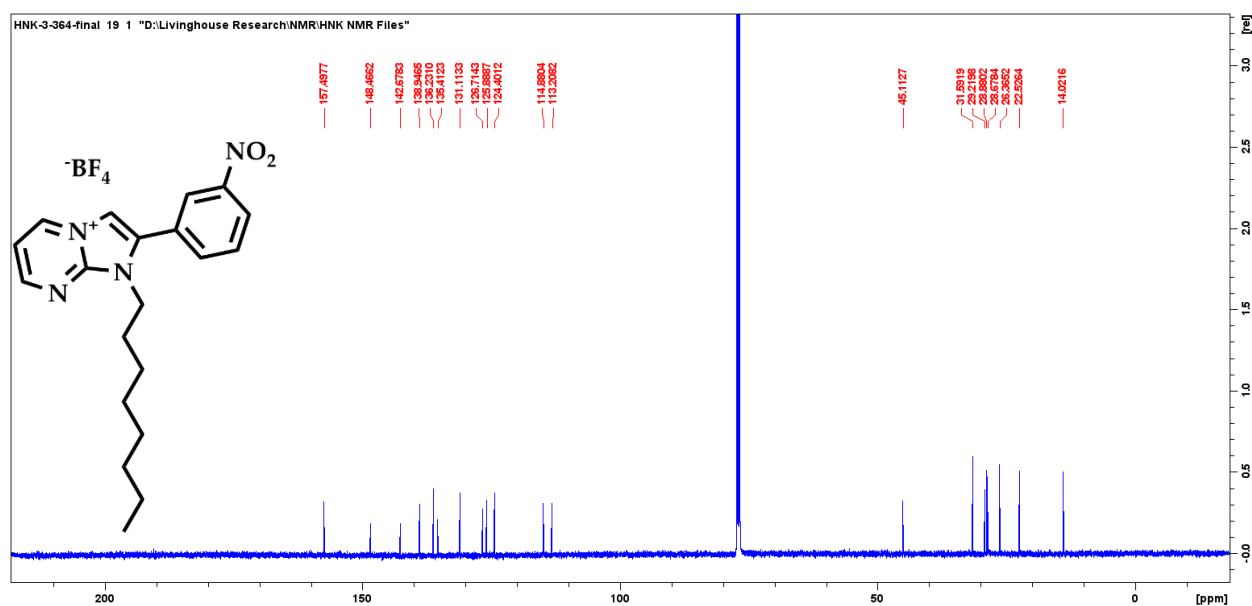


Figure 3.94B: ^{13}C -NMR Spectra of 2-(3-nitrophenyl)-1-octyl-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**1.2k**).

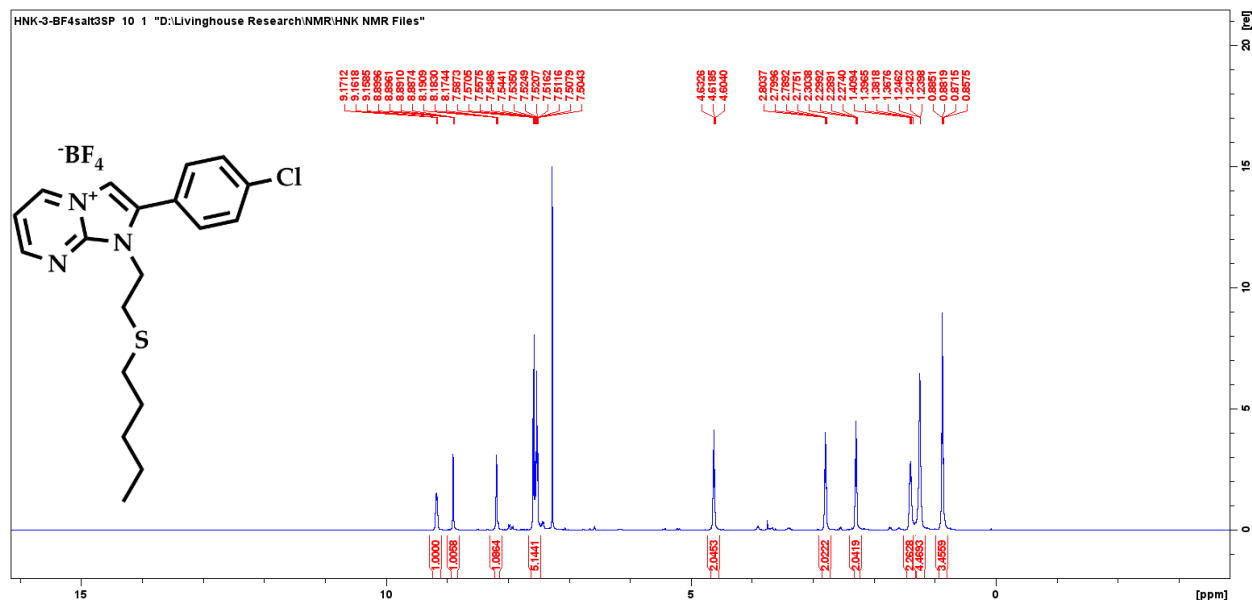


Figure 3.95B: ^1H -NMR Spectra of 2-(4-chlorophenyl)-1-(2-(pentylthio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**2.2a**).

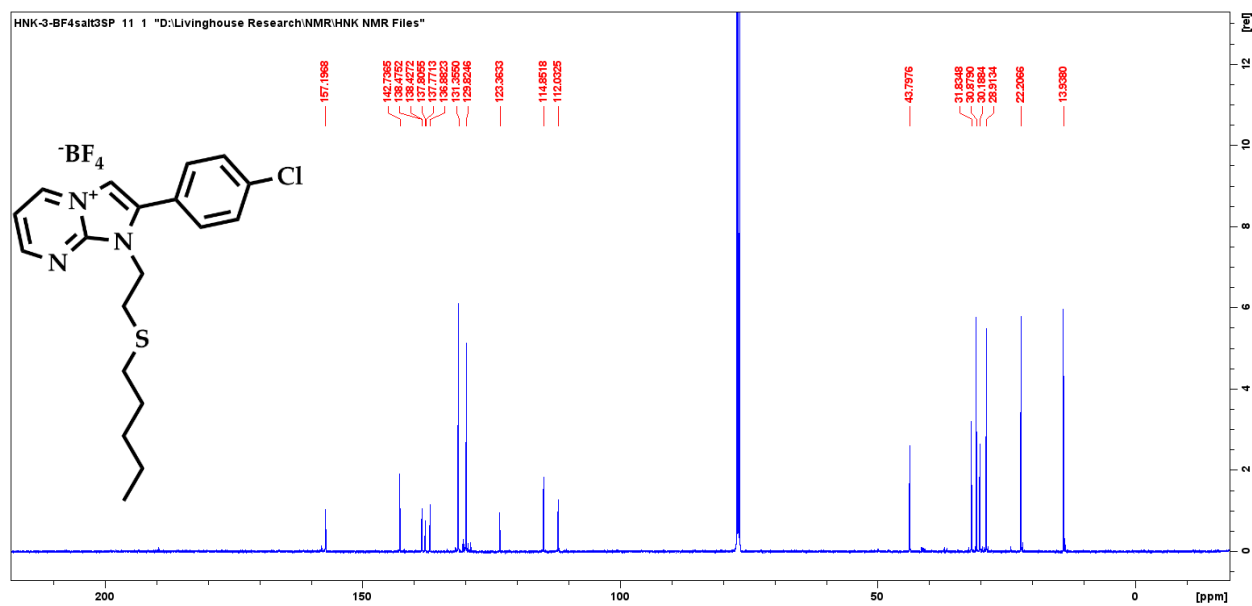


Figure 3.96B: ^{13}C -NMR Spectra of 2-(4-chlorophenyl)-1-(2-(pentylthio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**2.2a**).

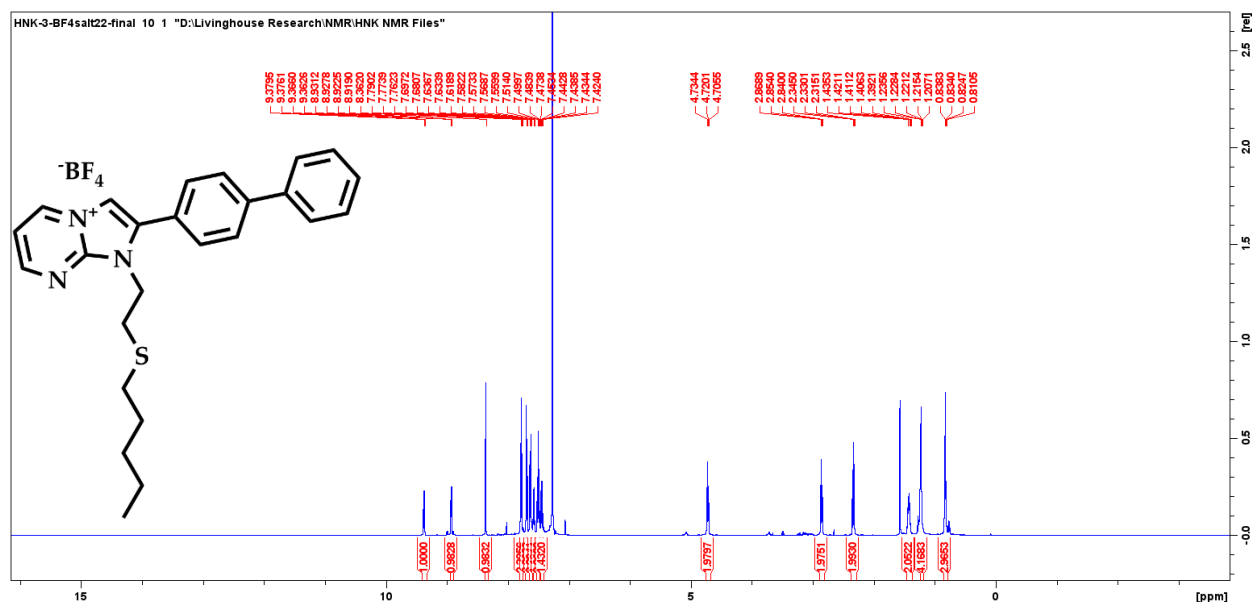


Figure 3.97B: ¹H-NMR Spectra of 2-([1,1'-biphenyl]-4-yl)-1-(2-(pentylthio)ethyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (**2.2b**).

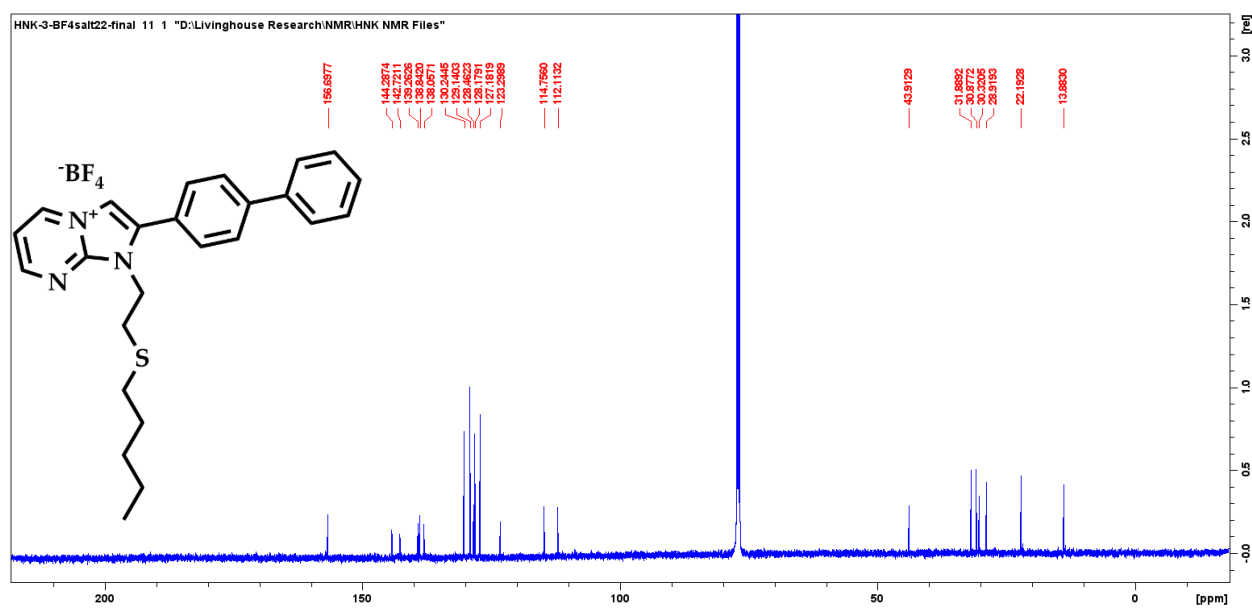


Figure 3.98B: ¹³C-NMR Spectra of 2-([1,1'-biphenyl]-4-yl)-1-(2-(pentylthio)ethyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (**2.2b**).

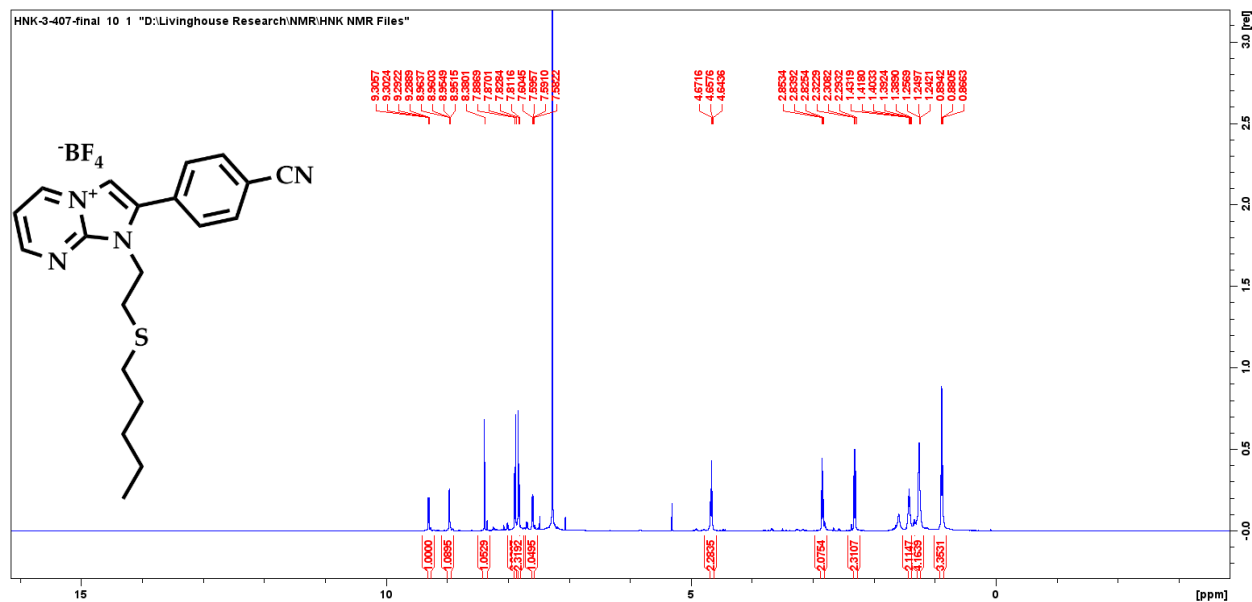


Figure 3.101B: ^1H -NMR Spectra of 2-(4-cyanophenyl)-1-(2-(pentylthio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**2.2d**).

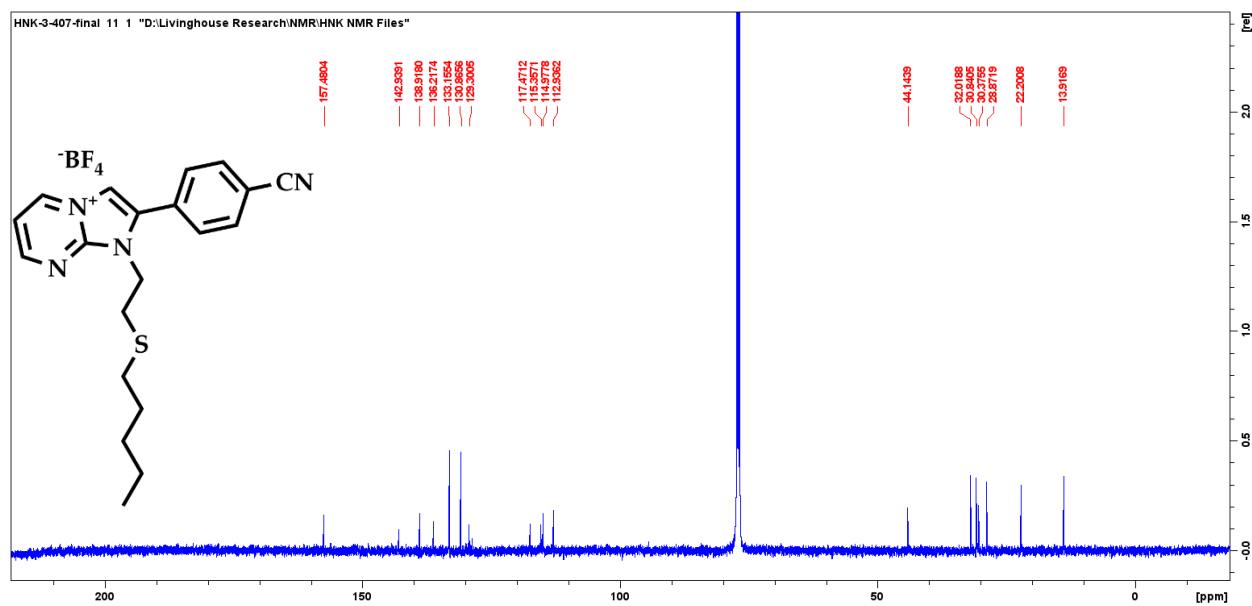


Figure 3.102B: ^{13}C -NMR Spectra of 2-(4-cyanophenyl)-1-(2-(pentylthio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**2.2d**).

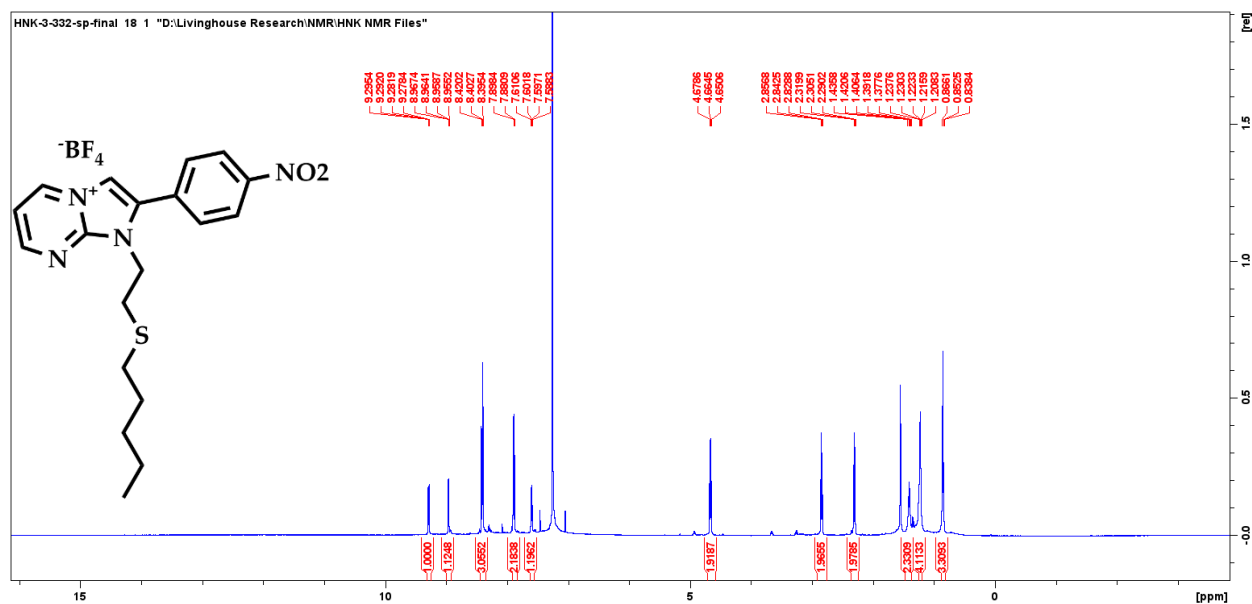


Figure 3.103B: ^1H -NMR Spectra of 2-(4-nitrophenyl)-1-(2-(pentylthio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**2.2e**).

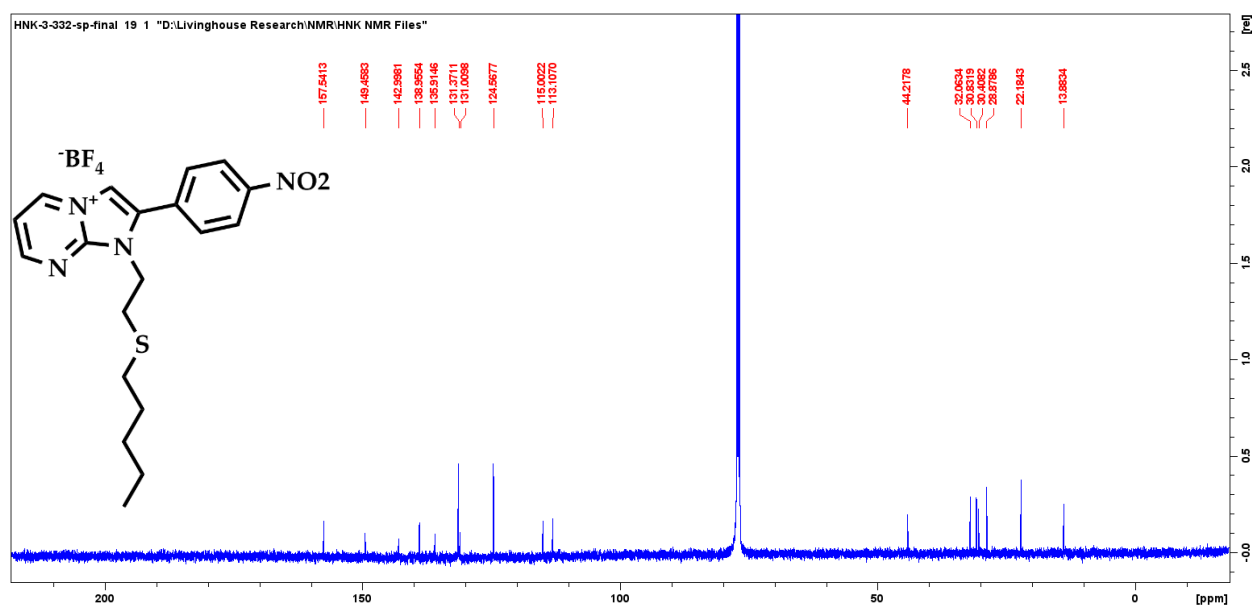


Figure 3.104B: ^{13}C -NMR Spectra of 2-(4-nitrophenyl)-1-(2-(pentylthio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**2.2e**).

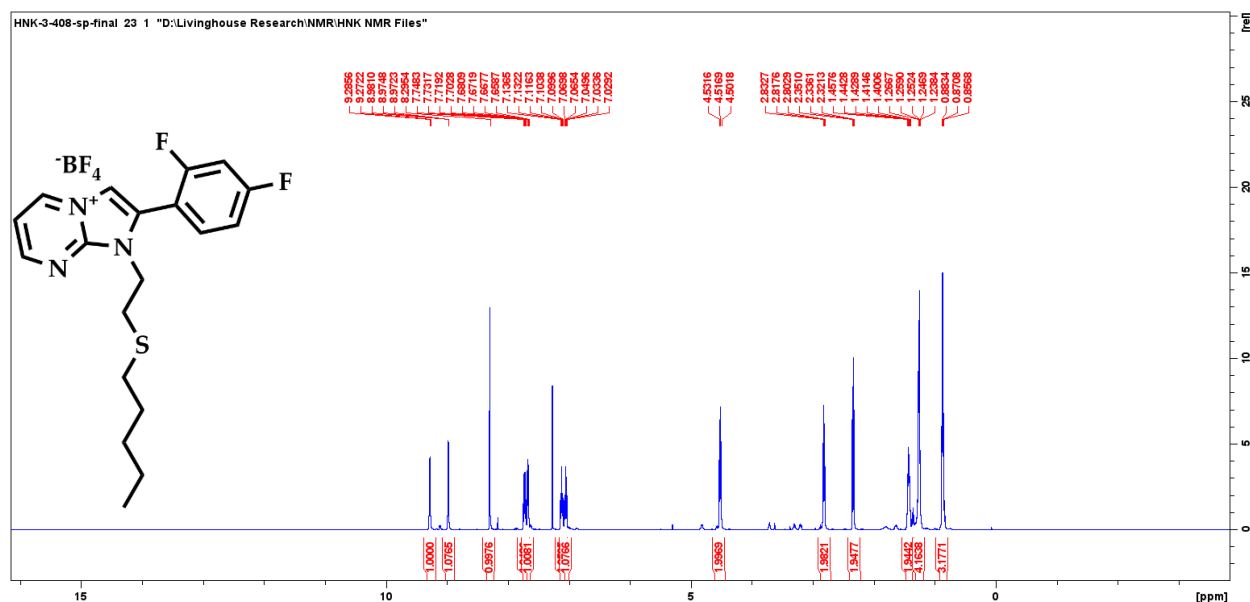


Figure 3.105B: ^1H -NMR Spectra of 2-(2,4-difluorophenyl)-1-(2-(pentylthio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**2.2f**).

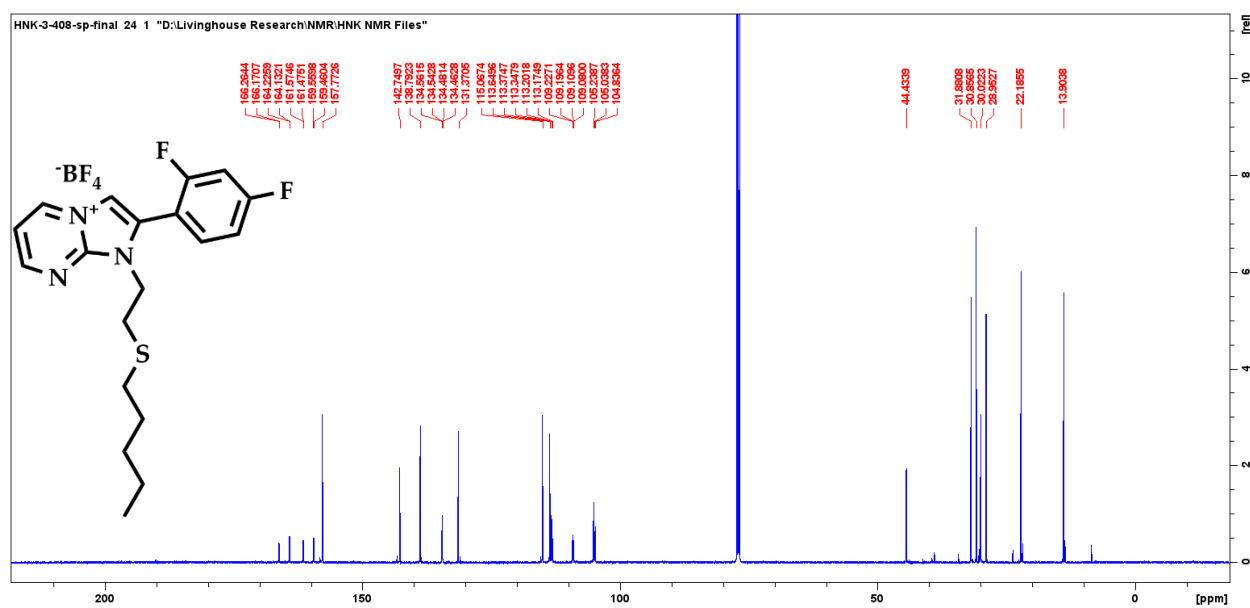


Figure 3.106B: ^{13}C -NMR Spectra of 2-(2,4-difluorophenyl)-1-(2-(pentylthio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**2.2f**).

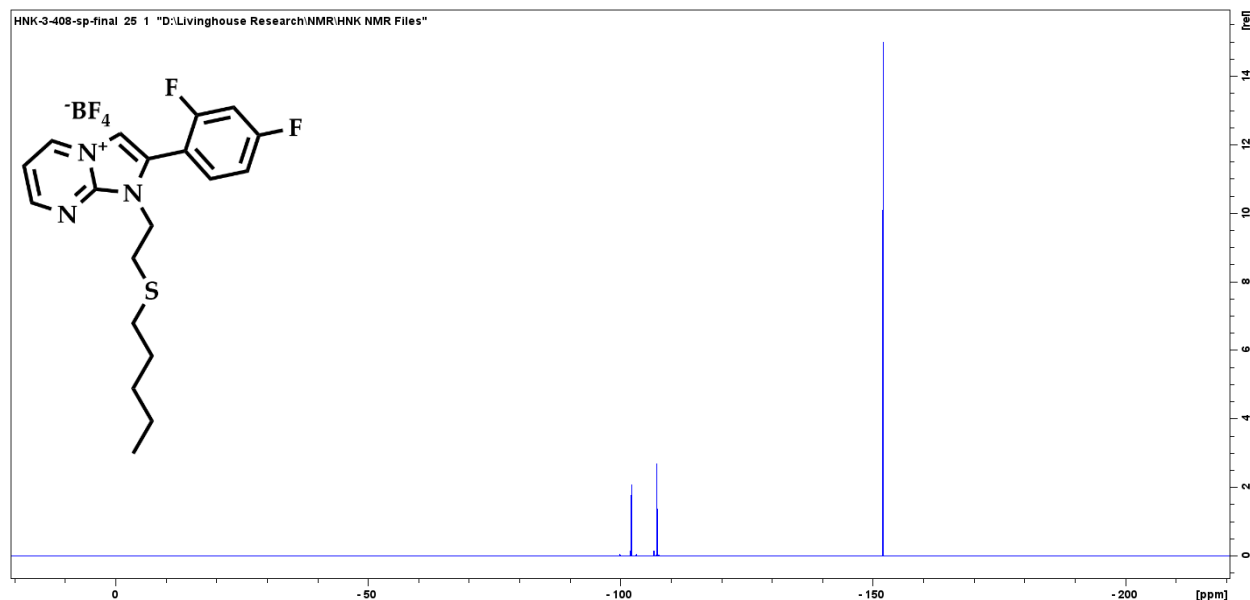


Figure 3.107B: ^{19}F -NMR Spectra of 2-(2,4-difluorophenyl)-1-(2-(pentylthio)ethyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (**2.2f**).

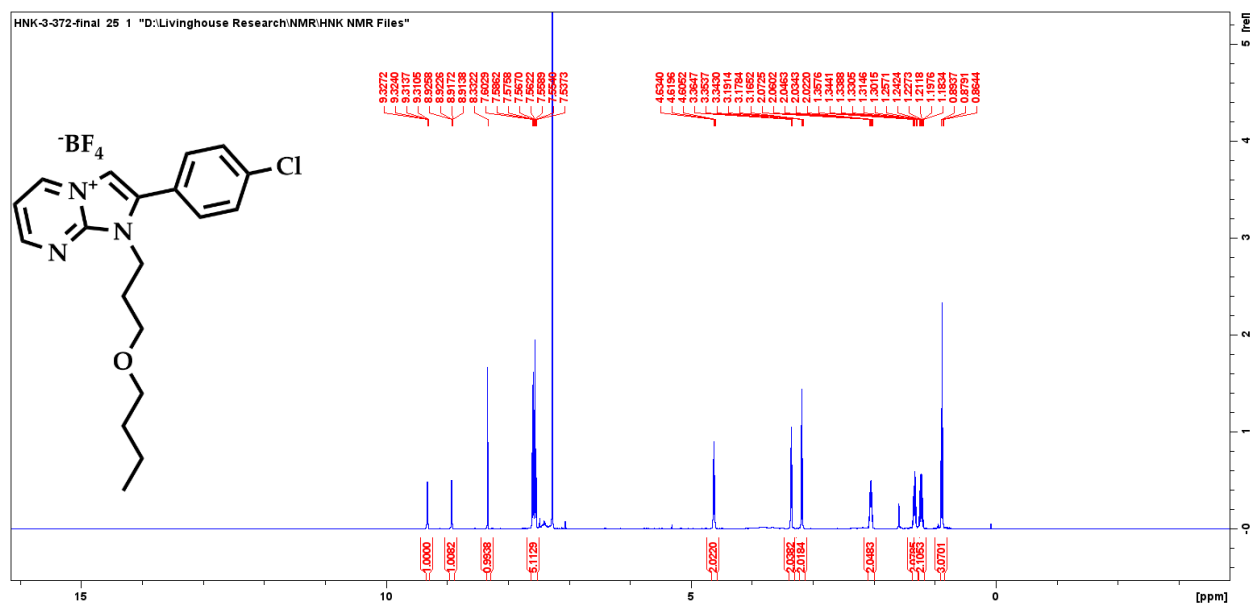


Figure 3.108B: ^1H -NMR Spectra of 2-(4-chlorophenyl)-1-(3-butoxypropyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (**3.2a**).

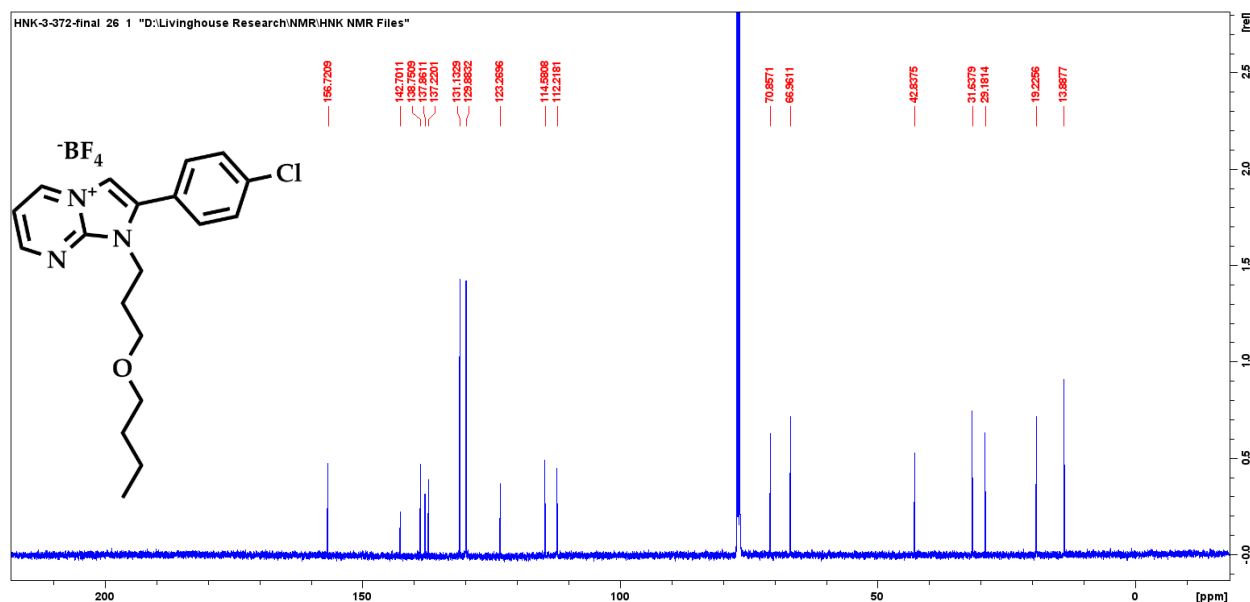


Figure 3.109B: ¹³C-NMR Spectra of 2-(4-chlorophenyl)-1-(3-butoxypropyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (3.2a).

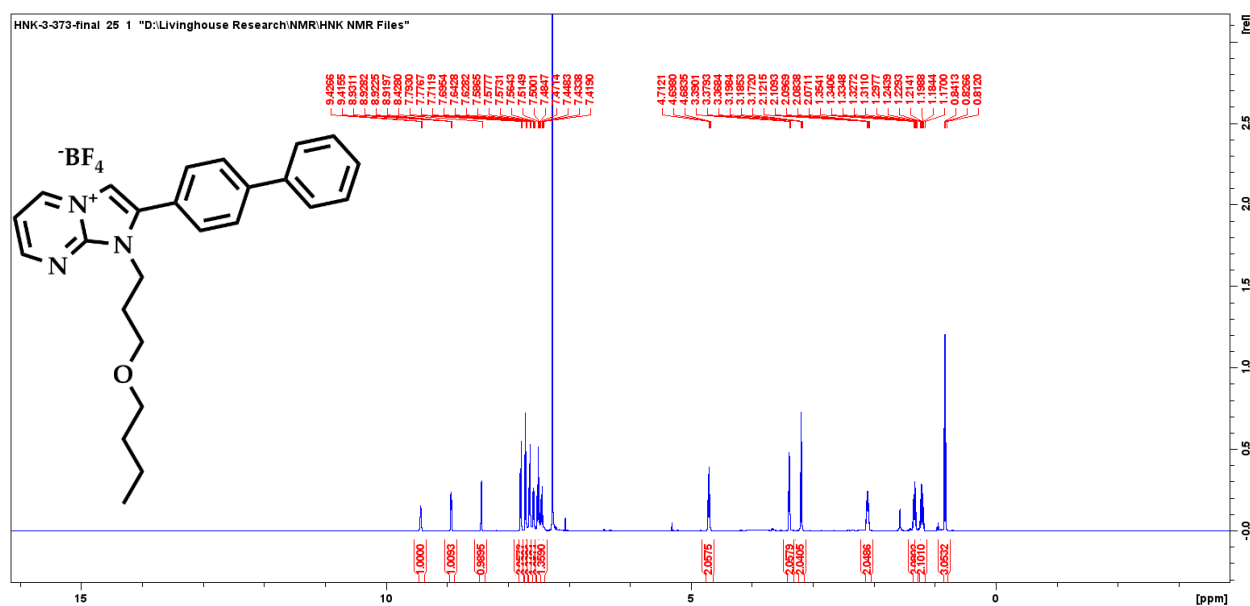


Figure 3.110B: ¹H-NMR Spectra of 2-([1,1'-biphenyl]-4-yl)-1-(3-butoxypropyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (3.2b).

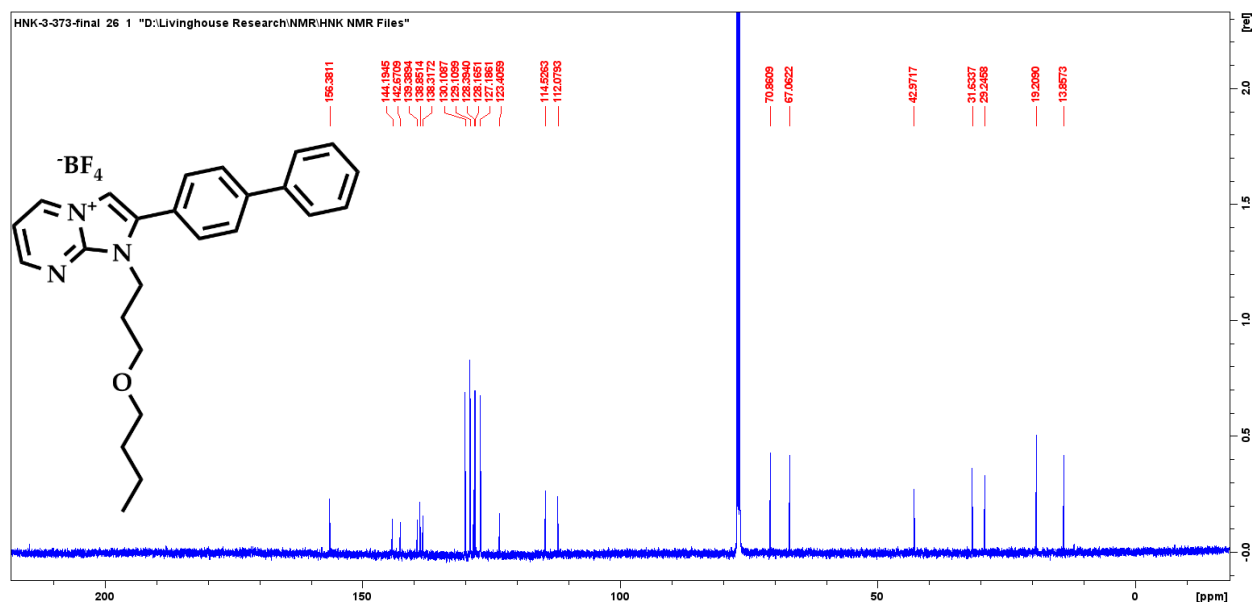


Figure 3.111B: ^{13}C -NMR Spectra of 2-([1,1'-biphenyl]-4-yl)-1-(3-butoxypropyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**3.2b**).

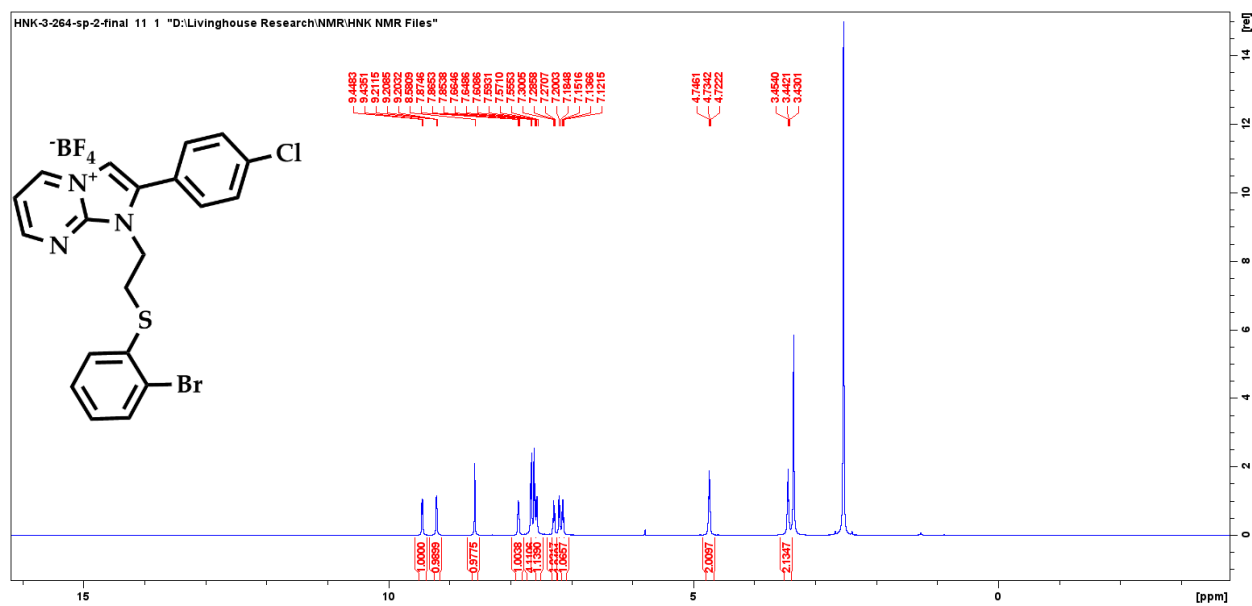


Figure 3.112B: ¹H-NMR Spectra of 1-((2-bromophenyl)thio)ethyl-2-(4-chlorophenyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**4.2a**).

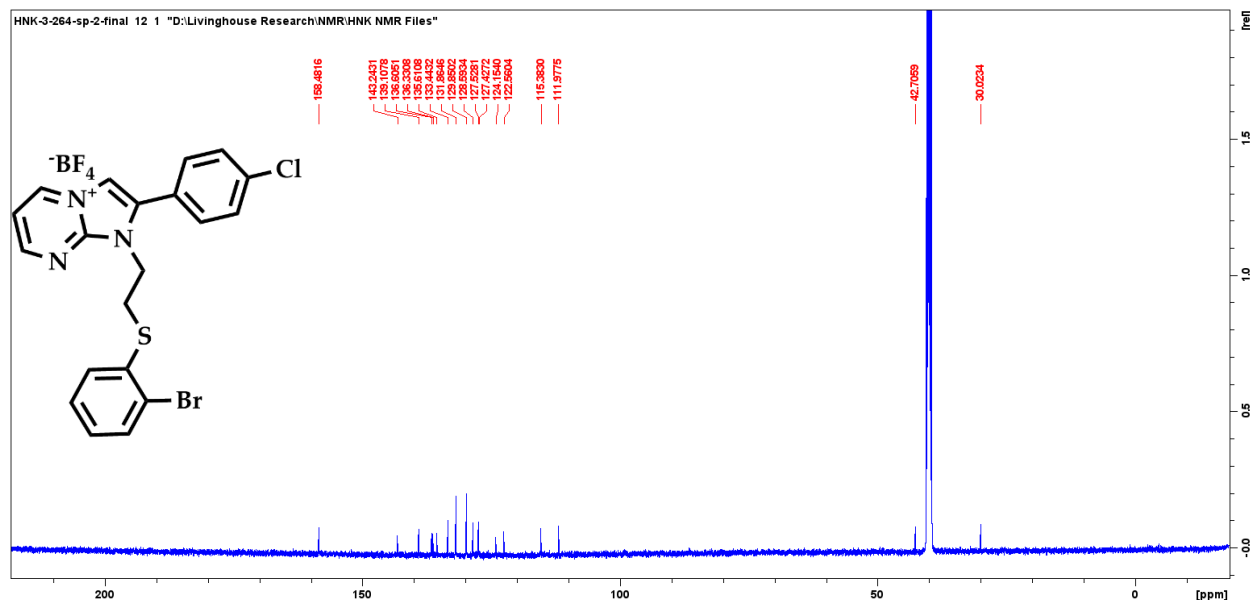
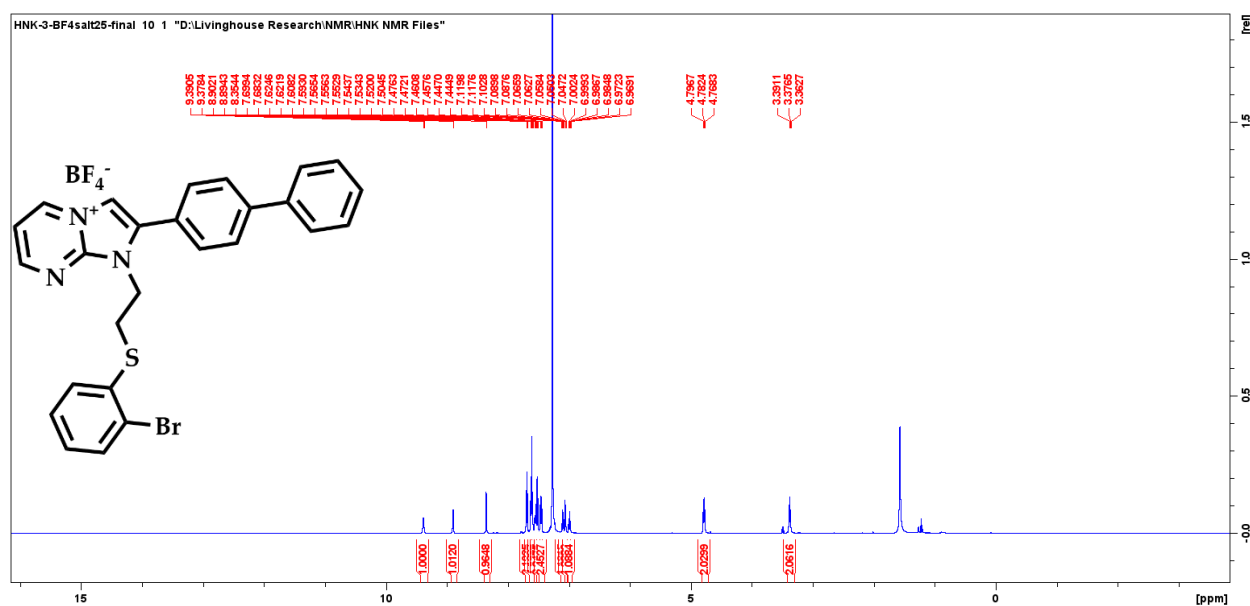


Figure 3.113B: ¹³C-NMR Spectra of 1-((2-bromophenyl)thio)ethyl-2-(4-chlorophenyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (**4.2a**).



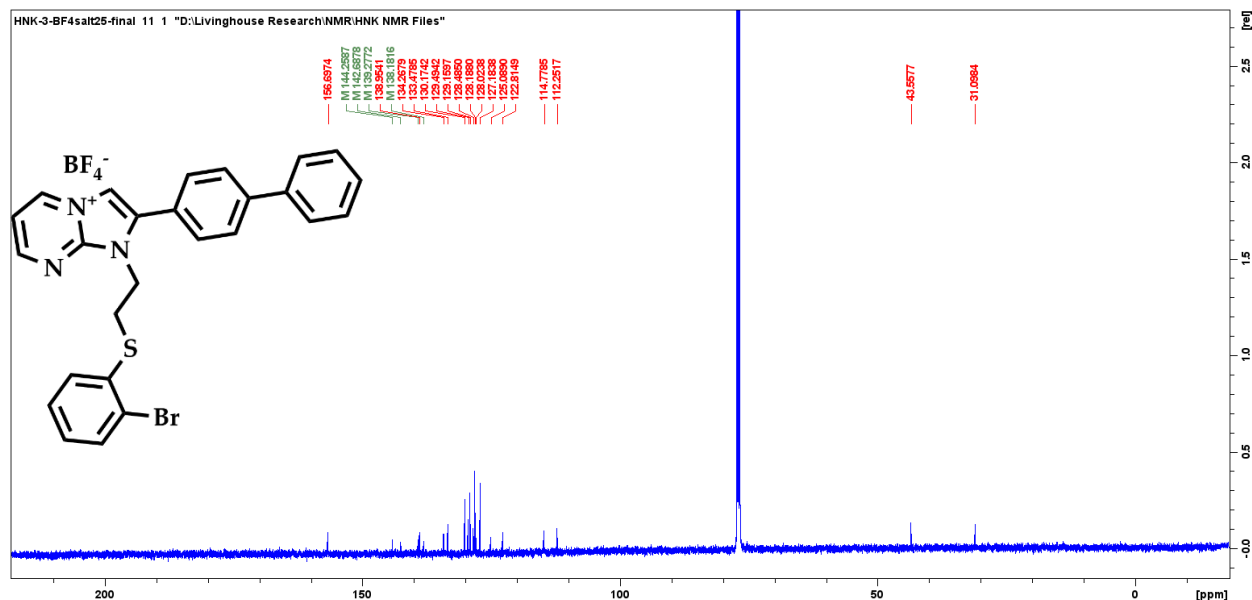


Figure 3.115B: ¹³C-NMR Spectra of 2-([1,1'-biphenyl]-4-yl)-1-(2-((2-bromophenyl)thio)ethyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (**4.2b**).

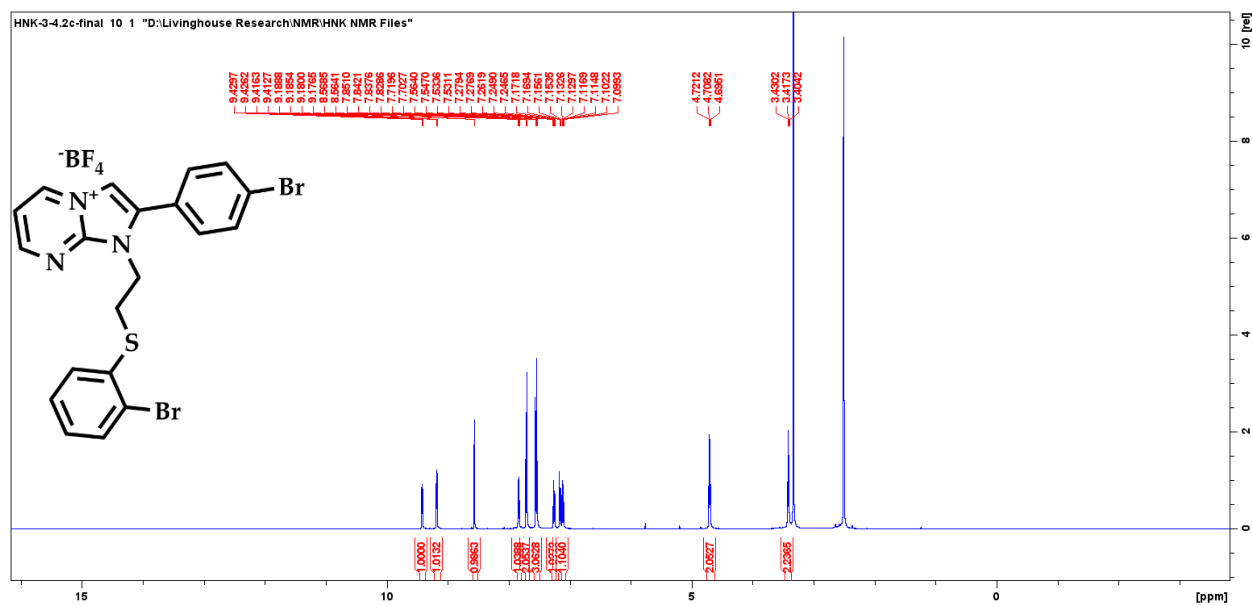


Figure 3.116B: ¹H-NMR Spectra of 1-(2-((2-bromophenyl)thio)ethyl)-2-(4-bromophenyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (**4.2c**).

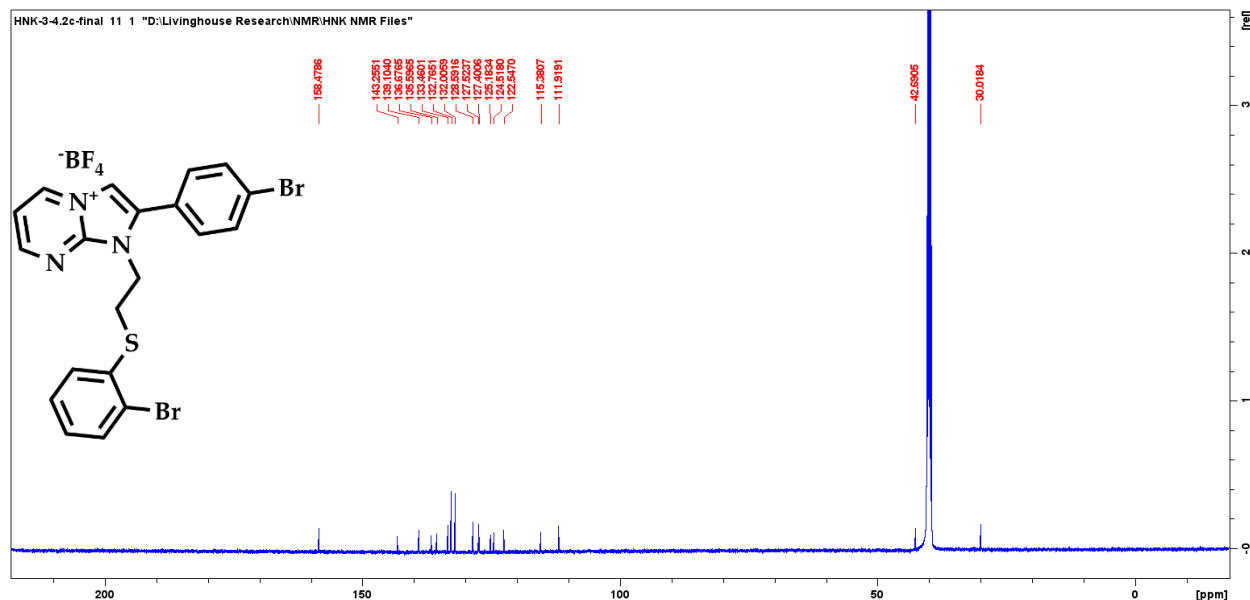


Figure 3.117B: ^{13}C -NMR Spectra of 1-((2-bromophenyl)thio)ethyl-2-(4-bromophenyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (**4.2c**).

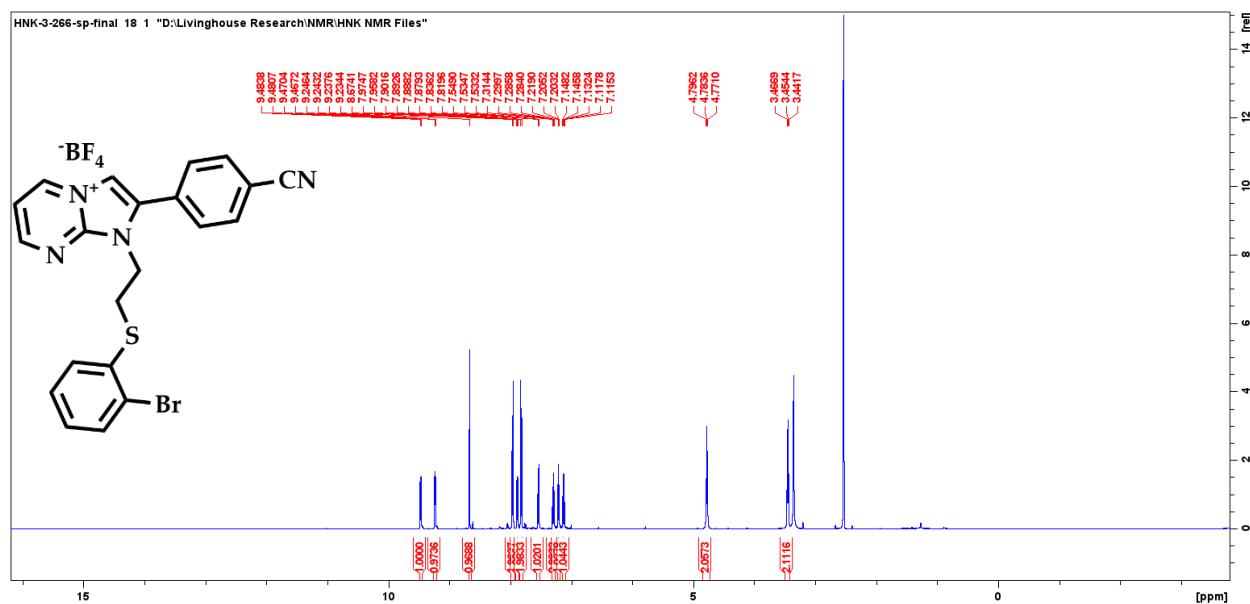


Figure 3.118B: ^1H -NMR Spectra of 1-((2-bromophenyl)thio)ethyl-2-(4-cyanophenyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (**4.2d**).

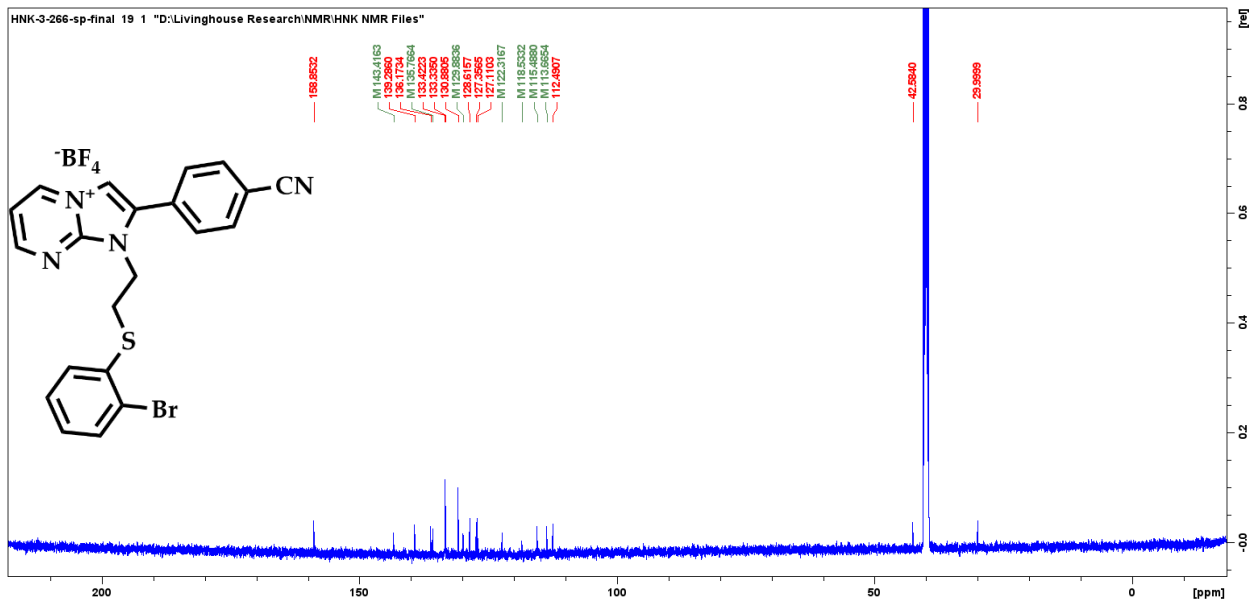


Figure 3.119B: ^{13}C -NMR Spectra of 1-(2-((2-bromophenyl)thio)ethyl)-2-(4-cyanophenyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**4.2d**).

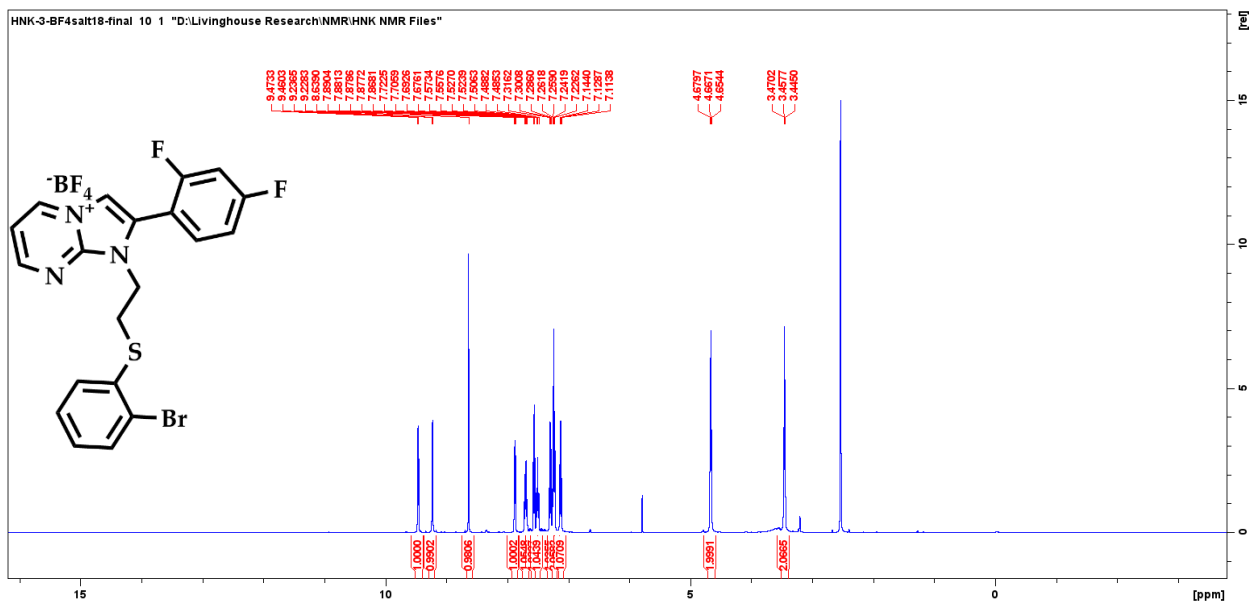


Figure 3.122B: ¹H-NMR Spectra of 1-(2-((2-bromophenyl)thio)ethyl)-2-(2,4-difluorophenyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**4.2f**).

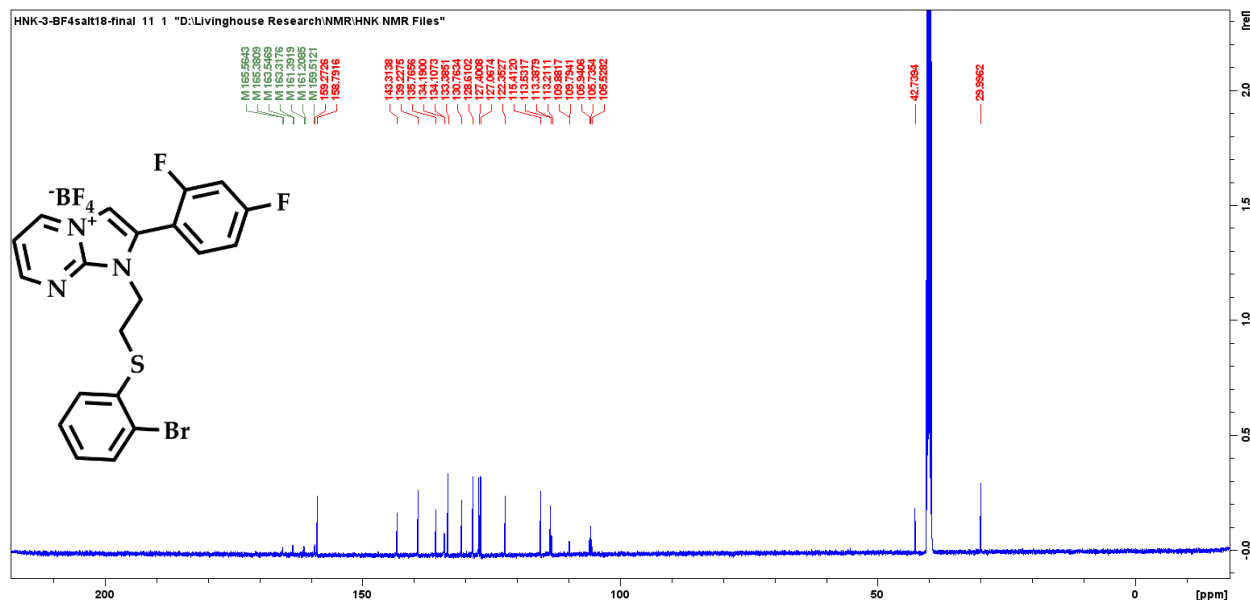


Figure 3.123B: ¹³C-NMR Spectra of 1-((2-bromophenyl)thio)ethyl-2-(2,4-difluorophenyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (**4.2f**).

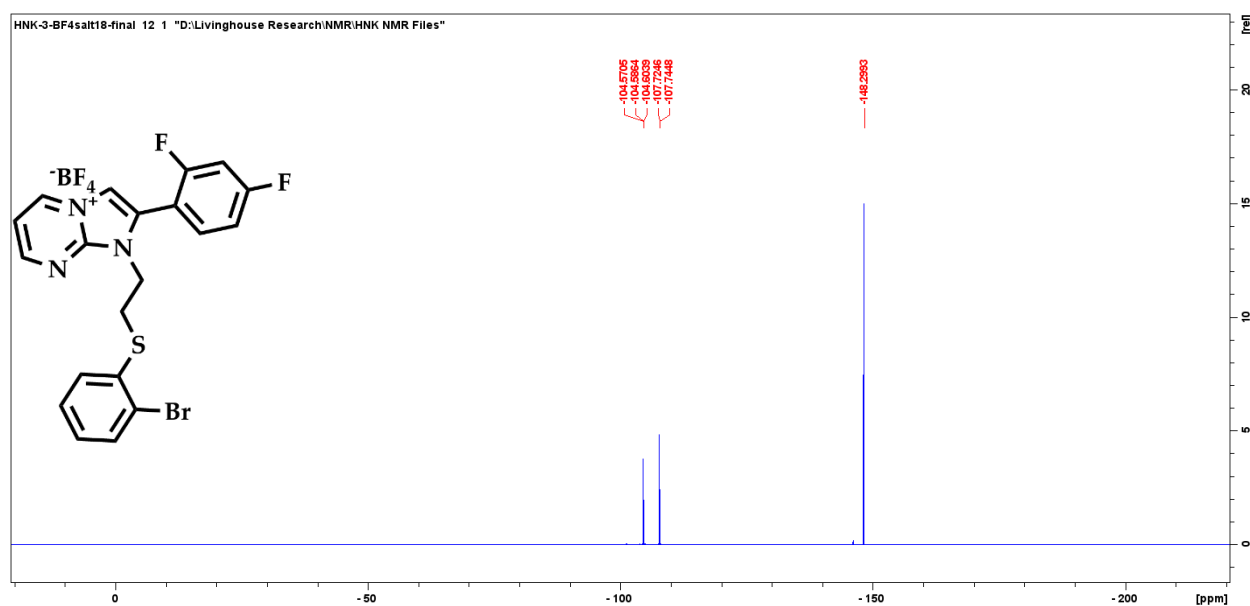


Figure 3.124B: ¹⁹F-NMR Spectra of 1-((2-bromophenyl)thio)ethyl-2-(2,4-difluorophenyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (**4.2f**).

HNK-3-303-final 23 1 "D:\Livinghouse Research\NMR\HNK NMR Files"

Chemical structure of compound 23 is shown as an inset. The structure is a 2-(4-chlorophenyl)-2-((2-chlorophenylthio)methyl)-1H-imidazole-5-carboxylate salt, with a BF_4^- counterion.

Peak list (ppm):

- 198.4762
- 153.3128
- 152.8581
- 138.5916
- 136.3507
- 135.3252
- 132.1538
- 131.8462
- 129.7775
- 129.8420
- 128.0776
- 127.7923
- 124.1712
- 115.3803
- 111.9824
- 42.8419
- 23.5861

Figure 3.126B: ^{13}C -NMR Spectra of 2-(4-chlorophenyl)-1-(2-((2-chlorophenyl)thio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**5.2a**).

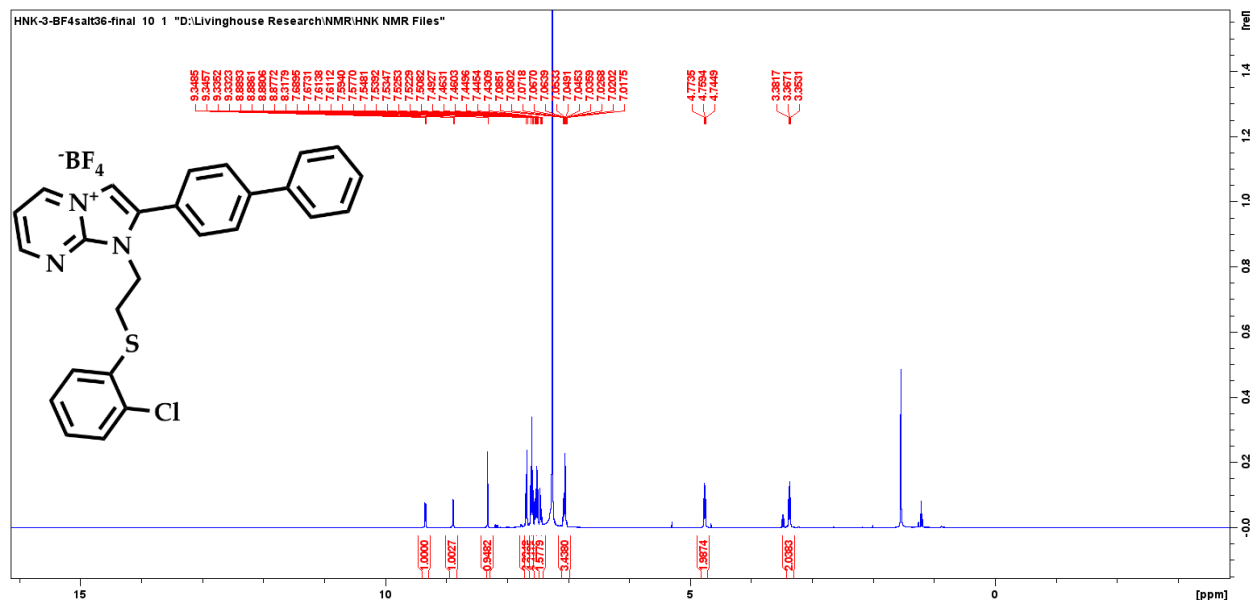


Figure 3.127B: ¹H-NMR Spectra of 2-([1,1'-biphenyl]-4-yl)-1-(2-((2-chlorophenyl)thio)ethyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (5.2b).

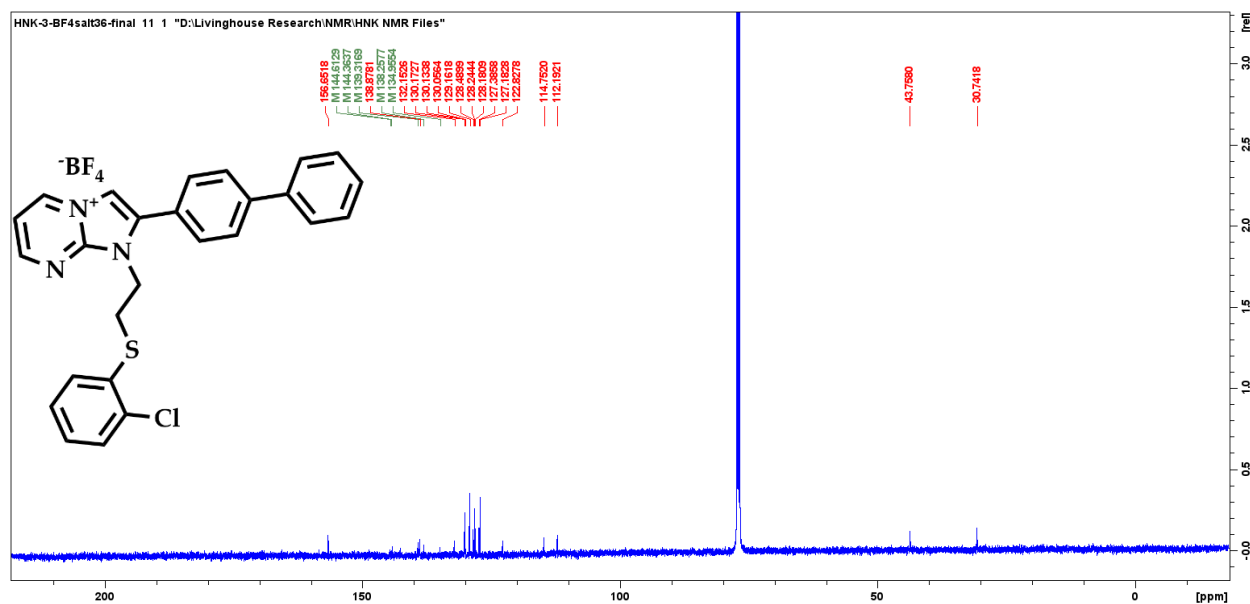


Figure 3.128B: ¹³C-NMR Spectra of 2-([1,1'-biphenyl]-4-yl)-1-(2-((2-chlorophenyl)thio)ethyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (5.2b).

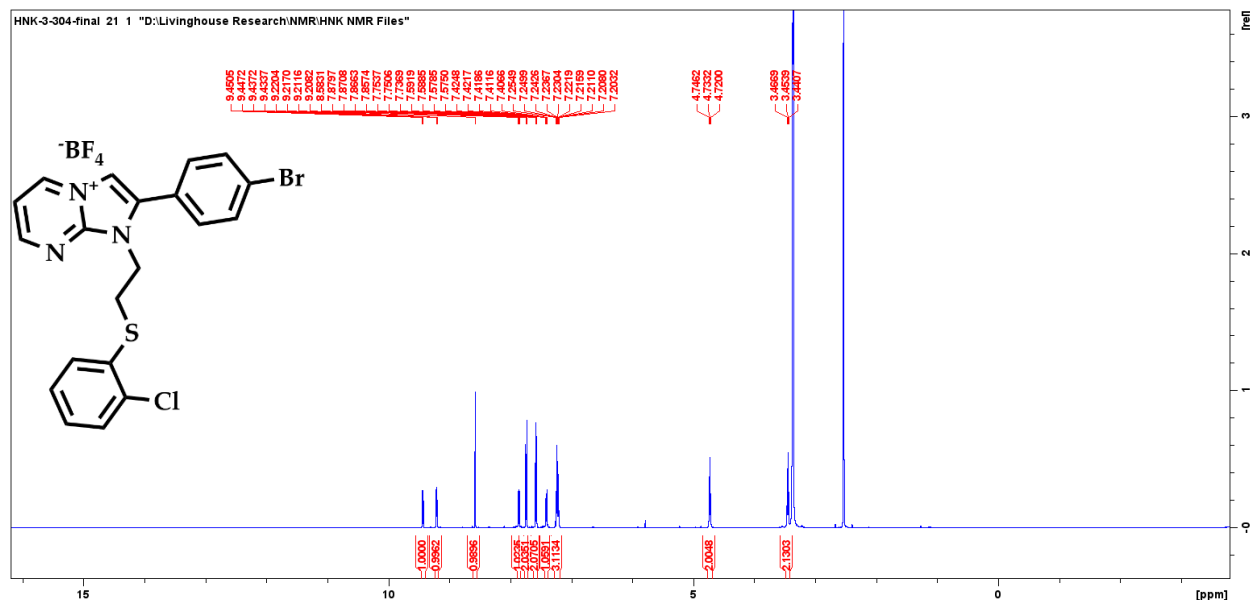


Figure 3.129B: ^1H -NMR Spectra of 2-(4-bromophenyl)-1-(2-((2-chlorophenyl)thio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (5.2c).

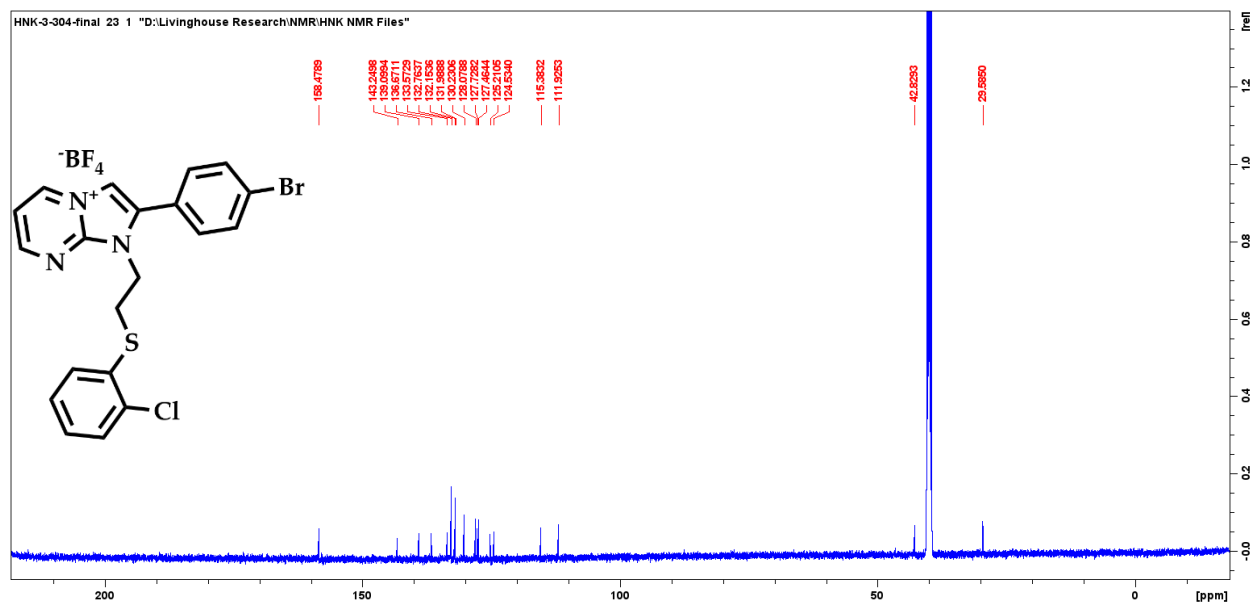


Figure 3.130B: ^{13}C -NMR Spectra of 2-(4-bromophenyl)-1-(2-((2-chlorophenyl)thio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (5.2c).

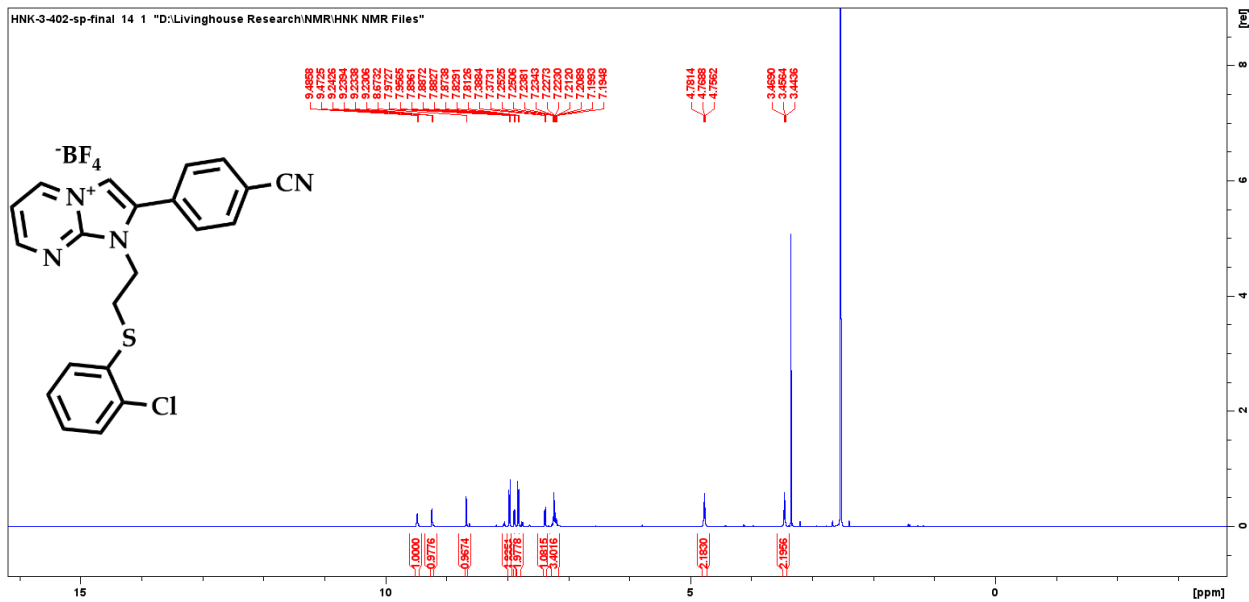


Figure 3.131B: ¹H-NMR Spectra of 1-(2-((2-chlorophenyl)thio)ethyl)-2-(4-cyanophenyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**5.2d**).

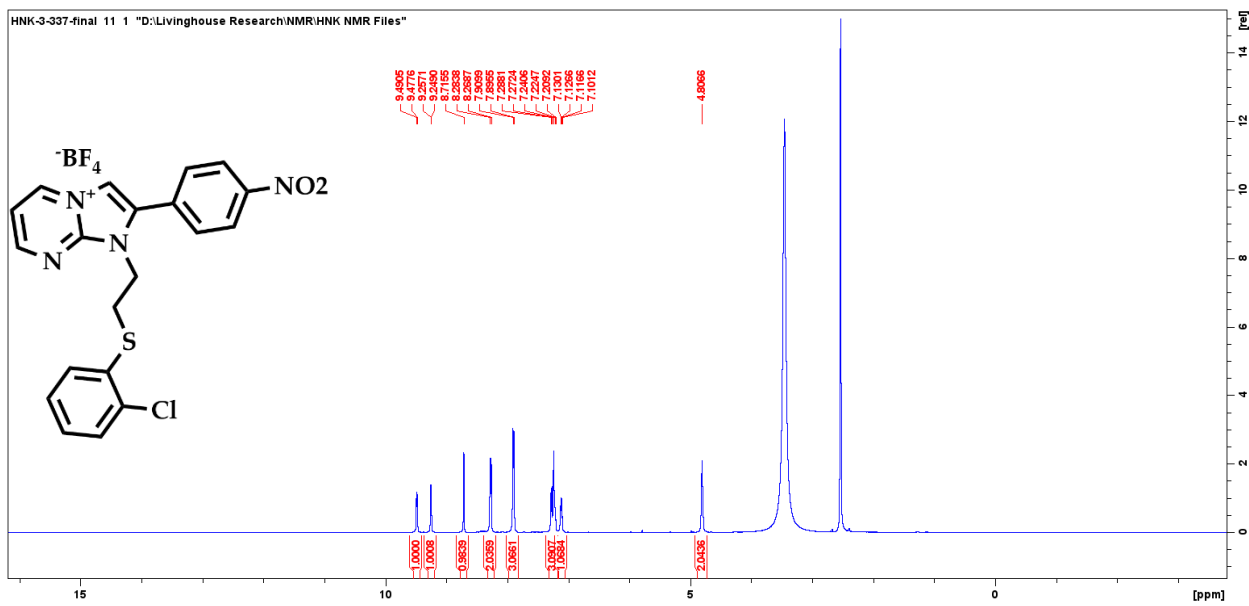


Figure 3.132B: ¹H-NMR Spectra of 1-(2-((2-chlorophenyl)thio)ethyl)-2-(4-nitrophenyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**5.2e**).

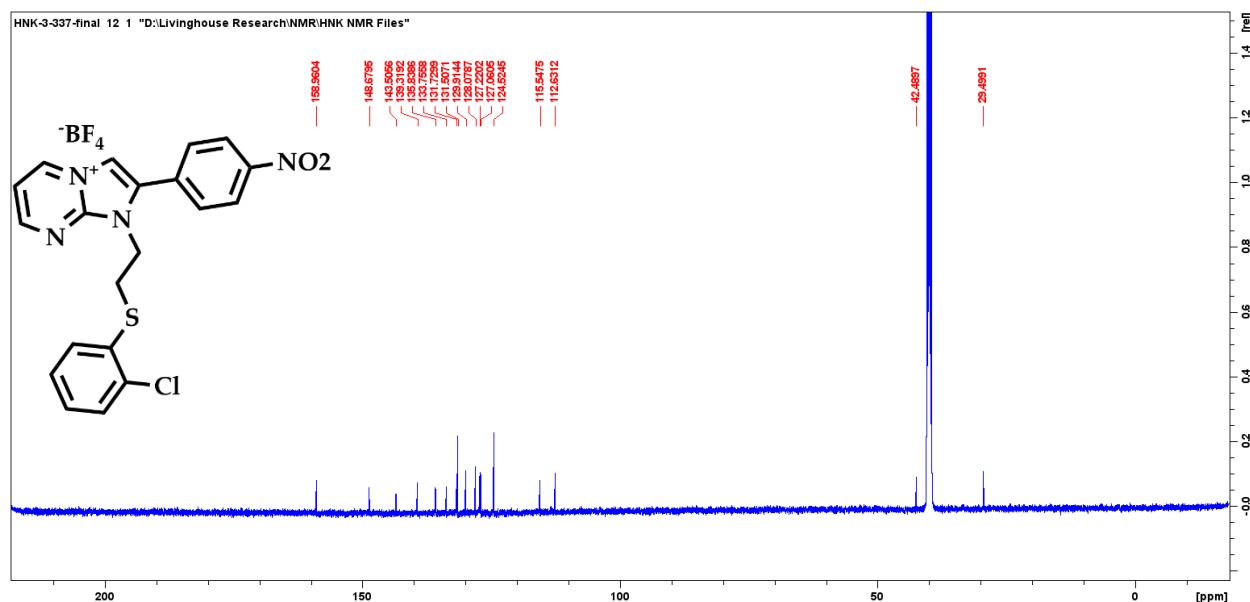


Figure 3.133B: ¹³C-NMR Spectra of 1-(2-((2-chlorophenyl)thio)ethyl)-2-(4-nitrophenyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (5.2e).

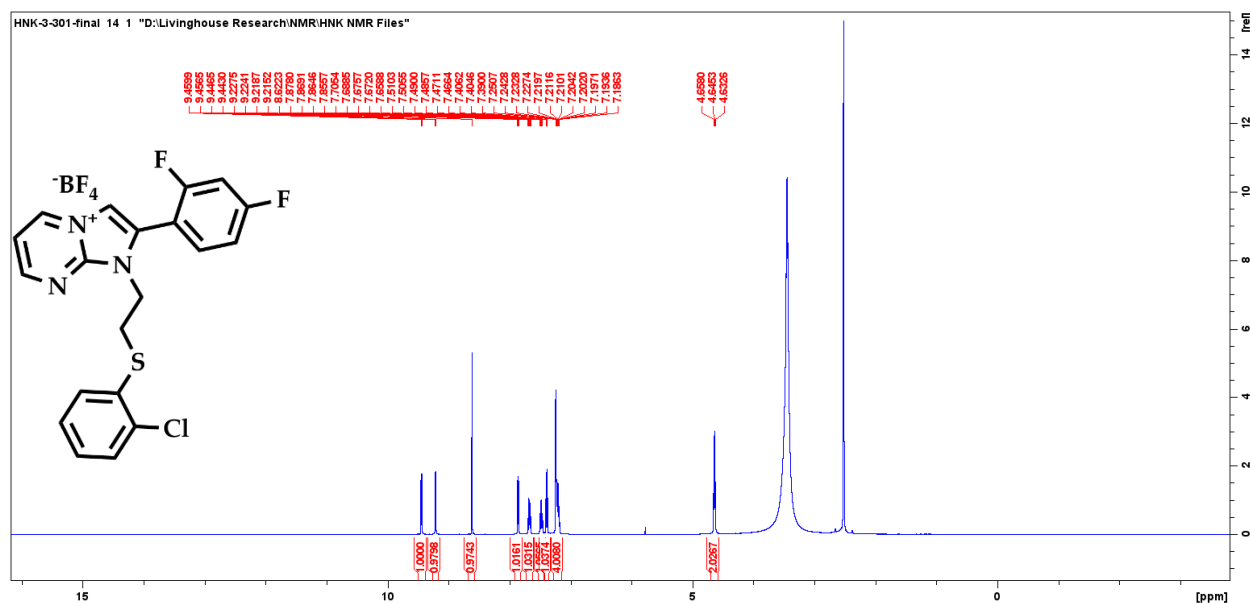


Figure 3.134B: ¹H-NMR Spectra of 1-(2-((2-chlorophenyl)thio)ethyl)-2-(2,4-difluorophenyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (5.2f).

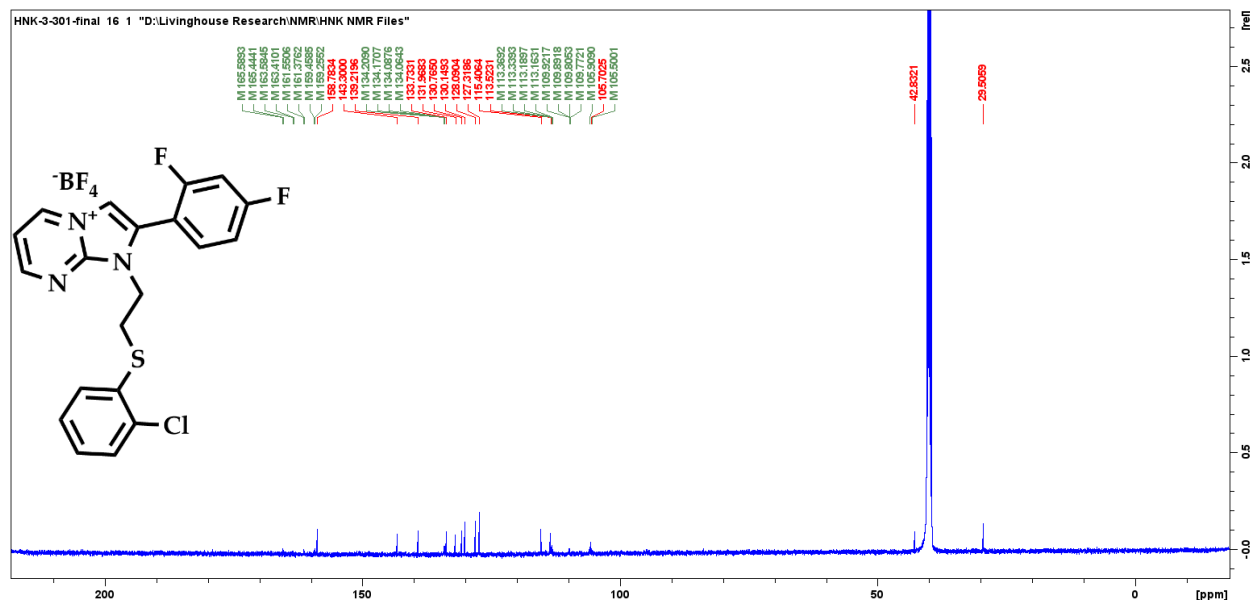


Figure 3.135B: ^{13}C -NMR Spectra of 1-(2-((2-chlorophenyl)thio)ethyl)-2-(2,4-difluorophenyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (5.2f).

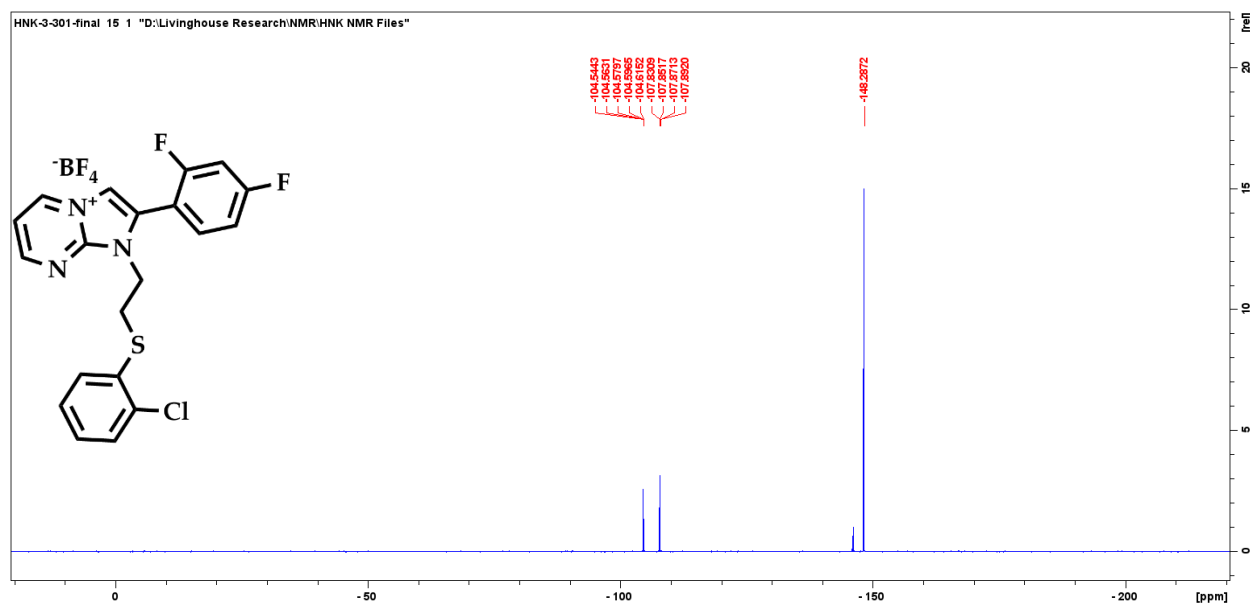


Figure 3.136B: ^{19}F -NMR Spectra of 1-(2-((2-chlorophenyl)thio)ethyl)-2-(2,4-difluorophenyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (5.2f).

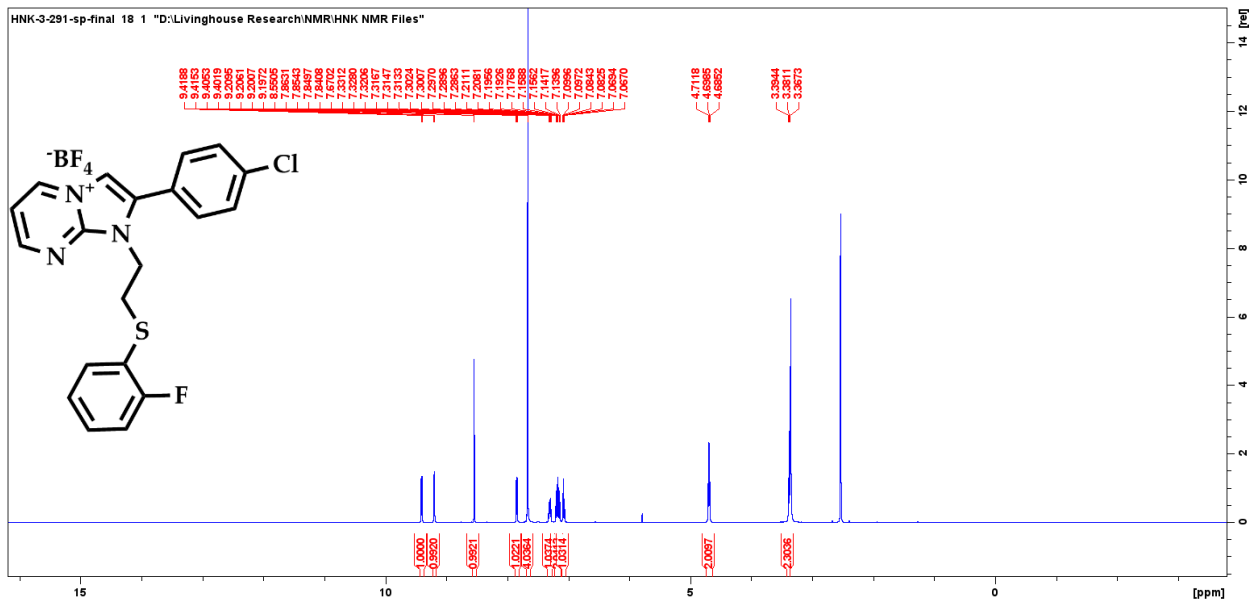


Figure 3.137B: ¹H-NMR Spectra of 2-(4-chlorophenyl)-1-((2-fluorophenyl)thio)ethyl-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**6.2a**).

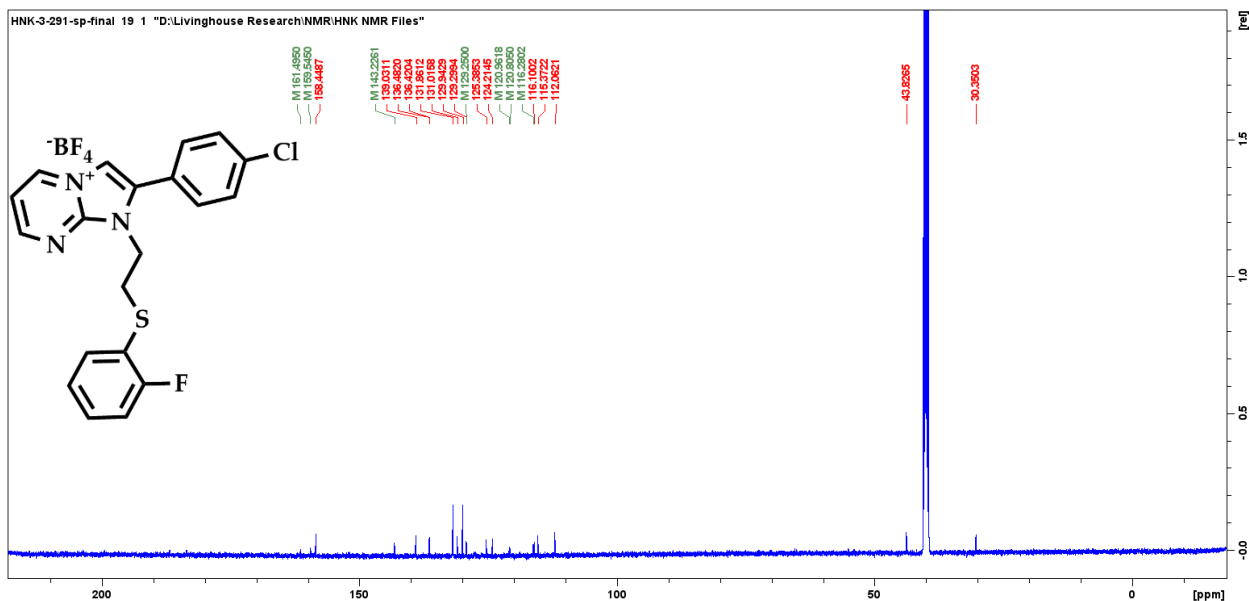


Figure 3.138B: ^{13}C -NMR Spectra of 2-(4-chlorophenyl)-1-(2-((2-fluorophenyl)thio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**6.2a**).

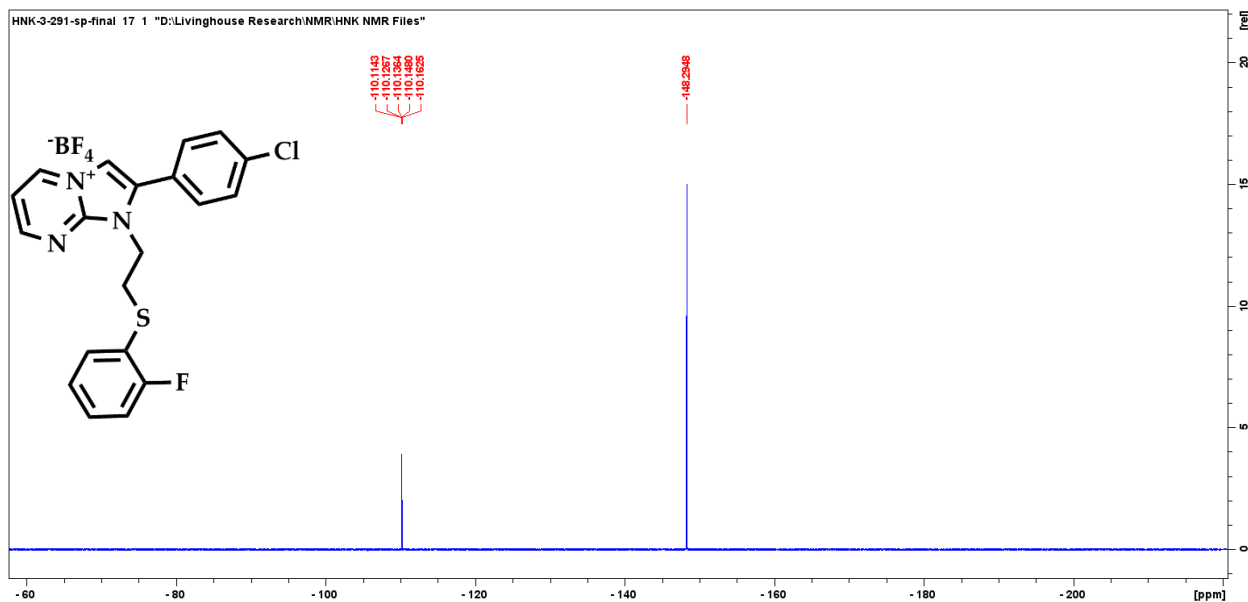


Figure 3.139B: ¹⁹F-NMR Spectra of 2-(4-chlorophenyl)-1-(2-((2-fluorophenyl)thio)ethyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (**6.2a**).

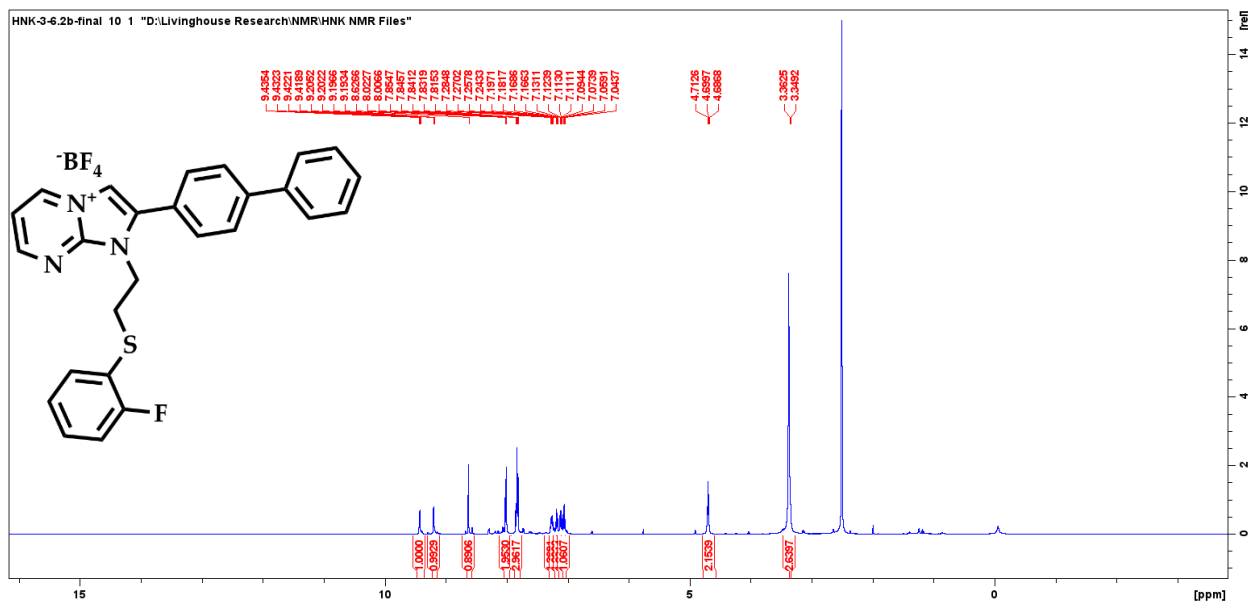


Figure 3.140B: ¹H-NMR Spectra of 2-([1,1'-biphenyl]-4-yl)-1-(2-((2-fluorophenyl)thio)ethyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (**6.2b**).

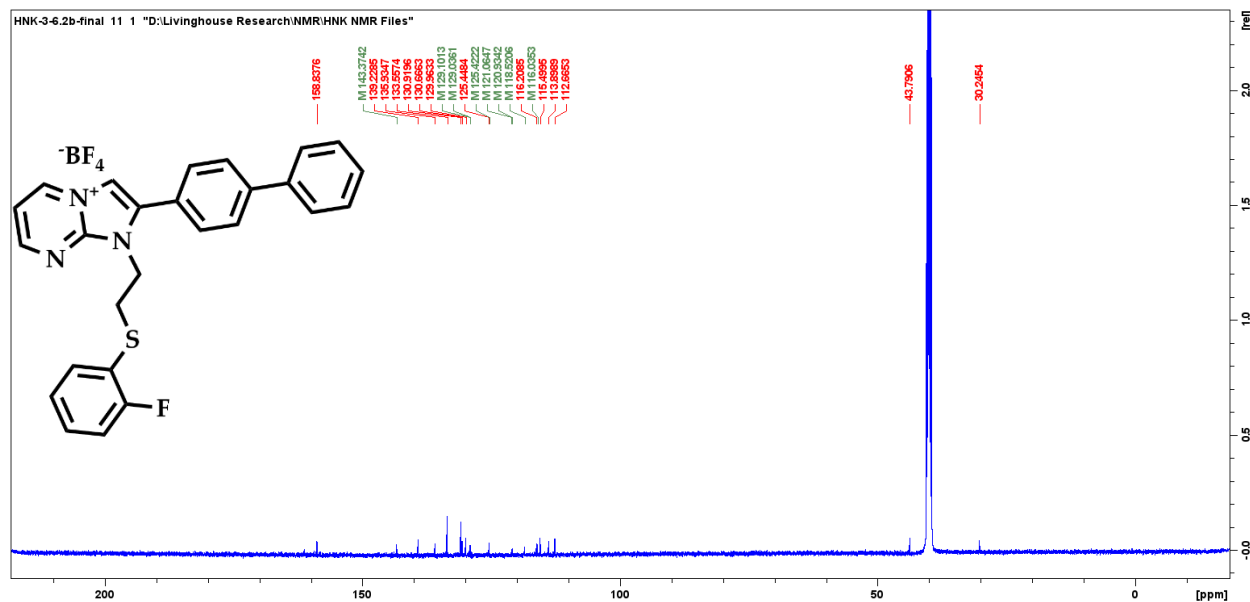


Figure 3.141B: ^{13}C -NMR Spectra of 2-([1,1'-biphenyl]-4-yl)-1-(2-((2-fluorophenyl)thio)ethyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (**6.2b**).

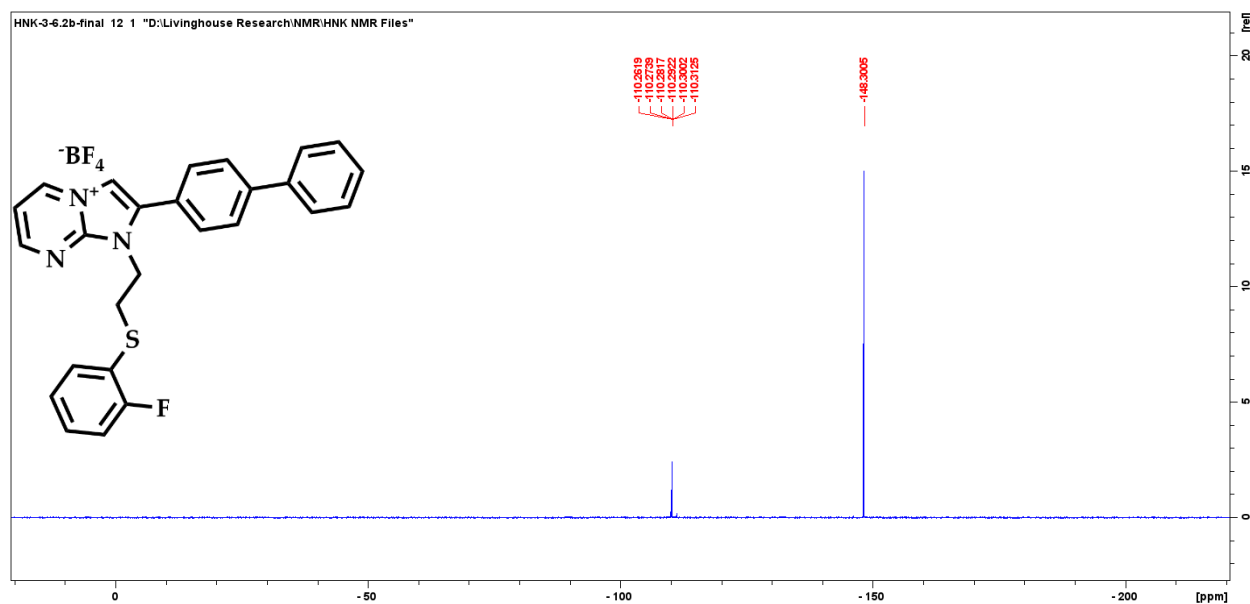


Figure 3.142B: ^{19}F -NMR Spectra of 2-([1,1'-biphenyl]-4-yl)-1-(2-((2-fluorophenyl)thio)ethyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (**6.2b**).

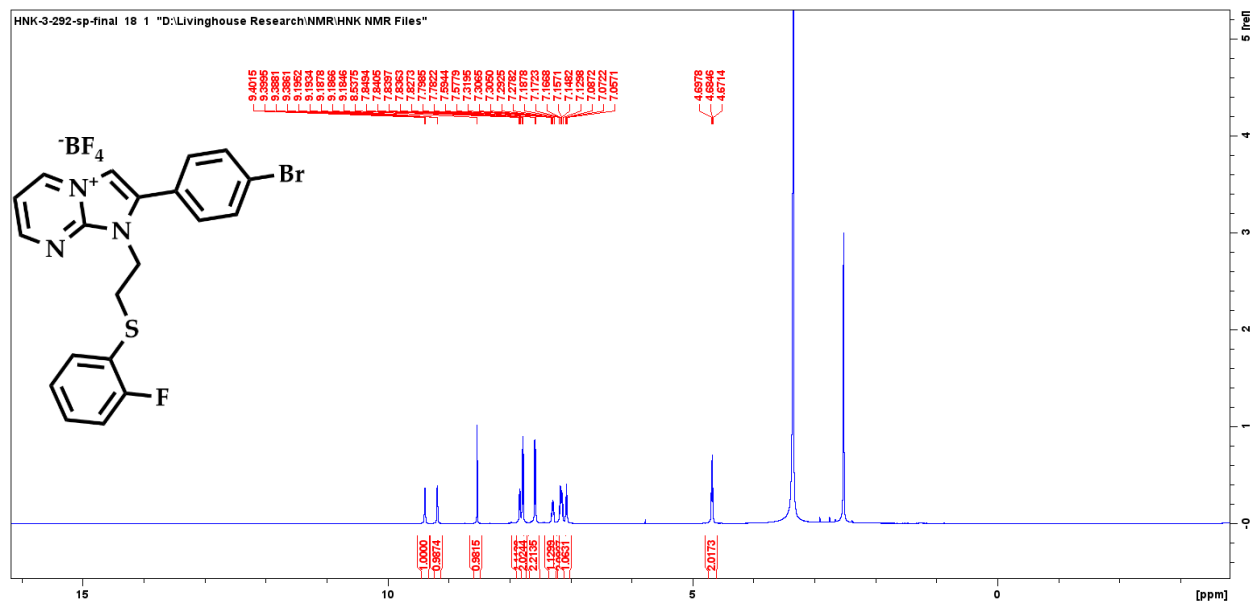


Figure 3.143B: ^1H -NMR Spectra of 2-(4-bromophenyl)-1-(2-((2-fluorophenyl)thio)ethyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (6.2c).

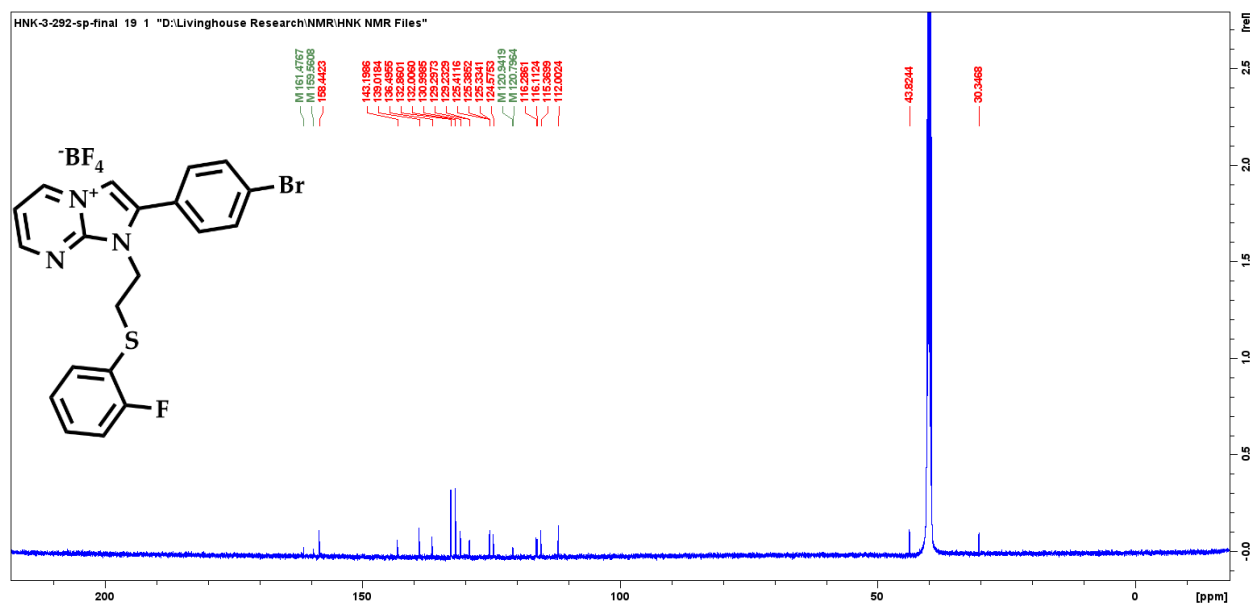


Figure 3.144B: ^{13}C -NMR Spectra of 2-(4-bromophenyl)-1-(2-((2-fluorophenyl)thio)ethyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (6.2c).

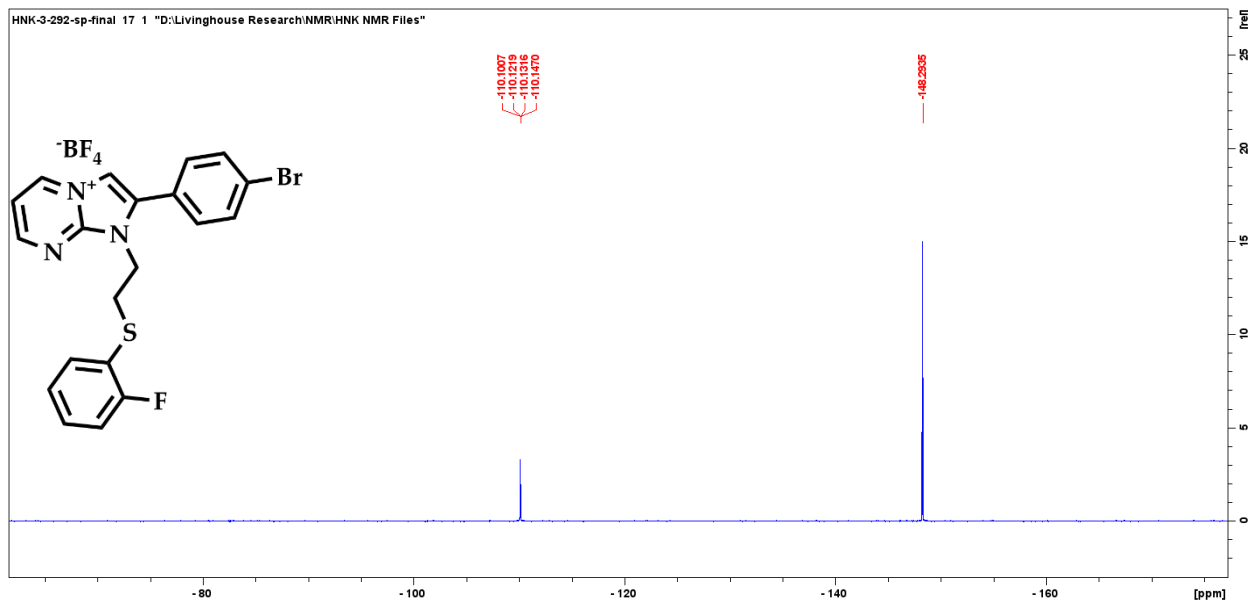


Figure 3.145B: ^{19}F -NMR Spectra of 2-(4-bromophenyl)-1-(2-((2-fluorophenyl)thio)ethyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (6.2c).

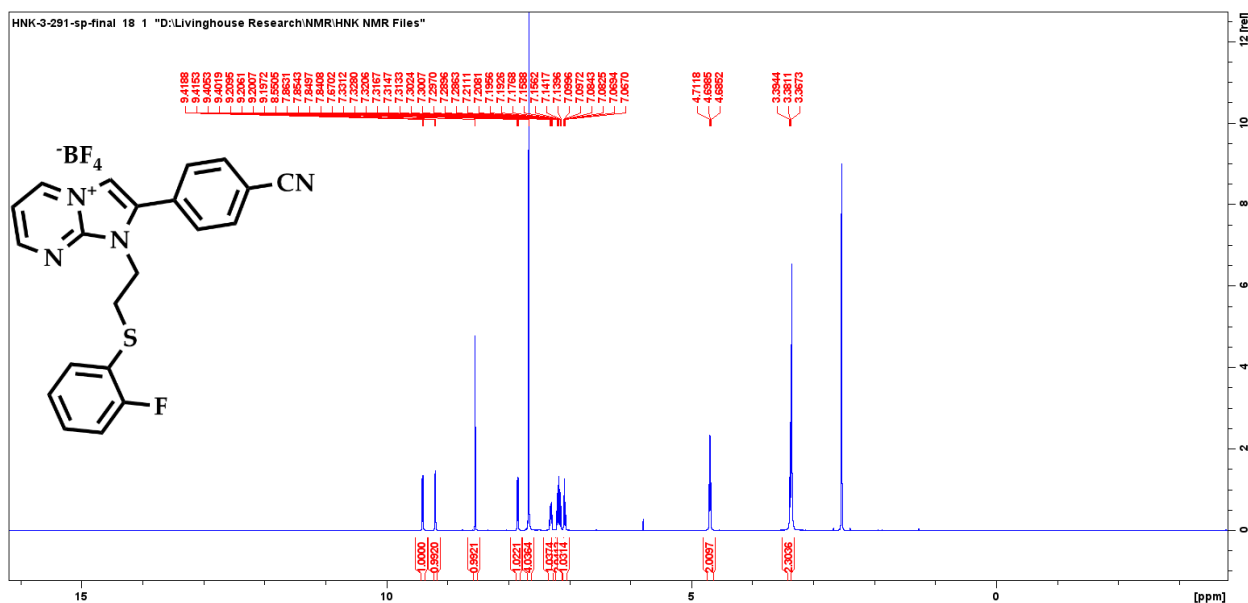


Figure 3.146B: ^1H -NMR Spectra of 2-(4-cyanophenyl)-1-(2-((2-fluorophenyl)thio)ethyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (6.2d).

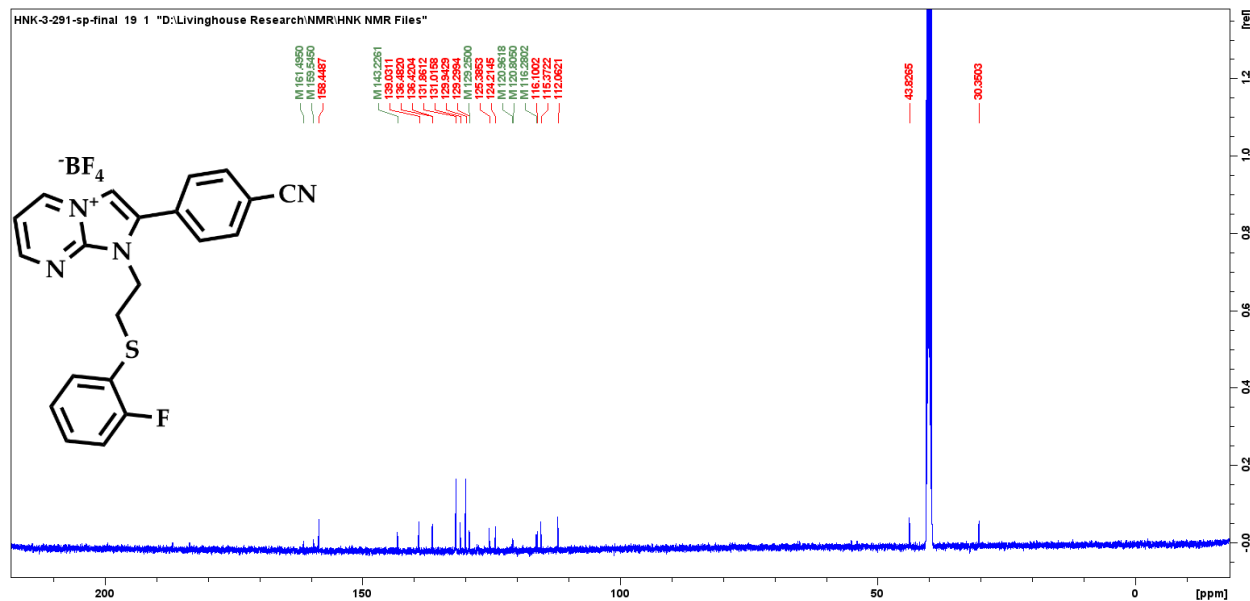


Figure 3.147B: ^{13}C -NMR Spectra of 2-(4-cyanophenyl)-1-(2-((2-fluorophenyl)thio)ethyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (**6.2d**).

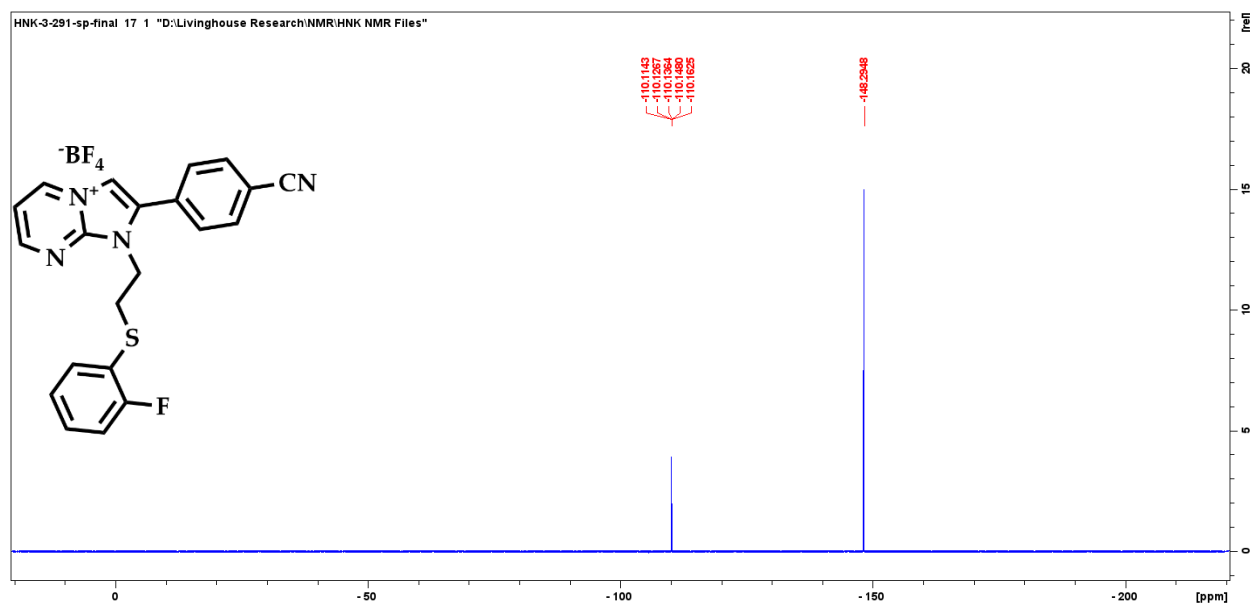


Figure 3.148B: ^{19}F -NMR Spectra of 2-(4-cyanophenyl)-1-(2-((2-fluorophenyl)thio)ethyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (**6.2d**).

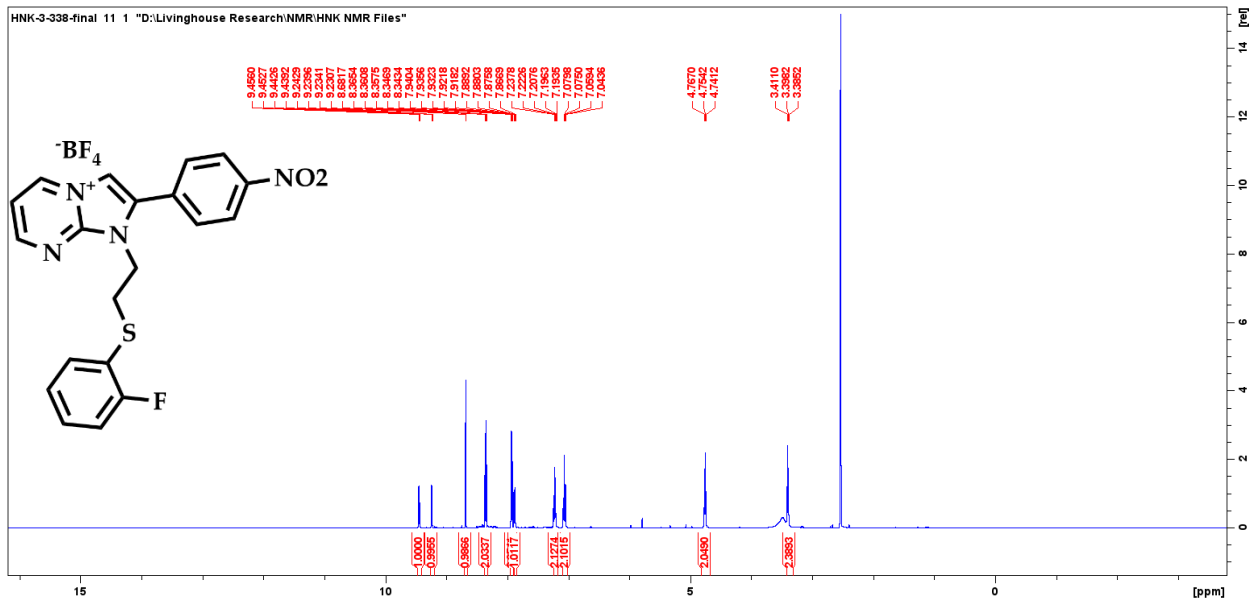


Figure 3.149B: ¹H-NMR Spectra of 1-(2-((2-fluorophenyl)thio)ethyl)-2-(4-nitrophenyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**6.2e**).

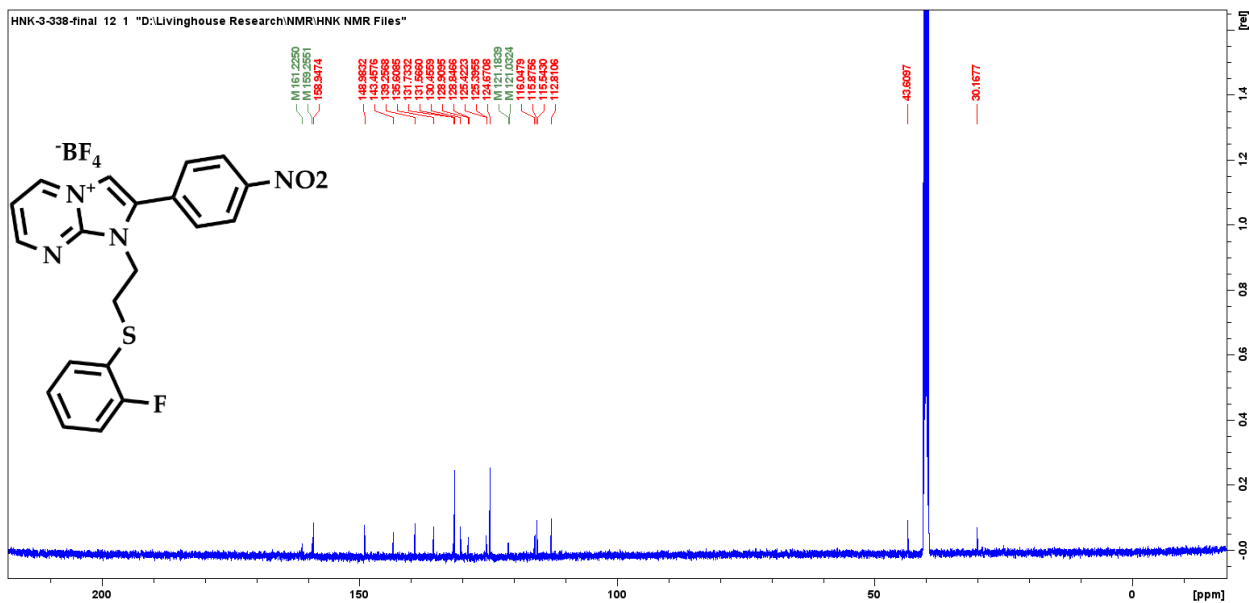


Figure 3.150B: ¹³C-NMR Spectra of 1-(2-((2-fluorophenyl)thio)ethyl)-2-(4-nitrophenyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**6.2e**).

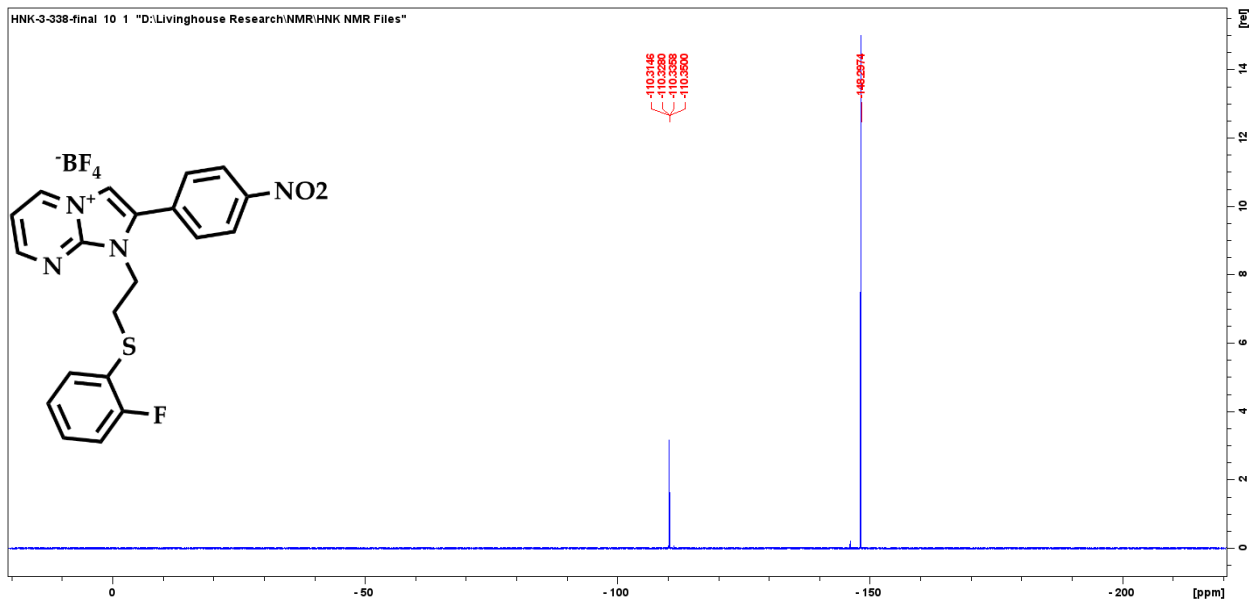


Figure 3.151B: ¹⁹F-NMR Spectra of 1-(2-((2-fluorophenyl)thio)ethyl)-2-(4-nitrophenyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**6.2e**).

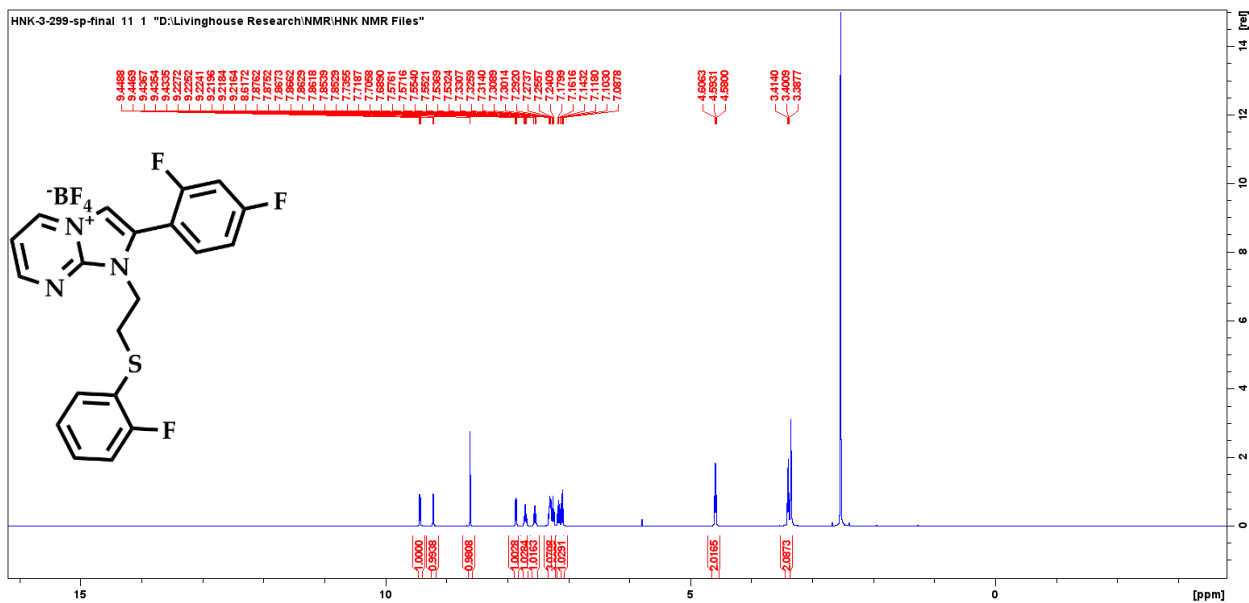


Figure 3.152B: ¹H-NMR Spectra of 2-(2,4-difluorophenyl)-1-(2-((2-fluorophenyl)thio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**6.2f**).

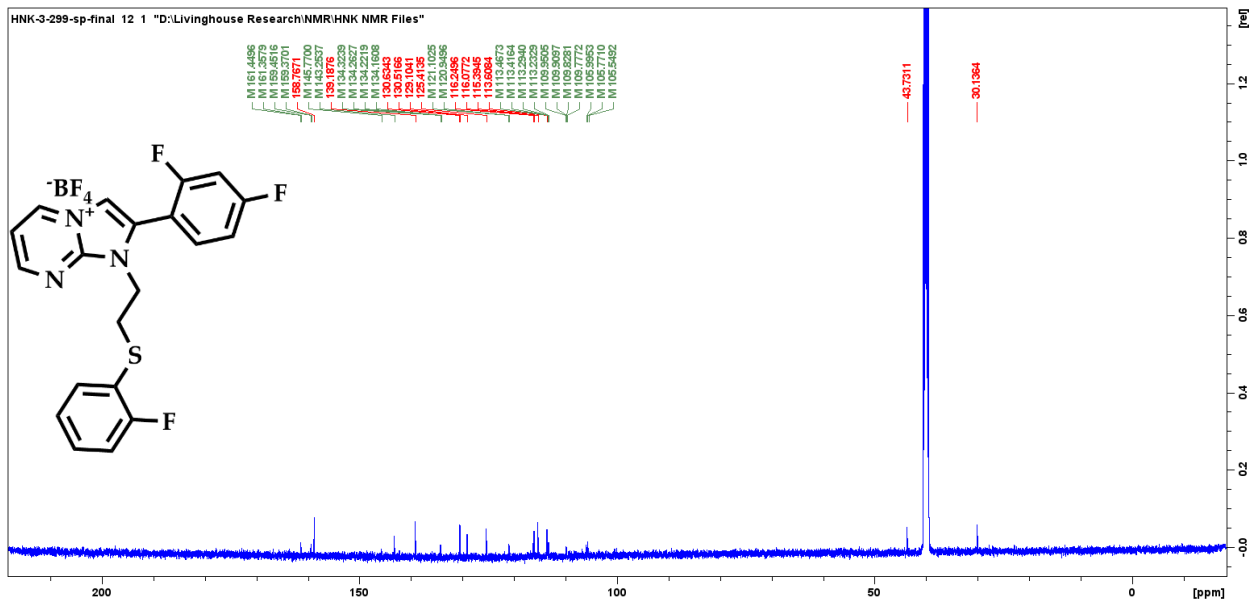


Figure 3.153B: ^{13}C -NMR Spectra of 2-(2,4-difluorophenyl)-1-(2-((2-fluorophenyl)thio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**6.2f**).

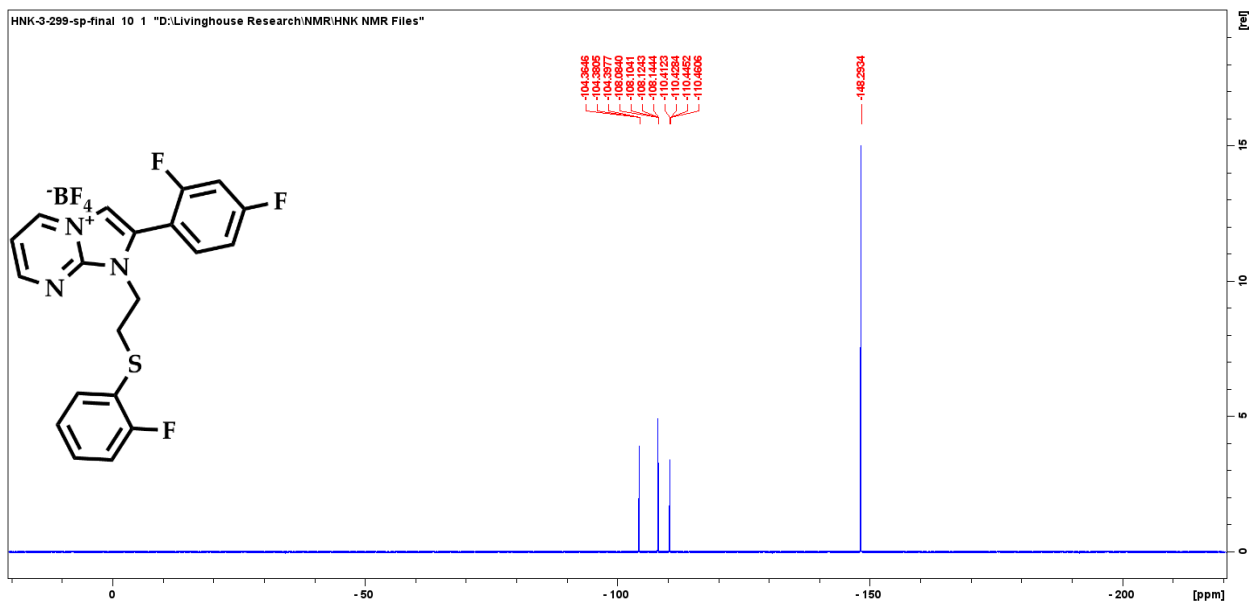


Figure 3.154B: ^{19}F -NMR Spectra of 2-(2,4-difluorophenyl)-1-(2-((2-fluorophenyl)thio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**6.2f**).

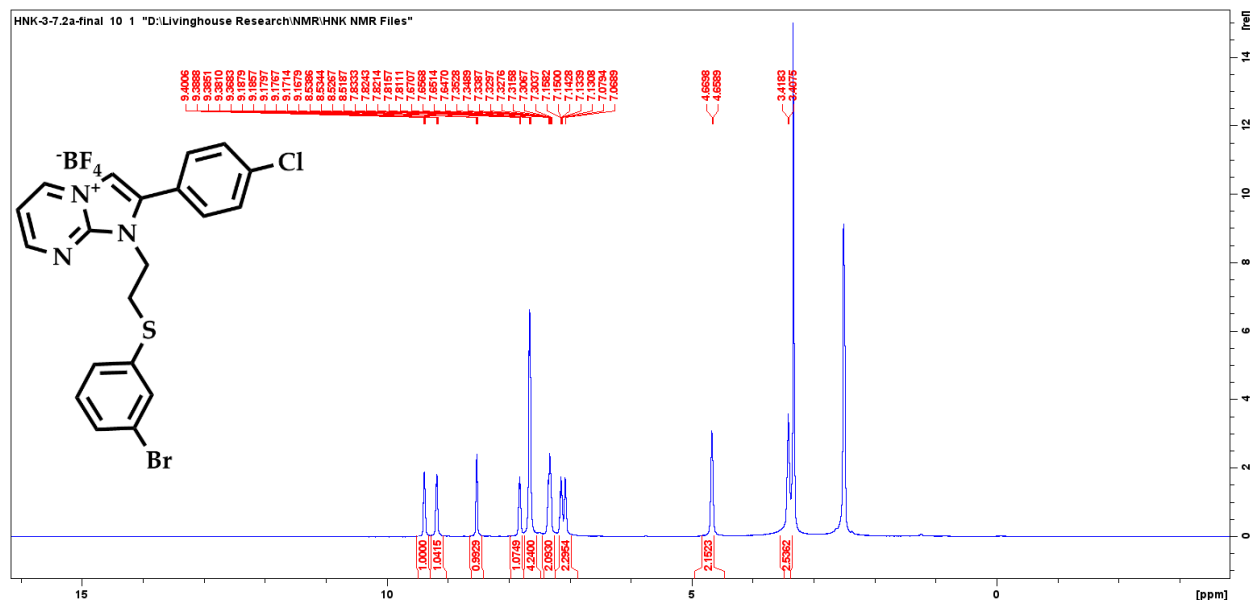


Figure 3.155B: ^1H -NMR Spectra of 2-(4-chlorophenyl)-1-(2-((3-bromophenyl)thio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (7.2a).

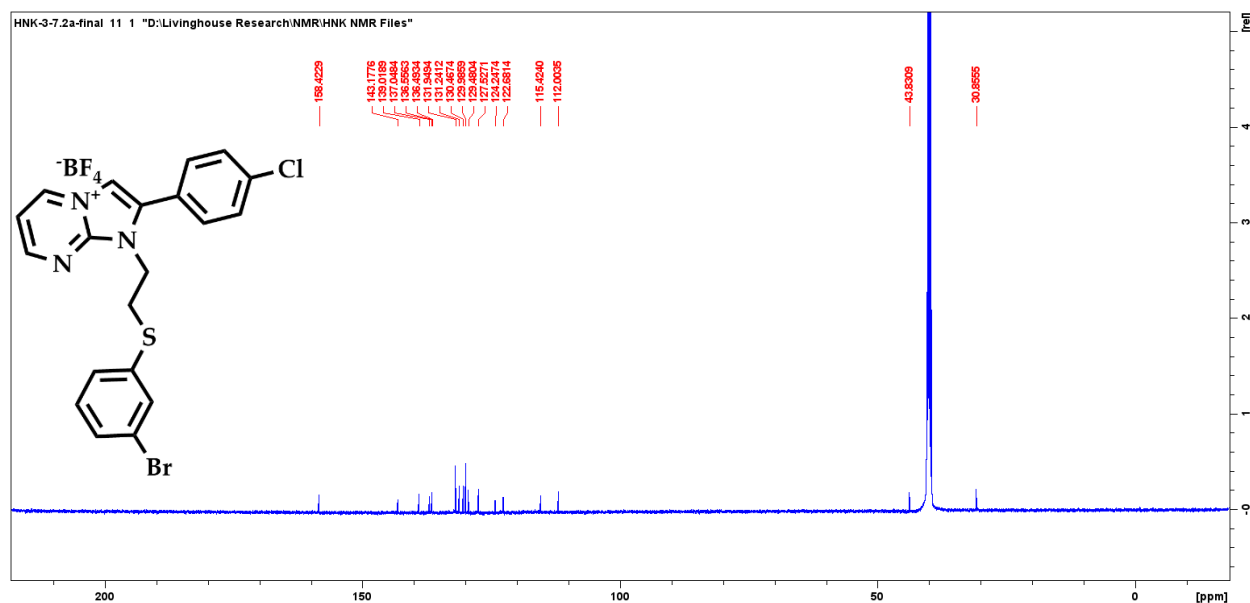


Figure 3.156B: ^{13}C -NMR Spectra of 2-(4-chlorophenyl)-1-(2-((3-bromophenyl)thio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (7.2a).

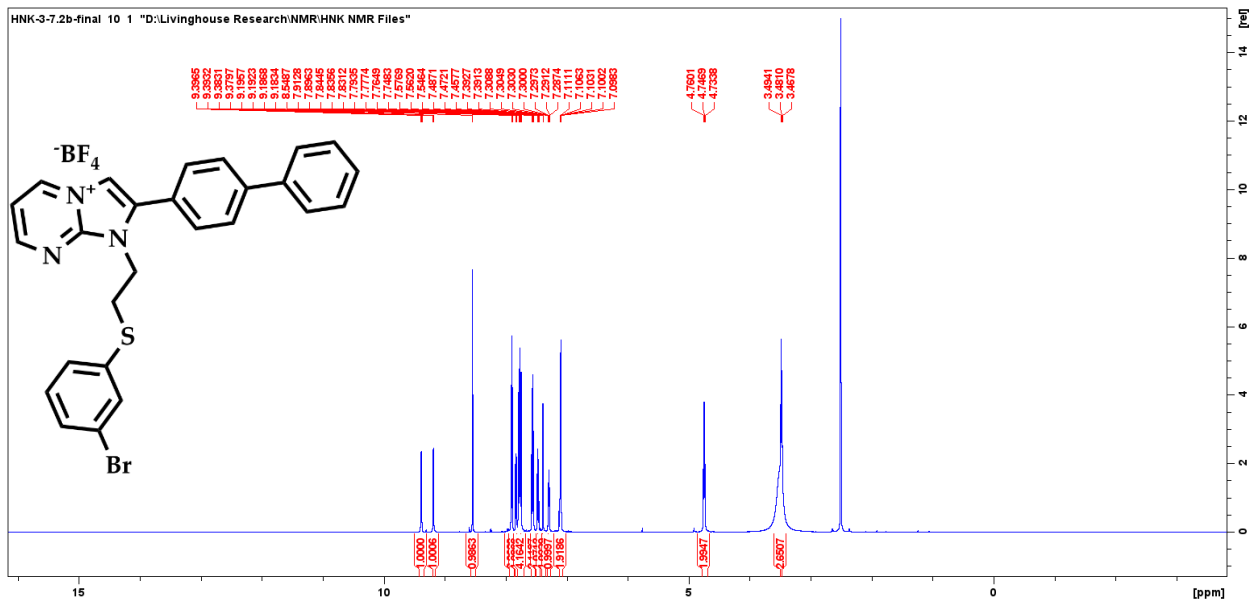


Figure 3.157B: ¹H-NMR Spectra of 2-([1,1'-biphenyl]-4-yl)-1-(2-((3-bromophenyl)thio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**7.2b**).

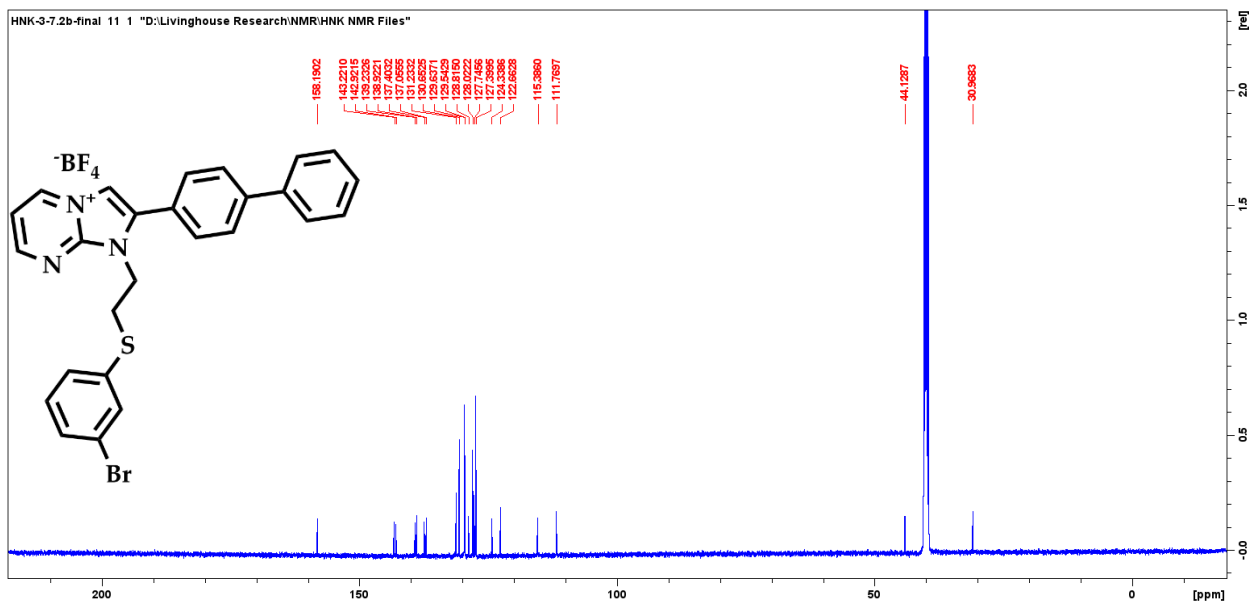


Figure 3.158B: ¹³C-NMR Spectra of 2-([1,1'-biphenyl]-4-yl)-1-(2-((3-bromophenyl)thio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**7.2b**).

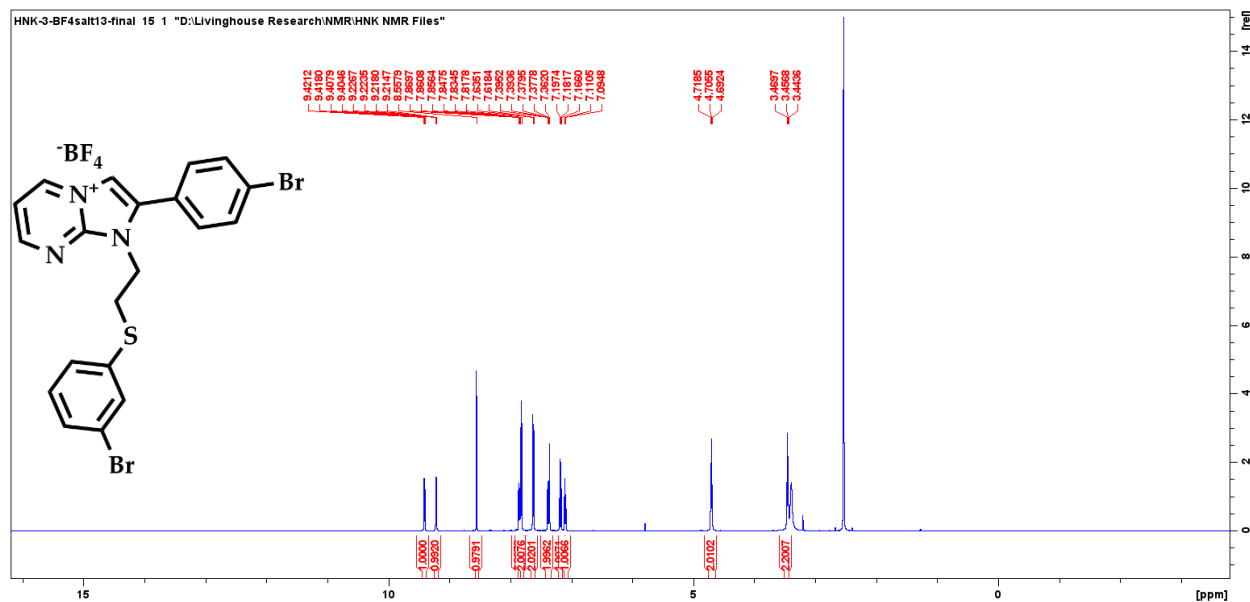


Figure 3.159B: ^1H -NMR Spectra of 2-(4-bromophenyl)-1-(2-((3-bromophenyl)thio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (7.2c).

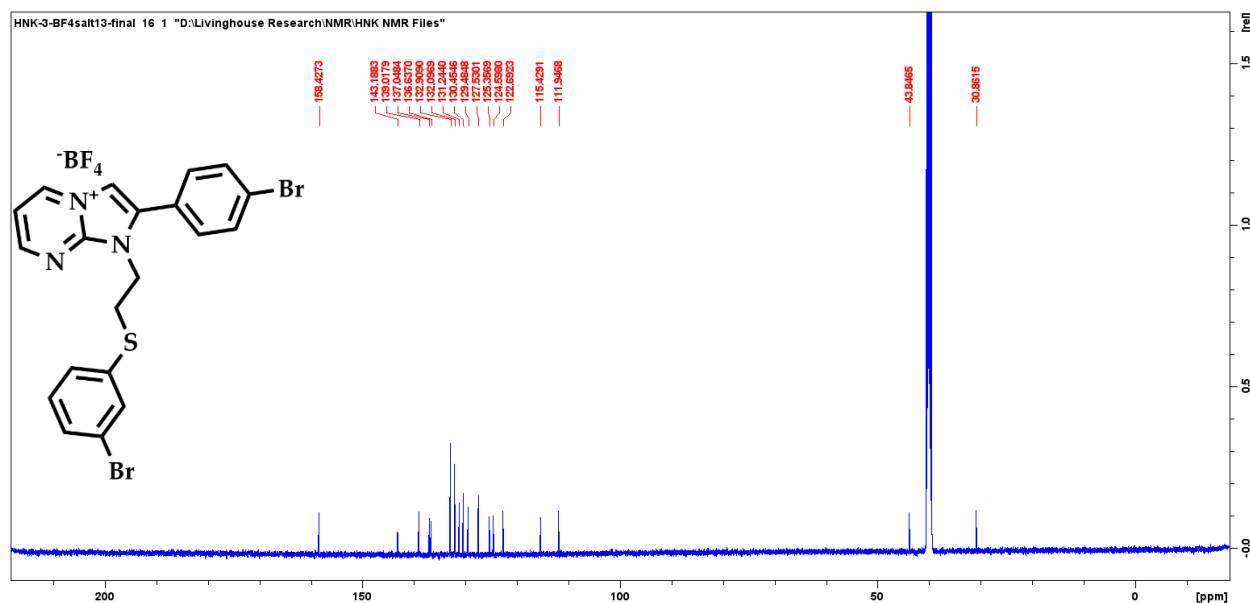


Figure 3.160B: ^{13}C -NMR Spectra of 2-(4-bromophenyl)-1-(2-((3-bromophenyl)thio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (7.2c).

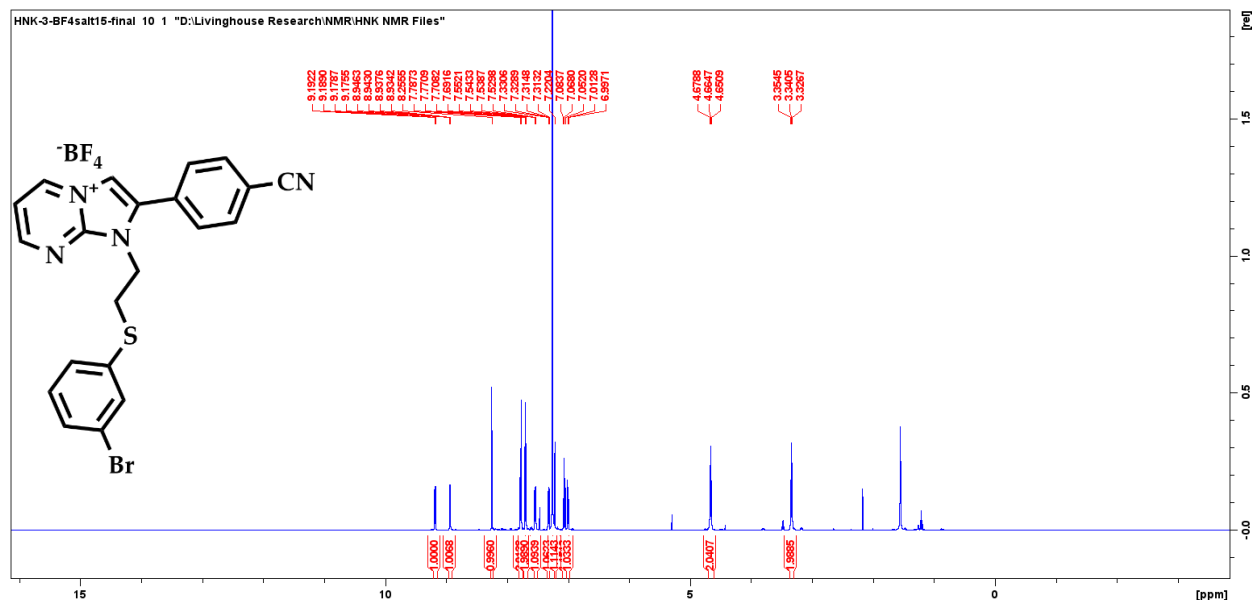


Figure 3.161B: ^1H -NMR Spectra of 1-(2-((3-bromophenyl)thio)ethyl)-2-(4-cyanophenyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**7.2d**).

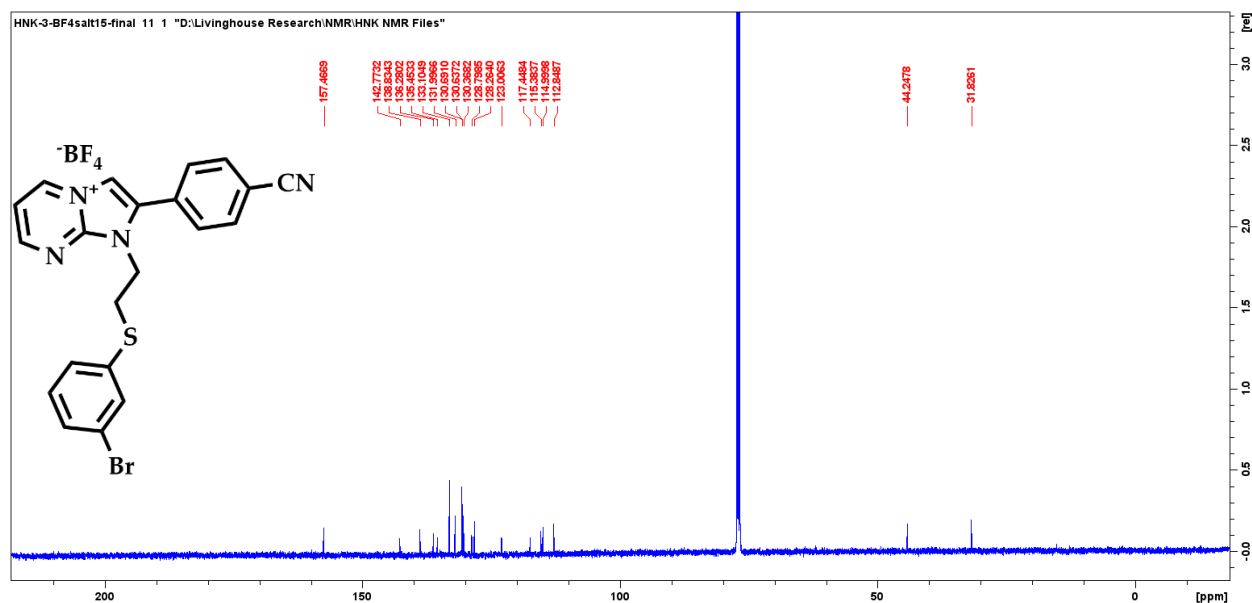


Figure 3.162B: ^{13}C -NMR Spectra of 1-(2-((3-bromophenyl)thio)ethyl)-2-(4-cyanophenyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**7.2d**).

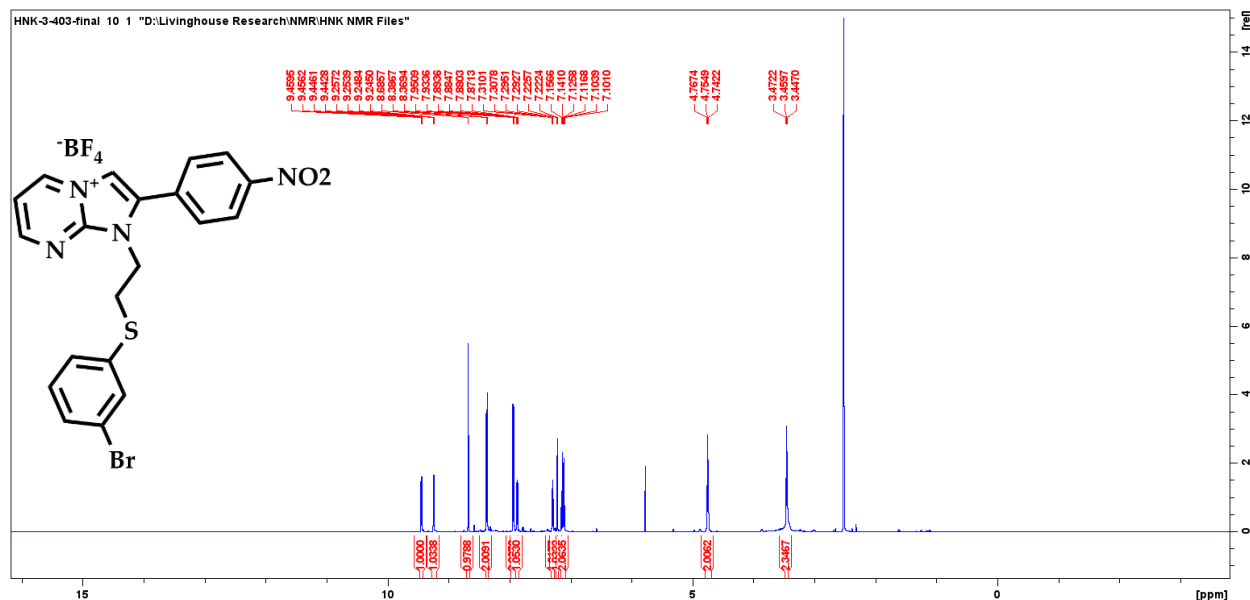
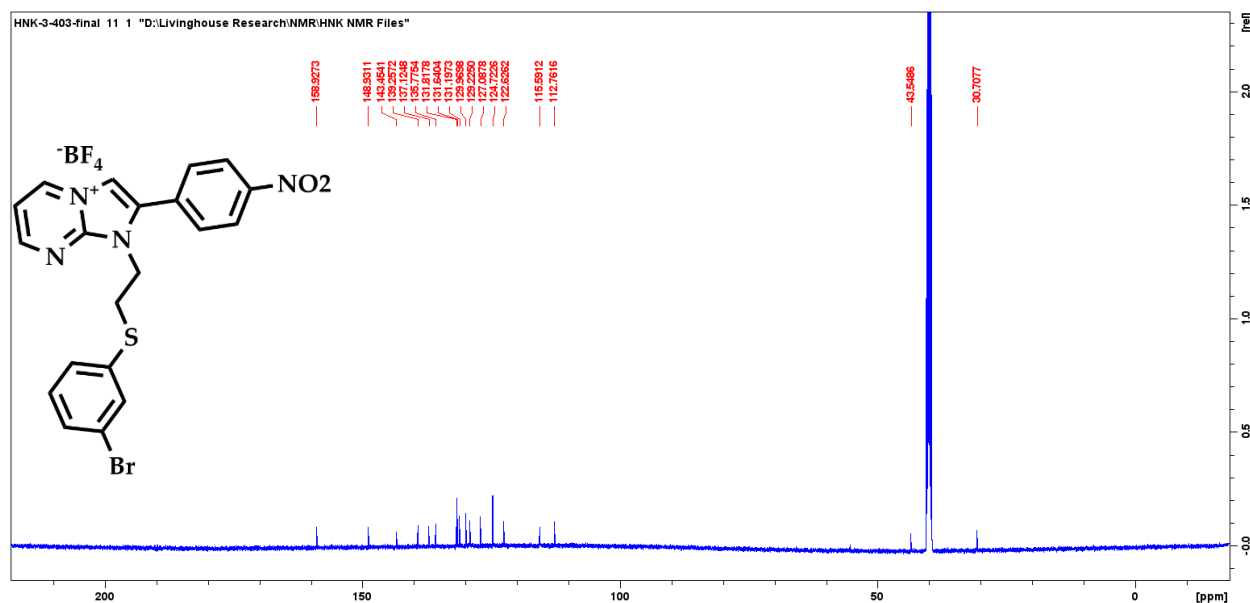


Figure 3.163B: ¹H-NMR Spectra of 1-(2-((3-bromophenyl)thio)ethyl)-2-(4-nitrophenyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (7.2e).



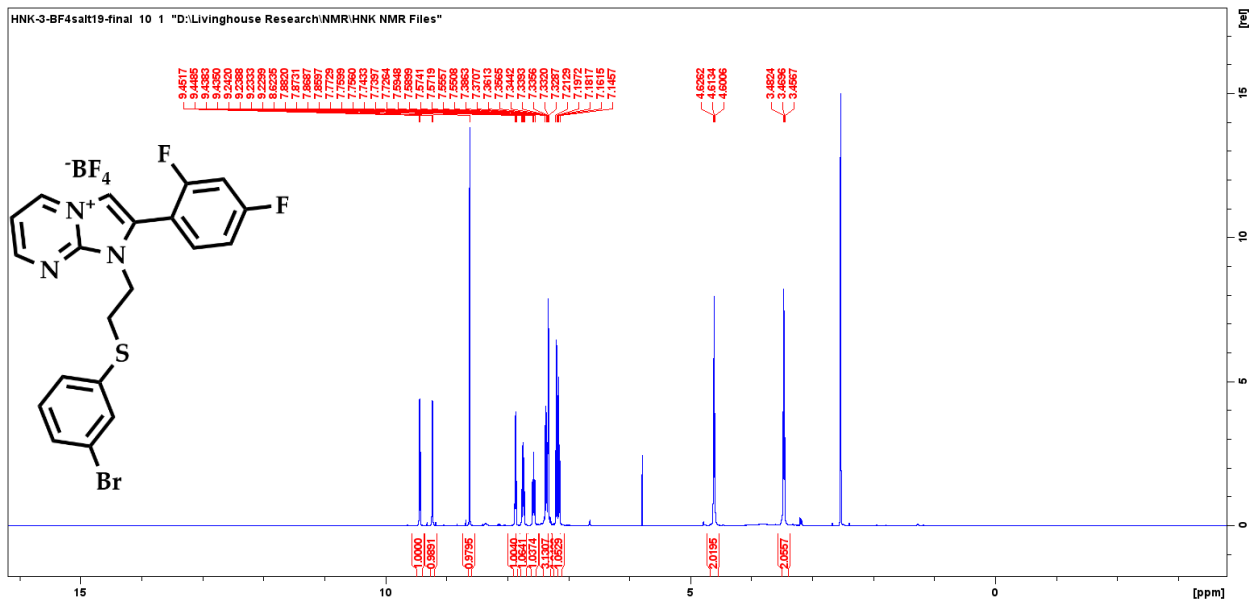


Figure 3.165B: ¹H-NMR Spectra of 1-(2-((3-bromophenyl)thio)ethyl)-2-(2,4-difluorophenyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**7.2f**).

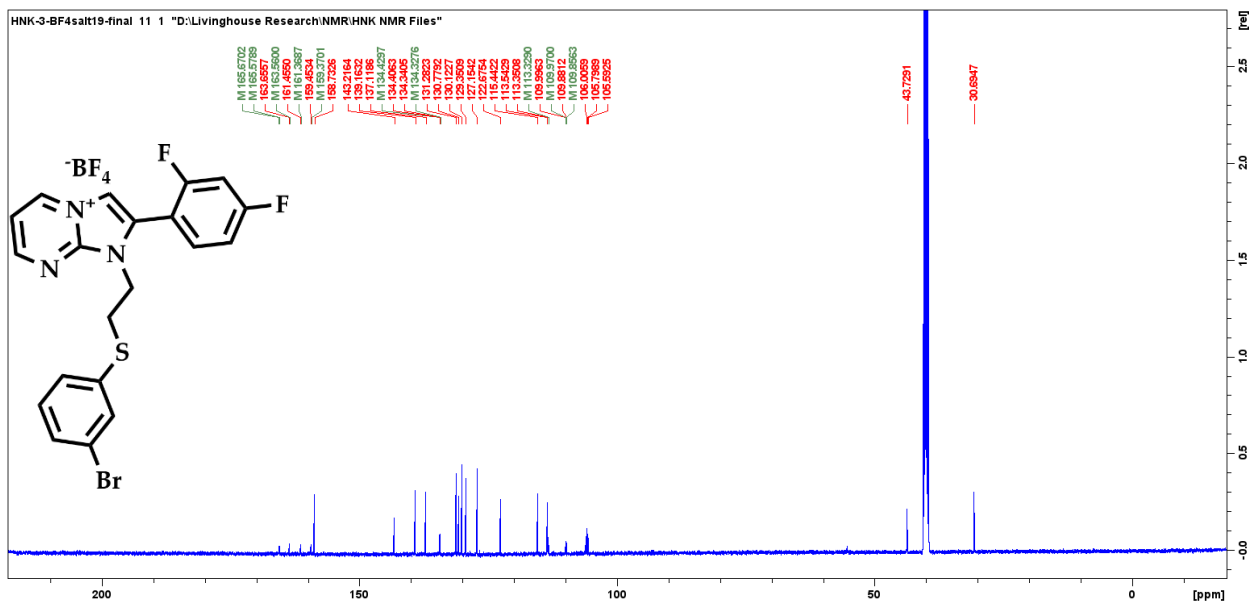


Figure 3.166B: ¹³C-NMR Spectra of 1-(2-((3-bromophenyl)thio)ethyl)-2-(2,4-difluorophenyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**7.2f**).

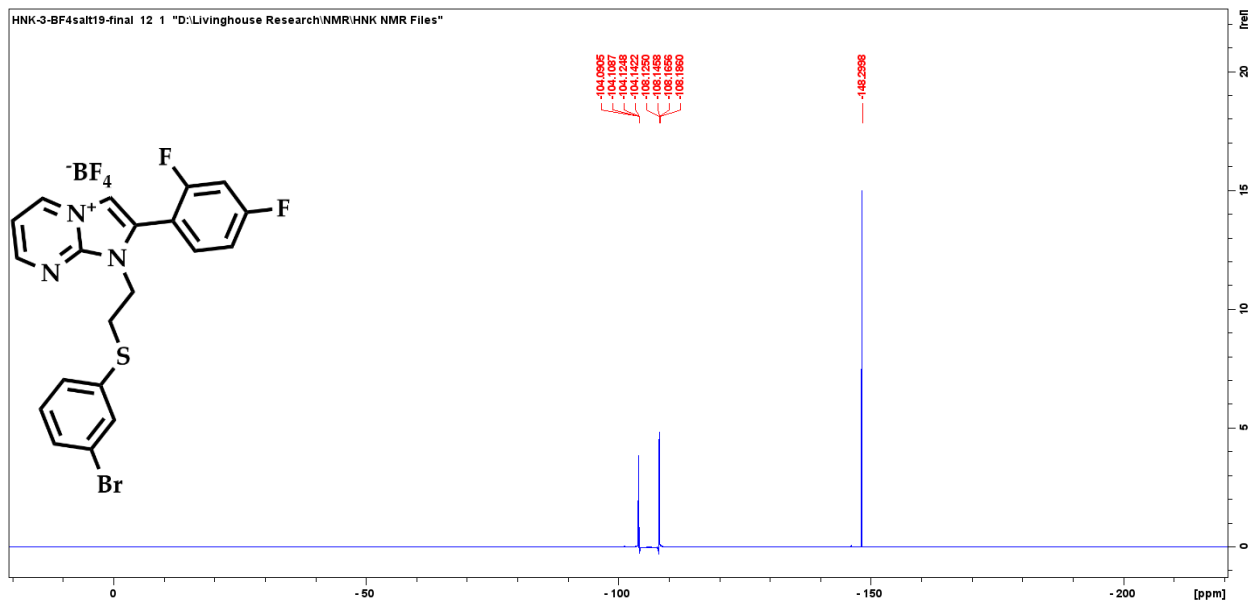


Figure 3.167B: ^{19}F -NMR Spectra of 1-((2-((4-bromophenyl)thio)ethyl)-2-(2,4-difluorophenyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (7.2f).

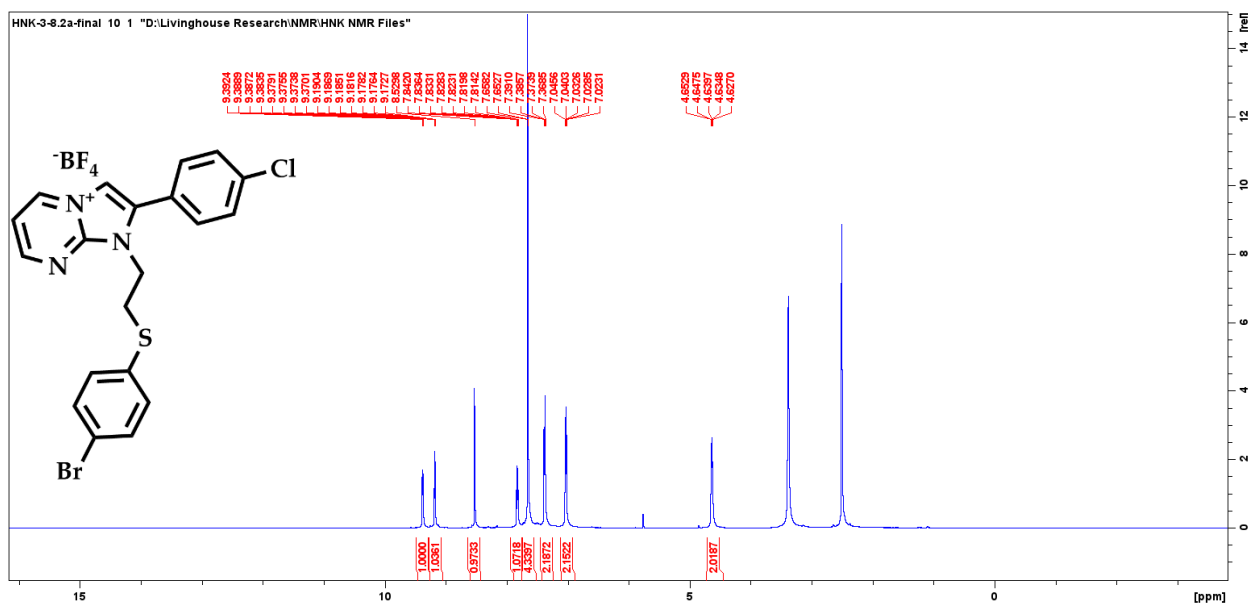


Figure 3.168B: ^1H -NMR Spectra of 2-(4-chlorophenyl)-1-((2-((4-bromophenyl)thio)ethyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (8.2a).

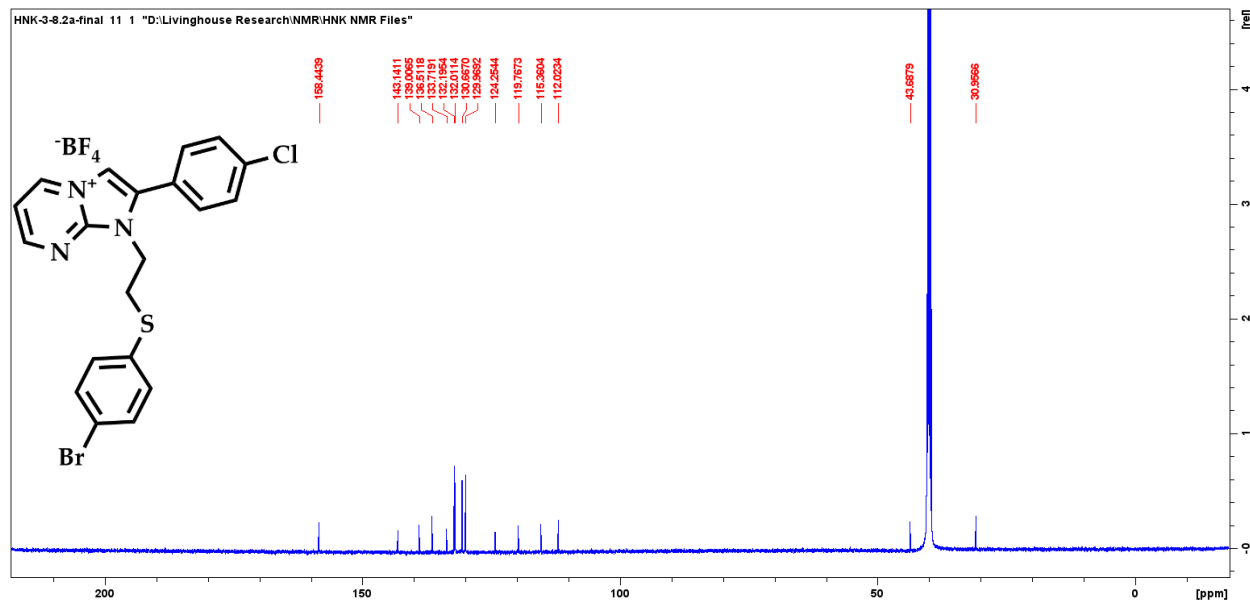


Figure 3.169B: ^{13}C -NMR Spectra of 2-(4-chlorophenyl)-1-(2-((4-bromophenyl)thio)ethyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (**8.2a**).

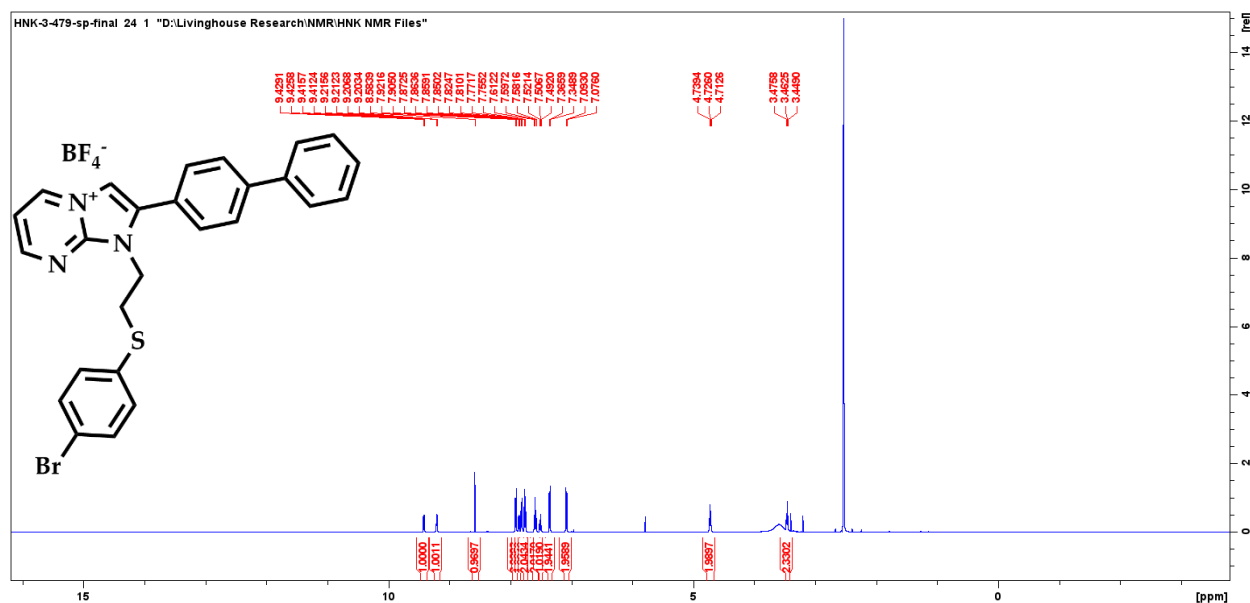


Figure 3.170B: ^1H -NMR Spectra of 2-([1,1'-biphenyl]-4-yl)-1-(2-((4-bromophenyl)thio)ethyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (**8.2b**).

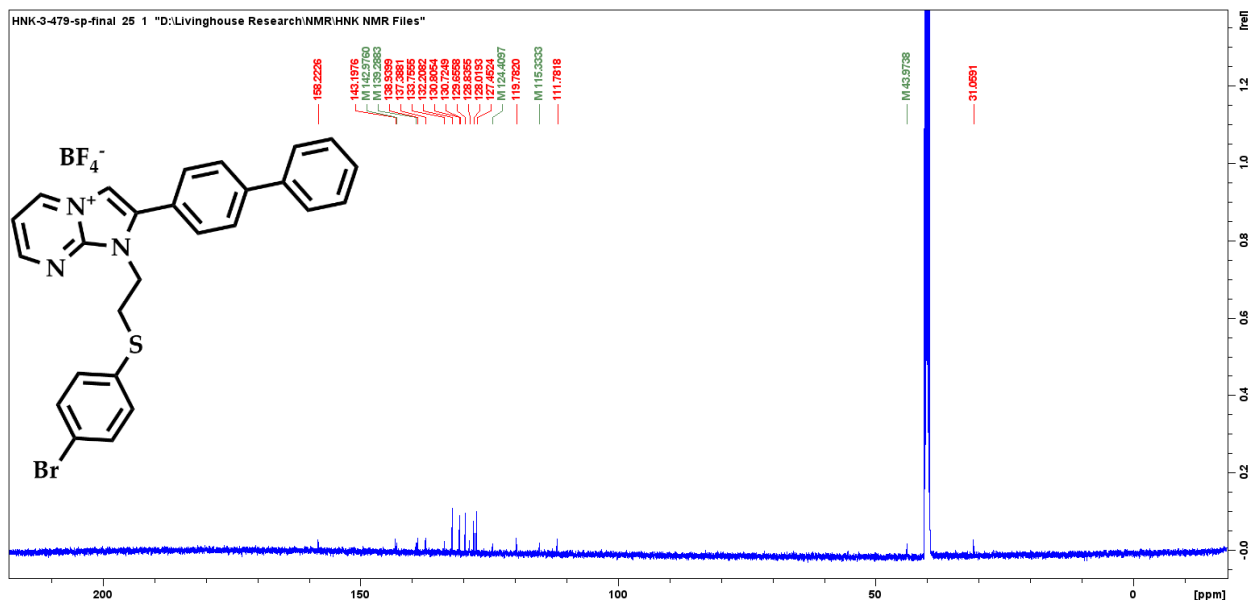


Figure 3.171B: ¹³C-NMR Spectra of 2-([1,1'-biphenyl]-4-yl)-1-(2-((4-bromophenyl)thio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**8.2b**).

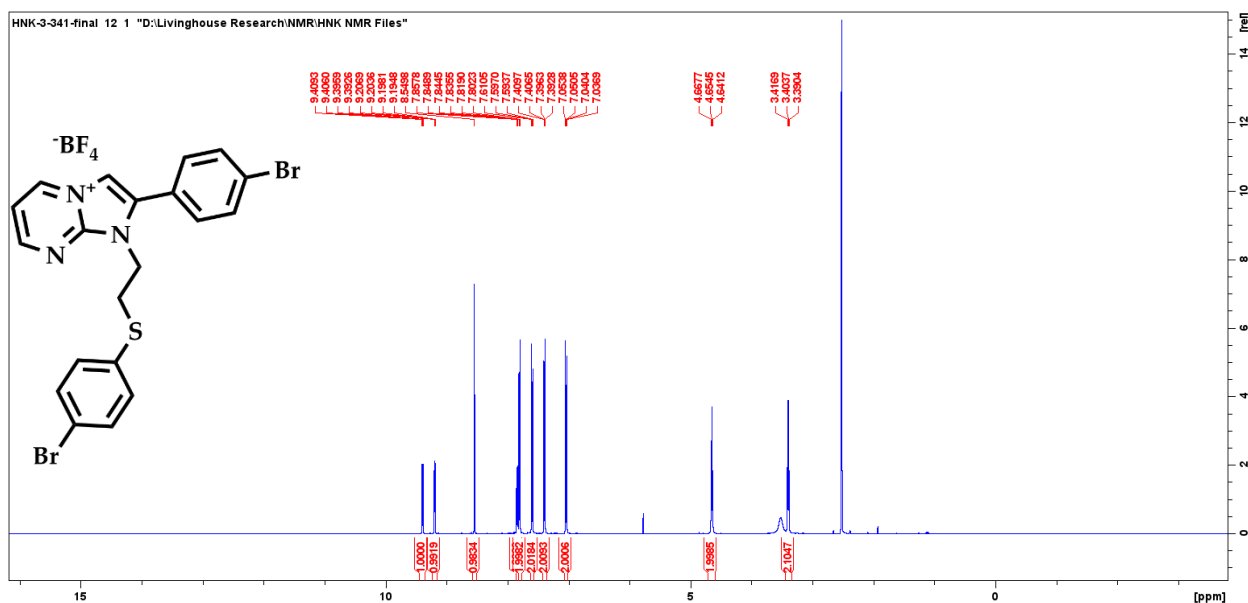


Figure 3.172B: ¹H-NMR Spectra of 2-(4-bromophenyl)-1-(2-((4-bromophenyl)thio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**8.2c**).

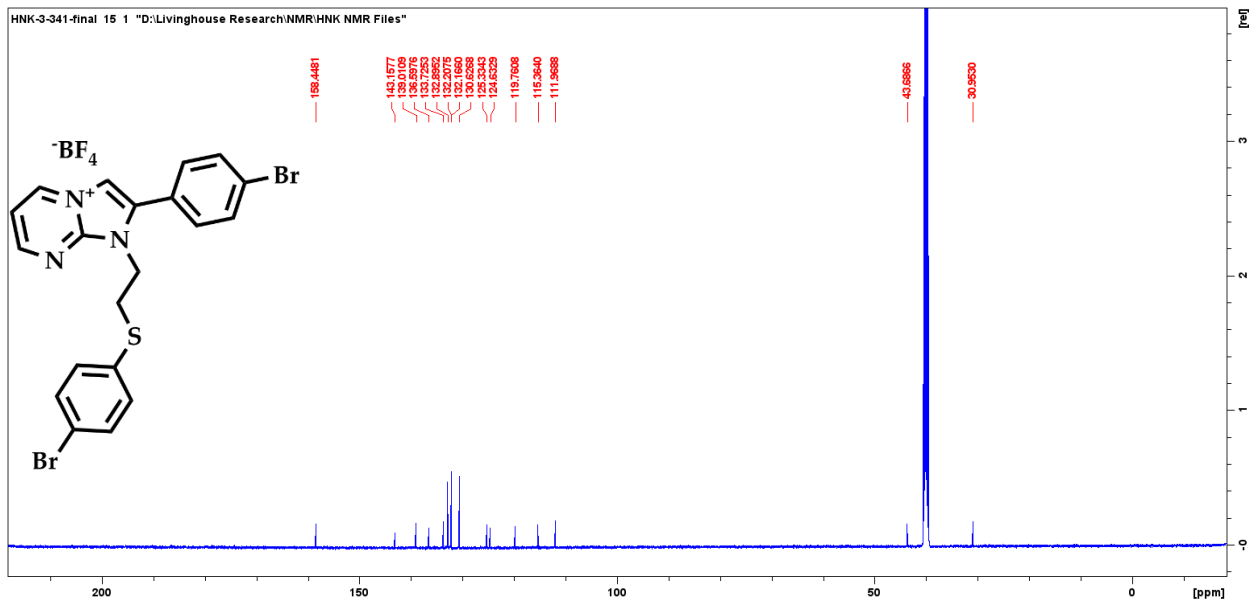


Figure 3.173B: ¹³C-NMR Spectra of 2-(4-bromophenyl)-1-(2-((4-bromophenyl)thio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**8.2c**).

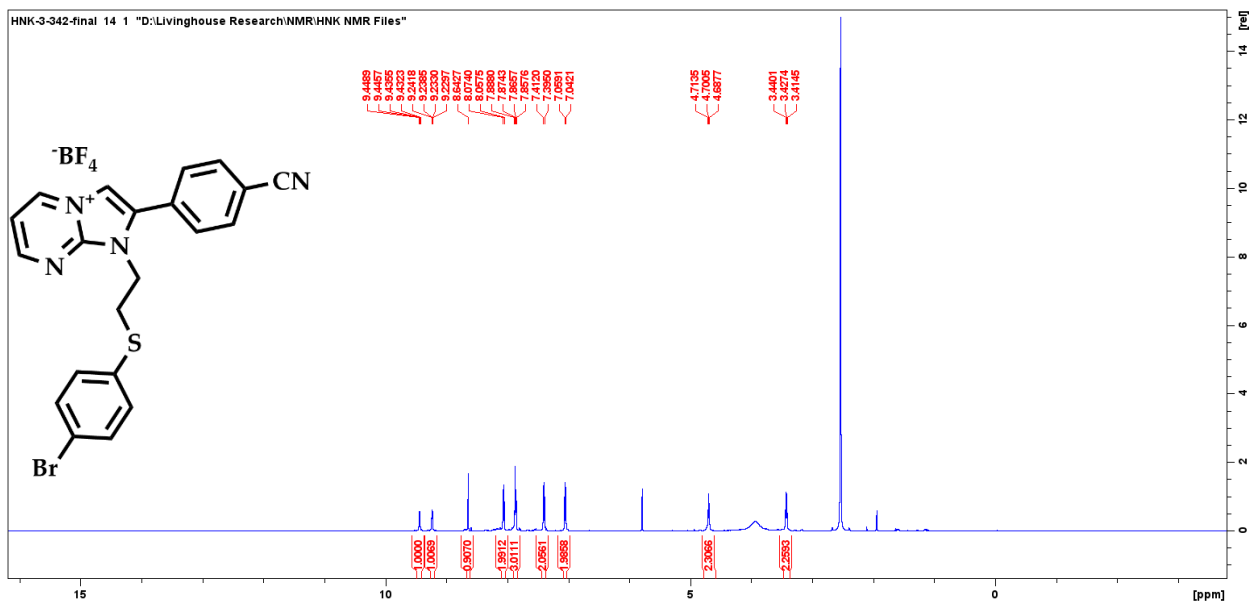


Figure 3.174B: ¹H-NMR Spectra of 1-((2-((4-bromophenyl)thio)ethyl)-2-(4-cyanophenyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (**8.2d**).

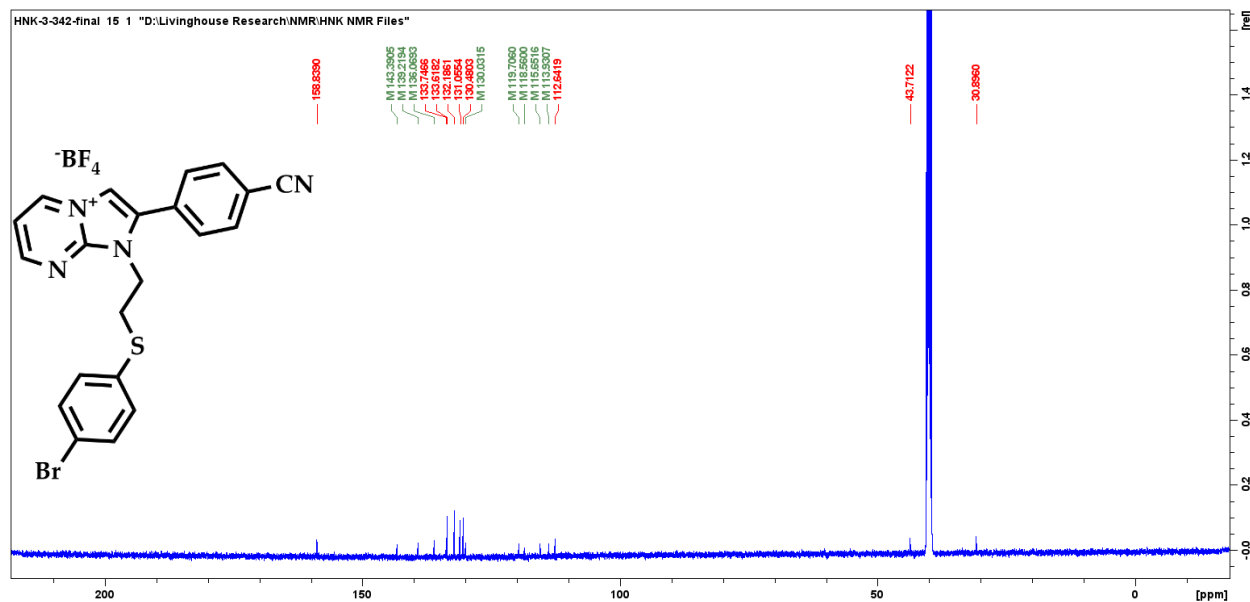


Figure 3.175B: ^{13}C -NMR Spectra of 1-(2-((4-bromophenyl)thio)ethyl)-2-(4-cyanophenyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (**8.2d**).

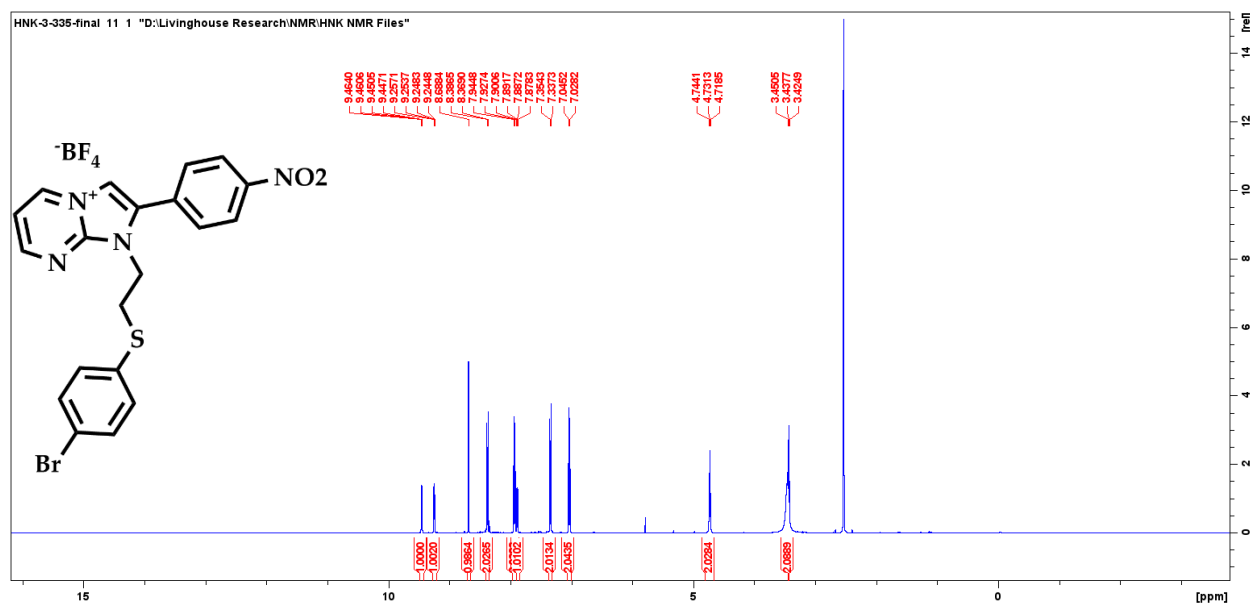


Figure 3.176B: ^1H -NMR Spectra of 1-(2-((4-bromophenyl)thio)ethyl)-2-(4-nitrophenyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (**8.2e**).

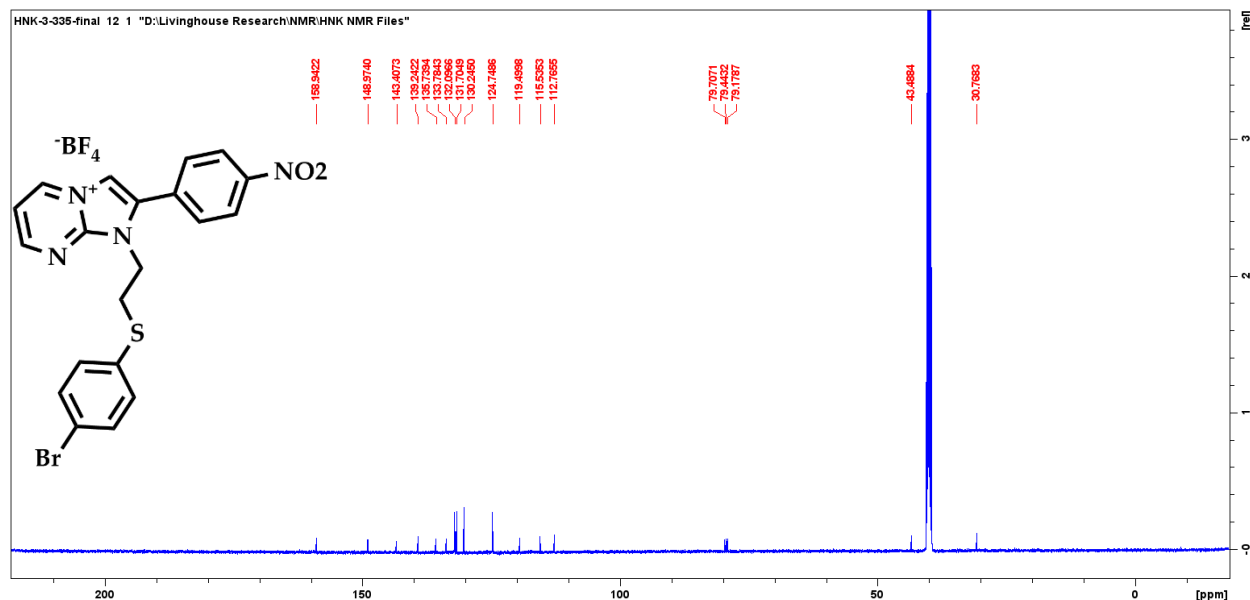


Figure 3.177B: ¹³C-NMR Spectra of 1-(2-((4-bromophenyl)thio)ethyl)-2-(4-nitrophenyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (**8.2e**).

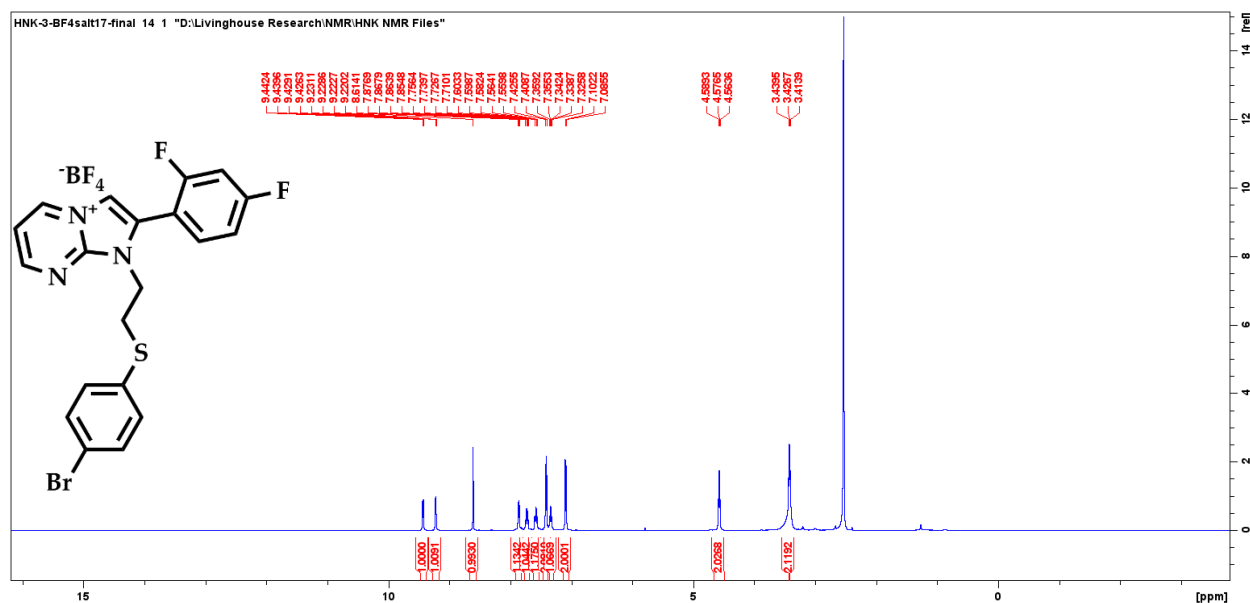


Figure 3.178B: ¹H-NMR Spectra of 1-(2-((4-bromophenyl)thio)ethyl)-2-(2,4-difluorophenyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (**8.2f**).

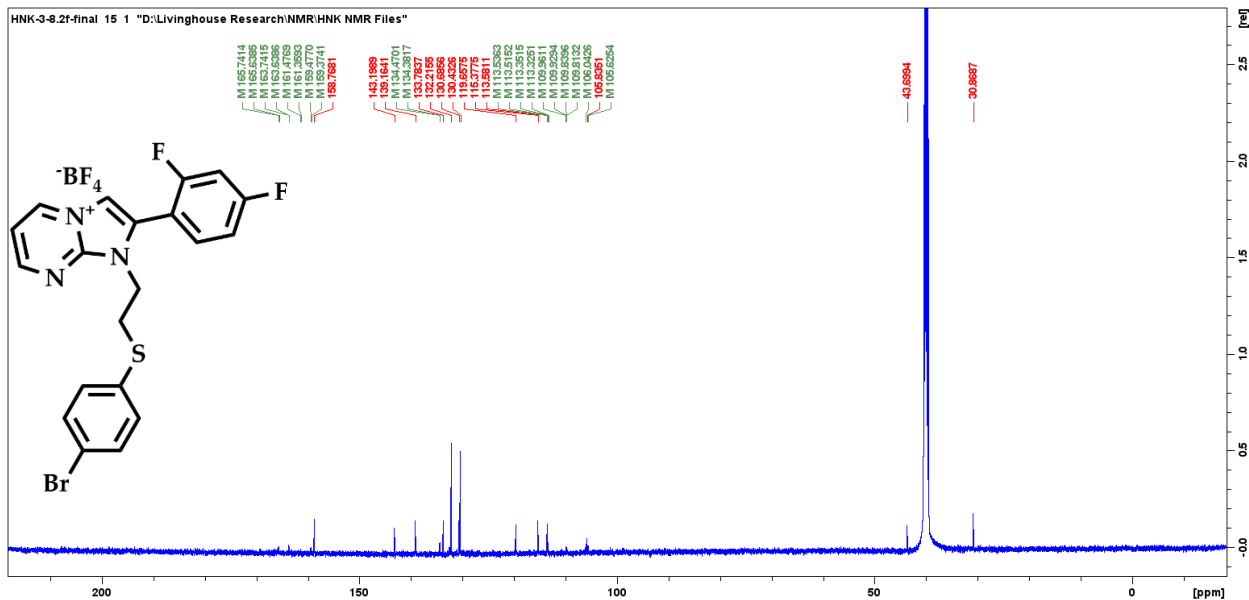


Figure 3.179B: ¹³C-NMR Spectra of 1-(2-((4-bromophenyl)thio)ethyl)-2-(2,4-difluorophenyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**8.2f**).

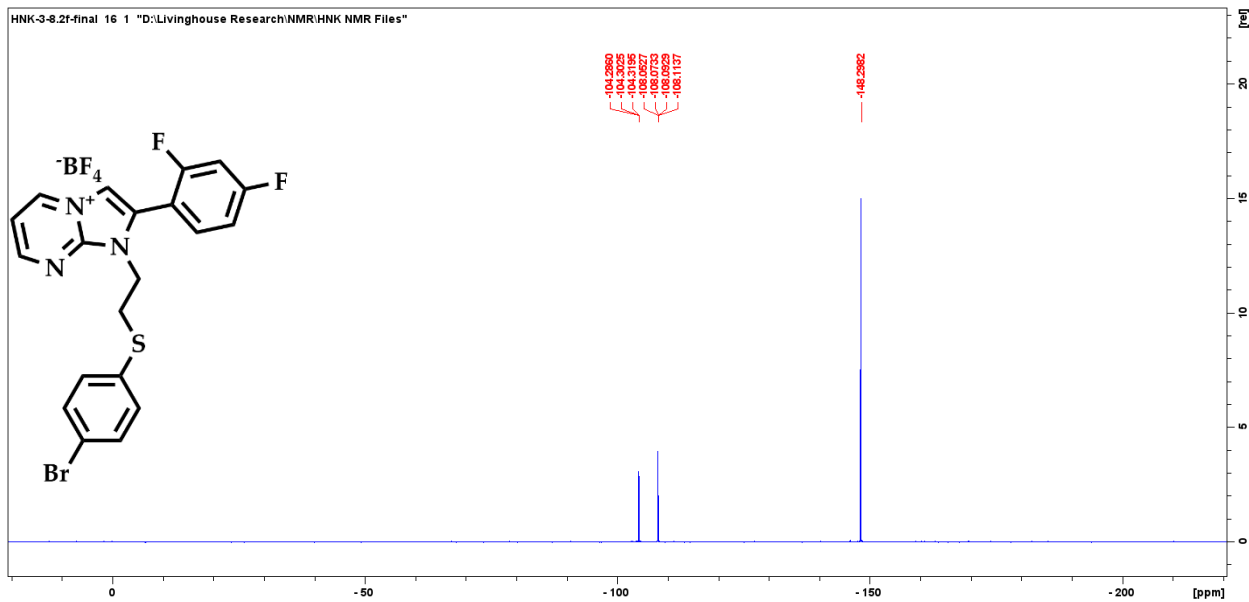


Figure 3.180B: ^{19}F -NMR Spectra of 1-(2-((4-bromophenyl)thio)ethyl)-2-(2,4-difluorophenyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**8.2f**).

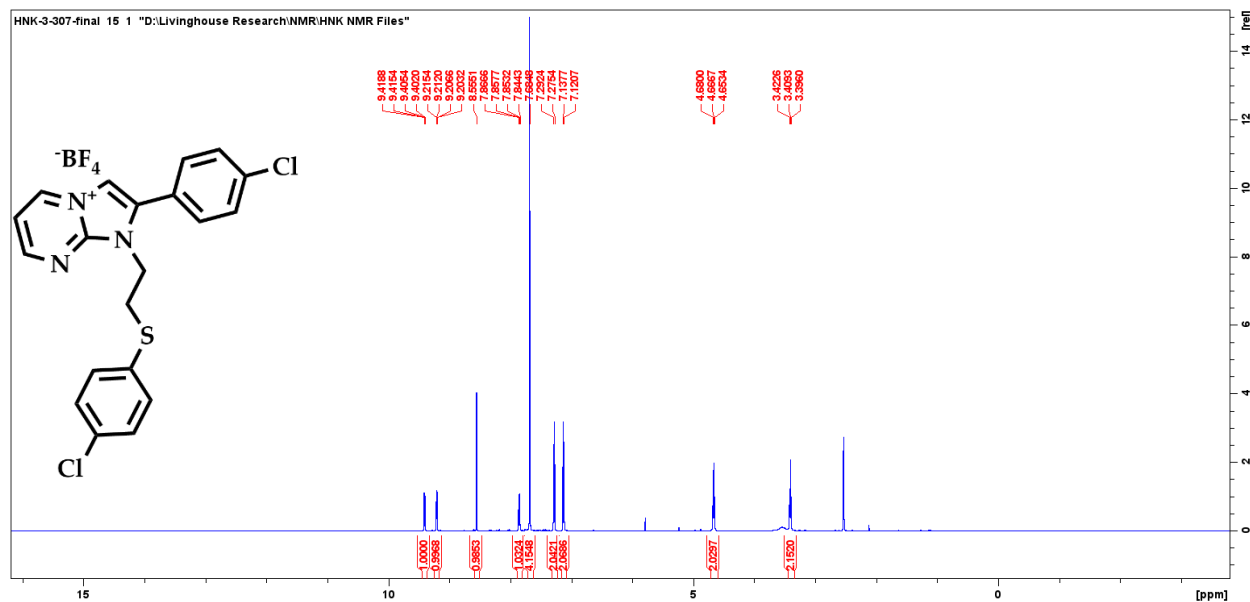


Figure 3.181B: ¹H-NMR Spectra of 2-(4-chlorophenyl)-1-(2-((4-chlorophenyl)thio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**9.2a**).

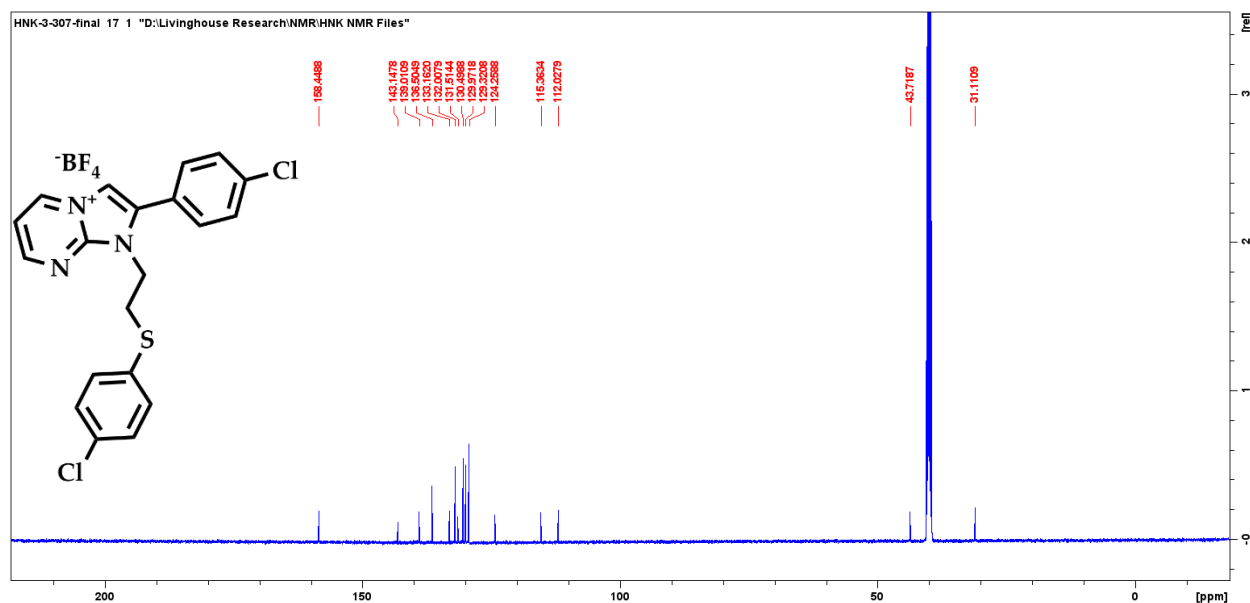


Figure 3.182B: ¹³C-NMR Spectra of 2-(4-chlorophenyl)-1-(2-((4-chlorophenyl)thio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**9.2a**).

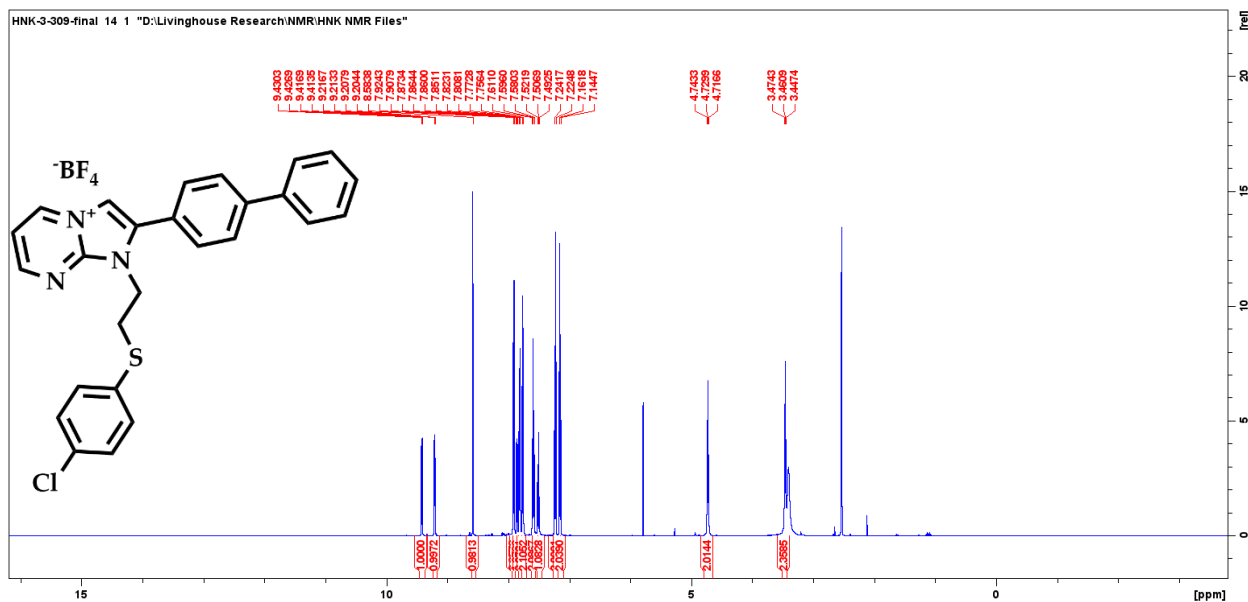


Figure 3.183B: ^1H -NMR Spectra of 2-([1,1'-biphenyl]-4-yl)-1-(2-((4-chlorophenyl)thio)ethyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (**9.2b**).

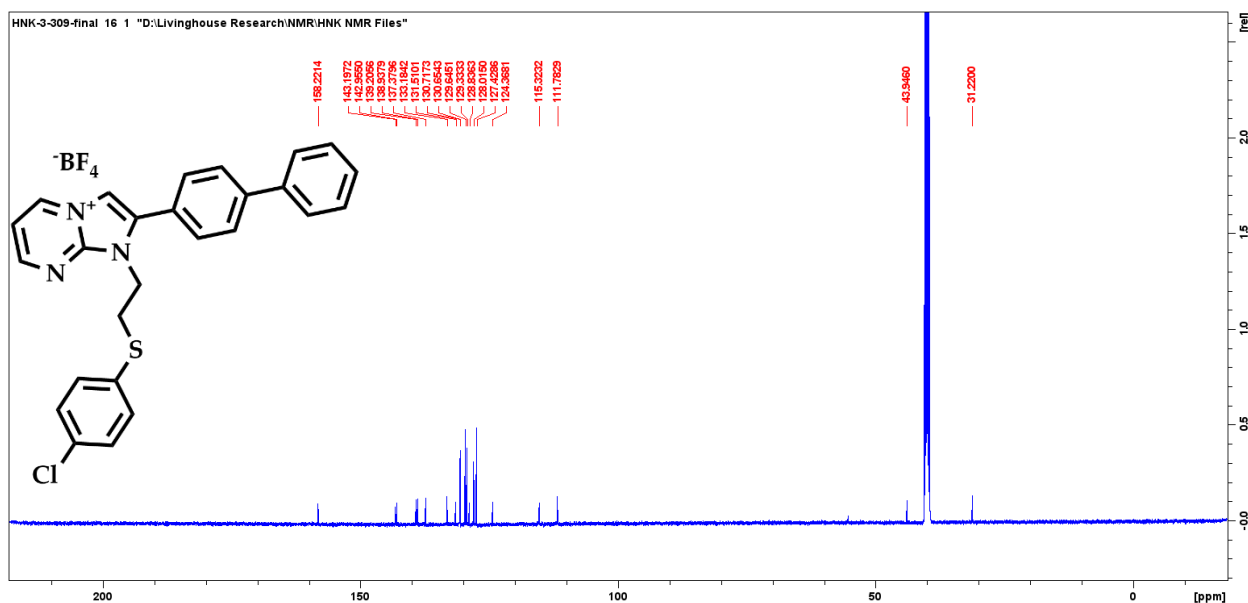


Figure 3.184B: ^{13}C -NMR Spectra of 2-([1,1'-biphenyl]-4-yl)-1-(2-((4-chlorophenyl)thio)ethyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (**9.2b**).

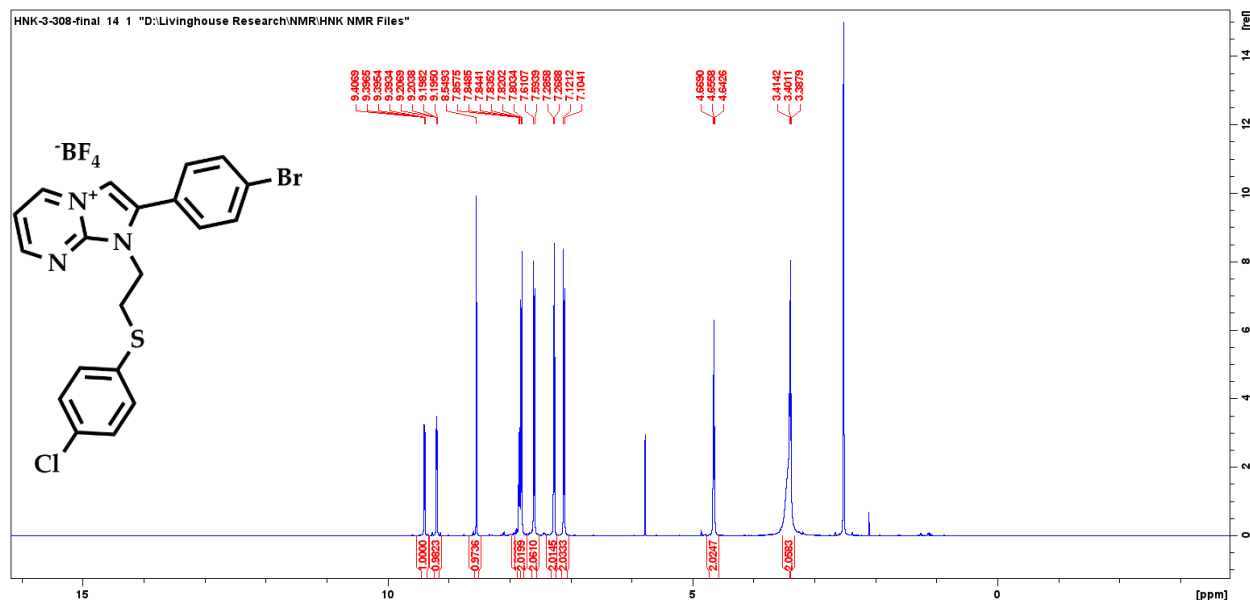


Figure 3.185B: ^1H -NMR Spectra of 2-(4-bromophenyl)-1-(2-((4-chlorophenyl)thio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (9.2c).

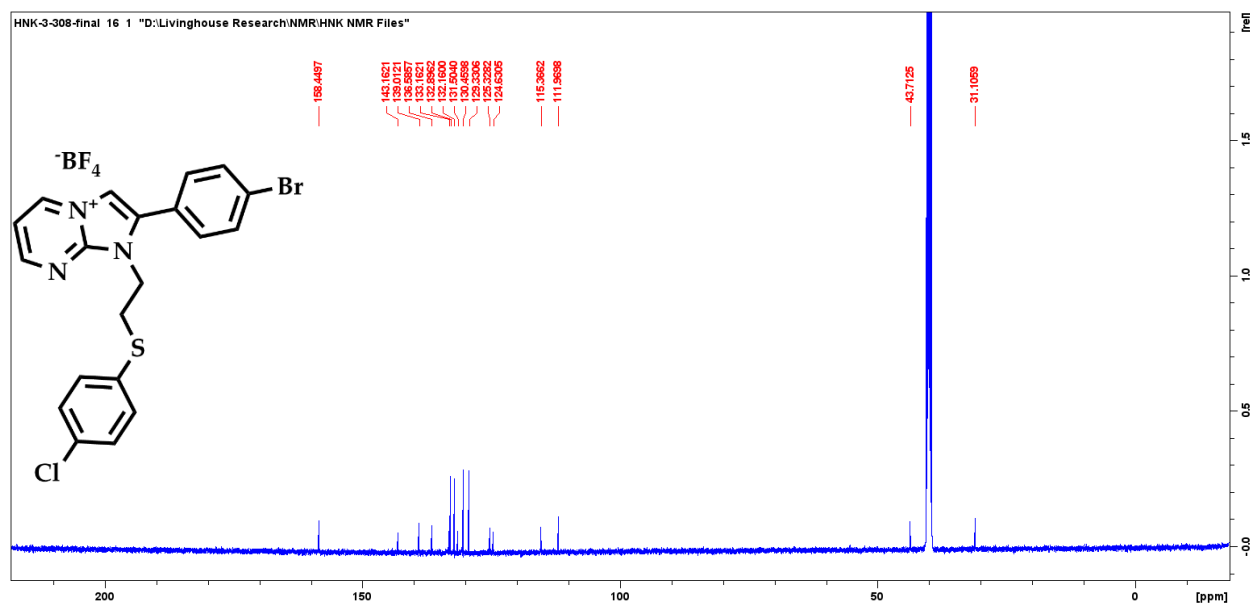


Figure 3.186B: ^{13}C -NMR Spectra of 2-(4-bromophenyl)-1-(2-((4-chlorophenyl)thio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (9.2c).

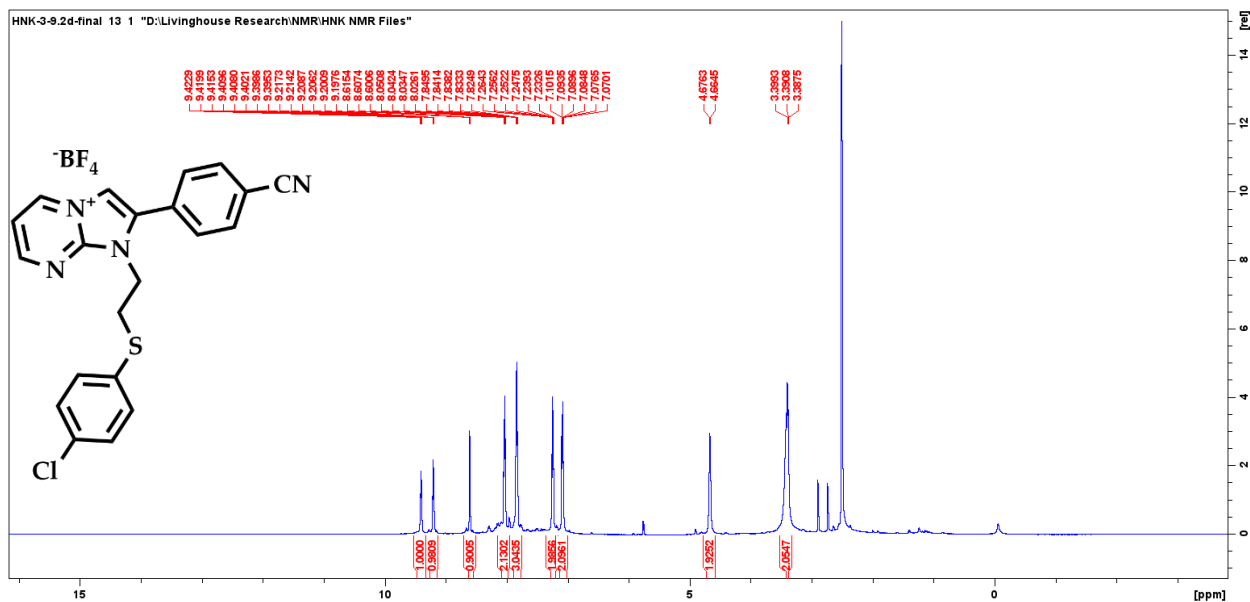


Figure 3.187B: ¹H-NMR Spectra of 1-(2-((4-chlorophenyl)thio)ethyl)-2-(4-cyanophenyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (**9.2d**).

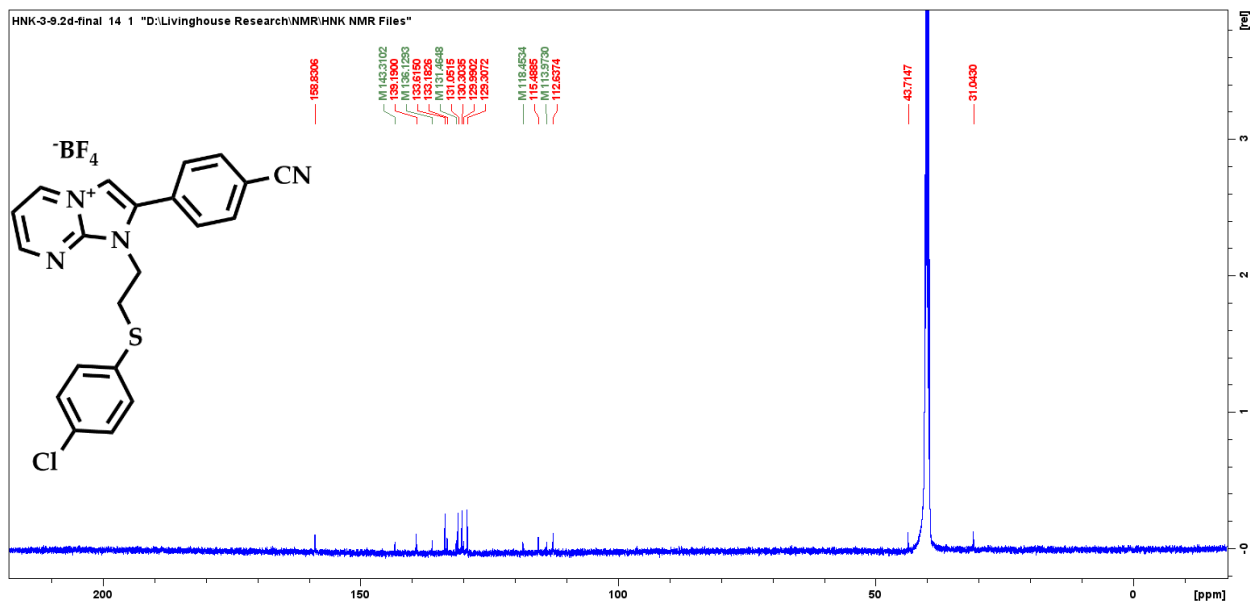


Figure 3.188B: ¹³C-NMR Spectra of 1-(2-((4-chlorophenyl)thio)ethyl)-2-(4-cyanophenyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (**9.2d**).

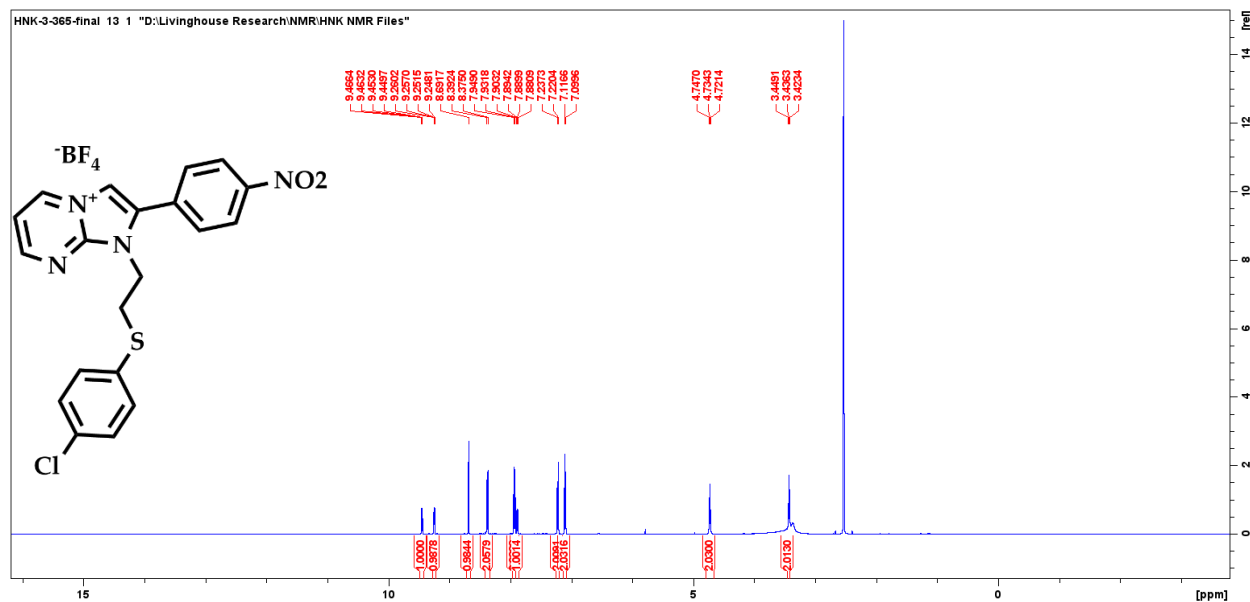


Figure 3.189B: ^1H -NMR Spectra of 1-(2-((4-chlorophenyl)thio)ethyl)-2-(4-nitrophenyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**9.2e**).

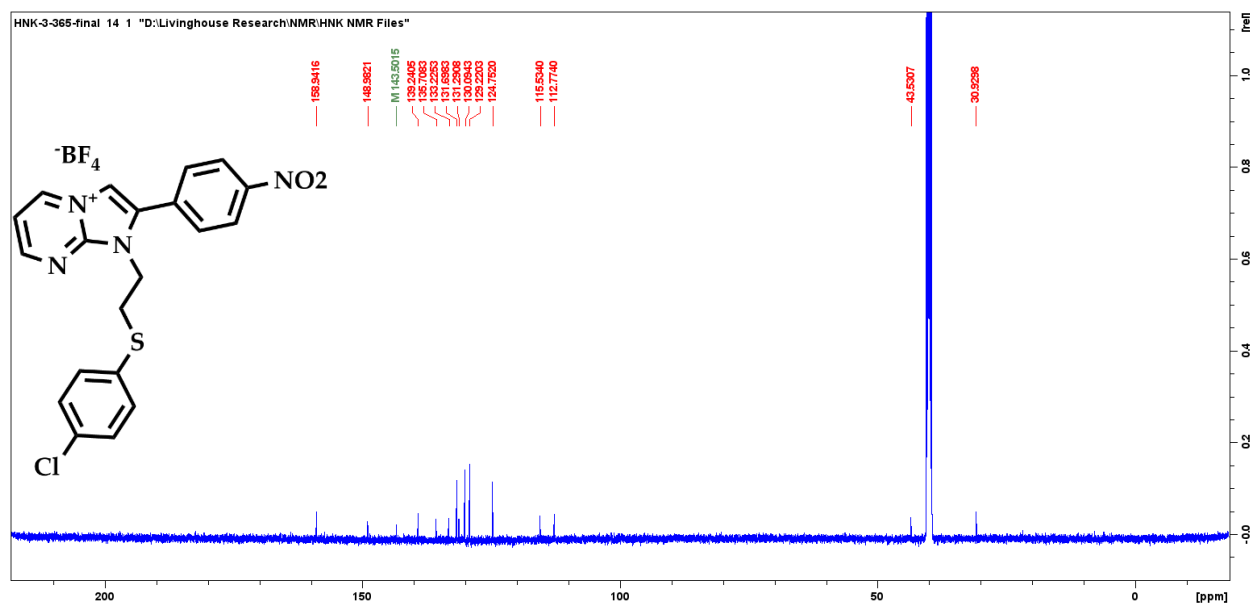
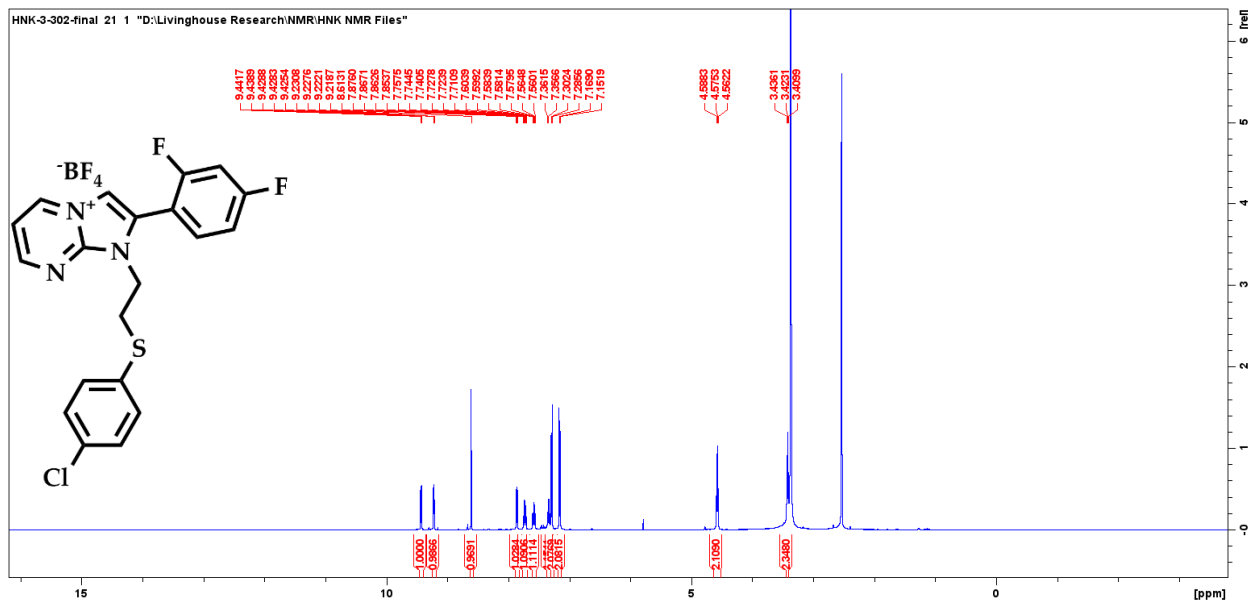


Figure 3.190B: ^{13}C -NMR Spectra of 1-(2-((4-chlorophenyl)thio)ethyl)-2-(4-nitrophenyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**9.2e**).



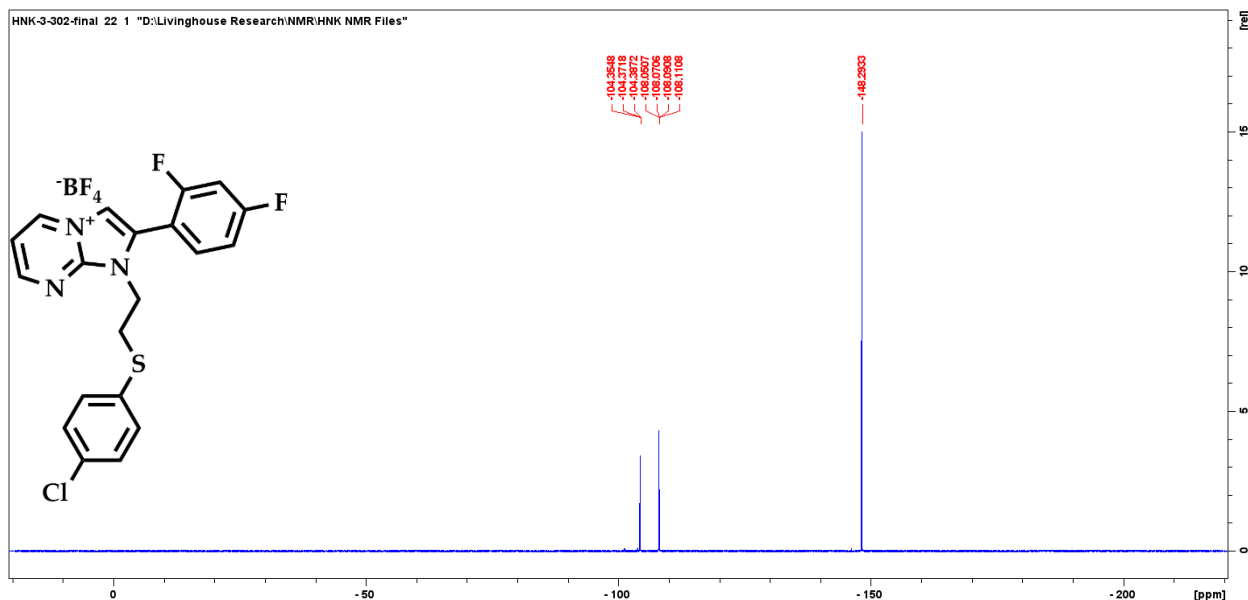


Figure 3.193B: ¹⁹F-NMR Spectra of 1-(2-((4-chlorophenyl)thio)ethyl)-2-(2,4-difluorophenyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (**9.2f**).

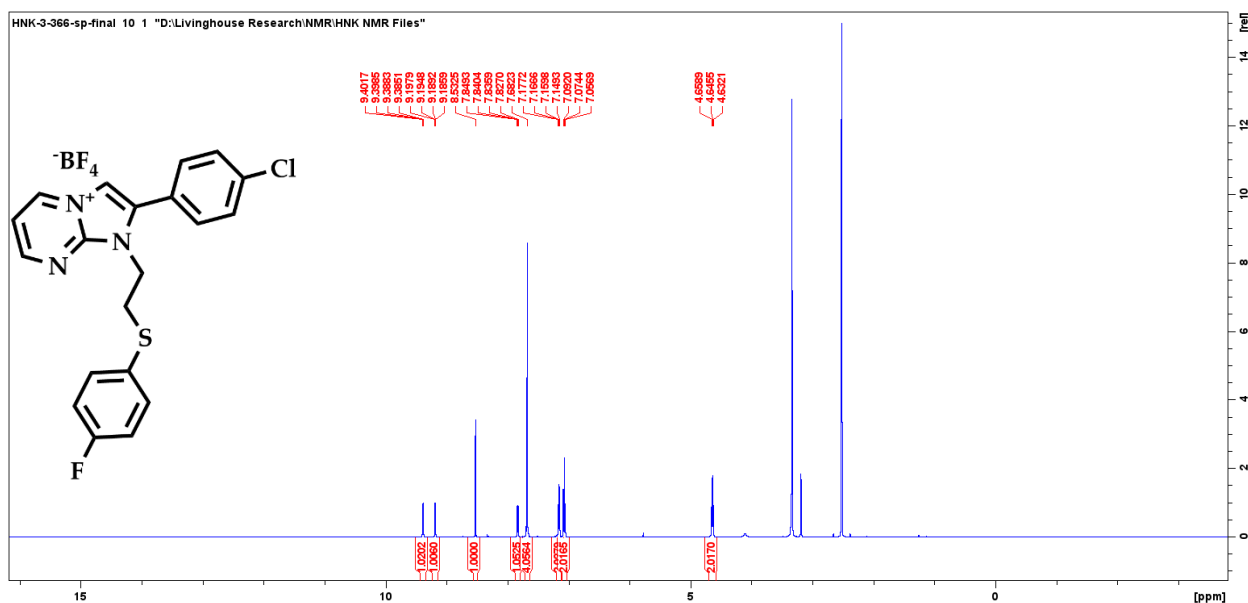


Figure 3.194B: ¹H-NMR Spectra of 2-(4-chlorophenyl)-1-(2-((4-fluorophenyl)thio)ethyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (**10.2a**).

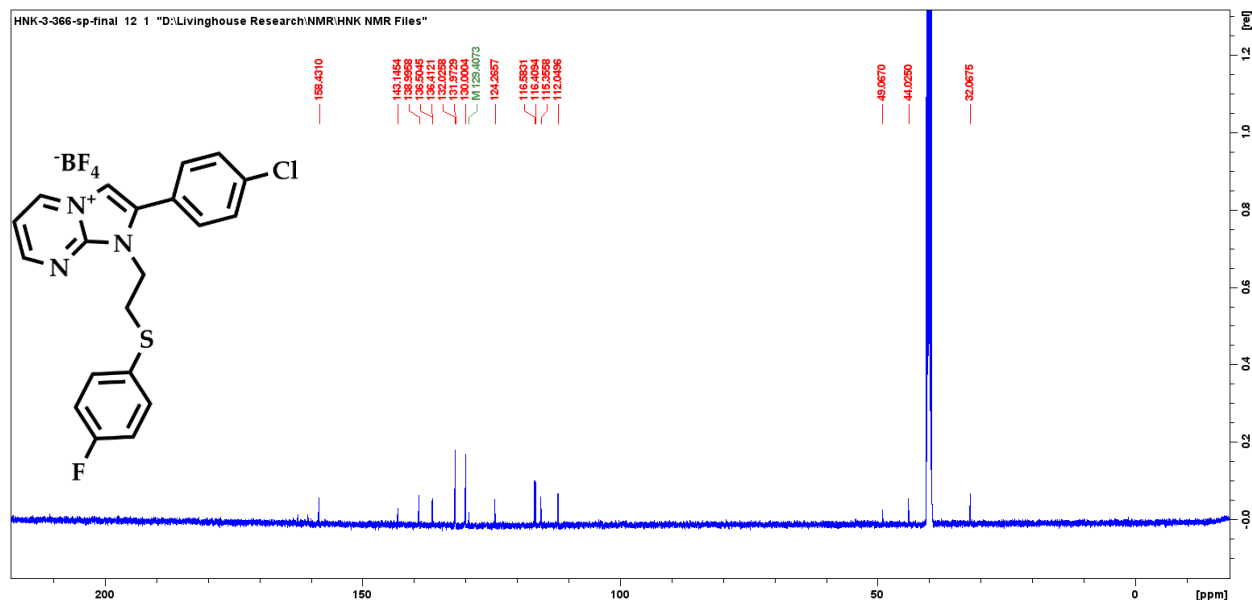


Figure 3.195B: ^{13}C -NMR Spectra of 2-(4-chlorophenyl)-1-(2-((4-fluorophenyl)thio)ethyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (**10.2a**).

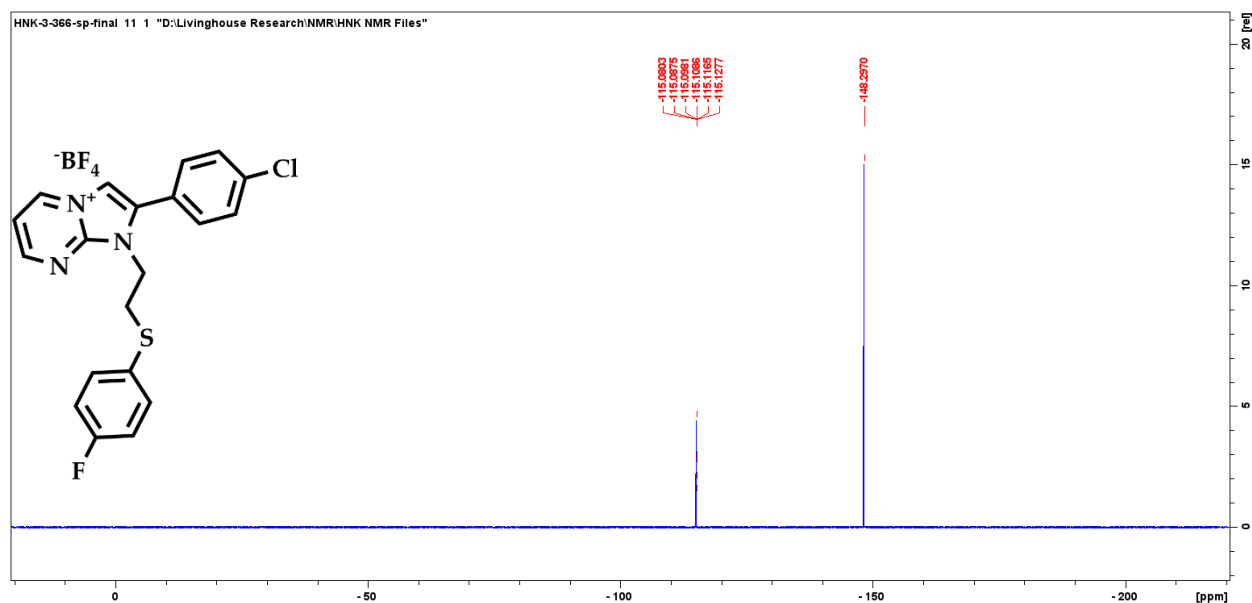


Figure 3.196B: ^{19}F -NMR Spectra of 2-(4-chlorophenyl)-1-(2-((4-fluorophenyl)thio)ethyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (**10.2a**).

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Chemical structure: c1ccc(cc1)-c2ccc(cc2)n3cc[n+]3CSC4=CC=C(F)C=C4.[B-](F)(F)F

¹³C NMR spectrum (ppm):

- 198.1961
- 143.1915
- 142.9532
- 138.5124
- 137.2009
- 132.7595
- 132.1597
- 130.6757
- 129.5900
- 128.8498
- 128.0414
- 124.3817
- 116.5835
- 116.4096
- 115.3156
- 111.0600
- 44.5372
- 32.2022

Figure 3.198B: ^{13}C -NMR Spectra of 2-([1,1'-biphenyl]-4-yl)-1-(2-((4-fluorophenyl)thio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**10.2b**).

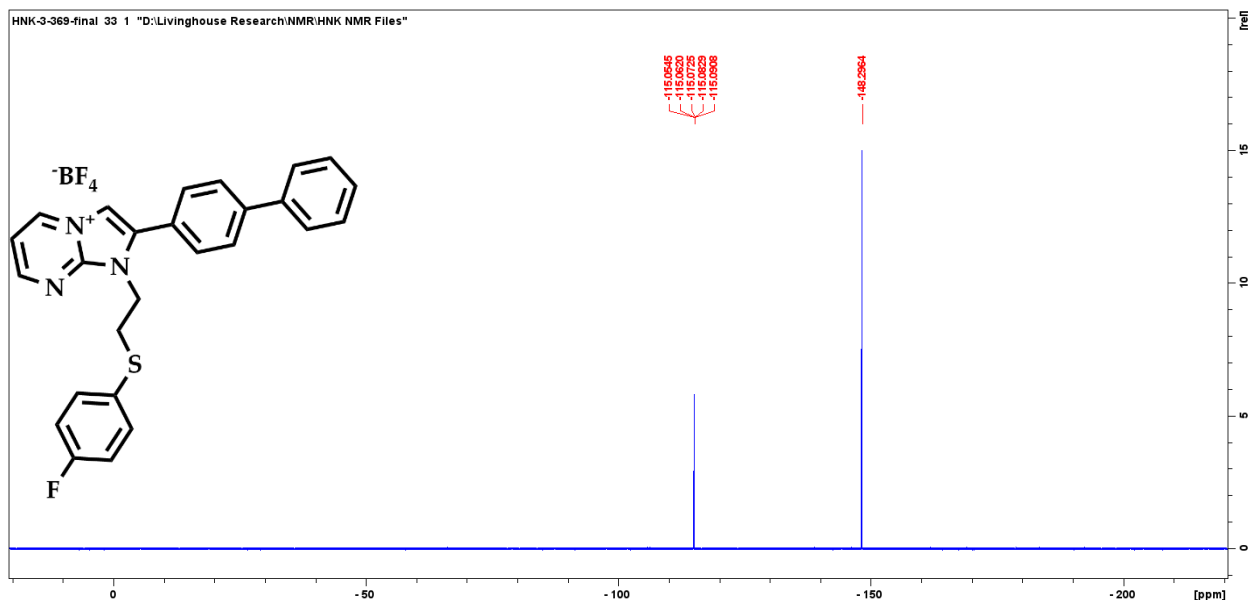


Figure 3.199B: ^{19}F -NMR Spectra of 2-([1,1'-biphenyl]-4-yl)-1-(2-((4-fluorophenyl)thio)ethyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (**10.2b**).

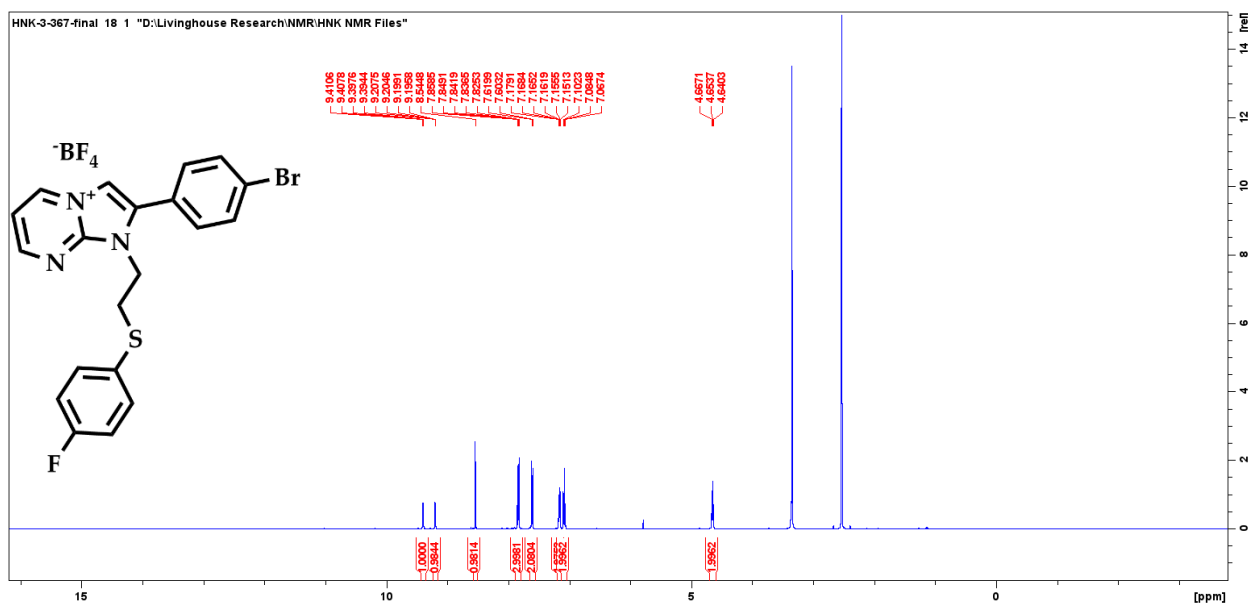


Figure 3.200B: ^1H -NMR Spectra of 2-(4-bromophenyl)-1-(2-((4-fluorophenyl)thio)ethyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (**10.2c**).

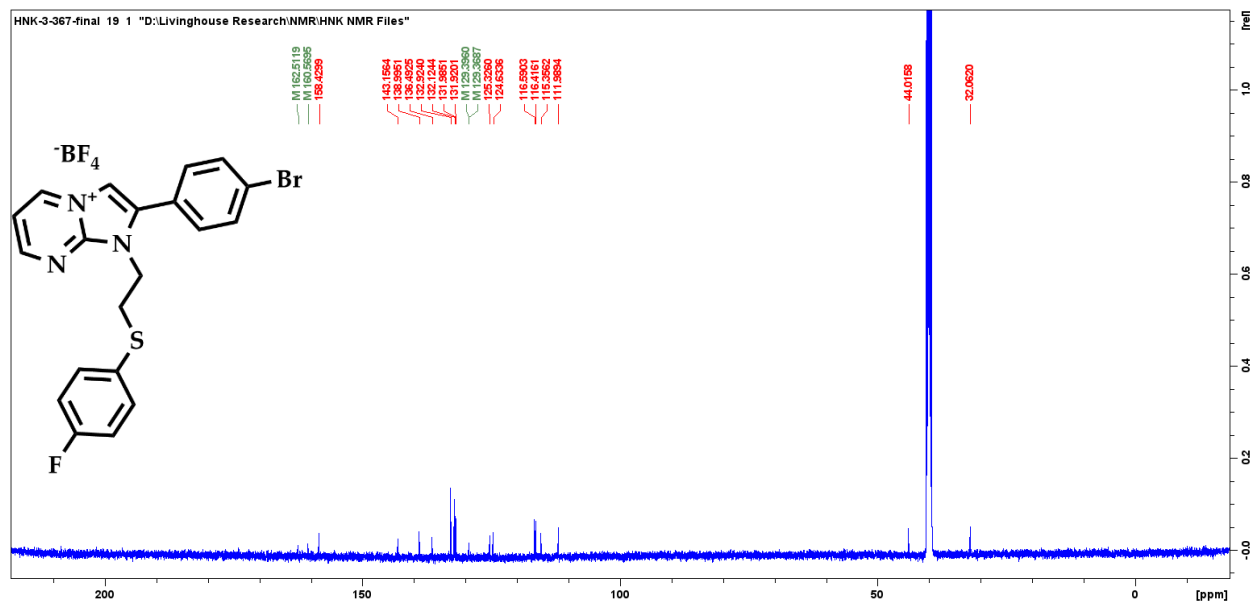


Figure 3.201B: ¹³C-NMR Spectra of 2-(4-bromophenyl)-1-(2-((4-fluorophenyl)thio)ethyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (**10.2c**).

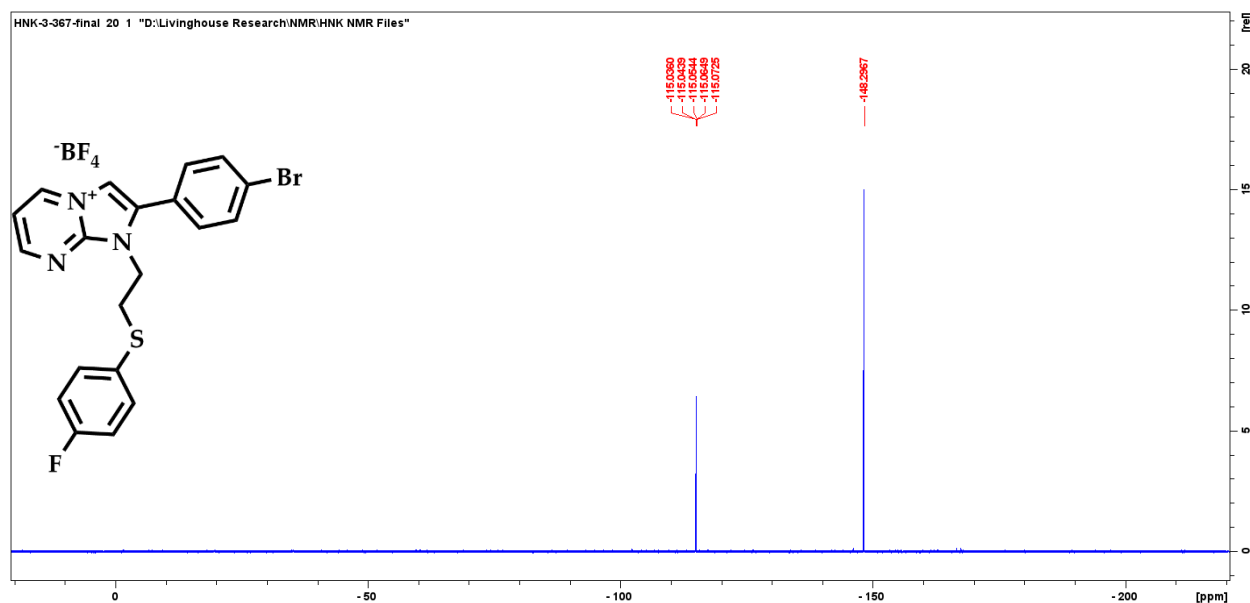


Figure 3.202B: ¹⁹F-NMR Spectra of 2-(4-bromophenyl)-1-(2-((4-fluorophenyl)thio)ethyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (**10.2c**).

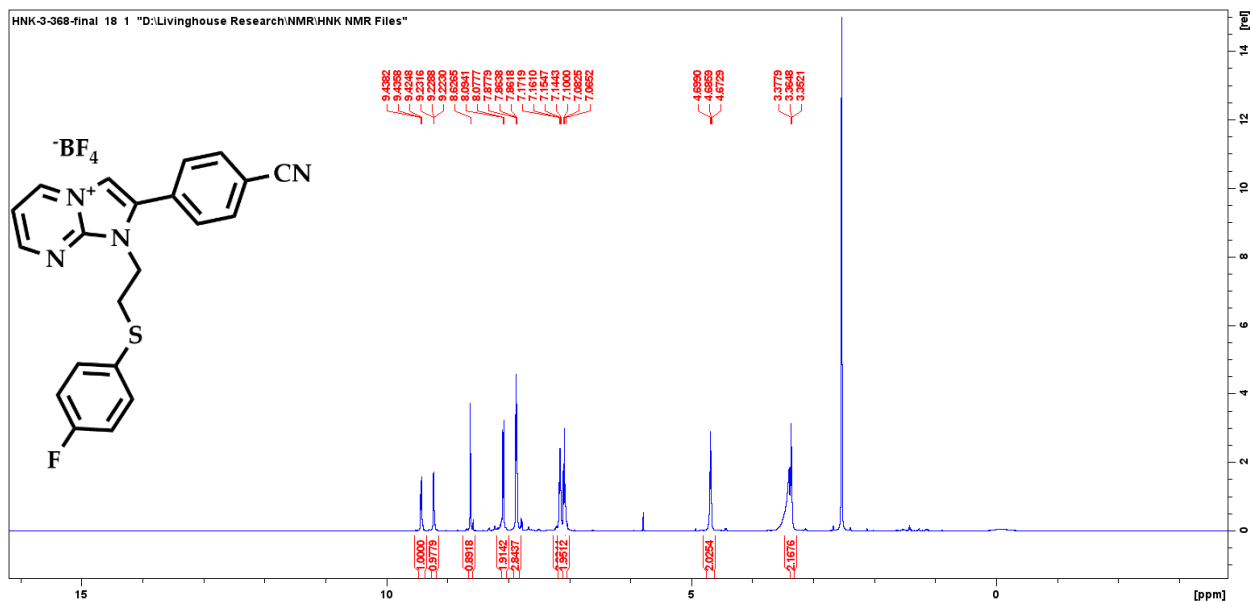


Figure 3.203B: ^1H -NMR Spectra of 2-(4-cyanophenyl)-1-(2-((4-fluorophenyl)thio)ethyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (**10.2d**).

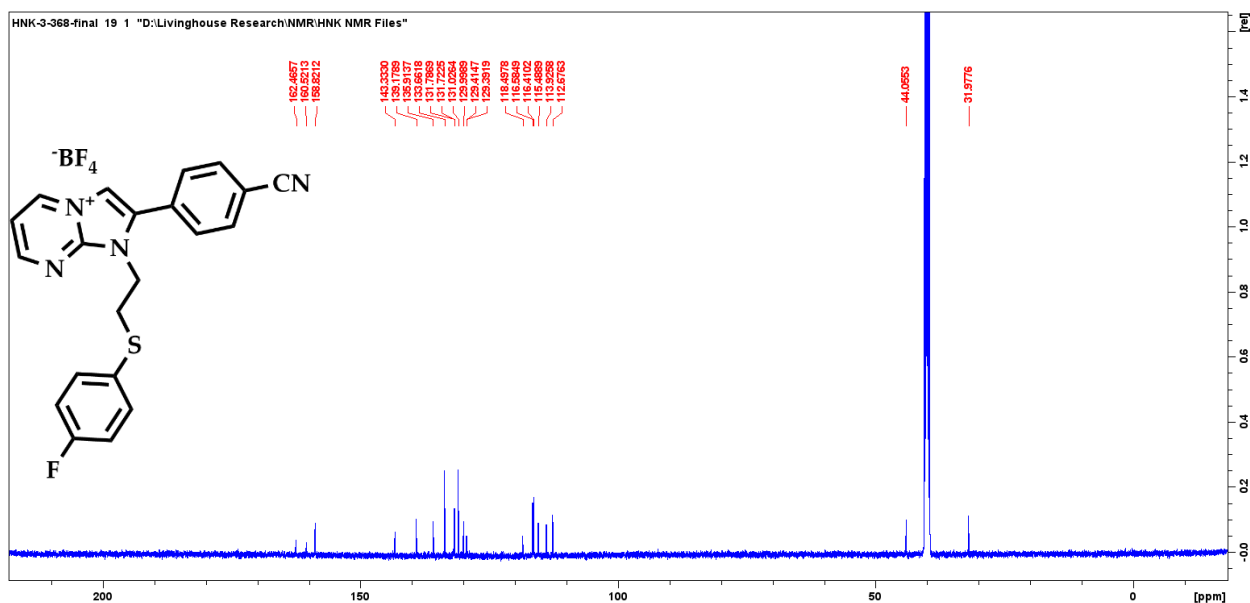


Figure 3.204B: ^{13}C -NMR Spectra of 2-(4-cyanophenyl)-1-(2-((4-fluorophenyl)thio)ethyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (**10.2d**).

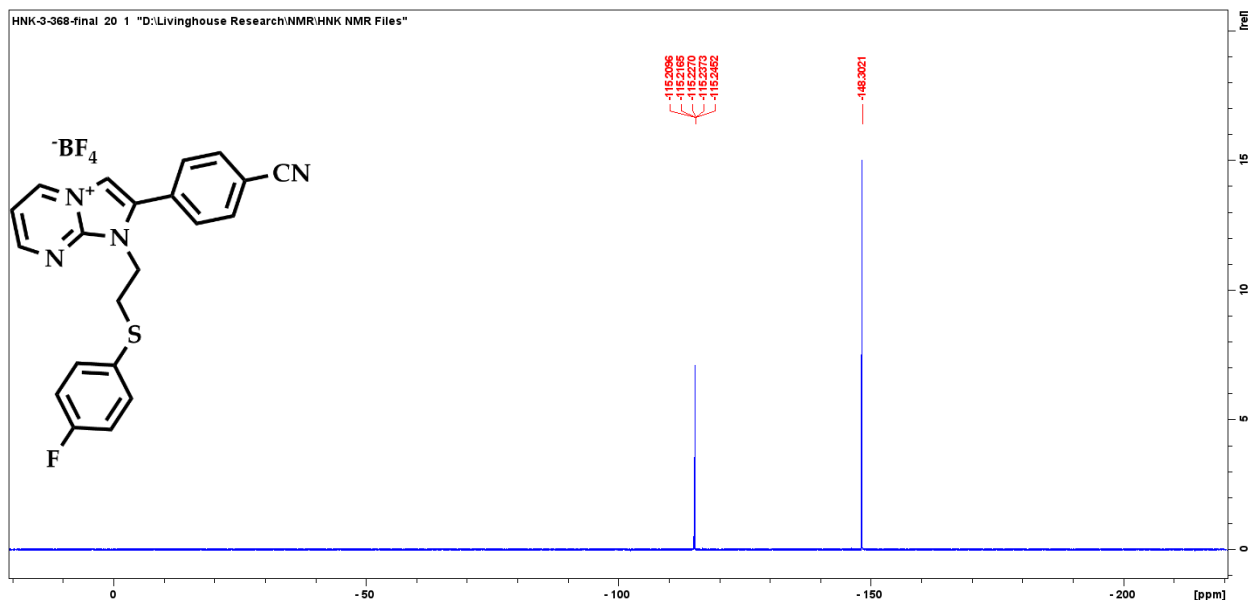


Figure 3.205B: ¹⁹F-NMR Spectra of 2-(4-cyanophenyl)-1-(2-((4-fluorophenyl)thio)ethyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (**10.2d**).

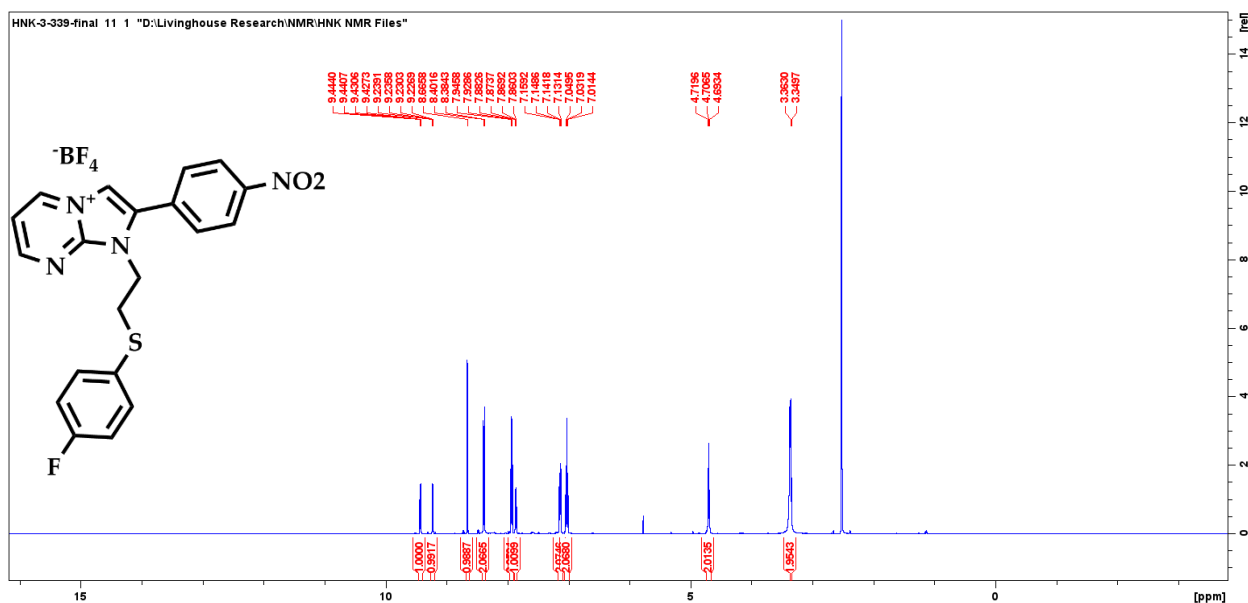


Figure 3.206B: ¹H-NMR Spectra of 1-(2-((4-fluorophenyl)thio)ethyl)-2-(4-nitrophenyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (**10.2e**).

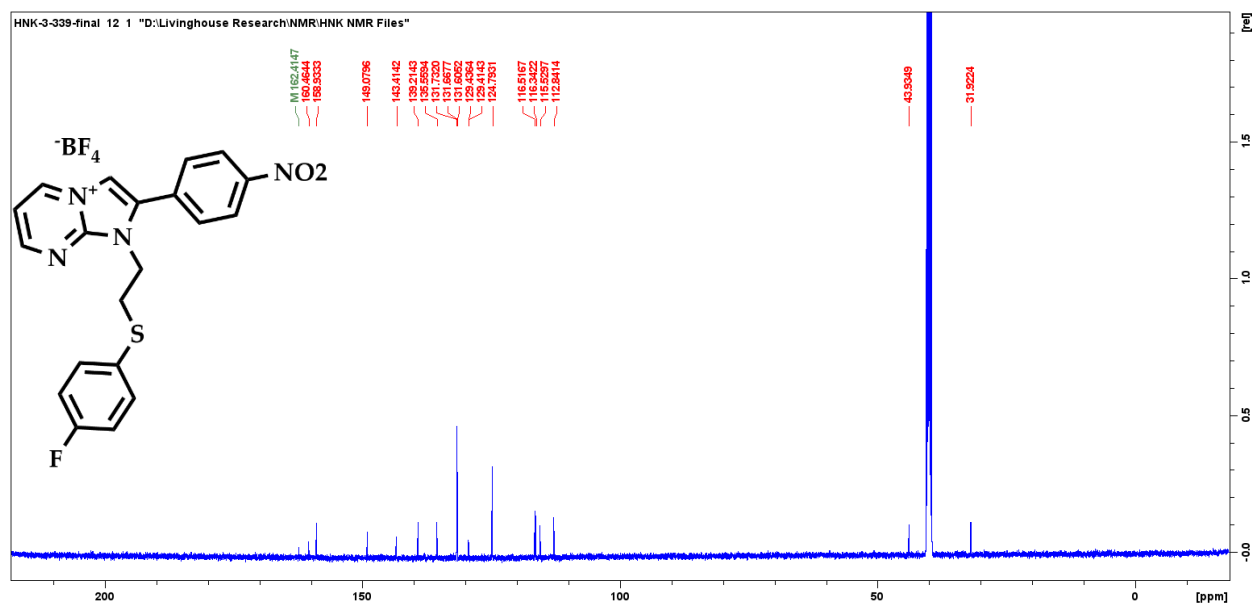


Figure 3.207B: ^{13}C -NMR Spectra of 1-(2-((4-fluorophenyl)thio)ethyl)-2-(4-nitrophenyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (**10.2e**).

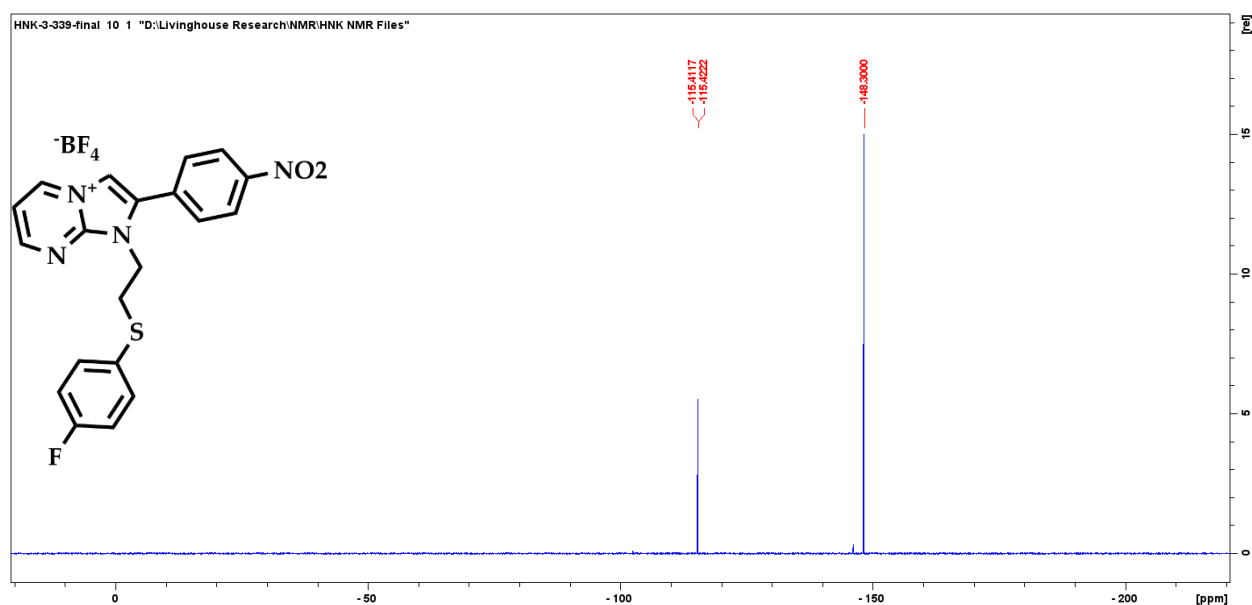


Figure 3.208B: ^{19}F -NMR Spectra of 1-(2-((4-fluorophenyl)thio)ethyl)-2-(4-nitrophenyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (**10.2e**).

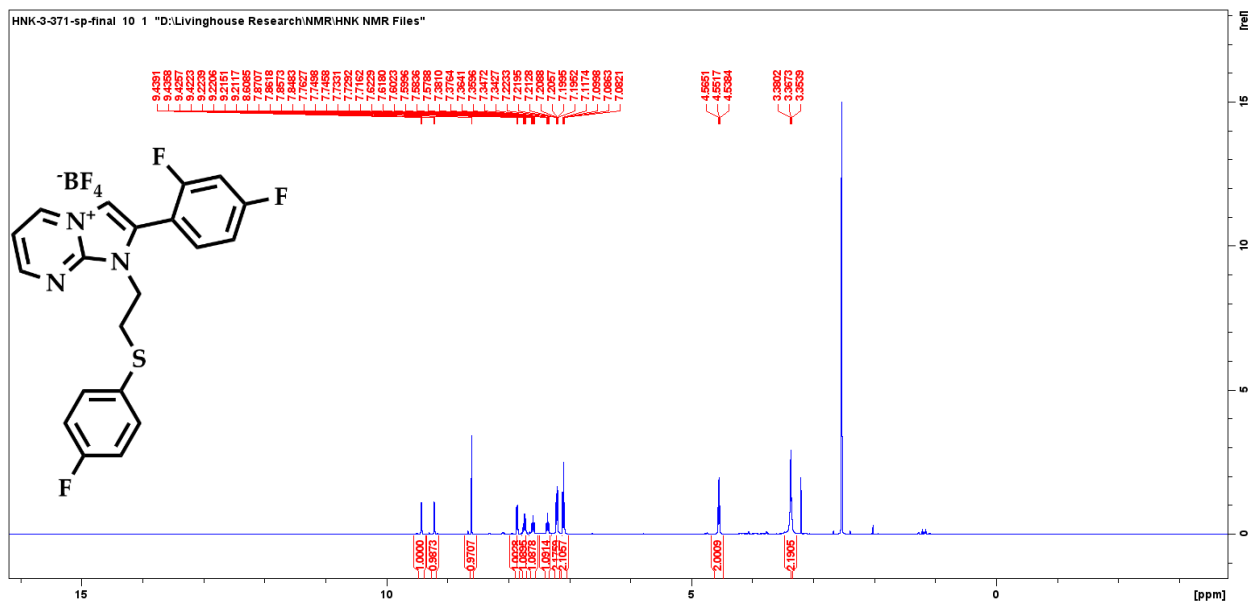


Figure 3.209B: ^1H -NMR Spectra of 2-(2,4-difluorophenyl)-1-(2-((4-fluorophenyl)thio)ethyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (**10.2f**).

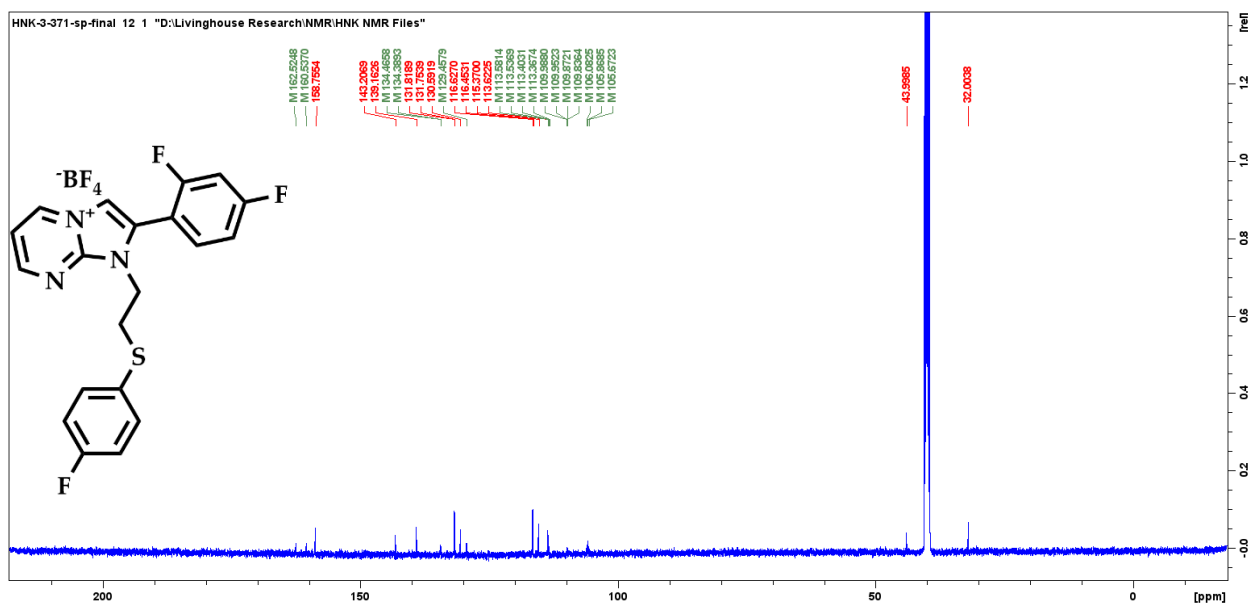


Figure 3.210B: ^{13}C -NMR Spectra of 2-(2,4-difluorophenyl)-1-(2-((4-fluorophenyl)thio)ethyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (**10.2f**).

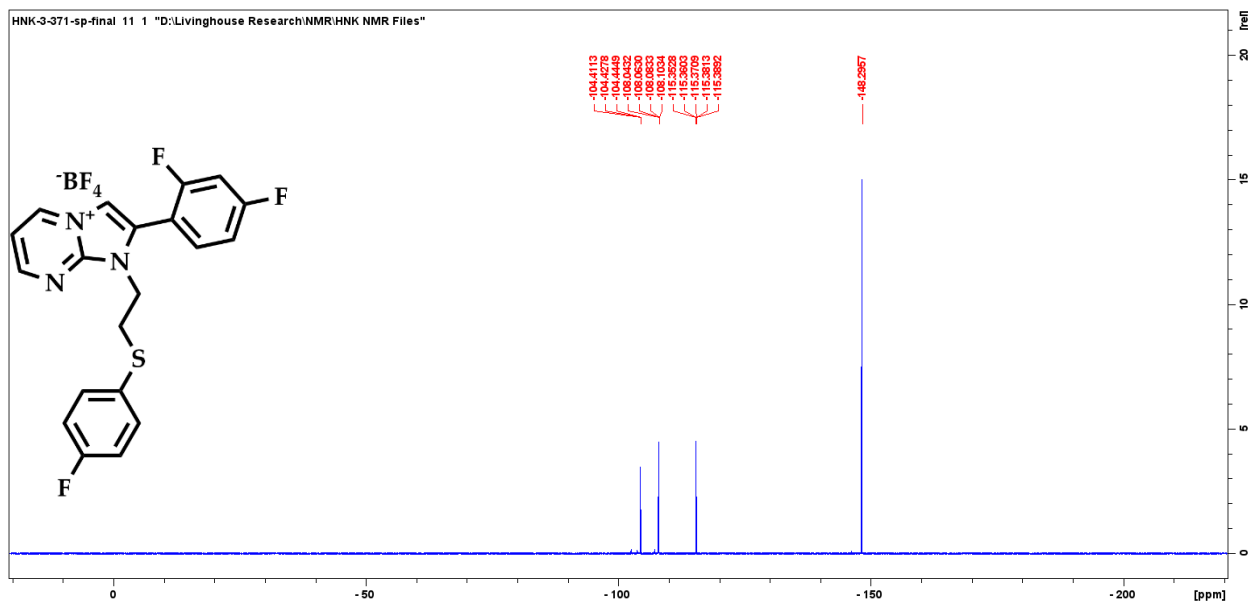


Figure 3.211B: ¹⁹F-NMR Spectra of 2-(2,4-difluorophenyl)-1-(2-((4-fluorophenyl)thio)ethyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (**10.2f**).

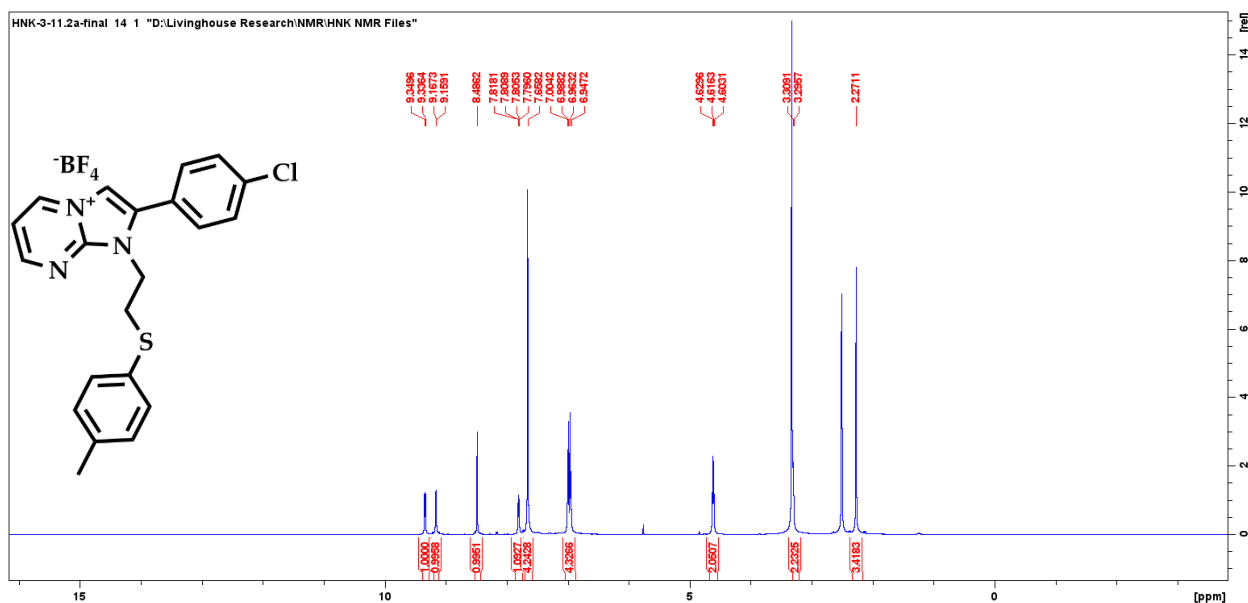


Figure 3.212B: ¹H-NMR Spectra of 2-(4-chlorophenyl)-1-(2-(p-tolylthio)ethyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (**11.2a**).

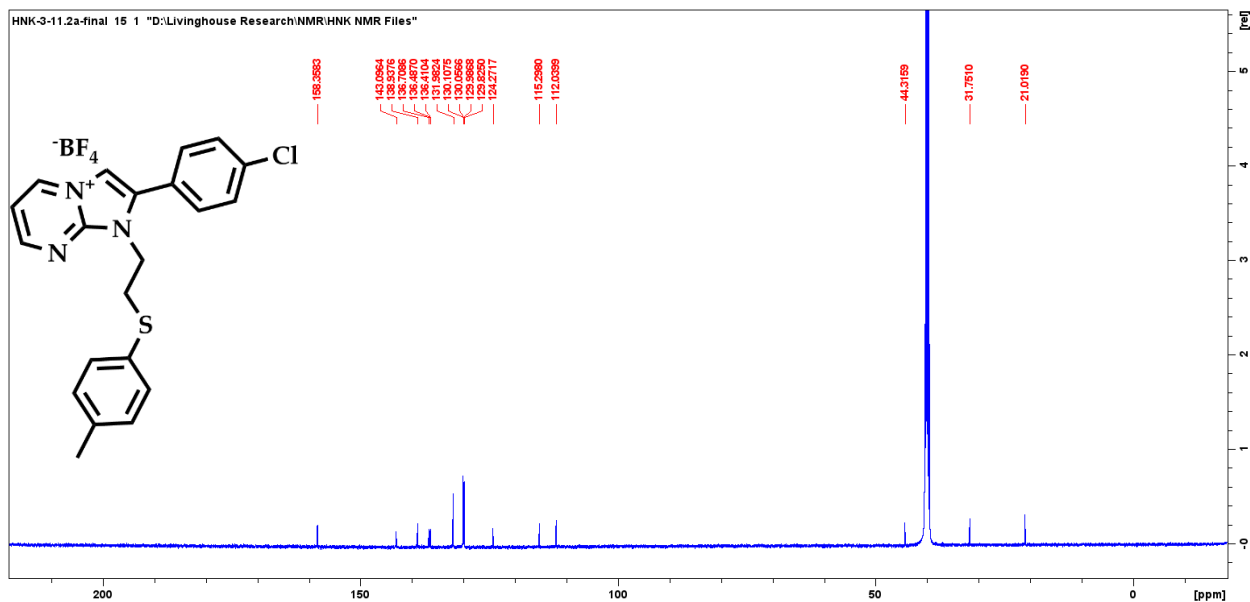


Figure 3.213B: ^{13}C -NMR Spectra of 2-(4-chlorophenyl)-1-(2-(*p*-tolylthio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**11.2a**).

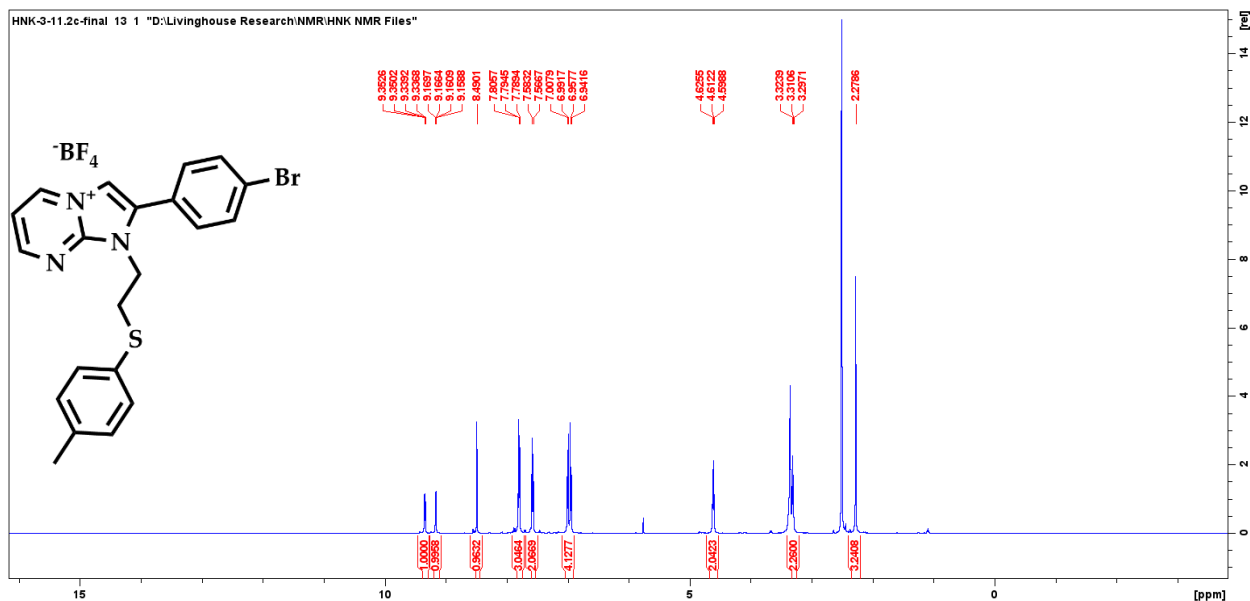


Figure 3.214B: ¹H-NMR Spectra of 2-(4-bromophenyl)-1-(2-(*p*-tolylthio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**11.2c**).

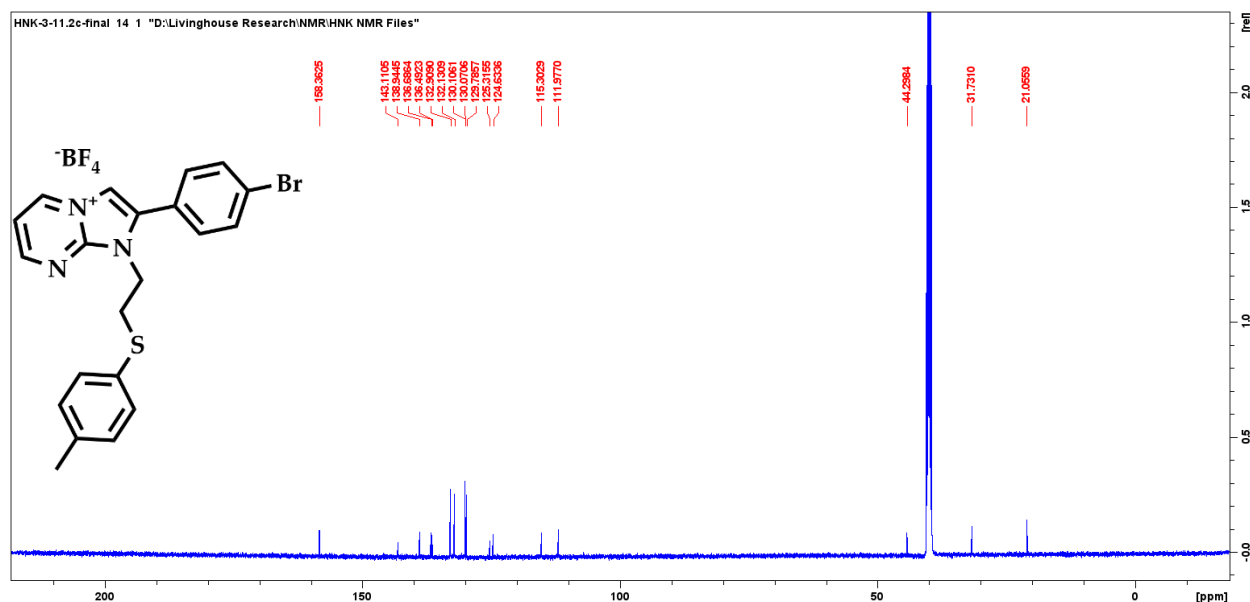


Figure 3.217B: ¹³C-NMR Spectra of 2-(4-bromophenyl)-1-(2-(p-tolylthio)ethyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (**11.2c**).

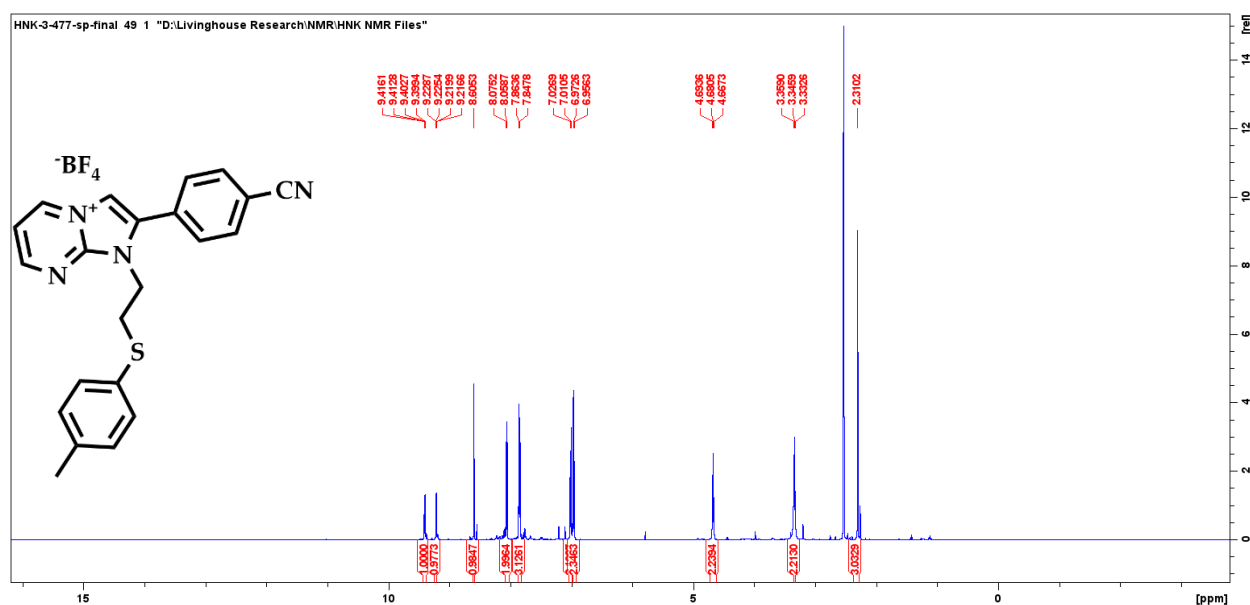


Figure 3.218B: ¹H-NMR Spectra of 2-(4-cyanophenyl)-1-(2-(p-tolylthio)ethyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (**11.2d**).

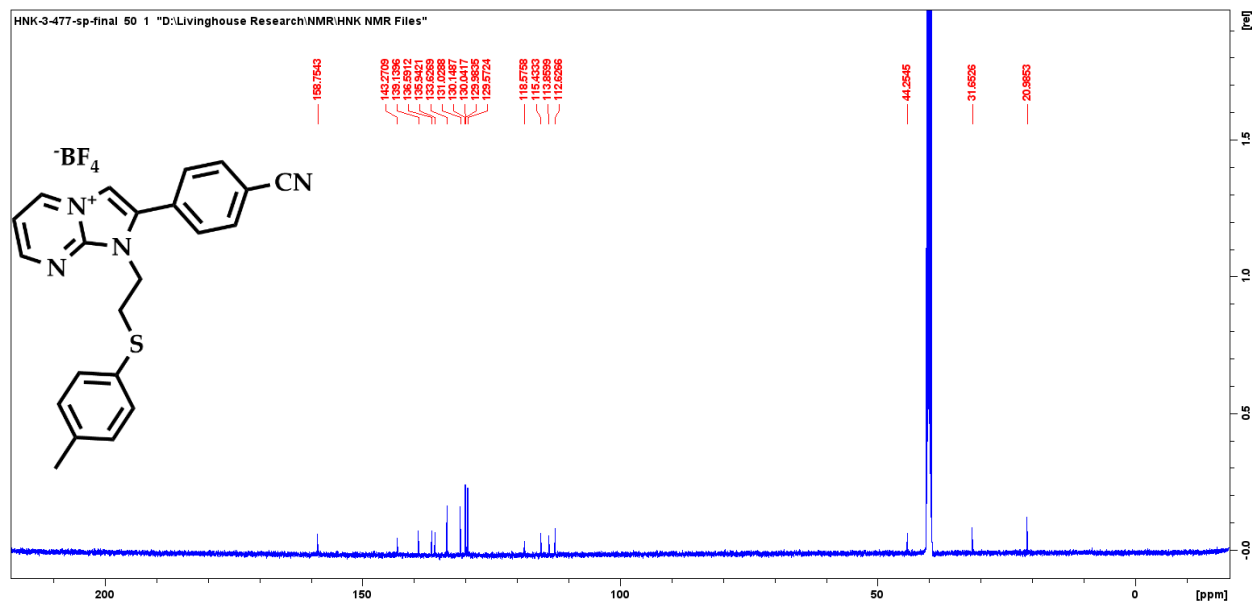


Figure 3.219B: ¹³C-NMR Spectra of 2-(4-cyanophenyl)-1-(2-(p-tolylthio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**11.2d**).

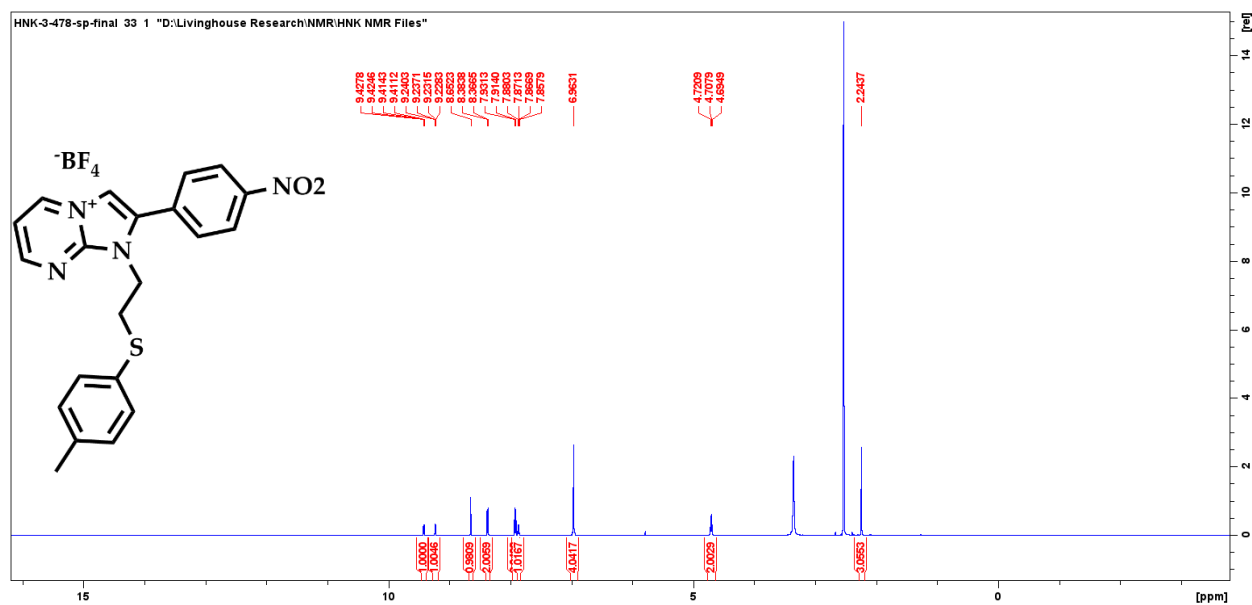


Figure 3.220B: ¹H-NMR Spectra of 2-(4-nitrophenyl)-1-(2-(p-tolylthio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**11.2e**).

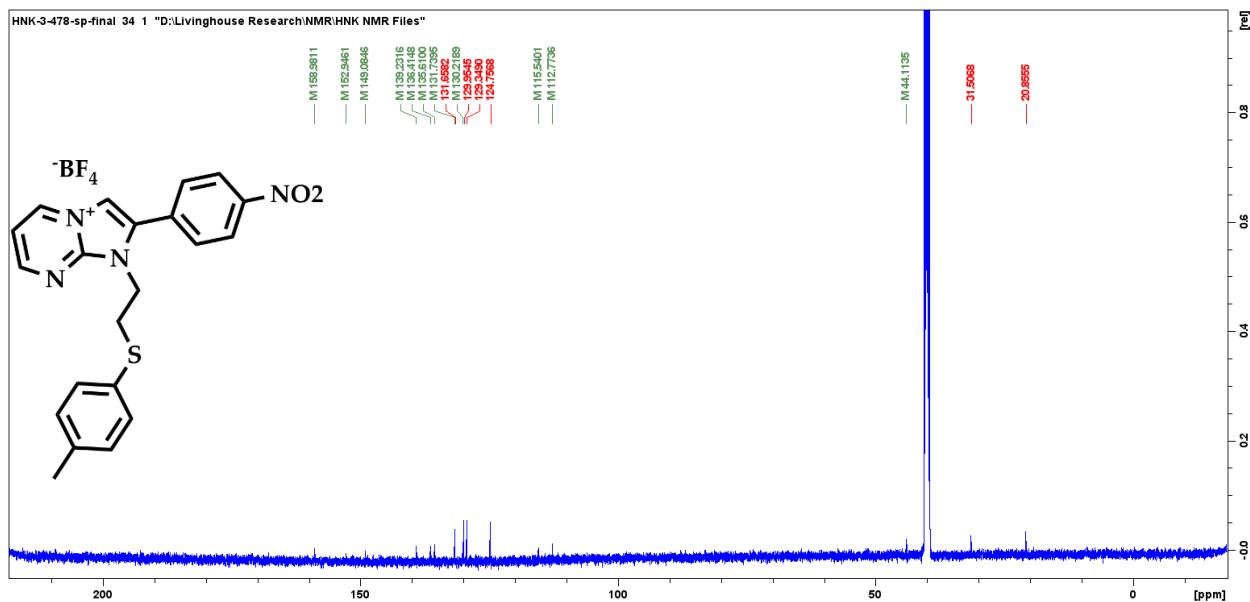


Figure 3.221B: ¹³C-NMR Spectra of 2-(4-nitrophenyl)-1-(2-(p-tolylthio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**11.2e**).

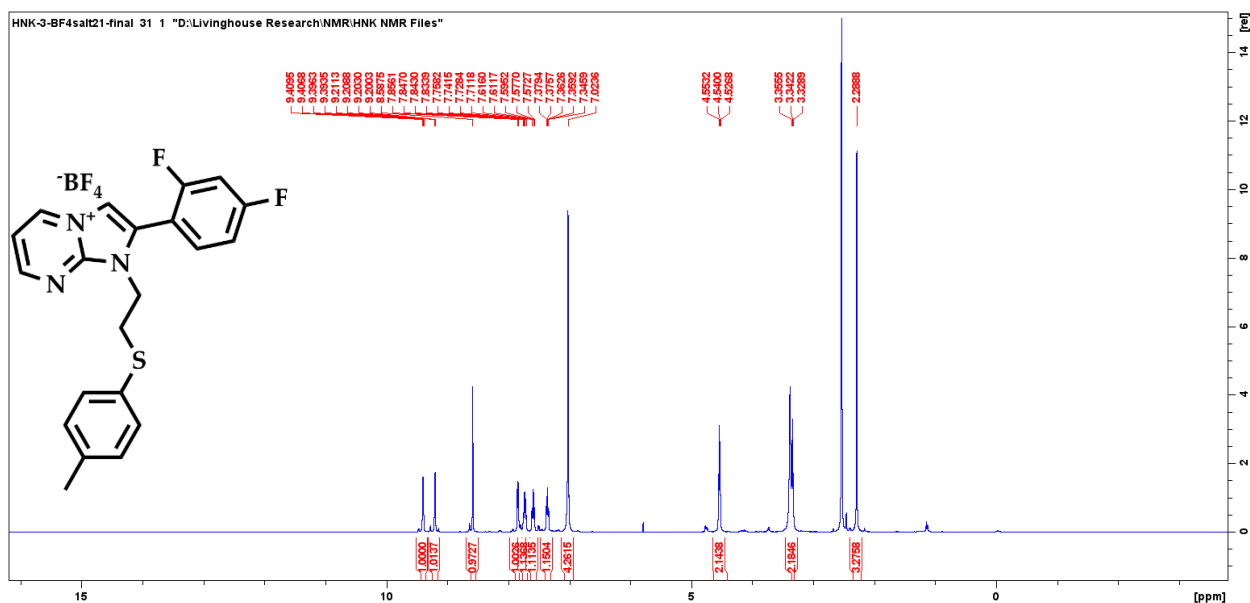


Figure 3.222B: ¹H-NMR Spectra of 2-(2,4-difluorophenyl)-1-(2-(p-tolylthio)ethyl)-1H-imidazo[1,2-a]pyrimidin-4-ium tetrafluoroborate (**11.2f**).

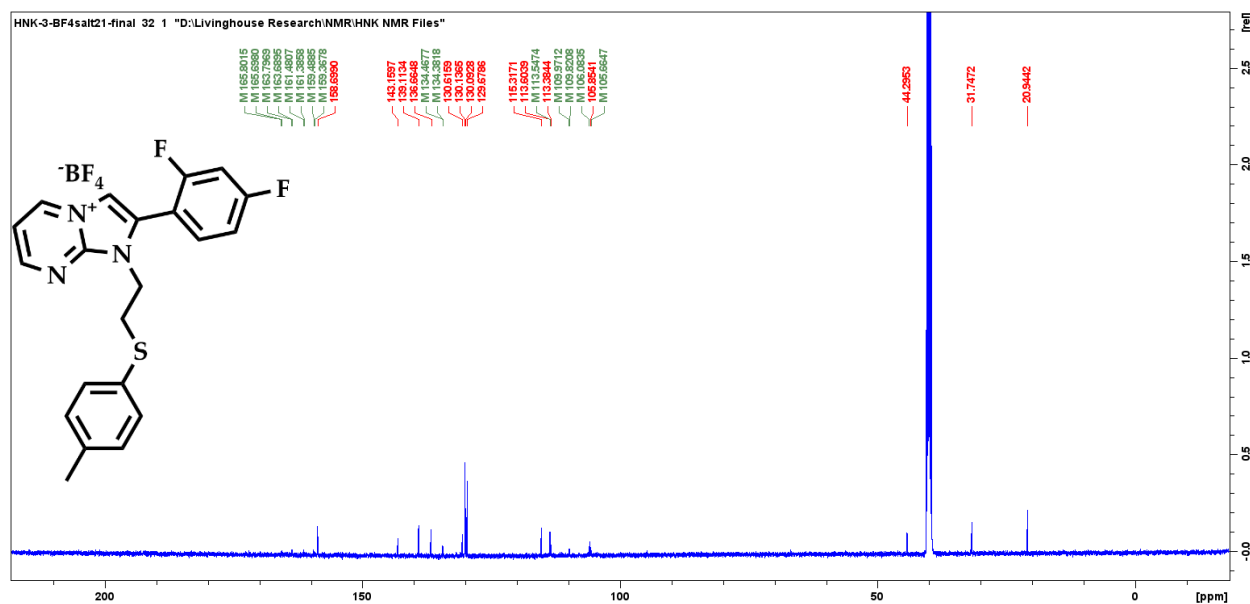


Figure 3.223B: ^{13}C -NMR Spectra of 2-(2,4-difluorophenyl)-1-(2-(p-tolylthio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**11.2f**).

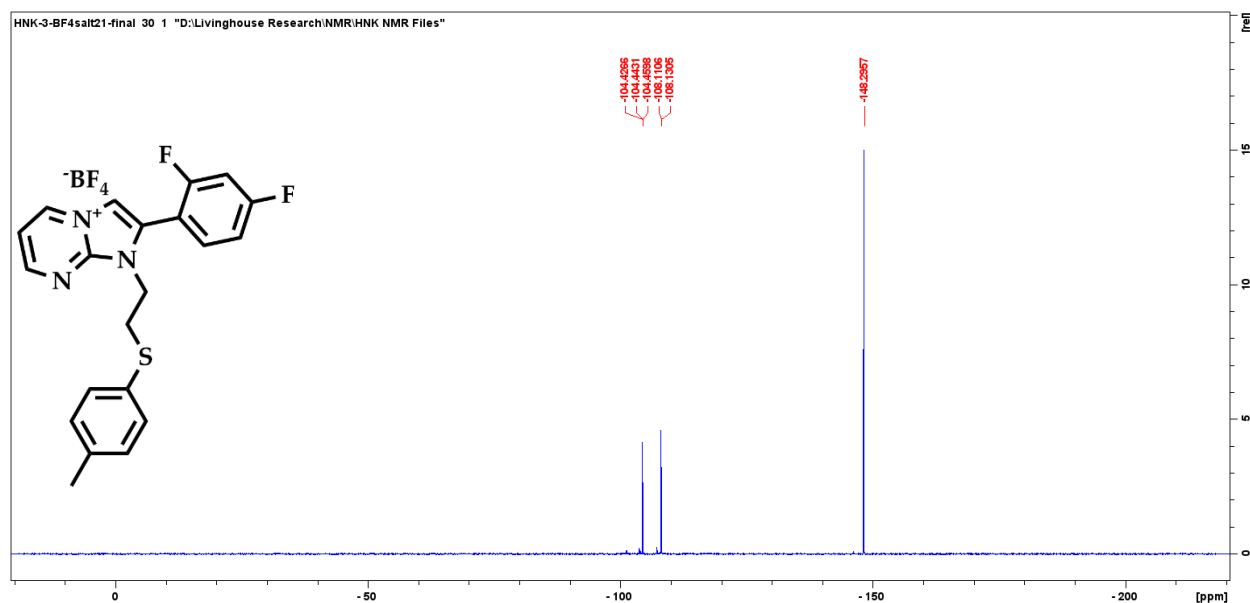


Figure 3.224B: ^{19}F -NMR Spectra of 2-(2,4-difluorophenyl)-1-(2-(p-tolylthio)ethyl)-1*H*-imidazo[1,2-*a*]pyrimidin-4-ium tetrafluoroborate (**11.2f**).

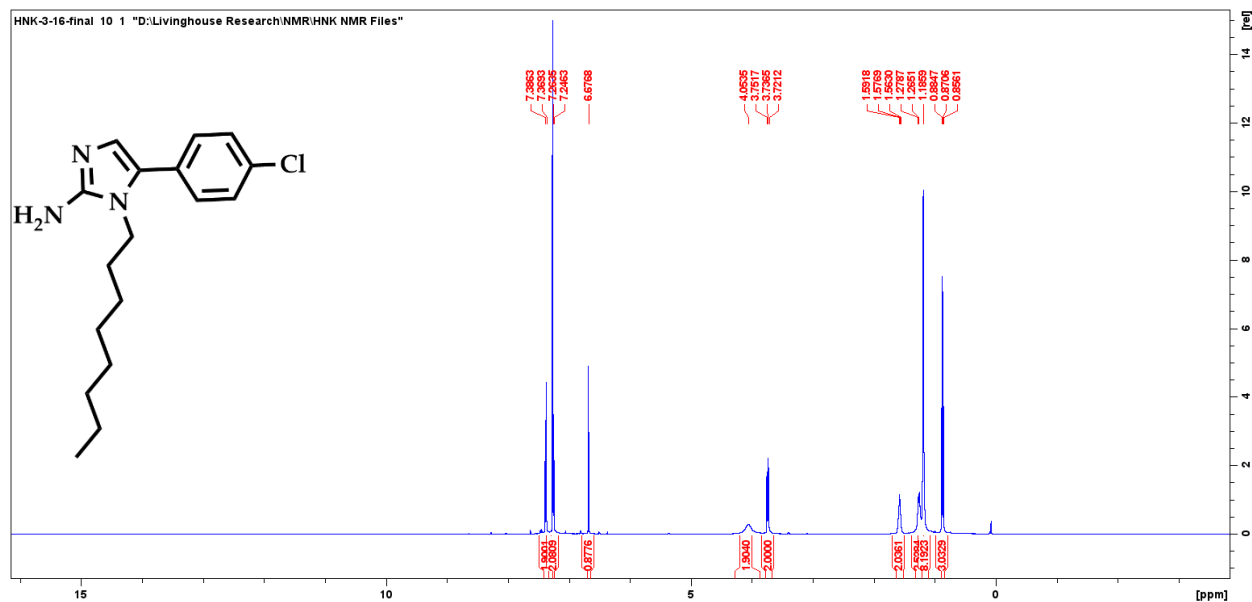


Figure 3.225B: ^1H -NMR Spectra of 5-(4-chlorophenyl)-1-octyl-1*H*-imidazol-2-amine (**1.3a**).

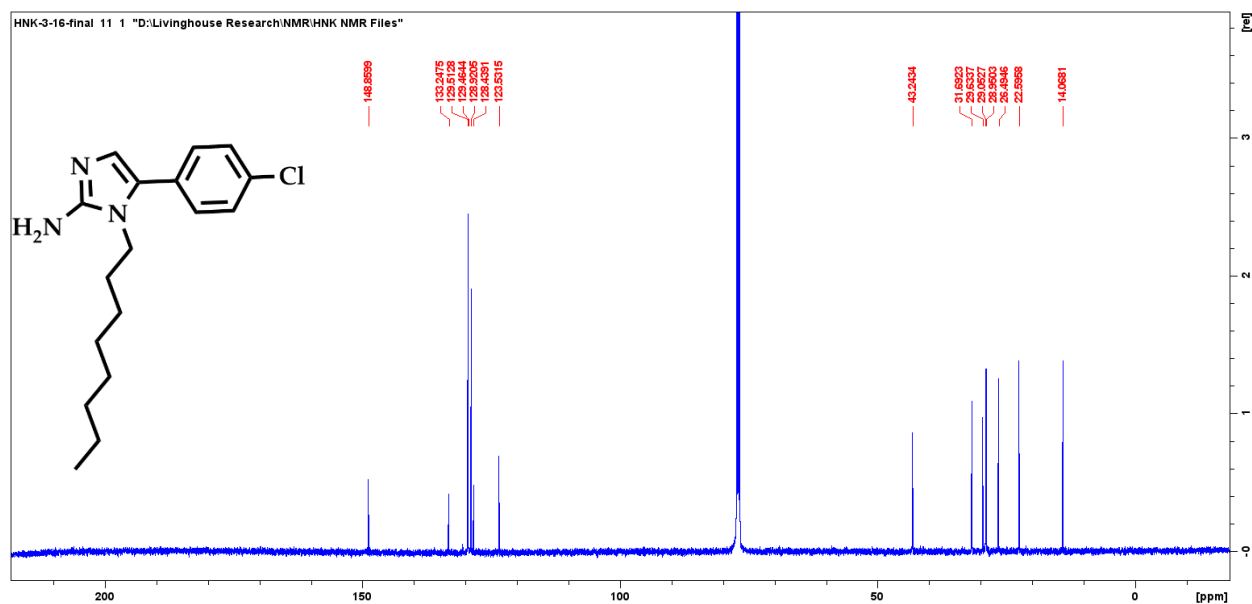


Figure 3.226B: ^{13}C -NMR Spectra of 5-(4-chlorophenyl)-1-octyl-1*H*-imidazol-2-amine (**1.3a**).

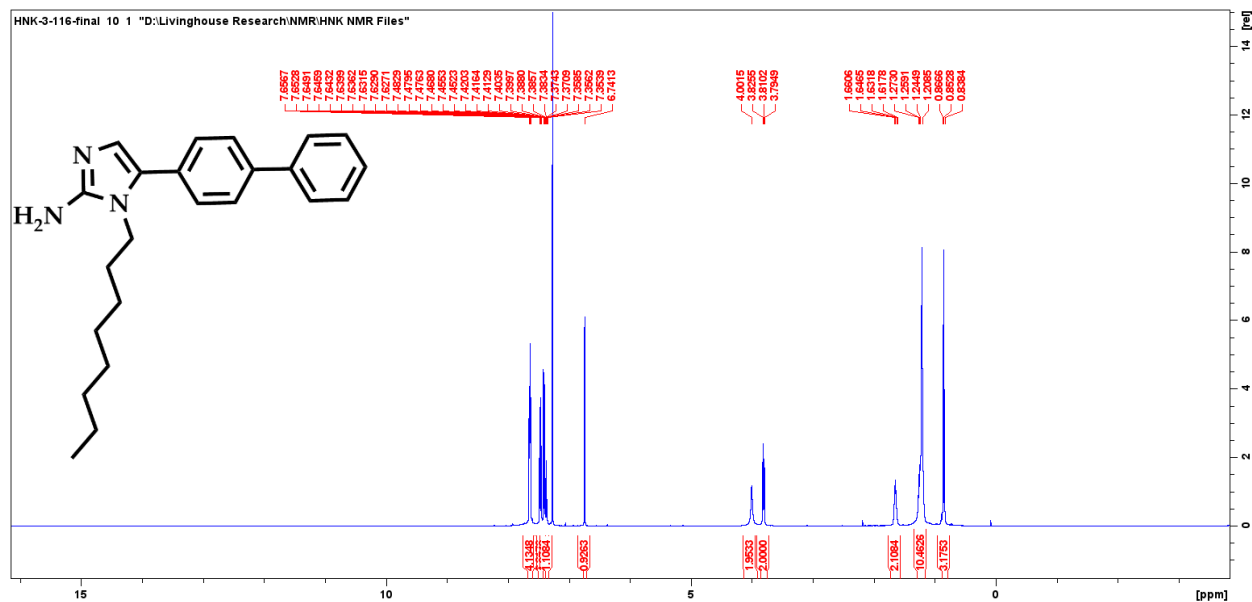


Figure 3.227B: ^1H -NMR Spectra of 5-([1,1'-biphenyl]-4-yl)-1-octyl-1*H*-imidazol-2-amine (**1.3b**).

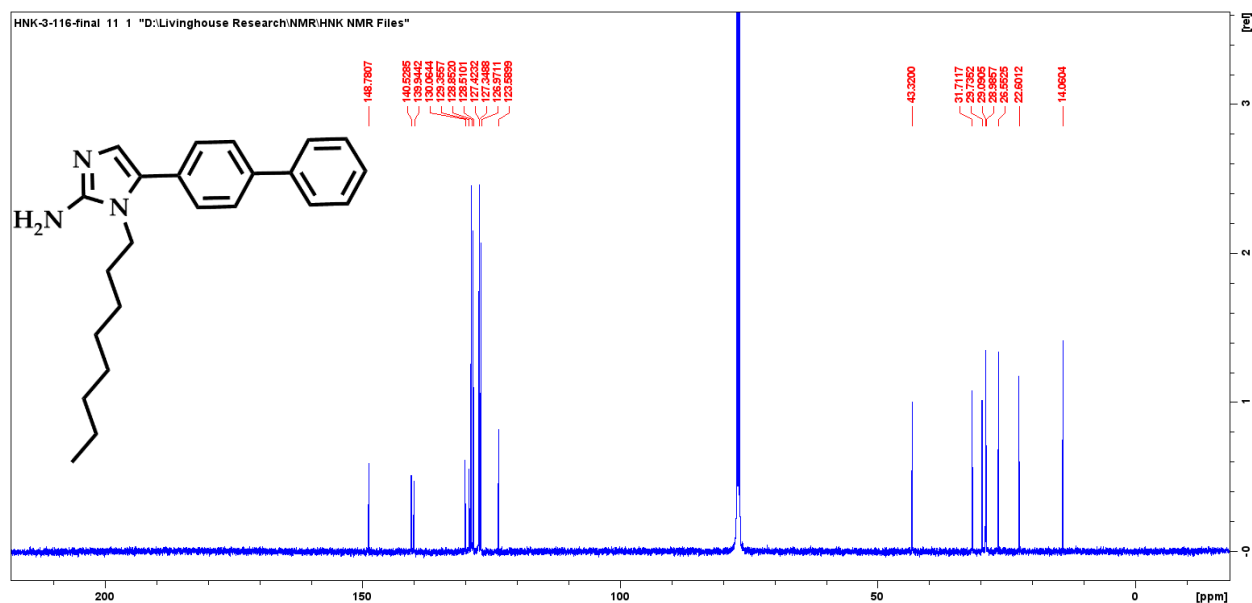


Figure 3.228B: ^{13}C -NMR Spectra of 5-([1,1'-biphenyl]-4-yl)-1-octyl-1*H*-imidazol-2-amine (**1.3b**).

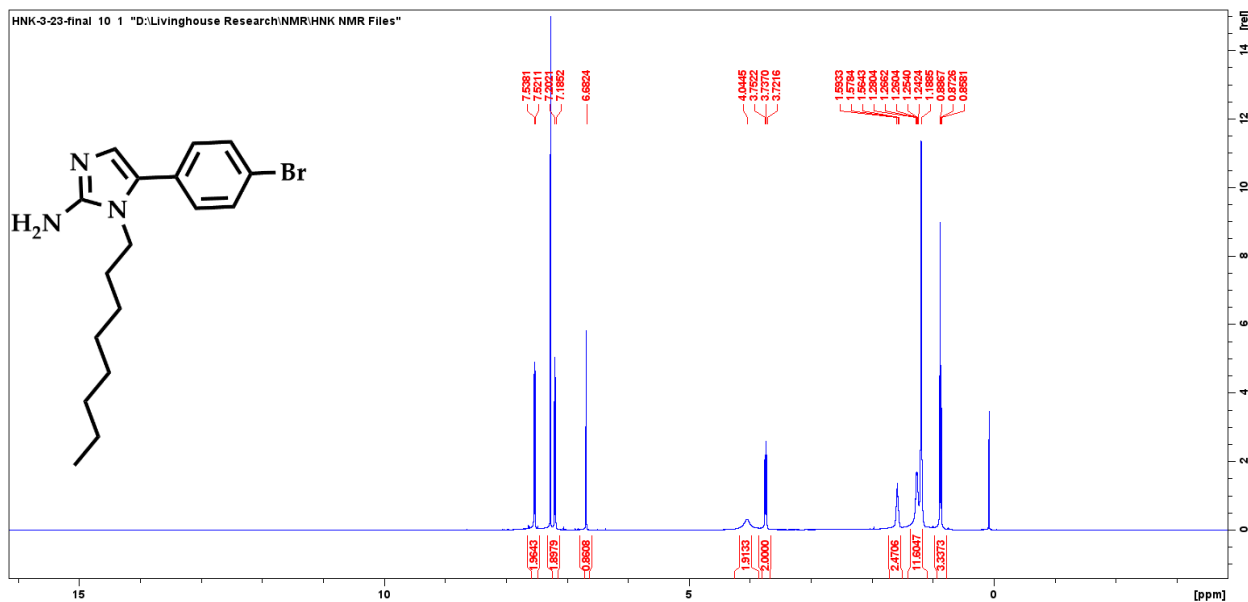


Figure 3.229B: ¹H-NMR Spectra of 5-(4-bromophenyl)-1-octyl-1H-imidazol-2-amine (1.3c).

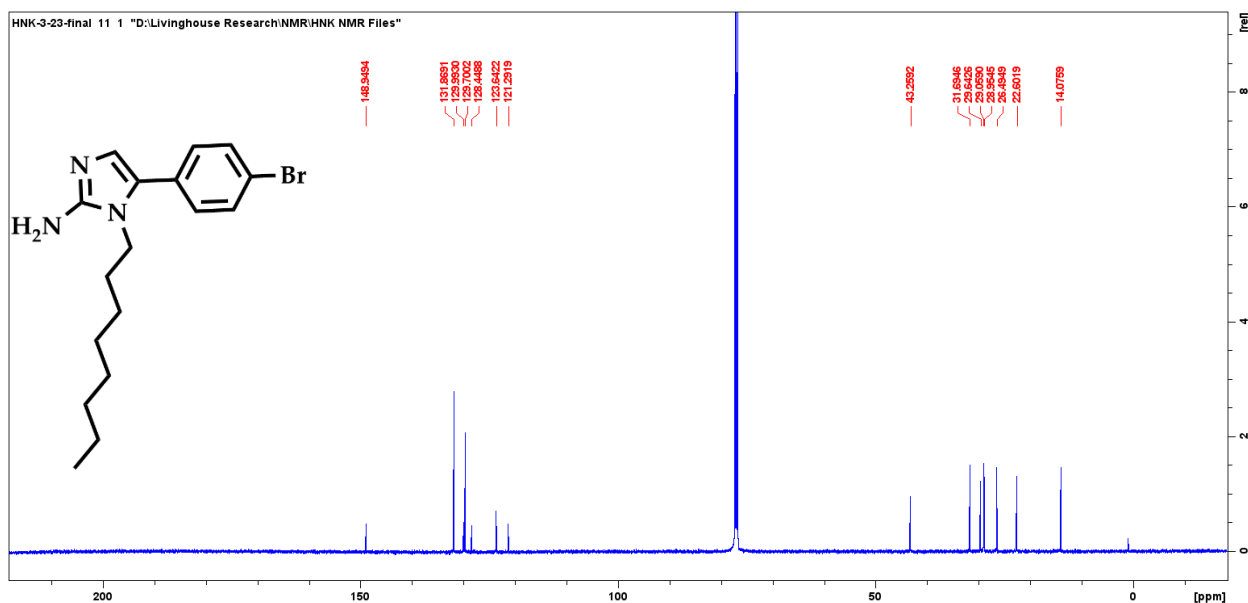


Figure 3.230B: ¹³C-NMR Spectra of 5-(4-bromophenyl)-1-octyl-1H-imidazol-2-amine (1.3c).

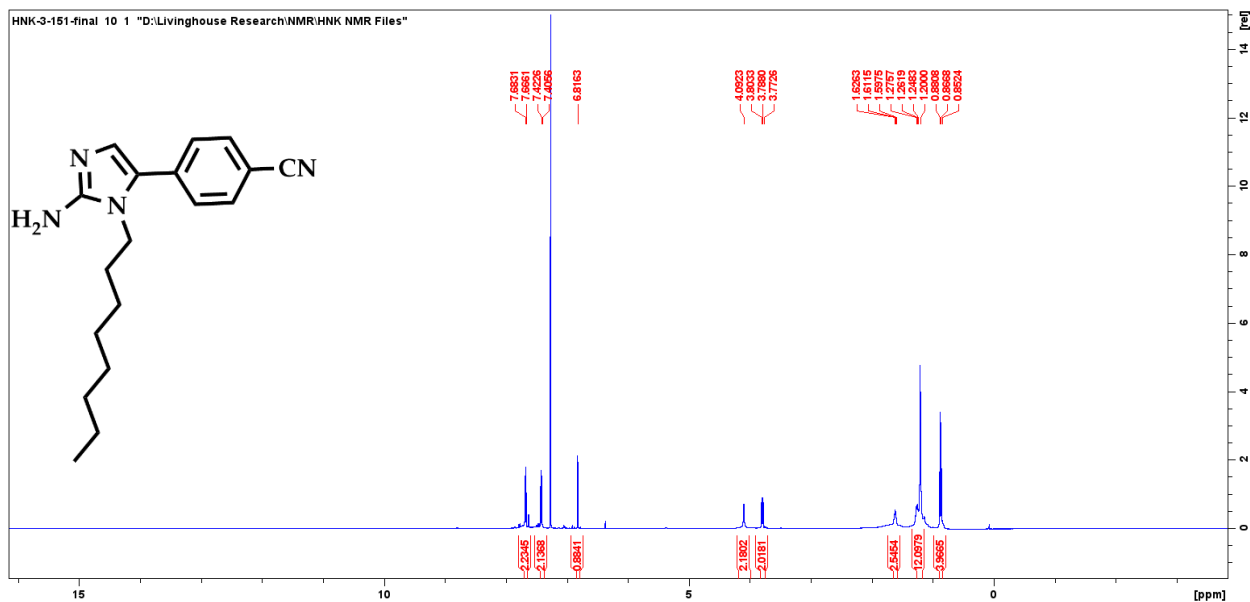


Figure 3.231B: ^1H -NMR Spectra of 5-(4-cyanophenyl)-1-octyl-1*H*-imidazol-2-amine (**1.3d**).

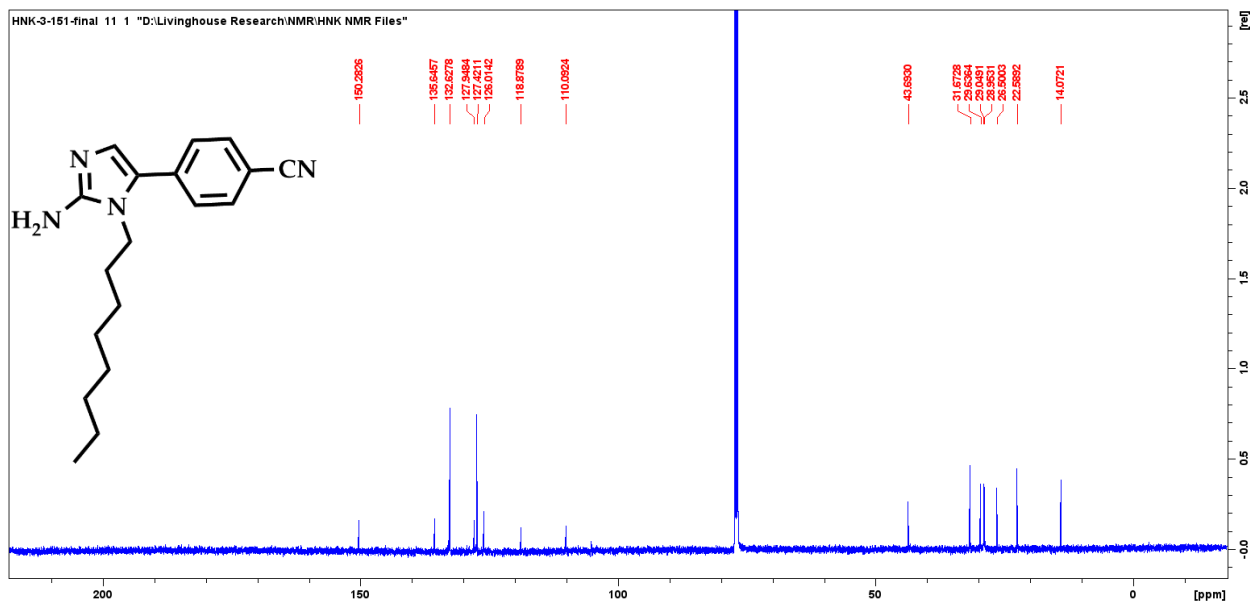


Figure 3.232B: ^{13}C -NMR Spectra of 5-(4-cyanophenyl)-1-octyl-1*H*-imidazol-2-amine (**1.3d**).

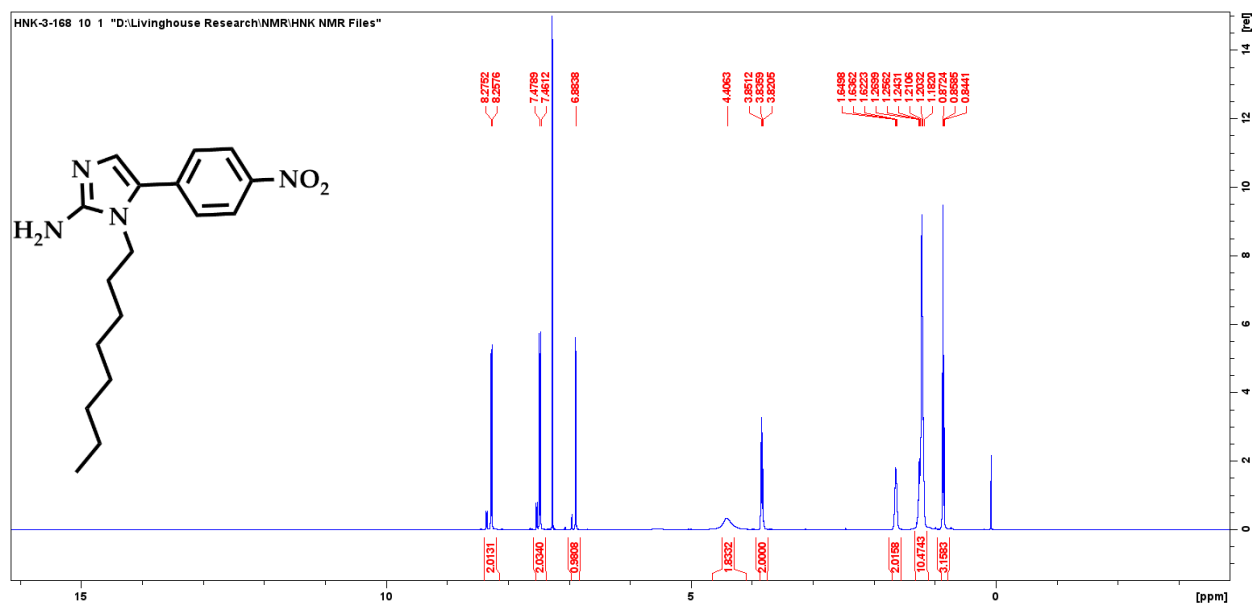


Figure 3.233B: ^1H -NMR Spectra of 5-(4-nitrophenyl)-1-octyl-1*H*-imidazol-2-amine (**1.3e**).

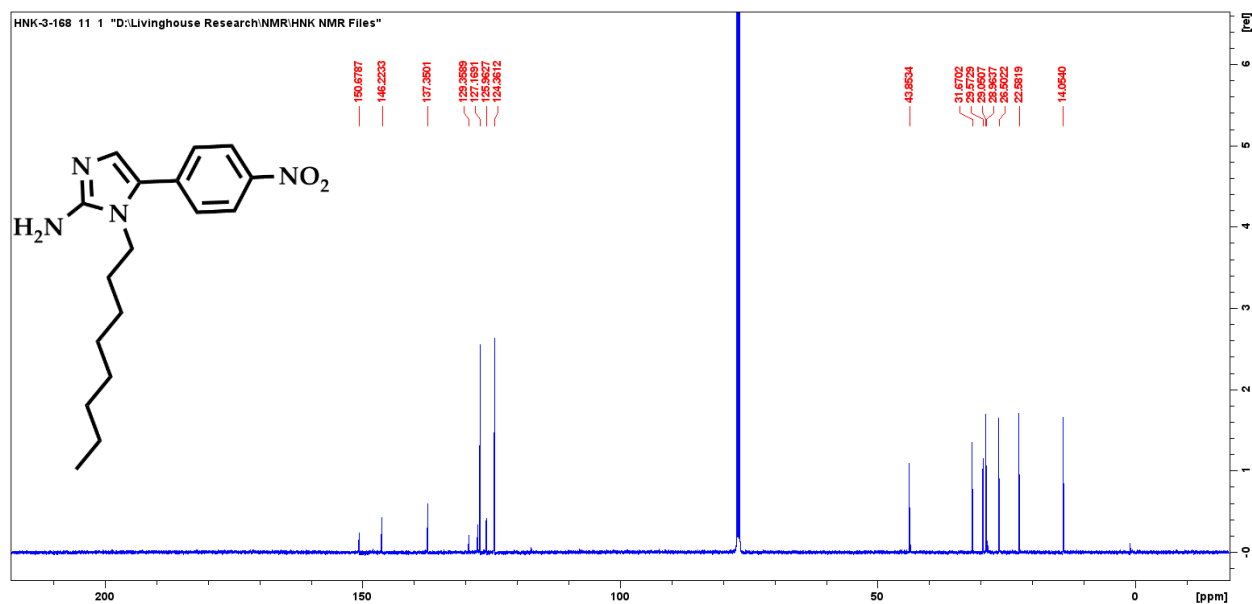


Figure 3.234B: ^{13}C -NMR Spectra of 5-(4-nitrophenyl)-1-octyl-1*H*-imidazol-2-amine (**1.3e**).

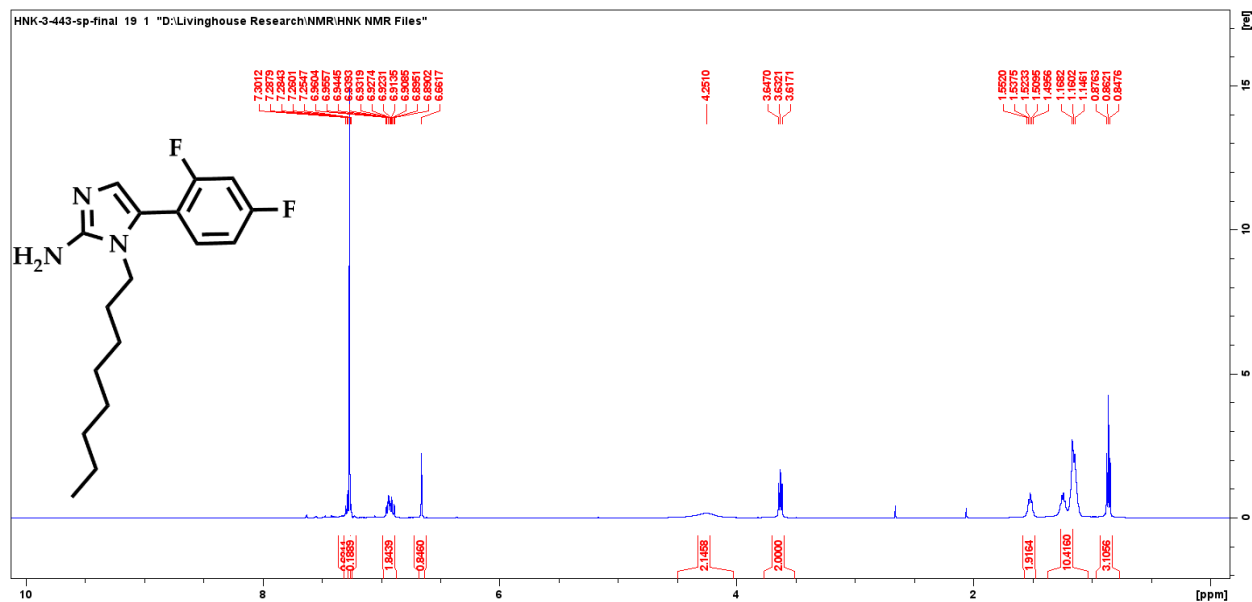


Figure 3.235B: ^1H -NMR Spectra of 5-(2,4-difluorophenyl)-1-octyl-1*H*-imidazol-2-amine (**1.3f**).

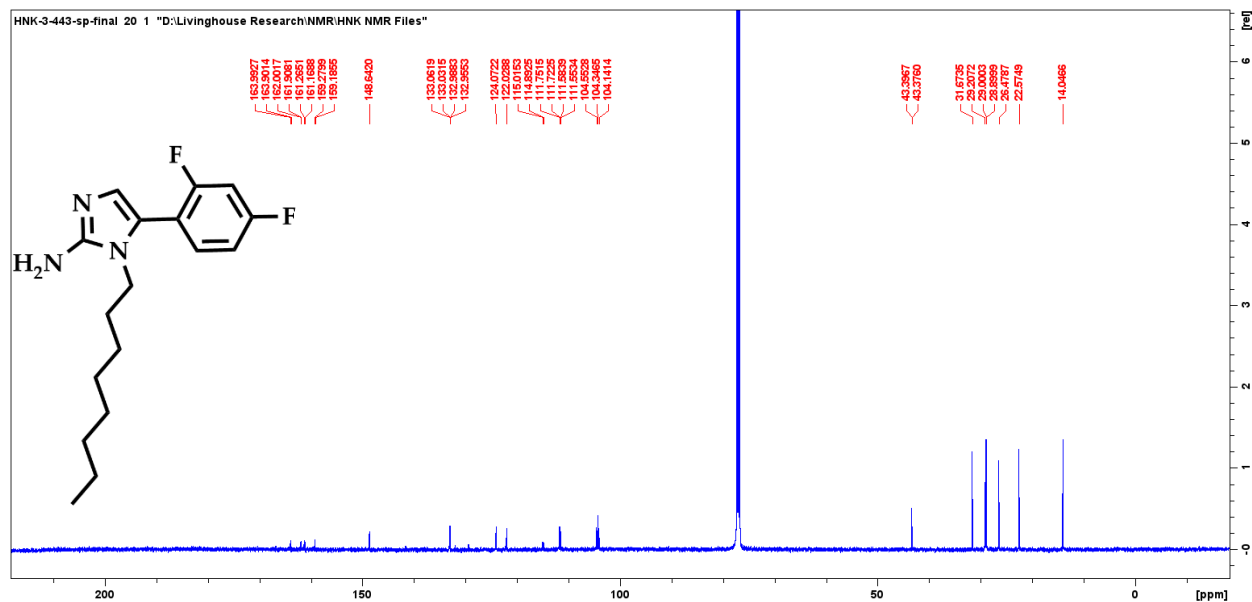


Figure 3.236B: ^{13}C -NMR Spectra of 5-(2,4-difluorophenyl)-1-octyl-1*H*-imidazol-2-amine (**1.3f**).

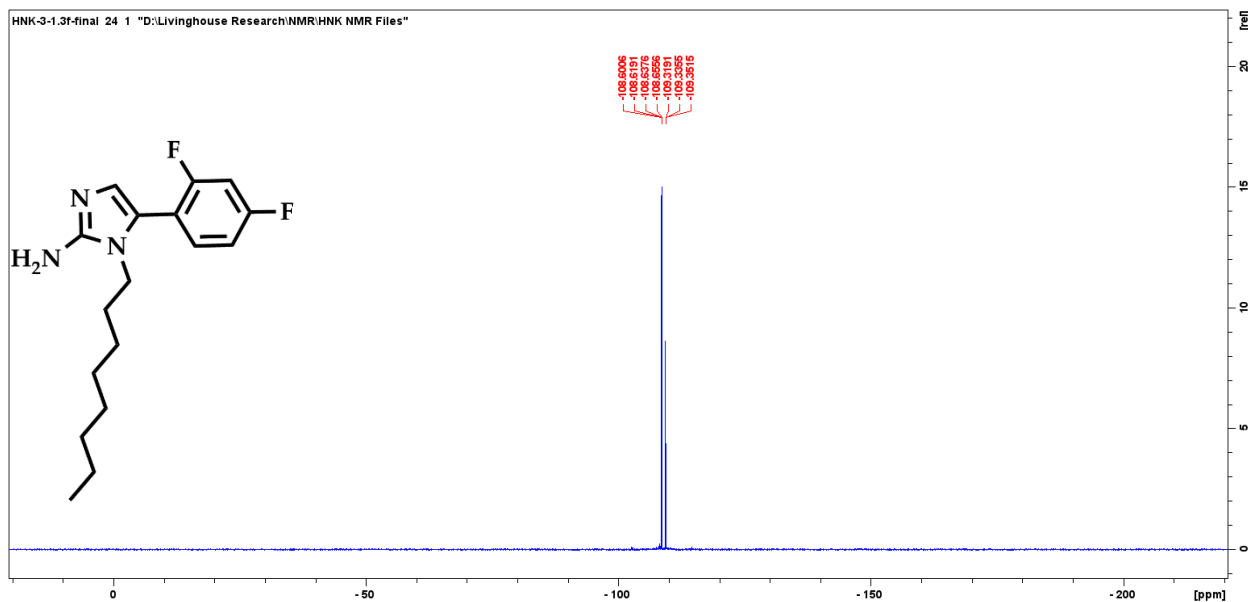


Figure 3.237B: ¹⁹F-NMR Spectra of 5-(2,4-difluorophenyl)-1-octyl-1H-imidazol-2-amine (1.3f).

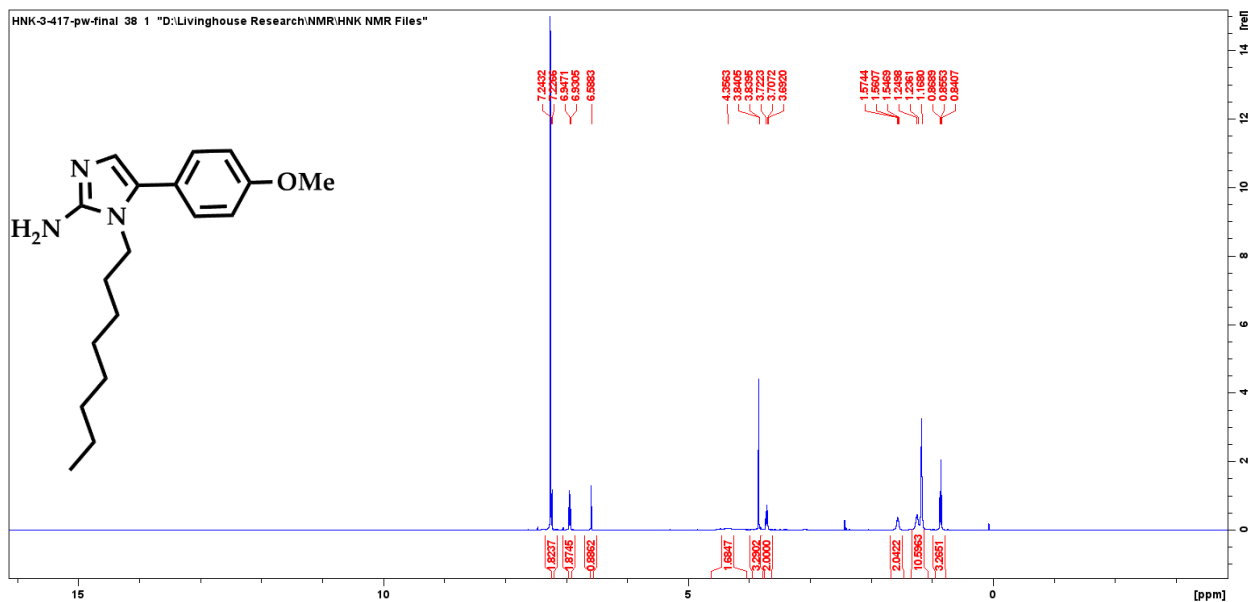


Figure 3.238B: ¹H-NMR Spectra of 5-(4-methoxyphenyl)-1-octyl-1H-imidazol-2-amine (1.3g).

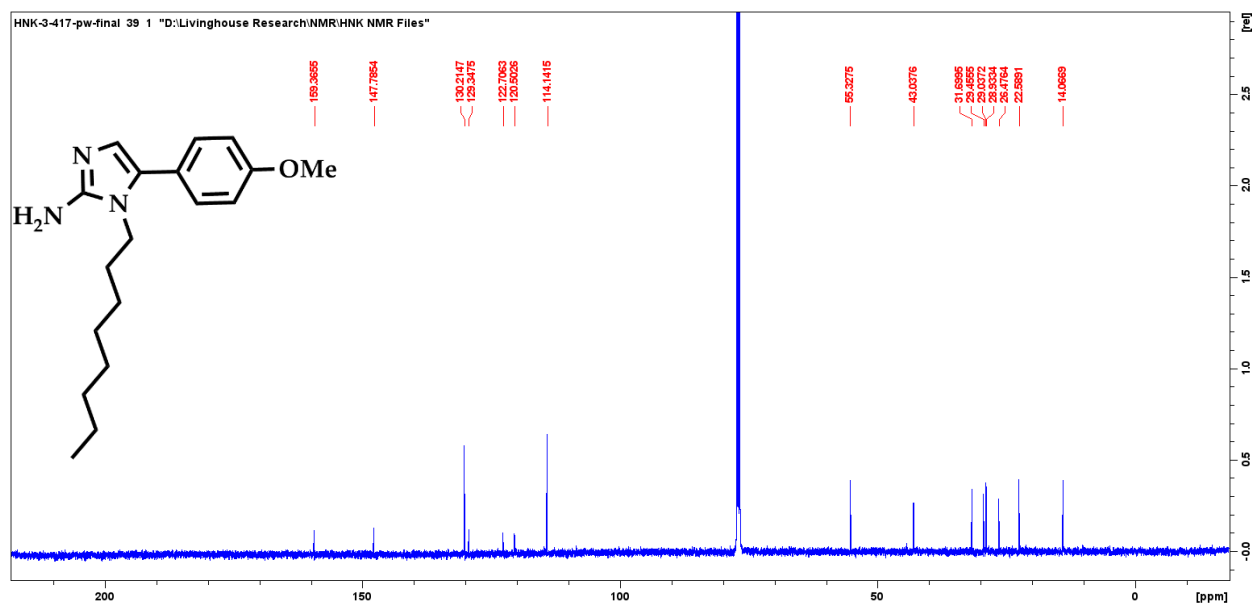


Figure 3.239B: ^{13}C -NMR Spectra of 5-(4-methoxyphenyl)-1-octyl-1H-imidazol-2-amine (**1.3g**).

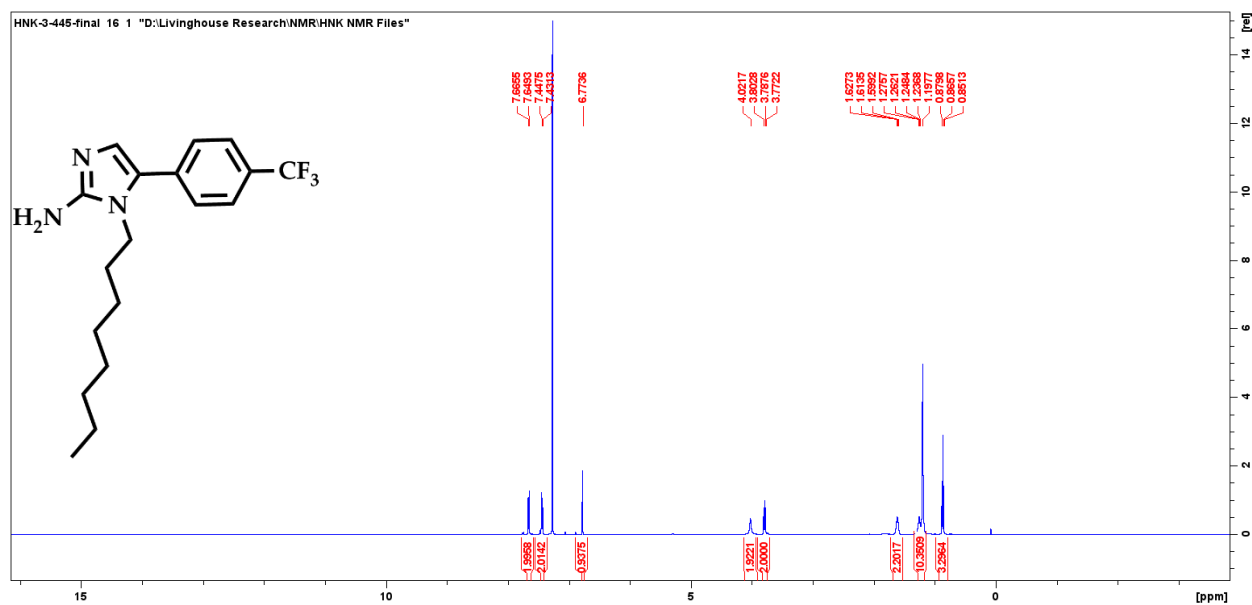


Figure 3.240B: ^1H -NMR Spectra of 1-octyl-5-(4-(trifluoromethyl)phenyl)-1H-imidazol-2-amine (**1.3h**).

HNK-3-1.3h-final 14 1 "D:\Livinghouse Research\NMR\HNK NMR Files"

Chemical structure: CCCCCN1C=NC=C1c2ccc(C(F)(F)F)cc2

Peak list:

Chemical Shift (ppm)	Intensity (a.u.)
62.5038	~15

Figure 3.242B: ^{19}F -NMR Spectra of 1-octyl-5-(4-(trifluoromethyl)phenyl)-1*H*-imidazol-2-amine (**1.3h**).

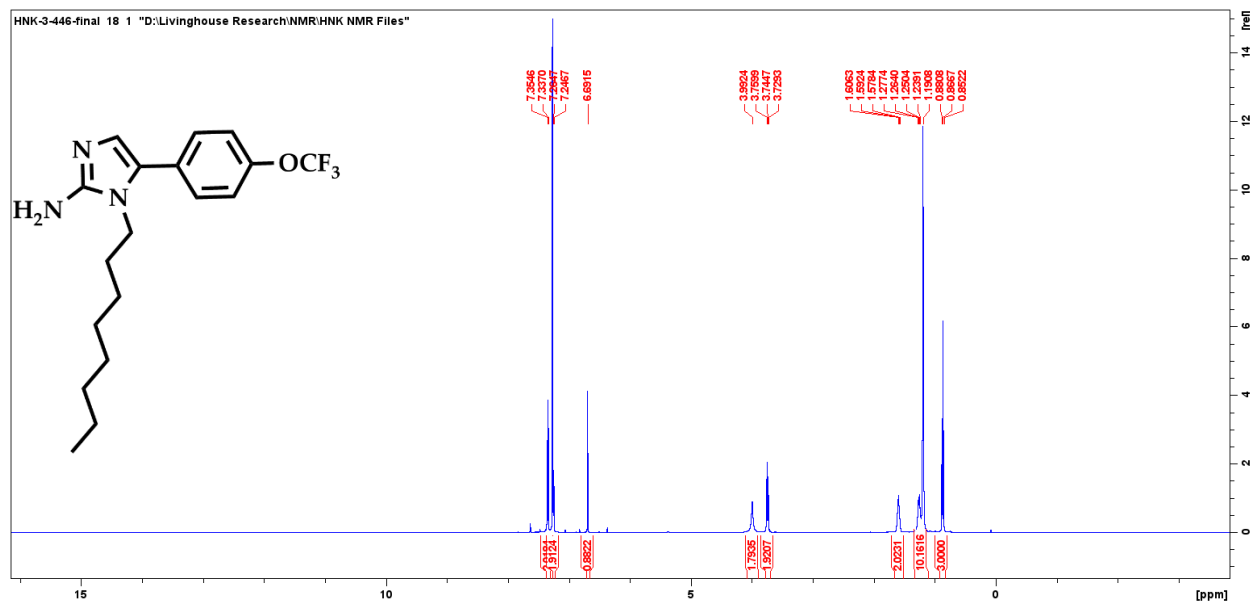


Figure 3.243B: ^1H -NMR Spectra of 1-octyl-5-(4-(trifluoromethoxy)phenyl)-1*H*-imidazol-2-amine (**1.3i**).

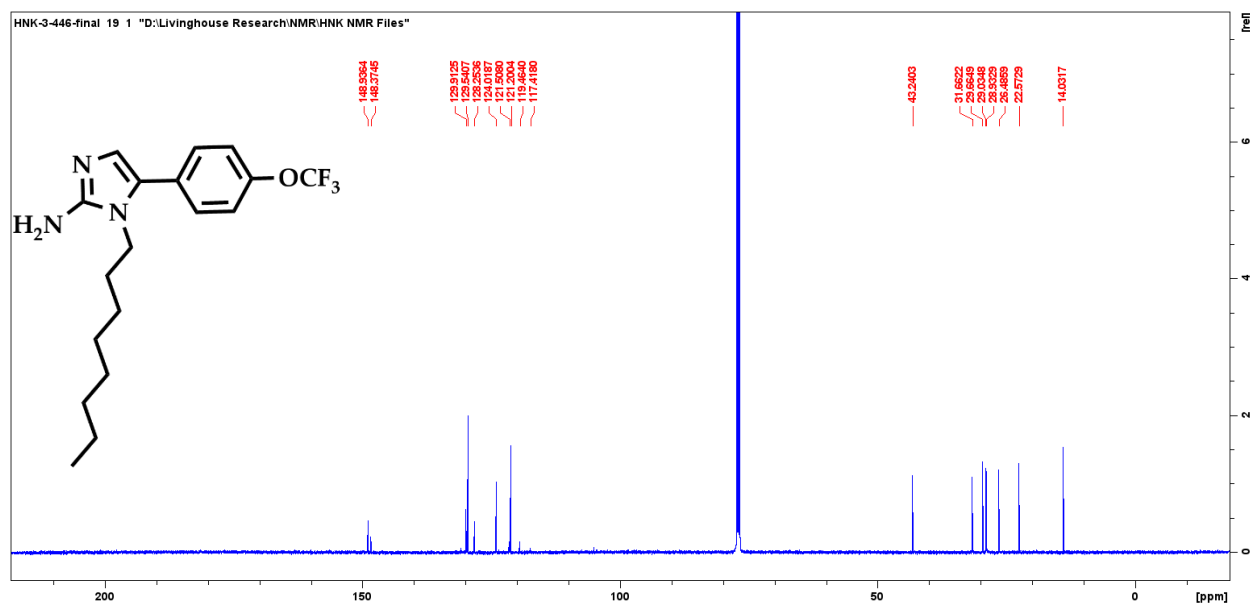


Figure 3.244B: ^{13}C -NMR Spectra of 1-octyl-5-(4-(trifluoromethoxy)phenyl)-1*H*-imidazol-2-amine (**1.3i**).

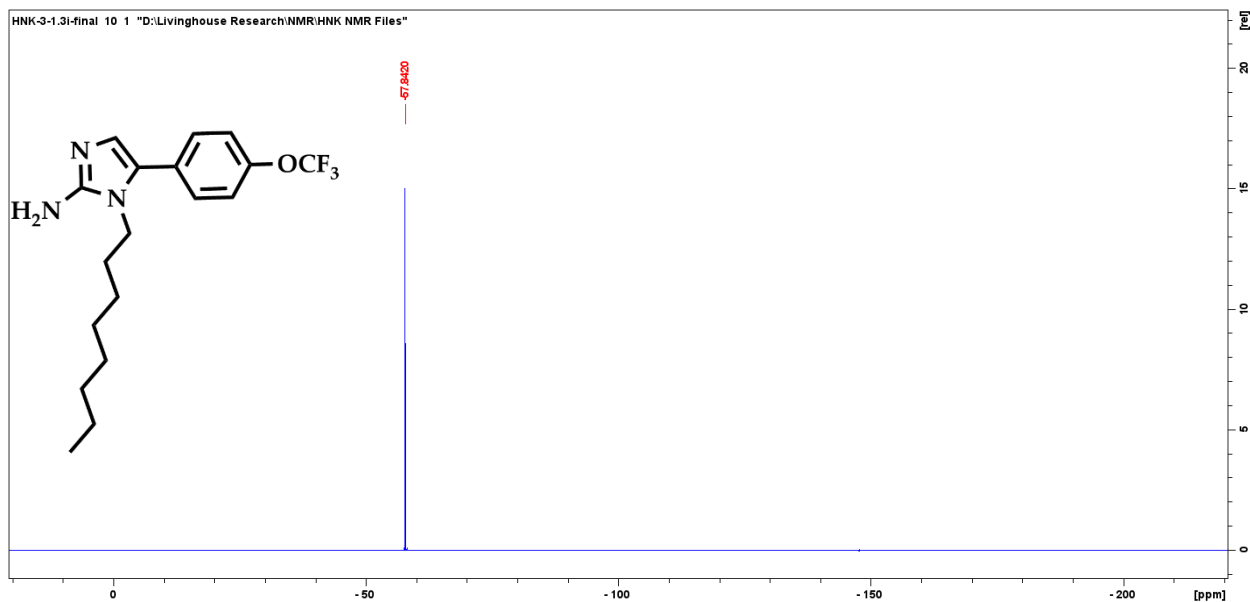


Figure 3.245B: ¹⁹F-NMR Spectra of 1-octyl-5-(4-(trifluoromethoxy)phenyl)-1H-imidazol-2-amine (1.3i).

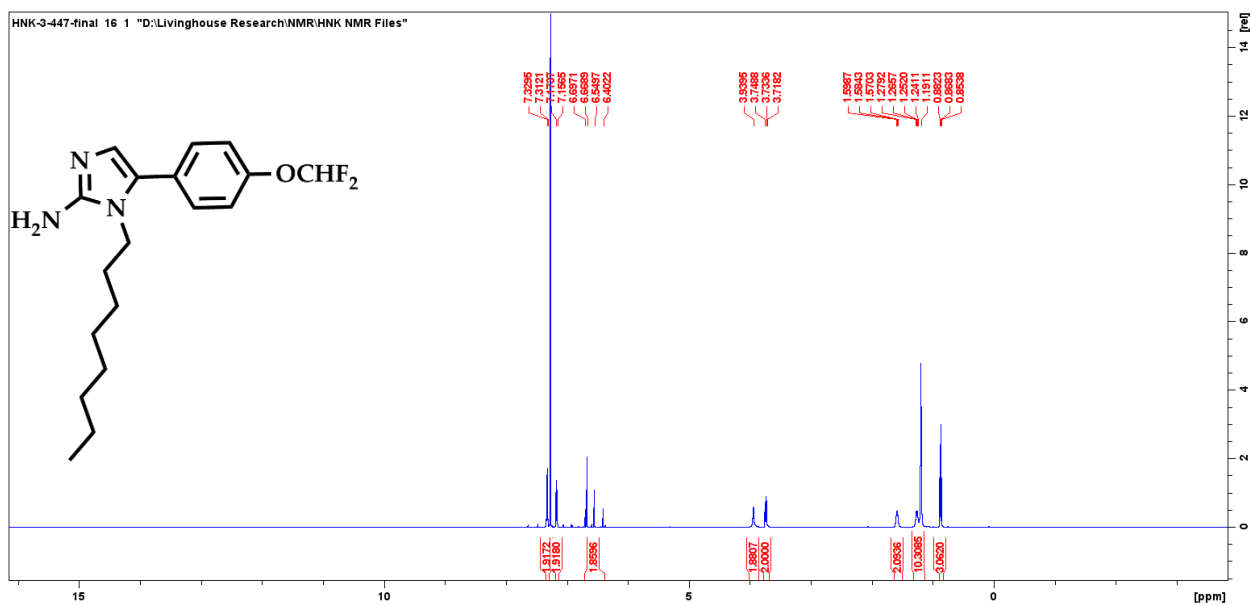


Figure 3.246B: ¹H-NMR Spectra of 5-(4-(difluoromethoxy)phenyl)-1-octyl-1H-imidazol-2-amine (1.3j).

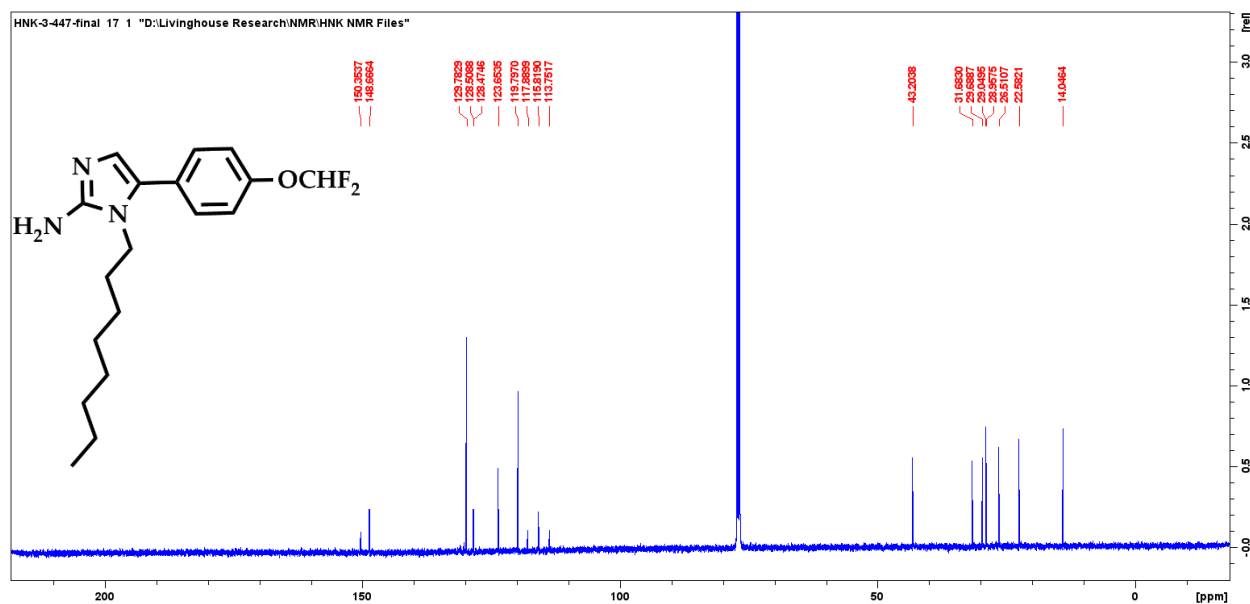


Figure 3.247B: ¹³C-NMR Spectra of 5-(4-(difluoromethoxy)phenyl)-1-octyl-1H-imidazol-2-amine (**1.3j**).

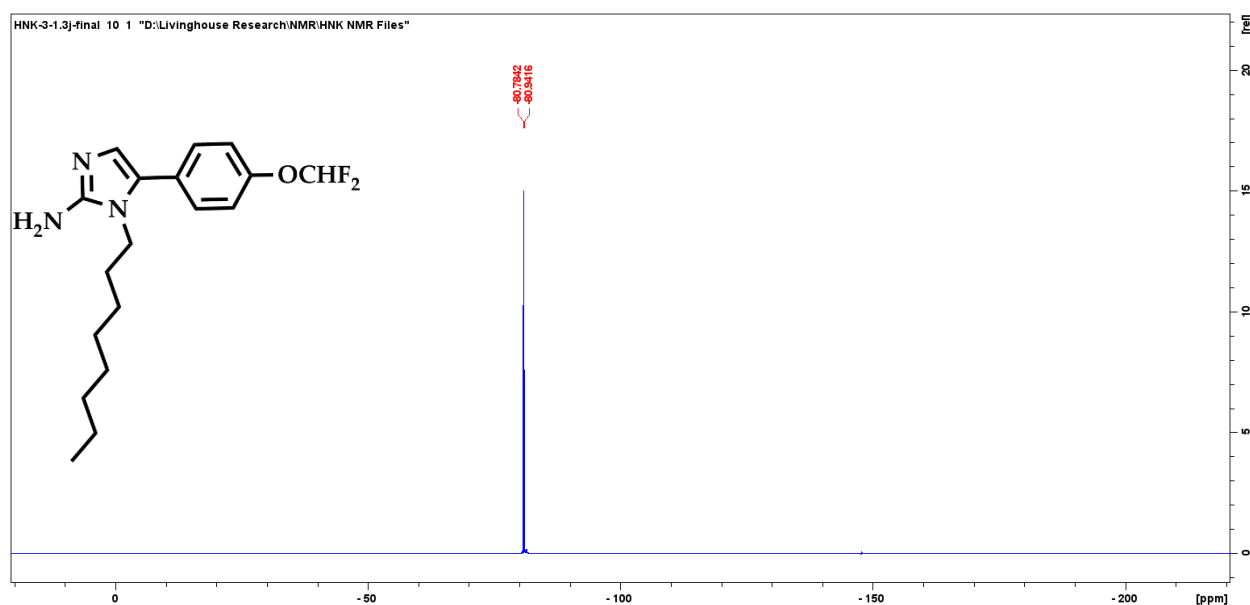


Figure 3.248B: ⁸⁹F-NMR Spectra of 5-(4-(difluoromethoxy)phenyl)-1-octyl-1H-imidazol-2-amine (**1.3j**).

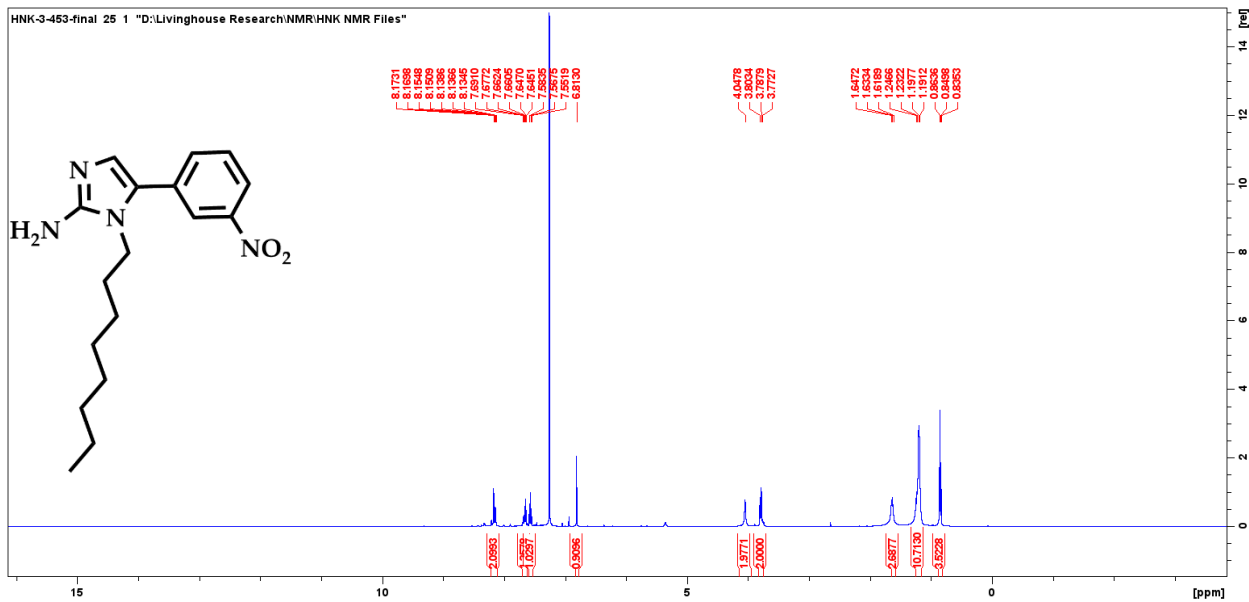


Figure 3.249B: ^1H -NMR Spectra of 5-(3-nitrophenyl)-1-octyl-1*H*-imidazol-2-amine (**1.3k**).

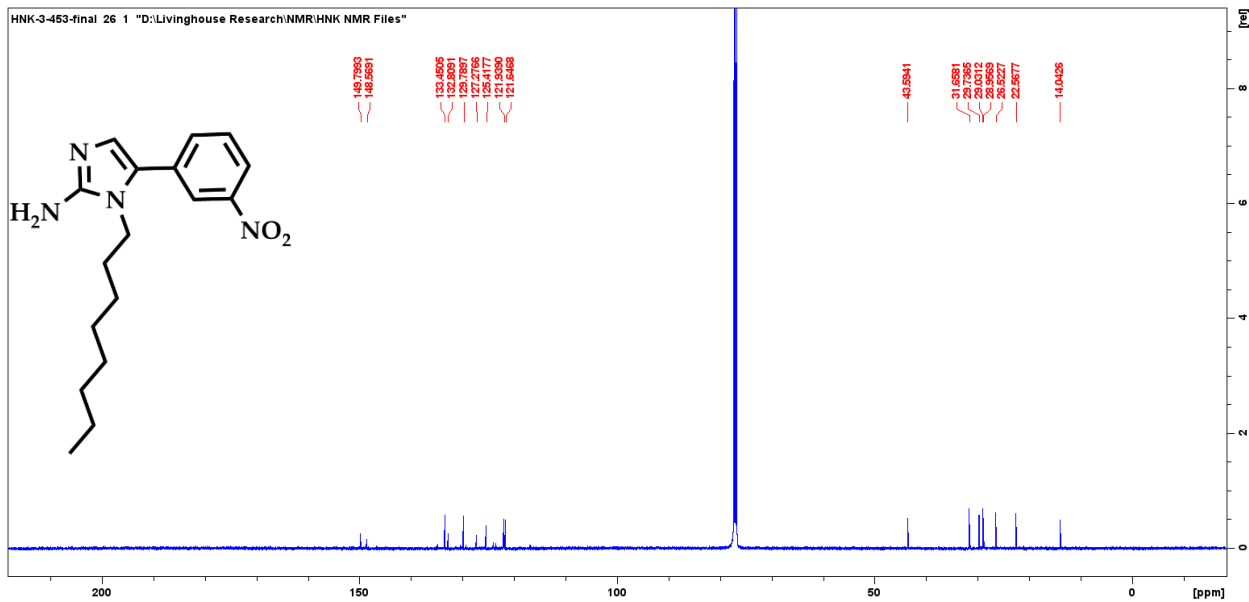


Figure 3.250B: ¹³C-NMR Spectra of 5-(3-nitrophenyl)-1-octyl-1*H*-imidazol-2-amine (**1.3k**).

HNK-3-42-final 11 1 "D:\Livinghouse Research\NMR\HNK NMR Files"

Chemical structure: Nc1nc(C2=CC=C(C=C2)Cl)n(CCCCS)cc1

¹H NMR spectrum (ppm):

- 149.2017
- 131.9843
- 128.9473
- 128.1525
- 126.0296
- 126.1696
- 121.9696
- 43.6594
- 39.5695
- 31.7065
- 30.5165
- 29.1885
- 22.2536
- 13.9555

Figure 3.252B: ¹³C-NMR Spectra of 5-(4-chlorophenyl)-1-(2-(pentylthio)ethyl)-1*H*-imidazol-2-amine (**2.3a**).

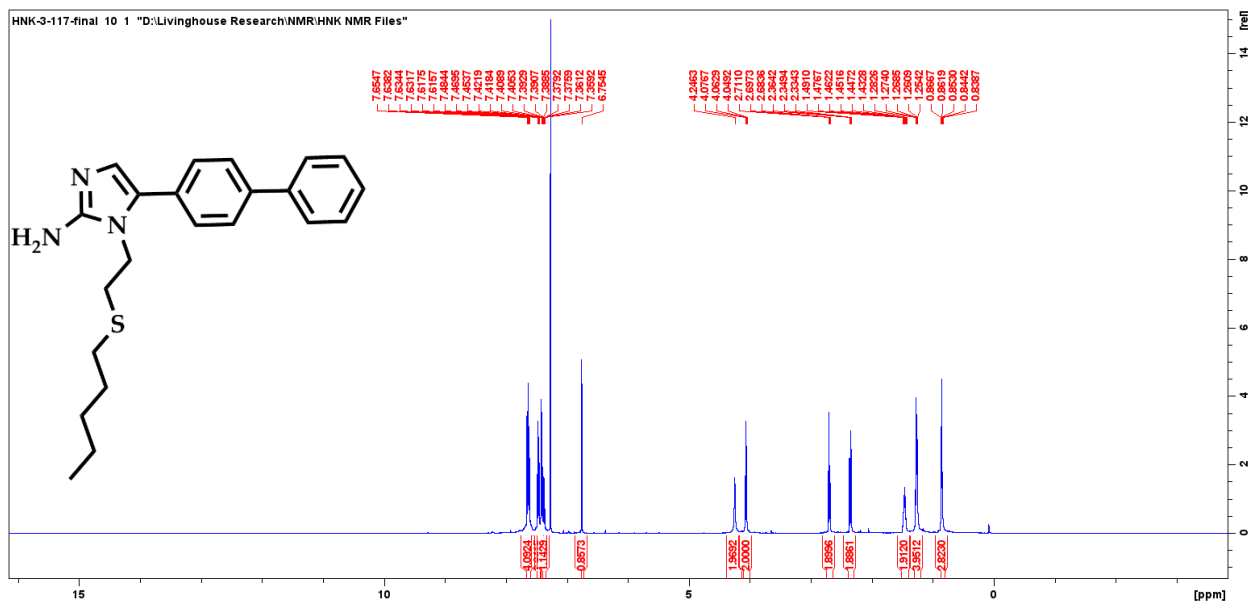


Figure 3.253B: ^1H -NMR Spectra of 5-([1,1'-biphenyl]-4-yl)-1-(2-(pentylthio)ethyl)-1*H*-imidazol-2-amine (**2.3b**).

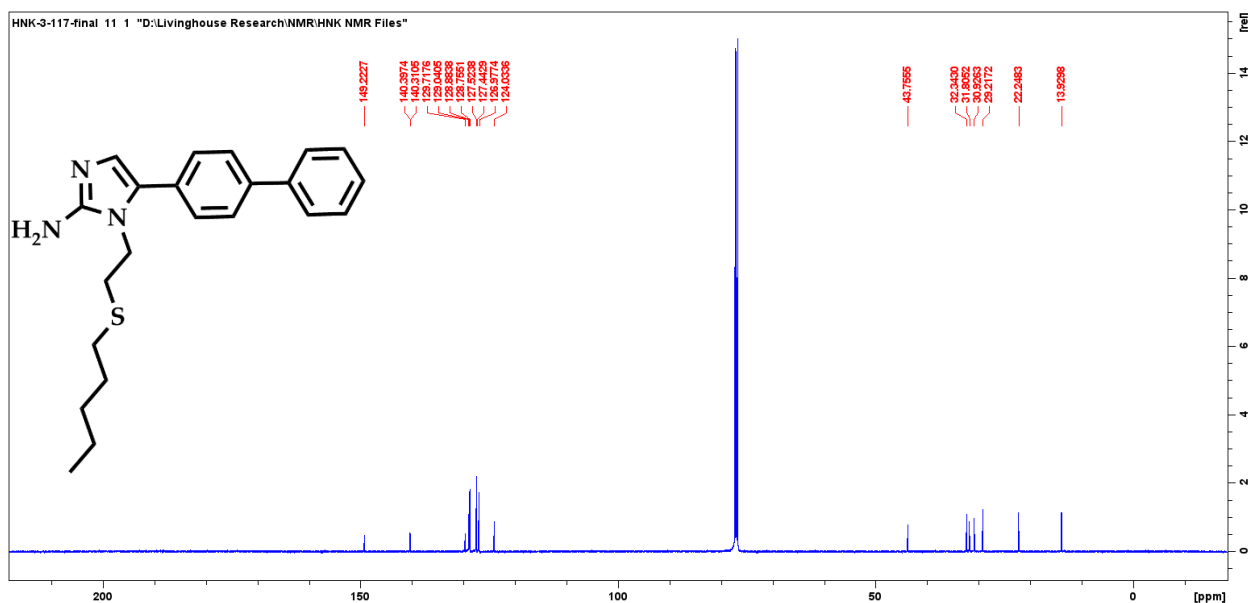


Figure 3.254B: ^{13}C -NMR Spectra of 5-([1,1'-biphenyl]-4-yl)-1-(2-(pentylthio)ethyl)-1*H*-imidazol-2-amine (**2.3b**).

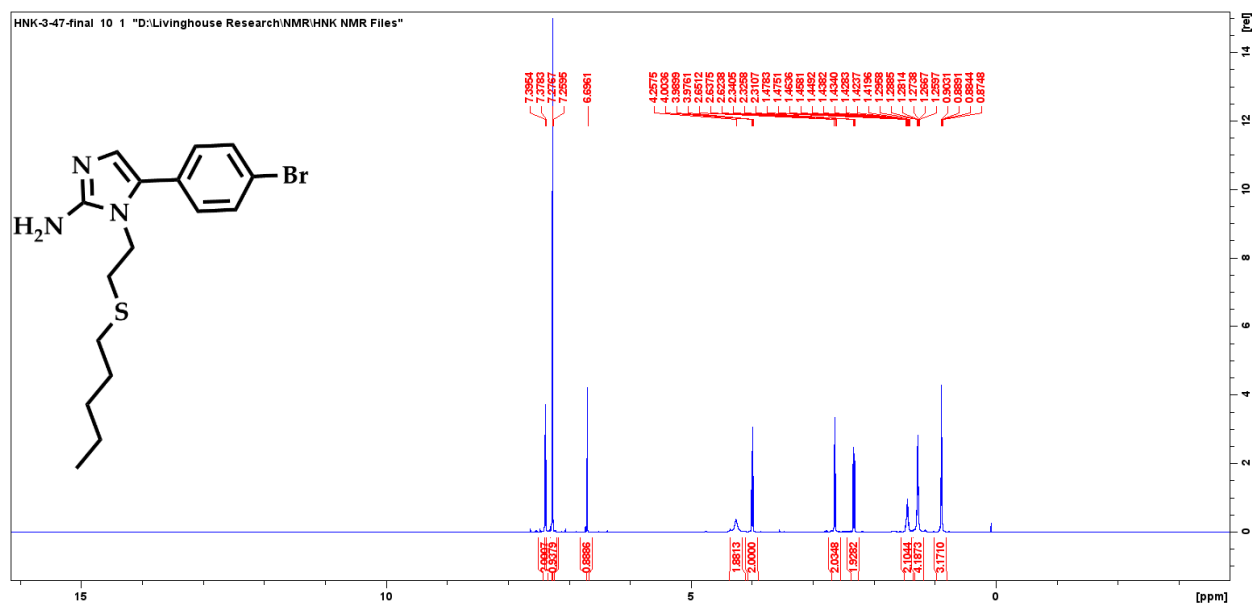


Figure 3.255B: ^1H -NMR Spectra of 5-(4-bromophenyl)-1-(2-(pentylthio)ethyl)-1*H*-imidazol-2-amine (**2.3c**).

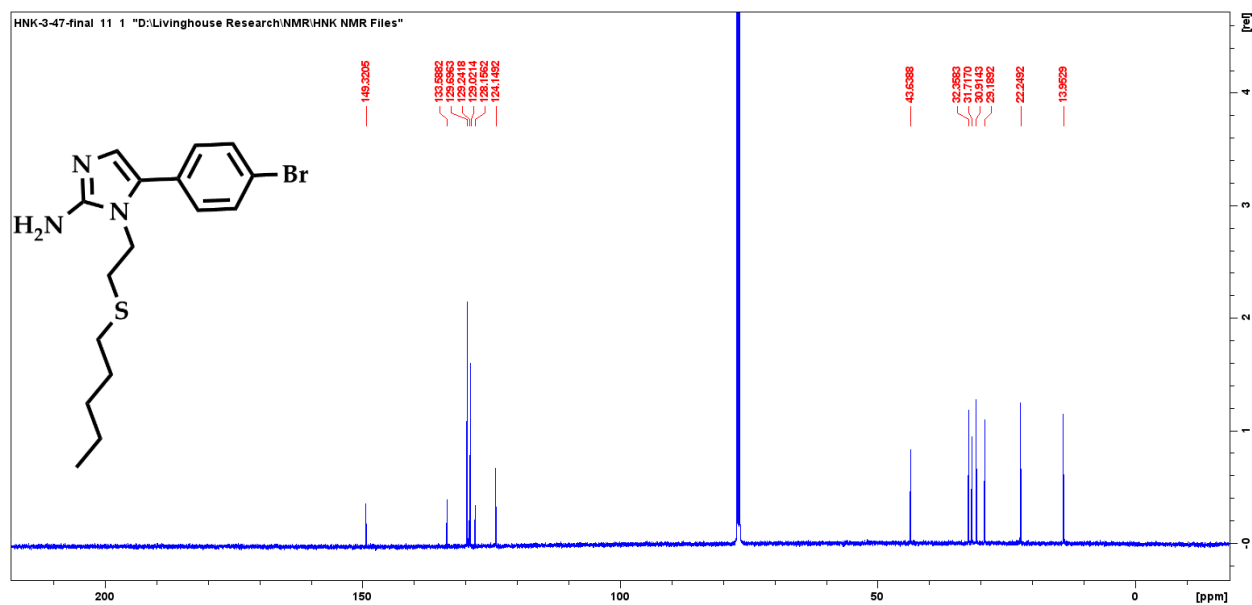


Figure 3.256B: ^{13}C -NMR Spectra of 5-(4-bromophenyl)-1-(2-(pentylthio)ethyl)-1*H*-imidazol-2-amine (**2.3c**).

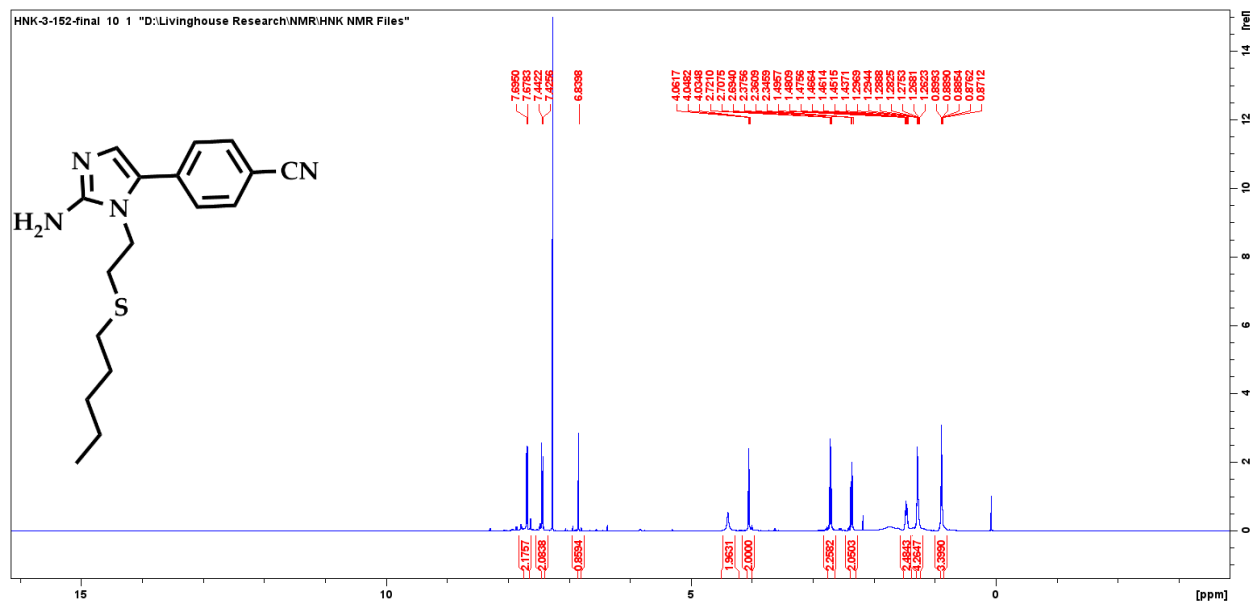


Figure 3.257B: ^1H -NMR Spectra of 4-(2-amino-1-(2-(pentylthio)ethyl)-1H-imidazol-5-yl)benzonitrile (2.3d).

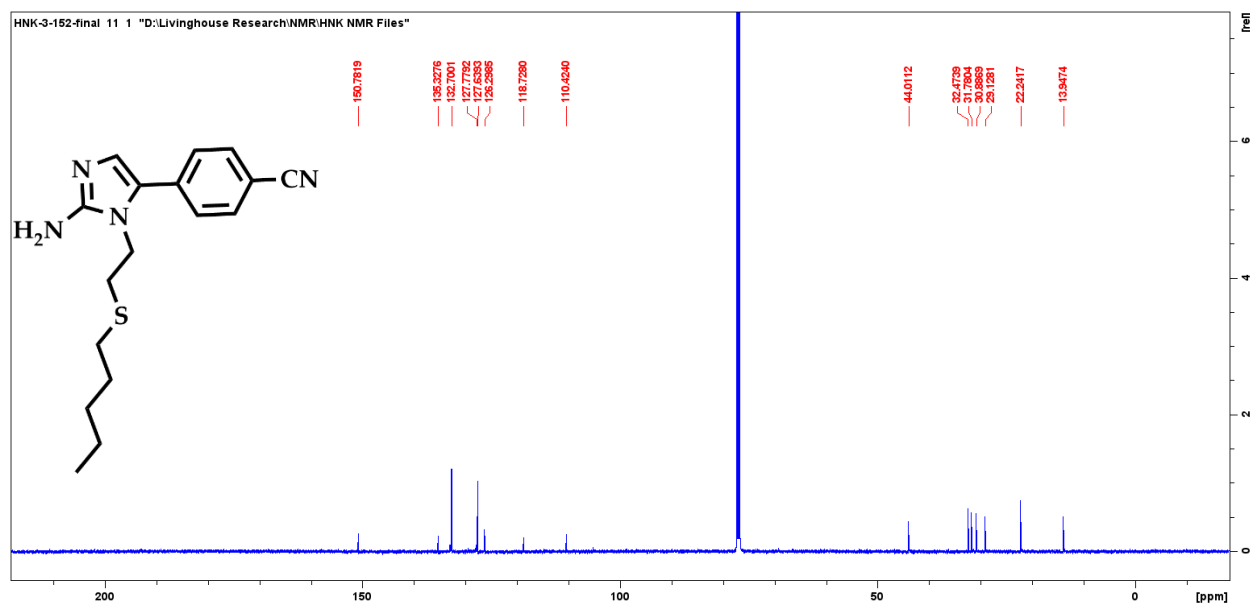


Figure 3.258B: ^{13}C -NMR Spectra of 4-(2-amino-1-(2-(pentylthio)ethyl)-1H-imidazol-5-yl)benzonitrile (2.3d).

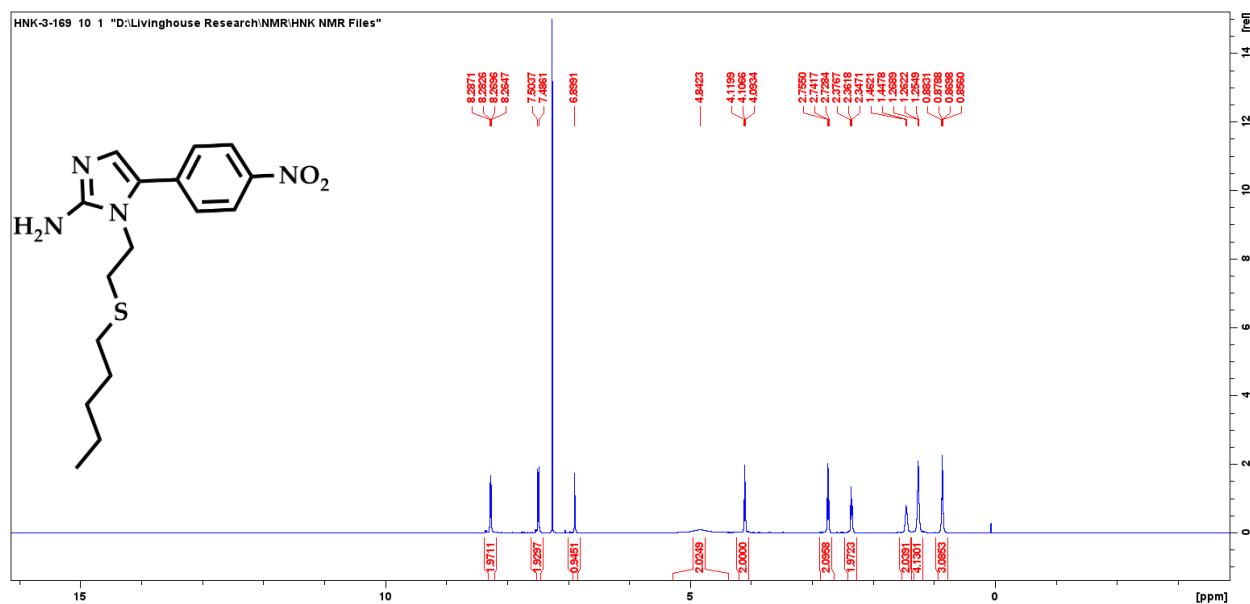


Figure 3.259B: ^1H -NMR Spectra of 5-(4-nitrophenyl)-1-(2-(pentylthio)ethyl)-1*H*-imidazol-2-amine (**2.3e**).

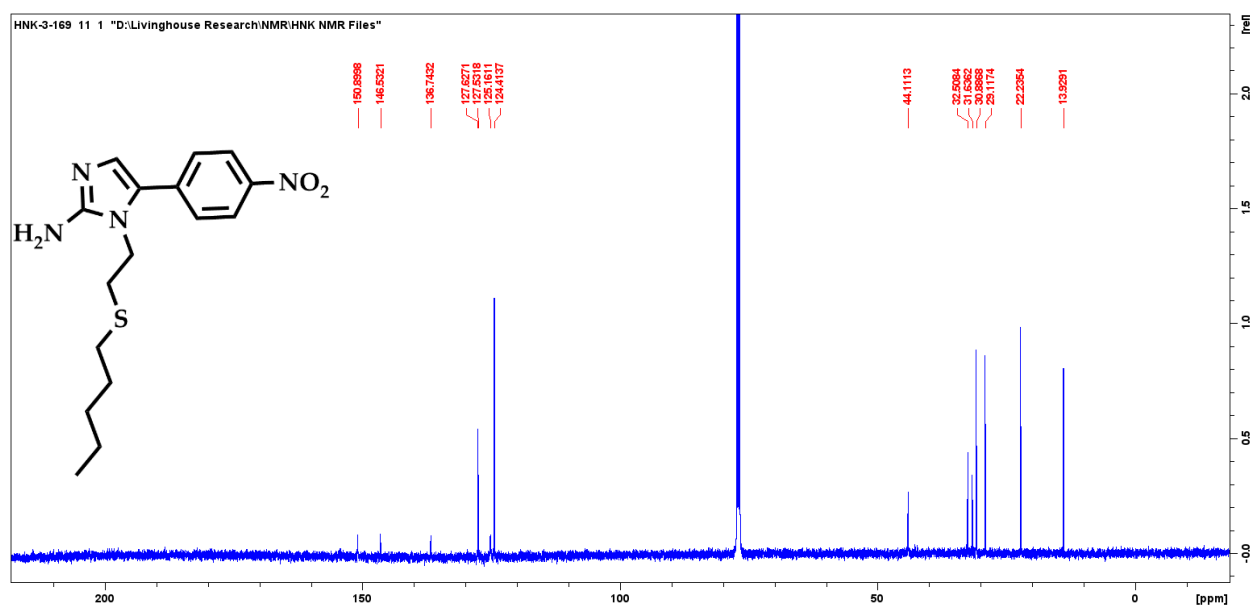


Figure 3.260B: ^{13}C -NMR Spectra of 5-(4-nitrophenyl)-1-(2-(pentylthio)ethyl)-1*H*-imidazol-2-amine (**2.3e**).

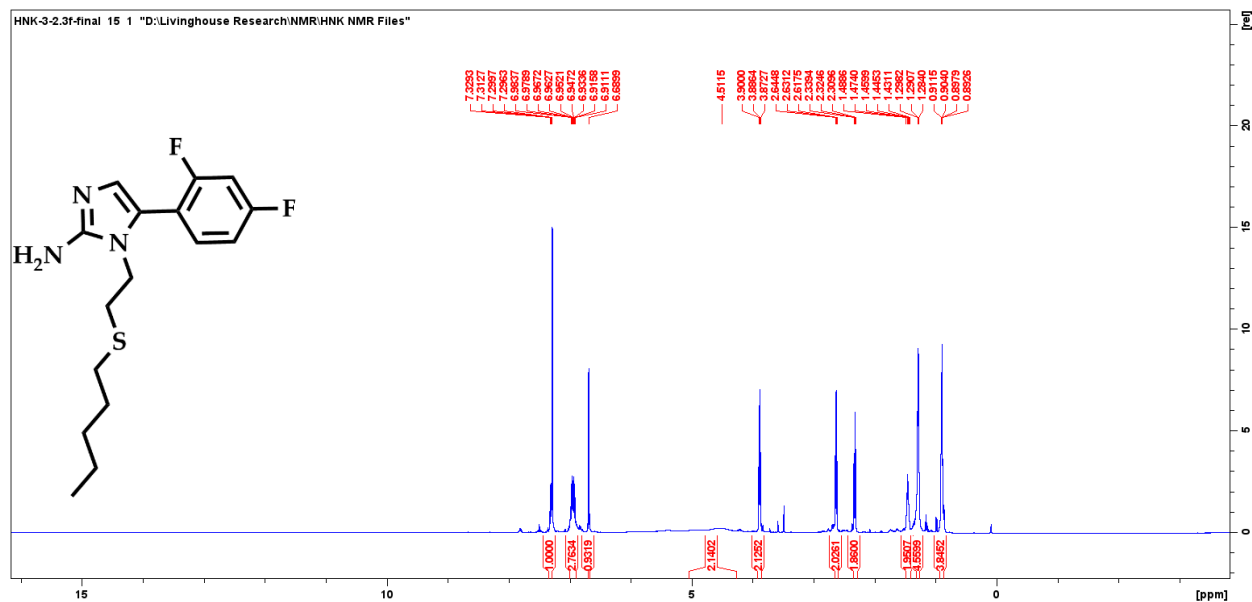


Figure 3.261B: ^1H -NMR Spectra of 5-(2,4-difluorophenyl)-1-(2-(pentylthio)ethyl)-1*H*-imidazole-2-amine (**2.3f**).

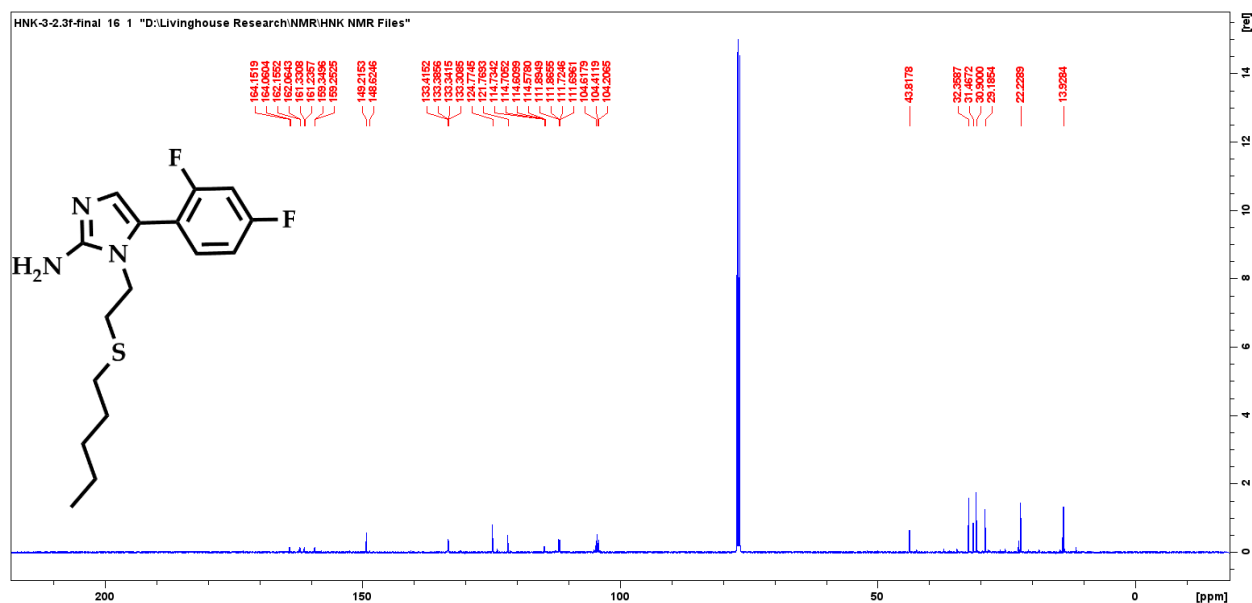


Figure 3.262B: ^{13}C -NMR Spectra of 5-(2,4-difluorophenyl)-1-(2-(pentylthio)ethyl)-1*H*-imidazole-2-amine (**2.3f**).

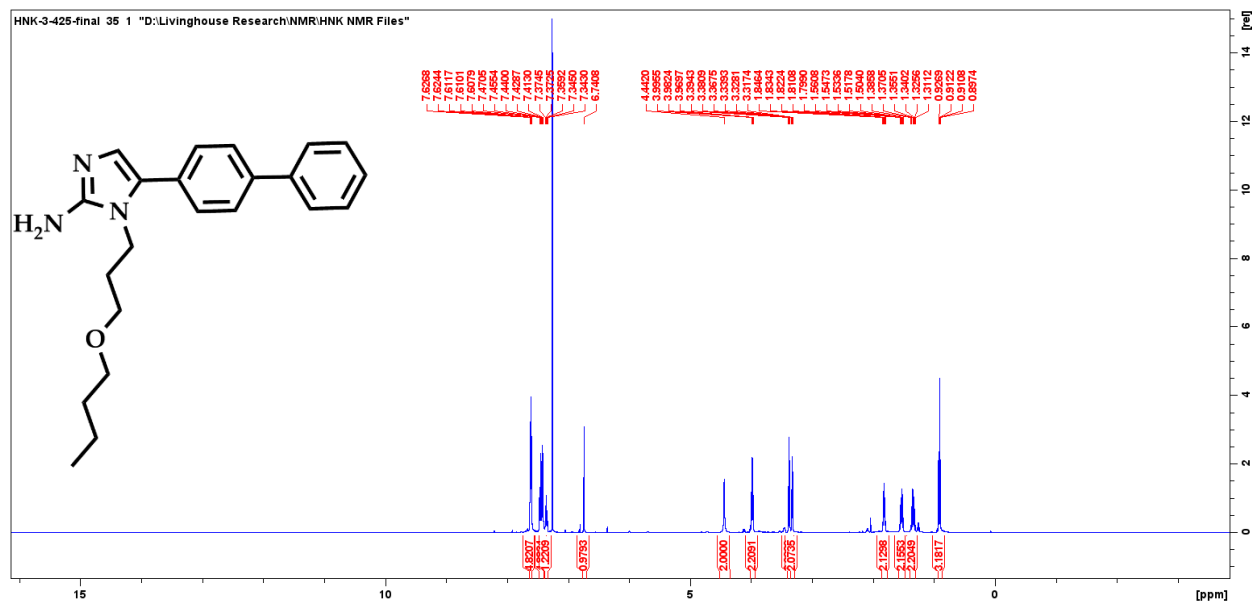


Figure 3.265B: ^1H -NMR Spectra of 5-([1,1'-biphenyl]-4-yl)-1-(3-butoxypropyl)-1H-imidazol-2-amine (3.3b).

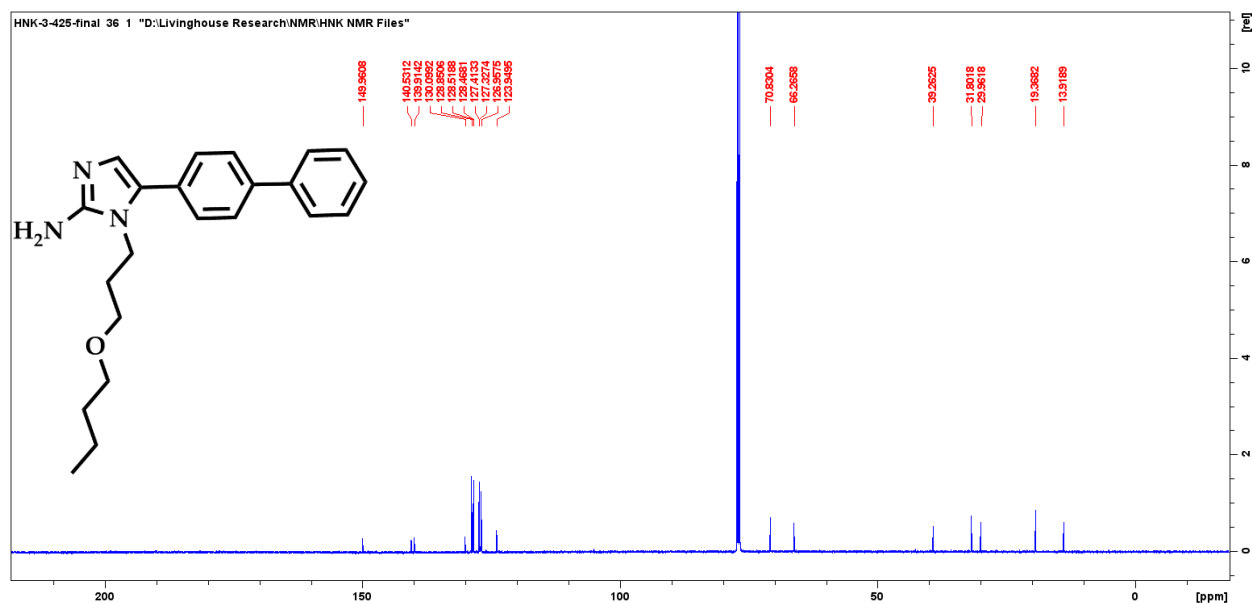


Figure 3.266B: ^{13}C -NMR Spectra of 5-([1,1'-biphenyl]-4-yl)-1-(3-butoxypropyl)-1H-imidazol-2-amine (3.3b).

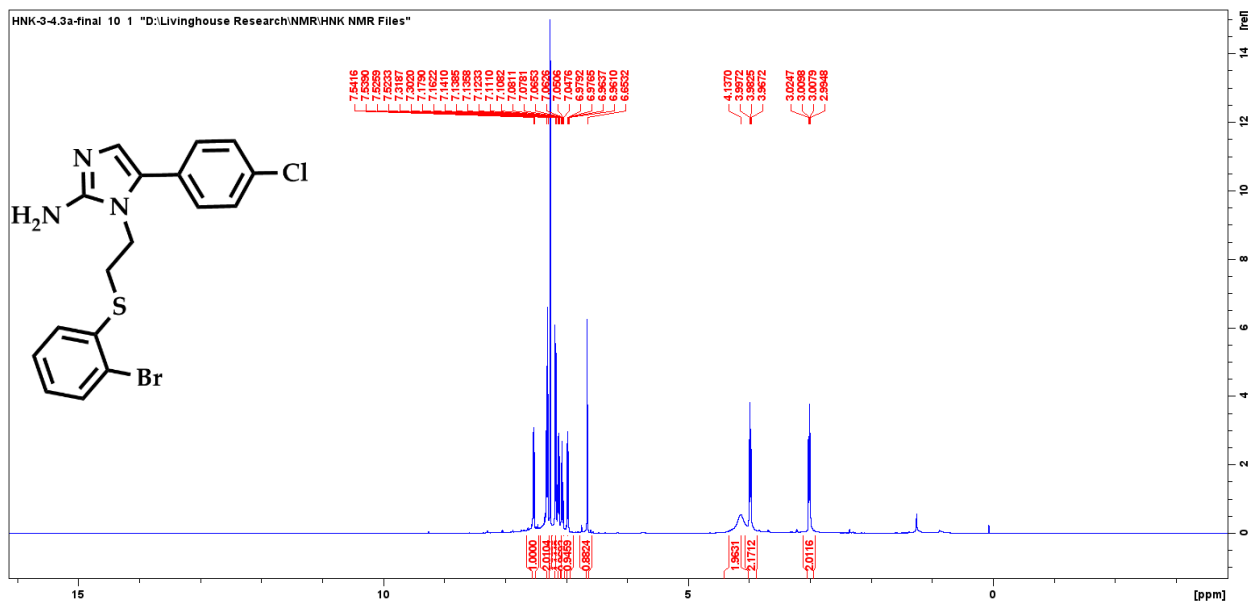


Figure 3.267B: ¹H-NMR Spectra of 1-(2-((2-bromophenyl)thio)ethyl)-5-(4-chlorophenyl)-1H-imidazol-2-amine (**4.3a**).

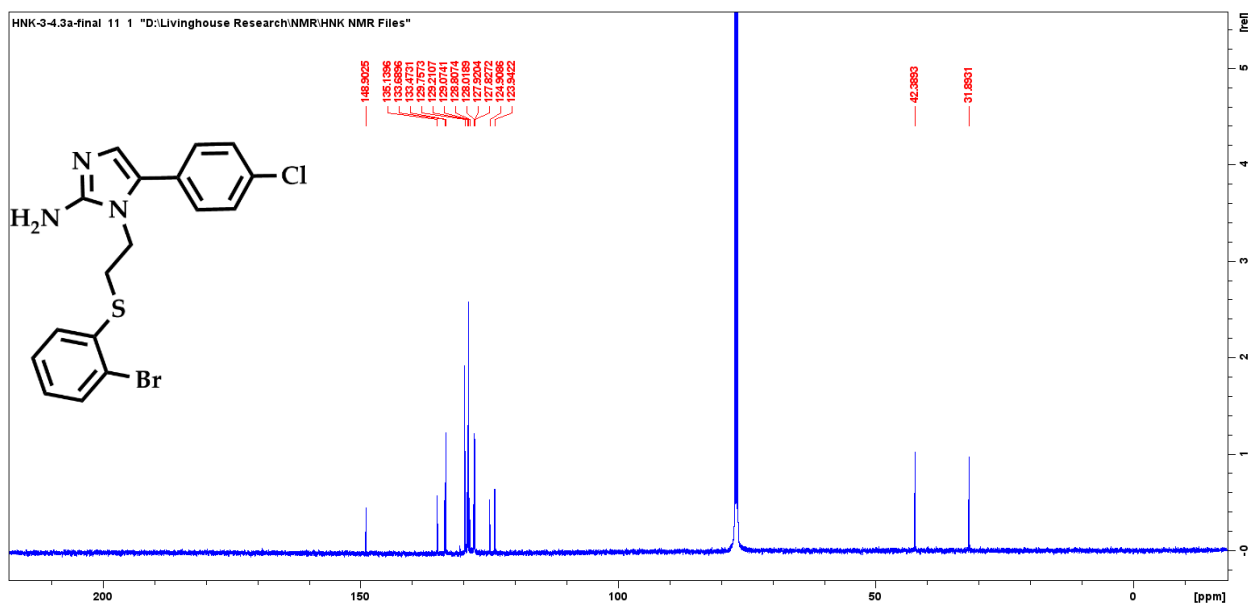


Figure 3.268B: ¹³C-NMR Spectra of 1-(2-((2-bromophenyl)thio)ethyl)-5-(4-chlorophenyl)-1H-imidazol-2-amine (**4.3a**).

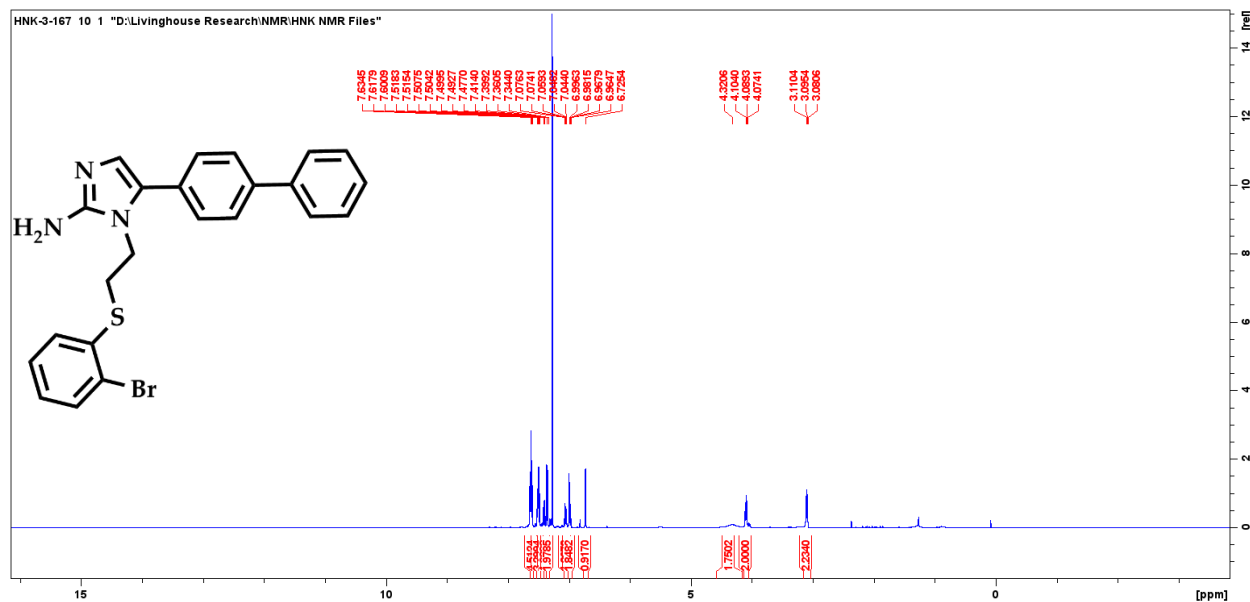
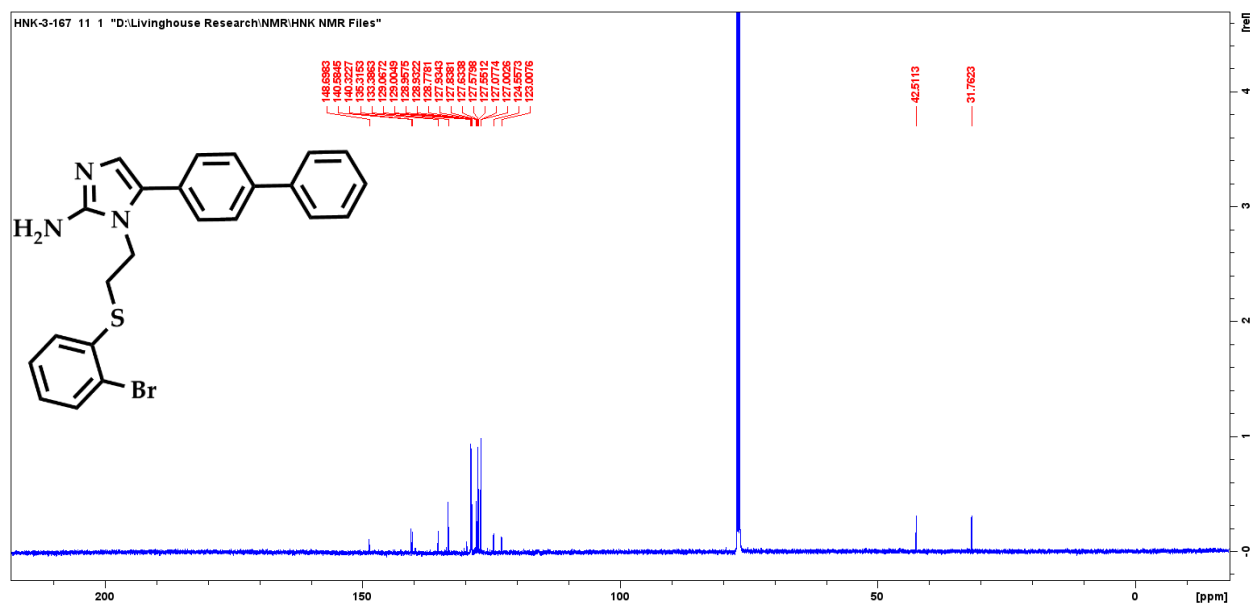
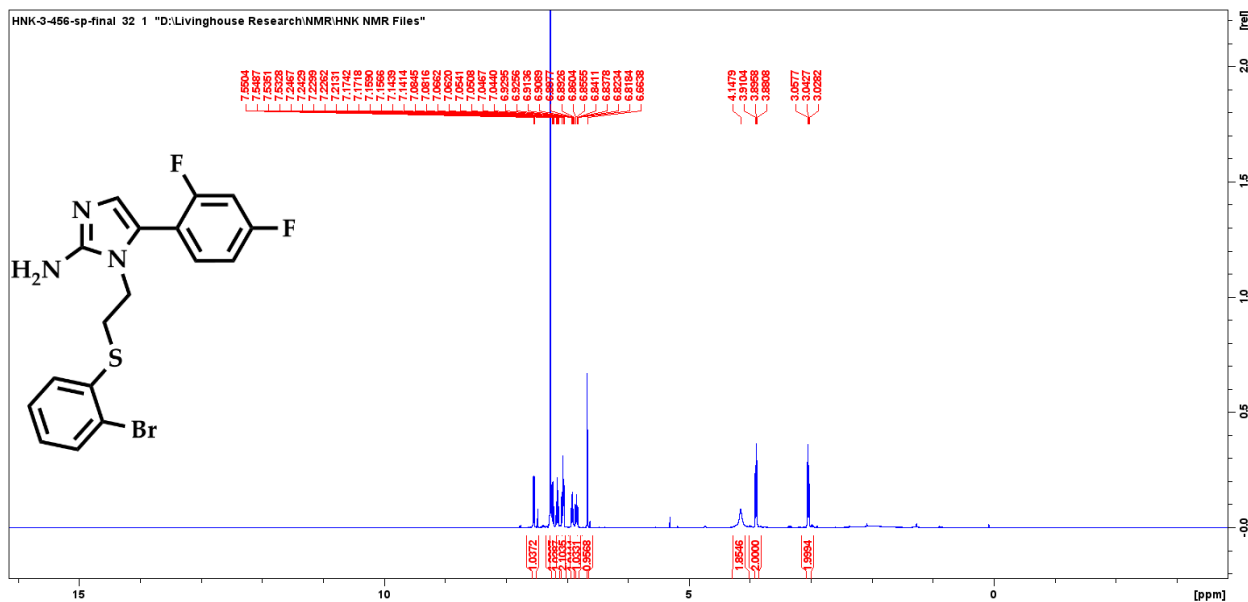


Figure 3.269B: ¹H-NMR Spectra of 5-([1,1'-biphenyl]-4-yl)-1-(2-((2-bromophenyl)thio)ethyl)-1H-imidazol-2-amine (**4.3b**).





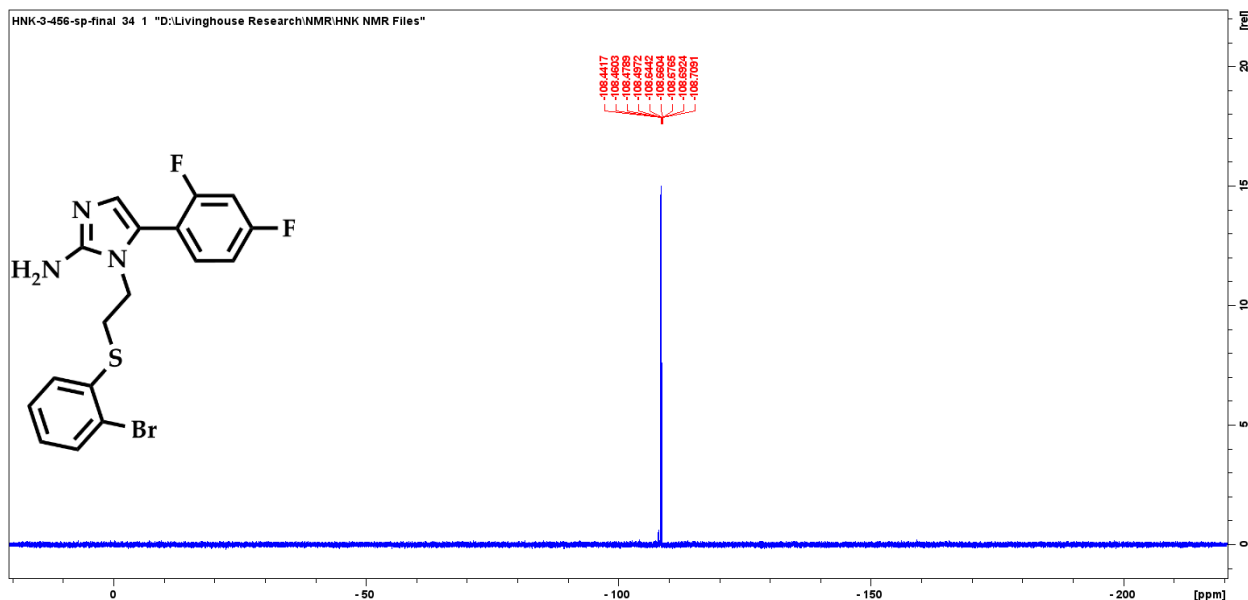
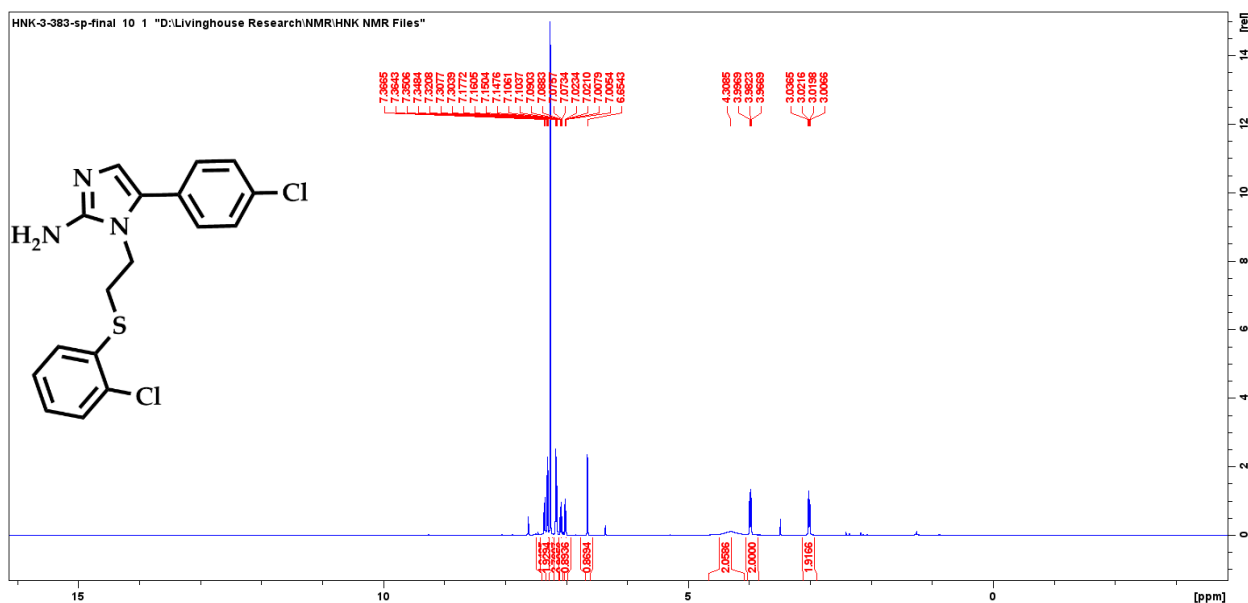


Figure 3.279B: ¹⁹F-NMR Spectra of 1-(2-((2-bromophenyl)thio)ethyl)-5-(2,4-difluorophenyl)-1H-imidazol-2-amine (4.3f).



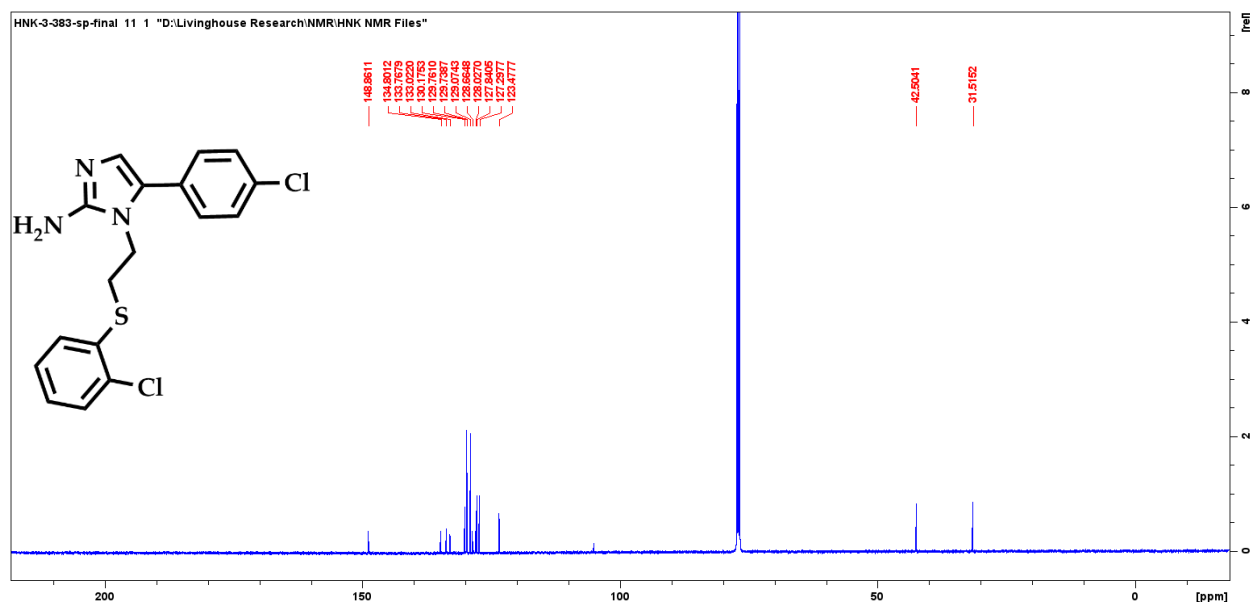


Figure 3.281B: ¹³C-NMR Spectra of 5-(4-chlorophenyl)-1-(2-((2-chlorophenyl)thio)ethyl)-1H-imidazol-2-amine (5.3a).

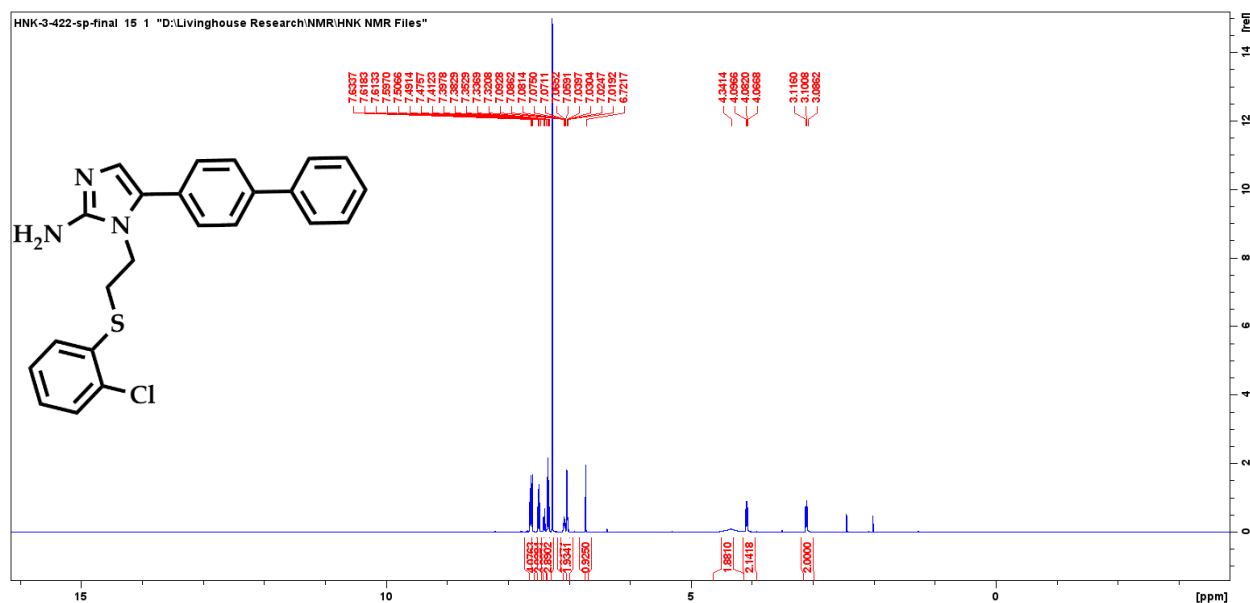


Figure 3.282B: ¹H-NMR Spectra of 5-([1,1'-biphenyl]-4-yl)-1-(2-((2-chlorophenyl)thio)ethyl)-1H-imidazol-2-amine (5.3b).

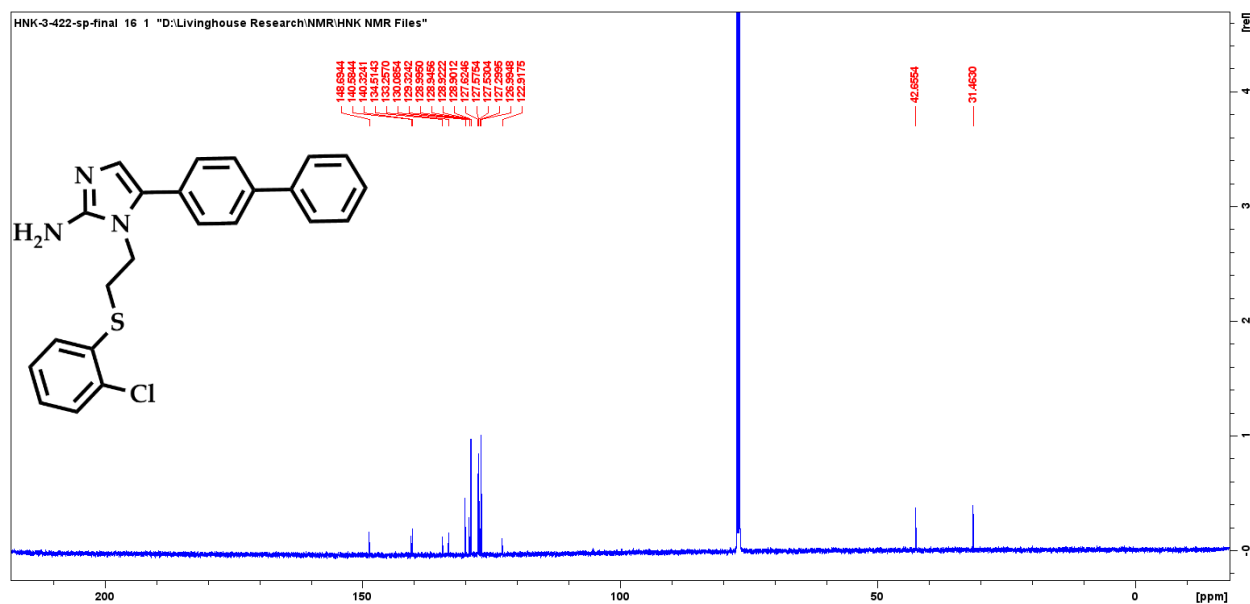


Figure 3.283B: ¹³C-NMR Spectra of 5-([1,1'-biphenyl]-4-yl)-1-(2-((2-chlorophenyl)thio)ethyl)-1H-imidazol-2-amine (5.3b).

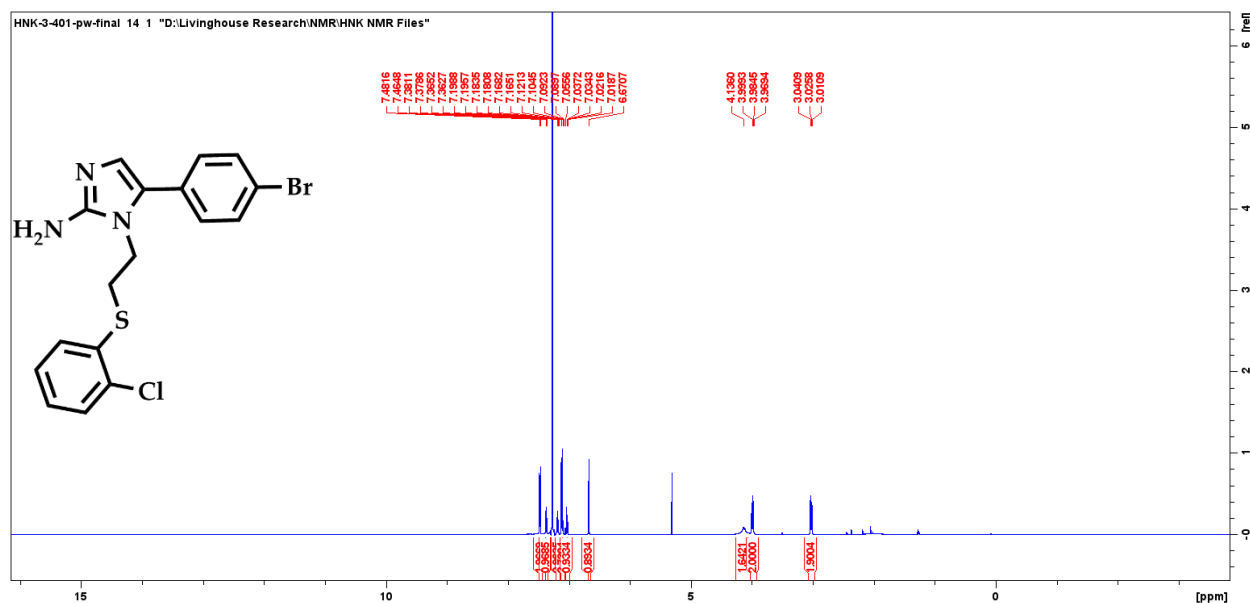


Figure 3.284B: ¹H-NMR Spectra of 5-(4-bromophenyl)-1-(2-((2-chlorophenyl)thio)ethyl)-1H-imidazol-2-amine (5.3c).

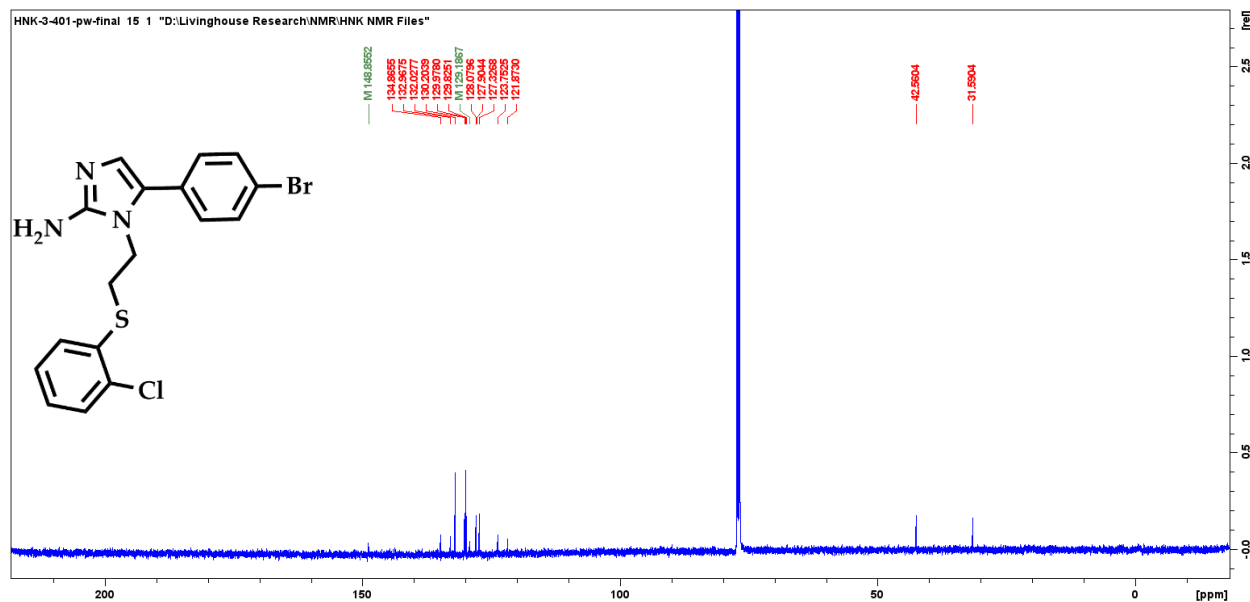


Figure 3.285B: ¹³C-NMR Spectra of 5-(4-bromophenyl)-1-(2-((2-chlorophenyl)thio)ethyl)-1H-imidazol-2-amine (5.3c).

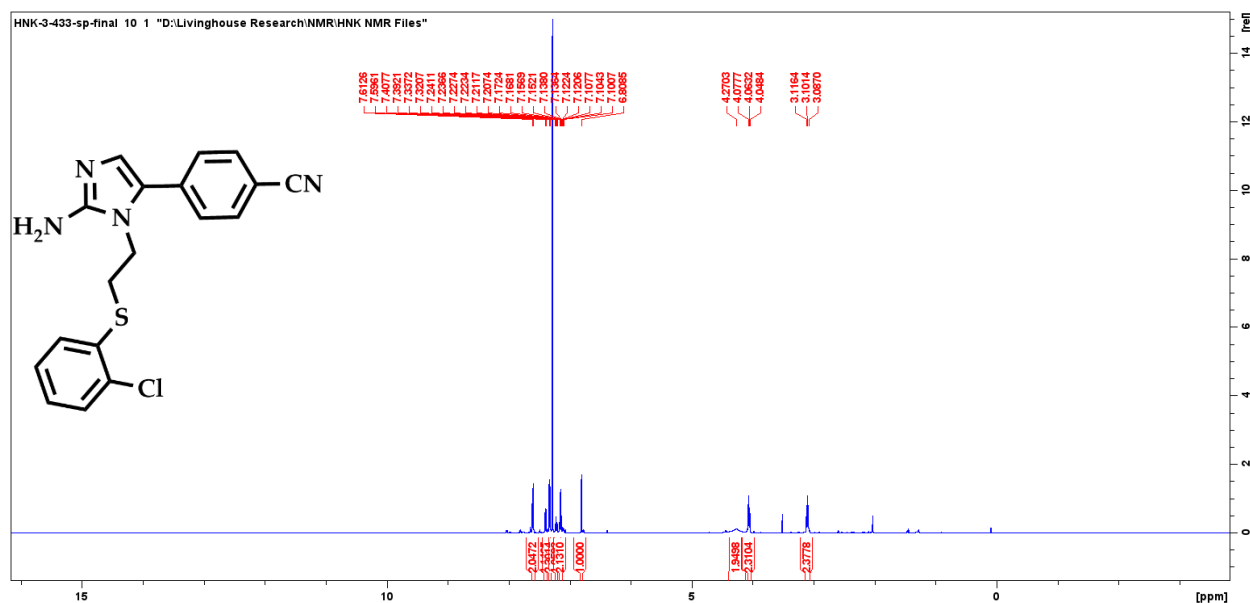


Figure 3.286B: ¹H-NMR Spectra of 4-(2-amino-1-(2-((2-chlorophenyl)thio)ethyl)-1H-imidazol-5-yl)benzonitrile (5.3d).

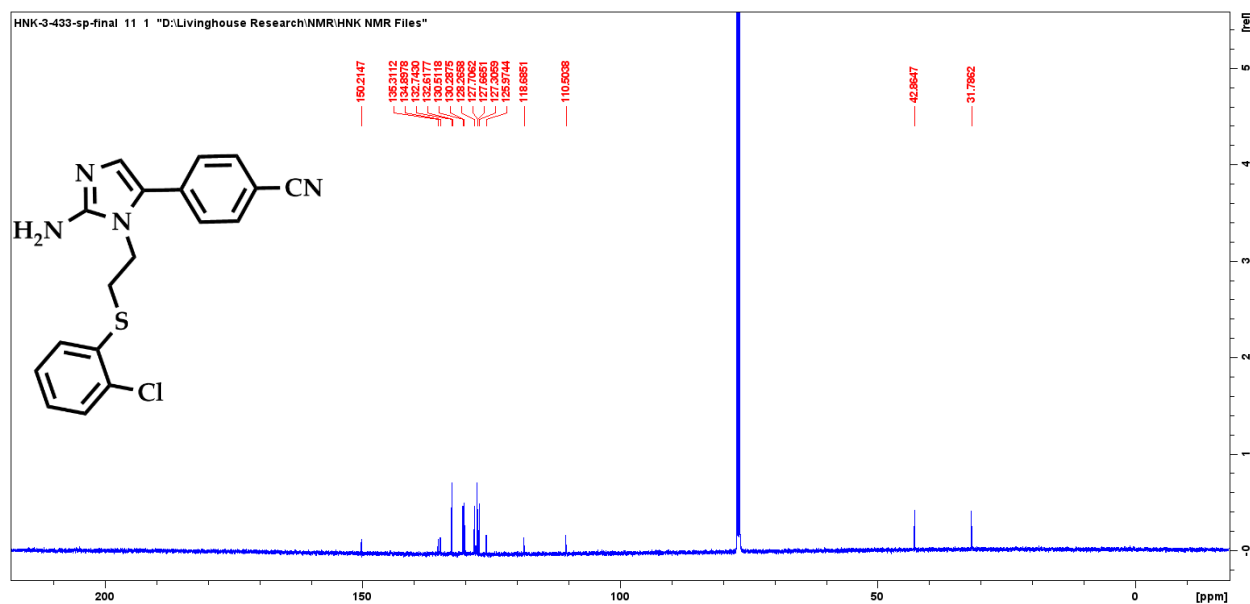


Figure 3.287B: ¹³C-NMR Spectra of 4-(2-amino-1-(2-((2-chlorophenyl)thio)ethyl)-1H-imidazol-5-yl)benzonitrile (5.3d).

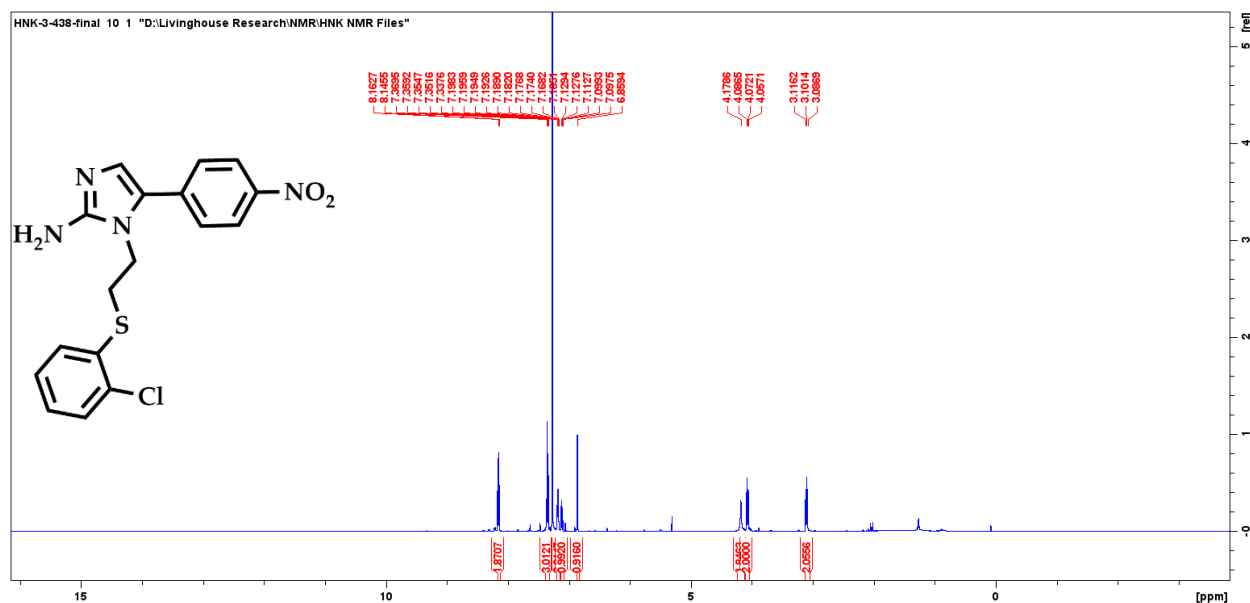


Figure 3.288B: ¹H-NMR Spectra of 1-(2-((2-chlorophenyl)thio)ethyl)-5-(4-nitrophenyl)-1H-imidazol-2-amine (5.3e).

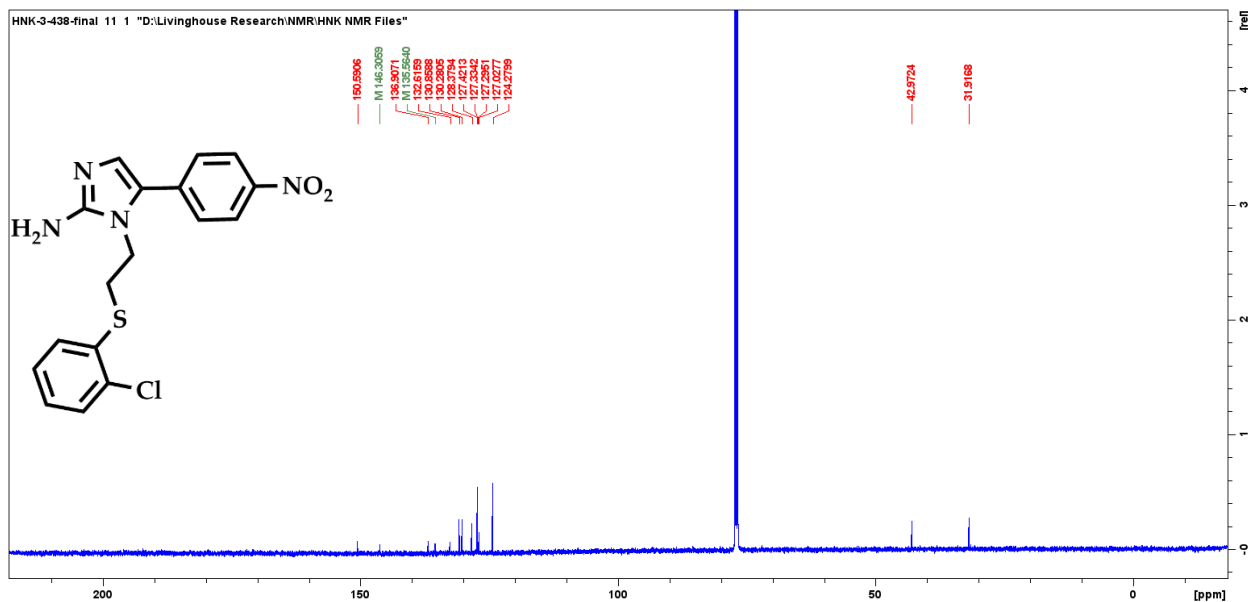


Figure 3.289B: ¹³C-NMR Spectra of 1-(2-((2-chlorophenyl)thio)ethyl)-5-(4-nitrophenyl)-1H-imidazol-2-amine (5.3e).

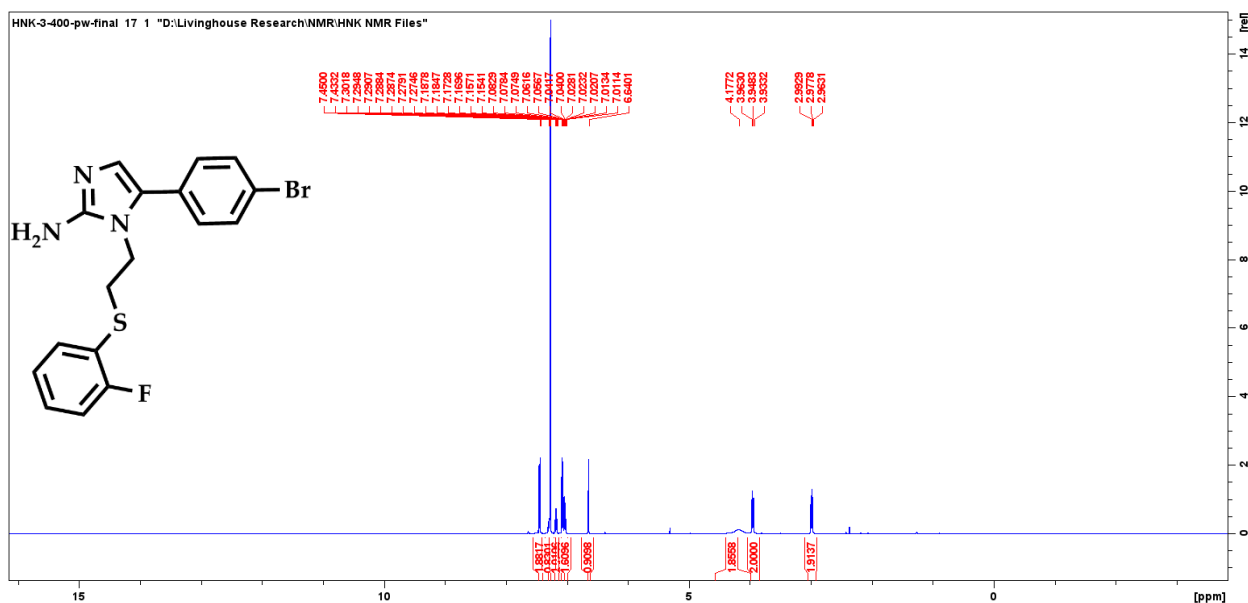


Figure 3.290B: ¹H-NMR Spectra of 5-(4-bromophenyl)-1-(2-((2-fluorophenyl)thio)ethyl)-1H-imidazol-2-amine (6.3c).

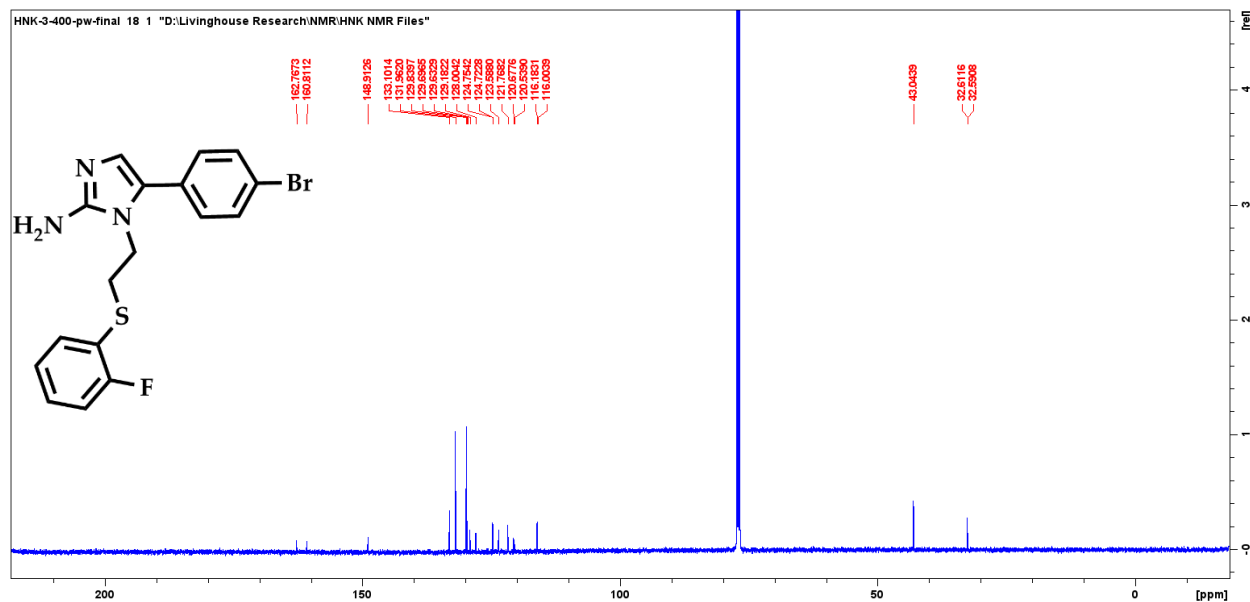


Figure 3.291B: ¹³C-NMR Spectra of 5-(4-bromophenyl)-1-(2-((2-fluorophenyl)thio)ethyl)-1H-imidazol-2-amine (6.3c).

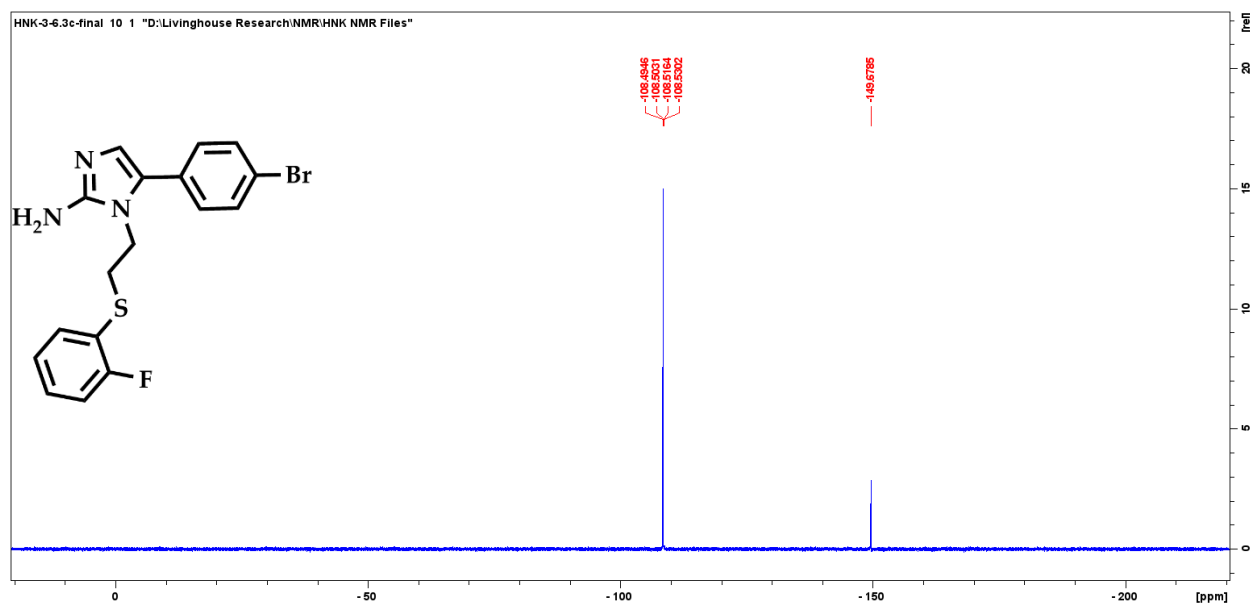


Figure 3.292B: ¹⁹F-NMR Spectra of 5-(4-bromophenyl)-1-(2-((2-fluorophenyl)thio)ethyl)-1H-imidazol-2-amine (6.3c).

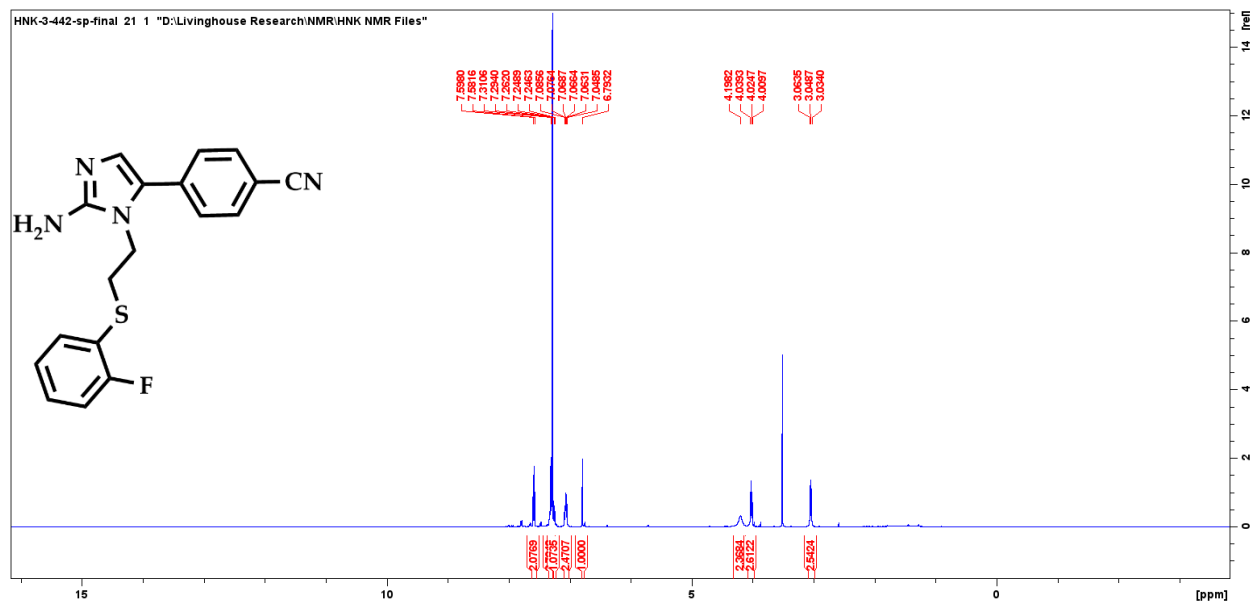


Figure 3.293B: ^1H -NMR Spectra of 5-(4-cyanophenyl)-1-(2-((2-fluorophenyl)thio)ethyl)-1H-imidazol-2-amine (**6.3d**).

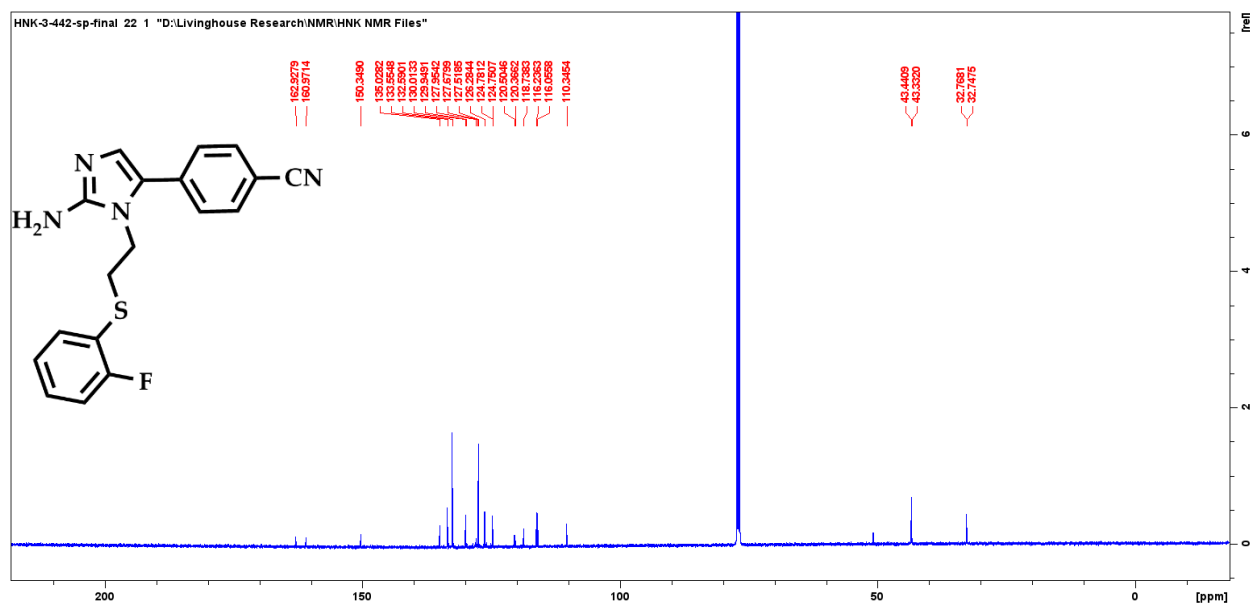


Figure 3.294B: ^{13}C -NMR Spectra of 5-(4-cyanophenyl)-1-(2-((2-fluorophenyl)thio)ethyl)-1H-imidazol-2-amine (**6.3d**).

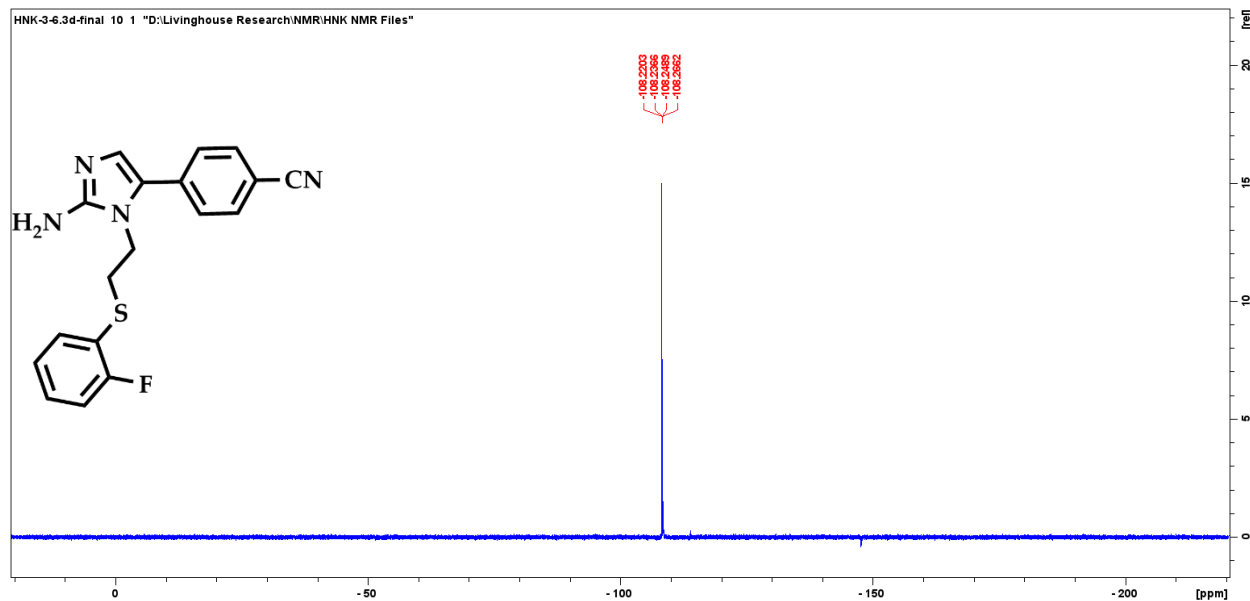


Figure 3.295B: ¹⁹F-NMR Spectra of 5-(4-cyanophenyl)-1-(2-((2-fluorophenyl)thio)ethyl)-1H-imidazol-2-amine (**6.3d**).

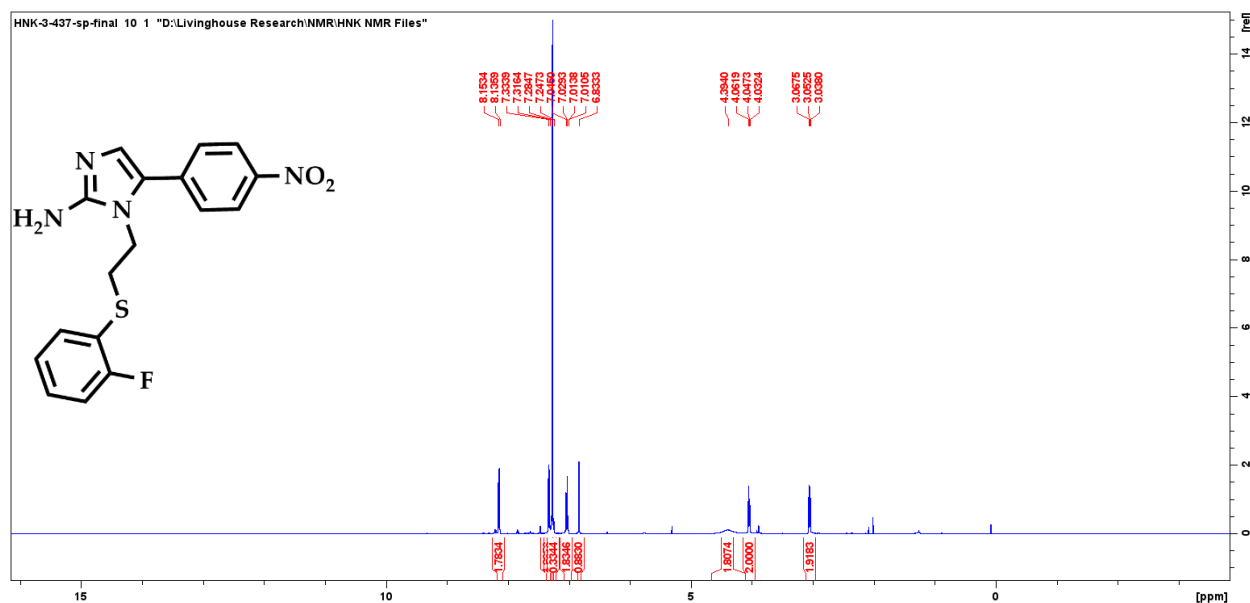


Figure 3.296B: ¹H-NMR Spectra of 1-(2-((2-fluorophenyl)thio)ethyl)-5-(4-nitrophenyl)-1H-imidazol-2-amine (**6.3e**).

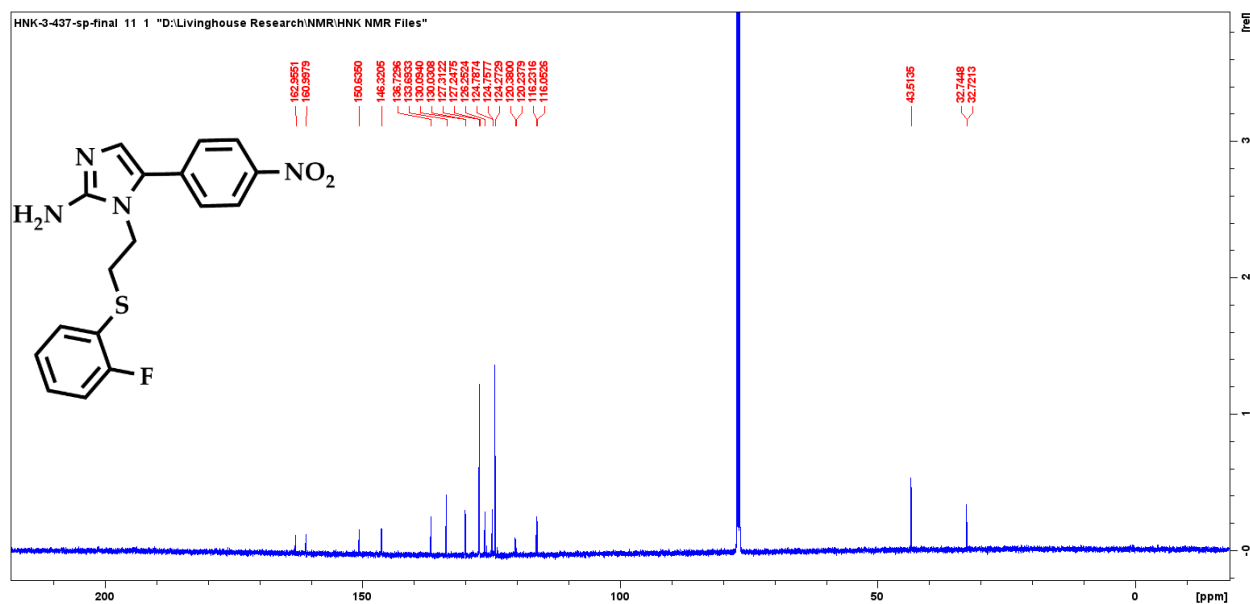


Figure 3.297B: ^{13}C -NMR Spectra of 1-(2-((2-fluorophenyl)thio)ethyl)-5-(4-nitrophenyl)-1H-imidazol-2-amine (**6.3e**).

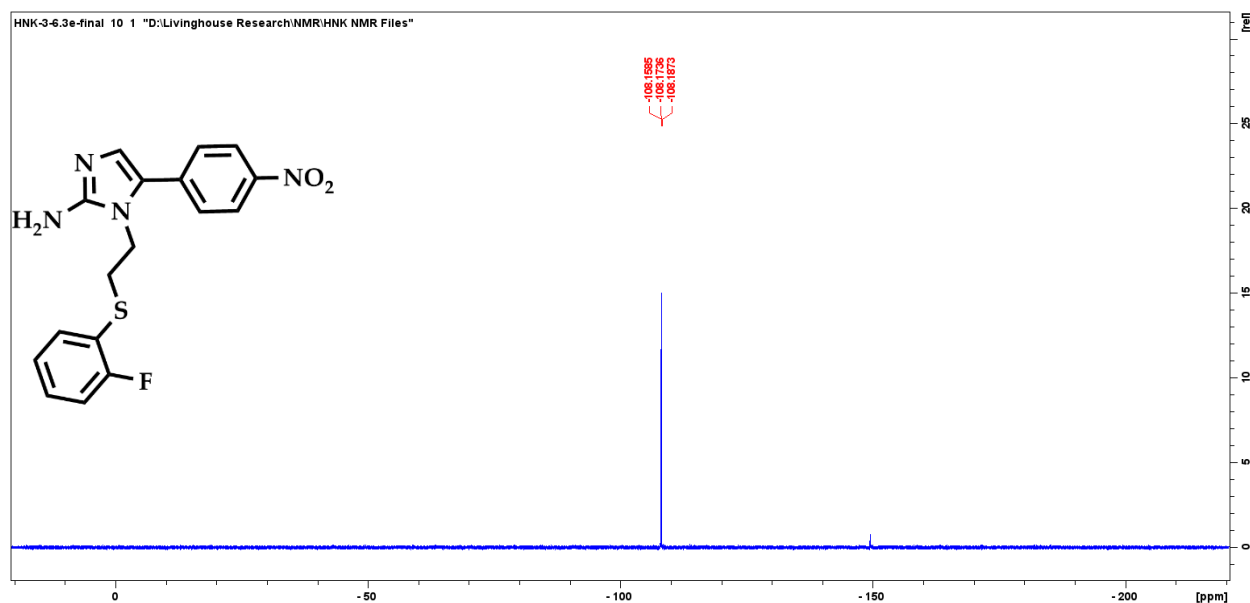


Figure 3.298B: ^{19}F -NMR Spectra of 1-(2-((2-fluorophenyl)thio)ethyl)-5-(4-nitrophenyl)-1H-imidazol-2-amine (**6.3e**).

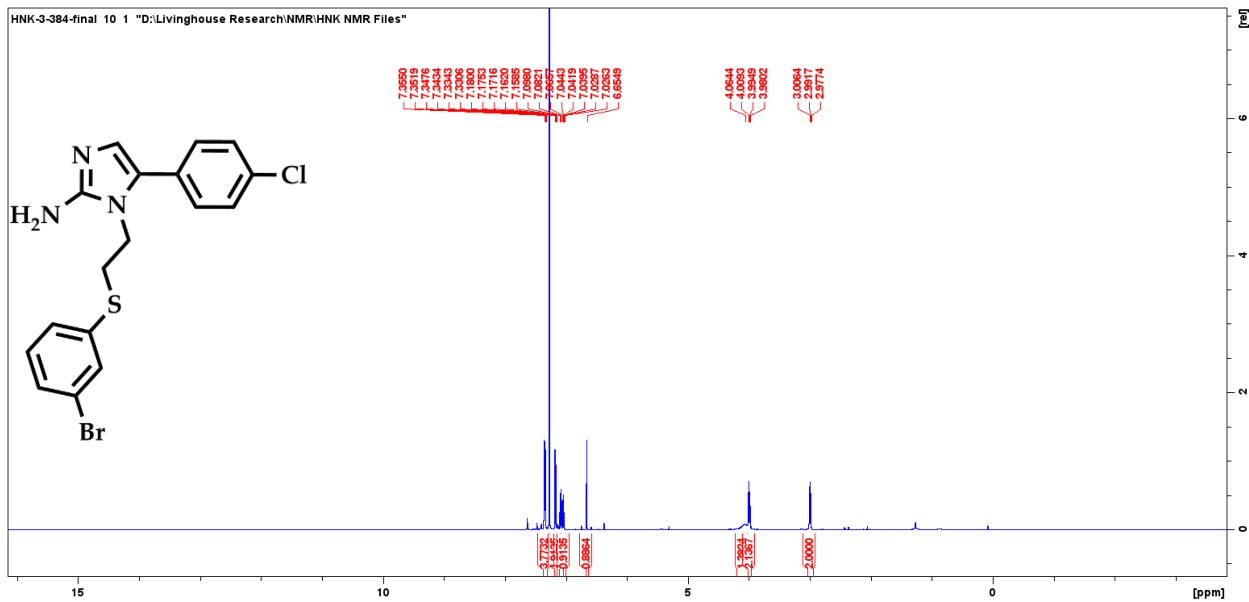


Figure 3.299B: ¹H-NMR Spectra of 1-(2-((3-bromophenyl)thio)ethyl)-5-(4-chlorophenyl)-1*H*-imidazol-2-amine (**7.3a**).

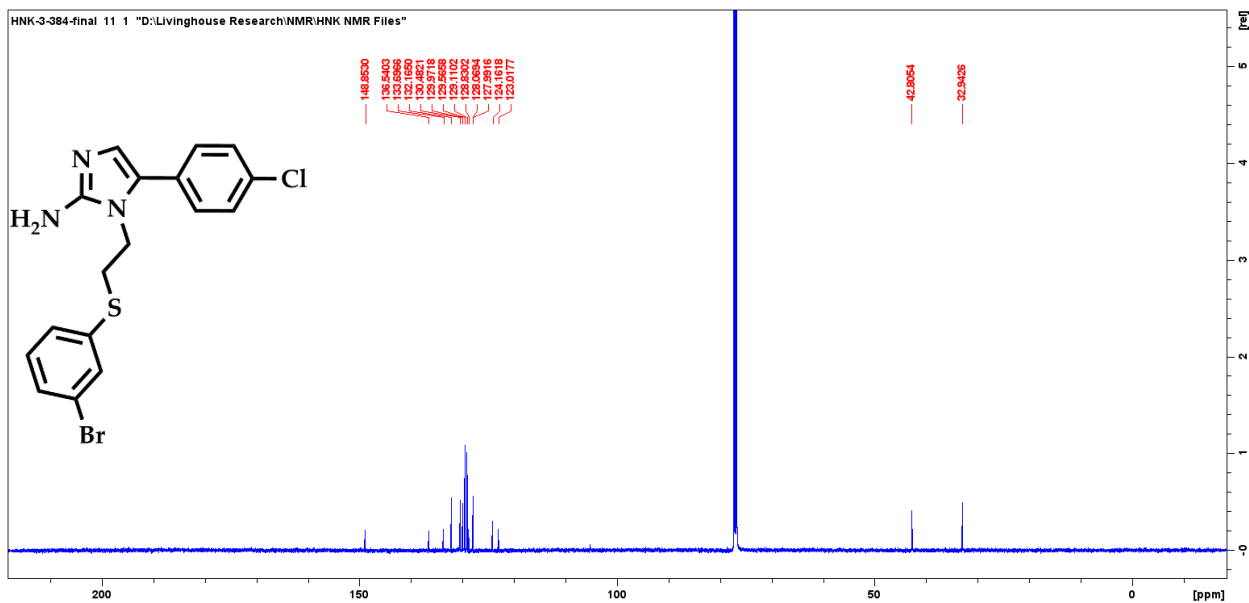


Figure 3.300B: ^{13}C -NMR Spectra of 1-(2-((3-bromophenyl)thio)ethyl)-5-(4-chlorophenyl)-1*H*-imidazol-2-amine (**7.3a**).

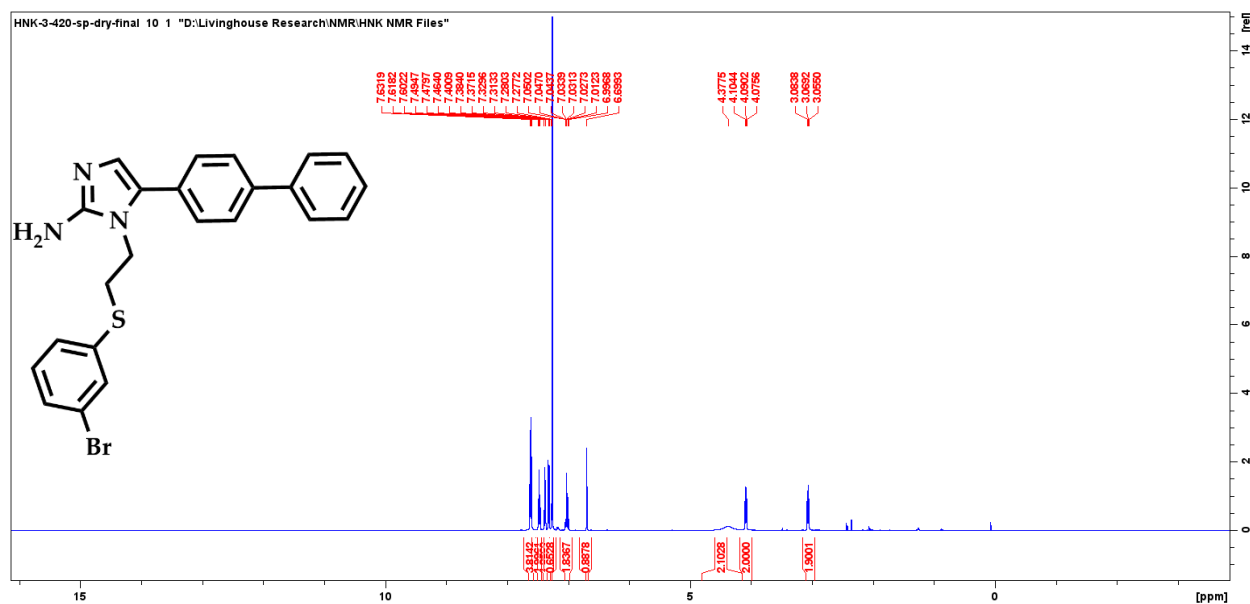


Figure 3.301B: ¹H-NMR Spectra of 5-([1,1'-biphenyl]-4-yl)-1-(2-((3-bromophenyl)thio)ethyl)-1H-imidazol-2-amine (7.3b).

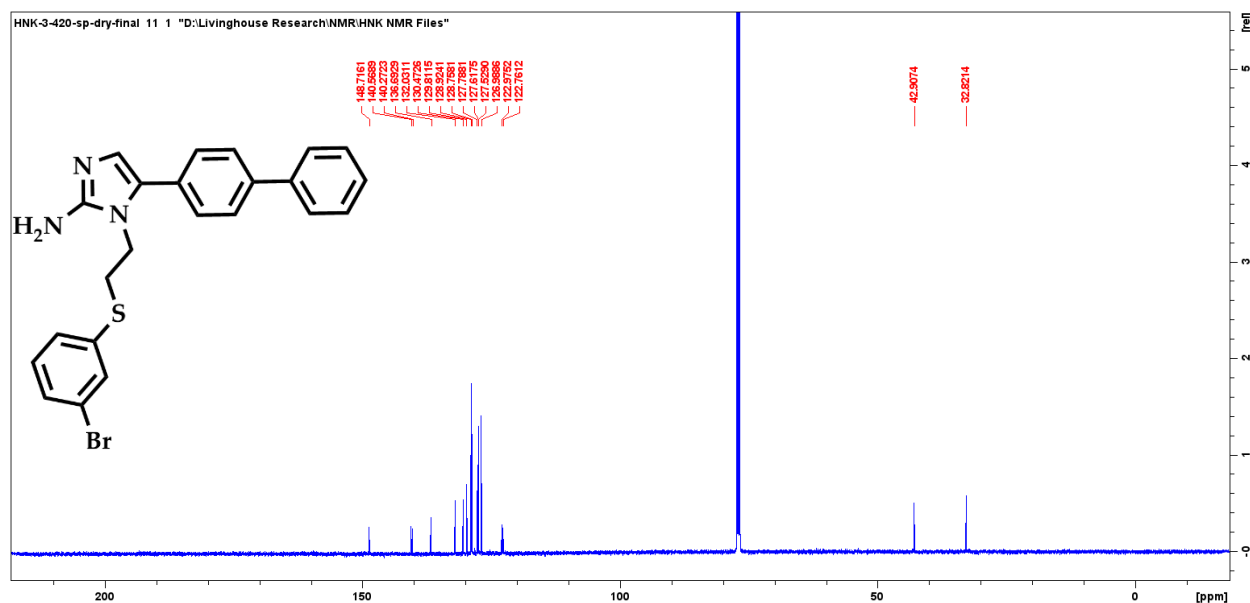


Figure 3.302B: ¹³C-NMR Spectra of 5-([1,1'-biphenyl]-4-yl)-1-(2-((3-bromophenyl)thio)ethyl)-1H-imidazol-2-amine (7.3b).

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Chemical structure of the compound: Nc1nc(Cc2ccc(Br)cc2)n(Cc3ccc(Br)cc3)c1

¹³C NMR peaks (ppm):

Peak Label	Chemical Shift (ppm)
148.8175	148.8175
136.4628	136.4628
132.1760	132.1760
132.0678	132.0678
131.0044	131.0044
130.0044	130.0044
129.8643	129.8643
128.1144	128.1144
128.0013	128.0013
127.5543	127.5543
123.0290	123.0290
121.9972	121.9972
42.8078	42.8078
32.8740	32.8740

Figure 3.304B: ^{13}C -NMR Spectra of 5-(4-bromophenyl)-1-(2-((3-bromophenyl)thio)ethyl)-1*H*-imidazol-2-amine (**7.3c**).

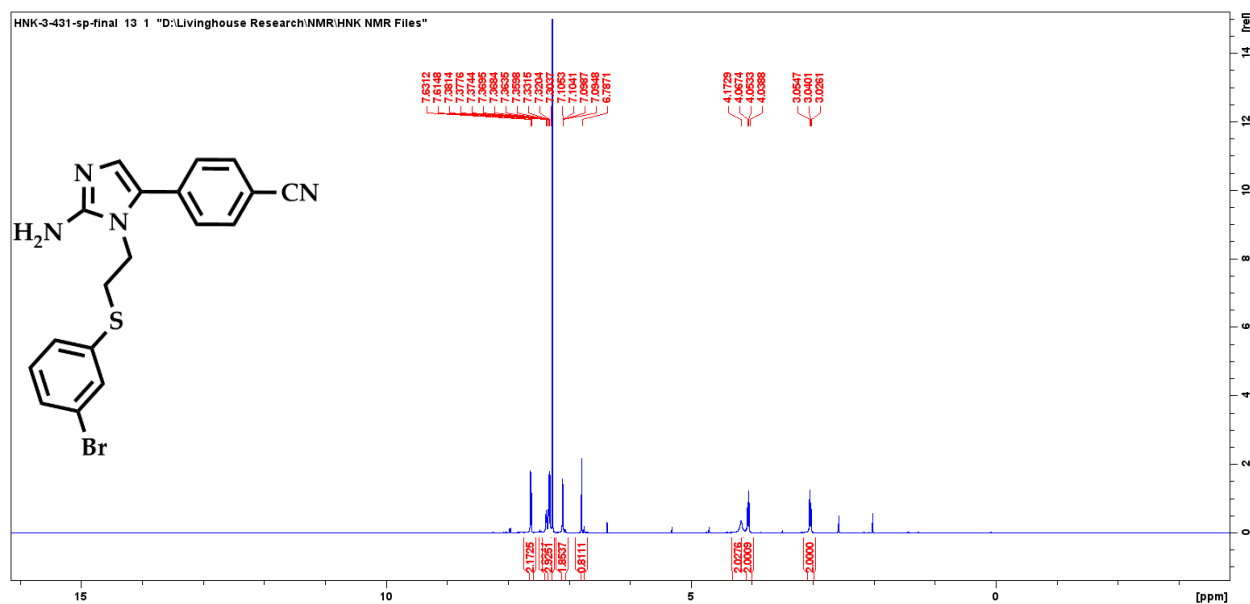


Figure 3.305B: ^1H -NMR Spectra of 4-(2-amino-1-(2-((3-bromophenyl)thio)ethyl)-1H-imidazol-5-yl)benzonitrile (7.3d).

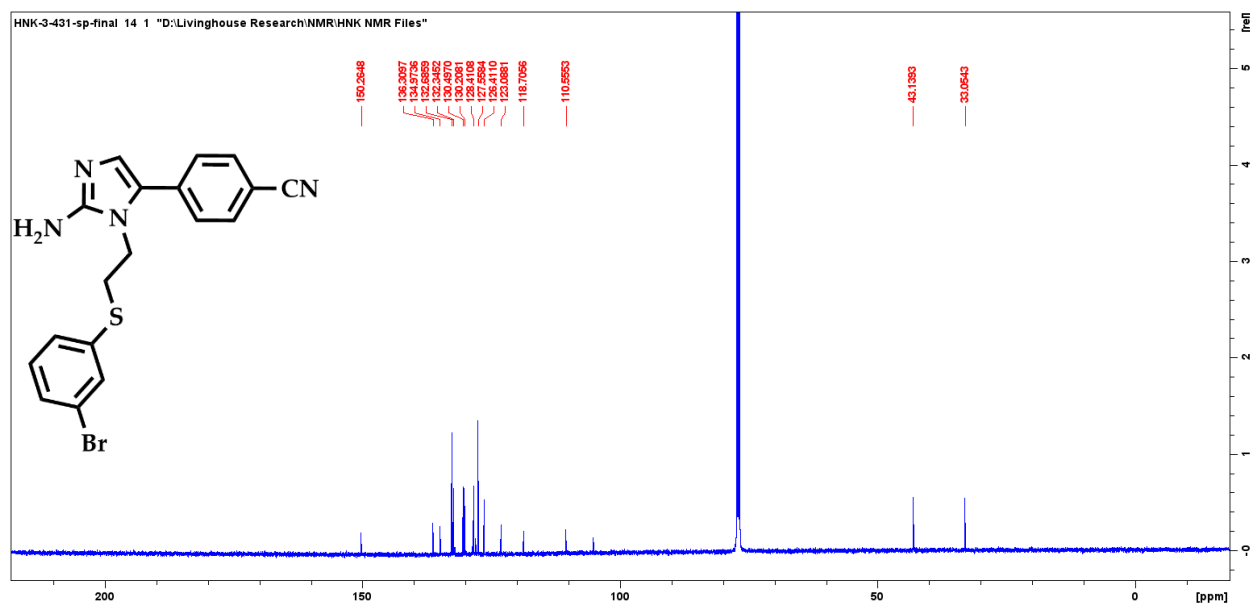


Figure 3.306B: ^{13}C -NMR Spectra of 4-(2-amino-1-(2-((3-bromophenyl)thio)ethyl)-1H-imidazol-5-yl)benzonitrile (7.3d).

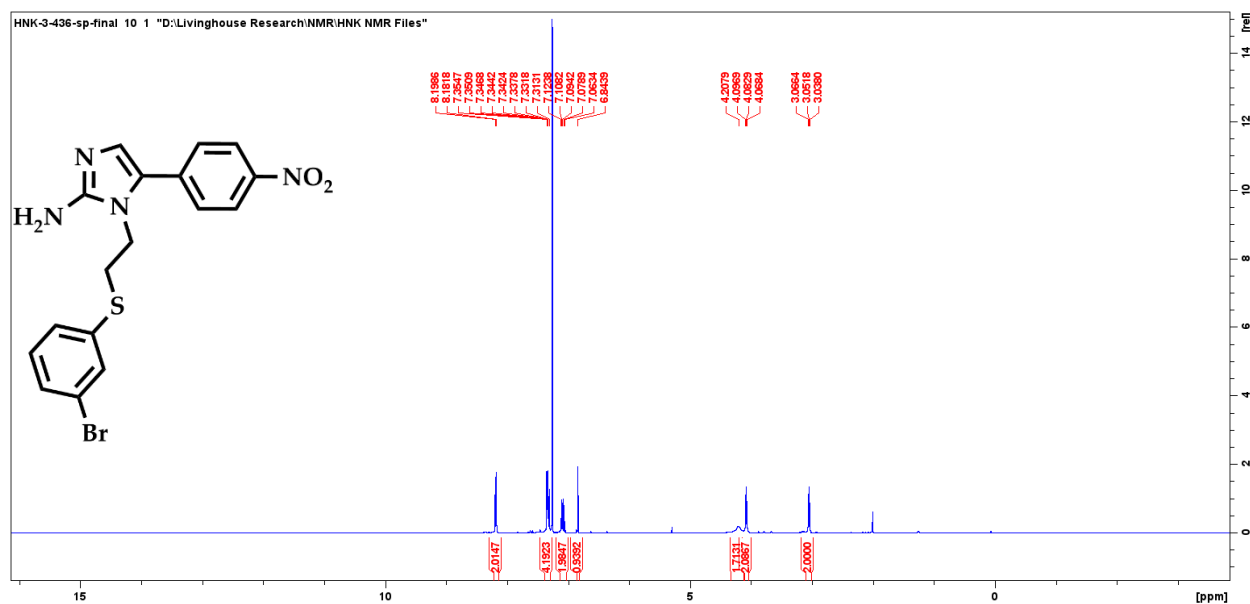


Figure 3.307B: ^1H -NMR Spectra of 1-(2-((3-bromophenyl)thio)ethyl)-5-(4-nitrophenyl)-1H-imidazol-2-amine (7.3e).

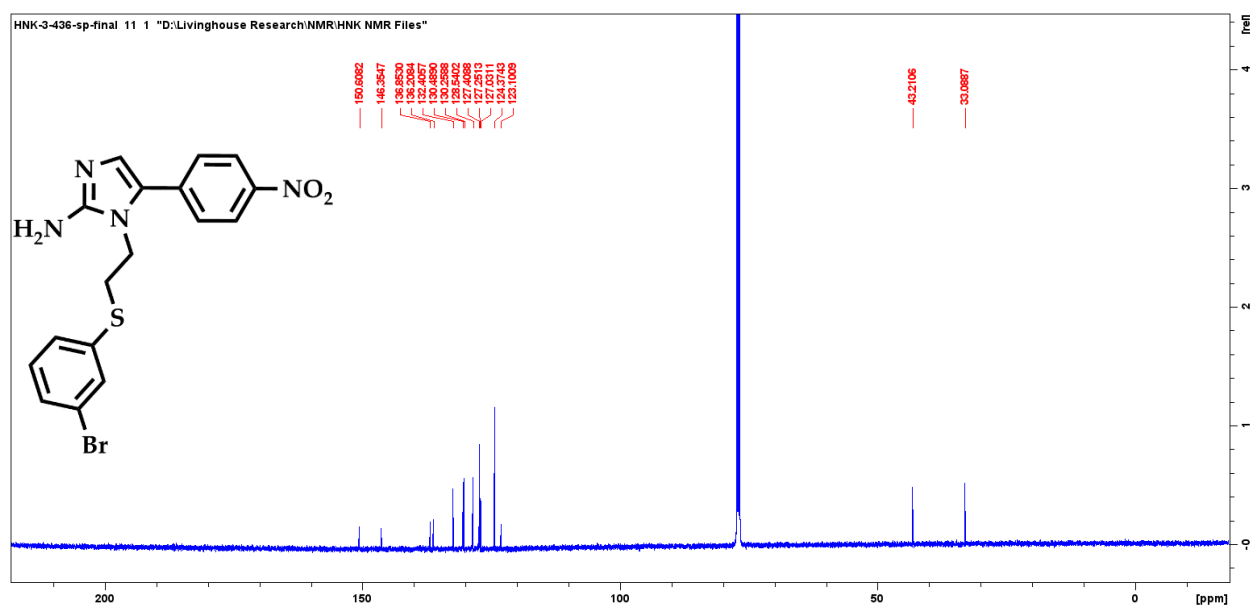


Figure 3.308B: ^{13}C -NMR Spectra of 1-(2-((3-bromophenyl)thio)ethyl)-5-(4-nitrophenyl)-1H-imidazol-2-amine (7.3e).

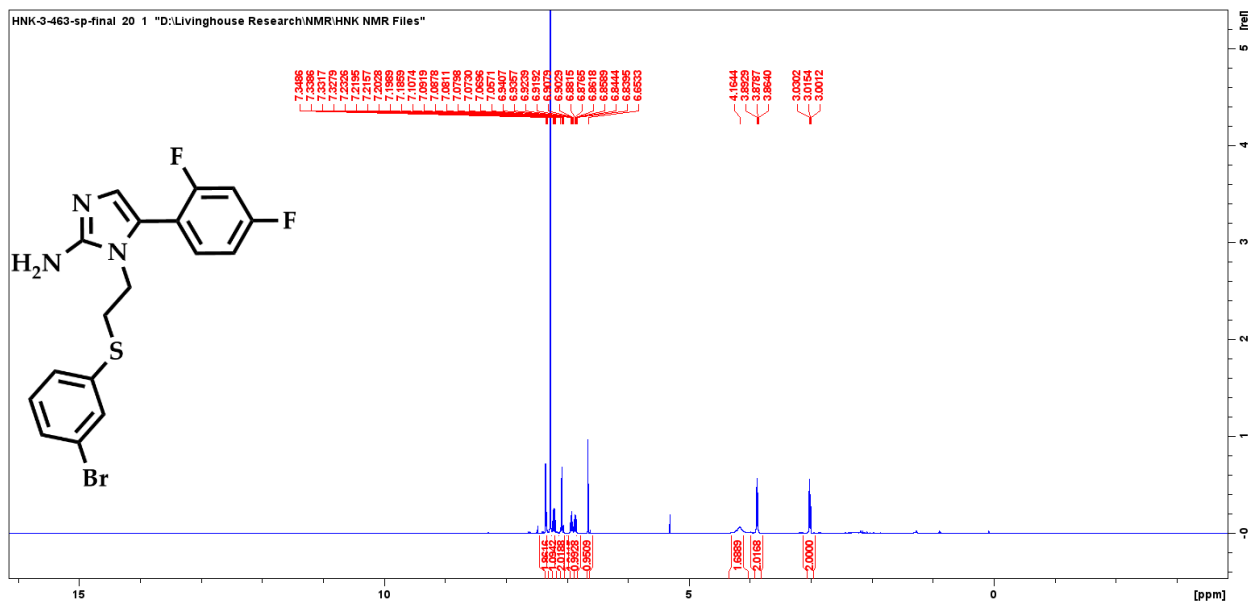


Figure 3.309B: ^1H -NMR Spectra of 1-(2-((3-bromophenyl)thio)ethyl)-5-(2,4-difluorophenyl)-1H-imidazol-2-amine (7.3f).

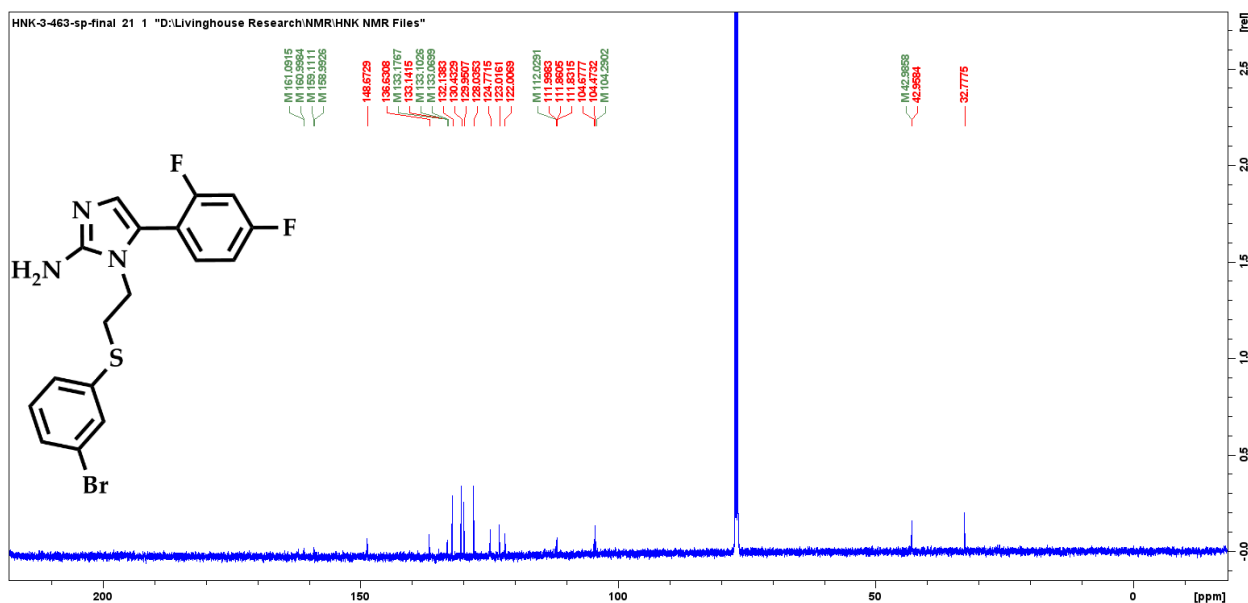


Figure 3.310B: ^{13}C -NMR Spectra of 1-(2-((3-bromophenyl)thio)ethyl)-5-(2,4-difluorophenyl)-1H-imidazol-2-amine (7.3f).

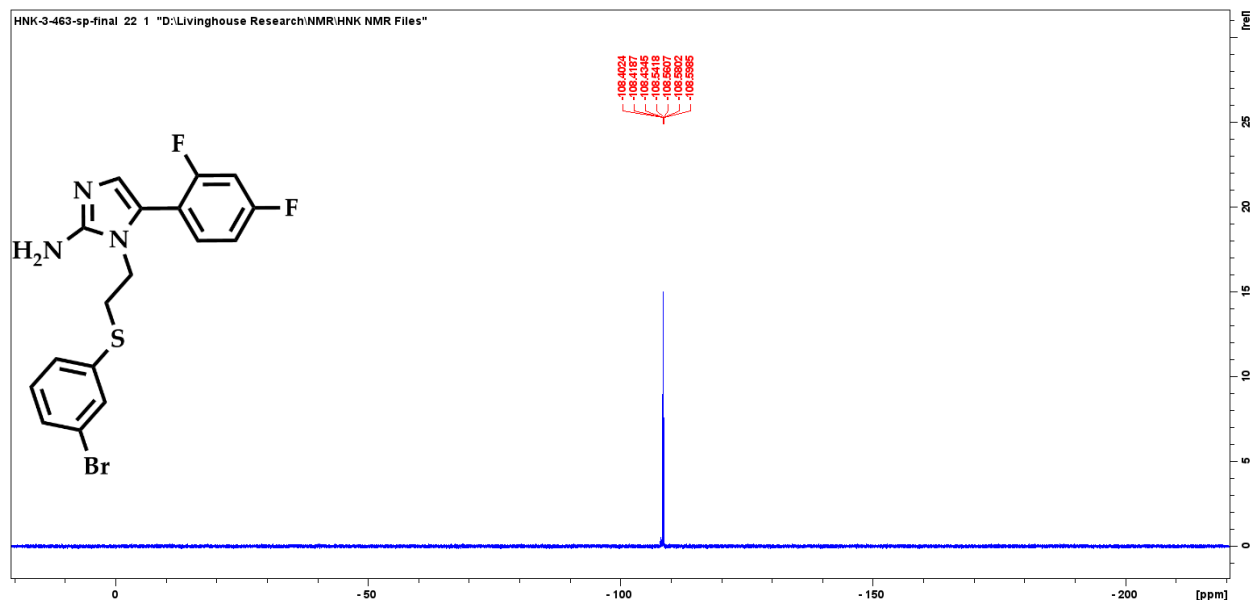


Figure 3.311B: ¹⁹F-NMR Spectra of 1-(2-((3-bromophenyl)thio)ethyl)-5-(2,4-difluorophenyl)-1H-imidazol-2-amine (7.3f).

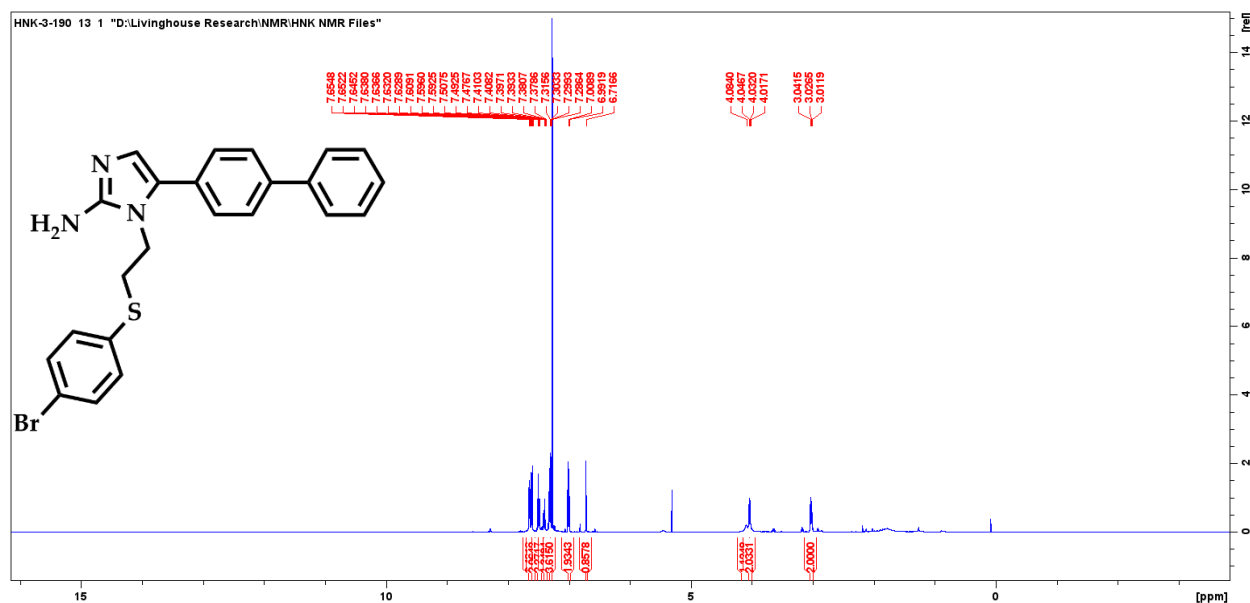


Figure 3.314B: ¹H-NMR Spectra of 5-([1,1'-biphenyl]-4-yl)-1-(2-((4-bromophenyl)thio)ethyl)-1H-imidazol-2-amine (8.3b).

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Chemical structure: Nc1nc(C2=CC=C(C=C2)SCC3=CC=C(C=C3)Br)c(C4=CC=C(C=C4)Br)n1

¹H NMR spectrum (ppm):

- 7.5105, 7.5025, 7.4841, 7.3783, 7.3689, 7.3595, 7.1068, 7.0522, 7.0427, 6.9965, 6.6701
- 4.3248, 3.9705, 3.9618
- 2.9921, 2.9770, 2.9625

Integration values (from left to right):

- 2.6634
- 2.3909
- 1.9302
- 0.9674
- 1.3176
- 2.0000
- 1.9986

Figure 3.316B: ¹H-NMR Spectra of 5-(4-bromophenyl)-1-(2-((4-bromophenyl)thio)ethyl)-1*H*-imidazol-2-amine (**8.3c**).

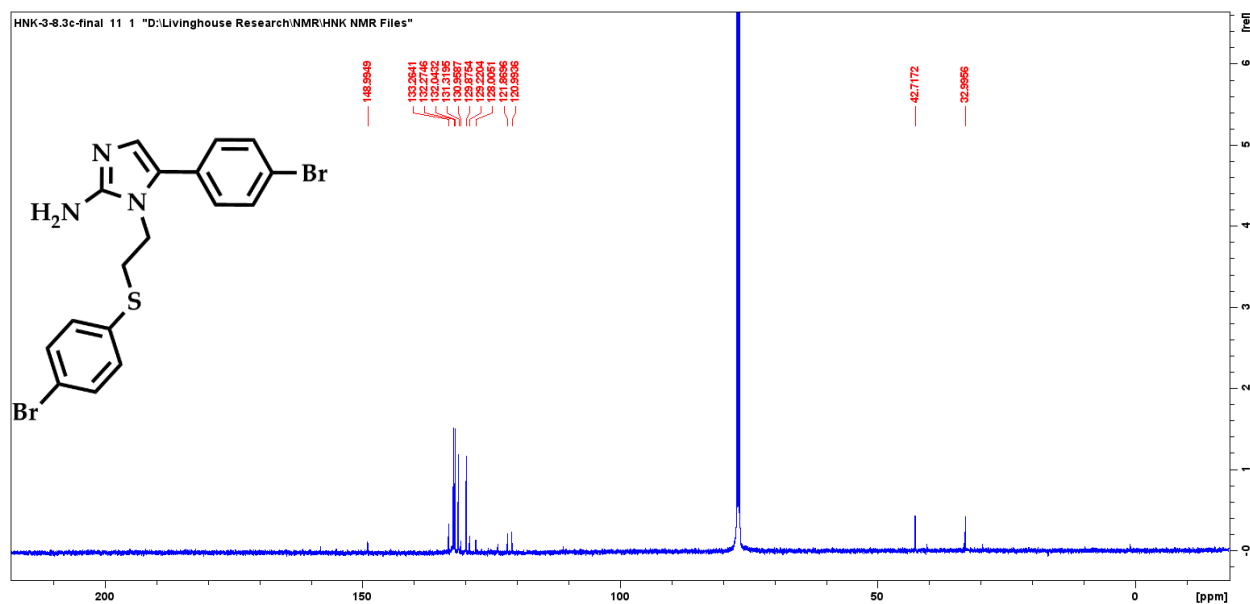


Figure 3.317B: ¹³C-NMR Spectra of 5-(4-bromophenyl)-1-(2-((4-bromophenyl)thio)ethyl)-1H-imidazol-2-amine (**8.3c**).

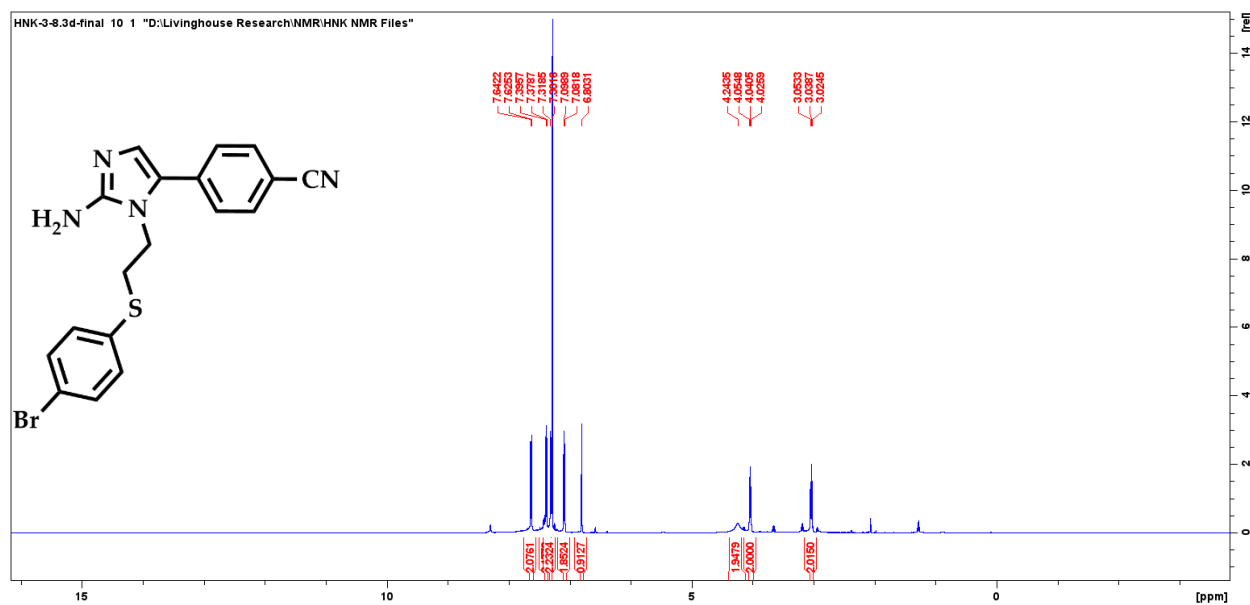


Figure 3.318B: ¹H-NMR Spectra of 4-(2-amino-1-(2-((4-bromophenyl)thio)ethyl)-1H-imidazol-5-yl)benzonitrile (**8.3d**).

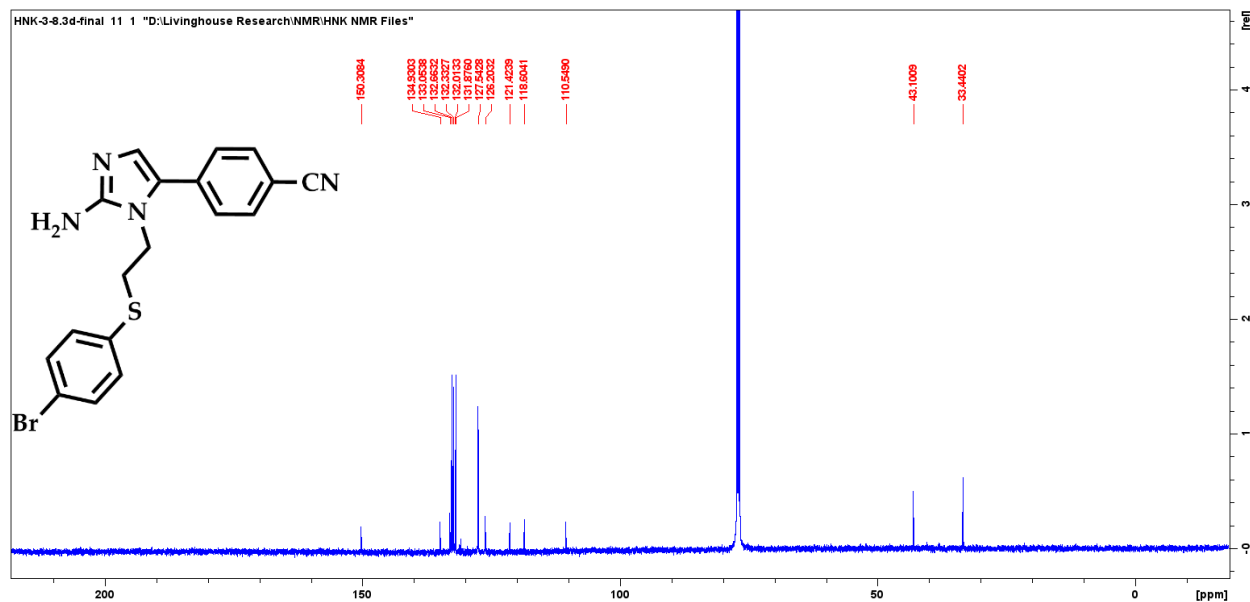


Figure 3.319B: ¹³C-NMR Spectra of 4-(2-amino-1-(2-((4-bromophenyl)thio)ethyl)-1H-imidazol-5-yl)benzonitrile (**8.3d**).

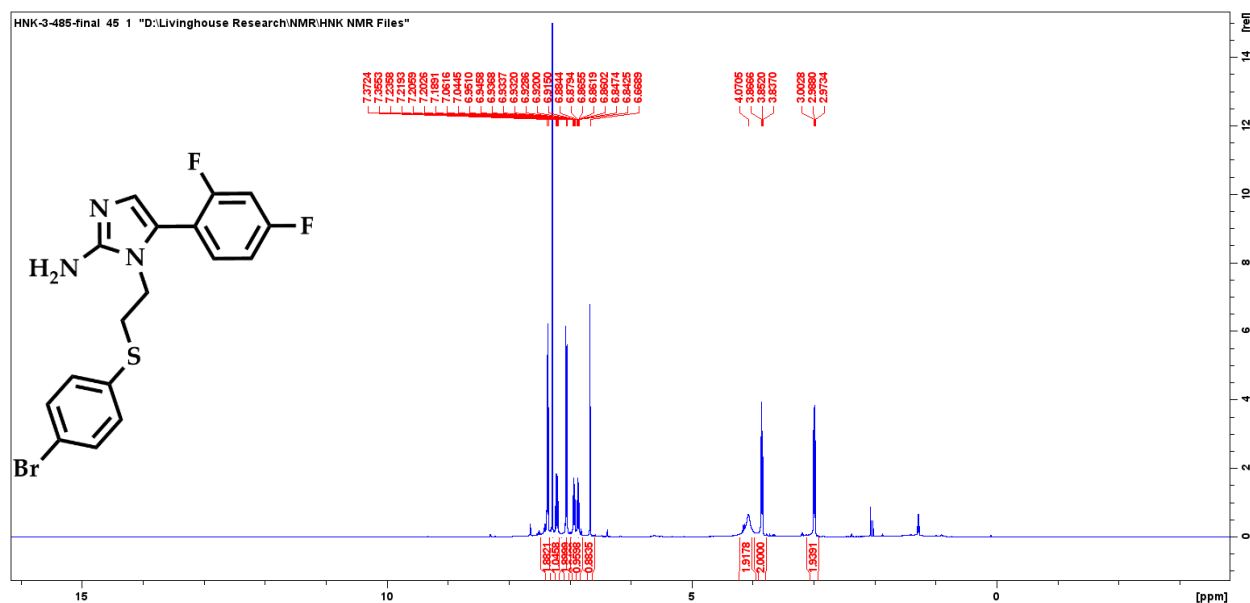


Figure 3.322B: ¹H-NMR Spectra of 1-(2-((4-bromophenyl)thio)ethyl)-5-(2,4-difluorophenyl)-1H-imidazol-2-amine (**8.3f**).

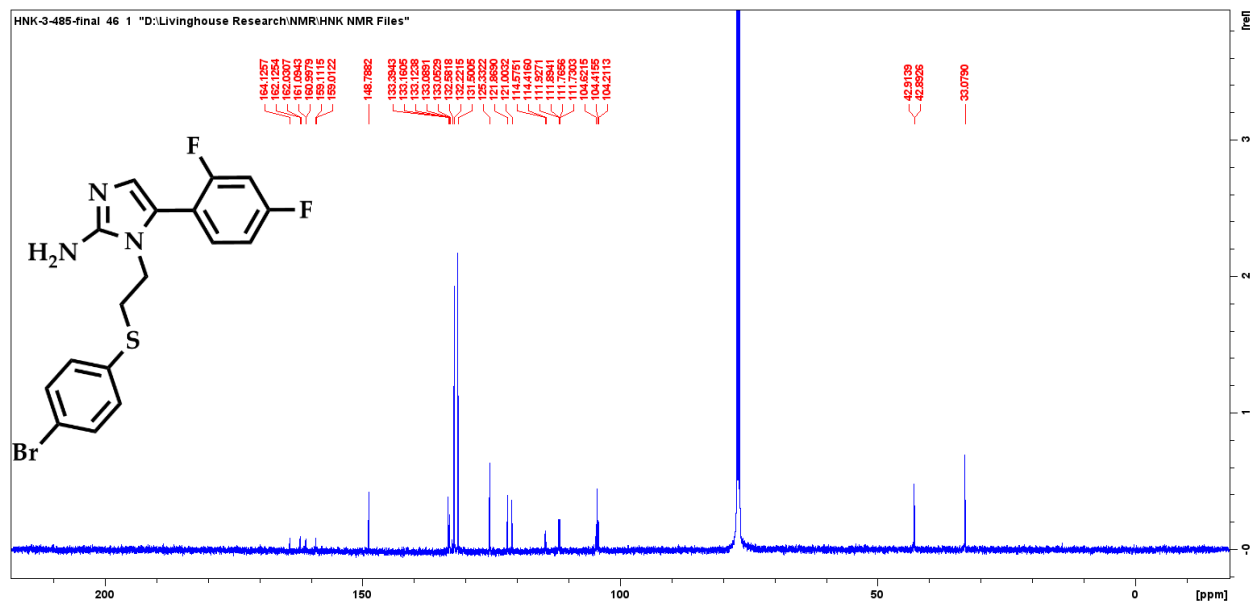


Figure 3.323B: ¹³C-NMR Spectra of 1-(2-((4-bromophenyl)thio)ethyl)-5-(2,4-difluorophenyl)-1H-imidazol-2-amine (8.3f).

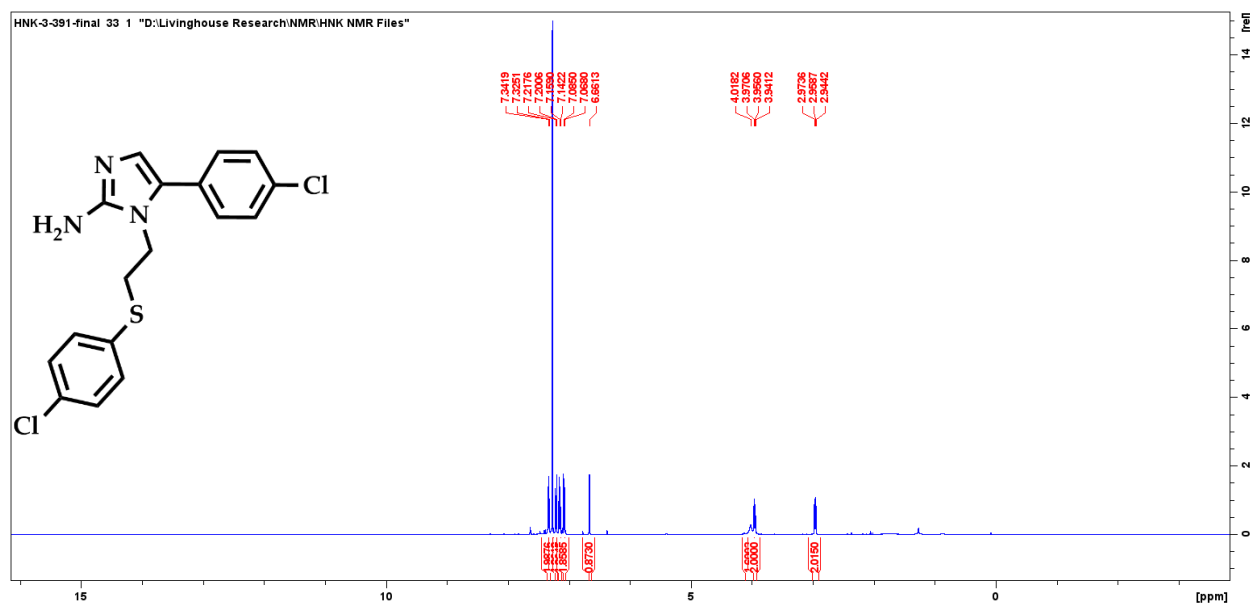


Figure 3.324B: ¹H-NMR Spectra of 5-(4-chlorophenyl)-1-(2-((4-chlorophenyl)thio)ethyl)-1H-imidazol-2-amine (9.3a).

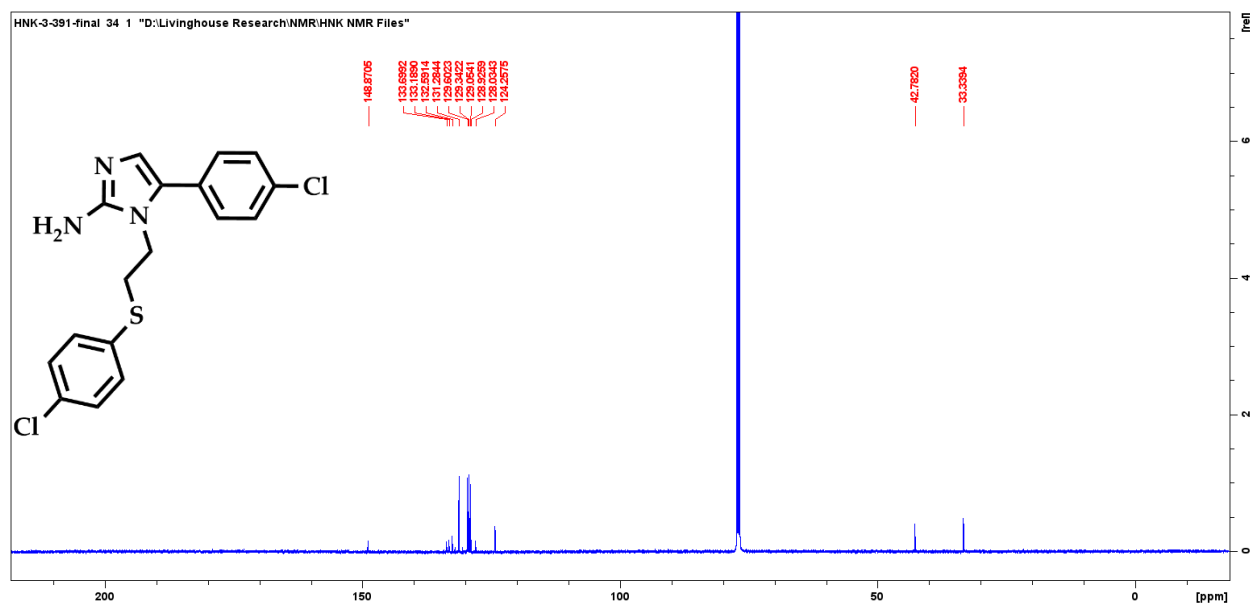


Figure 3.325B: ¹³C-NMR Spectra of 5-(4-chlorophenyl)-1-(2-((4-chlorophenyl)thio)ethyl)-1H-imidazol-2-amine (**9.3a**).

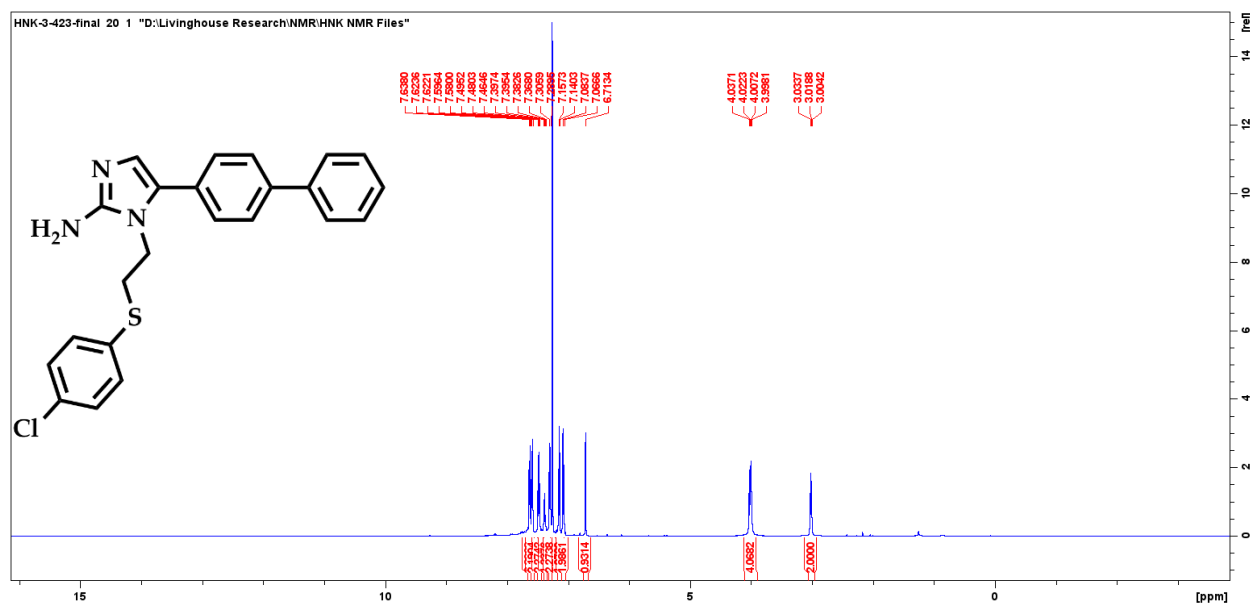


Figure 3.326B: ¹H-NMR Spectra of 5-([1,1'-biphenyl]-4-yl)-1-(2-((4-chlorophenyl)thio)ethyl)-1H-imidazol-2-amine (**9.3b**).

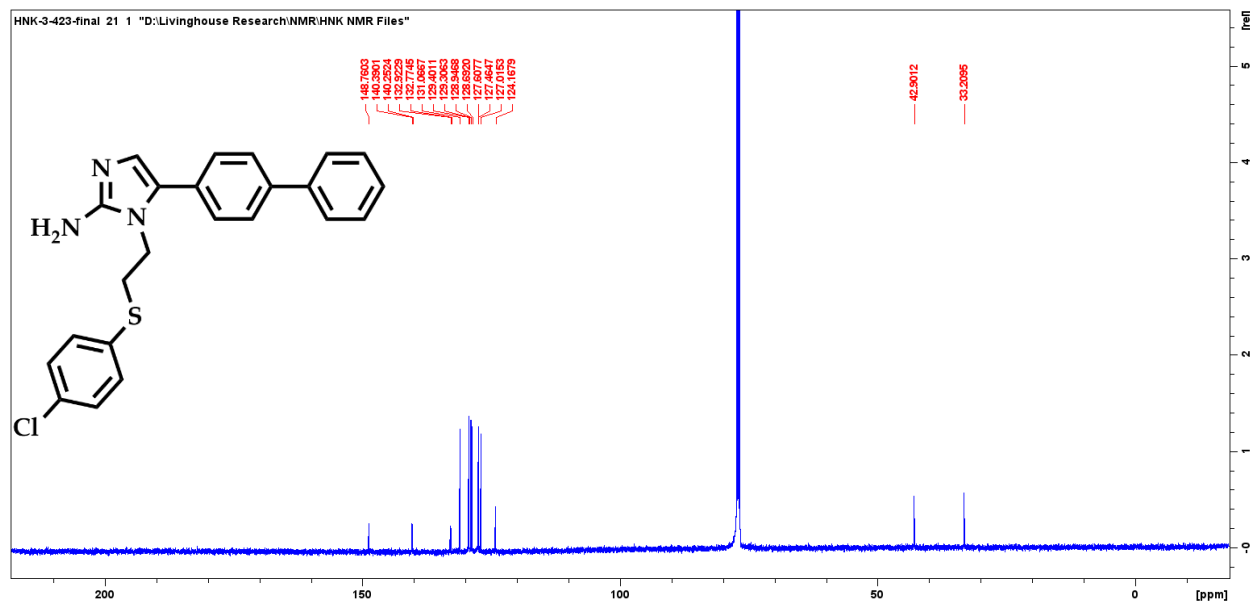


Figure 3.327B: ¹³C-NMR Spectra of 5-([1,1'-biphenyl]-4-yl)-1-(2-((4-chlorophenyl)thio)ethyl)-1H-imidazol-2-amine (**9.3b**).

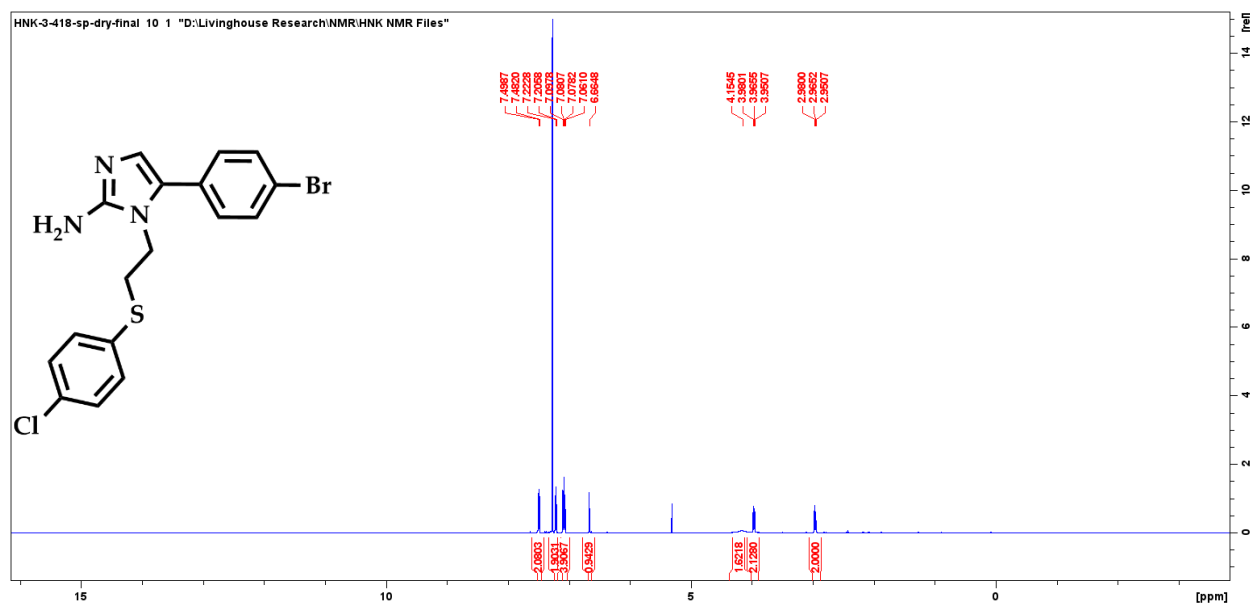


Figure 3.328B: ¹H-NMR Spectra of 5-(4-bromophenyl)-1-(2-((4-chlorophenyl)thio)ethyl)-1H-imidazol-2-amine (**9.3c**).

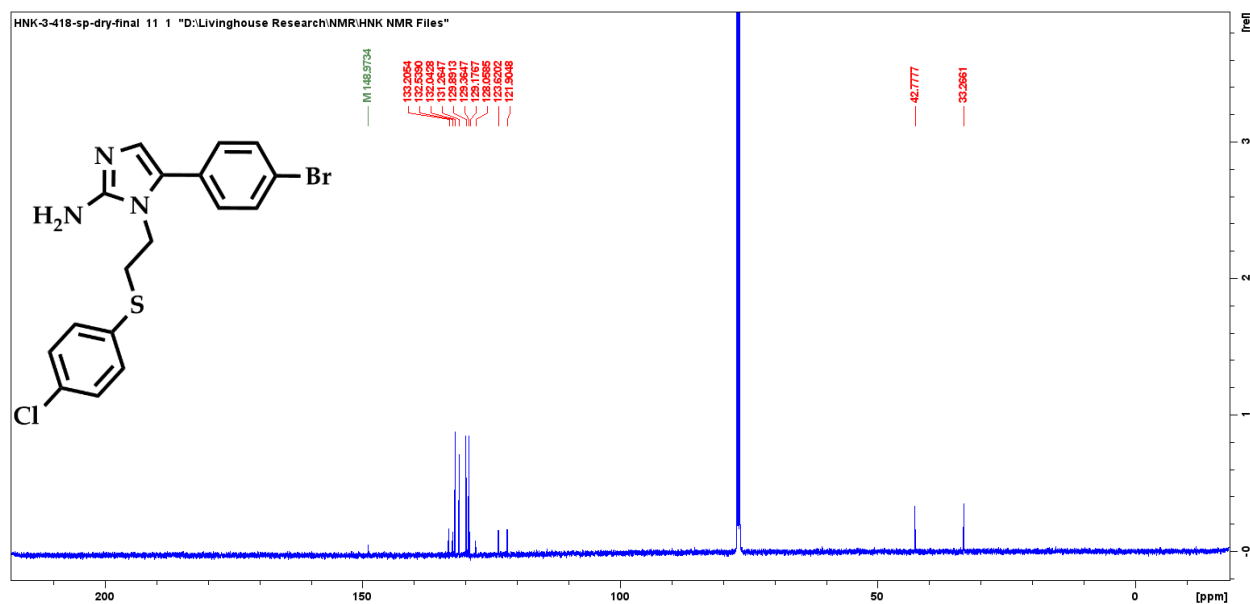


Figure 3.329B: ¹³C-NMR Spectra of 5-(4-bromophenyl)-1-(2-((4-chlorophenyl)thio)ethyl)-1H-imidazol-2-amine (9.3c).

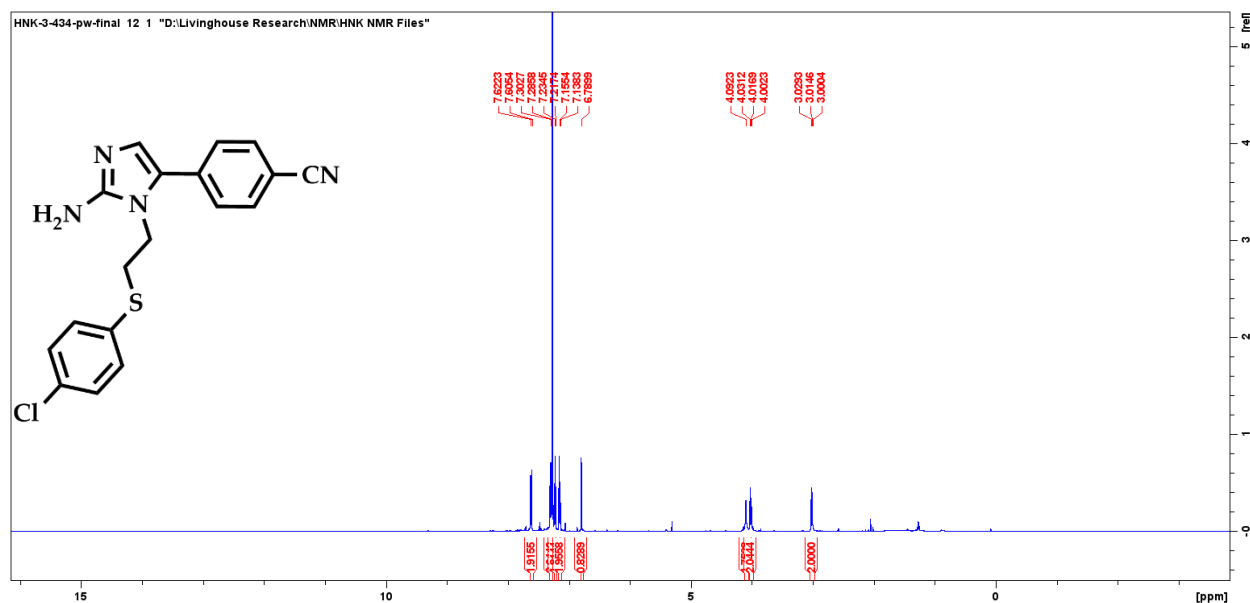


Figure 3.330B: ¹H-NMR Spectra of 4-(2-amino-1-(2-((4-chlorophenyl)thio)ethyl)-1H-imidazol-5-yl)benzonitrile (9.3d).

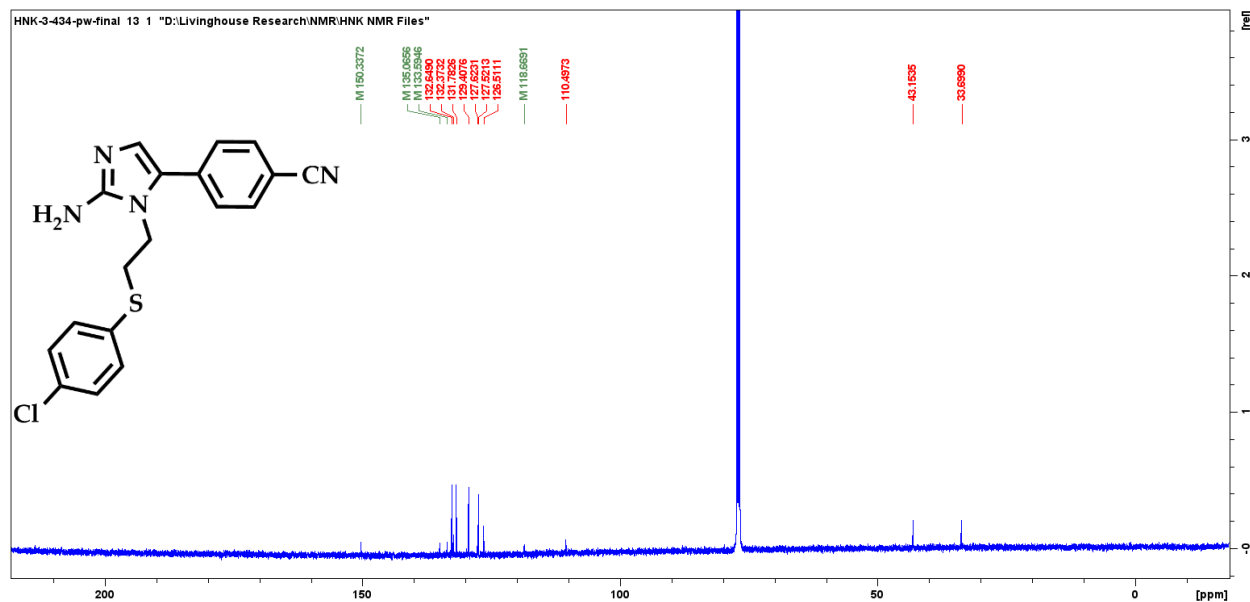


Figure 3.331B: ¹³C-NMR Spectra of 4-(2-amino-1-(2-((4-chlorophenyl)thio)ethyl)-1H-imidazol-5-yl)benzonitrile (**9.3d**).

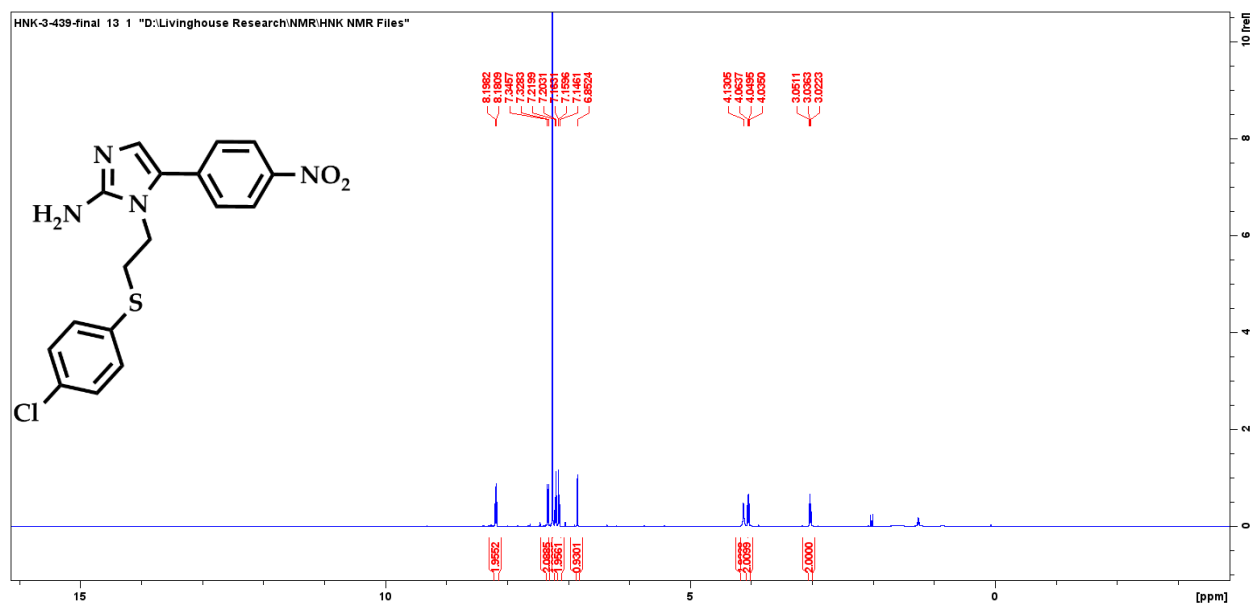


Figure 3.332B: ¹H-NMR Spectra of 1-(2-((4-chlorophenyl)thio)ethyl)-5-(4-nitrophenyl)-1H-imidazol-2-amine (**9.3e**).

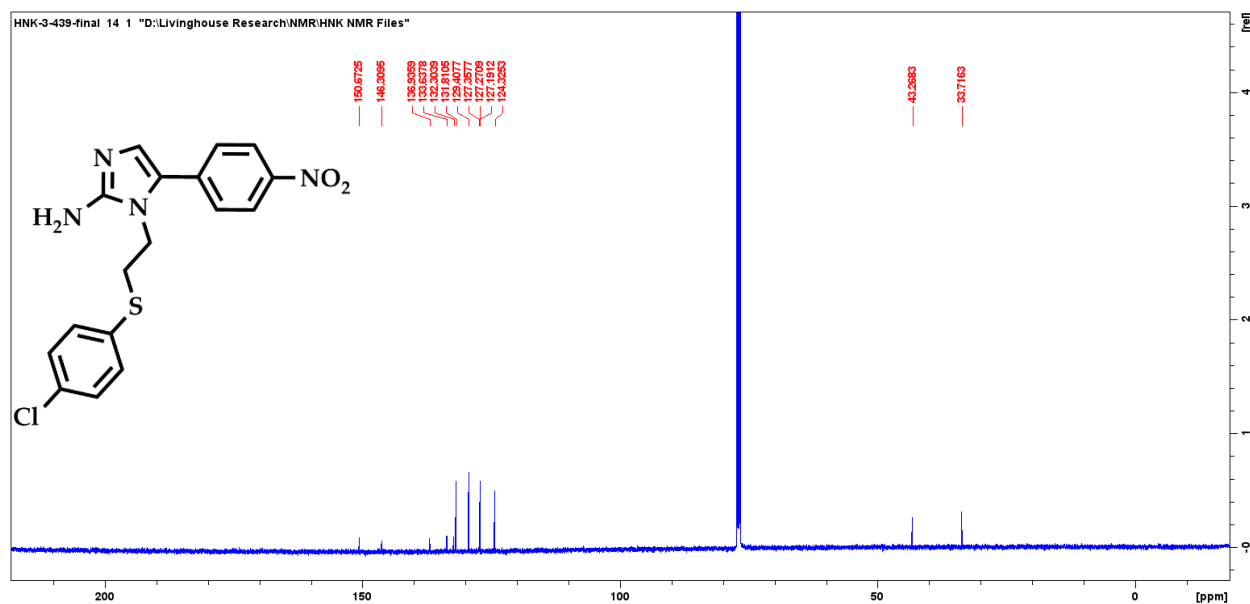


Figure 3.333B: ¹³C-NMR Spectra of 1-(2-((4-chlorophenyl)thio)ethyl)-5-(4-nitrophenyl)-1H-imidazol-2-amine (**9.3e**).

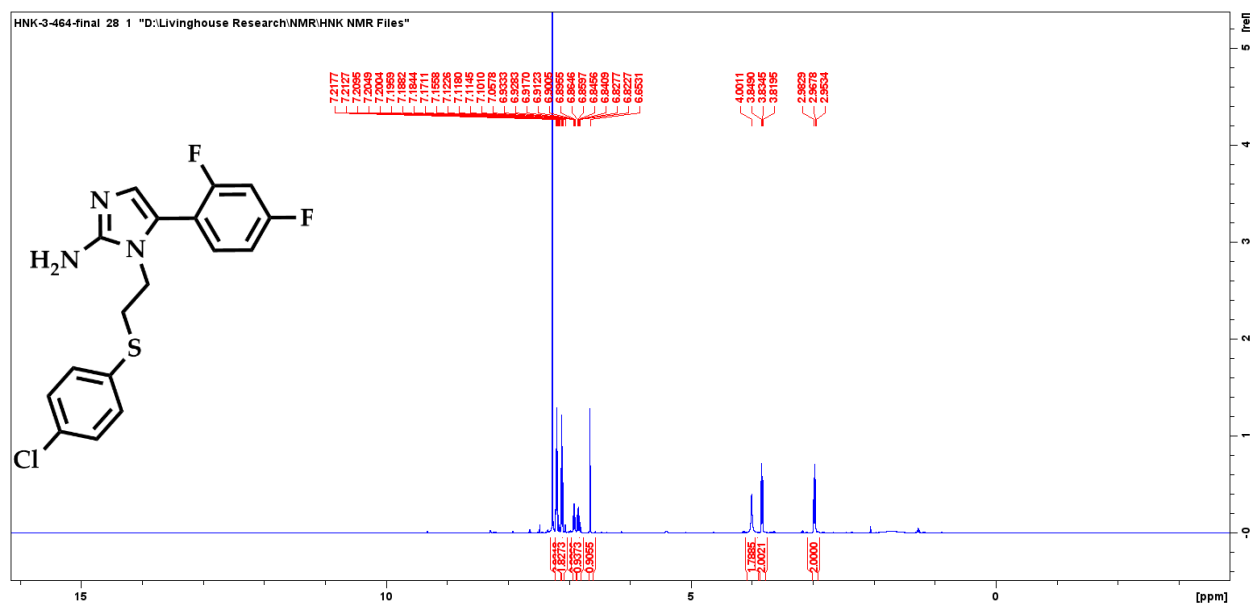


Figure 3.334B: ¹H-NMR Spectra of 1-(2-((4-chlorophenyl)thio)ethyl)-5-(2,4-difluorophenyl)-1H-imidazol-2-amine (**9.3f**).

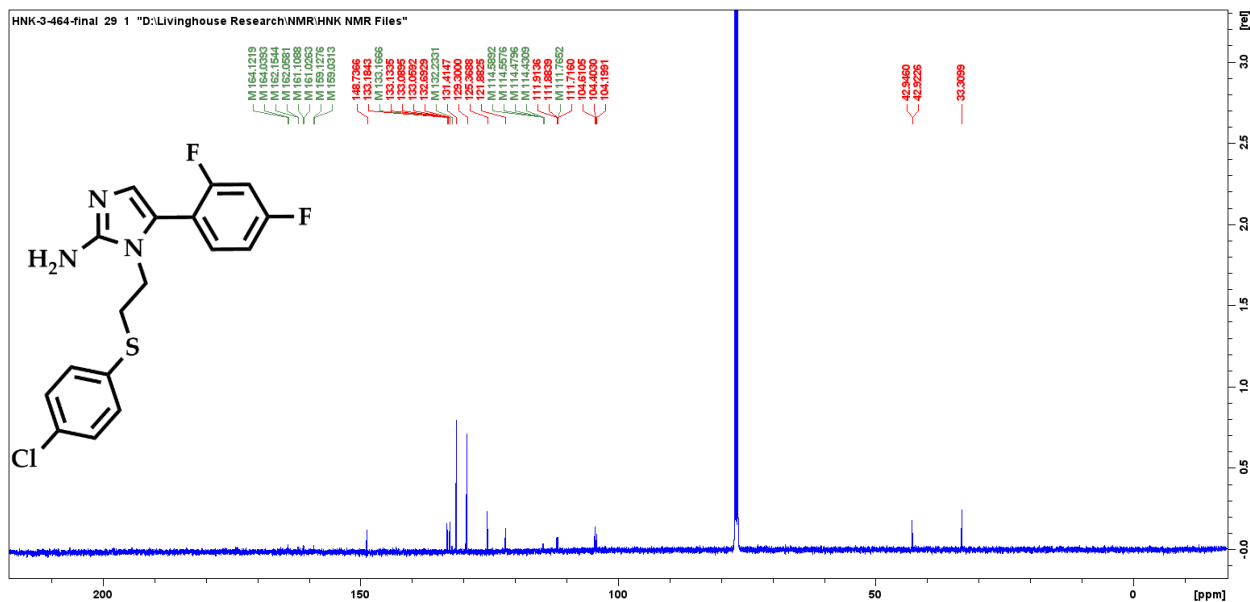


Figure 3.335B: ¹³C-NMR Spectra of 1-(2-((4-chlorophenyl)thio)ethyl)-5-(2,4-difluorophenyl)-1*H*-imidazol-2-amine (**9.3f**).

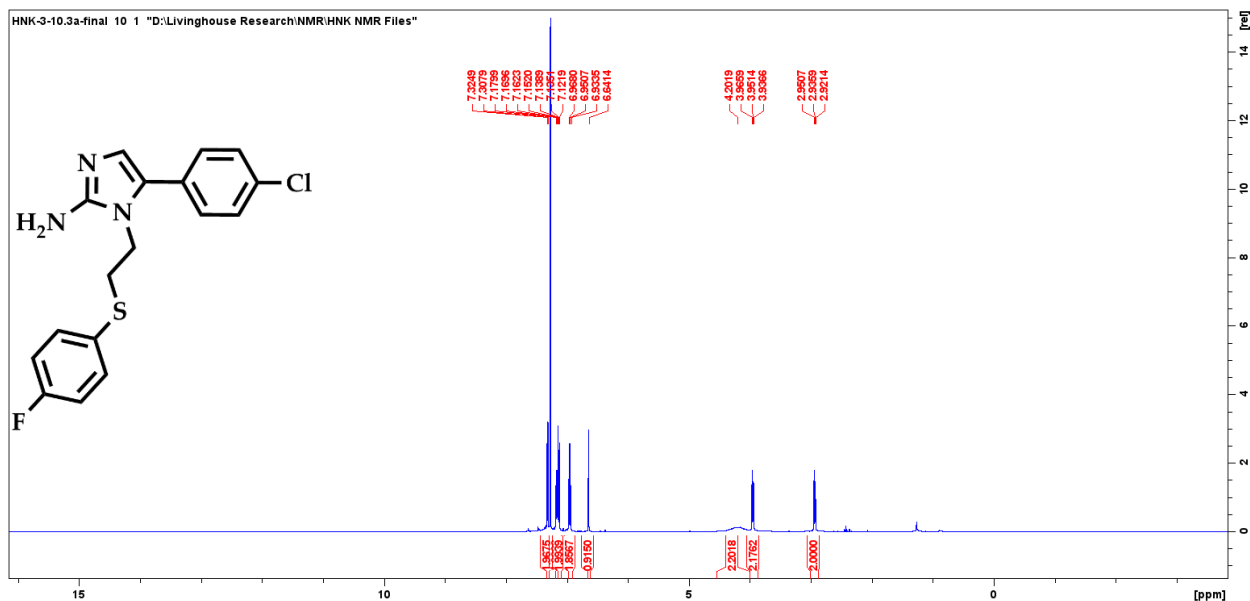


Figure 3.336B: ¹H-NMR Spectra of 5-(4-chlorophenyl)-1-(2-((4-fluorophenyl)thio)ethyl)-1*H*-imidazol-2-amine (**10.3a**).

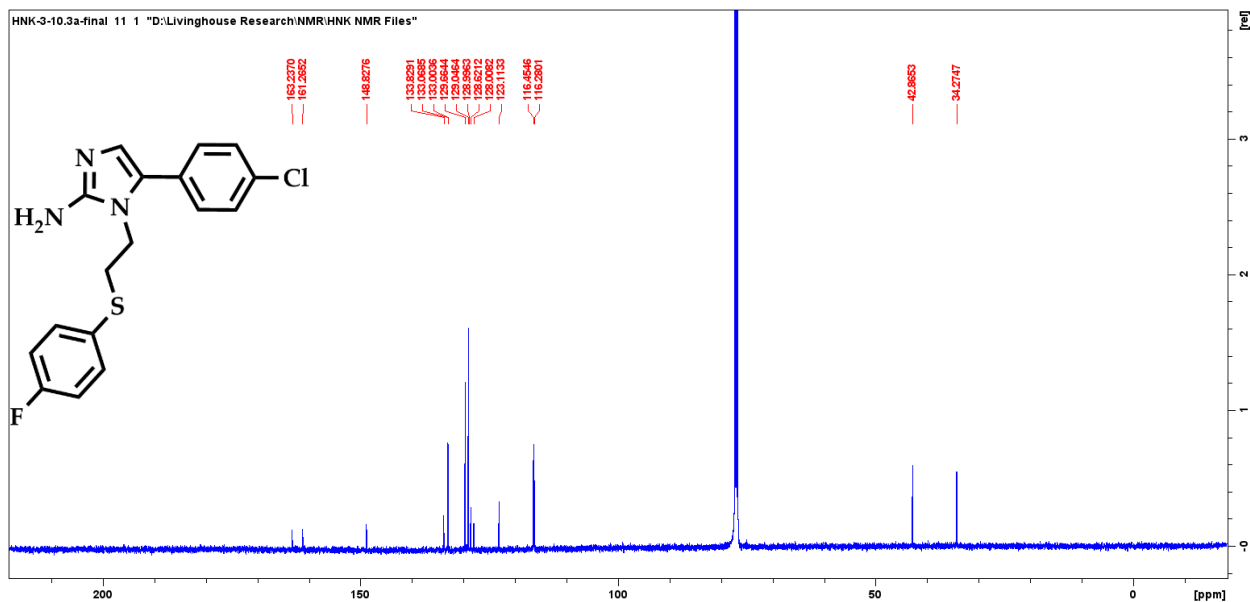


Figure 3.337B: ¹³C-NMR Spectra of 5-(4-chlorophenyl)-1-((4-fluorophenyl)thio)ethyl-1*H*-imidazol-2-amine (**10.3a**).

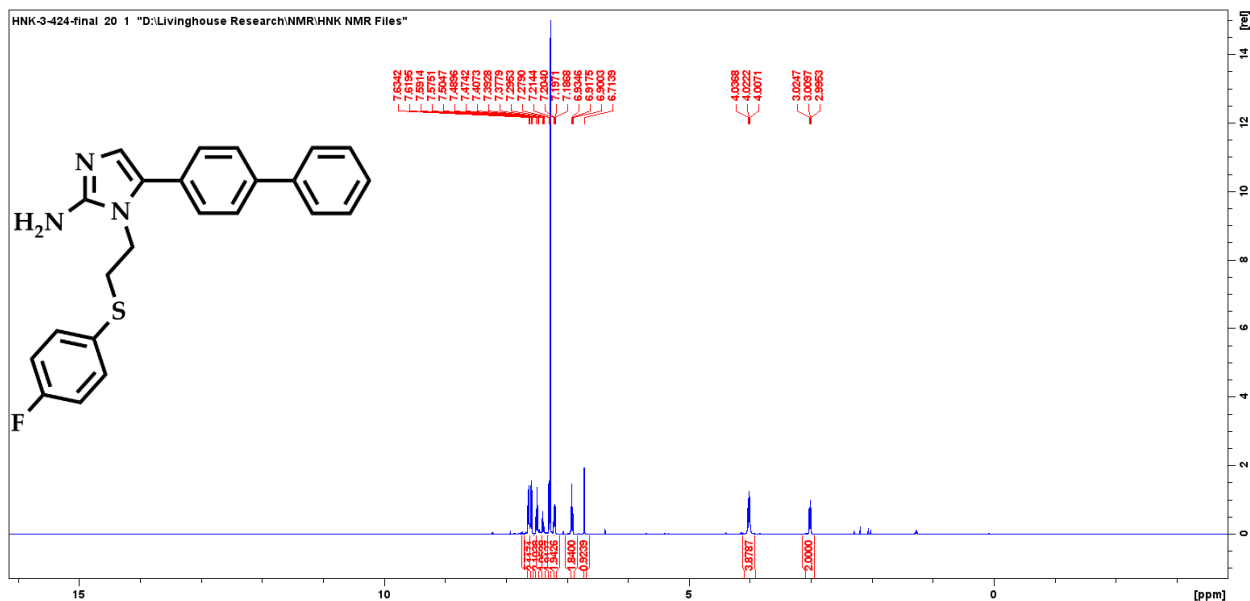


Figure 3.338B: ¹H-NMR Spectra of 5-([1,1'-biphenyl]-4-yl)-1-(2-((4-fluorophenyl)thio)ethyl)-1*H*-imidazol-2-amine (**10.3b**).

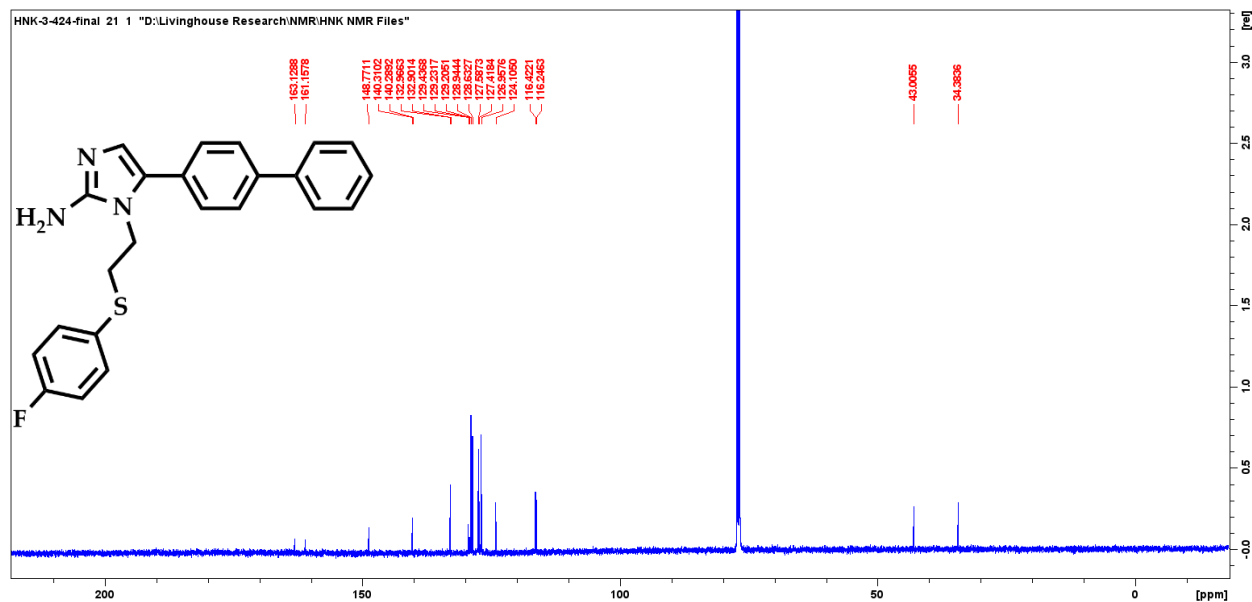


Figure 3.339B: ^{13}C -NMR Spectra of 5-([1,1'-biphenyl]-4-yl)-1-(2-((4-fluorophenyl)thio)ethyl)-1H-imidazol-2-amine (**10.3b**).

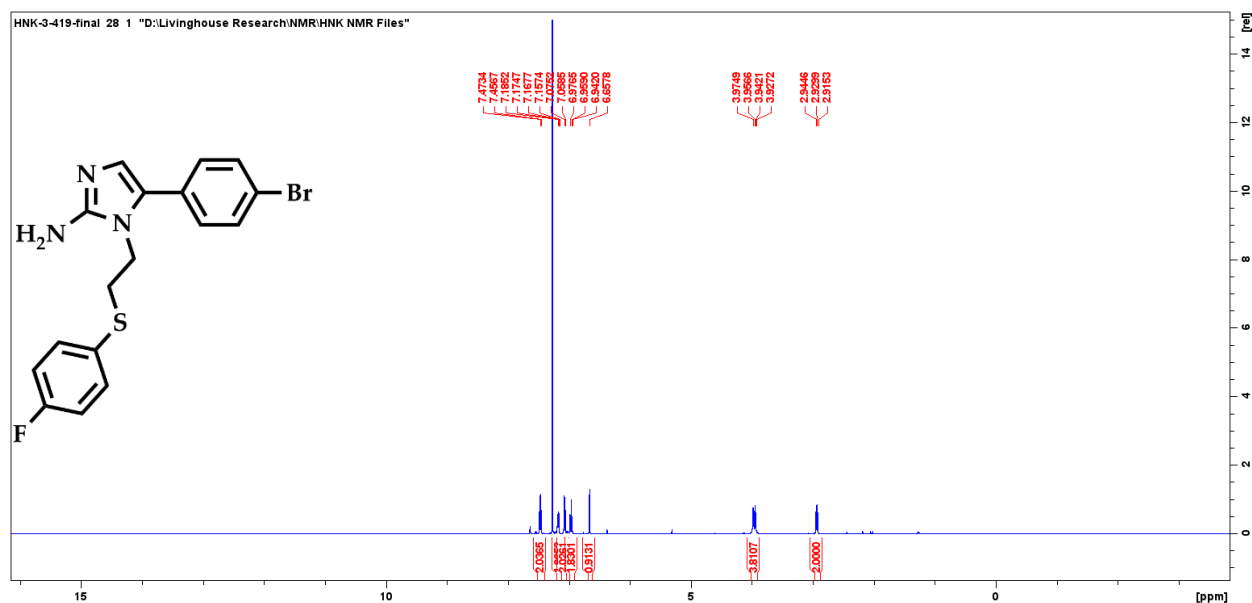


Figure 3.340B: ^1H -NMR Spectra of 5-(4-bromophenyl)-1-(2-((4-fluorophenyl)thio)ethyl)-1H-imidazol-2-amine (**10.3c**).

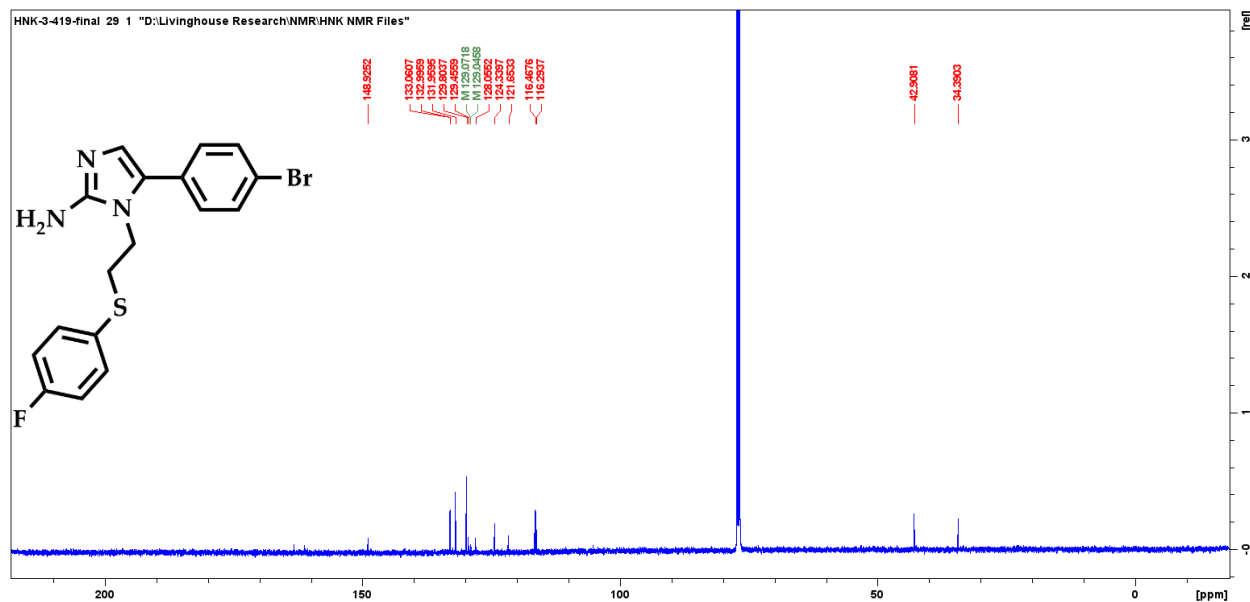


Figure 3.341B: ¹³C-NMR Spectra of 5-(4-bromophenyl)-1-(2-((4-fluorophenyl)thio)ethyl)-1H-imidazol-2-amine (**10.3c**).

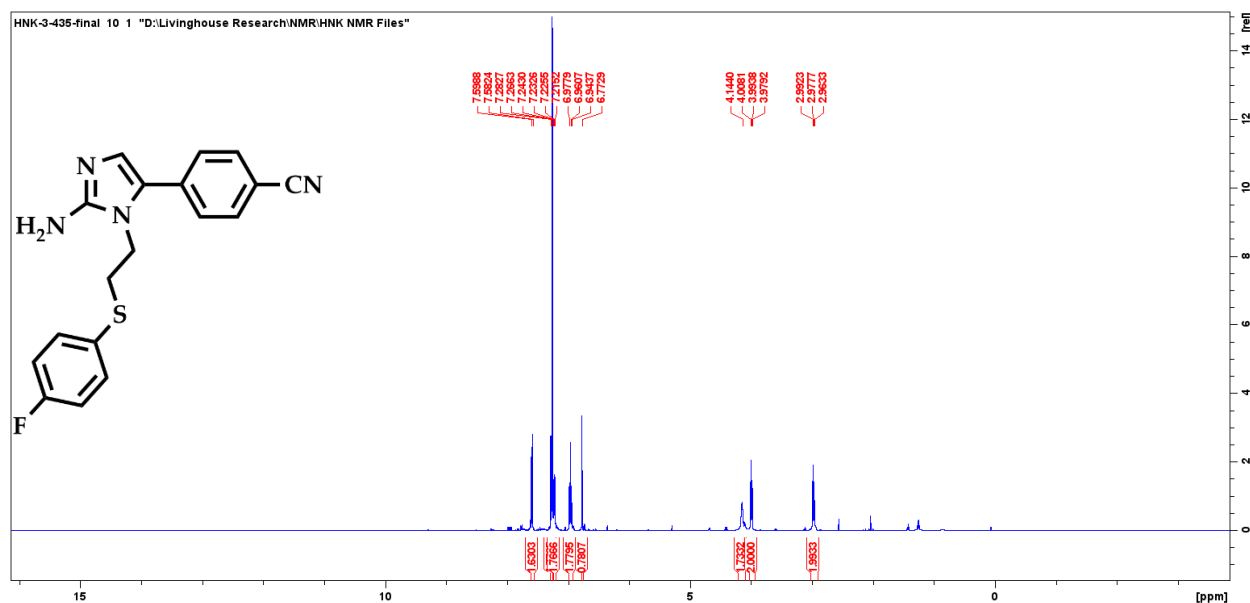


Figure 3.342B: ¹H-NMR Spectra of 4-(2-amino-1-(2-((4-fluorophenyl)thio)ethyl)-1H-imidazol-5-yl)benzonitrile (**10.3d**).

[illegible]

Figure 3.344B: ¹H-NMR Spectra of 1-(2-((4-fluorophenyl)thio)ethyl)-5-(4-nitrophenyl)-1H-imidazol-2-amine (**10.3e**).

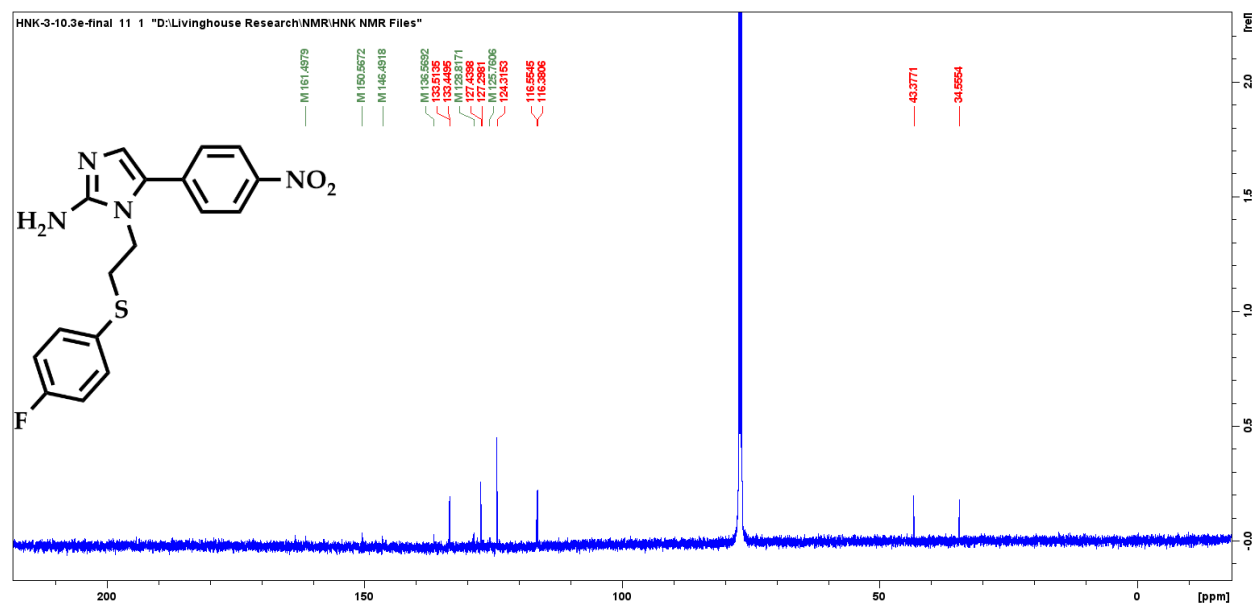


Figure 3.345B: ¹³C-NMR Spectra of 1-(2-((4-fluorophenyl)thio)ethyl)-5-(4-nitrophenyl)-1H-imidazol-2-amine (**10.3e**).

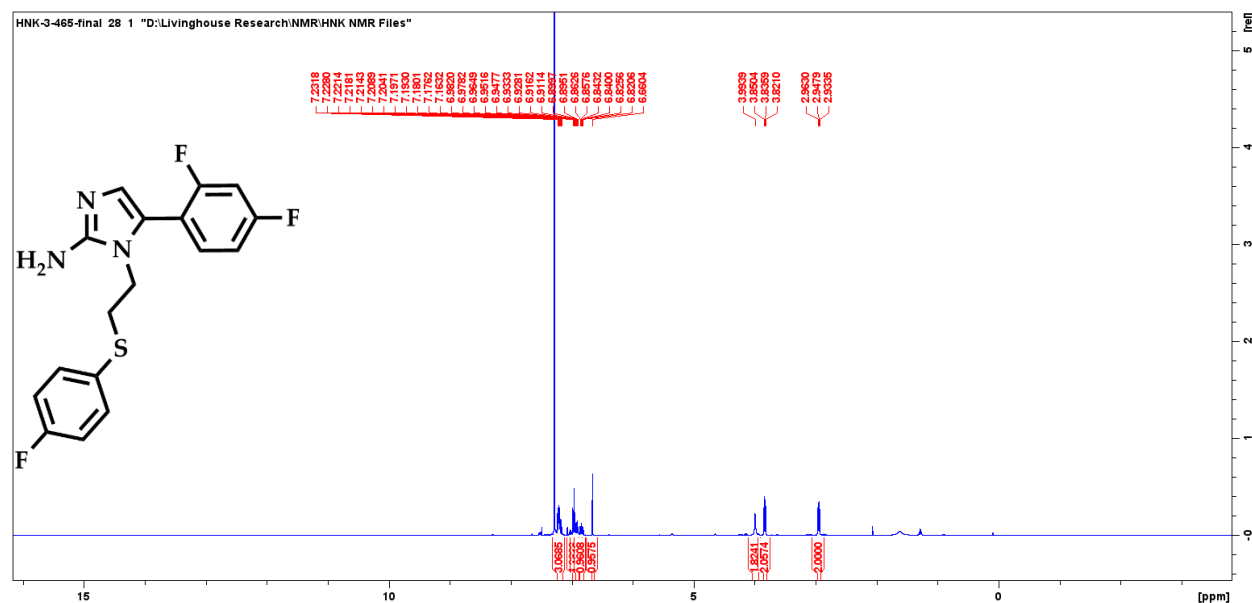


Figure 3.346B: ¹H-NMR Spectra of 5-(2,4-difluorophenyl)-1-(2-((4-fluorophenyl)thio)ethyl)-1H-imidazol-2-amine (**10.3f**).

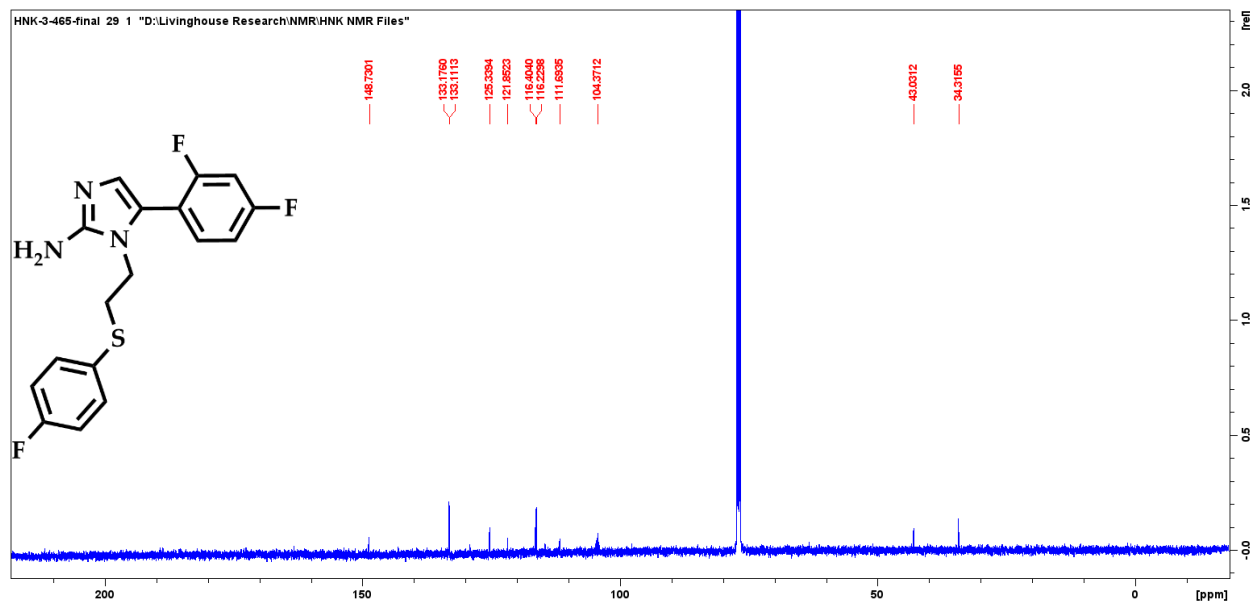


Figure 3.347B: ^{13}C -NMR Spectra of 5-(2,4-difluorophenyl)-1-(2-((4-fluorophenyl)thio)ethyl)-1H-imidazol-2-amine (**10.3f**).

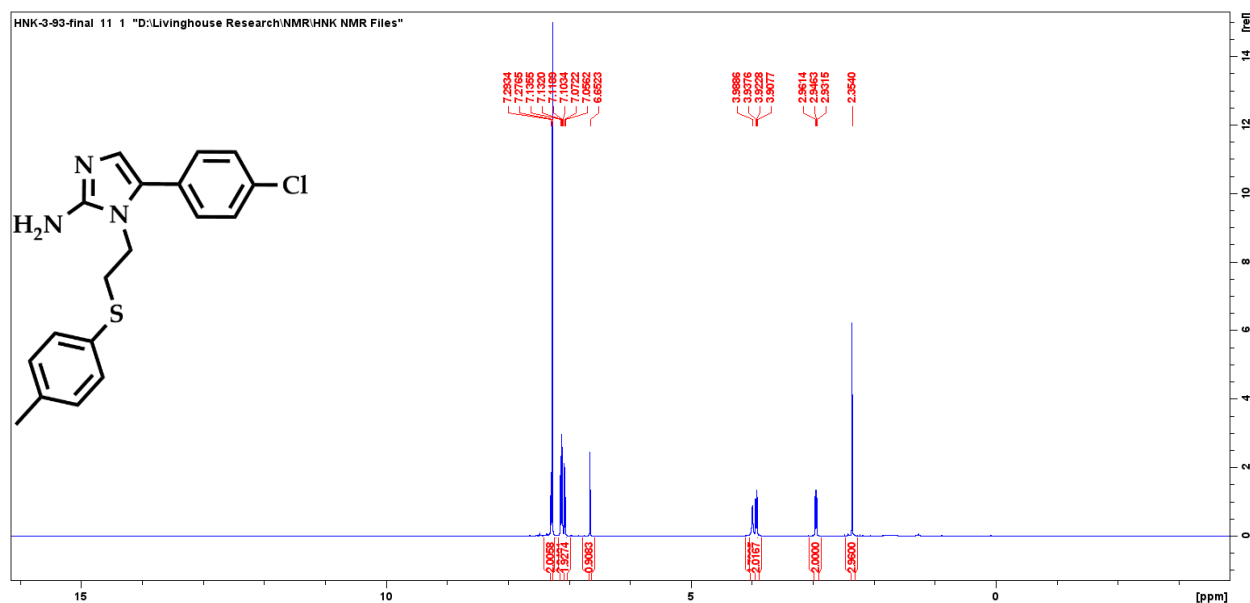


Figure 3.348B: ^1H -NMR Spectra of 5-(4-chlorophenyl)-1-(2-(p-tolylthio)ethyl)-1H-imidazol-2-amine (**11.3a**).

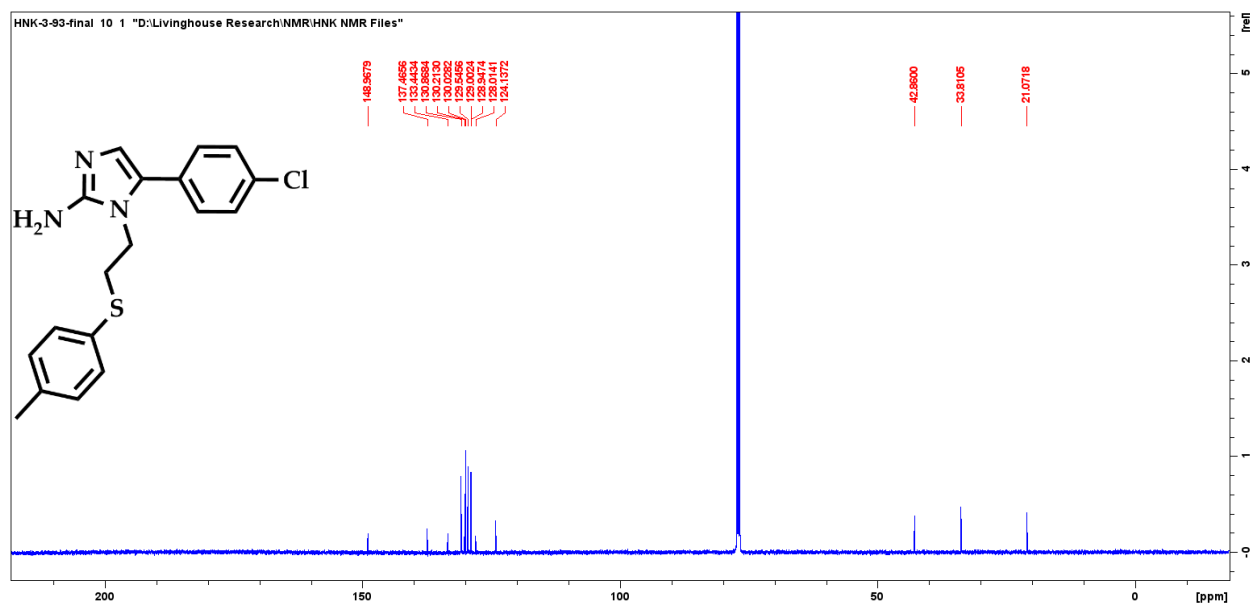


Figure 3.349B: ¹³C-NMR Spectra of 5-(4-chlorophenyl)-1-(2-(p-tolylthio)ethyl)-1H-imidazol-2-amine (**11.3a**).

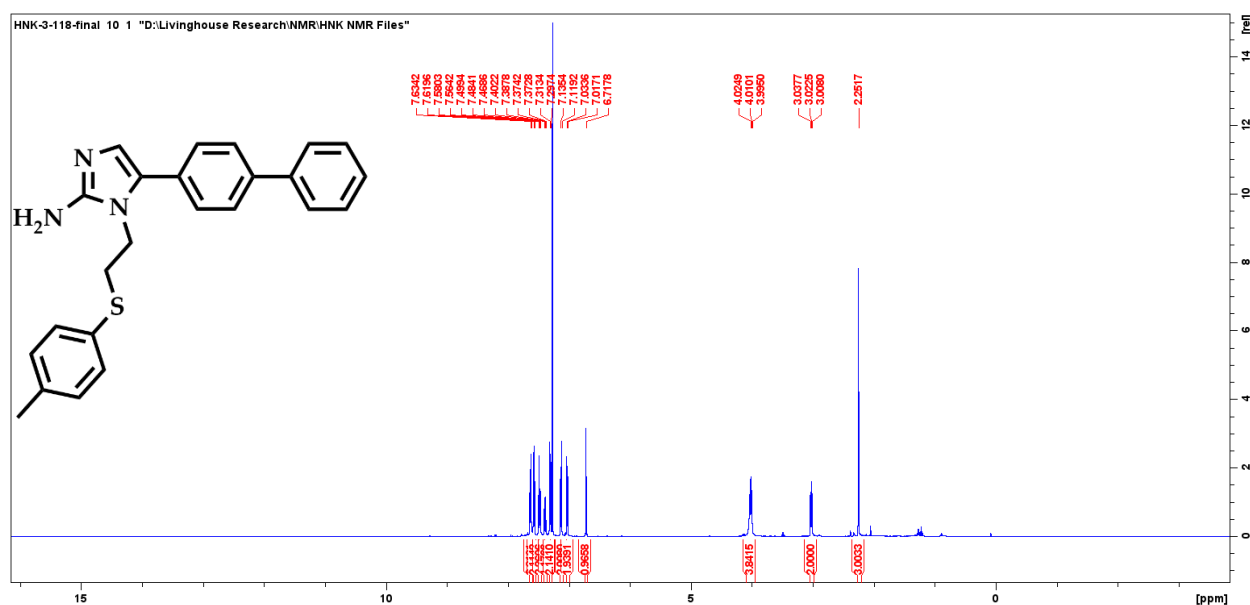


Figure 3.350B: ¹H-NMR Spectra of 5-([1,1'-biphenyl]-4-yl)-1-(2-(p-tolylthio)ethyl)-1H-imidazol-2-amine (**11.3b**).

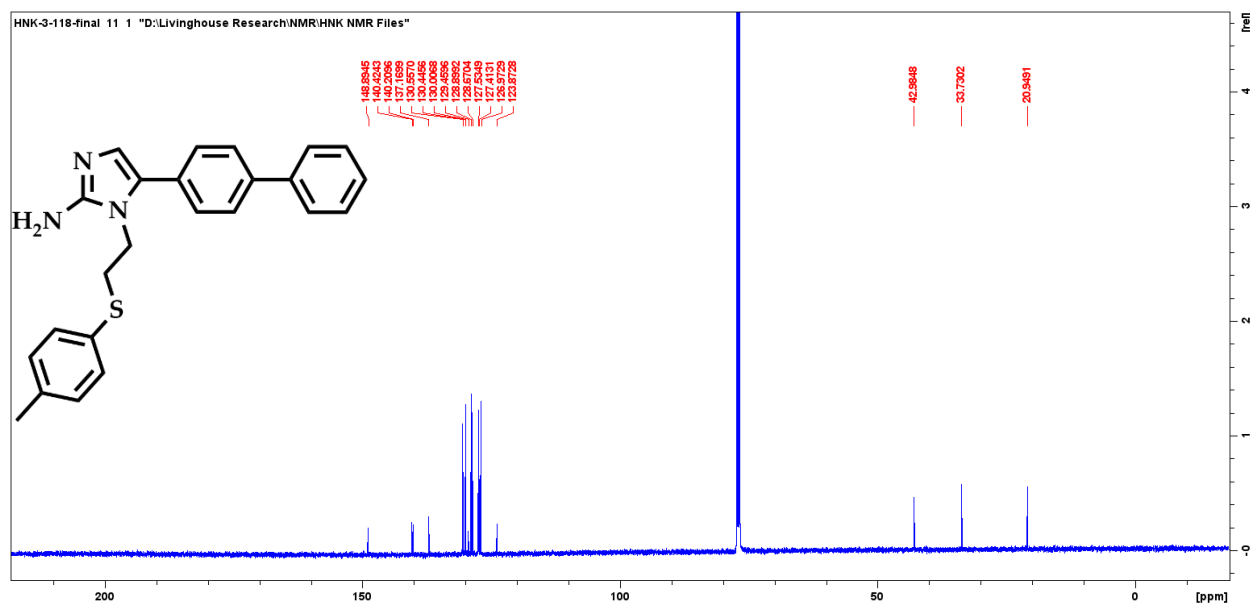


Figure 3.351B: ¹³C-NMR Spectra of 5-([1,1'-biphenyl]-4-yl)-1-(2-(p-tolylthio)ethyl)-1H-imidazol-2-amine (**11.3b**).

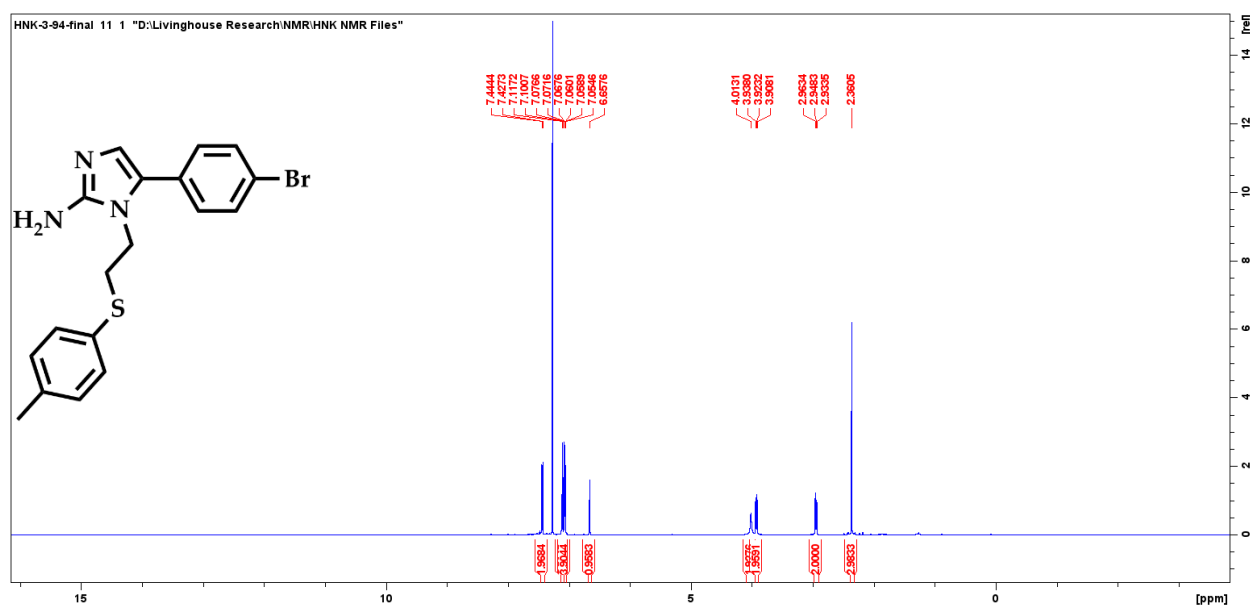


Figure 3.352B: ¹H-NMR Spectra of 5-(4-bromophenyl)-1-(2-(p-tolylthio)ethyl)-1H-imidazol-2-amine (**11.3c**).

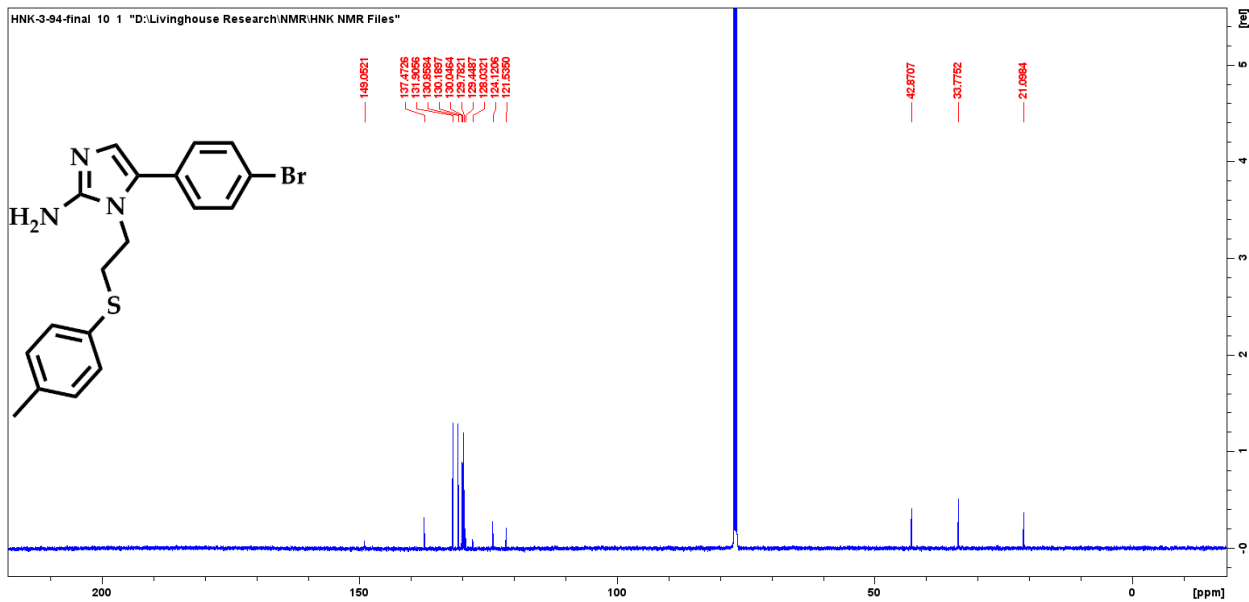


Figure 3.353B: ¹³C-NMR Spectra of 5-(4-bromophenyl)-1-(2-(*p*-tolylthio)ethyl)-1*H*-imidazol-2-amine (**11.3c**).

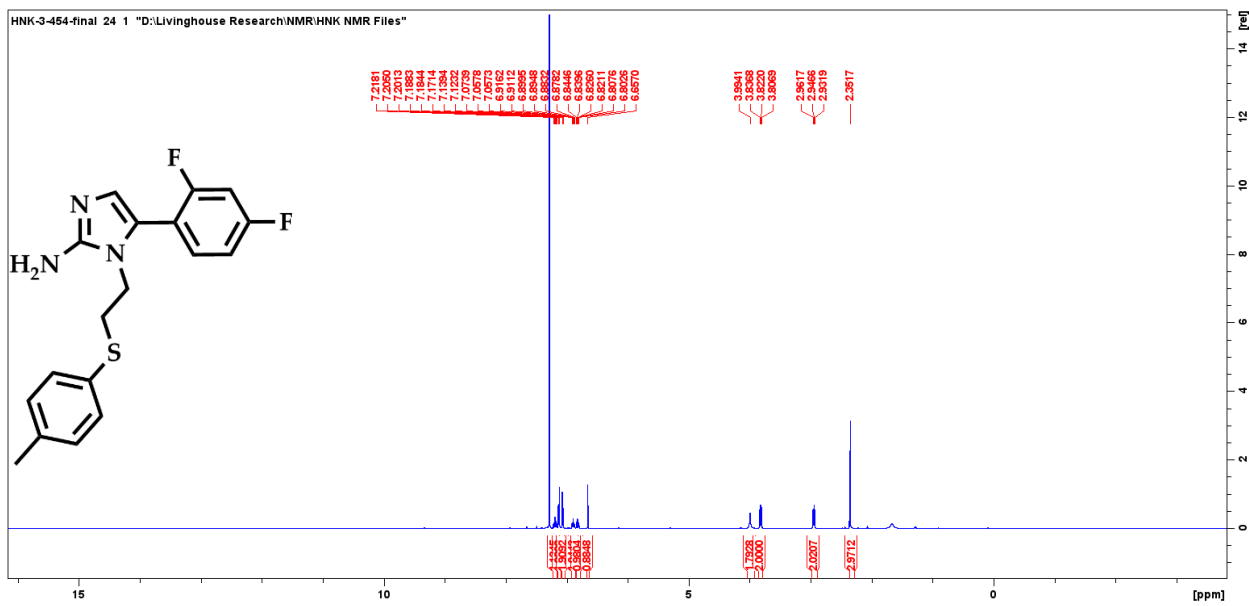


Figure 3.358B: ¹H-NMR Spectra of 5-(2,4-difluorophenyl)-1-(2-(*p*-tolylthio)ethyl)-1*H*-imidazol-2-amine (**11.3f**).

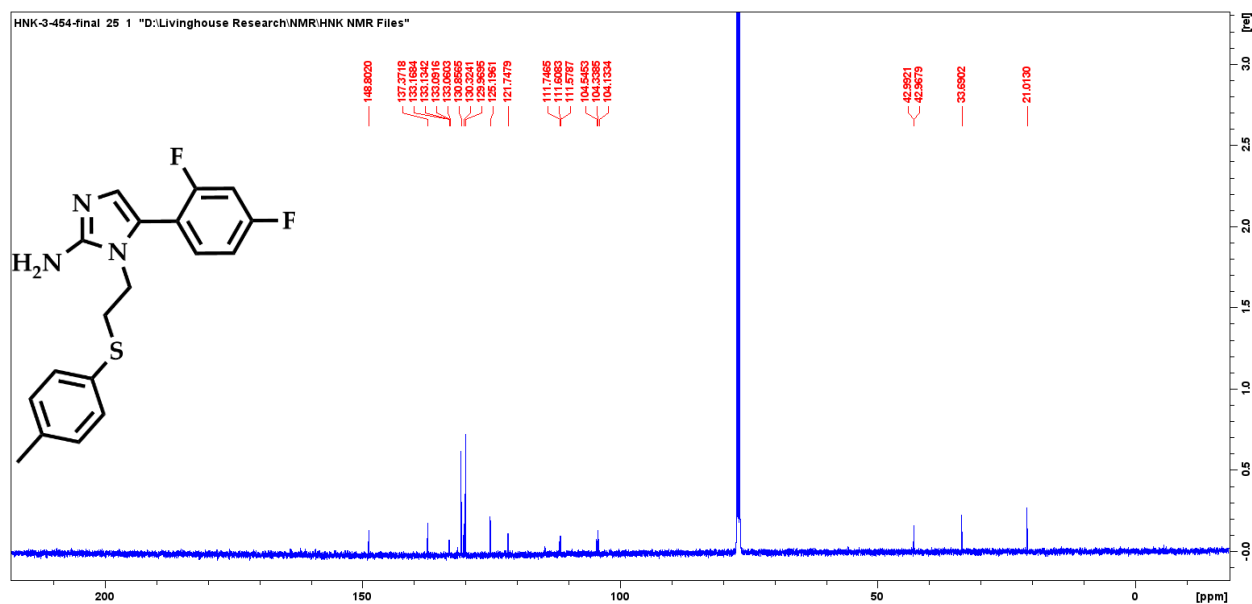


Figure 3.359B: ¹³C-NMR Spectra of 5-(2,4-difluorophenyl)-1-(2-(*p*-tolylthio)ethyl)-1*H*-imidazol-2-amine (**11.3f**).