Heteroannulations mediated by titanium imido complexes: methods development and applications to the total syntheses of (½)-monomorine I and (+)-preussin
by Paul Leo McGrane

A thesis submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Chemistry
Montana State University
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Abstract:
Highly reactive titanium imido complexes have been generated by the reaction of primary amines with monocyclopentadienyl titanium (IV) complexes. These transient imido complexes have been trapped via intramolecular [2 + 2] cycloadditions with tethered alkynyl moieties. This transformation has been used to prepare a variety of representative heterocycles via catalytic (CpTiCl3 mediated) and stoichiometric [CpTi(CH3)2Cl mediated] annulations of alkynlamines.

Additionally, the azatitanetines generated in stoichiometric [2+2] imido-alkyne cycloadditions have been shown to engage nucleophiles in subsequent bond-forming reactions.

The utility of these new methods in natural products synthesis was shown by their use in concise total syntheses of (±)-monomorine I and (+)-preussin.
HETEROANNULATIONS MEDIATED BY TITANIUM IMIDO COMPLEXES:
METHODS DEVELOPMENT AND APPLICATIONS TO THE TOTAL
SYNTHESES OF (±)-MONOMORINE I AND (+)-PREUSSIN

by

Paul Leo McGrane

A thesis submitted in partial fulfillment
of the requirements for the degree
of
Doctor of Philosophy
in
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Bozeman, Montana
January, 1993
APPROVAL

of a thesis submitted by

Paul Leo McGrane

This thesis has been read by each member of the thesis committee and has been found to be satisfactory regarding content, English usage, format, citations, bibliographic style, and consistency, and is ready for submission to the College of Graduate Studies.

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Date

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Date

Head, Major Department

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Graduate Dean
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Date: 1-10-93
Dedicated to the memory of my father and namesake, Leo Charles McGrane. May your Irish eyes always smile upon us.
ACKNOWLEDGEMENTS

As the successful compilation of a thesis is rarely an individual effort, there are a number of people who need to be acknowledged for their contributions.

Professor Tom Livinghouse has served most effectively as my research advisor and as a guide through the labyrinth of methods development and natural product synthesis. Professors A.C. Craig, P.W. Jennings and B.P. Mundy provided willing and capable guidance. The office staff, Mr. Lee David and Dr. Joe Sears furnished valuable services.

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Thank you all and God bless.
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ABSTRACT

Highly reactive titanium imido complexes have been generated by the reaction of primary amines with monocyclopentadienyl titanium (IV) complexes. These transient imido complexes have been trapped via intramolecular [2 + 2] cycloadditions with tethered alkynyl moieties. This transformation has been used to prepare a variety of representative heterocycles via catalytic [CpTiCl, mediated] and stoichiometric [CpTi(CH₃)₂Cl mediated] annulations of alkynylamines.

Additionally, the azatitanetines generated in stoichiometric [2 + 2] imido-alkyne cycloadditions have been shown to engage nucleophiles in subsequent bond-forming reactions.

The utility of these new methods in natural products synthesis was shown by their use in concise total syntheses of (±)-monomorine I and (+)-preussin.
INTRODUCTION

The development of transition metal mediated carboannulation methods has greatly enhanced the chemist's ability to elaborate the cyclic skeletons of many biologically active carbogens. Two powerful examples of these methods are intramolecular carbene cycloaddition\(^1\,^2\) and ligand cyclization reactions\(^3\) (Eq. 1 and Eq. 2).

\[
\begin{align*}
\text{Eq. 1} \\
\text{Eq. 2}
\end{align*}
\]

While the reactions in Eq. 1 and Eq. 2 both effect ring annulation, the \([2 + 2]\) cycloaddition of Eq. 1 has the added advantage of generating a metallocyclobutane or metallocyclobutene which may serve as an intermediate for further elaboration. The utility of intramolecular carbene-alkyne cycloadditions in natural product synthesis was
exemplified by Semmelhack's synthesis of deoxyfrenolicin (Scheme 1).

Scheme 1
The analogous transformations of amido and imido complexes that would lead to heterocyclic products have received little or no attention. Recently, Marks described the catalytic hydroamination of terminal alkenes proceeding via amidolanthanide complexes\(^5\)\(^\text{-}^6\) (Scheme 2).

Prior to the work reported in this thesis, there were no examples of the imido analog of the intramolecular carbene cycloaddition reaction. As with the carbene-olefin cycloaddition, imido complex-olefin cycloadditions could potentially provide exploitable metallocyclic intermediates (Eq. 3).
BACKGROUND

Transition metal imido complexes are defined as complexes bearing at least one imido ligand (N-R) on the metal. All monoimido complexes possess M-N-C bond angles greater than 155°, indicating extensive participation of the nitrogen lone pair in bonding interactions with the metal. With bisimido complexes it is possible to have smaller M-N-C bond angles due to saturation of the metal d-orbitals having $\pi$ symmetry. However, there is only one clear example of a bent imido ligand. The molybdenum complex Mo(NPh)$_2$(S$_2$CNEt$_2$)$_2$ shown below has both a linear (169°) and a bent (139°) imido ligand (Figure 1).

![Figure 1. Linear and Bent Molybdenum Bisimido Complex.](image)

The reaction chemistry of imido complexes, to the extent that it has been determined, is quite varied and depends largely on the metal and the other ligands present. For example, methylimido rhenium complexes are readily deprotonated due to the increased acidity of the methyl ($\beta$)
protons. This is a direct reflection of the electronegativity of the metal (Eq. 4).

\[
\begin{align*}
\text{Cl} & \quad \text{L} \\
\text{Cl-} & \quad \text{Re} \equiv \text{N-CH}_3 \\
\text{L'} & \quad \text{Cl} \\
\end{align*}
\]

\[\xrightarrow{2 \text{ py}}\]

\[
\begin{align*}
\text{Cl} & \quad \text{L} \\
\text{Cl-} & \quad \text{Re} \equiv \text{N} \equiv \text{CH}_2 \\
\text{L'} & \quad \text{py-HCl} \\
\end{align*}
\]

\[\text{L}=\text{PPh}_3, \text{PCH}_3\text{Ph}_2, \text{PEtPh}_2\]

Eq. 4

A more extreme case of the reactivity imparted on protons to the metal was seen with the related osmium complex \(\text{OsO}_3\text{NCH}_3\). Solutions of this methyl amidoo complex exploded when warmed to \(-40^\circ\text{C}\). The inherent instability of osmium imido complexes bearing \(\beta\) protons has been the major limitation in the otherwise useful oxyamination and diamination reactions mediated by imido osmium complexes\(^{12}\) (Eq. 5).

\[
\begin{align*}
\text{X} & \equiv \text{O, NR;}\ R=\text{tertiary alkyl} \\
\end{align*}
\]

Eq. 5

Another mode of reactivity of imido complexes is C-H insertion. Two interesting examples are presented here
(Eq. 6 and Eq. 7), and more recent examples with a direct bearing on the work in this thesis will be discussed later.

\[
\begin{align*}
\text{Eq. 6} & \quad \begin{array}{c}
\text{Ph} \\
\text{N} \\
\text{N} \\
\text{N} \\
\text{N} \\
\text{O} \\
\text{N} \\
\text{N} \\
\text{Ph}
\end{array}
\rightarrow
\begin{array}{c}
\text{HN} \\
\text{N} \\
\text{N} \\
\text{O} \\
\text{N} \\
\text{N} \\
\text{N} \\
\text{Ph}
\end{array}
\end{align*}
\]

In contrast to the [3 + 2] addition mode of the imido osmium complexes observed in oxyamination and diaminations, a trifluoroacetimido manganese complex<sup>15</sup> effects aziridine formation when treated with cyclooctene (Eq. 8). This is currently the single example of the imido analog of the epoxidations mediated by oxo complexes<sup>16</sup>.

Catalytic processes which have been suggested to proceed via imido complexes include the ammoxidation of
propylene and methylarenes\textsuperscript{7}. A partial mechanism for the ammoxidation of propylene that includes a molybdenum imido complex has been advanced\textsuperscript{17} (Scheme 3).

\begin{equation}
\text{CH}_2\text{CH}=\text{CH}_2 + \text{NH}_3 \xrightarrow{\text{Bi}_2\text{O}_3/\text{MoO}_3, 450 \degree \text{C}} \text{NOCOCF}_3
\end{equation}

Scheme 3

Although hundreds of transition metal-imido complexes are now known\textsuperscript{7,18}, only a few are known to engage olefins in cycloaddition reactions. Foremost among these are osmium
imido complexes which effect oxyamination or diamination of olefins via \([3 + 2]\) cycloadditions\(^{12}\) (Eq. 9).

\[
\begin{align*}
\text{O} &= \text{N} \\
\text{O} &= \text{Os} \\
\text{PhCH} &= \text{CH}_2
\end{align*}
\]

\(X = \text{O}, \text{N-}t-\text{Bu}\)

Eq. 9

Additionally, aziridine formation with trifluoracetimido manganese complexes likely proceed via \([2 + 2]\) cycloaddition onto the alkene\(^{15}\) (Eq. 10).

\[
\begin{align*}
\text{COCF}_3 &= \text{N} \\
\text{N} &= \text{L}_n\text{Mn}
\end{align*}
\]

Eq. 10

Prior to 1988, \([2 + 2]\) cycloaddition reactions of imido complexes onto alkynes were unknown. At this time, Bergman and Wolczanski, in concurrent publications, presented the first examples of monomeric zirconium imido complexes\(^{19-21}\).

The imido zirconocene complexes described by Bergman were generated by thermolysis of the corresponding methyl amido complexes. When alkynes were present in the reaction
mixture, they were engaged in intermolecular [2 + 2] cycloadditions to give azazirconetines. In the absence of alkynes or stabilizing ligands, imido zirconocene complexes dimerized to bridging complexes\(^1\) (Scheme 4).

\[
\begin{align*}
\text{Scheme 4}
\end{align*}
\]

An exception to this mode of reactivity was observed upon generation of the bulky t-butyl imido zirconocene complex. In this case the preferred pathway culminated in insertion into the C-H bonds of the solvent benzene. This was analogous to the reactivity observed by Wolczanski\(^2\) wherein activation of benzene C-H bonds was achieved (Eq. 11 and Eq. 12).

Our entry into the arena of Group IV imido chemistry was precipitated by a combination of Bergman’s report on
intermolecular couplings of imido zirconocene complexes with alkynes, and an earlier reaction observed by Teuben\textsuperscript{22}. Specifically, it was noted by Teuben that monocyclopentadienyl titanium amido complexes spontaneously dimerized in solution with concomitant loss of HCl to give bridging imido dimers (Eq. 13).

Though Teuben did not speculate that imido complexes were intermediates in this process, it seemed likely that the dimerization proceeded along a reaction pathway analogous to that later elucidated by Bergman for the formation of bridging imido zirconocene complexes. If true,
this would dictate imido complexes as intermediates (Eq. 14).

\[
\begin{align*}
\text{Cp-Ti-N-R} & \quad \text{HCl} \\
\text{Cl} & \quad \text{Cl}
\end{align*}
\]

Eq. 14

Teuben also observed anomalous behavior with amido complexes derived from t-butylamine. In this case, dimerization (and thus imido complex formation) could only be effected by treatment of the amido complex with PhLi or CH₃Li. However, dimerization was still the preferred reaction pathway, not C-H activation as observed by Bergman¹⁹.

It has not been determined whether addition of the organolithium to the t-butylamido titanium complex results in displacement of a chloride on titanium, or in metallation of the amide nitrogen. However, either process would give an intermediate more prone to elimination than the parent amido complex itself (Scheme 5).

The ease of formation of the bridging imido dimers suggested that the putative monomeric imido complexes formed readily from the amido complexes. Additionally, these monocyclopentadienyl complexes would be expected to be more electron deficient than imido zirconocene complexes.
Our goal at the outset of this research was to take advantage of this ease of imido complex formation and to exploit the reactivity of these transient species to effect intramolecular \([2 + 2]\) cycloadditions (Eq. 15).

Once the reactivity of these complexes had been ascertained, we hoped to utilize the \([2 + 2]\) cycloaddition in total syntheses of (+)-monomorine (1)\textsuperscript{23} and (+)-preussin (2)\textsuperscript{24} (Figure 2).
Figure 2. (+)-Monomorine I (1) and (+)-Preussin (2).

Since the inception of our research into Group IV imido complex [2 + 2] cycloaddition reactions, four publications dealing with monomeric, terminal titanium imido complexes have appeared. Inclusive in Rothwell's report was some preliminary data on the reactivity of bis-(aryloxy)-phenylimido complexes. Although these solvated species did not induce benzene C-H activation or undergo cycloaddition reactions with 3-hexyne, the corresponding bisamido complex was effective in catalyzing formation of the N-phenylimine of 3-hexanone from 3-hexyne and aniline (Scheme 6).

The authors suggested unsolvated imido complexes as the reactive intermediates in this process. If this was indeed the reactive intermediate, it would constitute the first probable example of a [2 + 2] cycloaddition of a titanium imido complex into an alkyne.

Roesky has detailed the preparation and x-ray diffraction study of a dichlorotitanium imido complex (Figure 3). Although no studies on the reactivity of this
complex have as yet been published, one might speculate that its unsolvated analog would exhibit either a marked reactivity towards olefins, or a propensity to dimerize (Scheme 7).
Scheme 7

More recently, Wolczanski\textsuperscript{27} has reported a series of titanium imido complexes that are closely related to the zirconium imido complex, described earlier\textsuperscript{21}. As with the analogous bisamido imido zirconium imido complex, bisamido imido titanium complexes (X=NH-t-Bu) promoted C-H activation of benzene (Figure 4).

Figure 4. Silyl Substituted Titanium Imido Complexes.

When one of the complexes of this series (X=t-Bu) was exposed to hydrogen, an interesting dimerization occurred.
This dimer was found, by x-ray diffraction, to contain a metal-metal bond (Eq. 16).

\[
\begin{align*}
\text{H}_2 & \quad \text{H}_2 \\
\text{t-Bu}_3\text{Si} & \quad \text{t-Bu}_3\text{Si}
\end{align*}
\]

Eq. 16

Doxsee\textsuperscript{28,29} reported the formation of vinylimidotitanocene complexes. The transient azatitanatines generated upon treatment of Tebbes' reagent with nitriles were isomeric to those obtained by Bergman\textsuperscript{19}. A retro [2 + 2] reaction gave the isolable vinylimidido complexes. Among the interesting chemistry associated with these vinylimidido complexes was addition of a second nitrile, via a [4 + 2] cycloaddition, to form diazatitanacyclohexadienes (Scheme 8).

In work pursued concurrently with that presented in this thesis, Mike Jensen, formerly of these laboratories, developed annulation methods based on the intramolecular [2 + 2] cycloaddition of monocyclopentadienyl zirconium imido complexes onto tethered alkynes\textsuperscript{30,31}. This method entailed treatment of CpZrCl\textsubscript{2}.DME\textsuperscript{32} with two equivalents of methyllithium to generate CpZr(CH\textsubscript{3})\textsubscript{2}Cl. The resultant solution could then be treated with a variety of alkynylamines to give, after workup, the annulated products (Eq. 17).
Another major focus of Jensen's work in this area was the selective functionalization of azametalletines. For example, azatitanetine 13 was selectively N-functionalized upon treatment with acyl chlorides, but C-functionalized upon exposure to acyl nitriles (Scheme 9).

Interestingly, this mode of functionalization was not observed when a similar azazirconetine was treated with
Scheme 9

ClCO₂CH₃. In this case, C-C bond formation was observed (Eq. 18).

Eq. 18

 Particularly noteworthy was the facile preparation of tetrahydropyridines 10 and 12 using this method. Table 1 contains the results of this study.
Table 1. Results of CpZr(CH₃)₂Cl Annulation Study

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<td>3 ( \text{NH}_2 \text{-} \text{Ph} )</td>
<td>(83)</td>
<td>4 ( \text{N} \text{-} \text{Ph} )</td>
</tr>
<tr>
<td>5 ( \text{NH}_2 \text{-} \text{n-Bu} )</td>
<td>(82)</td>
<td>6 ( \text{N} \text{-} \text{n-Bu} )</td>
</tr>
<tr>
<td>( \text{CH}_3 \text{-} \text{NH}_2 \text{-} \text{Ph} )</td>
<td>(77)</td>
<td>8 ( \text{N} \text{-} \text{Ph} )</td>
</tr>
<tr>
<td>9 ( \text{NH}_2 \text{-} \text{Ph} )</td>
<td>(69)</td>
<td>10 ( \text{N} \text{-} \text{Ph} )</td>
</tr>
<tr>
<td>11 ( \text{NH}_2 \text{-} \text{n-Bu} )</td>
<td>(74)</td>
<td>12 ( \text{N} \text{-} \text{n-Bu} )</td>
</tr>
</tbody>
</table>
RESULTS AND DISCUSSION

Methods Development

Our initial aim in this research was to establish the accuracy of our hypothesis that there existed a reactive monocyclopentadienyl titanium imido complex as an intermediate in the dimerization process observed by Teuben. Towards this end, 5-phenylpent-4-yn-1-ylamine (3) was prepared (Scheme 10). It was reasoned that the alkynyl moiety of amine 3 could serve as an intramolecular trap of imido complexes if they were generated.

We were quite pleased when an initial experiment in which amine 3 was added to CpTiCl₃ (1.0 eq.) and i-Pr₂NEt
(2.1 eq.) in THF at 25 °C yielded, after methanolysis, \( \Delta^1 \)-pyrroline 4 in 74 % yield (Scheme 11).

The mechanism proposed in Scheme 11 was based, at this early stage, solely on the known chemistry of imido and amido complexes of the Group IV elements. Specifically, the amine 3 would be expected to react with CpTiCl, to form the amido complex 17. This, along with a subsequent elimination of HCl to form the putative imido complex 18, would be in accord with Teuben’s observations \( ^{22} \). An intramolecular \([2 + 2]\) cycloaddition of 18 would then parallel the intermolecular cycloadditions of imidozirconocene complexes \( ^{19} \). The fact that \( \Delta^1 \)-pyrroline 4 was the only
isolable product of this reaction was certainly consistent with the proposed mechanism.

Bergman had noted that azazirconetines were intensely colored, presumably due to charge transfer from the azaallyl moiety to the empty orbital on the formally 16-electron zirconium center. As the titanium in azatitanetine 13 would be expected to be even more electron deficient, we were not surprised when amine addition in our pilot experiment induced formation of a deep burgundy color.

In a set of experiments designed to closely parallel those of Bergman, amine 3 was added to preformed solutions of CpTi(CH₃)₂Cl and CpTi(CH₃)₂OCH₃ (Scheme 12). It was anticipated that azatitanetine 13 would be generated by elimination of two equivalents of methane and subsequent [2 + 2] cycloaddition. Indeed, both dimethyltitanium complexes were found to be suitable precursors to 13. Addition of amine 3 to the solution of CpTi(CH₃)₂Cl was accompanied by immediate evolution of methane and formation of a deep burgundy color. It is noteworthy that these transformations were complete in less than two hours at 25 °C. By way of comparison, reaction of amine 3 with Cp₂Zr(CH₃)₂ gives less than 10 % conversion to Δ¹-pyrroline after 24 h at 80 °C. Although this rate differential was initially attributed to a more reactive imido complex being generated in our process, we have since determined that the reactivity difference in this case was due to a slow initial
reaction of the amine 3 with Cp₂Zr(CH₃)₂ to form an amido complex⁴⁰.

In an attempt to determine whether reactive nitrogen-titanium and carbon-titanium bonds were present, a solution of azatitanetine 13 was quenched with deuterium oxide. As anticipated, the dideuterated Δ¹-pyrroline 4D was formed in 92% yield. Indeed, azatitanetine 13 was also found to
react with nitriles as shown in Scheme 12, and with several other electrophiles, as demonstrated by Jensen.

Because all attempts at isolation and characterization of 13 have failed, we cannot state for certain that 13 is an intermediate in this process. The subsequent reactions observed for the intermediate are, however, consistent with structure 13.

\[
\text{PhC} = \text{C(CH}_2\text{)}_3\text{X} \xrightarrow{\text{NaCN}} \text{PhC} = \text{C(CH}_2\text{)}_3\text{CN} \xrightarrow{\text{LiAlH}_4} \text{NH}_2
\]

We next sought to extend this stoichiometric cycloaddition methodology to the formation of six-membered nitrogen heterocycles (e.g., tetrahydropyridines). For this purpose, 6-phenylhex-5-yn-1-ylamine 9 was prepared from the halide mixture 15 via nitrile displacement and subsequent reduction with LiAlH₄ (Eq. 19). Unfortunately, only starting material was recovered when amine 9 was added to CpTi(CH₃)₂Cl in THF at 25 °C. When more rigorous reaction conditions were employed (toluene, 85 °C, slow amine addition), we were able to obtain a mixture of tetrahydropyridine 10 and starting material (Eq. 20). As this conversion can be achieved at 25 °C with CpZr(CH₃)₂Cl, optimization with CpTi(CH₃)₂Cl was not pursued.
When a THF solution of CpTiCl₃ (1.0 eq.) and i-Pr₂NEt (2.1 eq.) was treated with amine 3 (vide infra, Scheme 11), but allowed to stir for a longer time, the initial dark burgundy color formed on amine addition begins to dissipate. Eventually (~2 h), the light red color of the CpTiCl₃/i-Pr₂NEt solution was restored. This suggested that the conversion of alkynylamine to Δ₁-pyrroline could be effected catalytically. Thus, addition of amine 3 to a solution of CpTiCl₃ (20 mole %) and i-Pr₂NEt (40 mole %) afforded Δ₁-pyrroline 4 in 94 % yield after two hours. A catalytic cycle that accounts for this transformation is proposed in Scheme 13. Note that dimer formation, if it did occur, would regenerate starting materials by a subsequent reaction with the amine hydrochloride present.

Although 6-phenylhex-5-yn-1-ylamine (9) was not cyclized under these conditions, the following modifications of the reaction conditions restored cyclization. For the generation of tetrahydropyridines, we found that addition of the amine to a preheated solution of CpTiCl₃, (20 mole %) and
N,N-dimethylaniline (40 mole %) gave the expected product in high yield (Eq. 21).

In an attempt to further probe the nature of the annulation, a series of experiments were run in which amine 3 was exposed to catalytic quantities of transition metal complexes possessing more (TiCl₄, ZnCl₂) or less (Cp₂TiCl₂, CpTi(CH₃)₂Cl) Lewis acidic character than CpTiCl₃. No other complex was found to effect Δ¹-pyrroline formation.
This observation, along with our results in the stoichiometric studies\textsuperscript{30,31}, strongly suggested that we were indeed dealing with a cycloaddition reaction and not a Lewis acid catalyzed hydroamination of alkynes.

With the two methods of cyclization fairly well developed, we sought to determine their generality. A variety of substrates were prepared for this reason (Scheme 14). In addition to the phenyl substituted
alkynylamines previously discussed, the substrates studied included dialkyl substituted alkynes, terminal alkynes, and substrates with the amine functionality on a secondary carbon. The results of this study on the facile preparation of 1-pyrrolines and tetrahydropyridines are shown in Table 2.

In the hope that the substrate amine and/or the product (1-pyrroline or tetrahydropyridine) could function in place of the auxiliary amine, cyclization was attempted in the absence of added tertiary amine. Addition of amine 26 to a THF solution of CpTiCl3, (10 mole %) gave complete conversion to 1-pyrroline 27 in two hours (Eq. 22).

\[
\text{CpTiCl}_3 (10 \text{ mol %}) \quad \text{THF, 25 °C}
\]

\[
\begin{align*}
\text{CH}_3 & \quad \text{NH}_2 \\
\text{C} & \quad \text{n-Bu}
\end{align*}
\]

\[
\begin{align*}
\text{CH}_3 & \quad \text{N} \\
\text{C} & \quad \text{n-Bu}
\end{align*}
\]

Eq. 22

Amines 20 and 23 were converted to their respective tetrahydropyridines in high yield (>90 %) by heating for three hours with CpTiCl3, (10 mole %) in benzene at 80 °C, This was quite gratifying in that we no longer had to deal with separating N,N-dimethylaniline from the products (Eq. 23).

The maximum turnover for CpTiCl3, in the catalytic cycle was measured with amine 26. The amine was added to a THF solution of CpTiCl3, in portions at intervals corresponding
Table 2. Results of CpTiCl₃ and CpTi(CH₃)₂Cl Annulation Studies

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Method⁻ᵃ</th>
<th>Yield, %ᵇ</th>
<th>Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>A</td>
<td>(94)</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>(96)</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>A</td>
<td>(94)</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>(94)</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>B</td>
<td>(92)</td>
<td>8</td>
</tr>
<tr>
<td>26</td>
<td>D</td>
<td>(94)</td>
<td>27</td>
</tr>
<tr>
<td>28</td>
<td>D⁻ᶜ</td>
<td>(100)ᵈ</td>
<td>29</td>
</tr>
<tr>
<td>9</td>
<td>C</td>
<td>(88)</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>E</td>
<td>(91)</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>C</td>
<td>(89)</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>E</td>
<td>(92)</td>
<td></td>
</tr>
</tbody>
</table>

a. A: 20 mol % CpTiCl₃, 40 mol % l-Pr₂NEt, THF, 25 °C. B: CpTi(CH₃)₂Cl, THF, 25 °C. C: 20 mol % CpTiCl₃, 40 mol % PhN(CH₃)₂, C₇H₈, 80 °C. D: 10 mol % CpTiCl₃, THF, 25 °C. E: 10 mol % CpTiCl₃, C₆H₆, 80 °C. b. All yields are isolated yields unless specified otherwise. c. C₆D₆, 25 °C. d. ¹H NMR yield.
to the dissipation of the color attributed to the metallocycle. The experiment was terminated when amine addition did not induce formation of the burgundy colored intermediate. The mass yield after workup was 96 % and was comprised of a 96:4 mixture of $\Delta^1$-pyrroline 27 and amine 26. By this method the turnover for CpTiCl$_3$, was between 50 and 55. Although this turnover is moderate, the ready availability of the catalyst should make the process extremely viable for many applications$^{34}$.

As carbenes were known to engage alkenes and dienes in cycloaddition reactions$^2$, we hoped to observe similar reactivity with imido complexes. We have made some preliminary attempts at inducing cycloaddition reactions between titanium imido complexes and other multiply bonded carbon-carbon systems. Specifically, alkenylamine 30 was subjected to all conditions found effective for the cycloaddition of alkynylamines (Eq. 24). Unfortunately, we were unable to obtain cyclized products. Even the more
electron-rich alkenylamine 31 failed to undergo the desired transformation (Eq. 25).

We also explored the possibility of inducing \([4 + 2]\) or \([2 + 2]\) cycloadditions of imido complexes onto diene functions. Dienylamine 32 was recovered unaltered from these attempted cycloadditions (Eq. 26).
Finally, we have not yet been able to use these new annulation methods in the preparation of azepines or azocines (Eq. 27).

As alkynyl amines 34 and 36 would both be expected to readily form imido complexes with either CpTiCl₃ or CpTi(CH₃)₂Cl, competitive, nonproductive reaction pathways must be responsible for the lack of observable annulation. Competitive, irreversible dimerization, as observed by Bergman for imidozirconocene complexes¹⁹, would account for the inefficiency of CpTi(CH₃)₂Cl. However, dimerization under catalytic conditions should not terminate formation of reactive imido complexes. In this case we speculate that the known propensity of cyclopentadiene to be displaced in the presence of an excess of amine⁴⁳ may give rise to an inactive amido complex of the general formula ClₙTi(NHR)ₘ, (n + m = 4). This observation was consistent with the inability of TiCl₄ to effect annulation of alkynyl amines. It also seems likely that displacement of cyclopentadiene accounts for the moderate turnover observed for CpTiCl₃, in the successful cyclizations discussed previously.
The Total Synthesis of (+)-Monomorine I (1).

The synthetic utility and functional group compatibility of CpTiCl₃ catalyzed cycloadditions of alkynylamines was demonstrated by a concise total synthesis of (+)-monomorine I (1)⁴⁴ (Figure 5).

Figure 5. (+)-Monomorine I (1).

This alkaloid is a trail pheromone of the Pharoah's Ant that also exhibits repellent activity toward other ant species²³,⁴⁵. Pharoah's Ants are common pests in the British Isles and are now becoming a problem in the United States. Infestations of these small ants are considered a serious problem because the ants have been shown to carry pathogenic bacteria and also possess the ability to penetrate sophisticated hospital isolation units⁴⁶.

Monomorine I was first described by Ritter in 1972²³. The absolute stereochemistry was confirmed by synthesis in 1975⁴⁷. Since then, 1 has been the subject of intense synthetic study. Although numerous syntheses have been
advanced, few are sufficiently high yielding to be of practical use in the preparation of I or similar indolizidine alkaloids. The most concise enantioselective synthesis of (+)-monomorine I utilized L-alanine as a chiral building block. The synthesis was completed in seven steps in an overall yield of 7-11% (Scheme 15).

With some improvement this method may be conducive to the large scale preparation of (+)-1. At this time the alternatives are a 22-step (<<7%) procedure starting with L-tartrate, or a >20-step (<4%) procedure commencing with diethyl L-tartrate.

The most promising racemic synthesis of monomorine I was advanced by Yamaguchi in 1987. This synthesis employed the nucleophilic addition of an alkynyl Grignard to a pyridinium chloride as a key bond forming step (Scheme 16).

The overall yield for this synthesis, based on the Grignard, was 28%. The addition of the Grignard to the pyridinium chloride was not, and likely could not be induced to be, enantioselective. Because the stereochemical outcome of the synthesis was set at this stage, it is doubtful that this approach could be parlayed into an enantioselective synthesis of (+)-monomorine I.

Our interest in I was based primarily on its use to probe the synthetic utility and functional group compatibility of the catalytic CpTiCl₃, mediated annulation
Scheme 15

51% $R_1 = R_2 = H$ (1)
21% $R_1 = OH, R_2 = H$
8% $R_1 = H, R_2 = OH$
of alkynylamines. A secondary goal was to facilitate a future enantioselective synthesis of 1 by developing a racemic synthesis that either 1) employed, at an early stage in the synthesis, an intermediate that could be derived in an enantiopure form from a readily available ("chiral pool") source, or 2) proceeded via an intermediate that was
stereogenic and, possibly, amenable to an asymmetric transformation (e.g., reduction, alkylation).

![Chemical structures]

Scheme 17

Retrosynthetic analysis of 1 revealed an intramolecular reductive amination that had been exploited previously by Stevens. We envisioned intermediate 37 to arise via a CpTiCl₃ mediated cycloaddition followed by selective reduction of the anticipated \( \Lambda^\prime \)-pyrroline 38. The precyclic alkynylamine 39 required as the key intermediate could likely be prepared via alkylation of an \( \delta \)-amino anion.
equivalent with an appropriate propargylic halide (Scheme 17). The successful application of this general strategy to the total synthesis of monomorine I is described below.

\[
\begin{align*}
\text{N-OH} & \xrightarrow{\text{a. THP}} \text{H}_2\text{N-O (40)} \xrightarrow{\text{b. H}_2\text{NNH}_2} \text{N-OTHP} \\
\text{2-hexanone} & \xrightarrow{\text{C}_6\text{H}_6} \text{N-OTHP} \\
\end{align*}
\]

Eq. 28

Hydroxylamine 40 was prepared using a modification of the literature procedure\(^5\). Condensation of 40 with 2-hexanone under Dean-Stark conditions gave oximes 41 in excellent yield (Eq. 28). THP-oximes of this type were known to react with LDA under equilibrating conditions to give anions corresponding to deprotonation of the methyl group selectively\(^6\). This method was applicable to oximes 41 as shown by the deprotonation-quenching experiment depicted in Eq. 29. Although lithiated oximes similar to 42 had previously been alkylated with acetone\(^6\), we needed to extend the field of alkylating agents to include halides in order to elaborate the carbon backbone of alkynylamine 39.
The halide required as the alkylating agent for lithiated oxime 42 was prepared as follows. 2-(2-bromoethyl)-2-methyl-1,3-dioxolane (43)\textsuperscript{61,62} was converted to the terminal alkyne 44 by displacement with lithium acetylide\textsuperscript{63,64}. Lithiation of alkyne 44 with n-BuLi followed by treatment with paraformaldehyde afforded the alcohol 45 (Scheme 18)\textsuperscript{65}. The crude alcohol 45 was mesylated\textsuperscript{66} using standard conditions, and the product was purified by recrystallization from Et\textsubscript{2}O to give the mesylate 46 as a white solid. Iodide mediated displacement\textsuperscript{67} of 46 gave the requisite propargylic iodide 47 (Scheme 19).

With the iodide 47 and the oximes 41 in hand, we were in a position to attempt the alkylation experiment. We were pleased to find that treatment of the oximes 41 first with LDA, and then with the iodide 47, gave oxime 48 in good
yield. Oxime 48 was converted directly to the key precyclic alkynylamine 39 by reduction with LiAlH₄ (Scheme 20).

Alkynylamine 39 was smoothly converted to the Δ¹-pyrroline 38 in 93% yield using the catalytic CpTiCl₃.
cycloaddition protocol described earlier. To this end, 39 was added to a solution of CpTiCl$_3$ and NEt$_3$ in THF at 25 °C. After the usual workup, 38 was recovered as the sole reaction product. Selective reduction of 38 to the cis-pyrrolidine 37 was accomplished with DiBAL-H (Scheme 20).

The synthesis was then completed using the general procedure of Stevens$^{56}$. Accordingly, 37 was treated with 5 % HCl followed by a basic workup. The unstable enamine 49 was immediately reduced with NaBH$_3$CN to furnish (±)-monomorine I in 72 % chromatographed$^{70}$ yield (Eq. 30). The spectroscopic characteristics of synthetic (±)-1 as prepared above were identical in all respects with those reported$^{10}$ for other synthetic samples of the alkaloid. The overall synthesis is illustrated in Scheme 21.

Some key points of merit for this synthesis are the high yield (53 % from the point of convergence), the functional group compatibility of the catalytic cyclization,
Scheme 21
and the novel use of oximes 41 as an $\delta$-amino anion equivalent. Because it was beyond the scope of this thesis, we have not attempted to utilize this general approach to indolizidines in the asymmetric synthesis of these alkaloids. However, it may be possible to apply the known methods$^{71-73}$ for the asymmetric reductions of oximes to oxime 48. If successful, this would generate (+)-39, leading eventually to (+)-monomorine (1) (Eq. 31).

The Enantioselective Total Synthesis of (+)-Preussin (2).

The synthetic utility of titanium imido-alkyne cycloaddition reactions was further demonstrated in a short, highly convergent and enantioselective synthesis of (+)-preussin (2) (Figure 6).

Preussin, first described by Schwartz in 1988, has been shown to be a broad spectrum antifungal agent possessing activity against both fungi and yeast$^{24}$. The relative and absolute stereochemistry of 2 were assigned in 1989$^{24}$, and
it has since been the subject of one synthesis\textsuperscript{75}. This interesting approach to \((+)-\)preussin employed D-glucose as the starting material (Scheme 22).

In contrast to this previous synthesis, we envisioned an approach that exploited the L-phenylalanine backbone inherent in 2. Our initial retrosynthetic analysis of 2 implicated \(\Delta^1\)-pyrroline 50 as a likely target. One-pot cis-reduction, N-methylation and hydrogenolysis of the benzyl protecting group would be expected to yield 2. The \(\Delta^1\)-pyrroline 50 was anticipated to arise via a \(\text{CpTiCl}_3\) mediated cycloaddition of the alkynylamine 51.

As alkynylamine 51 was a protected threo aminoalcohol, it seemed likely that it could be prepared by chelation-controlled addition of an organometallic to a phenylalaninalinal equivalent (Scheme 23). The application of this general strategy to the preparation of alkynylamine 51 is described below.

In recent publications\textsuperscript{76,77}, Polt has described the use of diphenylmethyldiene protected aminoesters as equivalents
D-glucose

1. NaN₃
2. anh. HCl/CH₃OH
3. Tf₂O

H₂/Pd

1. CICO₂CH₃
2. HCO₂H

H₂/Pd

n-C₁₇H₆P⁺Ph₃I⁻
n-BuLi

1. H₂/Pd
2. LiAlH₄

Scheme 22
for threeo aminoalcohols (Eq. 32). Although this work employed either aryl magnesium halides or vinyl lithums as the organometallic, it seemed likely that allenyl Grignards could also function in this capacity. For this purpose, the propargylic bromide 53 was prepared and converted to the allenyl Grignard 54 (Scheme 24).

Scheme 23

Eq. 32
The protected aminoester 55 required in this sequence was prepared according to Eq. 33. Much to our dismay, treatment of 55 with DiBAL-H/TriBAL, followed by three equivalents of the allenyl Grignard 54, did not lead to the expected alcohol. The product mixture was comprised of a mixture of ketones, most likely 56 and 57 based on their $^1$H and $^{13}$C NMR spectra. Interestingly, the same product mixture was obtained when first two equivalents of PhMgBr
and then one equivalent of the allenyl Grignard 54 were employed (Eq. 34).

\[
\begin{align*}
\text{Ph} & \quad \text{Ph} \\
\text{Ph} & \quad \text{N} \quad \text{Ph} & \quad \text{CO}_2\text{Me} \\
\text{a,b or} & \quad \text{a,c,d} \\
\rightarrow & \\
\text{Ph}_2\text{CN} & \quad \text{Ph} \\
\text{Ph}_2\text{CN} & \quad \text{Ph} \\
\text{C} & \quad \text{C} \\
\text{n-C}_8\text{H}_{17} & \\
\text{56} & \\
\text{57}
\end{align*}
\]

a. DIBAL-H/TriBAL (1 eq) b. 54 (3 eq)
c. PhMgBr (2 eq) d. 54 (1 eq)

Eq. 34

This obstacle was removed by substitution of the parent allenyl Grignard 58 for 54. Accordingly, we were able to obtain iminoalcohols 59 and 60 (Eq. 35). Chromatographic separation of the diastereomeric mixture gave 59 and 60 in a 3.2:1 ratio and 74 % combined yield.

\[
\begin{align*}
\text{Ph} & \quad \text{Ph} \\
\text{Ph} & \quad \text{N} \quad \text{Ph} & \quad \text{CO}_2\text{Me} \\
\text{a,b} & \\
\rightarrow & \\
\text{Ph}_2\text{CN} & \quad \text{Ph} \\
\text{H} & \quad \text{C} \\
\text{OH} & \\
\text{55} & \\
\text{59} & \\
\text{56} & \\
\text{60}
\end{align*}
\]

a. DIBAL-H/TriBAL (1 eq)
b. \text{H}_2\text{C}:\text{C}:\text{C}(\text{H})\text{MgBr} (58) (3 eq)

Eq. 35
Support for our initially intuitive assignment of the diastereomers was derived by hydrolysis of 59 and conversion of the resulting amine to the oxazolidinone 61⁶⁰ (Eq. 36). The vicinal coupling constant of 6.6 Hz for the -OCH-HCN- resonances was consistent with that reported for the similar oxazolidinone 62 (7.6 Hz)⁷⁷.

Additional support for this assignment was garnered from the observation that gelatinous 59 existed in equilibrium with its oxazolidine tautomer (Eq. 37), whereas crystalline 60 exhibited no tautomeric equilibrium as observed by ¹H or ¹³C NMR. This observation was consistent with the nonbonding interaction expected upon tautomerization of 60 (Eq. 38).

Iminoalcohol 59 was selectively O-alkylated to give 63 by deprotonation with KH followed by treatment with benzyl bromide⁶¹. The efficacy of C-lithiation was demonstrated
using CH$_3$SCN to yield 64 before n-octyl iodide was employed. Hydrolysis of the diphenylmethylidene protecting group of 65 afforded the desired alkynylamine 51 (Scheme 25).

Much to our dismay, alkynylamine 51 was not amenable to CpTiCl$_3$ mediated cyclization. Even the forcing conditions implemented to effect tetrahydropyridine formation (80 °C, C$_6$H$_6$) failed with 51. A likely cause of this failure was thought to be the unfavorable eclipsing interactions that would develop with syn coplaner approach$^{82}$ of the alkynyl moiety and the imido linkage. However, attempted cyclization of 51's (2S,3R) diastereomer, 66, in which the
developing eclipsing interactions during cyclization would be greatly diminished, also failed (Figure 7).

Although not conclusive, this result suggested that an unfavorable transition state was not the causative agent of annulation failure. In fact, it was determined by \(^1\)H NMR of an equimolar solution of 51 and CpTiCl\(_3\), that the elimination
of the second HCl equivalent did not occur. Thus, a reactive imido complex 67 was not being generated (Scheme 26).

In anticipation of a more facile elimination of methane from a methyl amido complex, refluxing solutions of CpTi(CH$_3$)$_2$Cl in THF, DME and benzene were treated with
alkynylamine 51. The reaction conducted in THF afforded only starting material, whereas both the reaction in DME and that in benzene yielded the pyrrole 68. Although it was encouraging that cyclization had occurred, we had lost the two key stereocenters via elimination of benzyl alcohol. We sought to circumvent this elimination by treating the putative metallocycle 69 with methyl chloroformate. In this case we recovered the N-carbomethoxy pyrrole 70 (Scheme 27).
Rather than attempt to elucidate a specialized set of conditions that would allow cyclization of 51 to 50 with retention of the two stereocenters, we sought a more general solution. We had noted earlier that terminal alkynes were markedly more reactive toward imido complexes. We planned to combine this reactivity difference with a nucleophilic addition of the metallocycle\textsuperscript{30} to generate a stabilized vinylogous amide or conjugated $\Delta^1$-pyrroline (Scheme 28).

![Scheme 28]

The terminal alkynylamine 71 was readily available via N-deprotection of the Schiff base 63 we had prepared previously (Eq. 39). This substrate was found to undergo
facile cycloaddition when added to CpTi(CH₃)₂Cl at 0 °C, followed by warming to 25 °C (Scheme 29).

Although Jensen had noted that acyl chlorides reacted with the Ti-N bond of azatitanetines, we had hoped that the
relatively unhindered Ti–C bond of azatitanetine 72 would allow for reaction at that site in preference to the Ti–N bond. Despite this, ketoamide 73 was obtained exclusively in accord with Jensen's observations.

The reaction of n-octanal with 72, to the extent that it did occur, did not yield an isolable, stabilized product. Fortuitously, Jensen had determined that acyl nitriles reacted exclusively with the Ti–C bond of azatitanetines. Accordingly, azatitanetine 72 was treated with n-octanoylnitrile (74). Formation of vinylogous amide 75 would have been in accord with Jensen's findings. Interestingly, the unhindered azatitanetine 72 gave the unsaturated nitrile 76 as the primary product (Scheme 30).

While nitrile 76 was unstable in pure form at 25 °C, it was stable in solution at 25 °C or neat at -20 °C. This stability, and the lack of a suitable alternative, motivated us to pursue the conversion of 76 to (+)-preussin. This was accomplished in a straightforward manner as described below. Treatment of the nitrile 76 with CH₃OTF, followed by NaBH₃CN afforded the N-methylated pyrrolidine 77. Conjugate reduction of 77 was accomplished with Mg/CH₂OH to afford the diastereomeric nitriles 78. Reductive decyanation and cleavage of the benzyl protecting group were then effected with K/HMPA in Et₂O/C₆H₆. It should be noted that the literature procedure does not employ toluene as a cosolvent, in which case reduction of aromatic rings was also observed.
The utilization of toluene as cosolvent eliminates this limitation. Also in accord with literature precedent, this procedure gave rise to some reductive elimination products. However, simple exposure of the crude reaction mixture to Pd-C/H₂ reduced these products to 2 (Scheme 31).
The spectroscopic properties of synthetic (+)-preussin 2 were in excellent agreement with those of authentic\textsuperscript{24} and synthetic\textsuperscript{75} preussin. The overall synthesis of (+)-preussin is presented in Scheme 32. The short length, high convergence and enantioselectivity of the synthesis are particularly noteworthy. Additionally, as can be seen from Scheme 32, this approach should be quite amenable to the preparation of analogs via substitution of alternative acyl nitriles or amino esters for those we employed in the synthesis of (+)-preussin (2).
Scheme 32
CONCLUSION

New methods for effecting formation of $\Lambda^3$-pyrrolines or tetrahydropyridines that rely on catalytic or stoichiometric $[2 + 2]$ cycloadditions of transient monocyclopentadienyl titanium imido complexes onto tethered alkynes have been developed. The CpTiCl₃ required for either method is a stable, readily accessible complex. More importantly, the azatitanetines generated via treatment of CpTi(CH₃)₂Cl with 1,3-disposed alkynylamines have been shown to engage in subsequent bond forming reactions. This combination of stoichiometric annulation and subsequent nucleophilic addition of the metallocycle has already shown itself to be a valuable synthetic tool by its application in the total synthesis of (+)-preussin. This stoichiometric cycloaddition methodology is a good complement to the intermolecular cycloadditions of zirconocene imido complexes.

Additionally, the facile CpTiCl₃ mediated catalytic annulation of alkynylamines has been employed in a concise total synthesis of (+)-monomorine. The catalytic formation of $\Lambda^3$-pyrrolines and tetrahydropyridines by CpTiCl₃ complements the amidolanthanide catalized formation of pyrrolidines and piperidines from alkenylamines, as well as the [(ArO)₂Ti=NR] mediated preparation of arylimines from alkynes.
EXPERIMENTAL

Physical Data: $^1$H NMR and $^{13}$C NMR were measured at 300 and 75 MHz respectively, with a Bruker AL-300 spectrometer. $^1$H NMR chemical shifts are reported as $\delta$ values in ppm relative to the residual protons of CDCl$_3$ (7.24) or C$_6$H$_6$ (7.15). $^{13}$C chemical shifts are reported in ppm relative to CDCl$_3$ (677.0) or C$_6$D$_6$ (6128). $^1$H NMR coupling constants are reported in Hz and refer to real or apparent multiplicities which are indicated as follows: s (singlet), d (doublet), t (triplet, q (quartet), p (pentet), sex (sextet), br (broad), m (multiplet) and app (apparent). Combinations of these descriptors were also used when appropriate. For example, a signal which appears as a triplet (t) but is truly an unresolved doublet of doublets (dd) would be reported as an apparent triplet (app t).

Infrared spectra were recorded with either a Perkin Elmer 1800 FTIR or 237B grating IR. High resolution mass spectra were measured on a VG Analytical 7070E spectrometer by Dr. L.J. Sears. Melting points were determined with a Fisher-Johns melting point apparatus and are uncorrected. Optical rotations were measured with a Perkins-Elmer 241 MC Polarimeter. Elemental analysis was performed by Desert Analytics, Tucson, AZ.
Chromatography: Gas chromatography was performed on a Varian Model 3700 Gas Chromatograph equipped with a flame ionization detector, a Hewlett-Packard 3390A Reporting Integrator and a 15m x 0.53mm ID column with a DB5 (or equivalent) bonded phase.

Thin layer chromatography was performed on plates supplied by Alltech Associates (K42-G). Visualization of plates was effected by one or more of the following: a) UV illumination; b) exposure to I₂ vapor; c) KMnO₄ oxidation; or d) anisaldehyde derivitization. All column chromatography was conducted on E. Merck silica gel 60. Solvent systems used for elution are reported in %volume/volume.

Materials: A listing of the common solvents and reagents purified by distillation is shown in Table 3. Atmospheric pressure distillations were conducted in an inert atmosphere of argon or nitrogen.

Commercially available 10M n-BuLi was diluted with heptane and then titrated against a standard solution of 2-butanol in xylene using 1,10-phenanthroline as indicator. Grignard reagents were titrated in the same manner as n-BuLi. These reagents were also checked periodically for total base content. This was accomplished by adding an aliquat to ice and titration of the resulting mixture with a standard solution of potassium biphthalate using phenolphthalein as the indicator.
Table 3. Solvent and Reagent Purification.

<table>
<thead>
<tr>
<th>Solvent/Reagent</th>
<th>Purification Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Et₂O⁹</td>
<td>Na-Ph₂CO</td>
</tr>
<tr>
<td>THF</td>
<td>K</td>
</tr>
<tr>
<td>CH₃CN</td>
<td>CaH₂</td>
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<tr>
<td>toluene</td>
<td>CaH₂</td>
</tr>
<tr>
<td>DME</td>
<td>K</td>
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<tr>
<td>CH₂Cl₂</td>
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<tr>
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<td>CaH₂</td>
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<tr>
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<td>Mg(OCH₃)₂</td>
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<td>xylene b</td>
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<td>pentane</td>
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<tr>
<td>hexane</td>
<td>K</td>
</tr>
<tr>
<td>amines*</td>
<td>CaH₂</td>
</tr>
</tbody>
</table>

a. Et₂O used in the preparation of CH₃Li was distilled from Na-K⁹.  b. reduced pressure.  c. vacuum pressure.  d. 1:3 Na:K.  e. Et₂NH, i-Pr₂NEt, i-Pr₂NH and PhN(CH₃)₂.

Unless indicated otherwise, reactions were performed in oven or flame dried vessels under an atmosphere of nitrogen or argon. Temperatures reported are bath temperatures unless noted otherwise. Concentrations were performed under reduced pressure with a Büchi rotary evaporator and "drying" of an organic solution was accomplished with anhydrous Na₂SO₄.

2,4-Cyclopentadien-1-yltrimethysilane. Three moles of freshly cracked cyclopentadiene were generated by heating a mixture of the dimer and silicone oil at 230-245 °C under an air cooled spiral condensor. The monomer (B.P. 36 °C) was
collected in a dry ice cooled receiver. The cyclopentadiene was then added slowly to NaH (72 g, 3 moles) suspended in THF (3L) at 0 °C. After stirring 1 h at 0 °C, the solution of sodium cyclopentadienide was added via cannula to a -78 °C solution of TMSCl (326 g, 3 moles) in THF (1L) over 40 min. After stirring an additional 20 min, H₂O (500 mL) was added. The resultant layers separated after 20-30 min, allowing the organics to be decanted. The organic layer was concentrated and the crude product distilled under reduced pressure to yield 187 g (45 %) of the title compound as a colorless oil. Dimerization can be minimized by storage at -20 °C35.

Cyclopentadienyltitanium trichloride. To a solution of TiCl₄ (12.5 g, 66 mmol) in toluene (30 mL) cooled to -78 °C was added dropwise over 20 min a solution of TMSCp (9.17 g, 66 mmol) in toluene (10 mL). Yellow solids precipitate during the addition of the TMSCp. After stirring an additional 45 min at -78 °C, the mixture was transferred quickly via cannula to a Schlenk filter. The solids were washed with cold toluene (10 mL), cold 1:1 toluene-heptane (10 mL) and cold 1:2 toluene-heptane (15 mL). Residual solvent was removed under high vacuum to yield bright yellow crystals (8.7 g, 60 %)33.

Mixture of 1-chloro-5-phenylpent-4-yne and 1-bromo-5-phenylpent-4-yne(15)86 n-Butyllithium (3 M in heptane,
13.33 mL, 40.0 mmol) was added over 5 min to a brine-ice cooled solution of phenylacetylene (4.09 g, 40.0 mmol) in THF (60 mL) and HMPA (6.5 mL). After 15 min, 1-bromo-3-chloropropane (6.30 g, 40 mmol) was added rapidly via syringe. After 2 h at 25 °C the reaction mixture was poured into sat. aqueous NH₄Cl (50 mL) and Et₂O (50 mL). The layers were separated, the organic phase was washed twice with sat. aqueous NH₄Cl (50 mL), and subsequently was concentrated to a yellow oil. Distillation of the crude product (75-85 °C and 0.025 torr) affords the product mixture as a colorless oil which was characterized as the iodide 16.

1-Iodo-5-phenylpent-4-yne (16). The halide mixture 15 (obtained from 100 mmol of phenylacetylene) was added to a solution of NaI (18.7 g, 125 mmol) in CH₃CN (250 mL). The resulting mixture was maintained at reflux overnight. The reaction mixture was then partitioned between H₂O (500 mL) and hexane (100 mL). The organic phase was separated and combined with three hexane extractions (100 mL) of the aqueous phase for drying. Filtration and concentration affords 16 (16.74 g, 62 % from phenylacetylene) as a colorless oil. ¹H NMR (300 MHz, CDCl₃) δ 7.45-7.2 (m, 5H, Ph); 3.35 (t, J = 6.7 Hz, 2H, CH₂I); 2.55 (t, J = 6.7 Hz, 2H, C:H₂CH₂); 2.08 (app p, J = 6.7 Hz 2H, CH₂); ¹³C NMR (75 MHz, CDCl₃) δ 131.30, 127.98, 127.50, 123.33, 87.66,
Mixture of 1-Chloronon-4-yne and 1-bromonon-4-yne(21). This mixture was prepared in a fashion analogous to that used to prepare 15, but employing 1-hexyne (3.29 g, 40 mmol) in place of phenylacetylene. After distillation (65-75 °C and 0.025 torr) the product mixture was obtained as a colorless oil that was characterized upon conversion to the iodide.

1-Iodonon-4-yne. The halide mixture 21 (obtained from 100 mmol of 1-hexyne) was added to CH$_3$CN (250 mL) containing NaI (18.7 g, 125 mmol). After refluxing overnight, the reaction was worked up as for 16 to afford the title compound (15.0 g, 60 % from 1-hexyne) as a colorless oil:

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 3.28 (t, J = 6.9 Hz, 2H, CH$_2$I); 2.27 (tt, J = 6.6 and 2.4 Hz, 2H, C:CCCH$_2$); 2.12 (tt, J = 6.9 and 2.4 Hz, 2H, C:CCCH$_2$); 1.94 (app p, J = 6.8 Hz, 2H, ICH$_2$CH$_2$); 1.55-1.25 (m, 4H, 2CH$_2$); 0.88 (t, J = 7.1 Hz, 3H, CH$_3$) $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 81.46, 77.61, 32.56, 31.06, 21.86, 19.77, 18.34, 13.53, 5.46; IR (film) 2950-2850, 1470, 1410, 1340, 1255, 1210, 1160 cm$^{-1}$.

7-Iodo-1-phenylhept-1-yne(35). A solution of phenylacetylene (8.78 mL, 80 mmol) in THF (120 mL) and HMPA (13.0 mL) at 0 °C was treated with n-BuLi (3.0 M in heptane, 26.7 mL, 80 mmol). After 15 min, Cl(CH$_3$)$_2$Cl (10.2 mL,
80 mmol) was added. The resultant mixture was allowed to warm to 25 °C and maintained overnight. Workup as for 15 and vacuum distillation provides 6.9 g of a colorless oil. Conversion to the iodide was accomplished as for 16, giving after vacuum distillation 9.5 g (40 % from phenylacetylene) of 35 as a colorless oil: 'H NMR (300 MHz, CDCl₃) δ 7.45 - 7.2 (m, 5H, Ph), 3.20 (t, J = 6.8 Hz, 2H, CH₂I), 2.41 (t, J = 6.6 Hz, 2H, C=CH₂), 1.87 (app pent, J = 7.1 Hz, 2H, CH₂), 1.59 (m, 4H, 2CH₂); ¹³C NMR (75 MHz, CDCl₃) δ 131.48, 128.13, 127.50, 123.86, 89.69, 80.91, 32.98, 29.69, 27.57, 19.20, 6.65; IR (film) 2920, 2850, 2215, 1590, 1480, 1430, 1200, 755, 690 cm⁻¹.

2-(2-Bromoethyl)-2-methyl-1,3-dioxolane(43). HBr (108 g, 1.34 mole) was dissolved in ethylene glycol (161 g, 2.6 mole) cooled in an ice bath. Freshly distilled methyl vinyl ketone (63 g, 0.9 mole) was then added slowly so that the internal temperature did not exceed 10 °C. The mixture was stirred 1 h at 25 °C and then extracted with pentane (3 x 100 mL). The combined extractions were washed with sat. aqueous NaHCO₃ (2 x 100 mL), dried and concentrated. Short path distillation under aspirator pressure afforded 43 (108 g, 65 %) as a colorless oil⁶¹,⁶².

2,2-Ethynenedioxydec-5-yne(24). n-BuLi (10.0 M, 10 mL, 100 mmol) was added dropwise to a -72 °C solution of 1-hexyne (11.5 mL, 100 mmol) and HMPA (15 mL) in THF (150 mL).
The resultant mixture was stirred 1 h at 0 °C and then recooled to -72 °C. 2-(2-bromoethyl)-2-methyl-1,3-dioxolane(24) (17.55 g, 90 mmol) in THF (50 mL) was added, followed by NaI (0.5 g). The mixture was allowed to slowly warm to 25 °C and, after 16 h, was extracted with sat. aqueous NH₄Cl (1 x 150 mL, 2 x 75 mL) and brine (1 x 100 mL). The organics were dried and concentrated. Distillation (60 °C and 0.025 torr) afforded 14.62 g (83 %) of 24 as a colorless oil. ¹H NMR (300 MHz, CDCl₃) δ 4.0-3.8 (m, 4H, 2CH₂O), 2.10 (tt, J = 6.8 and 2.3 Hz, 2H, C=CCH₂), 2.10 (tt, J = 6.6 and 2.3 Hz, 2H, C=CCH₂), 1.84 (t, J = 6.8 Hz, 2H, CH₂CO₂), 1.5-1.3 (m, 4H, 2CH₂), 1.29 (s, 3H, CH₃), 0.87 (t, J = 6.7 Hz, 3H, CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 109.08, 79.82, 79.56, 64.57, 38.58, 31.08, 23.63, 21.78, 18.29, 13.56, 13.46; IR (film) 2950-2850, 1370, 1210, 1130, 1055, 860 cm⁻¹.

Dec-5-yn-2-one(25). A solution of 24 (14.5 g, 74 mmol) in acetone (400 mL) and H₂O (40 mL) was treated with pyridinium tosylate (12.6 g, 50 mmol)⁸⁸. The mixture was maintained at reflux for 16 h and then concentrated to 100 mL. The concentrate was partitioned between H₂O (250 mL) and hexane (100 mL). The organic layer was separated and combined with two hexane extractions (50 mL) of the aqueous phase. The organics were washed with brine (100 mL), filtered, and concentrated to yield 25 as a colorless oil (10.8 g, 96 %). ¹H NMR (300 MHz, CDCl₃)
Dec-5-yn-2-ylamine (26). A mixture of alkynone 25 (7.6 g, 50 mmol), NH₄OAc (38.5 g, 500 mmol) and NaBH₃CN (2.2 g, 35 mmol) in absolute CH₃OH (150 mL) was stirred 48 h at 25 °C. The mixture was concentrated via rotovap and the resultant slurry diluted with H₂O (200 mL). Concentrated HCl was then added until a pH ~3 was obtained. The aqueous layer was extracted with hexane (2 x 50 mL) which was discarded. The aqueous phase was made basic by addition of NaOH and then saturated with NaCl. Three 1:1 Et₂O-hexane extractions (100 mL ea.) of the aqueous phase were then taken. The combined organics were concentrated. The resultant material was dried as a solution in 1:1 CH₂Cl₂-pentane and reconcentrated. Distillation (vacuum) afforded 5.74 g (75 %) of 26 as a colorless oil: ¹H NMR (300 MHz, CDCl₃) δ 2.99 (app sex, J = 6.3 Hz, 1H, NCH), 2.19 (tt, J = 7.1 and 2.3 Hz, 2H, C:CH₂), 2.11 (tt, J = 6.8 and 2.3 Hz, 2H, C:CH₂), 1.6-1.25 (m, 6H, 3CH₂), 1.09 (br s, 2H, NH₃), 1.04 (d, J = 6.3 Hz, 3H, CH₃), 0.87 (t, J = 7.0 Hz, 3H, CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 80.19, 79.19, 45.81,
38.87, 30.94, 23.57, 21.64, 18.13, 15.63, 13.29; IR (film) 3300, 2950-2850, 1590, 1460, 1370, 825 cm⁻¹.

6-Phenylhex-5-yn-2-ylamine(7). The title compound was prepared in a fashion similar to that used to prepare 26, but employing phenylacetylene in the place of 1-hexyne. Filtration of the crude dioxolane 22 through silica gel yielded 6.05 g (70 %) as a slightly yellow oil exhibiting the following ¹H NMR (300 MHz, CDCl₃): δ 7.45-7.25 (m, 5H, Ph), 3.95 (m, 4H, 2CH₂O), 2.49 (t, 2H, CH₃), 1.98 (t, 2H, CH₂), 1.35 (s, 3H, CH₃). The crude 6-phenylhex-5-yn-2-one obtained via dioxolane exchange was used in the reductive amination. Distillation of the crude alkynylamine (80 °C and 0.01 torr) afforded 3.53 g (51 % based on phenylacetylene) of 7 as a colorless oil: ¹H NMR (300 MHz, CDCl₃) δ 7.34 (m, 2H, Ph), 7.24 (m, 3H, Ph), 3.07 (m, 1H, NCH), 2.45 (t, J = 7.2 Hz, 2H, CH₂C:C), 1.59 (m, 2H, CH₂), 1.15 (br s, 2H, NH₂), 1.09 (d, J = 6.3 Hz, 3H, CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 131.56, 128.14, 127.50, 124.01, 89.76, 80.88, 46.19, 38.79, 23.94, 16.54, IR (film) 3300, 3656, 2962, 2926, 2870, 2234, 1576, 1560, 1490, 1442, 788, 756 cm⁻¹; high resolution mass spectrum calcd. for C₁₃H₁₅N(M⁺) 173.1204. Found 173.1202.

5-Phenylpent-4-yn-1-ylamine(3)⁹⁰. The halide mixture 15 (obtained from 40 mmol of phenylacetylene) was diluted with DMF (50 mL). To this solution was added potassium
phthalimide (9.26 g, 50 mmol), and the reaction mixture was brought to reflux for 10 h\textsuperscript{11}. The DMF was removed under reduced pressure (65 °C) and the resultant solids were triturated with 10 % KOH (2 x 30 mL) to yield pale yellow crystals. These were suspended in 95 % EtOH (50 mL), treated with hydrazine monohydrate (2.43 mL, 50 mmol) and brought to reflux for 4 h. The reaction mixture was then cooled to 0 °C, brought to pH 2 by addition of conc. HCl, and filtered. The solids were washed thoroughly with ethanol and the organic phase was concentrated to a solid mass. The solids were triturated with 1:1 Et\textsubscript{2}O-hexane until white, and then taken into H\textsubscript{2}O (50 mL), cooled to 0 °C and carefully saturated with K\textsubscript{2}CO\textsubscript{3}. The aqueous phase was then extracted with Et\textsubscript{2}O (4 x 30 mL). The combined organics were dried and concentrated. Distillation (67 °C and 0.025 torr) afforded 3 (3.94 g, 62 %) as a colorless oil: \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}) δ 7.35 (m, 2H, Ph), 7.24 (m, 3H, Ph), 2.83 (t, J = 6.8 Hz, 2H, NCH\textsubscript{2}), 2.45 (t, J = 7 Hz, 2H, CH\textsubscript{2}C\textsubscript{3}C), 1.71 (m, 2H, CH\textsubscript{2}CH\textsubscript{2}CH\textsubscript{2}), 1.16 (br s, 2H, NH\textsubscript{2}); \textsuperscript{13}C NMR (75 MHz, CDCl\textsubscript{3}) δ 131.55, 128.17, 127.53, 124.00, 89.61, 80.97, 41.36, 32.60, 16.88; IR (film) 3298, 3056, 2938, 2866, 2228, 1598, 1570, 1560, 1490, 1442, 756, 692 cm\textsuperscript{-1}; high resolution mass spectrum calcd. for C\textsubscript{11}H\textsubscript{13}N(M\textsuperscript{+}) 159.1048. Found 159.1043.

Non-4-yn-1-ylamine(5). This compound was prepared in analogous fashion to 3, but employing 21 (obtained from
40 mmol of 1-hexyne). After distillation, 3.11 g (56 %) of 5 was obtained as a colorless oil: \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 2.74 (t, \(J = 6.8\) Hz, 2H, NCH\(_2\)), 2.16 (m, 2H, CH\(_2\)C:C), 2.09 (m, 2H, CH\(_3\)C:C), 1.56 (m, 2H, NCH\(_2\)CH\(_2\)), 1.45-1.2 (m, 6H, 2CH\(_2\), NH\(_2\)), 0.85 (t, \(J = 6.8\) Hz, 3H, CH\(_3\)); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 80.60, 79.37, 41.29, 32.90, 31.20, 21.87, 18.37, 16.18, 13.49; IR (film) 3342, 2958, 2932, 2872, 2862, 154, 1484, 1468, 1434, 1320 cm\(^{-1}\); high resolution mass spectrum calcd. for C\(_9\)H\(_{17}\)N(M\(^+\)) 139.1361. Found 139.1357.

6-Phenylhex-5-yn-1-ylamine(9). The halide mixture 15 (obtained from 40 mmol of phenylacetylene) was slowly added to a solution of NaCN (2.11 g, 43 mmol) and NaI (0.6 g, 4 mmol) in DMSO (10 mL) at 25 °C. The reaction mixture was allowed to stir overnight at 25 °C and was then poured into a separatory funnel containing ice water (100 mL). The aqueous phase was extracted with hexane (5 x 100 mL) and the combined extractions were dried and concentrated. The nitrile obtained exhibits the following \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 7.45-7.2 (m, 5H, Ph), 2.56 (app pent, 4H, 2CH\(_2\)), 1.95 (m, 2H, CH\(_3\)). The crude nitrile was diluted with Et\(_2\)O (40 mL) and added slowly to a suspension of LiAlH\(_4\) (0.42 g, 11 mmol) in Et\(_2\)O (40 mL) cooled to 0 °C. After 2 h the reaction mixture was carefully quenched via sequential addition of H\(_2\)O (1 mL), 15 % NaOH (1 mL) and H\(_2\)O (2 mL). The organic phase was decanted, combined with two Et\(_2\)O washings of the solids, dried, and concentrated. Distilla-
tion (80-85 °C and 0.005 torr) afforded 5.40 g (78%) of 9 as a colorless oil: $^1$H NMR (300 MHz, CDCl₃) δ 7.36 (m, 2H, Ph), 7.25 (m, 3H, Ph), 2.73 (t, J = 6.5 Hz, 2H, NCH₂), 2.41 (t, J = 6.6 Hz, 2H, CH₂C:C), 1.62 (m, 4H, 2CH₂), 1.04 (s, 2H, NH₂); $^{13}$C NMR (75 MHz, CDCl₃) δ 131.53, 128.14, 127.46, 124.08, 90.00, 80.56, 41.83, 33.14, 26.15, 19.30; IR (film) 3346, 3056, 2936, 2864, 2232, 1560, 1542, 1522, 1490, 756, 692 cm⁻¹; high resolution mass spectrum calcd. for C₁₂H₁₅N(M⁺) 173.1204. Found 173.1207.

Dec-5-yn-1-ylamine(11)⁹². This amine was prepared in analogous fashion to 9, but utilizing the halide mixture 21 (obtained from 40 mmol of 1-hexyne). Distillation (66-72 °C and 0.75 torr) afforded 4.16 g (68%) of 11 as a colorless oil: $^1$H NMR (300 MHz, CDCl₃) δ 2.68 (t, J = 6.6 Hz, 2H, NCH₂), 2.15 (t, J = 6.9 Hz, 2H, CH₂C:C), 2.12 (t, J = 7.2 Hz, 2H, CH₂C:C), 1.5-1.4 (m, 10H, 4CH₂, NH₂), 0.88 (t, J = 7 Hz, 3H, CH₃); $^{13}$C NMR (75 MHz, CDCl₃) δ 79.95, 79.32, 41.40, 32.60, 30.85, 26.09, 21.51, 18.22, 18.00, 13.17; IR (film) 3338, 2958, 2936, 2862, 2158, 1570, 1488, 1466, 1434, 1382, 1328 cm⁻¹; high resolution mass spectrum calcd. for C₁₀H₁₅N(M⁺) 153.1517. Found 153.1516.

Pent-4-yn-1-ylamine(28)⁹³. A solution of 3-bromopropylamine hydrobromide (9.0 g, 41.1 mmol) in DMSO (20 mL) was added over 30 min to a 10 °C suspension of LiC:CH•H₂N(CH₂)₂NH₂ (9.2 g, 100 mmol) in DMSO (50 mL). The
resultant mixture was stirred 12 h at 25 °C and then quenched by cautious addition of ice. The fraction of the hydrolized reaction mixture that distilled under 130 °C was diluted with H₂O (10 mL), which was then made basic by addition of NaOH. The aqueous phase was extracted with Et₂O (3 x 15 mL) and the combined organics were dried and concentrated (rotovap, 0-5 °C). The concentrate was diluted with abs. EtOH (20 mL) and was then added to a suspension of AgNO₃ (7.14 g, 42 mmol) in abs. EtOH (100 mL). The silver acetylide so produced was collected on a frit and was washed with abs. EtOH (3 x 15 mL). The solids were treated with 3 % HCl (3 x 20 mL) while still on the frit. The aqueous filtrate collected was refiltered through celite and then made basic by addition of NaOH. After saturating with NaCl, the aqueous phase was extracted with 1:1 CH₂Cl₂-pentane (4 x 15). Drying and concentration of the combined organics afforded crude product which was subsequently distilled from CaH₂ (122-125 °C). ¹H NMR (300 MHz, CDCl₃) δ 2.79 (t, J = 6.9 Hz, 2H, NCH₂), 2.34 (dt, J = 7.0 and 2.6 Hz, 2H, C:CCH₂), 1.93 (t, J = 2.6 Hz, 1H, C:CH), 1.64 (app pent, J = 7.0 and 6.9 Hz, 2H, CH₂), 1.09 (br s, 2H, NH₂); ¹³C NMR (75 MHz, CDCl₃) δ 83.83, 68.36, 40.92, 32.01, 15.68; IR (film) 3250, 2920, 2840, 2110, 1580, 1420, 1080, 1050, 850, 750 cm⁻¹.

3,4-Dihydro-5-(phenylmethyl)-2H-pyrrole(4). Method A: To CpTiCl₃ (44 mg, 0.2 mmol) in THF (3 mL) was added
i-Pr$_2$NEt (70 μL, 0.4 mmol) followed by dropwise addition of a solution of 3 (159 mg, 1 mmol) in THF (2 mL). After 30 min a few drops of 5 % methanolic NaOH were added, and the reaction mixture was taken to dryness. The solids were triturated with hexane, the organic phases were filtered through powdered K$_2$CO$_3$ and concentrated to afford 149 mg (94 %) of 4 as the sole reaction product. Method B: To CpTiCl$_3$ (219 mg, 1 mmol) in THF (3 mL) at 0 °C was added CH$_3$Li (1.4 M in Et$_2$O, 1.43 mL, 2 mmol). The reaction mixture was warmed to 25 °C over 15 min and 3 (159 mg, 1 mmol) in THF (2 mL) was added dropwise over 5 min. After 1 h, 5 % methanolic NaOH (0.5 mL) was carefully added, and the reaction mixture was taken to dryness. Trituration with hexane, followed by filtration through powdered K$_2$CO$_3$ and concentration afforded 4 in 96 % yield. In cases where filtration through K$_2$CO$_3$ was not sufficient, the product was filtered through a small plug of silica (1:1 Et$_2$O-hexane).

$^1$H NMR (300 MHz, CDCl$_3$) δ 7.25 (m, 5H, Ph), 3.83 (m, 2H, NCH$_2$), 3.68 (s, 2H, PhCH$_2$), 2.39 (m, 2H, N=CCH$_2$), 1.83 (m, 2H, CH$_2$); $^{13}$C NMR (75 MHz, CDCl$_3$) δ 176.56, 137.12, 129.02, 128.57, 126.57, 61.05, 40.75, 36.53, 22.29; IR (film) 3100-2850, 1604, 1496 cm$^{-1}$; high resolution mass spectrum calcd. for C$_{11}$H$_{13}$N(M$^+$) 159.1048. Found 159.1046.

2-(Phenylmethyl)-3,4,5,6-tetrahydropyridine (10)$^{24}$. Method C: To a solution of CpTiCl$_3$ (44 mg, 0.2 mmol) and PhN(CH$_3$)$_2$ (51 μL, 0.4 mmol) in C$_6$H$_6$ (3 mL) at 80 °C was added
a solution of 9 (173 mg, 1 mmol) in C6H6 (2 mL). After 2 h at 80 °C, the reaction mixture was cooled to 25 °C and quenched by the addition of sat. aqueous K2CO3 (0.5 mL). The solvent was removed and the solids were tritutated with hexane while under a blanket of argon. The organic phase was filtered through powdered K2CO3 and then concentrated. The crude oil was subjected to high vacuum evaporation (<0.05 torr) to remove PhN(CH3)2 and yielded 10 (152 mg, 88 %) as an unstable oil. **Method E:** To a solution of CpTiCl3 (11 mg, 0.05 mmol) in C6H6 (1.5 mL) at 25 °C was added 9 (87 mg, 0.5 mmol). The mixture was heated to 80 °C for 3 h and then cooled to 25 °C and worked up as in Method C to give 10 (79 mg, 91 %). 1H NMR (300 MHz, CDCl3) δ 7.18 (m, 5H, Ph), 3.53 (m, 2H, NCH2), 3.40 (s, 2H, PhCH2), 1.97 (t, J = 7 Hz, 2H, N=CCH2), 1.50 (m, 4H, 2CH2); 13C NMR (75 MHz, CDCl3) δ 169.65, 137.91, 128.99, 128.43, 126.38, 49.45, 48.28, 28.20, 21.79, 19.54; IR (film) 3100-2850, 1673 cm⁻¹; high resolution mass spectrum calcd. for C12H15N(M⁺) 173.1204. Found 173.1200.

3,4-Dihydro-5-pentyl-2H-pyrrole(6). Submission of 5 to Method A gave 6 in 94 % yield. **Method B** also effected the desired transformation (94 %) to give 6 as a colorless oil: 1H NMR (300 MHz, CDCl3) δ 3.63 (m, 2H, NCH2), 2.29 (m, J = 7.9 and 1.5 Hz, 2H, N=CCH2), 2.16 (t, J = 7.5 Hz, 2H, N=CCH2), 1.68 (m, 2H, NCH2CH2), 1.44 (m, 2H, CH2), 1.16 (m, 4H, 2CH2), 0.73 (t, J = 6.8 Hz, 3H, CH3); 13C NMR (75 MHz,
CDCl_3) δ 177.87, 60.53, 36.85, 33.48, 31.45, 25.82, 22.32, 22.14, 13.58; IR (film) 2958-2856, 1478 cm⁻¹; high resolution mass spectrum calcd. for C₉H₁₇N(M⁺) 139.1361. Found 139.1358.

3,4-Dihydro-2-methyl-5-(phenylmethyl)-2H-pyrrole(8).
Submission of 7 to Method B afforded 8 (92%) as a clear oil: ¹H NMR (300 MHz, CDCl₃) δ 7.27 (m, 5H, Ph), 4.04 (m, 1H, NCH), 3.65 (s, 2H, PhCH₂), 2.34 (m, 2H, N=CCH₂), 2.00 (m, 1H), 1.4-1.25 (m, 1H), 1.22 (d, J = 6.7 Hz, 3H, CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 175.02, 137.06, 128.88, 128.50, 126.48, 67.79, 40.75, 36.56, 30.71, 21.93; IR (film) 3100-2855, 1493 cm⁻¹; high resolution mass spectrum calcd. for C₁₂H₁₅N(M⁺) 173.1204. Found 173.1207.

3,4-Dihydro-2-methyl-5-pentyl-2H-pyrrole(27).
Method D: A solution of CpTiCl₃ (11 mg, 0.05 mmol) in THF (2 mL) was treated with 26 (76 mg, 0.5 mmol). The mixture was stirred 2 h at 25 °C before working up as in Method A to give 27 (72 mg, 94%). ¹H NMR (300 MHz, CDCl₃) δ 3.96 (m, 1H, NCH), 2.55-2.41 (m, 1H), 2.41-2.29 (m, 1H), 2.25 (app dt, J = 7.7 and 0.8 Hz, 2H), 2.08-1.94 (m, 1H), 1.6-1.45 (m, 2H), 1.38-1.22 (m, 5H), 1.18 (d, J = 6.9 Hz, 3H, CH₃), 2.51 (t, J = 7.0 Hz, 3H, CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 176.47, 67.21, 36.88, 33.47, 31.33, 30.30, 25.85, 22.03, 21.69, 13.54; IR (film) 2950, 2920, 2860, 1620, 1425, 1410, 1360 cm⁻¹.
2-Pentyl-3,4,5,6-tetrahydropyridine(12). Submission of 11 to Method C or E afforded 12 (89 and 92 %, respectively) as a colorless oil: "H NMR (300 MHz, CDCl₃) δ 3.52 (m, 2H, NCH₂), 2.08 (m, 4H, N=C(CH₂)₂), 1.63 (m, 2H, CH₂), 1.51 (m, 4H, 2CH₂), 1.28 (m, 4H, 2CH₂), 0.86 (t, J = 7 Hz, 3H, CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 171.07, 49.20, 41.13, 31.75, 29.01, 26.19, 22.50, 21.98, 19.68, 13.94; IR (film) 2958, 2934, 2860, 1660 cm⁻¹; high resolution mass spectrum calcd. for C₁₀H₁₉N(M⁺) 153.1517. Found 153.1519.

3,4-Dihydro-5-methyl-2H-pyrrole(29)²⁵,²⁶. A solution of CpTiCl₃ (6 mg, 0.027 mmol) in C₆D₆ (0.4 mL) was treated with 28 (22 mg, 0.26 mmol). There ensued a mild exotherm accompanied by formation of a dark red color. A "H NMR spectrum collected within 10 min of amine addition shows only resonances attributed to A²-pyrroline 29 and none of the signals exhibited by amine 28. This sample, though frozen, showed significant (5-10 %) degradation after 12 h. "H NMR (300 MHz, C₆D₆) δ 3.98 (m, 2H, NCH₂), 2.17 (app t, J = 8.1 Hz, N:CCCH₃) 2.03 (s, 3H, CH₃), 1.69 (app pent, 2H, CH₂); ¹³C NMR (75 MHz, C₆D₆) δ 172.22, 61.26, 38.25, 22.93, 19.12.

Reaction of 13 with Isobutyronitrile. To 13 (0.5 mmol, prepared by Method B) was added isobutyronitrile (114 µL, 1.25 mmol). The septum was replaced with a screw cap and the reaction mixture was heated to 65 °C for 19 h. The reaction mixture was then heated with 20 % HCl (5 mL) for an
additional 2 h. After saturating the resultant solution with K₂CO₃, the product was extracted with 1:1 Et₂O-hexane. Filtration of the organic phases through silica gel and subsequent concentration gave the vinlylogous amide 14 (77 mg, 67%). An alternative workup procedure yields 19. In this case the reaction mixture was added to 5% HCl and the aqueous phase quickly extracted twice with Et₂O (which was found to contain small amounts of 14). The aqueous phase was then saturated with K₂CO₃ and extracted with hexane. Filtration of the organic phases through K₂CO₃ followed by concentration and distillation afforded 19 (72 mg, 63%) as a colorless oil: ¹H NMR (300 MHz, CDCl₃) δ 7.3-7.1 (m, 5H, Ph), 3.96 (t, J = 7.5 Hz, 2H, CH₂), 2.42 (app p, J = 6.9 Hz, H, CH), 2.17 (t, J = 8 Hz, 2H, CH₃), 1.65 (app p, J = 7.5 and 8 Hz, 2H, CH₂), 1.01 (d, J = 6.9 Hz, 6H, 2CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 176.39, 158.64, 141.44, 131.81, 128.01, 126.07, 102.06, 60.26, 38.39, 30.28, 22.01, 20.89; IR (film) 3451, 3054, 2964, 2853, 1614, 1514, 1488, 1336, 1298, 748, 704 cm⁻¹.

(E, E)-2,2-Dimethyl-4,6-octadiene-1-ylamine(32). ¹H NMR (300 MHz, CDCl₃) δ 5.99 (m, 2H, 2C:CH), 5.54 (m, 2H, 2C:CH), 2.41 (s, 2H, NCH₂), 1.93 (d, J = 7.6 Hz, 2H, C:CH₂CH₂), 1.70 (d, J = 6.6 Hz, 3H, C:CH₂), 0.95 (br s, 2H, NH₂), 0.81 (s, 6H, 2CH₃); ¹³C NMR (57 MHz, CDCl₃) δ 132.73, 131.64, 128.11, 127.07, 52.77, 42.76, 35.46, 24.68, 17.91; IR (film) 3350, 3000, 2920-2820, 1470, 1355, 985 cm⁻¹.
(Z)-5-Phenyl-4-penten-1-ylamine(30). A solution of Ni(OAc)$_2$$\cdot$4H$_2$O (187 mg, 0.75 mmol) in abs. EtOH (6 mL) under an atmosphere of H$_2$ was treated with ethanolic NaBH$_4$ (1 M, 0.75 mL, 0.75 mmol). To the resulting black solution was added H$_2$N(CH$_2$)$_2$NH$_2$ (99 µL, 1.25 mmol) and a solution of 3 (0.64 g, 4 mmol) in EtOH (1 mL). After stirring vigorously for 12 h under H$_2$, the reaction mixture was concentrated. The resultant solids were triturated with CH$_2$Cl$_2$. The organics were filtered through florisil and concentrated. Vacuum distillation affords 30 (0.55 g, 85 %) as a colorless oil: $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.4-7.1 (m, 5H, Ph), 6.43 (d, J = 11.6 Hz, 1H, C:CHPh), 5.65 (dt, J = 11.6 and 7.3 Hz, 1H, C:CHCH$_2$), 2.69 (t, J = 7.1 Hz, 2H, NCH$_2$), 2.36 (app dq, J = 7.4 and 7.3 Hz, 2H, C:CCH$_2$), 1.57 (app p, J = 7.4 and 7.1 Hz, 2H, CH$_2$), 1.09 (s, 2H, NH$_2$); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 137.52, 132.18, 129.12, 128.55, 127.96, 126.35, 41.66, 33.85, 25.76.

6-Methyl-5-hepten-2-ylamine(31). A refluxing solution of HONH$_2$•HCl (16.6 g, 240 mmol) and NaOAc (19.7 g, 240 mmol) in H$_2$O (80 mL) and EtOH (3.2 mL) was treated with 6-methylhept-5-en-2-one (11.8 mL, 80 mmol). The mixture was maintained at reflux 40 h and then cooled to 25 °C. The layers were separated and the aqueous layer was extracted with 1:1 Et$_2$O-hexane (2 x 30 mL). The combined organics were concentrated and then rediluted with Et$_2$O (100 mL).
This solution was added over 2 h to a brine-ice cooled suspension of LiAlH₄ (10.4 g, 274 mmol) in Et₂O (250 mL). After refluxing 23 h, the reaction mixture was cooled in a brine-ice bath and quenched via sequential addition of H₂O (10 mL), 15 % NaOH (10 mL) and H₂O (30 mL). The mixture was stirred 1 h, saturated with K₂CO₃, and then allowed to settle. The organics were decanted and combined with two Et₂O washes of the solids. The combined organics were dried and concentrated. Distillation affords 6.35 g (62 % from ketone) of 31 as a colorless oil: ¹H NMR (300 MHz, CDCl₃) δ 5.09 (app tt, J = 6.2 and 1.1 Hz, 1H, C:CH), 2.85 (app sex, J = 6.2, 1H, NCH), 1.99 (app q, J = 7.1 Hz, 2H, CH₂), 1.66 (s, 3H, CH₃), 1.59 (s, 3H, CH₃), 1.33 (m, 2H, CH₂), 1.17 (br s, 2H, NH₂), 1.03 (d, J = 6.2 Hz, 3H, CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 131.39, 124.21, 46.53, 40.18, 25.59, 24.94, 23.90, 17.54; IR (film) 3300, 2895, 2830, 1600, 1450, 1390, 820 cm⁻¹.

5,5-Ethylenedioxyhex-2-yne (44). To a slurry of LiC·CH·H₂N(CH₂)₂NH₂ (22 g, 222 mmol) in DMSO (75 mL) at 5 °C was slowly added 2-(2-bromoethyl)-2-methyl-1,3-dioxolane 43 (27.3 g, 148 mmol). After 2 h at 25 °C the reaction mixture was carefully poured into ice water (500 mL) and the aqueous layer was extracted with hexane (6 x 100 mL). The combined organic phases were then back extracted sequentially with H₂O (2 x 200 mL), sat. aqueous NH₄Cl (2 x 200 mL) and brine.
(200 mL). Drying, concentration and distillation (< 60 °C and 0.1 torr) gave 44 (13.9 g, 67 %) as a colorless oil:

\(^1^H\) NMR (300 MHz, CDCl\(_3\)) \(\delta\) 3.91 (m, 4H, 2CH\(_2\)O), 2.23 (m, 2H, C\(\cdot\)CH\(_2\)), 1.90 (m, 3H, CH\(_2\), C\(\cdot\)CH), 1.30 (s, 3H, CH\(_3\)); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 108.97, 84.31, 67.88, 64.72, 37.92, 23.81, 13.24; IR (film) 3294, 2984, 2962, 2936, 2884, 2118, 1718, 1448, 1378, 1256, 1220, 1144, 1102, 1056, 948, 862, 642 cm\(^{-1}\); high resolution mass spectrum calcd. for C\(_8\)H\(_{13}\)O\(_2\)(MH\(^+\)) 141.0916. Found 141.0920.

2,2-Ethylenedioxyhept-5-yn-7-ol (45). To 44 (7.46g, 53.3 mmol) in THF (90 mL) at 0 °C was added n-BuLi (1.7 M in hexane, 34.5 mL, 58.65 mmol). After 15 min, dry paraformaldehyde (2.23g, 74.5 mmol) was added in one portion. The reaction mixture was stirred 2 h at 25 °C and was then poured into sat. aqueous NH\(_4\)Cl (75 mL). The organic layer was separated, combined with three Et\(_2\)O extractions of the aqueous layer and dried. Concentration and distillation of the residue afforded 45 (8.61 g, 95 %) as a colorless oil: \(^1^H\) NMR (300 MHz, CDCl\(_3\)) \(\delta\) 4.15 (t, J = 2 Hz, 2H, CH\(_2\)O), 3.88 (m, 4H, 2CH\(_2\)O), 2.57 (br s, 1H, OH), 2.45 (m, J = 8 and 2 Hz, 2H, C\(\cdot\)CH\(_2\)), 1.84 (t, J = 8 Hz, 2H, CH\(_2\)), 1.26 (s, 3H, CH\(_3\)); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 109.02, 85.67, 78.23, 64.60, 50.99, 37.84, 23.69, 13.46; IR (film) 3418, 2982, 2958, 2934, 2888, 1448, 1378, 1256, 1222, 1146, 1132, 1102, 1054, 1024, 860, 788 cm\(^{-1}\); high
resolution mass spectrum calcd. for C₈H₁₅O₃(M⁺) 171.1021. Found 171.1024.

2,2-Ethylene dioxy-7-iodohept-5-yne (47). CH₃SO₂Cl (3.4 mL, 44 mmol) was added dropwise to a solution of 45 (6.8 g, 40 mmol) and Et₃N (8.36 mL, 60 mmol) in CH₂Cl₂ (200 mL) at 0 °C. The reaction mixture was stirred 1 h at 25 °C and then transferred to a separatory funnel containing ice water (200 mL). The organic phase was separated and washed sequentially with sat. aqueous solutions of NH₄Cl, NaHCO₃, and NaCl. Concentration gave the crude mesylate 46 which was recrystallized from Et₂O (-70 °C) to give white crystals (9.0 g, 91 %, m.p. 34 °C). Although this mesylate was not extremely stable, we were able to obtain satisfactory ¹H and ¹³C spectra (Appendix). The mesylate was dissolved in CH₃CN (200 mL) containing NaI (11.6 g, 77.5 mmol). The reaction mixture was protected from light and, after 4 h, concentrated to a sludge which was diluted with 1:1 Et₂O-hexane and filtered through basic alumina. Concentration and distillation of the residue (0.05 torr) gave 47 (10.2 g, 94 %) as a colorless oil: ¹H NMR (300 MHz, CDCl₃) δ 3.85 (m, 4H, 2CH₂O), 3.61 (t, J = 2.5 Hz, 2H, CH₂I), 2.21 (tt, J = 8 Hz and 2.5, 2H, C:CH₂), 1.78 (t, J = 8 Hz, 2H, CH₂), 1.23 (s, 3H, CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 108.76, 96.90, 86.11, 64.66, 37.43, 23.68, 13.80, -16.87; IR (film) 2982, 2958, 2934, 2882, 2230, 2204, 1446, 1378, 1254, 1220, 1176, 1144, 1100, 1054,
862 cm⁻¹; high resolution mass spectrum calcd. for C₈H₁₃IO₂(M⁺) 279.9960. Found 279.9966.

O-2,3,5,6-Tetrahydropyran-2-ylhydroxylamine (40). N-hydroxyphthalimide (36.63 g, 0.2 mol) suspended in C₆H₆ (400 mL) was treated with dihydropyran (20.1 mL, 0.22 mol) and a few drops of POCl₃. The reaction mixture was brought to reflux for 16 h, at which time the heating bath was removed. The reaction mixture was subsequently maintained at reflux by the slow addition of hydrazine monohydrate (12.01 g, 0.24 mol). After an additional 4 h at reflux, the reaction mixture was cooled to 25 °C and filtered. The solids were washed with C₆H₆ and the combined organic phases were dried. Concentration gave a red oil which upon distillation yielded 40 (20.1 g, 85%) as a white solid (m.p. 38 °C): ¹H NMR (300 MHz, CDCl₃) δ 5.44 (br s, 2H, NH₂), 4.59 (t, J = 3.4 Hz, 1H, HCO₂), 3.79 (m, 1H, OCH₂), 3.46 (m, 1H, OCH₂), 1.8-1.3 (m, 6H, 3 CH₂); ¹³C NMR (75 MHz, CDCl₃) δ 102.09, 62.06, 28.52, 24.96, 19.34.

(E) and (Z)-O-(2,3,5,6-Tetrahydropyran-2-yl)-hexan-2-one oxime (41). A solution of 2-hexanone (5.0 g, 50 mmol) and 40 (5.9 g, 50 mmol) in C₆H₆ (100 mL) was refluxed under Dean-Stark conditions for 1 h. Concentration of the reaction mixture followed by distillation (74-76 °C and 16 mm) gave 41 (9.77 g, 98%) as a clear oil composed of a mixture of the E and Z isomers. For characterization, the
isomer mixture (0.2 g, 1 mmol) in THF (0.5 mL) was added to LDA (1.1 mmol) in THF (1.5 mL) at -48 °C. After 5 h at -48 °C the reaction mixture was quenched by slow addition of absolute CH₃OH. Filtration and concentration afforded the E isomer of 41 (0.192 g, 96 %) as a colorless oil: ¹H NMR (300 MHz, CDCl₃) δ 5.14 (m, 1H, O₂CH), 3.95-3.45 (m, 2H, OCH₂), 2.15 (m, 2H, N:CH₂), 1.83 (s, 3H, CH₃), 1.8-1.0 (m, 10H, 5CH₂), 0.84 (t, J = 7.2 Hz, 3H, CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 159.62, 100.27, 63.11, 35.49, 29.04, 28.60, 25.17, 22.28, 20.14, 13.86, 13.68; IR (film) 2954, 2872, 1466, 1456, 1368, 1202, 1112, 1080, 1042, 982, 936 cm⁻¹; high resolution mass spectrum calcd. for C₁₁H₂₁NO₂(M⁺) 199.1573. Found 199.1572.

O-(2,3,5,6-Tetrahydropyran-2-yl)-2,2-ethylene-dioxytridec-5-yn-7-one oxime(48). To i-Pr₂NH (1.62 mL, 11.55 mmol) in THF (8 mL) at 0 °C was added n-BuLi (3M in heptane, 3.85 mL, 11.55 mmol). After 15 min the reaction mixture was cooled to -48 °C and 41 (2M in THF, 5.25 mL, 10.5 mmol) was added. After 5h at -45 to -48 °C, 47 (2.80 g, 10 mmol) in THF (6 mL) was added dropwise, and the reaction mixture was maintained for 1 h at -48 °C. CH₃OH (1 mL) was then added and the reaction mixture was concentrated. Dilution with 1:1 Et₂O-hexane (20 mL) followed by filtration through neutral alumina and concentration afforded 48 (3.44 g, 98 %) as a light yellow oil which could not be distilled: ¹H NMR (300 MHz, CDCl₃)
δ 5.17 (m, 1H, HCO₂), 3.90 (m, 5H, OCH₂CH₂O, OCH₂), 3.60 (m, 1H, OCH₃), 255-2.15 (m, 8H, 4CH₂), 1.9-1.2 (m, 12H, 6CH₂), 1.29 (s, 3H, CH₃), 0.88 (t, J = 7.3 Hz, 3H, CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 161.6, 109.00, 100.15, 80.35, 78.73, 64.61, 62.80, 38.36, 34.26, 28.95, 28.56, 28.00, 25.19, 23.68, 22.45, 19.88, 15.49, 13.73, 13.51; IR (film) 2956, 2930, 2874, 2852, 1456, 1376, 1204, 1134, 1112, 1078, 1058, 1042, 946, 788, 764 cm⁻¹; high resolution mass spectrum calcd. for C₂₀H₃₄NO₄(MH⁺) 352.2488. Found 352.2448.

(±) 7-amino-2,2-ethylenedioxytridec-5-yne(39). A solution of 48 (19.7 g, 56 mmol) in Et₂O (100 mL) was slowly added to LiAlH₄ (4.25 g, 112 mmol) in Et₂O (100 mL) which was cooled to -78 °C. The reaction mixture was brought to reflux for 2 h, cooled to -78 °C and was subsequently quenched with 10 % KOH. The organic phase was decanted, concentrated, dried as a solution in 1:1 CH₂Cl₂-pentane and reconcentrated. Distillation (100 °C and 0.1 torr) gave 39 (12.04 g, 85 %) as a colorless oil: ¹H NMR (300 MHz, CDCl₃) δ 3.80 (m, 4H, OCH₂CH₂O), 2.69 (m, 1H, NCH), 2.11 (m, 4H, CH₂C:CH₂), 1.74 (m, 2H), 1.55-1.4 (m, 1H), 1.35-1.1 (m, 10H), 1.03 (br s, 2H, NH₂), 0.79 (t, J = 7.6 Hz, 3H, CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 108.93, 79.84, 79.34, 64.48, 50.15, 38.41, 37.57, 36.91, 28.09, 23.56, 22.62, 15.52, 13.87, 13.45; IR (film) 3374, 3306, 2980, 2956, 2930, 2874, 2860, 1582, 1448, 1378, 1254, 1220, 1132, 1102, 1056, 860 cm⁻¹;
high resolution mass spectrum calcd. for \( \text{C}_{15}\text{H}_{27}\text{NO}_2(\text{M}^+) \) 253.2042. Found 253.2046.

(±) 2-Butyl-3,4-dihydro-5-(4,4-ethylenedioxypentyl)-2H-pyrrole(38). To Et\(_3\)N (260 µl, 1.9 mmol) and CpTiCl\(_3\) (208mg, 0.95 mmol) in THF (10 mL) at 25 °C was added 39 (1.20 g, 4.74 mmol) in THF (10 mL). After 1 h, 5 % methanolic NaOH (4 mL) was added, and the reaction mixture brought to dryness. The resultant mass was triturated with hexane (3 x 10 mL) which was then filtered through powdered K\(_2\)CO\(_3\). Concentration yielded 38 (1.12 g, 93 %) as a slightly colored oil: \(^1\)H NMR (300 MHz, CDCl\(_3\)) \( \delta \) 3.88 (m, 4H, OCH\(_2\)CH\(_2\)O), 2.55-2.2 (m, 5H, N=C(CH\(_2\))\(_2\), NCH), 2.1-1.7 (m, 1H), 1.7-1.55 (m, 5H), 1.45-1.1 (m, 9H), 0.86 (m, J = 7, 3H, CH\(_3\)); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \( \delta \) 176.70, 109.83, 72.48, 64.56, 38.71, 36.81, 36.36, 33.90, 28.82, 28.55, 23.69, 22.80, 21.14, 14.02; IR (film) 2956, 2928, 2872, 1644, 1458, 1376, 1256, 1218, 1132, 1060; high resolution mass spectrum calcd. for \( \text{C}_{15}\text{H}_{27}\text{NO}_2(\text{M}^+) \) 253.2042. Found 253.2034.

(±) 2-Butyl-5-(4,4-ethylenedioxypentyl)-2B,3,4,5B-tetrahydro-1H-pyrrole(37). A\(^1\)-pyrroline 38 (1.265 g, 5 mmol) was added over 10 min to a solution of DiBAL-H (1M in C\(_7\)H\(_8\), 20 mL, 20 mmol) in THF (15 mL) at -78 °C. After 30 min the reaction mixture was warmed to -50 °C, and then to 0 °C over 3 h. The reaction mixture was quenched by careful addition of 10 % aqueous KOH (6 mL) and then
saturated with K$_2$CO$_3$. The organic phase was separated and combined with two Et$_2$O extractions of the aqueous phase. Concentration gave 37 (1.21 g, 95 %) as an unstable red oil which was used without purification: $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 3.81 (m, 4H, OCH$_2$CH$_2$O), 2.8 (m, 2H, 2NCH), 1.72 (m, 2H, CH$_2$), 1.53 (m, 2H, CH$_2$), 1.45-1.0 (m, 15H, 6CH$_2$, CH$_3$), 0.96 (app d, J = 6.6 Hz, 1H), 0.77 (t, J = 7 Hz, 3H, CH$_3$); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 109.84, 64.40, 59.19, 59.10, 39.19, 36.84, 36.32, 31.12, 29.51, 23.53, 22.71, 21.86, 20.40, 13.86; IR (film) 3854, 2954, 2872, 1652, 1462, 1376, 1252, 1220, 1142, 948 cm$^{-1}$; high resolution mass spectrum calcd. for C$_{15}$H$_{29}$NO$_2$(M$^+$) 255.2198. Found 255.2191.

(±)-Monomorine(1). A solution of 37 (1.275 g, 5 mmol) in THF (15 mL) was stirred overnight with 5 % HCl (5 mL). The reaction mixture was saturated with K$_2$CO$_3$, the organic phase was separated and combined with two Et$_2$O extractions of the aqueous phase. The solvent was removed and the resultant oil was diluted with THF (10 mL) to which NaBH$_3$CN (0.314 g, 5 mmol) in CH$_3$OH (3 mL) and 5 % HCl (1 mL) were added. After 2 h the reaction mixture was saturated with K$_2$CO$_3$, the organic phase was separated and combined with two Et$_2$O extractions of the aqueous phase. Concentration and flash chromatography of the residue (silica gel, 10 % Et$_2$O/hexane) gave 1 (0.70 g, 72 %) as colorless oil: $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 2.44 (tt, J = 10 and 2.5 Hz, 1H, NCH), 2.18 (m, 1H, NCH), 2.03 (m, 1H, NCH), 1.87-1.15 (m, 16H,
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\[8 \text{CH}_2\), 1.10 (d, J = 6.4 Hz, 3H, \text{CH}_3), 0.86 (t, J = 7 Hz, 3H, \text{CH}_3); ^{13}\text{C NMR (75 MHz, CDCl}_3) \delta 67.07, 62.77, 60.14, 39.68, 35.85, 30.91, 30.30, 29.70, 29.26, 24.87, 22.85, 22.79, 14.07; \text{IR (film) 3402, 2956, 2930, 2872, 2860, 1456, 1378, 1320, 1302, 1206, 1130, 788 cm}^{-1}; \text{high resolution mass spectrum calcd. for C}_{13}\text{H}_{22}\text{N}(M^+) 195.1987. \text{Found 195.1982.}

\text{Undec-2-yn-1-ol(52). Lithium metal (3.82 g, 0.55 mole) was added in small portions to a dry ice condensor equipped flask containing liquid NH}_3 (350 mL) and a crystal of ferric nitrate. After the blue color was discharged, propargyl alcohol (14.5 mL, 0.25 mole) was added dropwise over 15 min. After an additional 15 min, octyl bromide (34.5 mL, 0.2 mole) was added, followed by DMSO (175 mL). The reaction mixture was allowed to warm to 25 °C overnight and was then diluted to 750 mL with ice water. The aqueous layer was extracted with Et}_2\text{O (4 x 150 mL). The combined extractions were washed with brine, dried and filtered. Following concentration, the crude product was distilled through an 8" vigeroux column (72 °C and 0.025 torr) to afford 27 g (80 %) of 52 as a colorless oil: } ^{1}H \text{NMR (300 MHz, CDCl}_3) \delta 4.22 (dt, J = 6.0 and 2.2 Hz, 2H, CH}_2\text{O), 2.33 (s, 1H, OH), 2.18 (tt, J = 7.0 and 2.2 Hz, 2H, C:CH}_2\text{), 1.48 (app pent, J = 7.2 Hz, 2H, CH}_3\text{), 1.4-1.15 (m, 10H, 5CH}_2\text{), 0.86 (t, J = 6.7 Hz, 3H, CH}_3\text{); } ^{13}\text{C NMR (75 MHz, CDCl}_3) \delta 86.27, 78.28, 51.07, 31.74, 29.08, 29.01, 28.80, 28.55,
22.54, 18.64, 13.94; IR (film) 3300, 2900, 2820, 2200, 1460, 1130, 1010 cm\(^{-1}\).

1-Bromoundec-2-yne(53). A solution of Br\(_2\) (6.3 g, 39.5 mmol) in CCl\(_4\) (25 mL) was added dropwise to a 0 °C solution of Ph\(_3\)P (10.3 g, 39.5 mmol) in CCl\(_4\) (100 mL). After 15 min a solution of 52 (6.72 g, 40 mmol) in CCl\(_4\) (25 mL) was added. The reaction mixture was brought to reflux for 1 h and was then cooled to 0 °C and filtered. The solids were washed with CCl\(_4\) (2 x 20 mL) and the combined organics were concentrated to a white mass. The solids were triturated with hexane (2 x 50 mL) which was subsequently concentrated to an oil. Vacuum distillation affords 7.56 g (81 %) of 53 as a colorless oil: \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 3.90 (t, \(J = 2.4\) Hz, 2H, CH\(_2\)Br), 2.21 (tt, \(J = 7.0\) and 2.4 Hz, 2H, C\(\equiv\)CCH\(_2\)), 1.48 (app pent, \(J = 7.2\) Hz, 2H, CH\(_2\)), 1.55-1.15 (m, 10H, 5CH\(_2\)), 0.86 (t, \(J = 6.7\) Hz, 3H, CH\(_3\)); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 88.32, 75.24, 31.80, 29.12, 29.02, 28.81, 28.36, 22.62, 18.93, 15.69, 14.05; IR (film) 2890, 2820, 2210, 1450, 1200 cm\(^{-1}\).

L-Phenylalanine methyl ester hydrochloride. A -5 °C suspension of phenylalanine (20 g, 121 mmol) in CH\(_2\)OH (120 mL) was treated with SOCl\(_2\) (15.7 mL, 1.78 eq) at such a rate that the internal temperature did not exceed 0 °C. The mixture was allowed to stir 4 h at 25 °C and was then concentrated. The resultant solids were diluted with and
stripped of CH₃OH (60 mL) four times. The solids were then slurried with Et₂O (150 mL) and filtered. After washing the solids with Et₂O (2 x 50 mL) the residual solvent was removed under vacuum. Grinding in a mortar with a pestle yields 25.5 g (98 %) of the title compound as a white powder. Due to the limited solubility of this salt, it was converted to the free amine for characterization. ¹H NMR (300 MHz, CDCl₃) 6 7.25-7.05 (m, 5H, Ph), 3.63 (dd, J = 7.8 and 5.2 Hz, 1H, NCH), 3.61 (s, 3H, CH₃), 2.99 (dd, J = 13.5 and 5.2 Hz, PhCH₂), 2.77 (dd, J = 13.5 and 7.8 Hz, PhCH), 1.42 (s, 2H, NH₂); ¹³C NMR (75 MHz, CDCl₃) 6 174.99, 136.96, 128.90, 128.14, 126.40, 55.47, 51.48, 40.76.

Methyl N-(diphenylmethylene)-L-phenylalaninate(55).
The preparation of this compound has been described by Polt. ¹H NMR (300 MHz, CDCl₃) 6 7.7-6.6 (m, 15H, Ph), 4.29 (dd; J = 9.3 and 4.3 Hz, 1H, NCH), 3.74 (s, 3H, CH₃), 3.31 (dd, J = 13.3 and 4.3 Hz, 1H, PhCH₂), 3.21 (dd, J = 13.3 and 9.3 Hz, 1H, PhCH); ¹³C NMR (75 MHz, CDCl₃) 6 172.17, 170.74, 139.29, 137.82, 135.97, 130.17, 129.76, 128.68, 128.24, 128.06, 127.90, 127.53, 126.22, 67.13, 52.06, 39.70.

(2S, 3S) and (2S, 3R)-2-[N-(diphenylmethylene)amino]-1-phenylhex-5-yn-3-ol(59) and (60). A 1 L flask charged with methyl N-(diphenylmethylene)-L-phenylalaninate (19.5 g, 57 mmol) and CH₂Cl₂ (440 mL) was cooled to -73 °C. A mixture of TriBAL (1 M in C₆H₆, 57 mL, 1 eq) and DiBAL-H
(1 M in C$_2$H$_4$, 57 mL, 1 eq) was then added slowly via addition funnel so that the temperature did not exceed -68 °C. Upon completion of the addition, the yellow solution was treated with H$_2$C:C:C(H)MgBr (1.8 M in Et$_2$O, 95 mL, 3 eq), again at a rate such that the temperature did not exceed -68 °C. The resulting green reaction mixture was stirred 10 h at -73 °C before slowly warming to 15 °C for 4 h. After cooling to 0 °C, aqueous NaOH (5 M, 63 mL) was added slowly over 1 h. The red organic layer was then decanted and combined with 3 x 100 CH$_2$Cl$_2$ washes of the green solids for drying. The concentrated organics were rediluted with CC$_4$ and filtered through a pad of basic alumina. Concentration gave 19.15 g (55.8 mmol, 95 %) of the diastereomeric mixture as a viscous red oil. When 10 g of this mixture was chromatographed on 600 mL of silica gel (10 % EtOAc/Hexane) there was obtained 5.755 g (16.8 mmol, 55 %) of the 2S,3S diastereomer (59) as a yellow-green, gelatinous solid and 1.761 g (4.99 mmol, 16.8 %) of the 2S,3R diastereomer (60) as a white solid:

(2S,3S)-2-[N-(diphenylmethylene)amino]-1-phenylhex-5-yn-3-ol (59). $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.8-6.7 (m, 15H, Ph), 3.93 (app q, $J$ = 6.7 and 6.0 Hz, 0.6H, NCH), 3.83 (app t, $J$ = 6.4 Hz, 0.4H), 3.75 (app dt, $J$ = 7.0, 6.2 and 1.7 Hz, 0.4H), 3.47 (app q, $J$ = 7.4 and 5.7 Hz, 0.6H), 3.06, 2.95, 2.88 and 2.86 (all dd, $J$ = 13.2 and 6.8 Hz, 14.1 and 5.7 Hz, 13.2 and 4.5 Hz, and 14.1 and 8.0 Hz, respectively, 2H,
PhCH₂), 2.46 and 2.40 (m, 1H, C:CCH), 2.32-2.18 (m, 1H, C:CCH), 1.97 (app t, J = 2.7 and 2.4, 0.6H, C:CH), 1.92 (app t, J = 2.7 and 2.4, 0.4H, C:CH); ¹³C NMR (75 MHz, CDCl₃) δ 169.92, 144.94, 144.78, 139.10, 138.42, 138.32, 136.09, 130.33, 129.77, 129.02, 128.41, 128.19, 128.10, 128.04, 127.98, 127.62, 127.49, 127.28, 126.40, 126.19, 126.09, 126.05, 99.45, 80.89, 80.62, 79.91, 71.00, 70.14, 65.50, 64.77, 39.54, 39.37, 25.52, 24.00; (note: oxazolidine-imine tautomerism); IR (film) 3460, 3250, 3050, 3030, 2990, 2890, 2100, 1655, 1615, 1595, 1485, 1445, 1310, 1275, 1240, 1065, 1030, 950, 780, 755, 710 cm⁻¹.

(2S,3R)-2-[N-(diphenylmethylene)amino]-1-phenylhex-5-yn-3-ol(60). ¹H NMR (300 MHz, CDCl₃) δ 7.7-6.3 (m, 15H, Ph), 3.94 (app q, J = 5.4 Hz, 1H, OCH), 3.64 (ddd, J = 9.5, 5.4 and 3.1 Hz, 1H, NCH), 3.05 (dd, J = 13.0 and 3.1 Hz, 1H, PhCH), 2.90 (dd, J = 13.0 and 9.5 Hz, 1H, PhCH), 2.68 (br s, 1H, 0H), 2.57 (ddd, J = 16.7, 5.6 and 2.7 Hz, 1H, C:CCH), 2.48 (ddd, J = 16.7, 7.5 and 2.5 Hz, 1H, C:CCH), 1.98 (app t, J = 2.7 and 2.5 Hz, 1H, C:CH); ¹³C NMR (75 MHz, CDCl₃) δ 168.79, 139.56, 138.94, 136.30, 130.18, 130.00, 128.46, 128.11, 127.97, 127.85, 127.65, 125.94, 80.88, 73.01, 70.75, 67.03, 37.83, 23.73; IR (KBr) 3230, 3050, 3010, 2990, 2905, 2850, 2100, 1605, 1480, 1440, 1325, 1280, 1105, 1045, 1015, 775, 690 cm⁻¹.
(4S,5S)-5-(Phenylmethyl)-4-(prop-2'-yn-1'-yl)-2-oxazolidinone (61). A solution of (2S,3S)-3-hydroxy-1-phenylhex-5-yn-2-ylamine (140 mg, 0.74 mmol), prepared by hydrolysis of 59) and carbonyldiimidazole (156 mg, 0.96 mmol) in THF (3 mL) was stirred at 25 °C for 2 h. The mixture was concentrated and the resultant solids dissolved in Et₂O. The organic phase was washed with 1 M HCl (2 x 5 mL) and sat. aqueous NaHCO₃ (5 mL). Filtration of the organics through powdered K₂CO₃ and concentration provided a viscous oil. Chromatography (50 % EtOAc/Hex) affords 100 mg (47 %) of 61 as a white solid: ¹H NMR (300 MHz, CDCl₃) δ 7.4-7.1 (m, 5H, Ph), 6.21 (s, 1H, NH), 4.36 (app q, J = 6.6 and 5.1 Hz, 1H), 3.9Q (app q, J = 6.6 and 5.1 Hz, 1H), 2.88 (d, J = 7.0 Hz, 2H, PhCH₂), 2.46 (m, 2H, C:CH₂), 1.97 (app t, J = 2.7 Hz, C:CH); ¹³C NMR (7.5 MHz, CDCl₃) δ 158.18, 135.65, 129.12, 128.85, 127.16, 78.36, 77.42, 71.56, 58.04, 41.62, 24.19; IR (CCl₄) 3300, 2900, 1750, 1390, 1240, 790, 760, 710 cm⁻¹.

(2S,3S)-3-benzyloxy-2-[N-(diphenylmethylene)amino]-1-phenylhex-5-yn-2-yl(63). A solution of 59 (5.4 g, 15.3 mmol) in THF (30 mL) was added over 15 min to a suspension of KH (1.2 g, 30 mmol) in THF (50 mL) at 25 °C. After 2 h at 25 °C, the dark red solution was cooled to 0 °C and PhCH₂Br (3.57 mL, 30 mmol) was added. After 10 min at 0 °C, the mixture was warmed to 25 °C for 1 h. The mixture was then poured into ice water (100 mL) and Et₂O (100 mL). The
organics were separated, dried and concentrated. After redrying as a solution in 1:1 CH$_2$Cl$_2$-pentane, the organics were again concentrated to yield 6.916 g (102\% \text{ of crude 63. An analytical sample was prepared by chromatography on silica gel (5 \% EtOAc/Hexane): \text{ }^1H \text{ NMR (300 MHz, CDCl}_3) \delta 7.6-6.4 \text{ (m, 20 H, Ph), 4.76 (d, J = 11.8 Hz, 1H, PhCHO), 4.62 (d, J = 11.8 Hz, 1H, PhCHO), 3.89 (ddd, J = 9.8, 5.35 and 3.0 Hz, 1H, NCH), 3.75 (ddd, J = 7.6, 5.35 and 3.7 Hz, 1H, OCH), 3.09 (dd, J = 12.8 and 3.0 Hz, 1H, PhCH), 2.96 and 2.94 (overlapping dd, J = 12.8 and 9.8 Hz, 1H, PhCH and ddd, J = 17, 3.7 and 2.4 Hz, 1H, C:CCH), 2.69 (ddd, J = 17, 7.6 and 2.7 Hz, 1H, C:CCH), 1.34 (app t, J = 2.7 and 2.4 Hz, 1H, C:CH); \text{ }^{13}C \text{ NMR (75 MHz, CDCl}_3) \delta 168.52, 139.67, 139.30, 138.49, 136.50, 129.80, 129.73, 128.36, 128.12, 127.97, 127.88, 127.82, 127.75, 127.65, 127.58, 127.37, 125.74, 82.14, 80.47, 72.51, 69.53, 66.36, 37.31, 20.94; \text{ IR (film) 3270, 3050, 3000, 2900, 2115, 1740, 1650, 1625, 1490, 1455, 1445, 1910, 1275, 1240, 1060, 1025, 745, 695 cm}^-; \text{ high resolution mass spectrum calcd. for C}_{32}H_{23}NO(M-H\text{)} 442.2211. Found 442.2216.

(2S,3S)-3-benzyloxy-2-[N-(diphenylmethylene)amino]-1-phenyl-6-(thiomethyl)hex-5-yne(64). A solution of i-Pr$_2$NET (73 \mu l, 0.522 mmol, 1.05 eq) in THF (3 mL) at 0 °C was treated with n-BuLi (2.53 M in heptane, 206 \mu l, 0.522 mmol, 1.05 eq). After 30 min the mixture was cooled to -35 °C and 63 (0.25 M in THF, 2 mL, 0.497 mmol) was added dropwise.
HMPA (86 μl, 0.497 mmol) was added after 1 h and the mixture was then warmed to 0 °C for 1 h. CH₃SCN (40 μl, 0.577 mmol) was then added dropwise. After 30 min at 25 °C the reaction mixture was partitioned between Et₂O and sat. aqueous NH₄Cl. The layers were separated and the organic phase was washed with sat. aqueous NH₄Cl. Concentration of the organics gave a red oil which was filtered through neutral alumina (20 % EtOAc/Hexane). Concentration affords 0.234 g (96 %) of 64 as a red oil: ¹H NMR (300 MHz, CDCl₃) δ 7.8-6.5 (m, 20H, Ph), 4.78 (d, J = 11.9 Hz, 1H, PhCHO), 4.67 (d, J = 11.9 Hz, 1H, PhCHO), 3.94 (m, 1H), 3.79 (m, 1H), 3.17 (dd, J = 12.7 and 3.0 Hz, 1H), 3.08 (dd, J = 17.2 and 4.0 Hz, 1H), 3.02 (dd, J = 12.7 and 9.8 Hz, 1H), 2.85 (dd, J = 17.2 and 7.3 Hz, 1H), 2.36 (s, 3H, CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 168.33, 139.57, 139.23, 138.41, 136.43, 129.70, 129.62, 128.25, 128.02, 127.86, 127.74, 127.66, 127.53, 127.50, 127.26, 125.64, 90.52, 80.37, 72.24, 71.37, 68.35, 37.35, 22.44, 18.75; IR (film) 3050, 3020, 2940, 1970, 1670, 1620, 1600, 1500, 1455, 1450, 1320, 1280, 1080, 1030, 780, 690 cm⁻¹.

(2S,3S)-3-benzyloxy-2-[N-(diphenylmethylene)amino]-1-phenyltetradec-5-yn-65. A solution of 63 (3.46 g of crude product, ~7.65 mmol) in THF (25 mL) was added to a solution of LDA (9.56 mmol, 1.25 eq) in THF (50 mL) maintained at -35 °C. After 10 min, HMPA (1.33 mL, 1.0 eq) was added and the mixture was warmed to 0 °C for 45 min. The blue-green
solution was then treated with n-C₈H₁₇I (2.76 mL, 2 eq) and allowed to stir 11 h at 25 °C. The reaction mixture was then partitioned between Et₂O (100 mL) and sat. aqueous NH₄Cl (100 mL). The organics were separated and washed twice with sat. aqueous NH₄Cl (50 mL) and were then dried and concentrated. The crude material was chromatographed on silica gel (5 % EtOAc/Hexane) to afford 2.22 g (52 % from 59) of 65 as a light orange, viscous oil: ¹H NMR (300 MHz, CDCl₃) δ 7.7-6.4 (m, 20H, Ph), 4.73 (d, J = 11.8 Hz, 1H, PhCHO), 4.59 (d, J = 11.8 Hz, 1H, PhCHO), 3.87 (ddd, J = 9.6, 5.6 and 3.0 Hz, 1H, NCH), 3.68 (ddd, J = 7.1, 5.6 and 4.0 Hz, 1H, OCH), 3.06 (dd, J = 12.8 and 3.0 Hz, 1H, PhCHC), 2.92 (dd, J = 12.8 and 9.6 Hz, 1H, PhCHC), 2.84 (app d pent, J = 16.9, 4.0 and 2.3 Hz, 1H, C:CHCO), 2.63 (ddt, J = 16.9, 7.1 and 2.3 Hz, 1H, C:CHCO), 2.19 (m, J = 6.9 and 2.3 Hz, 2H, C:CH₂), 1.50 (p, J = 6.9, 2H, C:CH₂CH₂), 1.43-1.28 (br s, 10H, 5CH₂), 0.96 (t, J = 6.6, 3H, CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 168.30, 139.88, 139.52, 138.80, 136.67, 129.86, 129.62, 128.34, 128.08, 127.94, 127.85, 127.81, 127.74, 127.67, 127.55, 127.27, 125.69, 81.59, 80.98, 77.42, 72.41, 66.62, 37.66, 31.83, 29.17, 29.14, 28.98, 28.95, 22.61, 21.30, 18.84, 14.06.

(2S,3S)-3-benzyloxy-1-phenyltetradec-5-yn-2-ylamine(51). To 65 (0.812 g, 1.48 mmol) in THF (14 mL) was added oxalic acid (0.317 M, 5 mL, 1.585 mmol, 1.07 eq). After 7 h at 25 °C, the reaction mixture was stirred
vigorously with KOH (0.5 M, 15 mL) and Et₂O (10 mL) for 10 min. The organics were separated and combined with three additional Et₂O extractions (8 mL) of the aqueous phase. Chromatography of the concentrated organics (10 % EtOAc/Hex - 10 % CH₃OH/CH₂Cl₂) affords 51 (0.376 g, 65 %) as a colorless oil: ¹H NMR (300 MHz, CDCl₃) δ 7.4-7.1 (m, 10H, Ph), 4.75 (d, J = 11.6 Hz, 1H, PhCHO), 4.51 (d, J = 11.6 Hz, 1H, PhCHO), 3.44 (app q, J = 10, 5.8 and 4.1 Hz, 1H, NCH), 3.27 (app p, J = 8.8, 4.5 and 4.1 Hz, 1H, OCH), 2.89 (dd, J = 13.3 and 5.1 Hz, 1H, PhCHC), 2.62 (dd, J = 13.3 and 9.0 Hz, 1H, PhCHC), 2.58 (m, J = 8.8 and 2.7 Hz, 2H, OCCH₂), 2.16 (app t, J = 6.9 Hz, 2H, C=CCH₂), 1.55-1.20 (m cont br s, 14H, 6CH₂, NH₂), 0.90 (t, J = 6.5, 3H, CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 139.45, 138.45, 129.15, 128.36, 128.28, 127.73, 127.56, 126.10, 82.32, 80.27, 76.35, 72.04, 55.09, 41.06, 31.79, 29.14, 29.08, 28.92, 28.86, 22.58, 20.96, 18.75, 14.02.

(2S,3S)-3-benzylxyloxy-1-phenylhex-5-yn-2-ylamine(71). A solution of 63 (7.24 g, 16.35 mmol) and oxalic acid monohydrate (2.6 g, 20 mmol) in THF (30 mL), H₂O (1 mL) and CH₃OH (6 mL) was allowed to stir 3 h at 25 °C. A solution of KOH (1.2 g) in H₂O (25 mL) was added. The mixture was transferred to a separatory funnel and extracted with hexane (1 x 20 mL) and 1:1 Et₂O-hexane (2 x 50 mL). The combined organics were dried and concentrated. Chromatography of the crude product (10 % EtOAc/Hexane-5 % CH₃OH/CH₂Cl₂) afforded
3.42 g (75%) of 71 as a viscous light yellow oil: ¹H NMR (300 MHz, CDCl₃) δ 7.45-7.1 (m, 10H, Ph), 4.74 (d, J = 11.5 Hz, 1H, PhCHO), 4.51 (d, J = 11.5 Hz, 1H, PhCHO), 3.48 (m, 1H), 3.24 (app pent, J = 4.6 Hz, 1H), 2.87 (dd, J = 13.3 and 5.0 Hz, 1H, PhCH), 2.7-2.5 (m, 3H, C:CH), 2.01 (app t, J = 2.7 Hz, 1H, C:CH), 1.41 (s, 2H, NH₂). ¹³C NMR (75 MHz, CDCl₃) δ 139.29, 138.25, 129.20, 128.47, 128.40, 127.84, 127.73, 126.24, 81.12, 79.92, 72.31, 70.23, 55.09, 41.18, 20.76. IR (film) 3290, 3010, 2900, 2110, 1590, 1490, 1450, 1340, 1060, 1020, 770, 690 cm⁻¹; high resolution mass spectrum calcd. for C₁₉H₂₂NO(MH⁺) 280.1702. Found 280.1703. Anal. Calcd. for C₁₉H₂₁NO: C, 81.68; H, 7.58. Found: C, 81.13; H, 7.51.

5-Nonyl-2-(phenylmethyl)pyrrole (68). A solution of HNEt₂ (62 µl, 0.6 mmol) in DME (2 mL) was treated with n-BuLi (2.58 M in heptane, 233 µl, 0.6 mmol). The resultant mixture was added to a solution of CpTiCl₃ (66 mg, 0.3 mmol) in DME (1 mL). The mixture was brought to reflux and amine 51 (98 mg, 0.25 mmol) in DME (1 mL) was added dropwise over 1 h. After an additional 1 h the mixture was cooled to 25 °C and quenched with sat. aqueous NaHCO₃. The aqueous phase was extracted with Et₂O (3 x 5 mL) and the combined extractions were concentrated. Chromatography (10% ETOAc/Hexane) provides a 53% unoptimized yield of pyrrole 68 as an unstable oil. The same product was obtained upon treatment of DME or C₆H₆ solutions of CpTi(CH₃)₂Cl with 51.
$^1$H NMR (300 MHz, CDCl$_3$) δ 7.50 (br m, 1H, NH), 7.45-7.15 (m, 5H, Ph), 5.89 (app t, J = 2.8 Hz, 1H, NC:CH), 5.83 (app t, J = 2.8 Hz, 1H, NC:CH), 3.96 (s, 2H, PhCH$_2$), 2.53 (t, J = 7.7 Hz, 2H, NCCH$_2$), 1.60 (app pent, J = 7.5 Hz, 2H, CH$_2$), 1.30 (br s, 12H, 6CH$_2$), 0.92 (t, J = 7.0 Hz, 3H, CH$_3$);

$^{13}$C NMR (75 MHz, CDCl$_3$) δ 139.87, 132.30, 128.82, 128.60, 128.49, 126.25, 106.39, 104.68, 34.17, 31.86, 29.63, 29.50, 29.41, 29.36, 29.37, 27.78, 22.64, 14.06; IR (film) 3350, 2900, 2840, 1450, 1255, 1225, 770, 700 cm$^{-1}$.

**N-Carbomethoxy-5-nonyl-2-(phenylmethyl)pyrrole(70).** A solution of CpTiCl$_3$ (96 mg, 0.44 mmol) in C$_6$H$_6$ (2 mL) at 25 °C was treated with CH$_3$Li (0.644 M, 1.37 mL, 0.88 mmol). The mixture was brought to reflux and amine 51 (0.4 M in C$_6$H$_6$, 1 mL, 0.4 mmol) was added over 0.5 h. After 15 min the mixture was cooled to 25 °C and ClCO$_2$CH$_3$ (78 µl, 1 mmol) was added. After 2 h the reaction mixture was quenched with CH$_3$OH and concentrated. Trituration of the resultant solids with 30 % EtOAc/Hexane followed by filtration of the organics through a silica plug and concentration provided crude product. Chromatography (5 % EtOAc/Hexane) afforded 70 (61 mg, 45 %) as an unstable oil: $^1$H NMR (300 MHz, CDCl$_3$) δ 7.35-7.1 (m, 5H, Ph), 5.89 (d, J = 3.4 Hz, 1H, NC:CH), 5.78 (d, J = 3.4 Hz, 1H, NC:CH), 4.15 (s, 2H, PhCH$_2$), 3.77 (s, 3H, CH$_3$O), 2.80 (t, J = 7.6 Hz, 2H, NCCH$_2$), 1.60 (app pent, 2H, CH$_2$), 1.45-1.15 (m, 12H, 6CH$_2$), 0.91 (t, J = 6.8, 3H, CH$_3$); $^{13}$C NMR (75 MHz, CDCl$_3$) δ 152.19, 140.02,
Octanoyl Nitrile (74). Octanoyl chloride (4.27 mL, 25 mmol) was added to a suspension of CuCN (2.69 g, 30 mmol) in CH₃CN (30 mL). The resultant mixture was brought to reflux for 30 min, at which time the CH₃CN was allowed to distill from the reaction mixture. The residue was then distilled from the copper salts under aspirator pressure. Redistillation at aspirator pressure (98-102 °C) afforded 2.5 g (65 %) of 74 as a colorless oil: ¹H NMR (300 MHz, CDCl₃) δ 2.71 (t, J = 7.3 Hz, 2H, CH₂CO), 1.71 (app pent, J = 7.3 Hz, 2H, CH₂CH₂CO), 1.4-1.2 (m, 8H, 4CH₃), 0.87 (t, J = 6.7 Hz, 3H, CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 177.06, 113.24, 44.98, 31.38, 28.68, 28.48, 22.72, 22.43, 13.89; IR (film) 2910, 2845, 2205, 1725, 1460, 1380, 1370, 1120, 1070, 1015, 740 cm⁻¹.

(4S,5S)-4-benzyoxy-2-[2'-cyano-1'-nonen-1'-yl]-5-(phenylmethyl)-2H-pyrrole (76). A solution of CpTiCl₃ (230 mg, 1.05 mmol) in THF (3 mL) at 25 °C was treated with CH₃Li (1.8 M in Et₂O, 1.17 mL, 2.10 mmol). After 15 min the mixture was cooled to 0 °C and 71 (270 mg, 0.97 mmol) in THF (1 mL) was added. The mixture was stirred 2 h in the dark at 25 °C. The dark burgundy solution was then cooled to
0 °C and 74 (168 mg, 1.1 mmol) was added. After 2 h at 25 °C florisil (~0.5 g) and hexane (5 mL) were added. The resultant slurry was filtered through florisil (2") with the aid of 1:1 Et₂O-hexane (50 mL). Concentration of the organics yields crude 76 (307 mg, 76 %) as a yellow oil. The major product can be isolated by column chromatography (10 % EtOAc/Hexane) in 40-60 % yield. However, better overall yields were obtained when crude 76 was employed in the preparation of 77: 1H NMR (300 MHz, CDCl₃) δ 7.5-7.15 (m, 10H, Ph), 6.92 (s, 1H, C:CH), 4.56 (d, J = 11.7 1H, PhCHO), 4.33 (d, J = 11.7 1H, PhCHO), 4.25-4.12 (m, 2H, NCH, OCH), 3.41 (d, J = 17.7 Hz, 1H, PhCH), 3.33 (dd, J = 13.8 and 6.5 Hz, 1H, N:CCH), 3.23 (dd, J = 13.8 and 8.2 Hz, 1H, N:CCH), 2.97 (ddd, J = 17.7, 5.0 and 1.3 Hz, 1H, PhCH), 2.39 (t, J = 7.46 Hz, 2H, C:CCH₂), 1.64 (m, 2H, CH₂), 1.45-1.25 (m, 10H, 5CH₂), 0.93 (t, J = 6.7 Hz, 3H, CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 168.63, 139.83, 139.80, 137.74, 129.02, 128.20, 128.13, 127.45, 125.86, 120.29, 117.51, 78.20, 76.81, 71.20, 41.82, 35.98, 34.84, 31.43, 28.68, 28.43, 27.66, 22.40, 13.85; IR (film) 3020, 3000, 2930, 2900, 2850, 2195, 1700, 1495, 1455, 1345, 1100, 1060, 1030, 730, 690 cm⁻¹; MS (ESI⁺) chemical mass calcd for C₂₈H₃₆N₂O(MH⁺) 415.6. Found 415.6. Anal. Calcd for C₂₈H₃₄N₂O: C, 81.12; H, 8.27. Found: C, 80.30; H, 8.54.

(2S,3S,5R)-4-benzyloxy-2-[2'-cyano-1'-nonen-1'-yl]-1-methyl-5-(phenylmethyl)-pyrrolidine(77). To a solution of
crude 76 (307 mg, 0.741 mmol) in CH₂Cl₂ (3 mL) at 0 °C was added CH₃OTF (100 μL, 0.888 mmol). After 2 h at 25 °C the mixture was cooled to −72 °C and a solution of NaBH₄CN (56 mg, 0.888 mmol) in CH₃OH (1 mL) was added via syringe. The cooling bath was removed and the mixture was stirred vigorously for 2 h at 25 °C. After quenching with 1 M NaOH (3 mL), the mixture was diluted with pentane (4 mL). The organic phase was separated and combined with two 1:1 CH₂Cl₂-pentane extractions (3 mL) of the aqueous phase. The organics were dried and concentrated to afford 77 (258 mg, 81 %) as an orange oil. An analytical sample was prepared by column chromatography (5 % EtOAc/Hexane): ¹H NMR (300 MHz, CDCl₃) δ 7.4–7.1 (m, 10H, Ph), 6.17 (d, J = 9.3 Hz, 1H, C:CH), 4.43 (d, J = 11.6 Hz, 1H, PhCHO), 4.22 (d, J = 11.6 Hz, 1H, PhCHO), 3.72 (m, J = 2.3 Hz, 1H, OCH₃), 3.25 (app q, J = 8.6 Hz, 1H, NCHC:C), 3.04 (dd, J = 13.2 and 10.1 Hz, 1H, PhCH), 2.83 (dd, J = 13.2 and 4.3 Hz, 1H, PhCH), 2.56 (app p, J = 5.0 and 4.5 Hz, 1H, NCHBn), 2.31 (s, 3H, NCH₃), 2.28–2.17 (m, 3H, C:CCH₂, β-H), 1.64 (ddd, J = 13.9, 7.4 and 2.3 Hz, 1H, α-H), 1.53 (m, 2H, CH₂), 1.26 (m, 8H, 4CH₂), 0.87 (t, J = 6.6 Hz, 3H, CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 149.32, 139.69, 139.25, 129.26, 128.23, 128.17, 127.97, 127.52, 125.89, 117.37, 115.94, 77.55, 72.64, 71.02, 66.00, 39.30, 36.45, 34.16, 33.87, 31.62, 28.81, 28.52, 27.84, 22.52, 13.95; IR (film) 3050, 3000, 2900, 2850, 2190, 1470, 1440, 1330, 1140, 1085, 1055, 1020, 755, 690 cm⁻¹.
high resolution mass spectrum calcd. for $C_{29}H_{38}N_2O(M^+)$ 430.2985. Found 430.2988.

**Diastereomeric Nitriles 78.** To crude 77 (250 mg, 0.58 mmol) in abs. CH$_3$OH (5 mL) was added magnesium turnings (0.56 g, 23 mmol). The flask was then placed in a water bath at 25 °C and stirred 5 h. The mixture was concentrated and then subjected to vacuum. The resultant mass was triturated with hexane (3 x 4 mL). After filtering through a plug of florisil the organics were concentrated to afford 78 (230 mg, 90 %) as a reddish oil. Chromatographic purification (5 % EtOAc/Hexane) provided 147 mg (35 % from 71) of the diastereomeric mixture 78. The $^1$H NMR spectrum of the mixture (Appendix) exhibits two NCH$_3$ resonances in a ratio of 0.76:1. IR (film) 3040, 3000, 2900, 2830, 2215, 1470, 1450, 1430, 1330, 1110, 1080, 1050, 1015, 755, 690 cm$^{-1}$; high resolution mass spectrum calcd. for $C_{29}H_{40}N_2O(M^+)$ 432.3140. Found 432.3147.

$(2S,3S,5R)-1$-methyl-$5$-nonyl-$2$-(phenylmethyl)-3-pyrrolidinol(2). To potassium (100 mg, 2.6 mmol) in Et$_2$O (2 mL) at 0 °C was added first HMPA (0.5 mL), followed by a solution of the nitriles 78 (43.3 mg, 0.1 mmol) and t-BuOH (100 mg, 1.35 mmol) in Et$_2$O (0.8 mL) and toluene (0.8 mL). In the absence of toluene as cosolvent, reduction of the phenylmethyl substituent was also observed. The resultant mixture was stirred 4 h at 25 °C and then diluted with
hexane (4 mL). The organics were decanted and extracted with sat. aqueous NH₄Cl (6 x 3 mL). Drying and concentration afforded crude product which exhibited olefinic resonances in its ¹H NMR spectrum. The crude material was diluted with abs. EtOH (5 mL) and 10 % Pd-C (3 mg) was added. The flask was flushed with H₂ and the mixture then stirred 4 h under H₂ (40 psi). After filtering through celite with the aid of EtOAc/Hexanes, the organics were concentrated to a red oil. Chromatography on silica gel (5 % CH₃OH/CH₂Cl₂) afforded 2 (27 mg, 85 %) as a waxy solid: [α]²⁵D +30.0° (c 1.0, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 7.35-7.1 (m, 5H, Ph), 3.86 (m, 1H, OCH), 2.90 (dd, J = 13.3 and 10.4 Hz, 1H, NCH), 2.87 (dd, J = 13.3 and 4.3 Hz, 1H, NCH), 2.40 (s, 3H, NCH₃), 2.35-2.1 (m, 3H), 1.8-1.15 (m, 17H), 0.85 (t, J = 6.3 Hz, 3H, CH₃); ¹³C NMR (75 MHz, CDCl₃, δ 138.96, 129.36, 128.45, 126.24, 74.10, 70.19, 66.45, 39.29, 38.34, 34.03, 33.19, 31.87, 29.76, 29.56, 29.52, 29.26, 26.31, 22.64, 14.03; IR (film) 3360, 3015, 3000, 2920, 2900, 2830, 2760, 1480, 1455, 1130, 1025, 780, 695 cm⁻¹; high resolution mass spectrum calcd. for C₂₁H₃₄NO(M⁺-H) 316.2641. Found 316.2644.
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34. Though CpTiCl₃ is commercially available, both it and the TMSCp³ used in the preparation of CpTiCl₃ are quite expensive. For this reason, these compounds were prepared in-house by modifications of the literature procedures³³,³⁵.


37. Prepared in situ via treatment of CpTiCl₂OCH₃ with two equivalents of CH₃Li.


39. Effluent from the reaction was submitted to Dr. L.J. Sears and was analyzed by GLC on a 6 ft x 2 mm i.d. glass column packed with 100-120 mesh alumina. Methane was confirmed by comparison to an authentic sample.

40. Subsequent elimination and cycloaddition are quite rapid. Treatment of an equimolar solution of Cp₂ZrCl₂ and 5-phenylpent-4-yn-1-ylamine with 2 eq. of CH₃Li gives the expected pyrrole in reasonable yield in less than two hours.


Polt, R.L.; Peterson, M.A.; DeYoung, L. J. Org. Chem. 1992, 57, 5469. We thank Professor Polt for providing us a copy of this manuscript prior to publication.


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82. This mode of approach has been demonstrated for ligand cyclization reactions (ref. 3 and ref. therein) and may be applicable to this system.


86. Although it was initially thought that 1-chloro-3-iodopropane would provide the best selectivity for monosubstitution, it was found that 1-bromo-3-chloropropane is superior in this respect. This is due to the relative propensities of iodide and bromide ion to displace chloride ion.


90. The published protocol for workup of phthalimide forming (Gabriel) reactions is less than optimal. Specifically, extraction of the phthalimide from aqueous DMF is cumbersome, complicated by formation of emulsions, and accompanied by coextraction of DMF. We found it efficacious simply to remove the DMF at 60-65 °C on a rotovaporator and then rid the product of inorganic salts by trituration with water. Alternative workup procedures for the initial step of the Gabriel amine synthesis have since been published$^5$.$^6$


92. Miesel, J.L. U.S. Pat. #3927020 (Cl. 260-309.2; C07D), 1975, CA #85:94361y.


99. A potentially more direct approach to alkynols of this type involves alkylation of dimetallated propargyl alcohol. Unfortunately, neither 2-(2-bromoethyl)-1,3-dioxolane nor the corresponding iodide functioned adequately as an alkylating agent.
Figure 8. $^1$H NMR Spectrum of 1-Iodo-5-phenylpent-4-yne(16).
Figure 9. $^{13}$C NMR Spectrum of 1-Iodo-5-phenylpent-4-yne(16).
Figure 10. $^1H$ NMR Spectrum of 1-Iodonon-4-yne.
Figure 11. $^{13}$C NMR Spectrum of 1-Iodonon-4-yne.
Figure 12. $^1$H NMR Spectrum of 7-Iodo-1-phenylhept-1-yne(35).
Figure 13. $^{13}$C NMR Spectrum of 7-Iodo-1-phenylhept-1-yne(35).
Figure 14. $^1$H NMR Spectrum of 2,2-Ethylene-dioxydec-5-yne(24).
Figure 15. $^{13}$C NMR Spectrum of 2,2-Ethylene-dioxydec-5-yne(24).
Figure 16. $^1$H NMR Spectrum of Dec-5-yn-2-one(25).
Figure 17. $^{13}$C NMR Spectrum of Dec-5-yn-2-one(25).
Figure 18. $^1$H NMR Spectrum of Dec-5-yn-2-ylamine(26).
Figure 19. $^{13}$C NMR Spectrum of Dec-5-yn-2-ylamine(26).
Figure 20. $^1$H NMR Spectrum of 2,2-ethylenedioxy-5-phenylhex-5-yne (23).
Figure 21. \(^1\)H NMR Spectrum of 6-Phenylhex-5-yn-2-ylamine(7).
Figure 22. $^{13}$C NMR Spectrum of 6-Phenylhex-5-yn-2-ylamine(7).
Figure 23. $^1$H NMR Spectrum of 5-Phenylpent-4-yn-1-ylamine(3).
Figure 24. $^{13}$C NMR Spectrum of 5-Phenylpent-4-yn-1-ylamine(3).
Figure 25. $^1$H NMR Spectrum of Non-4-yn-1-ylamine(5).
Figure 26. $^{13}$C NMR Spectrum of Non-4-yn-1-ylamine(5).
Figure 27. $^1$H NMR Spectrum of 6-Phenylhexanenitrile.
Figure 28. $^1$H NMR Spectrum of 6-Phenylhex-5-yn-1-ylamine(9).
Figure 29. $^{13}$C NMR Spectrum of 6-Phenylhex-5-yn-1-ylamine(9).
Figure 30. $^1$H NMR Spectrum of Dec-5-yn-1-ylamine(11).
Figure 31. $^{13}$C NMR Spectrum of Dec-5-yn-1-ylamine(11).
Figure 32. $^1$H NMR Spectrum of Pent-4-yn-1-ylamine(28).
Figure 33. $^{13}$C NMR Spectrum of Pent-4-yn-1-ylamine(28).
Figure 34. $^1$H NMR Spectrum of 3,4-Dihydro-5-(phenylmethyl)-2H-pyrrole(4).
Figure 35. $^{13}$C NMR Spectrum of 3,4-Dihydro-5-(phenylmethyl)-2H-pyrrole(4).
Figure 36. $^1$H NMR Spectrum of 2-(Phenylmethyl)-3,4,5,6-tetrahydro-pyridine(10).
Figure 37. $^{13}$C NMR Spectrum of 2-(Phenylmethyl)-3,4,5,6-tetrahydro-pyridine(10).
Figure 38. $^1$H NMR Spectrum of 3,4-Dihydro-5-pentyl-2H-pyrrole(6).
Figure 39. $^{13}$C NMR Spectrum of 3,4-Dihydro-5-pentyl-2H-pyrrole(6).
Figure 40. $^1$H NMR Spectrum of 3,4-Dihydro-2-methyl-5-(phenylmethyl)-2H-pyrrole(8).
Figure 41. $^{13}$C NMR Spectrum of 3,4-Dihydro-2-methyl-5-(phenylmethyl)-2H-pyrrole(8).
Figure 42. $^1$H NMR Spectrum of 3,4-Dihydro-2-methyl-5-pentyl-2H-pyrrole(27).
Figure 43. $^{13}$C NMR Spectrum of 3,4-Dihydro-2-methyl-5-pentyl-2H-pyrrole(27).
Figure 44. $^1$H NMR Spectrum of 2-Pentyl-3,4,5,6-tetrahydropyridine(12).
Figure 45. $^{13}$C NMR Spectrum of 2-Pentyl-3,4,5,6-tetrahydropyridine(12).
Figure 46. $^1$H NMR Spectrum of 3,4-Dihydro-5-methyl-2H-pyrrole(29).
Figure 47. $^{13}$C NMR Spectrum of 3,4-Dihydro-5-methyl-2H-pyrrole(29).
Figure 48. $^1$H NMR Spectrum of (E,E)-2,2-Dimethyl-4,6-octadiene-1-ylamine(32).
Figure 49. $^{13}$C NMR Spectrum of (E,E)-2,2-Dimethyl-4,6-octadiene-1-ylamine(32).
Figure 50. $^1$H NMR Spectrum of (Z)-5-Phenyl-4-penten-1-ylamine(30).
Figure 51. $^{13}$C NMR Spectrum of (Z)-5-Phenyl-4-penten-1-ylamine(30).
Figure 52. $^1$H NMR Spectrum of 6-Methyl-5-hepten-2-ylamine(31).
Figure 53. $^{13}$C NMR Spectrum of 6-Methyl-5-hepten-2-ylamine(31).
Figure 54. $^1$H NMR Spectrum of 5,5-Ethyleneoxyhex-2-yne(44).
Figure 55. $^{13}$C NMR Spectrum of 5,5-Ethlenedioxyhex-2-yne(44).
Figure 56. $^1$H NMR Spectrum of 2,2-Ethylendioxyhept-5-yn-7-ol(45).
Figure 57. $^{13}$C NMR Spectrum of 2,2-Ethylenedioxyhept-5-yn-7-ol(45).
Figure 58. $^1$H NMR Spectrum of 2,2-Ethylendioxyhept-5-yn-7-ol methane sulfonate ester(46).
Figure 59. $^{13}$C NMR Spectrum of 2,2-Ethylenedioxyhept-5-yn-7-ol methane sulfonate ester (46).
Figure 60. $^1$H NMR Spectrum of 2,2-Ethyleneoxy-7-iodohept-5-yne(47).
Figure 61. $^{13}$C NMR Spectrum of 2,2-Ethylendioxy-7-iodohept-5-yne(47).
Figure 62. $^1$H NMR Spectrum of 0-2,3,5,6-Tetrahydropyran-2-ylhydroxyl-amine(40).
Figure 63. $^{13}$C NMR Spectrum of 2,3,5,6-Tetrahydropyran-2-ylhydroxyl-amine(40).
Figure 64. $^1$H NMR Spectrum of (E) and (Z)-O-(2,3,5,6-Tetrahydropyran-2-yl)-hexan-2-one oxime(41).
Figure 65. $^{13}$C NMR Spectrum of (E) and (Z)-$O$-(2,3,5,6-Tetrahydropyran-2-yl)-hexan-2-one oxime(41).
Figure 66. $^1$H NMR Spectrum of O-(2,3,5,6-Tetrahydro-pyran-2-yl)-2,2-ethylene-dioxytridec-5-yn-7-one oxime(48).
Figure 67. $^{13}$C NMR Spectrum of O-(2,3,5,6-Tetrahydro-pyran-2-yl)-2,2-ethylene-dioxytridec-5-yn-7-one oxime(48).
Figure 68. $^1$H NMR Spectrum of (±) 7-amino-2,2-ethylene-dioxytridec-5-yne(39).
Figure 69. $^{13}$C NMR Spectrum of (±) 7-amino-2,2-ethylene-dioxytridec-5-yne(39).
Figure 70. $^1$H NMR Spectrum of (±) 2-Butyl-3,4-dihydro-5-(4,4-ethylene-dioxy)pentyl)-2H-pyrrole(38).
Figure 71. $^{13}$C NMR Spectrum of (±) 2-Butyl-3,4-dihydro-5-((4,4-ethylene-dioxypentyl)-2H-pyrrole(38).
Figure 72. \(^1\)H NMR Spectrum of (±) 2-Butyl-5-(4,4-ethylenedioxy)pentyl)-2β,3,4,5β-
tetrahydro-1H-pyrrole(37).
Figure 73. $^{13}$C NMR Spectrum of (±) 2-Butyl-5-(4,4-thylenedioxypropyl)-2β,3,4,5β-tetrahydro-1H-pyrrole(37).
Figure 74. $^1$H NMR Spectrum of $(t)$-Monomorine(1).
Figure 75. $^{13}$C NMR Spectrum of (±)-Monomorine(1).
Figure 76. $^1$H NMR Spectrum of Undec-2-yn-1-ol(52).
Figure 77. $^{13}$C NMR Spectrum of Undec-2-yn-1-ol(52).
Figure 78. $^1$H NMR Spectrum of 1-Bromoundec-2-yne(53).
Figure 79. $^{13}$C NMR Spectrum of 1-Bromoundec-2-yn(53).
Figure 80. $^1$H NMR Spectrum of Methyl L-Phenylalaninate.
Figure 81. $^{13}$C NMR Spectrum of Methyl L-Phenylalaninate.
Figure 82. $^1$H NMR Spectrum of Methyl N-(diphenylmethylene)-L-phenylalaninate(55).
Figure 83. $^{13}$C NMR Spectrum of Methyl N-(diphenylmethylen)-L-phenylalaninate(55).
Figure 84. $^1$H NMR Spectrum of (2S,3S)-2-[N-(diphenylmethylene)amino]-1-phenylhex-5-yn-3-ol(59).
Figure 85. $^{13}$C NMR Spectrum of (2S,3S)-2-[$N$-(diphenylmethylene)amino]-1-phenylhex-5-yn-3-ol(59).
Figure 86. $^1$H NMR Spectrum of (2S,3R)-2-[N-(diphenylmethylene)amino]-1-phenylhex-5-yn-3-ol (60).
Figure 87. $^{13}$C NMR Spectrum of (2S,3R)-2-[N-(diphenylmethylene)amino]-1-phenylhex-5-yn-3-ol (60).
Figure 88. $^1$H NMR Spectrum of (4S,5S)-5-(Phenylmethyl)-4-(prop-2'-yn-1'-yl)-2-oxazolidinone(61).
Figure 89. $^{13}$C NMR Spectrum of (4S,5S)-5-(Phenylmethyl)-4-(prop-2'-yn-1'-yl)-2-oxazolidinone(61).
Figure 90. $^1$H NMR Spectrum of (2S,3S)-3-benzyloxy-2-[N-(diphenylmethylen)amino]-1-phenylhex-5-yne(63).
Figure 91. $^{13}$C NMR Spectrum of (2S,3S)-3-benzyloxy-2-[N-(diphenylmethylene)amino]-1-phenylhex-5-yne(63).
Figure 92. $^1$H NMR Spectrum of (2S,3S)-3-benzyloxy-2-[N-(diphenylmethylen)amino]-1-phenyl-6-(thiomethyl)hex-5-yne(64).
Figure 93. $^{13}$C NMR Spectrum of (2S,3S)-3-benzyloxy-2-[N-(diphenylmethylen)amino]-1-phenyl-6-(thiomethyl)hex-5-yne(64).
Figure 94. $^1$H NMR Spectrum of (2S,3S)-3-benzyloxy-2-[N-(diphenylmethylene)amino]-1-phenyltetradec-5-yne(65).
Figure 95. $^{13}$C NMR Spectrum of (2S,3S)-3-benzyloxy-2-[N-(diphenylmethyIene)amino]-1-phenyltetradec-5-yne(65).
Figure 96. $^1$H NMR Spectrum of (2S,3S)-3-benzyloxy-1-phenyltetradec-5-yn-2-ylamine(51).
Figure 97. $^{13}$C NMR Spectrum of (2S,3S)-3-benzylxoy-1-phenyltetradec-5-yn-2-ylamine (51).
Figure 98. $^1$H NMR Spectrum of (2S,3R)-3-benzyloxy-1-phenyltetradec-5-yn-2-ylamine(66).
Figure 99. $^{13}$C NMR Spectrum of (2S,3R)-3-benzyloxy-1-phenyltetradec-5-en-2-ylamine(66).
Figure 100. $^1$H NMR Spectrum of (2S,3S)-3-benzylxy-1-phenylhex-5-yn-2-ylamine(71).
Figure 101. $^{13}$C NMR Spectrum of (2S,3S)-3-benzyloxy-1-phenylhex-5-yn-2-ylamine(71).
Figure 102. $^1$H NMR Spectrum of 5-Nonyl-2-(phenyl-methyl)pyrrole(68).
Figure 103. $^{13}$C NMR Spectrum of 5-Nonyl-2-(phenyl-methyl)pyrrole (68).
Figure 104. $^1$H NMR Spectrum of N-Carbomethoxy-5-nonyl-2-(phenylmethyl)pyrrole(70).
Figure 105. $^{13}$C NMR Spectrum of N-Carbomethoxy-5-nonyl-2-(phenylmethyl)pyrrole(70).
Figure 106. $^1$H NMR Spectrum of Octanoyl Nitrile(74).
Figure 107. $^{13}$C NMR Spectrum of Octanoyl Nitrile(74).
Figure 108. $^1$H NMR Spectrum of (4S,5S)-4-benzyoxy-2-[2'–cyano-1'-nonen-1'-yl]-5-(phenylmethyl)-2H-pyrrole(76).
Figure 109. $^{13}$C NMR Spectrum of (4S,5S)-4-benzyoxy-2-[2'-cyano-1'-nonen-1'-yl]-5-(phenyl-methyl)-2H-pyrrole(76).
Figure 110. $^1$H NMR Spectrum of (2S,3S,5R)-4-benzyloxy-2-[2'-cyano-l'-nonen-l'-yl]-1-methyl-5-(phenylmethyl)-pyrrolidine(77)
Figure 111. $^{13}$C NMR Spectrum of $(2S,3S,5R)$-4-benzyloxy-2-$[2'$-cyano-$1'$-nonen-$1'$-yl]-$1'$-methyl-5-$(phenylmethyl)$-pyrrolidine(77)
Figure 112. $^1$H NMR Spectrum of Diastereomeric Nitriles(78)
Figure 113. $^{13}$C NMR Spectrum of (2S,3S,5R)-1-methyl-5-nonyl-2-(phenylmethyl)-3-pyrrolidinol(2)