



Heterocyclic chemistry : unique role of heteroatoms in structure and reactivity
by Changjoo Lee

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:

To examine the influences of heteroatom and ring size of structures and reactivity in propellane series, propellanes are prepared using dianion ring annulation and Diels-Alder reaction.

A formal synthesis of maleimycin, an antibiotic natural product, was completed using, dianion chemistry and flash vacuum thermolysis (F.V.T.) conditions.

Under F.V.T. condition, 1,2-dicarbomethoxycyclopentene was prepared in nearly 100% yield. This is the key intermediate of cyclopentanoids such as antibiotic sarkomycin.

In a hydroboration study, the reactivities of propellanes are shown to depend on the HOMO energy and the atomic coefficient of olefin. Also, we see an interesting correlation between the reactivity and interatomic distance of heteroatom and the olefinic carbon atom, which is the steric control. And the stereoisomer ratio of electrophilic additions to olefins depend on the steric hinderance.

In a solvolysis study, the rate enhancement (1.6 times) was observed for the anti-tosylate of [10] relative to the syn-tosylate. Again, the big rate enhancement (70 times) was observed for the anti-tosylate of [30] relative to the syn-tosylate. This was interpreted to mean that the heteroatom does influence reactivity in these compounds. In examining the solvolysis of the different ring size and dioxo-propellane series, steric and transannular dipole effects were observed.

The major ions in the (EI) mass spectrum of [2] and propellanes have been determined and investigated. Mechanisms, illustrating the oxygen atom's role in the fragmentation process, have been proposed.

Stereospecific hydrogenation was observed in the catalytic hydrogenation of [112] and modest stereoselectivity, was observed in catalytic hydrogenation of [113] and [114].

HETEROCYCLIC CHEMISTRY-
UNIQUE ROLE OF HETEROATOMS
IN STRUCTURE AND REACTIVITY

By
Changjoo Lee

A thesis submitted in partial fulfillment
of the requirements for the degree
of
Doctor of Philosophy
in
Chemistry

MONTANA STATE UNIVERSITY
Bozeman, Montana

August 1991

D378
L5

ii

APPROVAL

of a thesis submitted by

Changjoo Lee

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.

July 29, 1991
Date

Bradford Philip Mundy
Chairperson, Graduate Committee

Approved for the Major Department

July 29, 1991
Date

Dr. P.W. Jennings
Head, Major Department

Approved for the college of Graduate Studies

August 6, 1991
Date

Henry L. Parsons
Graduate Dean

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To

My wife, parents and parents in law.

ACKNOWLEDGEMENTS

This endeavor would not have been possible without the help of a number of people. Special thanks are extended to.....

Dr. Mundy, for his everlasting encouragements,
understanding, and most of all, his support of
students.

Dr. Hong, for teaching me to love organic chemistry.

Dr. Howald, for his help on kinetic experiments.

Dr. Callis, for his helpful discussions of our
calculation data.

Dr. Sears, for his 1,000,000 th mass spectrum!! and
discussions following.

Dr. Craig, for his enthusiastic discussions on physical
organic chemistry.

Dr. Jennings, for his discussions on platinum catalyst.

Dr. Livinghouse, for his discussions on synthesis.

Dr. Houk, for providing advanced copies of his
manuscript on hydroboration study.

Mr. Larson, for his help on X-ray crystallography.

Mr. Rees, for his friendship and his help on 'life USA'

Mr. Muño, for showing me how to 'calculate'

Mr. Dunham, for his unselfish assistance.

My wife, for her understanding....

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ABSTRACT

To examine the influences of heteroatom and ring size of structures and reactivity in propellane series, propellanes are prepared using dianion ring annulation and Diels-Alder reaction.

A formal synthesis of maleimycin, an antibiotic natural product, was completed using dianion chemistry and flash vacuum thermolysis (F.V.T.) conditions.

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The major ions in the (EI) mass spectrum of [2] and propellanes have been determined and investigated. Mechanisms, illustrating the oxygen atom's role in the fragmentation process, have been proposed.

Stereospecific hydrogenation was observed in the catalytic hydrogenation of [112] and modest stereoselectivity was observed in catalytic hydrogenation of [113] and [114].

CHAPTER 1

INTRODUCTION

Neighboring Heteroatom Participation

Our lab has been interested in the unique role of heteroatoms in determining the structure and reactivity of heterocyclic compounds^{1,2,3}.

In heteroatom containing molecules, the influence of the heteroatom on reactivity has been related to the degree in which it can stabilize positive charges, as interpreted through solvolysis reactions⁴. In some cases an oxygen atom has been shown to enhance reaction rates; while in other compounds, an oxygen has been shown to retard reactivity. Interpreting oxygen's effect in imparting reactivity on the molecule has been difficult because oxygen does not easily share its lone pair electrons in the stabilization of positive charges, a consequence of its high electronegativity. Yet, oxygen is very effective at stabilizing positive charge on an adjacent bonded carbon atom. As a result of these many differences, the various effects oxygen imparts on structure and reactivity are not completely understood.

Oxygen's influence is generally to be more subtle than that of nitrogen or sulfur, which have lower

electronegativities and more diffuse lone pair orbital. Often this subtle influence is reflected in small rate differences. Schleyer⁵ suggests, however, "the detection of any rate enhancement due to anchimeric assistance, no matter how small, is indicative of strong (not weak!) participation by the neighboring group". We, and others, have tried to analyze the participation effects.

Gratz and Wilder⁶ have proposed the possibility of an intermediate of the type, [1], to account for the large (750 fold) rate increase of the endo-tricyclic sulfide relative to the carbon analog. This can be compared to the much smaller 2.52 rate increase of endo-tricyclic ether relative to the carbon analog. (Figure 1)

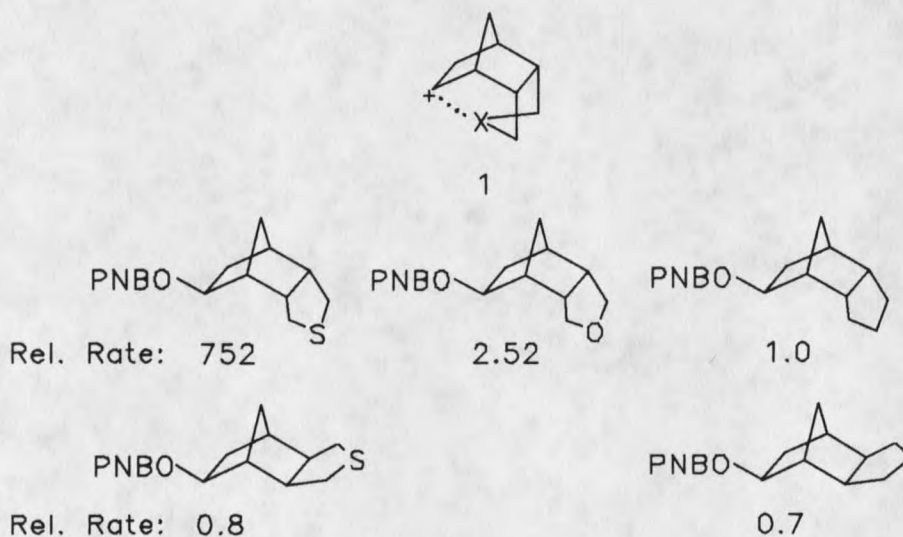
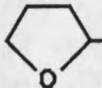


Figure 1. A Remote Heteroatom Participation.

Closson⁷ also has found anchimeric assistance by the tetrahydrofuranlyl group. This rate enhancement was shown to

Table 1. Relative Rates of Solvolysis of p-Bromobenzenesulfonates in Acetic Acid at 50°C.

<u>Compound</u>	<u>Relative Rate.</u>
$\text{CH}_3\text{---CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{OBs}$	1
$\text{CH}_3\text{O---CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{OBs}$	657
 $(\text{CH}_2)_n\text{---OBs}$	
$n=1$	13.1
$n=2$	26.3
$n=3$	1510
$n=4$	12400
$n=5$	1380

These systems are unlike the conformationally rigid norbornyl systems of Wilder, and greater conformational flexibility exists. As a result, oxygen is better able to stabilize positive charge through Neighboring Group Participation (NGP) (Figure 2).

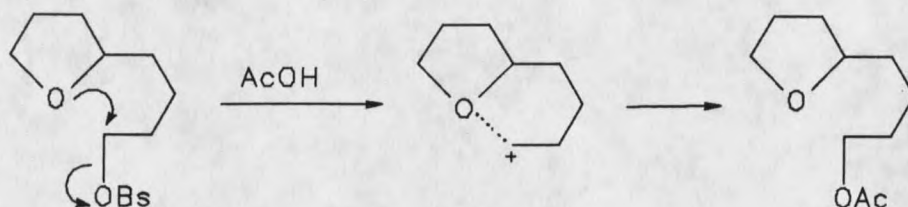


Figure 2. Oxygen Intermediate Stabilization.

Tarbell and Hazen⁸ investigated the effects of oxygen on the rates of solvolysis of carbo- and heterocyclic brosylates. They observed the rates of solvolysis to be an order of magnitude slower than would be expected from a simple through-bond dipole effect of the oxygen (Figure 3). This information, coupled with the fact that the corresponding heterocyclic ketones had higher carbonyl stretching frequencies than their carbocyclic counterparts, led Tarbell and Hazen to conclude that they were dealing with a transannular dipole effect as illustrated in Figure 4.

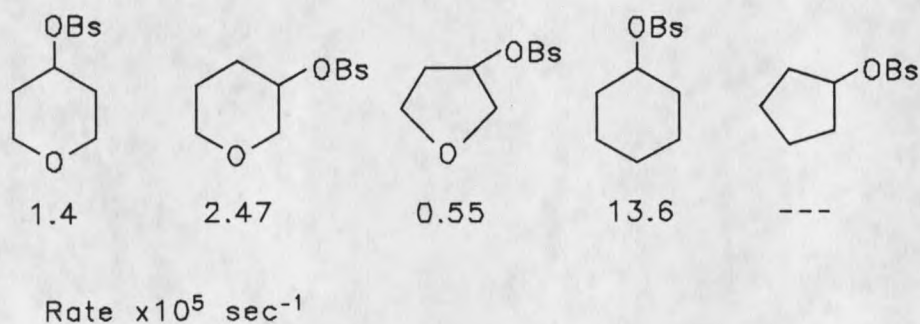


Figure 3. Solvolysis of Oxygen Heterocyclic Compounds.

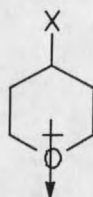
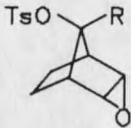
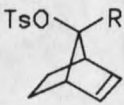
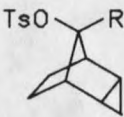
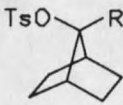


Figure 4. Transannular Dipole Effect.

The dipole associated with the ether oxygen was destabilizing the incipient carbonium ion in the solvolysis and increasing the double bond character of the carbonyl group in the corresponding ketones.

Gassman⁹ used the method of "increasing electron demand" to determine the relative ability of the carbon-carbon bond of an epoxide, a cyclopropyl group, and a pi-bond to stabilize the carbonium ion formed during solvolyses of the compounds shown in Table 2.

Table 2. Oxygen's Inductive Effect on Carbon-Carbon Bond Participation.

<u>Compound</u>	<u>Relative Ratio(Me/H)</u>
	10^8
	10^{11}
	10^{14}
	1

By examining the α -methyl/hydrogen ratio, the changing electronic effects could be isolated from the changing steric effects of the molecule. This method is based on the assumption that if the electron demand of the incipient carbonium ion in the transition states is satisfied by the electron density donated by a substituent on the carbon atom, then a remote functional group will not participate in the reaction. The relative ability of a functional group to be involved in NGP was determined by comparing the rate when the electron demand was satisfied by substituents (tertiary

carbocations) to the ratio when electron demand was satisfied by remote functional groups. Note, however, the significantly reduced rate enhancement of the epoxide relative to its cyclopropyl group analog. This is attributed to oxygen's inductive effect on carbon-carbon bond participation.

In a study done by Otzenberger¹ in 1971, oxymercuration of the tetrahydrophthalan, [2] was found to give predominantly syn-alcohol, [3] (Figure 5).

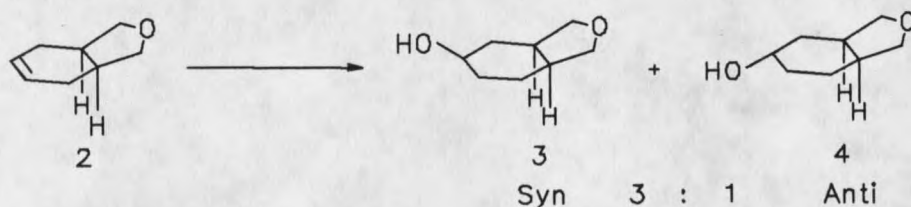


Figure 5. Oxymercuration of *cis*-8-Oxabicyclo[4,3,0]oct-3-ene.

It had been previously demonstrated for norbornyl systems¹⁰ that heteroatom participation in the transition state leading to the products was responsible for the observed stereoselectivity of chemistry occurring at the double bond (Figure 6). Isolation of the nitrogen alkylated product, [6] was interpreted as firm evidence for remote heteroatom participation in these systems.

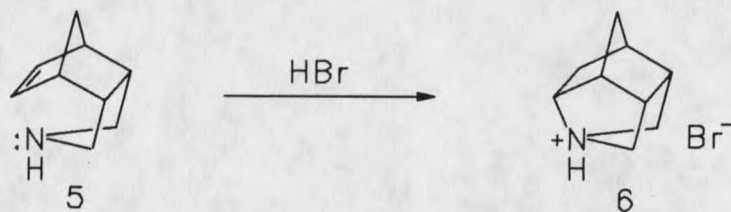


Figure 6. Heteroatom Participation in Aza-norbornyl System.

The question which faced Otzenberger was, could the same type of heteroatom effect be operating in the tetrahydrophthalan case? In his experimental results, Otzenberger suggested that the heteroatom effect was probably the main causative factor in determining the outcome of the oxymercuration of [2].

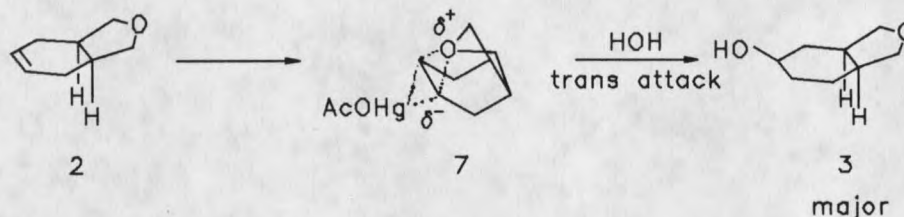


Figure 7. Charge Stabilization by Oxygen Atom in *cis*-Tetrahydrophthalan.

Figure 7 shows the transformation of the tetrahydrophthalan, [2], to the *syn*-alcohol, [3] via intermediate, [7], for which Otzenberger proposed that the developing charge of the mercurinium ion was stabilized by the neighboring oxygen atom. One unexplored possibility was the potential for simple steric effects to dominate the course of the

reaction. As illustrated below, the pi-system of the cyclohexene ring is facially dissimilar (Figure 8);

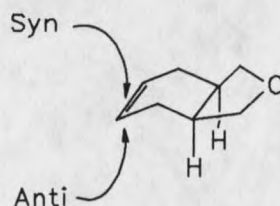


Figure 8. Steric Bias in *cis*-Tetrahydrophthalan.

One face of the double bond is *syn* to the oxapropano group while the opposite face of the double bond experiences only two hydrogen atoms.

Thus, the question to be asked was: could observed product ratios be attributed to merely steric factors? Nuclear magnetic resonance experiments had suggested¹¹ that the conformation of the tetrahydrophthalan molecule was predominantly the more stable unfolded isomer depicted in Figure 9.

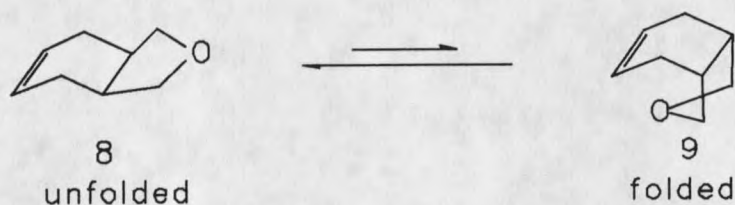


Figure 9. Conformational Equilibrium in *cis*-Tetrahydrophthalan.

In spite of these facts, the question of steric control remained insoluble for the system at hand. Clearly, in order to unambiguously address this question, a more

propitious molecule should eliminate the steric discrepancies inherent in the tetrahydrophthalan system, while concomitantly retaining the relationship of the oxygen atom to the alkene function. The best such molecule presented itself as the propellane, [10] illustrated below (Figure 10).



10

Figure 10. 8-Oxatricyclo[4,3,3,0]dodec-3-ene.

As can be seen from the drawing, the propellane presents nearly identical steric bulk to each face of the double bond; thereby permitting facial distinction only on the basis of heteroatom character. A possible objection to this statement could be proposed on the basis of a conformational preference for the double bond to fold toward or away from the heteroatom (Figure 11); however, [11] and [12] would seem to have equivalent reactivity by calculational methods. The ground state energies, energies of HOMO's and Pz-orbital coefficients are essentially identical.

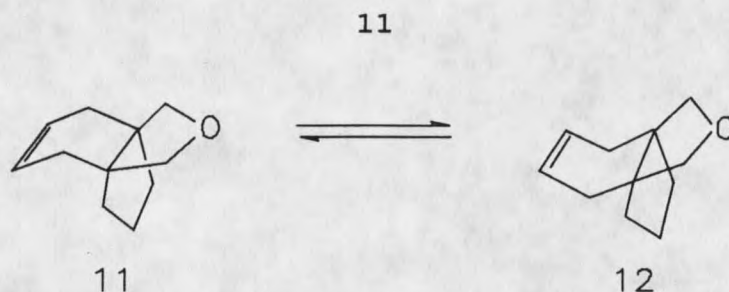


Figure 11. Conformational Equilibrium of Oxa-propellane.

When Wilkening¹² subjected [11] to an epoxidation study using mCPBA and to an oxymercuration study catalyzed by trace amounts of nitric acid in methanol, he found no indication of oxygen participation influencing product stereochemistry. The product ratios in both studies were 1:1 (Figure 12). As a result, he concluded that simple steric effect, not oxygen participation, controlled the reaction.

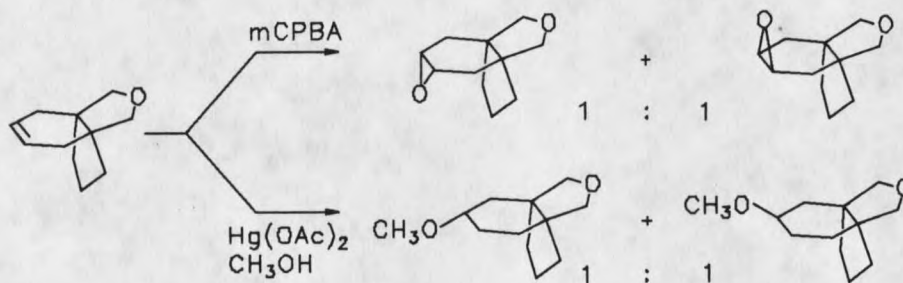


Figure 12. Absence of Oxygen Participation in 8-Oxatricyclo[4,3,3,0]dodec-3-ene.

Johnson³ carried out the solvolyses of the *syn*- and *anti*- tosylate derived from [2] and [10] (Tables 3 and 4). A slight rate enhancement (1.53 times) was observed for the *anti*- tosylate, [16] relative to the *syn*- isomer. But,

identical reactivities were observed in the solvolysis of the *syn*- and *anti*- tosylates, [13] and [14].

Table 3. Kinetic Results of the Solvolysis of [13] and [14].

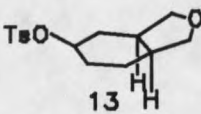
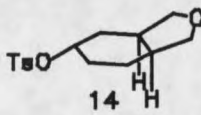
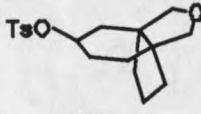
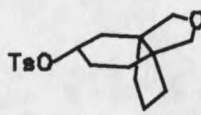
<u>Compound</u>	<u>Temp. (°C)</u>	<u>k x 10⁴ (s⁻¹)</u>	<u>E_a (Kcal/mol)</u>
 13	35.84	0.607	26.2
	50.00	3.47	
	62.87	14.3	
 14	35.78	0.607	25.8
	50.20	3.32	
	63.00	13.9	

Table 4. Kinetic Results of the Solvolysis of [15] and [16].

<u>Compound</u>	<u>Temp. (°C)</u>	<u>k x 10⁴ (s⁻¹)</u>	<u>E_a (Kcal/mol)</u>
 15	35.82	1.91	22.7
	50.10	9.35	
	63.00	37.9	
 16	35.70	2.90	21.9
	50.15	14.7	
	62.90	52.7	

Since there remain many unanswered questions concerning the influences of the heteroatoms on structure and reactivity, an effort has been made to obtain further insight into heteroatom effects. To examine the heteroatom's role on structure and reactivity, the following investigations were proposed.

- (1) Prepare the sulfur analogues of [10] and determine the role of the sulfur atom in influencing the stereochemistry of electrophilic addition to the alkene bond. Examine the solvolysis of tosylates derived from this compound. The lone pair electron orbitals of the sulfur are more polarizable than oxygen, and one would expect greater influences in imparting both stereochemistry and reactivity on the molecule.
- (2) Synthesize 8,11-dioxatricyclo[4,3,3,0]dodec-3-ene and examine the influence of the solvolysis of the tosylates derived from this compound. One would expect either an oxygen participation or a transannular dipole effect. What then is the experimental effect?
- (3) Examine the role the oxygen atom plays in influencing structure and reactivity in a more conformationally flexible system. A system to address this question is found with 8,12-dioxatricyclo[5,4,3,0]tetradec-3-ene and the tosylates derived from this alkene.
- (4) Build different ring size analogues of [10] by using dianion ring annulation. It would be interesting to

examine the effect ring size plays in influencing structure and reactivity in the different ring size propellane systems.

- (5) Synthesize a natural product such as maleimycin by using dianion chemistry and F.V.T.
- (6) Synthesize and subject to catalytic hydrogenation 3-methyl-*cis*-1,6-dicarbomethoxybicyclo[4,3,0]non-3-ene, 3-methyl-*cis*-1,6-dihydroxymethyl bicyclo[4,3,0]non-3-ene, and 3-methyl-8-oxatricyclo[4,3,3,0]dodec-3-ene. If oxygen is complexing with catalyst, one would expect a particular stereoselective reduction. If hydrogenation is controlled by steric factor, one would expect opposite stereochemistry.
- (7) As a new experimental probe to observe oxygen's role in imparting reactivity on the molecule, elucidate the electron impact mass spectroscopy fragmentation mechanisms of a number of heterocyclic compounds, and determine oxygen's role in this process.
- (8) Examine the MSU-developed interface for its use in measuring absolute kinetic experiments.
- (9) Use calculational approaches, particularly MM2 and MNDO, to investigate the propellane systems and their derivatives.
- (10) Confirm the relative stereochemistry for the tricyclic para-nitrobenzoates, by X-ray data.

CHAPTER 2

SYNTHETIC STUDIES

Propellane Synthesis

Previous work suggested that the tetrahydrofuran ring of the propellane was constructed by dehydration of a 1,4-diol. Since the 1,4-dihydroxy functionality is easily obtained from succinate derivatives, the key intermediate for a synthesis of the desired propellanes was the diester, [17]; which presented two practical options for synthesis (Figure 13). The first of these required an addition of butadiene to a 1,2-dicarboxycyclopentene such as the dimethyl ester, [18]. Literature preparations of [18] gave unsatisfactory yield¹³. There was ample reason for concern regarding the Diels-Alder reaction of [18] with butadiene as well; as tetra-substituted alkene are often sterically and/or electronically inhibited as dienophiles¹⁴.

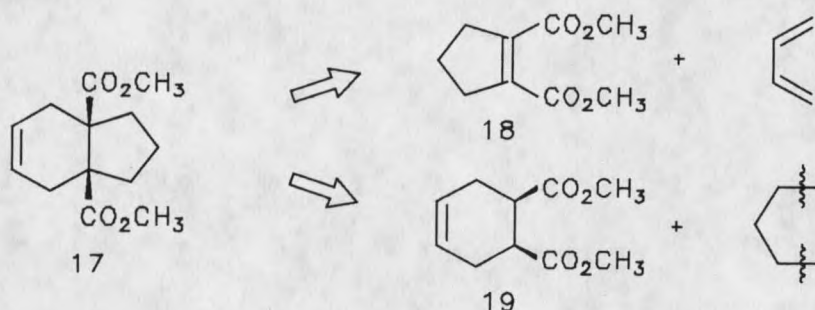


Figure 13. Synthetic Routes to *cis*-1,6-Dicarbomethoxybicyclo[4,3,0]non-3-ene.

The alternative approach proceeded from the readily available 3,4-dicarbomethoxycyclohexene, [19], by attaching different rings through dianion ring annulation methodology. One goal of this project was to demonstrate this type of ring annulation for constructing 4, 5, 6, and 7 membered rings.

It was postulated that a vicinal ester dianion generated from [19] might be a legitimate intermediate if a disubstituted alkane could be found to act as an electrophile in the dianion ring annulation reaction (Figure 14).

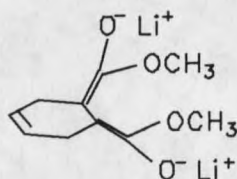


Figure 14. Dianion of 3,4-Dicarbomethoxycyclohexene.

Additional credence to this approach was gleaned from the anticipated stability of the dianion generated from the vicinal diester, as conjugation of the enolates would serve to stabilize the developing charge. Also, this reaction offered the expected formation of only a *cis*-vicinal diester. The dienolate, being presumably planar to permit conjugation, implied that once the first alkylation has occurred the second displacement would proceed from the same face, since formation of the *trans* ring juncture would require the alkyl group to twist between the two ester residues. This hypothesis was examined by performing the experiments outlined in Figure 15.

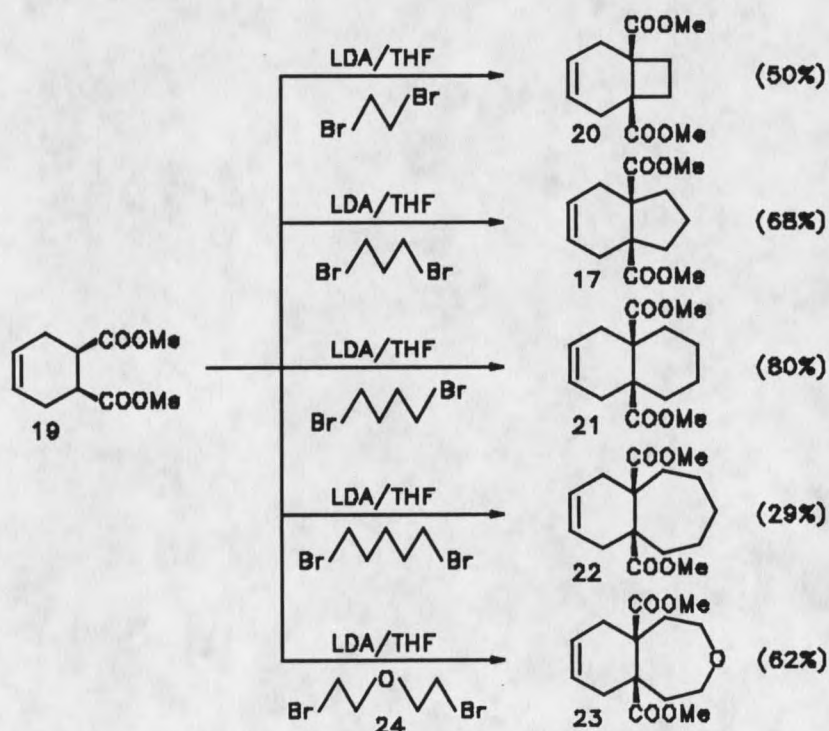


Figure 15. Dianion Mediated Syntheses of Different Ring Size Diester Compounds.

When 1.5 equivalents of dibromoalkane were added to the cooled, bright red THF solution of the dienolate of 3,4-dicarbomethoxy cyclohexene, the bicyclic ester was obtained (Diester, [22], showed low yield, 29%, due to elimination bi-product). The synthesis of the heterocyclic propellane was accomplished in a straight-forward manner as described in Figure 16.

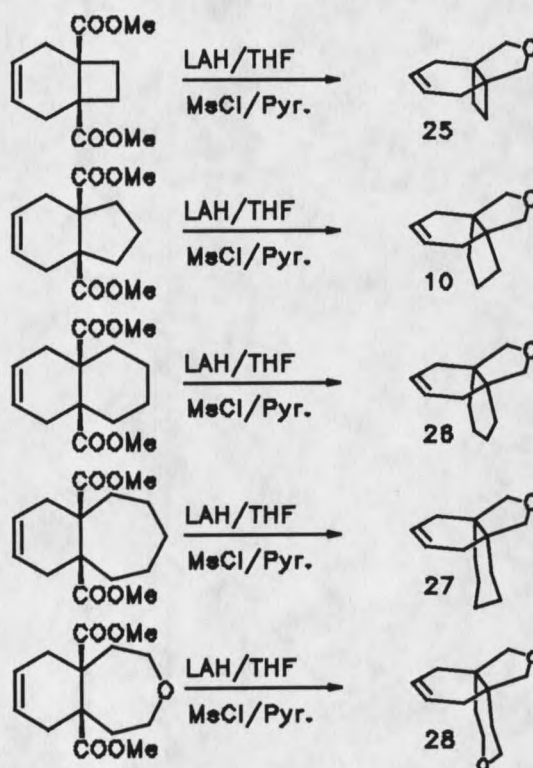


Figure 16. Syntheses of Propellanes.

To make the sulfur-containing propellane, [30], the diester, [17] was first reduced with lithium aluminum hydride. Treatment of the resulting diol with methanesulfonyl chloride in pyridine gave the dimesylate,

[29] in 78% yield. Heating the dimesylate in dry hexamethylphosphoramide (HMPA) with anhydrous sodium sulfide led to sulfide, [30] in 86% yield. Paquette¹⁵ reported that the use of dry HMPA is essential to the success of this two-fold S_N2 displacement-cyclization. The high cation-solvating capacity of HMPA, which greatly reduces the effective size of the nucleophile relative to its bulk in other (especially protic) media, causes a marked acceleration of desired chemical change. The synthesis of propellane, [30] is illustrated in Figure 17.

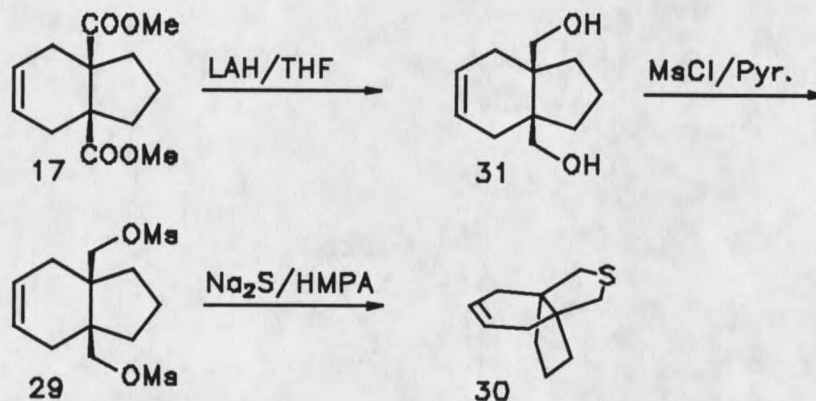


Figure 17. Synthesis of 8-Thiatricyclo[4,3,3,0]dodec-3-ene.

The reaction of tetraethylethylene tetracarboxylate, [32] with butadiene provided cyclohex-4-ene-(1,1,2,2)-tetraethylester, [33]. The synthesis of [32] was accomplished in a procedure used by Krapcho¹⁶ (Figure 18).

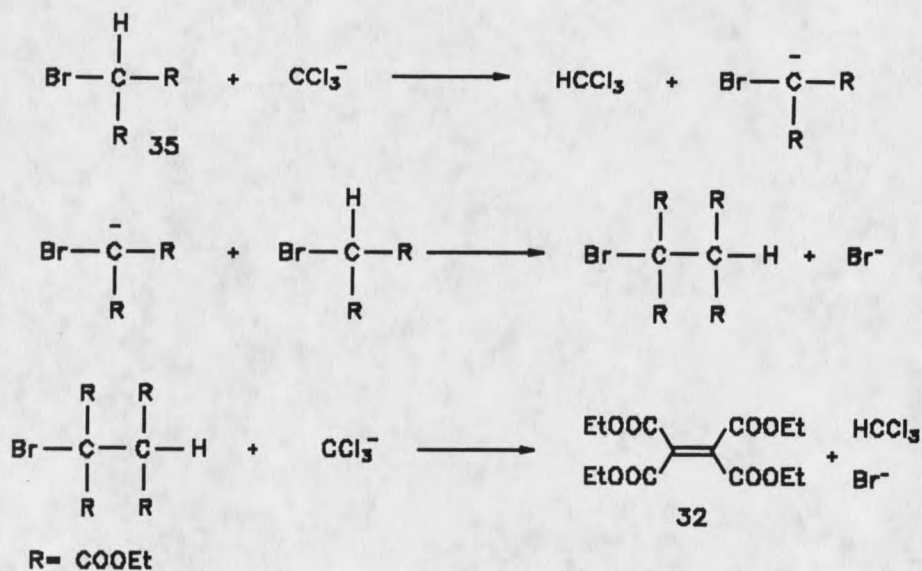


Figure 18. Synthesis of Tetraethylethylene-tetracarboxylate.

The tetra ester, [33] was reduced with lithium aluminum hydride and the resulting tetraol was extracted by continuous extraction. Treatment of the tetraol with KHSO_4 at 190-200°C gave the desired 8,11-dioxatricyclo[4,3,3,0]dodec-3-ene, [34]. This dioxapropellane synthesis is described by Figure 19.

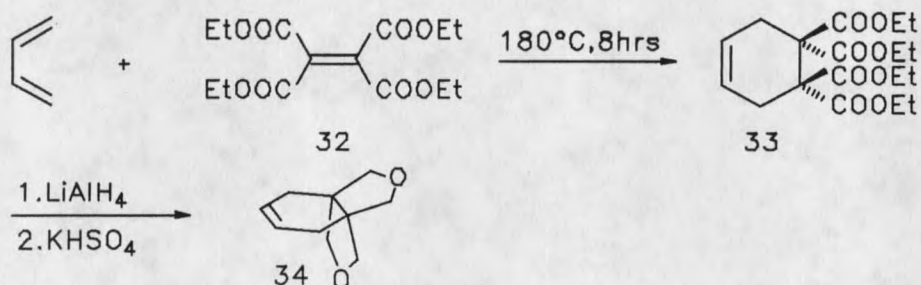
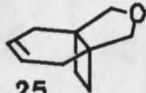
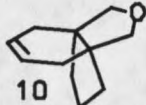
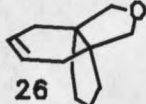
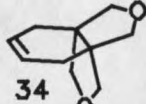
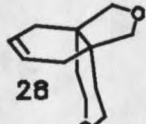


Figure 19. Synthesis of 8,11-Dioxatricyclo[4,3,3,0]dodec-3-ene.

In the purification of propellanes, for example [10], [25], [26], [28], and [34], a florisil separation was employed to cleanly separate unreacted starting material from the propellane system. Although structurally very similar, different solvent systems were needed for effective separations. The solvent systems are reported in Table 5.

Table 5. Solvent Systems for Propellane Purification.

<u>Compound</u>	<u>Ethylacetate:Hexane</u>
 25	1 : 19
 10	1 : 9
 26	2 : 98
 34	2 : 8
 28	3 : 7

In general, the *syn*- and *anti*-tosylates, were synthesized from its parent propellane alkene system. After hydroboration, the corresponding alcohol mixture was

converted to the *para*-nitrobenzoate derivatives. Flash chromatography was then employed to cleanly separate this mixture into isomerically pure *syn*- and *anti*-tricyclic-*para*-nitrobenzoates. Saponification of the isomerically pure *syn*- and *anti*-tricyclic-*para*-nitrobenzoates afforded the respective *syn*- and *anti*-alcohols, which maintained their isomeric purity. The hydrolyzed alcohols were compared to known samples. No isomerization took place during hydrolysis. The alcohols were then easily converted to *syn*- and *anti*-tricyclic-tosylates (Figure 20).

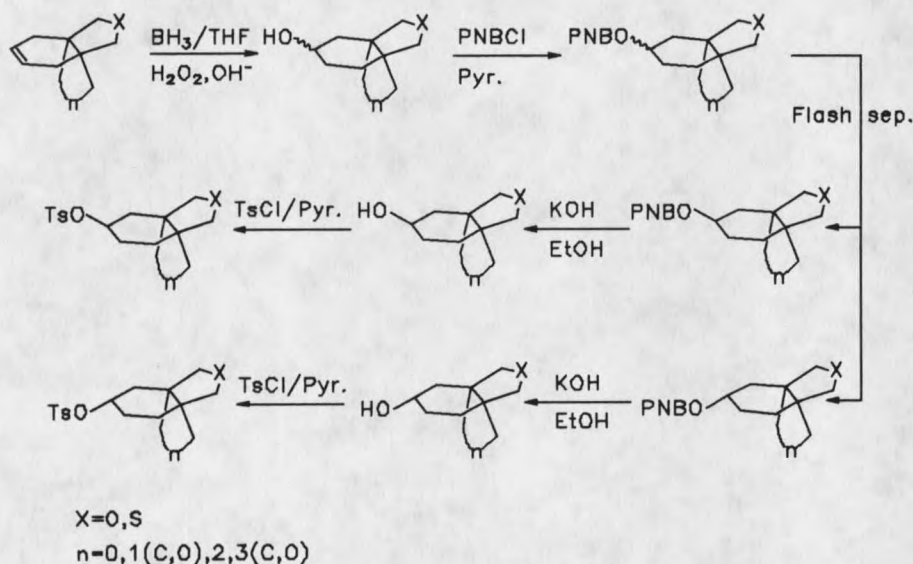
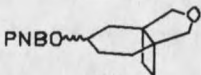
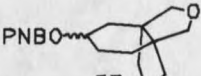
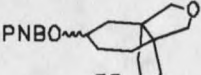
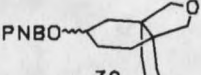
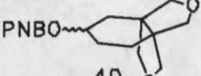
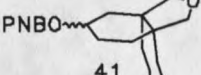
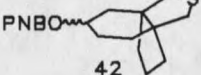


Figure 20. Syntheses of *syn*- and *anti*-Tricyclic-tosylates Derived from the Corresponding Propellane.

Solvent systems used for *para*-nitrobenzoate separations are reported in Table 6.

Table 6. Solvent Systems for *para*-Nitrobenzoate Separation.

Compound	CH ₂ Cl ₂ :EtOAc:Hexane		
 36	10	:1	:1
 37	10	:1	:1
 38	10	:1	:1
 39	10	:1	:1
 40	0	:1	:1
 41	0	:1	:1
 42	25	:1	:1

As part of our continuing interest in the chemistry of propellanes, we have already applied the methodology to the synthesis of valerane¹⁷ and modhephene¹⁸. A consequence of our immediate concern was the realization that we could synthesize maleimycin. Our approach is outlined below.

Maleimycin Synthesis

Maleimycin is a bicyclic maleimide antibiotic elaborated by Streptomyces Showdoensis, and assigned structure [43] by Suhadolnik¹⁹ (Figure 21). Maleimycin

shows activity against bacteria and is also active against leukemia L-1210 cells.

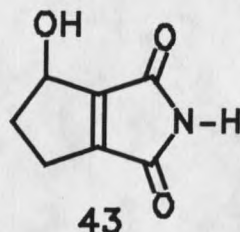
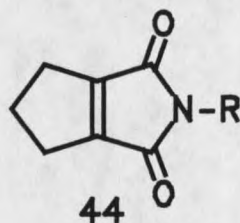
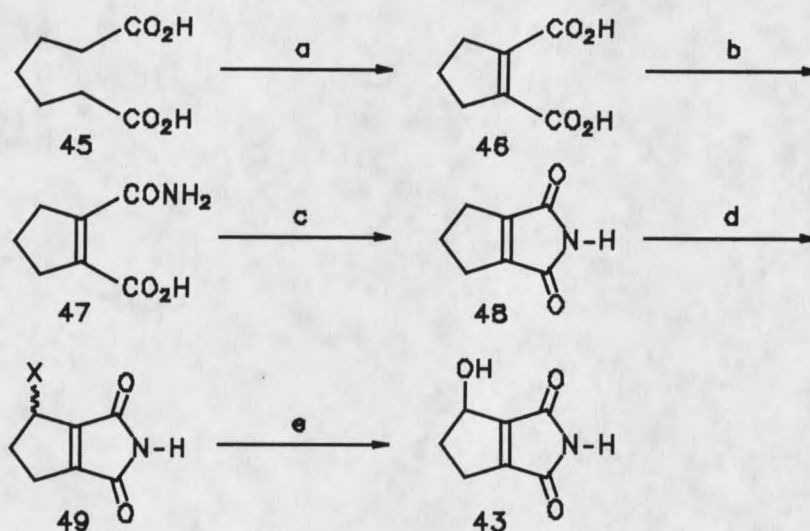


Figure 21. Structure of Maleimycin.

Kasugai²⁰ reported that N-substituted imides of general structure, [44] are also known to have fungicidal and herbicidal activity.



Maleimycin was prepared by Weinreb²¹ according to the steps outlined in Figure 22.



X=Br, OCOCF_3

a. (1) SOCl_2 , (2) Br_2 , (3) MeOH , (4) NaH , DMF

b. AcO_2 , NH_4OH c. TFAC_2

d. NBS, then Ag^+ TFAC^- e. $\text{PH}=4$

Figure 22. Weinreb's Synthesis of Maleimycin.

Our interest in making the five-five fused ring system of this molecule using dianion annulation suggested a simpler approach. Jun¹⁷ chose succinimide as a starting material for his earlier attempt. This was N-substituted with the benzyl group because the imide proton hinders formation of the needed dianion. Succinimide, [50], benzyl chloride and potassium carbonates were refluxed and to give N-benzyl succinimide, [51], (Figure 23).

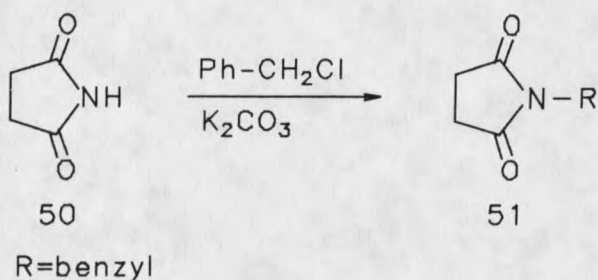


Figure 23. Synthesis of N-benzyl succinimide.

When 2.5 equivalents of lithium diisopropyl amide were mixed with [51], a reddish black color of the dienolate was formed; but, this dianion did not react with 3-bromoethylpropionate. Yamamoto²² reported difficulty in employing 3-bromoethylpropionate in condensations with the dianion and he suspected that the proton exchange process was fast (Figure 24).

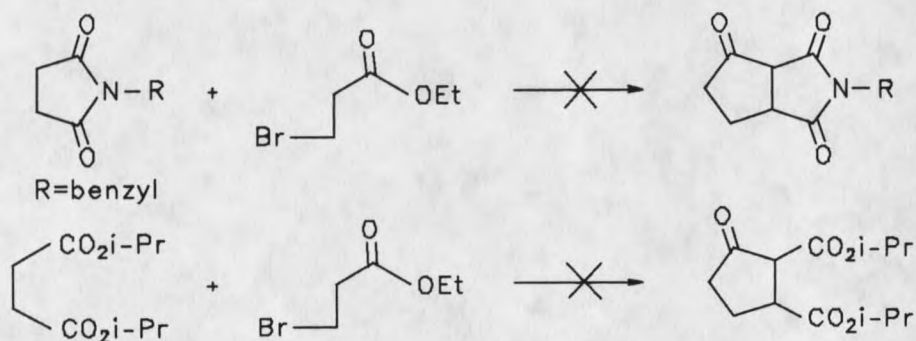


Figure 24. Attempted Synthesis of Cyclopentanones.

We used 1,3-dibromopropane for this dianion reaction and made *cis*-3-(N-benzyl)-2,4-dioxo-3-azabicyclo[3,3,0]heptane, [52], in 60% yield (Figure 25).

In order to introduce the 1,2-double bond in [52], Wilkening's²³ method was used. The dienolate of [52] was reacted with 1.1 equivalents of iodine in the established method, but this reaction did not result in formation of the double bond (Figure 26)¹⁷.

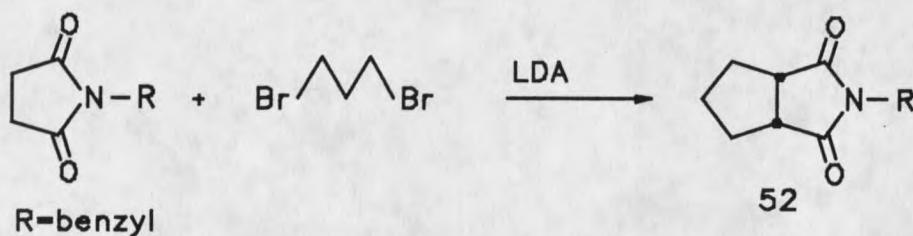


Figure 25. Synthesis of *cis*-3-(N-benzyl)-2,4-dioxo-3-azabicyclo[3,3,0]octane.

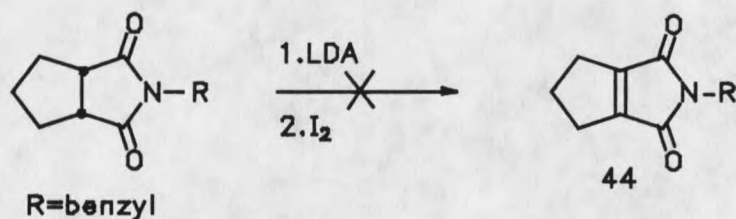


Figure 26. Attempted Synthesis of 3-(N-benzyl)-2,4-dioxo-3-azabicyclo[3,3,0]oct- $\Delta^{1,5}$ -ene.

The synthesis required modification. Readily available *cis*-1,2,3,6-tetrahydrophthalimide, [53], treated with potassium carbonate, and benzylchloromethyl ether, was refluxed to give N-benzyloxymethyl-*cis*-1,2,3,6-tetrahydrophthalimide [54] (91% yield). When 2.5 equivalents of lithium diisopropyl amide were mixed with [54], a red-colored dienolate was formed, and this dianion,

when reacted with 1,3-dibromopropane, gave N-benzyloxymethyl-7,9-dioxo-8-azatricyclo[4,3,3,0]dodec-3-ene, [55] (61% yield). Deprotection with BBr₃ provided 7,9-dioxo-8-azatricyclo[4,3,3,0]dodec-3-ene, [56] (83% yield). Finally, this molecule readily underwent retro-Diels Alder reaction under F.V.T. condition (~600°C) to provide 60% [48], and 35% starting material (Figure 27). The four-step synthesis of [48], including the protection and deprotection steps, constitutes a formal synthesis of maleimycin and shows a simple, general entry to these molecules.

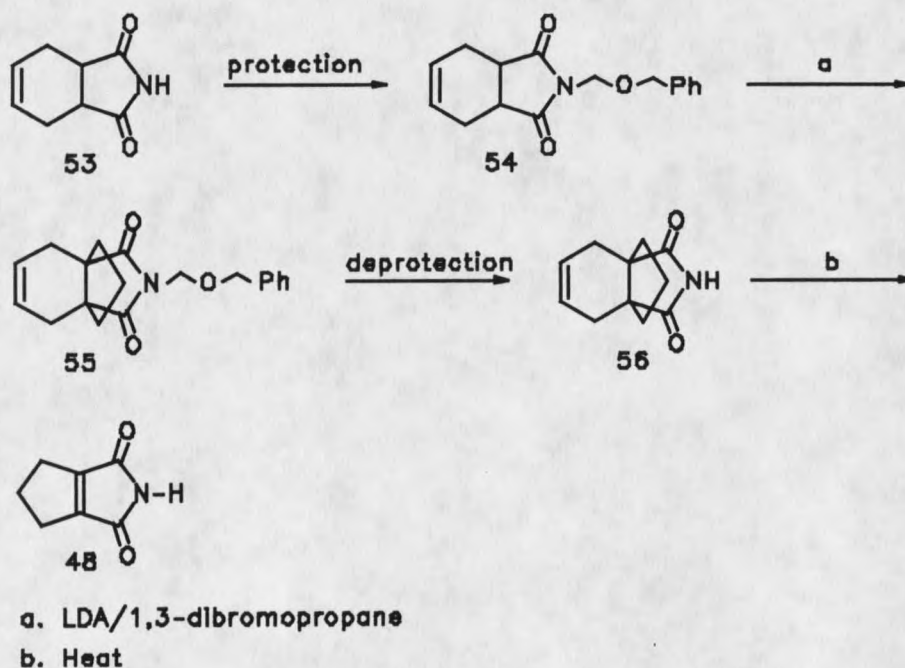


Figure 27. Synthesis of 2,4-Dioxo-3-azabicyclo[3,3,0]oct- $\Delta^{1,5}$ -ene.

1,2-Dicarbomethoxycyclopentene Synthesis

Another versatile aspect of the vicinal ester dianion was revealed during the course of experimentation aimed at the synthesis of 1,2-dicarbomethoxycyclopentene. Due to some interest in simple cyclopentanoids such as the antibiotic sarkomycin (Figure 26)²⁴, and the related compounds shown below^{25,26,27}, (Figure 28), we felt that the dianion methodology could be fruitfully employed in this area.

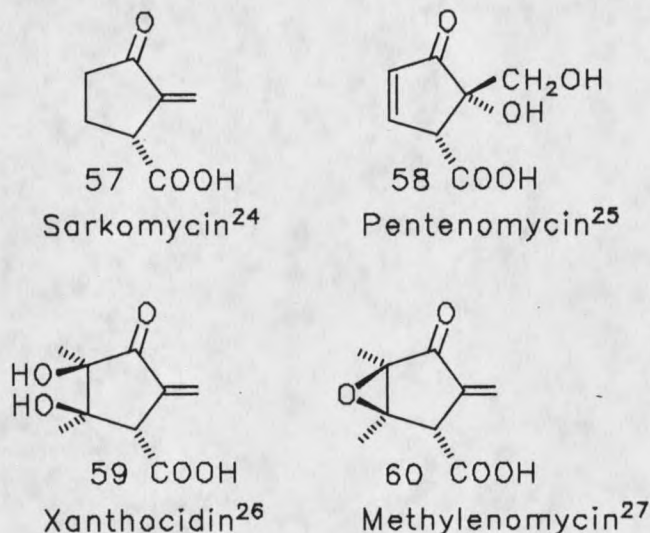
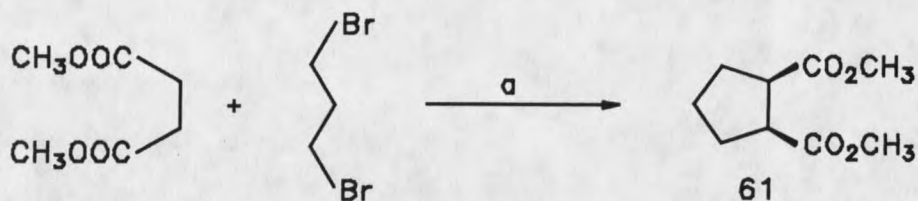


Figure 28. Simple Cyclopentanoid Natural Products.

When the dianion of dimethylsuccinate was treated with 1,3-dibromopropane, 1,2-dicarbomethoxycyclopentane, [61] was obtained in 51% yield following distillation (Figure 29).



α . 2.5equi.LDA/THF, -78°C

Figure 29. Synthesis of 1,2-Dicarbomethoxycyclopentane

In order to introduce the 1,2-double bond in [61], a number of suitable oxidizing agents were tried - all to no avail. However, when the dienolate of [61] was prepared and reacted with 1.1 equivalent of iodine, the desired cyclopentene, [18] was formed in 85% yield (Figure 30)¹⁸.

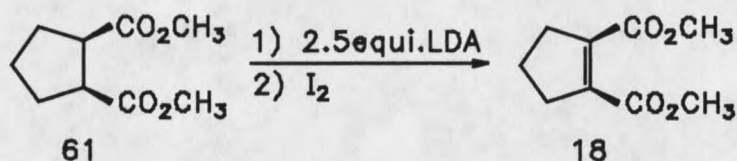


Figure 30. Synthesis of 1,2-Dicarbomethoxycyclopentene.

The proposed mechanism of this transformation is shown in Figure 31. In subsequent experiments, it was discovered that cuprous iodide also affected this transformation in high yield.

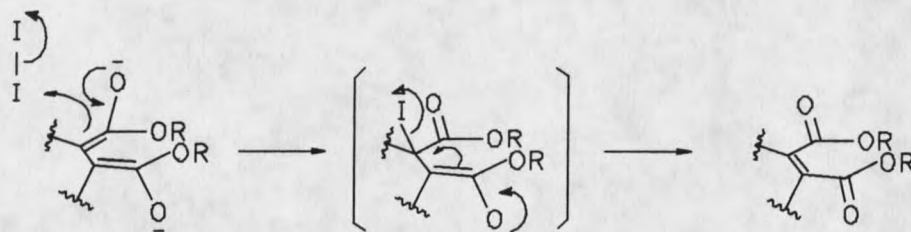


Figure 31. Mechanism of the Dienolate Mediated Oxidation of 1,2-Dicarbomethoxycyclopentane.

Using F.V.T. condition, we converted *cis*-1,6-dicarbomethoxybicyclo[4,3,0]non-3-ene, [17] to the desired product, [18] in 99% yield (Figure 32). Also, we can prepare different ring size analogues of [18]. For future work, it will be interesting to examine the effect of ring size in the retro-Diels Alder reaction.

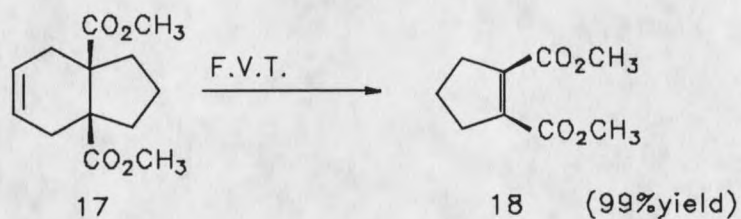


Figure 32. Synthesis of 1,2-Dicarbomethoxycyclopentene.

CHAPTER 3

STERIC EFFECTS OF RING SIZE AND HETEROATOM EFFECTS

Competitive Hydroboration Studies

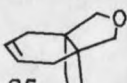
The hydroboration competition studies on compounds, [10], [25], [26], [27] reported in Table 7, demonstrate steric effects of ring size and electronic effects of heteroatom.

After our initial studies, we found that the GC peak area indicated that there was a non-linear dependency on molecular size which would have to be determined for each set of compounds in some manner. The problem could be avoided if the GC analyses were carried out in such a manner that peak areas could be determined for both reactants with an internal standard, such as anthracene. The competitions were carried out with 1 equivalent of each propellane systems, internal standard and 0.1 equivalent of $\text{BH}_3\text{:THF}$. The large reactant peaks and very small product peaks had to be recorded in the GC trace of reaction mixture. The relative rate was determined from the equation below.

$$\text{Relative Rate} = \frac{\ln \left(\frac{[\text{P1}]}{[\text{IS}]} / \frac{[\text{P2}]}{[\text{IS}]} \right)}{\ln \left(\frac{[\text{SP1}]}{[\text{IS}]} / \frac{[\text{SP2}]}{[\text{IS}]} \right)}$$

[P1]	G.C. peak area of propellane in a product
[P2]	G.C. peak area of propellane in a reactant
[SP1]	G.C. peak area of standard propellane, [10] in a product
[SP2]	G.C. peak area of standard propellane, [10] in a reactant
[IS]	G.C. peak area of internal standard, anthracene

Table 7. Hydroboration Competition Results of [10], [25], [26] and [27].

<u>Compound</u>	<u>Relative Rate $\pm$ 5%</u>
 24	0.42*
 10	1.00*
 25	0.17*
 26	1.10

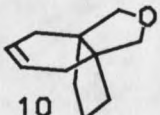
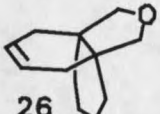
*: Average of three runs

On the basis of hard and soft acid base theories²⁸, electrophilic attack on olefins is governed by the Coulombic interactions between reactant and substrate at the reactive

site (charge control) and the interactions between the highest occupied molecular orbital of the olefin and the lowest unoccupied molecular orbital of the electrophile (orbital control). According to HSAB Theory, a soft acid (electrophile) is most likely to interact at the positions with the largest coefficients, ie. orbital control. We considered its LUMO to be constant. Therefore, the entire HOMOs of the olefins were examined to see if there were large coefficients, especially on the oxygen atom, that could favorably interact with the electrophile.

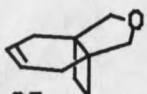
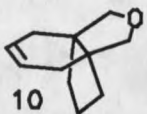
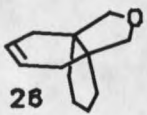
Within the framework of the FMO model, the reactivity of a olefin toward an electrophile should increase with decreasing energy separation between the olefin HOMO and LUMO on the electrophile. Since the LUMO of the electrophile remains constant for each study, this relative reactivity should parallel the relative HOMO energies, which are reported in Table 8. MNDO calculation suggested that these propellanes have similar HOMO energy (± 15 cal) except for [25]. Therefore, based solely on orbital influences, three propellanes should have equal reactivities. But, experimentally, there were some differences on reactivities towards electrophile.

Table 8. HOMO Energies of [10], [25], [26], and [27].

<u>Compound</u>	<u>Energy(eV)(HOMO)</u>
 25	-9.92926
 10	-9.93314
 26	-9.93404
 27	-9.93293

Based on FMO theory, the reactivity of electrophilic additions to olefins assumes that electrophilic attack will occur where the π -bond is most heavily concentrated. The HOMO Pz atomic orbital coefficients are reported in Table 9.

Table 9. HOMO Pz Atomic Orbital Coefficients of Olefinic Propellanes.

<u>Compound</u>	<u>Contribution(%) to MO(Av.ofPzi²,Pzj²)</u>	<u>CPzi</u>	<u>CPzj</u>
 25	42.461%	-0.64967	-0.65357
 10	42.506%	-0.65102	-0.65291
 28	42.383%	0.65056	0.65147
 27	42.464%	-0.65163	-0.65165

According to above data, we can see that there is a corresponding relationship between the relative reactivity and atomic coefficient of the double bond (Pz orbital) (Figure 33). It is still questionable about the relationship between the relative reactivity and atomic coefficient of the double bond (Pz orbital) since the differences of the coefficient (Pz orbital) shown between the four propellane are within 0.14% of contribution to HOMO (Figure 34).

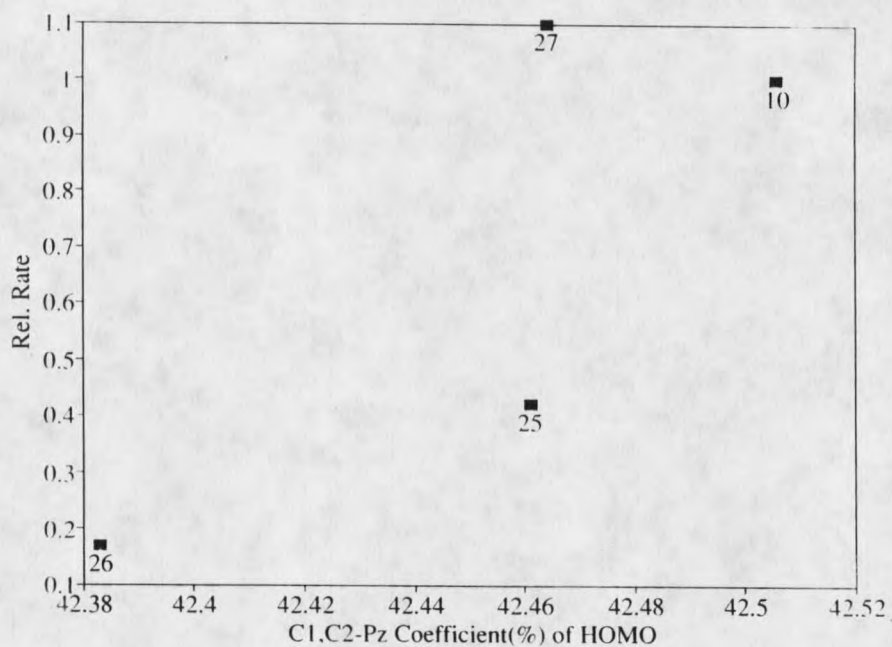
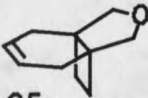
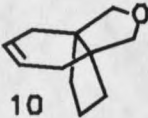
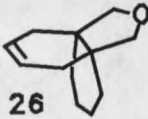
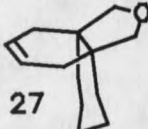


Figure 33. Relationship between the Relative Rate and Atomic Coefficient of Double Bond.

One would expect that the larger coefficient of the heteroatom would retard reactivity of hydroboration, due to this complexing effect. In examining the HOMO's coefficient on oxygen, it is obvious that a small coefficient exists on oxygen (less than 1% contribution to HOMO) (Table 10).

Table 10. HOMO Coefficient of Oxygen.

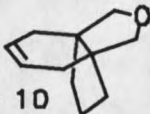
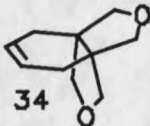
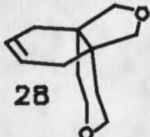
<u>Compound</u>	<u>Contribution(%) to MO</u> <u>(S²+Px²+Py²+Pz²)</u>	<u>Coefficient</u>
 25	0.079%	S -0.00365
		Px -0.00000
		Py -0.00565
		Pz 0.02734
 10	0.12%	S 0.00593
		Px 0.00139
		Py 0.02208
		Pz 0.02594
 26	0.33%	S 0.01053
		Px 0.00012
		Py 0.01202
		Pz 0.05526
 27	0.13%	S 0.00548
		Px 0.00061
		Py 0.02977
		Pz 0.02056

It also appears that molecules in these series, [10], [25], [26], and [27] have very little contribution by oxygen (which could possibly complex with borane) in their HOMO. Wood and Rickborn²⁹ studied intramolecular dehydroboration-hydroboration of alkylborane, which indicated that THF plays no role in the transition state.

We have considered the effect of varying ring size on the carbocyclic portion of the molecule. What will be the consequence of additional heteroatom influences?

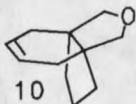
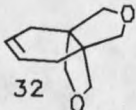
In examining two unique dioxapropellane molecules, the HOMO energies of both propellanes are lower than the HOMO energy of [10]. The HOMO energies are reported in Table 11.

Table 11. HOMO Energies of [10], [28], and [34].

<u>Compound</u>	<u>Energy(eV)(HOMO)</u>
 10	-9.93314
 34	-10.11293
 28	-10.00041

So, these low HOMO energy seem to correspond with retardation of the reactivities of dioxapropellanes in competitive hydroboration. The hydroboration competition results are reported in Table 12.

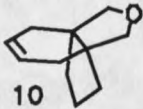
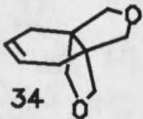
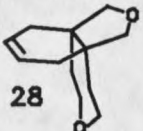
Table 12. Hydroboration Competition Results.

<u>Compound</u>	<u>Relative Rate $\pm$ 5%</u>
 10	1.00*
 32	0.49*
 27	0.36*

*: Average of three runs

Again, the electrophilic attack will occur where the π -bond density is most heavily concentrated. The HOMO Pz atomic orbital coefficient are reported in Table 13.

Table 13. HOMO Pz Atomic Orbital Coefficients of Olefinic Propellanes.

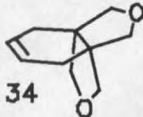
<u>Compound</u>	<u>Contribution(%) to MO(Av.ofPzi²,Pzj²)</u>	<u>CPzi</u>	<u>CPzj</u>
 10	42.506%	-0.65102	-0.65291
 34	42.503%	-0.65101	-0.65288
 28	41.703%	0.64410	0.64746

The difference of the coefficients (Pz orbital) between [10] and [34] were 0.001%, about the same contribution. However, 4.14 Kcal difference of HOMO energies in [10] and [34] has decreased by half the reactivity between [10] and [34]. The propellane, [28] also has lower HOMO energy (1.55 Kcal), and a smaller Pz coefficient (0.8%). These differences again are reflected in a retarding of the reactivity of [28] in competitive hydroboration.

It also appears that these dioxapropellane [28], [34] have no contribution by oxygen (which could possibly complex with borane) in their HOMO. In examining the HOMO's

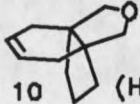
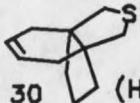
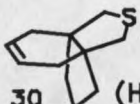
coefficient existing on oxygen, we see less than 1% contribution to HOMO (Table 14).

Table 14. HOMO Heteroatom Coefficients.

Compound	Contribution(%) to MO (S ² +Px ² +Py ² +Pz ²)		Coefficient		
	<u>O1</u>	<u>O2</u>	<u>O1</u>	<u>O2</u>	
 34	0.30%	0.089%	S	-0.00994	-0.00539
			Px	0.00099	-0.00050
			Py	0.00820	-0.01746
			Pz	0.05311	0.02356
 28	0.48%	0.23%	S	0.01000	0.00275
			Px	-0.00037	0.00647
			Py	0.02376	0.02271
			Pz	0.06419	0.04114

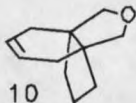
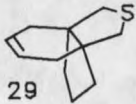
The thiapropellane has a different HOMO energy level and contribution of Pz on olefin and heteroatom (Table 15).

Table 15. HOMO Energies and Contribution (%) to Molecular Orbital.

Compound	Energy(eV)	Contribution(%) to MO	
		$\frac{\text{Av. of } P_z^2, P_z^2}{(\text{Olefin})}$	$\frac{S^2 + P_x^2 + P_y^2 + P_z^2}{(\text{Hetero Atom})}$
 10 (HOMO)	-9.93314	42.51%	0.12%
 30 (HOMO)	-9.42667	0.11%	86%
 30 (HOMO-1)	-9.92524	41.87%	0.25%

MNDO calculation suggested that the thiapropellane's HOMO energy and HOMO-1 energy were higher than the oxapropellane's by 11.67 Kcal, and 0.18 Kcal. In the HOMO of the thiapropellane, the coefficient of olefin is 0.11% of contribution from Pzi and Pzj, and 41.87% contribution in HOMO-1. Although the thiapropellane, [30] has 0.18 Kcal of the HOMO energy higher than oxapropellane, [10] but 0.632% difference of the Pzi, Pzj contribution to MO has decreased the reactivity between [10] and [30]. The hydroboration competition results are reported in Table 16.

Table 16. Hydroboration Competition Results.

<u>Compound</u>	<u>Relative Rate $\pm$ 5%</u>
 10	1.00*
 29	0.48* 0.65(with BH ₃ :DMS)

* Average of three runs
 DMS: Dimethyl sulfide

When the competition was carried out with both propellane, [10] and [30] with BH₃:DMS reacted with olefin easier than BH₃:THF. The BH₃:THF can complex with the sulfur of [30]. This results in a decrease in reactivity. However, when we use BH₃:DMS in hydroboration, the chances of complexing with same sulfur atom of thiapropellane are less.

We have considered the HOMO energies and coefficients of propellanes. From these combined data, the reactivity of competitive hydroboration of propellanes would seem to be dependent on these two factors. However these studies have not provided a definitive answer to why the reactivities are observed in these propellanes series. Examination of the conformations might be helpful to understand these reactivity differences.

Brown and coworkers³⁰ have shown that the rates of hydroborations are influenced by the nature of alkene substrates and solvents, while the order of the rates are similar in various solvents. Ab initio calculations for the gas phase reactions indicate that reaction rates are similarly influenced by the structural variation of alkenes³¹.

From the MNDO calculations of propellanes, interatomic distance between the heteroatom and the olefinic carbon atom was available. We see an interesting correlation between the reactivity (competitive hydroboration) and distance (steric control) (Figure 34).

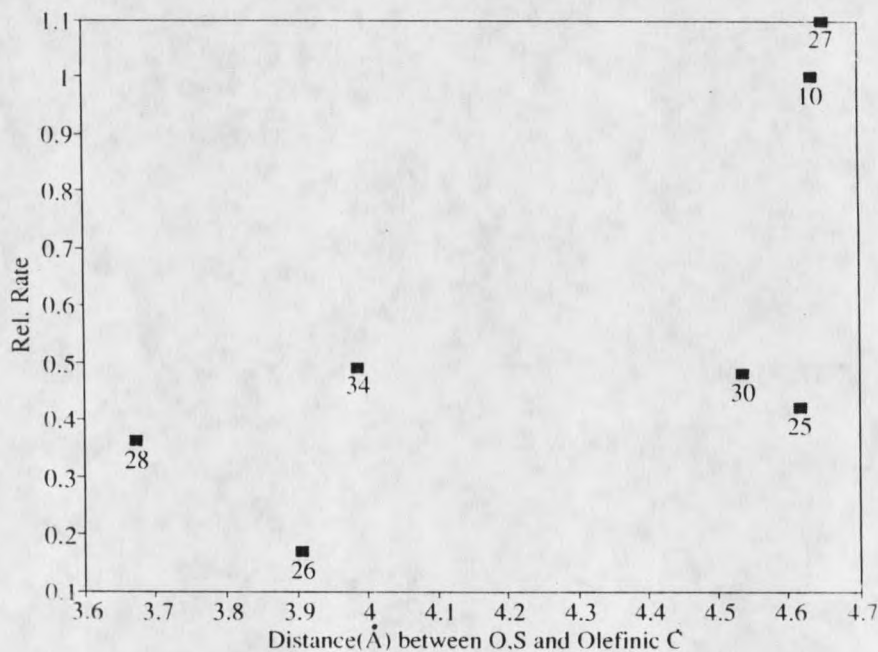
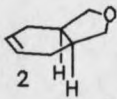
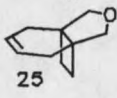
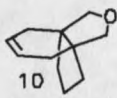
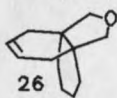
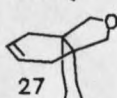
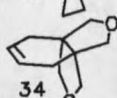
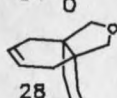


Figure 34. Relationship between the Relative Rate and the Interatomic Distance of the Heteroatom and the Olefinic Carbon Atom.

Hydroboration Studies and Stereochemistry

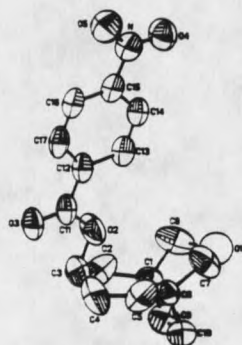
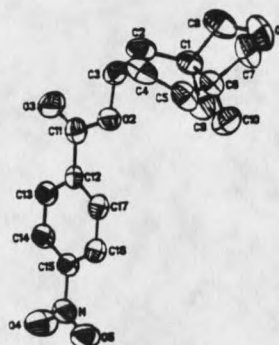
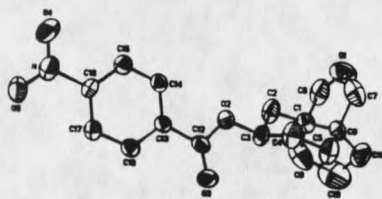
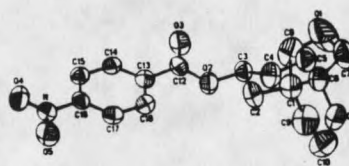
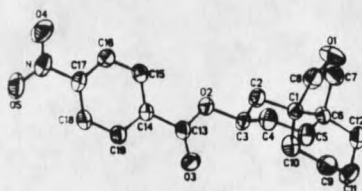
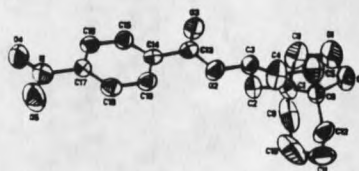
In order to distinguish simple steric effects from any electronic effects imparted by the heteroatom in influencing the stereochemistry of electrophilic additions to the olefins, a hydroboration study was conducted on a series of propellanes (Table 17).

Table 17. Hydroboration Study of Propellanes.

<u>Compound</u>	<u>G.C</u> <u>Syn*:Anti</u>	<u>¹³C INV.GATE</u> <u>Syn*:Anti</u>
 2	10 : 90	N.A
 25	not separated	57 : 43
 10	53 : 47	51 : 49
 26	57 : 43	57 : 43
 27	59 : 41	N.A
 34	one isomer	
 28	not separated	26 : 74
 30	43 : 57	45 : 55

*:Syn to the 5-membered ring heteroatom bridge
The reported stereochemistries are
those of the alcohol products.

The product ratios were obtained from peak integrations of the GLC traces obtained on the VG-7070E-HF mass spectrometer and the peak integration of ^{13}C -Inverse Gate experiment. The relative stereochemistries of the alcohols derived from propellanes were determined from the X-ray crystal structure obtained for the *syn*-tricyclic-*para*-nitrobenzoates and *anti*-tricyclic-*para*-nitrobenzoate (Figure 35) (See chapter 5 for larger X-ray structure).

[36]-*syn*[36]-*anti*[37]-*syn*[37]-*anti*[38]-*syn*[38]-*anti*

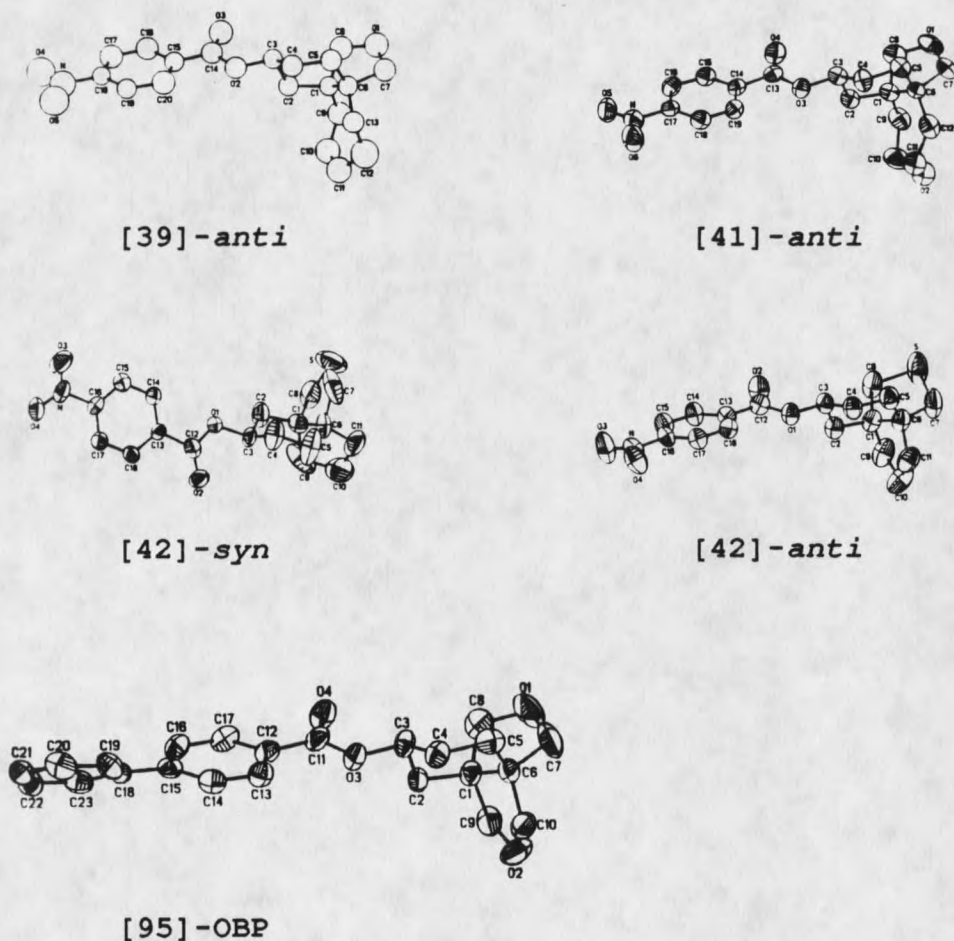


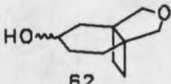
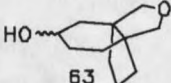
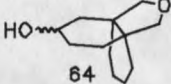
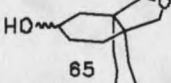
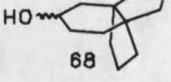
Figure 35. X-ray Structures of *para*-Nitrobenzoates.

In general, when a *syn*-tricyclic-*para*-nitrobenzoate was subjected to saponification (KOH in absolute ethanol) only one alcohol resulted, the corresponding *syn*-alcohol. The other alcohol, having a similar pattern, and ¹H NMR spectra was obviously the corresponding *anti*-alcohol.

In the mass spectra of *syn*- and *anti*-alcohols of propellanes, different peak intensity of parent molecular ion and a loss of water was observed (Table 18). In the

generally observed trend, the *syn*-OH of propellanes have a strong intensity of M^+-H_2O and weak intensity of M^+ because *syn*-OH is near the oxapropano ring.

Table 18. Intensity of M^+ and M^+-H_2O of Hydroxypropellanes.

Compound	M^+		M^+-H_2O	
	Syn*-OH	Anti-OH	Syn*-OH	Anti-OH
 62	0.77	0.56	26	14
 63	0.97	3.2	49	23
 64	1.2	13	23	28
 65	0	2.1	13	11
 66	0	0	37	37
 67	0	2.0	7.2	6.8
 68	39	94	46	8.3

Syn*:Syn to the 5-membered ring heteroatom bridge

Analysis of the NMR spectrum for *syn*- and *anti*-alcohols of the propellane systems showed a unique d,d of H_a and H_b , and multiplet of H_c (Figure 36).

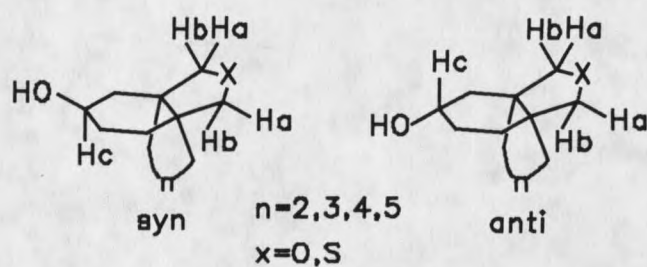
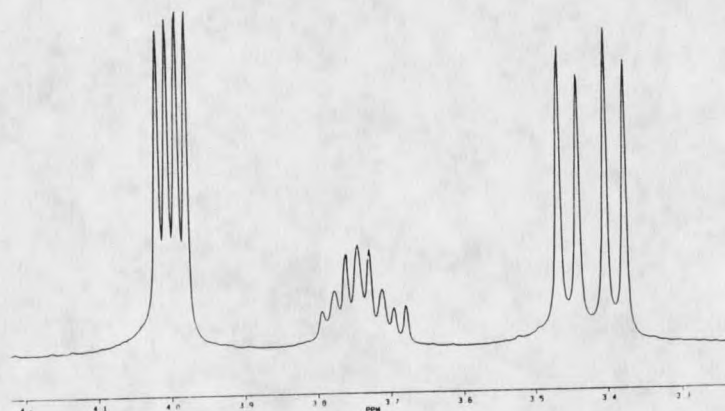
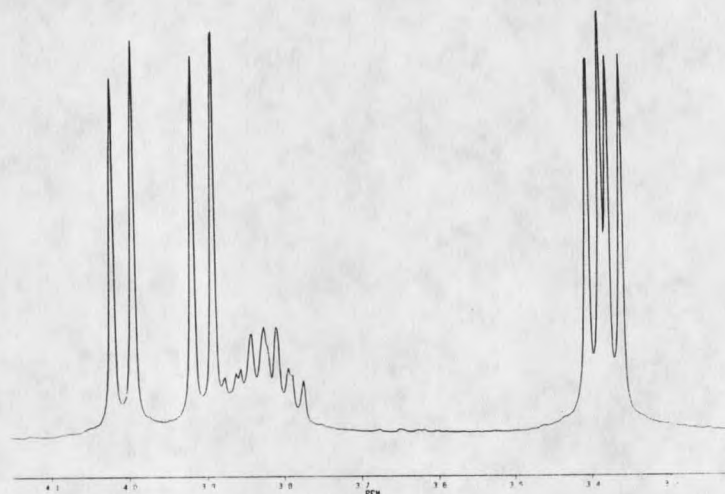


Figure 36. *syn*- and *anti*- Alcohol of Propellane.

In Figure 37 is illustrated examples of Ha coupled with Hb and Hc. The mutiplets seen in different chemical shift versus *syn*- and *anti*- alcohols of [64] are reported.



[64]-*syn*



[64]-*anti*

Figure 37. Partial NMR Spectrum of [64]-*syn* and [64]-*anti*.

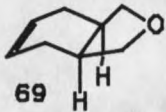
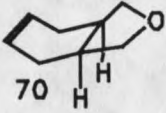
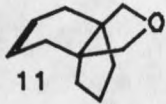
Johnson³ used the MM2 and MNDO methods to determine the relative equilibrium abundances of olefin [10]. One strength of the MM2 method is its ability to determine conformational minima of a compound by calculating steric energies for all possible conformations of the molecule³². MM2 considers a molecule as a collection of atoms held together by harmonic forces which can be described by potential energy functions of structural features such as bond lengths, bond angles, nonbonded interactions and so on. The combination of these potential energy functions constitutes the force field. The steric energy (ES) of the molecule in the force field arises from deviations from "identical" structural features and can be approximated by a sum of energy contributions.

$$ES = E_b + E_{st} + E_{nb} + \dots$$

Where E_b is the energy arising from bending bond angles from their "ideal" values, E_{st} is the energy arising from stretching bond lengths from their "ideal" lengths, and E_{nb} is the energy of nonbonded interactions. The steric energy of the molecule is, therefore, the difference in energy between the actual molecule and a hypothetical molecule where all bond lengths and bond angles have exactly their "ideal" values³³. The MNDO method is a semi-empirical molecular orbital calculation developed by Dewar and has, as one of its strengths, the ability to accurately calculate heats of formation (H_f) while requiring only modest

computational time. The initial geometries for the MNDO calculation were the optimized geometries obtained by the SIMS and PC MODEL molecular modeling programs. These geometries were then optimized at the SCF level by minimizing the energy with the Davidon-Fletcher-Powell (DFP) algorithm³⁴. From these calculation methods, Johnson reported the energies of the two anticipated boat formations (Table 19).

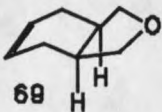
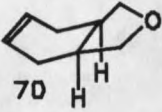
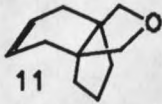
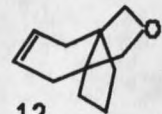
Table 19. Ground State Conformational Energies for [69], [70], [11] and [12].

<u>Conformation</u>	<u>Energy(Kcal/mol)</u>	
	<u>MM2(Steric)</u>	<u>MNDO(H_r)</u>
 69	18.78	-42.90
 70	18.73	-42.84
 11	27.39	-48.77
 12	27.24	-48.81

These results suggest that the minima for the two anticipated boat conformation are energetically equivalent within the errors reported for each calculation³⁵. As a

result, the relative conformational equilibrium abundances, as calculated as $\exp(-\Delta E/RT)$ where ΔE is the conformational energy differences, R is the gas constant and $T=298^\circ\text{K}$, are approximately equal for the two anticipated boat conformations. Also, he calculated the olefin HOMO. According to the FMO theory, the reactivity of a olefin towards an electrophile should increase with decreasing energy separation between the olefin HOMO and the LUMO on the electrophile. Since LUMO of the electrophile remains constant for hydroboration study, this relative reactivity should parallel the relative HOMO energies, which are reported in Table 20.

Table 20. HOMO Conformational Energies of [69], [70], [11] and [12].

<u>Conformation</u>	<u>Energy(eV)(HOMO)</u>
 69	-9.96
 70	-9.94
 11	-9.69
 12	-9.69

The above calculation suggests that conformation of [69] and [70] have nearly identical reactivities and conformation [11] and [12] have identical reactivities.

The results of Table 17 suggest that the stereochemistry ratio of electrophilic additions to olefins depends on steric hinderance. With the different size of ring systems, one face of the double bond is *syn* to the oxapropano group while the opposite face experiences a different ring size. Also, in the different sulfur heteroatom system, one face of the double bond is *syn* to a thiapropano group ring while the opposite face experiences the propano group. Since the π -faces of propellanes have different steric environments, electrophilic addition went to the sterically less hindered side. Again, there are obvious steric differences between the π -faces of [2]. In [2], the face *anti* to oxygen is much less hindered and the initial electrophilic attack *anti* to oxygen would be favored. In X-ray structures of para-nitrobenzoates of [25] and [28], we found two different conformational isomers (Figure 38). For [25], the ratio of stereoisomers favors *syn* to oxygen because one of the isomers provides more space. Also, compound [28] has two different conformational isomers. One conformational isomer provides more space, therefore, ratio of stereoisomer is favorable to *syn* to oxygen of 7-membered ring.

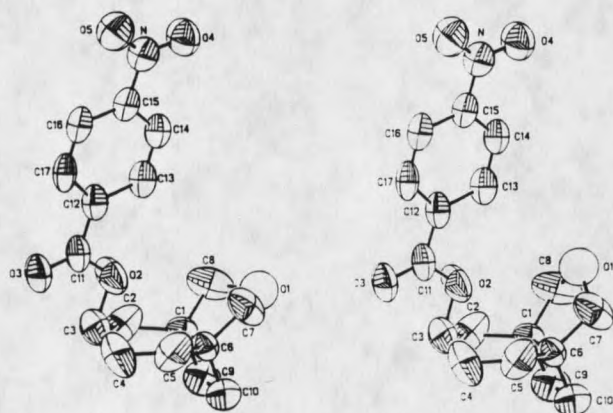
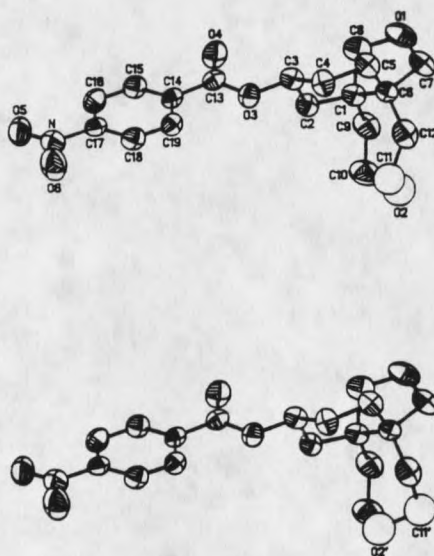
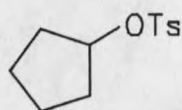
[36]-*syn*[41]-*anti*

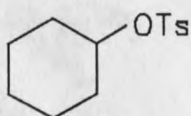
Figure 38. ORTEP Drawings of X-ray Structure of Two Conformational Isomers of [36]-*syn* and [41]-*anti*.

Solvolysis Studies

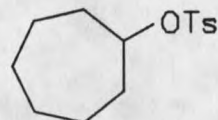
It was about thirty years ago that Brown and coworkers published their paper on Chemical Effects of Steric Strain³⁶. In this work, Brown determined the rate constants and activation parameters associated with the solvolysis of cycloalkyltosylates with different ring sizes. We have tested an MSU-developed interface on these particular reactions. One of the unique features of this method is that research quality data are routinely gathered on milligram quantities. Efforts were thus focused on the preparation and solvolytic behavior of tosylate, 71~73.



71



72



73

Table 21 shows the observed individual first order rate constants for the three starting compounds. The last column shows Brown's rate constants for the tosylates at three temperatures of which there is a direct comparison.

Table 21. Rate Constants for the Tosylates.

Ring size	Temp (°C)	K exp ($\times 10^{-5}$)	K Ref ³⁶ ($\times 10^{-5}$)
5	50	3.80	3.82
	60	11.35	-
	70	31.80	33.20
	80	106.45	-
	90	261.80	-
6	70	2.39	2.37
	80	7.25	-
	90	22.70	22.20
7	50	6.49	6.45
	60	19.73	-
	70	60.55	60.00
	80	165.68	-
	90	399.00	395.00

For these experiments, we have plotted $\ln(k/T)$ vs $1000/T$. The excellent data allow us to assign the values of $\Delta S^\ddagger$ of activation shown in the Table 22. Literature values are also included in this table. Our data support Brown's values and his conclusions.

Table 22. Activation Parameters.

	5-ring		6-ring		7-ring	
	$\Delta H^\ddagger$	$\Delta S^\ddagger$	$\Delta H^\ddagger$	$\Delta S^\ddagger$	$\Delta H^\ddagger$	$\Delta S^\ddagger$
Ref ³⁶	24.1	-4.2	27.3	-0.5	23.3	-5.7
This Work	24.4	-3.4	27.6	-0.4	23.7	-4.6

With the knowledge that we could carry out precise solvolysis studies using the equipment, we next investigated

whether we could measure long-range heteroatom influences. The series of propellane's tosylates were designed to attempt to elucidate the heteroatom's role in influencing reactivity in solvolysis. If NGP is occurring, an increase in rate would be predicted for the *anti*-tosylate relative to the corresponding *syn*-tosylate.

The tosylates, [15] and [16], are unique in that the steric environments for the two compounds (Figure 39) seem to be identical. In [15], the tosylate group is *syn* to the oxapropano group while in [16] the tosylate group is *anti* to the oxapropano group. Therefore, the backside attack by solvent, on the carbon bearing the tosylate, should experience the same steric environment. So, any observed rate enhancement of [16] over [15] might then be attributed solely to oxygen participation.

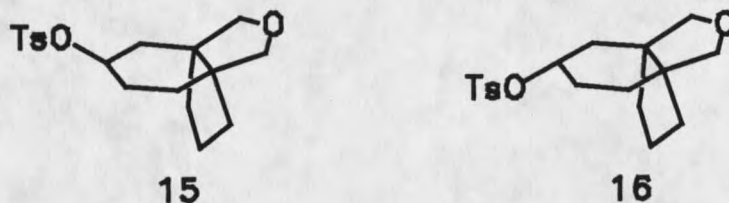


Figure 39. *syn*- and *anti*-Tosylate of [10].

We initially chose *para*-nitrobenzoate as our leaving group. As previously described, the propellane systems were subject to hydroboration yielding the corresponding alcohol mixtures which were subsequently converted to the *para*-nitrobenzoate mixture. Flash chromatography was then

employed to isolate the product. Unfortunately, these *para*-nitrobenzoates proved to be surprisingly stable. In order to increase the reactivity of this series, we completed two new syntheses derivatizing the alcohols with tosylate, a better organic leaving group. We therefore used the schemes shown in Figure 20 to obtain the isomerically pure tosylates. Examples of ^1H NMR spectra of tosylates are illustrated in Appendix B. *para*-Nitrobenzoates were white solids, which after a number of crystallizations yielded crystals in hexane (or ethanol) and dichloromethane (10:1, respectively) from which X-ray structures were obtained. These X-ray structures confirmed the relative stereochemistries reported for the *para*-nitrobenzoate in the syntheses. Their ORTEP drawings are illustrated in Figure 35.

All the solvolysis experiments used 50% aqueous methanol. The kinetic studies were completed conductrimetrically. A conductance cell and thermistor were interfaced to a computer allowing for the simultaneous acquisition of conductance, temperature, and time measurements. A standard solution of 50% aqueous methanol was used. The standard solution (20 mL) was added to the pretreated conductance cell which was then placed in the constant temperature bath. The reaction system was allowed to equilibrate for 2 hours, then approximately 1 mg of the tosylate was added to the cell and upon temperature

equilibration, data acquisition began. Data were collected approximately every second over 3 to 5 half-lives of the reaction and an infinity point was obtained after approximately 15 half-lives. Least squares method treatment on $\ln (C_{\infty}-C_x)$ vs time (seconds) yielded first order rate constant (k) for each tosylate. From examination of the rate constants obtained from tosylate of [10] and [30], there appears to be rate enhancement of the *anti*-tosylate over *syn*-tosylate.

By MNDO calculation of Wilder's molecules, [74] and [75], interatomic distances between the heteroatom and the carbon bearing the hydroxyl group are 3.671Å (oxygen), and 3.888Å (sulfur) (Figure 40).

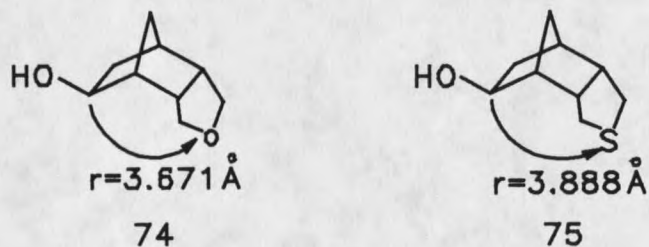


Figure 40. Interatomic Distance of Wilder's Molecules.

In X-ray structures of *anti*-tricyclic-para-nitrobenzoate, [76] and [77] the interatomic distances between the heteroatom and the carbon which has OPNB group are 4.067Å (oxygen), 4.465Å (sulfur) (Figure 41).

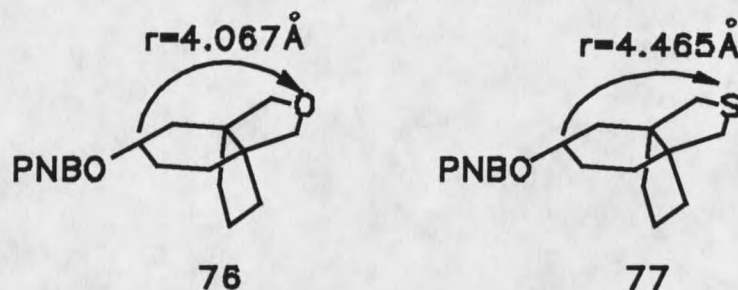


Figure 41. Interatomic Distance of *para*-Nitrobenzoates of propellane.

MNDO calculation of hydroxy propellane, [78] and [79] also have similar interatomic distance, $3.814\text{\AA}$ (oxygen), $4.261\text{\AA}$ (sulfur) (Figure 42).

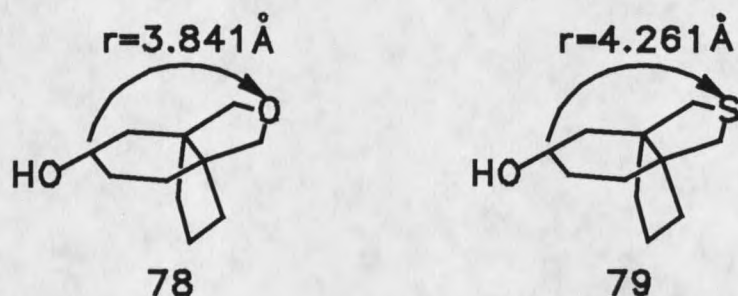
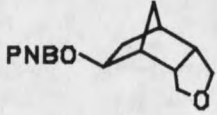
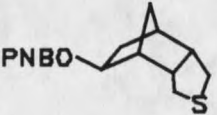


Figure 42. Interatomic Distance of Hydroxy Propellanes.

This investigation suggested that the distance between the heteroatom and the carbon atom which was connected to the leaving group was related to reactivity of solvolysis. These reactivity versus the distance relationships are illustrated in Table 23.

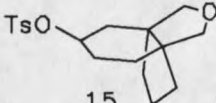
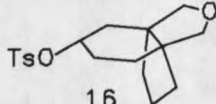
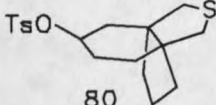
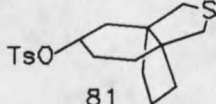
Table 23. The Reactivity vs. the Distance Relationship.

<u>Compound</u>	<u>Relative Rate (vs. Carbon)</u>	<u>Distance(Å) (by MNDO, X=OH)</u>
	2.53	3.671Å
	1.6	3.841Å
	752	3.888Å
	70	4.261Å

The rate enhancement (1.6 times) was observed for the anti-tosylate of [10] relative to the syn-isomer. Also, the big rate enhancement (70 times) was observed for the anti-tosylate of [30] relative to the syn-isomer. This was interpreted to mean that the heteroatom does influence reactivity in these compounds.

The lone pair electron orbital of the sulfur are more polarizable than oxygen. The big rate enhancement was observed for anti-tosylate of [30] versus anti-tosylate of [10]. The results of these kinetic studies are reported in Table 24.

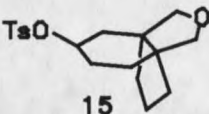
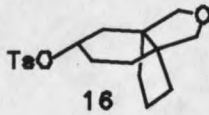
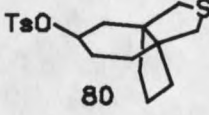
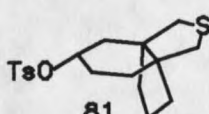
Table 24. Kinetic Results of the Solvolysis of *syn*- and *anti*-Tosylates of [10] and [30].

Compound	Temp(°C)±0.05	k x 10 ⁻⁴ (s ⁻¹)
 15	39.7	3.00
	50.1	9.65
	59.9	27.5
 16	40.1	5.09
	49.8	15.0
	59.9	43.6
 80	40.3	0.67
	50.1	1.75
	60.1	3.79
 81	19.3	4.67
	29.0	13.5
	40.9	54.2
	49.2	122

For these solvolysis studies, a plot of the logarithm of the rate constant against the reciprocal of the absolute temperature is approximately linear with negative gradient (i.e. the reaction is faster at higher temperature.). The Arrhenius equation was used to obtain energies of activation, E_a . E_a represents a critical energy which the molecule must possess in order for reaction to occur; for a given value of A , the rate constant decreases as E_a becomes larger. And the transition-state theory was employed to obtain the enthalpy, $\Delta H^\ddagger$ and entropy, $\Delta S^\ddagger$ of activation. The term $\Delta H^\ddagger$, the enthalpy of activation, corresponds

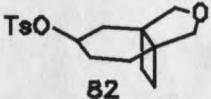
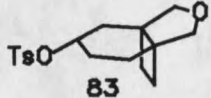
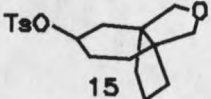
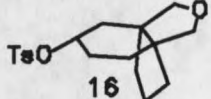
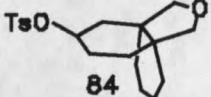
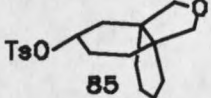
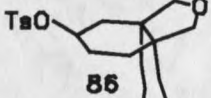
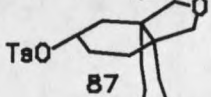
closely to the activation energy term, E_a , in the Arrhenius equation (for liquids and solids, $\Delta E = \Delta H^\ddagger + RT$) $\Delta S^\ddagger$ is known as the entropy of activation. One important merit of transition-state theory is that it rationalizes the probability factor, P . A reaction in which the transition state is highly organized will have a large, negative $\Delta S^\ddagger$, corresponding to a small value for P . The results of these studies are reported in Table 25.

Table 25. Activation Parameters of the Solvolysis of *syn*- and *anti*-Tosylates of [10] and [30].

<u>Compound</u>	<u>E_a(Kcal/mol)</u>	<u>$\Delta H^\ddagger$(Kcal/mol)</u>	<u>$\Delta S^\ddagger$(eu)</u>
 15	22.7	22.0	-4.61
 16	22.5	21.8	-4.29
 80	18.2	17.5	-21.9
 81	20.6	20.0	-5.58

In examining the solvolysis of the different ring size analogues propellane, it appeared that the reaction rate constant depended on steric hinderance except for [86] and [87]. The results of these studies are reported in Table 26 and Figures 43~44.

Table 26. Kinetic Results of the Solvolysis of *syn*- and *anti*-Tosylates of [10], [25], [26], and [27].

<u>Compound</u>	<u>Temp(°C)±0.05</u>	<u>k x 10⁻⁴(s⁻¹)</u>
 82	40.5	9.55
	50.1	27.9
	59.8	71.1
 83	40.1	10.3
	49.9	29.5
	59.7	73.5
 15	39.7	3.00
	50.1	9.65
	59.9	27.5
 16	40.1	5.09
	49.8	15.0
	59.9	43.6
 84	40.1	0.39
	50.0	1.21
	59.7	3.53
 85	40.3	0.49
	50.1	1.58
	59.9	4.99
 86	39.2	2.96
	49.1	12.2
	57.8	24.3
 87	29.7	26.5
	40.0	81.9
	49.4	173

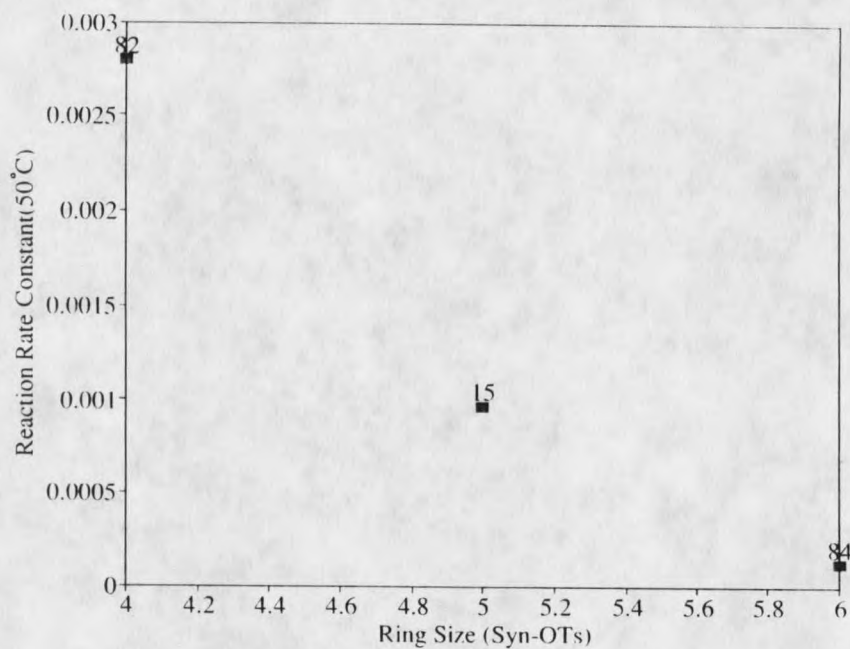


Figure 43. Plot of Reaction Rate Constant vs. Ring size (*syn*-Tosylate).

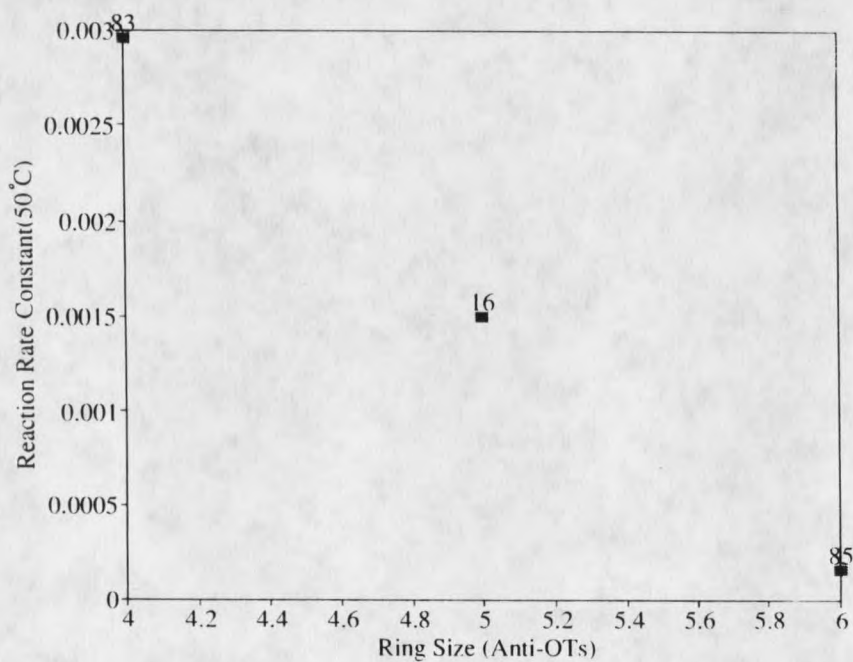
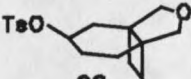
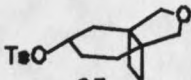
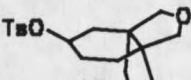
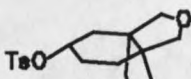
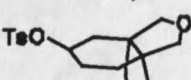
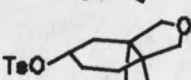
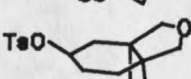
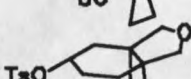


Figure 44. Plot of Reaction Rate Constant vs. Ring size (*anti*-Tosylate).

Again, the Arrhenius equation was used to obtain energies of activation, E_a and the transition-state theory was employed to obtain the enthalpy, $\Delta H^\ddagger$, and entropy, $\Delta S^\ddagger$ of activation. The results of these analyses are reported in Table 27.

Table 27. Activation Parameters of the Solvolysis of *syn*- and *anti*-Tosylates of [10], [25], [26], and [27].

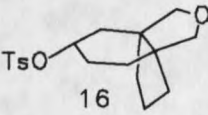
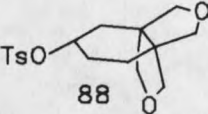
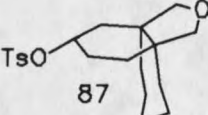
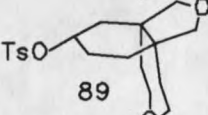
Compound	E_a (Kcal/mol)	$\Delta H^\ddagger$ (Kcal/mol)	$\Delta S^\ddagger$ (eu)
 82	21.6	20.9	-5.91
 83	20.8	20.1	-8.23
 15	22.7	22.0	-4.61
 16	22.5	21.8	-4.29
 84	23.3	22.6	-6.86
 85	24.5	23.9	-2.33
 86	23.4	22.8	-1.45
 87	18.4	17.8	-11.80

Rate enhancements were again observed for *anti*-tosylate relative to *syn*-tosylate for each of the different ring size

series. We found a significant E_a difference (5 Kcal/mol) between the *anti*- and *syn*-tosylate of 7 membered ring propellanes, [86] and [87]. The relative rate of [87]/[86] is 14 times at 50°C.

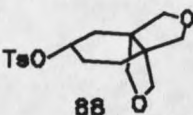
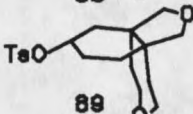
From an examination of the rate constants obtained from the tosylates of [16], [88], [87] and [89] we observed a rate retarding effect by the second oxygen (Table 28).

Table 28. Kinetic Results of the Solvolysis of [16], [87], [88] and [89].

Compound	Temp(°C)±0.05	$k \times 10^{-4}(s^{-1})$
 16	40.1	5.09
	49.8	15.0
	59.9	43.6
 88	39.3	0.79
	49.9	2.87
	60.0	8.58
 87	29.7	26.5
	40.0	61.9
	49.4	173
 89	40.9	6.94
	49.7	20.6
	60.2	61.7

These results lead us to believe that we are dealing with a transannular dipole effect. The dipole associated with the second ether oxygen was destabilizing the incipient carbonium ion in the solvolysis, thus retarding the rate. The results of activation parameters are reported in Table 29.

Table 29. Activation Parameters of the Solvolysis of [88] and [89].

<u>Compound</u>	<u>Ea(Kcal/mol)</u>	<u>$\Delta H^\ddagger$(Kcal/mol)</u>	<u>$\Delta S^\ddagger$(eu)</u>
 88	23.8	23.2	-3.27
 89	23.5	22.9	-0.23

Product studies were carried out by combining the three runs for each tosylate, distilling most of the methanol, and then extracting the resulting residue repeatedly with dichloromethane. Product studies were completed by comparing ^1H spectra and GC-MS spectra of the observed products to those of the authentic samples that were synthesized and characterized previously. Product ratios were obtained from peak integration completed on GLC

capillary column equipped with a flame ionization detector. The results of those studies are summarized in Figures 45~49.

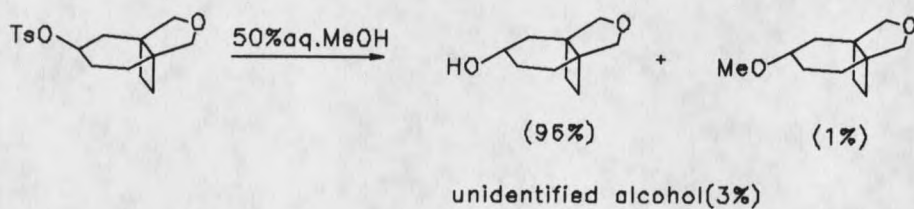


Figure 45. Product Studies of the Solvolysis of [82].

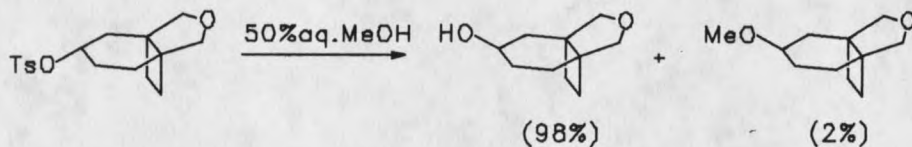


Figure 46. Product Studies of the Solvolysis of [83].

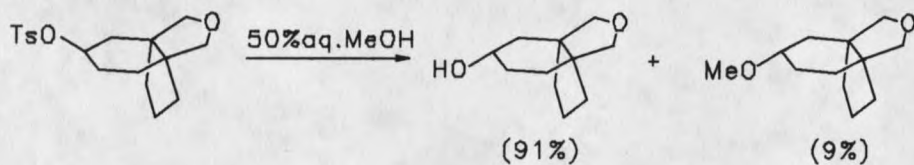
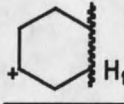
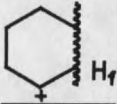
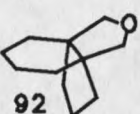
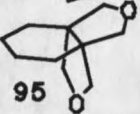


Figure 47. Product Studies of the Solvolysis of [15].

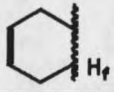
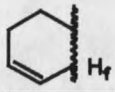
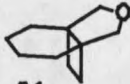
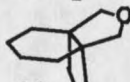
methoxy and alcohol compounds in the relative ratio of 47% : 38%. These processes have been found to result in products formed by substitution (S_N2 mechanism), and elimination (this elimination is the only example in these series). However, mass spectral fragmentation patterns of the substitution products are different to those of the authentic samples that were synthesized and characterized previously. The 1H spectra of the substitution products are very similar to authentic samples. From this data, we suggest a 1,2 hydride shift. A 1,2 hydride shift, followed by substitution, accounts for the hydroxy and methoxy compound at C_2 . Because the driving force to migration in solvolysis is the formation of a more stable carbocation³⁷, carbocation stabilities were determined by the MNDO method (Table 30). These calculations illustrate a thermodynamic driving force promoting this rearrangement. The carbocation at C_2 is favored by approximately 3-6 Kcal/mol over carbocation at C_3 .

Table 30. Calculated Carbocation Stabilities (Kcal/mol).

Compound		
 91	169.85	165.81
 92	161.26	155.58
 93	165.34	159.25
 94	170.14	166.29
 95	132.48	129.62
 96	143.00	141.72
 97	198.52	197.05

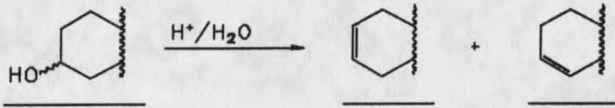
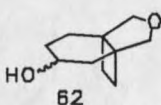
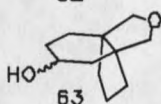
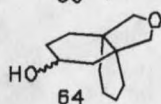
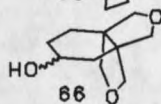
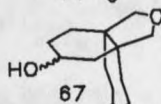
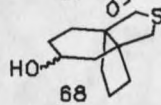
Elimination of *para*-toluenesulfonic acid results in a mixture of olefins. An examination of the stabilities of olefins by MNDO calculation indicates that [90] is thermodynamically more stable than alkene, [34] by 3 Kcal/mol (Table 31)

Table 31. Calculated Olefinic Energies (Kcal/mol).

Compound	 H _f	 H _f
 91	-27.504	-28.718
 92	-37.551	-41.075
 93	-34.688	-37.389
 94	-28.652	-31.821
 95	-68.193	-71.292
 96	-57.445	-55.089
 97	0.439	-3.243

Also, dehydration of hydroxy propellanes with catalytic amount of sulfuric acid provide two alkenes. Again, major alkenes are more stable by ~3 Kcal/mol thermodynamically by MNDO calculation (Table 32).

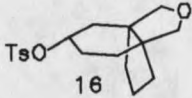
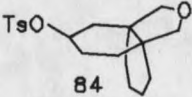
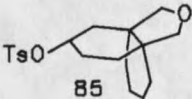
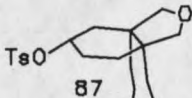
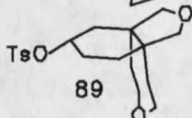
Table 32. Dehydration of Alcohols.

		
 62	1	: 3.29
 63	1	: 8.39
 64	1	: 6.44
 65	N.A	N.A
 66	1	: 8.10
 67	1	: 2.10
 68	1	: 1.51

Other tosylates, mostly *anti*-tosylates, have the same trends as [88] except for the elimination process. The product studies for [16], [84], [85], [87], and [89] show the alcohol and methoxy compound (Table 33). Again, mass spectral fragmentation patterns of these substitution products are different from those of the authentic samples that were synthesized and characterized previously. But ^1H spectra of the substitution products are similar to one of

the authentic spectrum. And the stabilities of carbocation at C₂ and C₃ position were determined by MNDO calculation (Table 30). These calculations suggest the 1,2-hydride shift possibility for these processes.

Table 33. Product Studies of the Solvolysis of [16], [84], [85], [87] and [89].

<u>Compound</u>	<u>Alcohol Compound</u>	<u>Methoxy Compound</u>
 16	93%	7%
 84	79%	21%
 85	58% 26% (two kinds)	16%
 87	87%	13%
 89	66% 9% (two kinds)	25%

In order to absolutely establish the identities of the products from these studies, future work will require the synthesis of authentic samples of hydroxy and methoxy compounds at C₂ position.

Mass Spectrum Fragmentation of Propellanes
and *cis*-8-Oxabicyclo[4,3,0]non-3-ene

Our interest was the preparation and characterization of a number of unique tricyclic (propellanes) and bicyclic non-aromatic heterocycles. In the spectrum of each compound, a loss of water is observed. It is obvious where the oxygen comes from in the loss. The fundamental question to account for the loss is the identification of the source of hydrogens. Assuming a similar mechanism accounts for the loss of water in each compound, we prepared propellanes and three specially deuterium-labeled substrates for study. To address the question as to where the protons originate in the loss of water, Johnson³ prepared a series of deuterium labelled analogues of [2]. In this series, the C₂-C₃ positions were labelled to form [99], the C₇-C₈ positions were labelled to form [98], and both of these positions were labelled to form [100] (Figure 50).

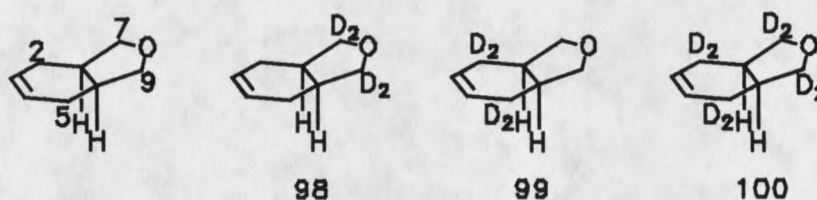


Figure 50. Deuterium Labeled Analogue of *cis*-8-Oxabicyclo[4,3,0]non-3-ene, [2].

For the synthesis of [98], the known anhydride, [101], was reduced with lithium aluminum deuteride. The resulting

1,4-diol was immediately cyclized to [98] with TsCl/Pyr. The syntheses of [99] and [100] developed from a common intermediate, [102]. Non-labelled butadiene sulfone, [103], was dissolved in D₂O to which was added a catalytic amount of sodium metal. After stirring at room temperature for 48 hours, exchange had taken place to >95%. The labeled sulfone, [104], was refluxed with maleic anhydride in xylene to yield the Diels-Alder product, [102]. Reduction and cyclization of [102] led to [99] [100] (Figure 51 outlines these synthesis).

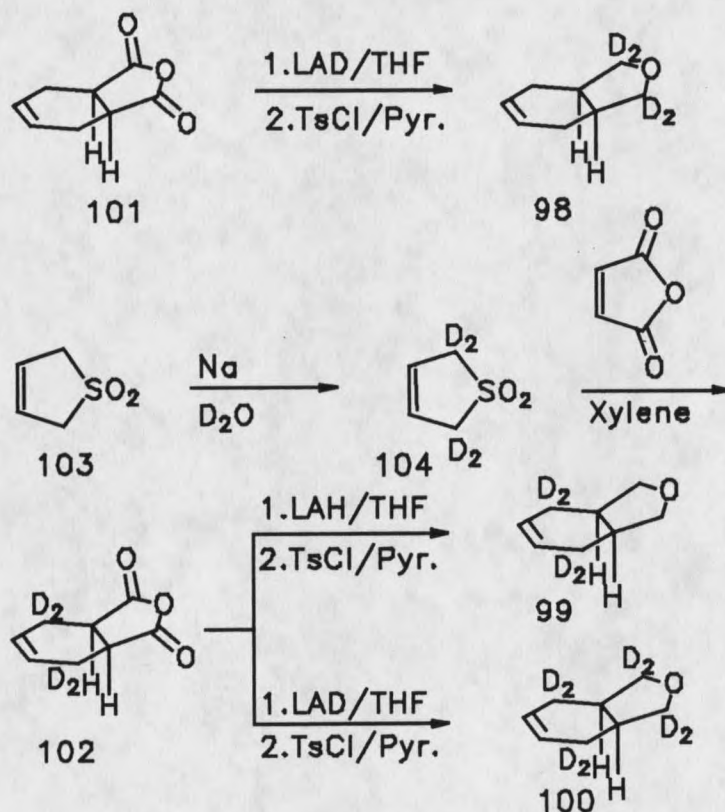


Figure 51. Synthesis of [98], [99], and [100].

The EI mass spectra of these compounds are recorded in Figures 52-54.

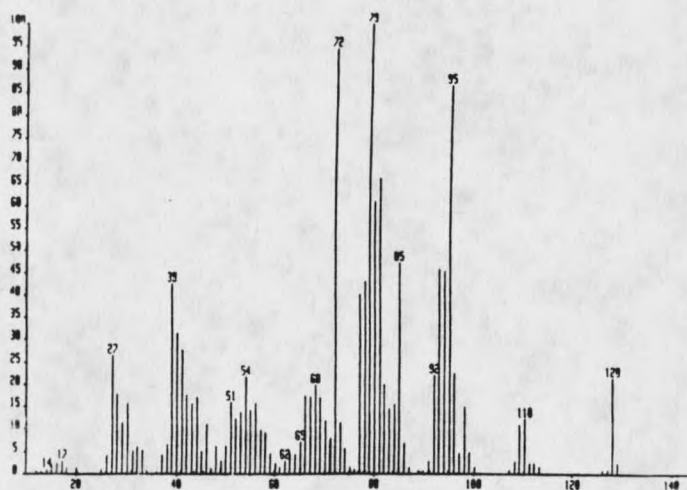


Figure 52. 70eV EI mass spectrum of *cis*-7,7,9,9-Tetradeutero-8-oxabicyclo[4,3,0]non-3-ene, [98].

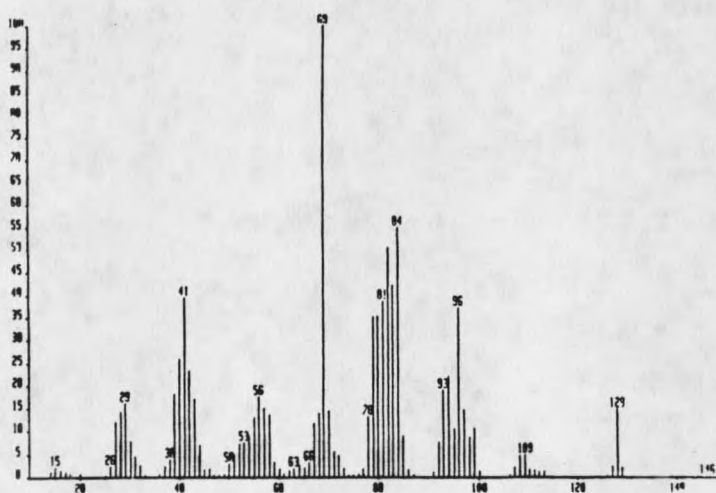


Figure 53. 70 eV EI mass spectrum of *cis*-2,2,5,5-Tetradeutero-8-oxabicyclo[4,3,0]non-3-ene, [99].

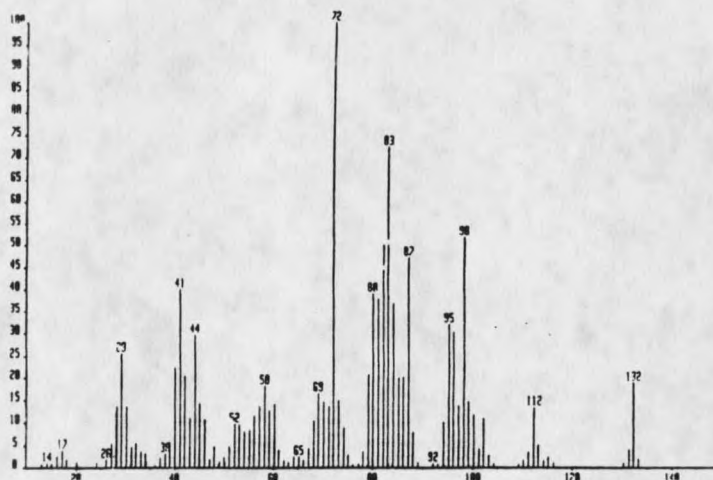
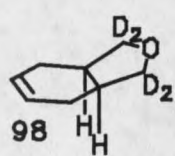
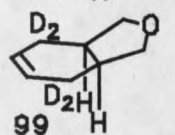
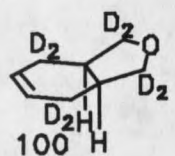


Figure 54. 70 eV EI Mass Spectrum of *cis*-2,2,5,5,7,7,9,9,-Octadeutero-8-oxabicyclo[4,3,0]non-3-ene, [100].

From an examination of these spectra, there is a loss of 20 mmu from [100]. For [98] there is loss of 18 mmu and 19 mmu; which for [99] there is loss of 19 mmu and 20 mmu. These data require that the protons associated with the water loss come from different sources. In loss of 18 from [98], the two protons must originate from the C₂-C₅ position. In the loss of 19 mmu from [98], a proton comes from the C₂-C₅ position, and a deuterium atom is required from the C₇-C₉ position. Similarly, for the loss of 20 mmu from [99] two deuterium atoms originate from the C₂-C₅ position; while for the loss of 19 mmu a deuterium atom originates from the C₂-C₅ position and a proton is derived

from the C₇-C₉ position. The loss of water from [98], [99], and [100] is summarized in Table 34.

Table 34. Water Loss Summary.

<u>Compound</u>	<u>Loss of H₂O</u>	<u>Loss of HDO</u>	<u>Loss of D₂O</u>
 98	110(12%)	109(10%)	---
 99	---	109(5%)	108(5%)
 100	---	113(5%)	112(13%)

These data suggest that the loss of water results from at least two different processes. The following mechanism appears to account for the two different processes of the loss of water (Figure 55).

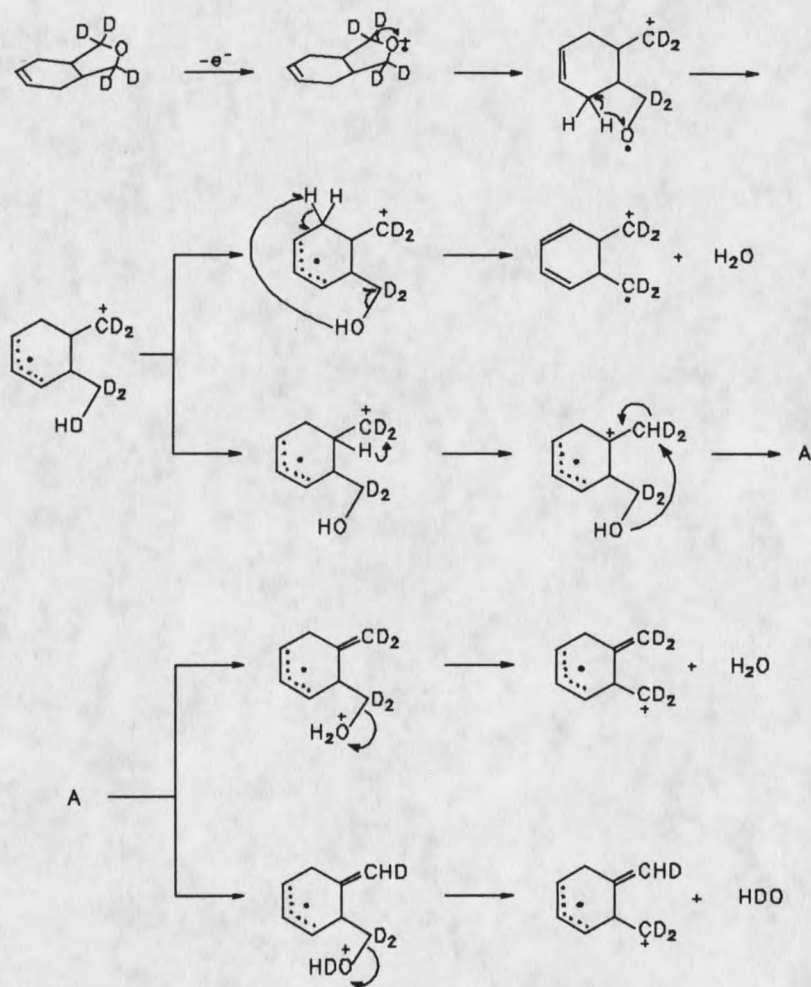


Figure 55. Loss of Water from *cis*-7,7,9,9-Tetradeutero-8-oxabicyclo[4,3,0]non-3-ene, [98].

Interestingly, there is a loss of 19 (HDO) with weak intensity (5%) and a loss of 20 (D_2O) with strong intensity (13%) in [100]. These data also support our mechanism (Figure 56).

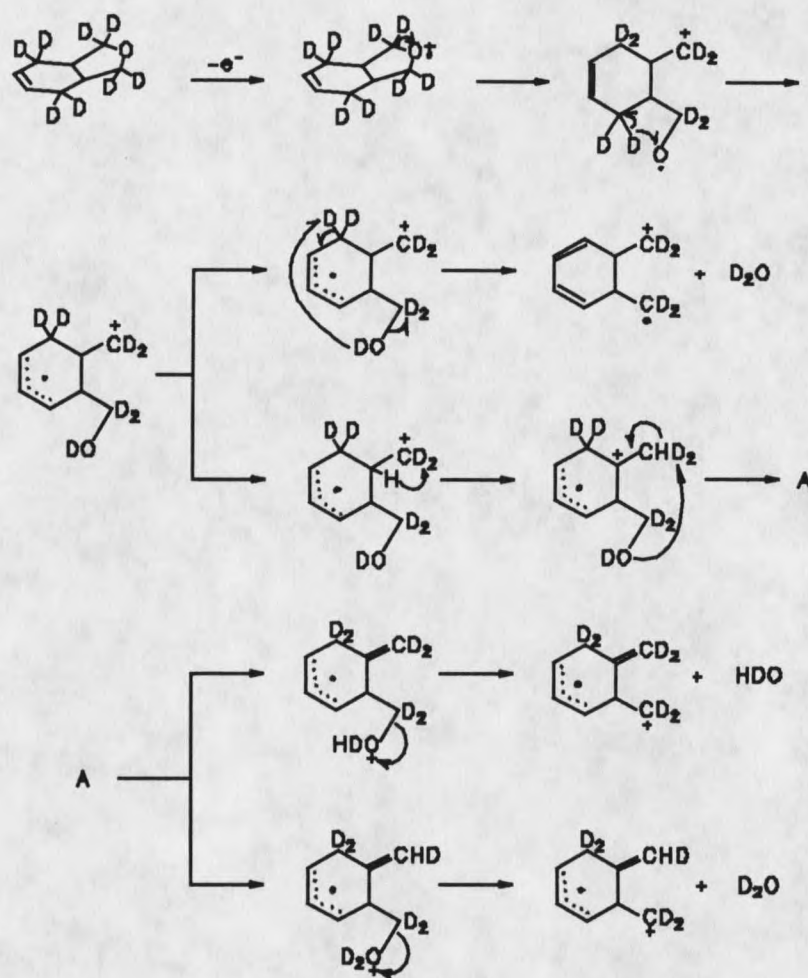


Figure 56. Loss of Water from *cis*-2,2,5,5,7,7,9,9-Octadeutero-8-oxabicyclo[4,3,0]non-3-ene, [100].

In the electron impact (EI) mass spectra of propellanes, [10], [25], [26], [27], and [34], the loss of water is observed with different intensity. The intensities of the peaks are illustrated in Figure 57. It appears that there is the loss of water in [34] with 32% intensity. It is obvious that this propellane has two ethereal oxygen atoms, which is a main factor for the loss of water. By

changing ring size on the propellanes, the difference of the peak intensities for loss of water changes from 1% to 21%.

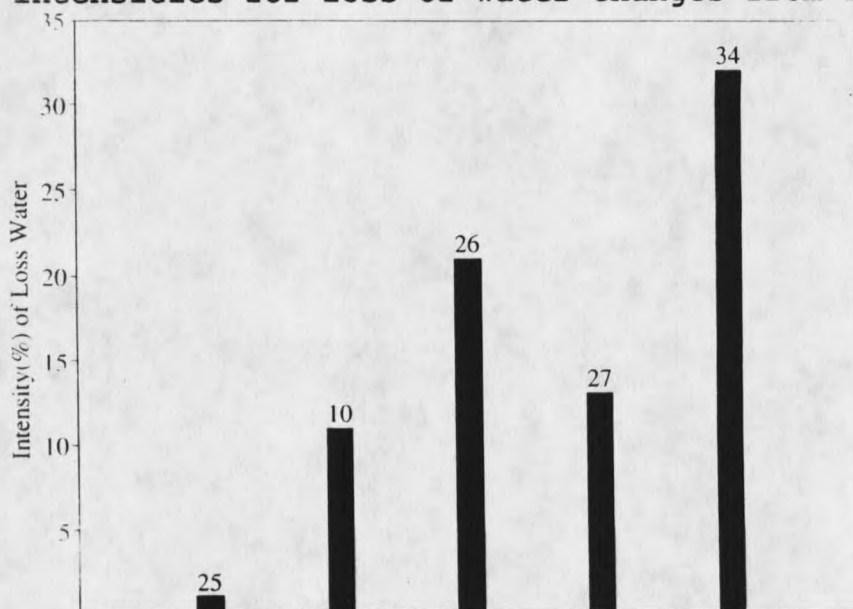


Figure 57. Loss of Water of Propellanes.

The following mechanism appears to account for the process of the loss of water in propellane systems (Figure 58).

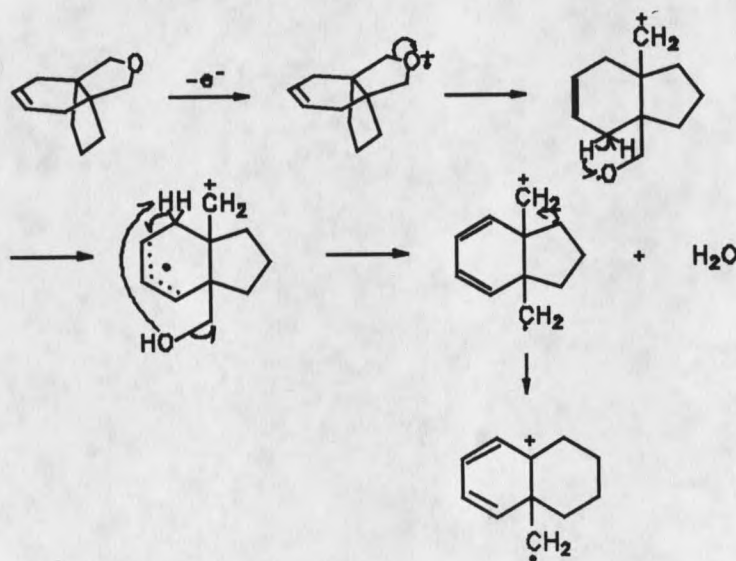


Figure 58. Loss of Water from [10].

The rigidity of the 4-membered ring propellane, [25] appears to account for a small intensity of the loss of water (1%). In the EI mass spectrum of [25], the first major peak was (M^+-28), which suggest the loss of (C_2H_4) from the 4-membered ring.

In [10] second loss results in a ion $m/z=133$, in [26] $m/z=147$, in [27] $m/z=161$, in [34] $m/z=135$. This is a loss of 31 for [10], [26], [27], and [34]. These data suggest the loss of ($HO\dot{C}H_2$). The following mechanism illustrates the observed $HO\dot{C}H_2$ loss (Figure 59).

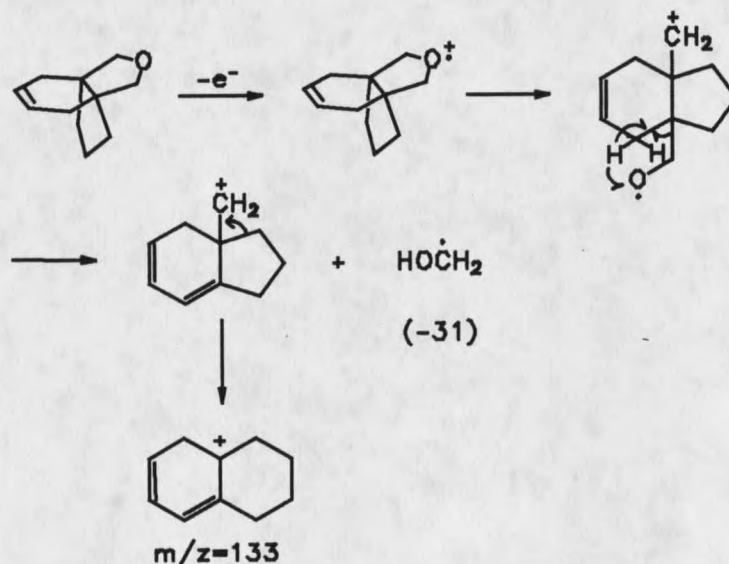
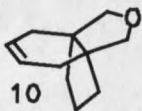
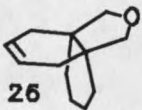
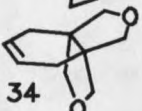


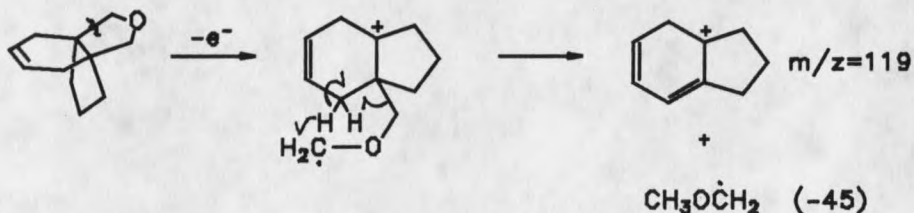
Figure 59. Loss of $HO\dot{C}H_2$ from [10].

Loss of $HO\dot{C}H_2$ is observed with similar intensity for the four molecules of interest as illustrated in Table 35.

Table 35. Loss of HOCH₂ in Propellanes.

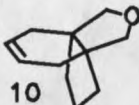
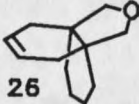
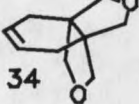
<u>Compound</u>	<u>Intensity</u>
 10	31%
 26	34%
 27	23%
 34	32%

The major ion, $m/z=119$ in [10] seems to correspond to the major ion, $m/z=133$ in [26], $m/z=147$ in [27], $m/z=121$ in [34]. This is a loss of 45 for [10], [26], [27], and [34]. These data suggest the loss of $(CH_3-O-\dot{C}H_2)$. The following mechanism illustrates the observed losses (Figure 60).

Figure 60. Loss of $CH_3-O-\dot{C}H_2$ from [10].

The intensities of these peaks are summarized in Table 36.

Table 36. Loss of $\text{CH}_3\text{-O-}\dot{\text{C}}\text{H}_2$ in Propellanes.

<u>Compound</u>	<u>Intensity</u>
	32%
	15%
	23%
	24%

The major ion, $m/z=109$ in [10] seems to correspond to the major ion, $m/z=123$ in [26] $m/z=137$ in [27], $m/z=111$ in [34]. This is a loss of 55 for [10], [26], [27], and [34]. These data suggest the loss of $\dot{\text{C}}_4\text{H}_7$. The following mechanism illustrates the observed losses (Figure 61). The intensities of these peaks are summarized in Table 37.

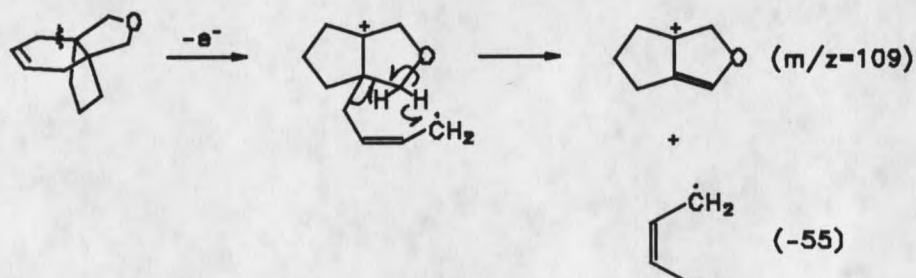
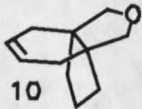
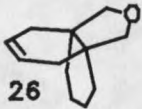
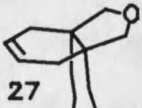
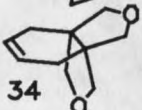
Figure 61. Loss of $\dot{\text{C}}_4\text{H}_7$ from [10].

Table 37. Loss of C_4H_7 in propellanes.

<u>Compound</u>	<u>Intensity</u>
 10	25%
 26	71%
 27	64%
 34	7%

From this examination, we found somewhat different intensity of each propellant. Obviously, bicyclic major ion of [10] and [34] show weak intensity (10%-20%) while the bicyclic major ion of [26] and [27] exhibit strong intensity (60%-70%). Probably, the stability of major ion depends on the strain of bicyclic system, and stable major ion shows strong intensity. Also we found strong ion (40%), $m/z=112$ in [34]. The following mechanism illustrates the observed loss (Figure 62).

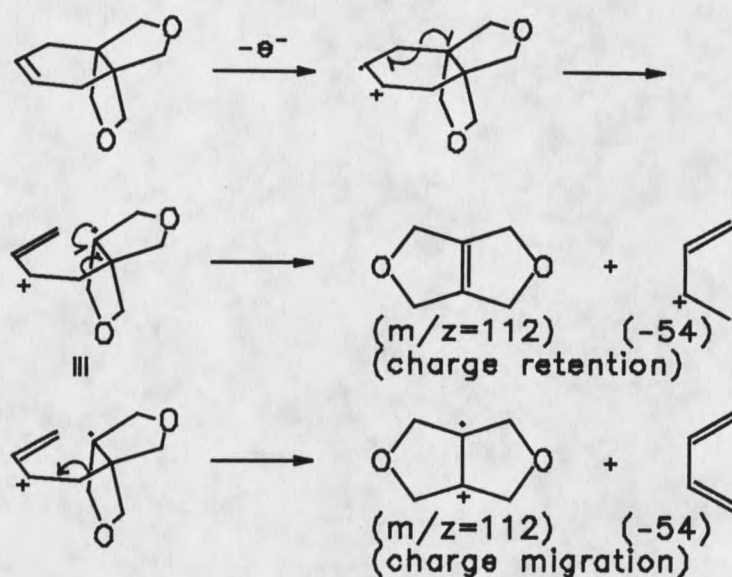


Figure 62. Loss of C_4H_6 from [32], Retro-Diels-Alder Process.

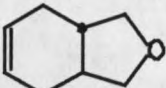
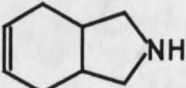
From this study, the oxygen atom's role in a number of fragmentation processes has been studied. The major ions in the (EI) mass spectrum of [2] and propellanes have been determined and investigated mechanisms, illustrating the oxygen atom's role in the fragmentation processes, have been proposed.

Steric and Oxygen Effect on the Stereoselective Hydrogenation

The catalytic hydrogenation of olefins has been studied by a number of investigators using a variety of reaction techniques. Theodore² investigated a series of catalytic hydrogenation studies. In the competitive study, the experiment was carried out by mixing the bicyclic alkene

with cyclohexene in the same reaction vessel. Each competition was carried out for a specified length of time and quenched by the removal of hydrogen. The catalyst used was 10% pd/c and the reactant-product distribution was monitored by gas chromatography. Bicyclic alkene, [2] in Table 38 seem to indicate a heteroatom rate enhancing effect (1.3 fold) over the carbon analogue, [106]. Also, the fact that [105] is slower (3.5 fold) than [2] is probably due, as a result of the trans configuration at the ring juncture of [105], to the steric difficulty encountered by the double bond in resulting on the catalytic surface. From these results, we are now dealing with the two effects (steric and heteroatom) in the catalytic hydrogenation.

Table 38. Relative Rates of Catalytic Hydrogenation.

<u>Compound</u>	<u>Competitive</u>	<u>Non-competitive</u>
	1.0	1.0
 2	6.59	0.78
 105	1.33	0.55
 106	4.92	0.13
 107	23.63	0.0039

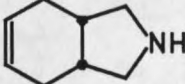
The fact that [106] appears to reduce faster than cyclohexene under competitive conditions can be attributed to a "bulk effect". Since an equivalent amount of [106] will occupy more space than cyclohexene in a fixed volume, and given a substrate to catalyst ratio of 1000:1, it seems reasonable that the probability of a catalyst particle coming in contact with [106] is high.

In the non-competitive study, carried out in separate reaction vessels for the same time period, the rates of reduction of all the bicyclic compounds were slower than

that of cyclohexene. The 7.7 fold rate difference between [106] and cyclohexene can be rationalized on the basis of steric arguments. In the case of [107], the nitrogen atom is complexing with the catalyst, tying up the catalyst sites, and prohibiting cyclohexene from being reduced under competitive conditions.

Theodore also completed a number of competitive and non-competitive hetroatom/catalyst affinity studies (Table 39). These results represent the ratios of complexed to free substrate relative to the ratio of complexed to free cyclohexene.

Table 39. Relative Catalyst Affinities.

<u>Compound</u>	<u>Competitive</u>	<u>Non-competitive</u>
	1.00	1.00
 106	0.88	0.13
 2	3.36	0.75
 107	40.20	4.22

In the affinity studies, a substrate to catalyst ratio of 2:1 was used to allow monitoring of the change in concentration of free substrate and minimize the "bulk effect".

The results of the competitive study suggest a greater affinity of heteroatom bicyclic compound, [2] to bind to the catalyst over carbon analogue, [106] or cyclohexene. And the results of the non-competitive study were also used to argue for a positive oxygen/catalyst affinity. We therefore envisioned one molecule of [2] having the ability to complex to more than one catalyst site as shown in Figure 63.

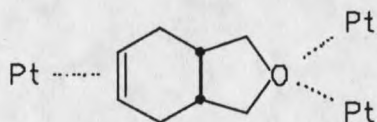


Figure 63. Complexation of *cis*-8-Oxabicyclo[4,3,0]non-3-ene.

Glancy³⁸ also observed an oxygen/catalyst interaction. He studied the effect of oxygen heterocycles on the catalytic hydrogenation of cyclohexene (Figure 64).

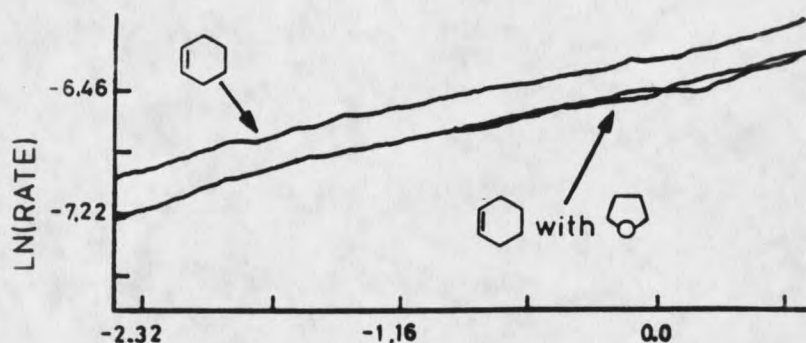


Figure 64. Effect of Tetrahydrofuran on the Reduction of Cyclohexene.

He rationalized these results by reasoning that the ethereal oxygen in tetrahydrofuran absorbed on to catalyst sites normally used for hydrogen absorption. This prevented cyclohexene from reaching the catalyst surface thus decreasing its rate of reduction.

Wilkening^{39,40} used the heteroatom interaction with catalyst in the reduction of 2-methyl-*cis*-1,5-dicarbomethoxy[3,3,0]oct-2-ene (Figure 65). This was used as a key step in his stereospecific synthesis of (dl) modhephene.

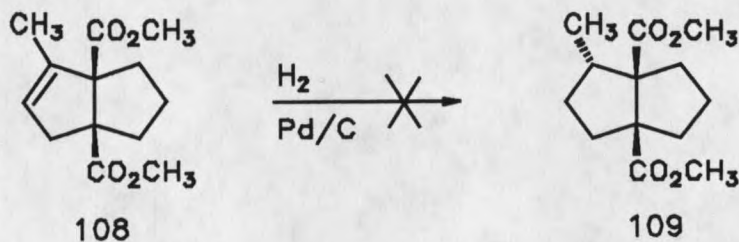


Figure 65. Stereospecific Hydrogenation of 2-Methyl-*cis*-1,5-dicarbomethoxy[3,3,0]oct-2-ene.

Unexpectedly, catalytic hydrogenation of [108] produced one isomer by reduction from the less hindered face without any interaction between the heteroatom and catalyst (Figure 66).

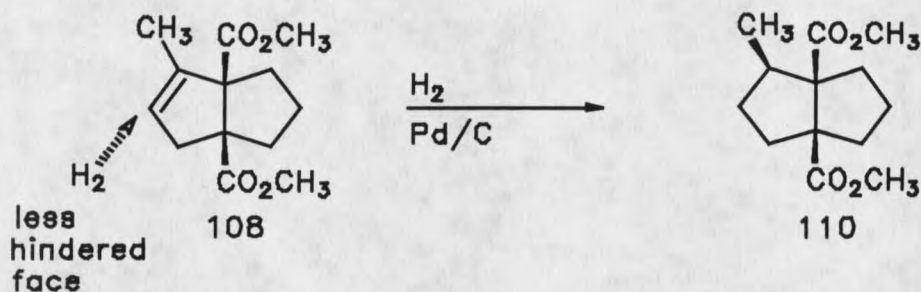


Figure 66. Synthesis of the Intermediate of epi-Modhephene.

Recently, Kraus⁴¹ reported the synthesis of epi-modhephene. In this article, he suggests an alternative catalyst which is $[\text{Ir}(\text{COD})(\text{PCy}_3)\text{py}]\text{PF}_6$ for the stereospecific hydrogenation toward modhephene.

However, Theodore and Glancy both observed the oxygen/catalyst interaction and some steric effect. In the catalytic hydrogenation, we should consider both the heteroatom coordination with the catalyst and steric effect of the substrate itself. In order to detect this proposed question, new systems, [112], [113], and [114] were synthesized and subjected to catalytic hydrogenation. In the synthesis of [112], [113], and [114], 1.2 equivalents of 1,3-dibromopropane were added to the lithium dienolate of *cis*-1,6-dicarbomethoxy-3-methylcyclohex-3-ene, [111]. The diester, [112], was obtained in 72% yield. Reduction of the

diester with LAH afforded the diol, [113] (82% yield) which was subsequently ring-closed to the desired propellane, [114] (86% yield) (Figure 67).

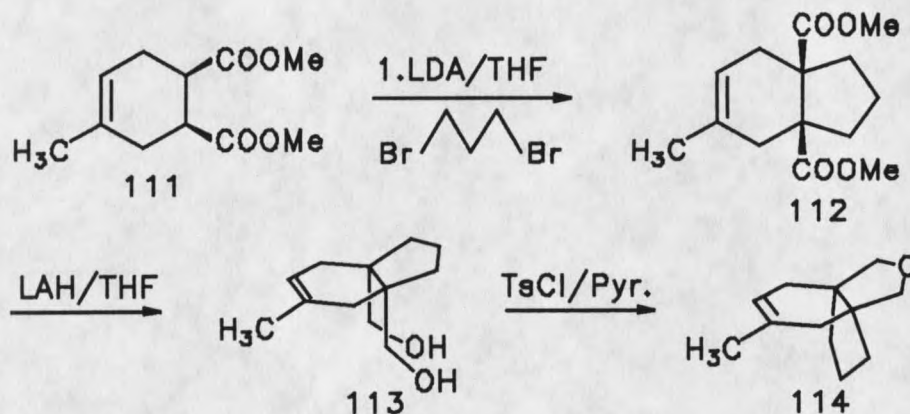


Figure 67. Synthesis of [112], [113], and [114].

In the catalytic hydrogenation of olefinic diester, [112], the experiment was carried out by mixing substrate and Pt/c in ethanol at 20 psi for overnight. A stereospecific addition was observed. In an identical procedure olefinic diol, [113] was reduced. A stereoselective addition was observed, and products were formed in the relative ratio of 65:35. Again, in the propellane, [114], the reduced products were formed in the relative ratio of 75:25 (Figure 68).

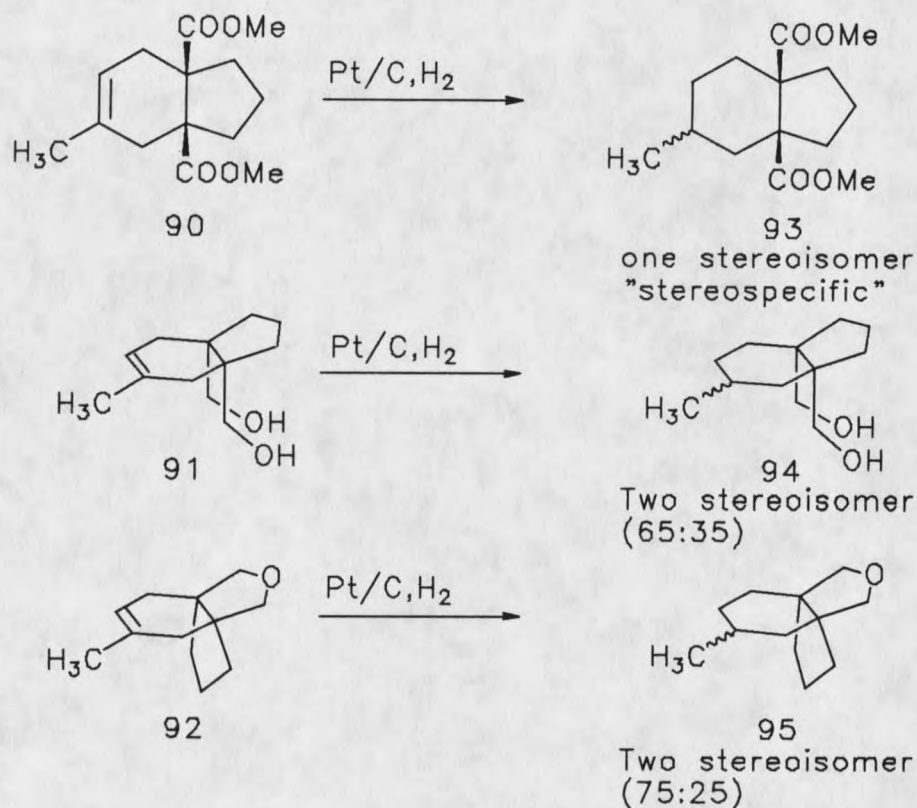


Figure 68. Stereospecific and Stereoselective Hydrogenation with Different Functional Group.

The reduced diester, [115] was formed as one stereoisomer (stereospecific hydrogenation). Reduction of this diester, [115] with LAH afforded the one stereoisomer diol, which is the same stereoisomer as the major isomer from [116]. Again, this major isomer subsequently ring-closed to the propellane, which is the same stereoisomer as major isomer from [117].

A difference Nuclear Overhauser Effect (NOE)⁴² ^1H NMR experiment was employed on the major isomer of [117] to

determine the stereochemistry of the methyl group. In the ^1H NMR spectrum, one of the doublets (3.52 ppm) was irradiated and a positive 4.7% NOE enhancement was observed at the methyl proton at 0.87 ppm. This is a first piece of evidence to support the structure as shown in Figure 69.

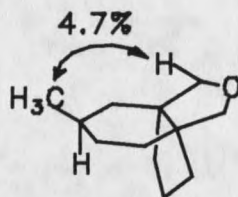


Figure 69. % Enhancement of NOE Experiment of the 3-Methyl-8-oxatricyclo[4,3,3,0]dodecane, [117]-Major Isomer.

In the electron impact mass spectroscopy fragmentations of the major and minor isomers of [117], different peak intensity due to the loss of water was observed, 1% and 18% respectively. (Figures 70-71)

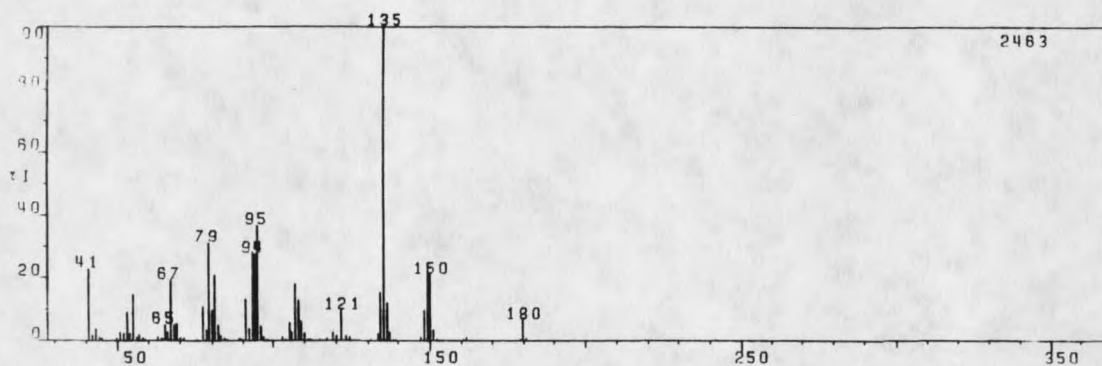


Figure 70. 70eV EI Mass Spectrum of Major Isomer of [117].

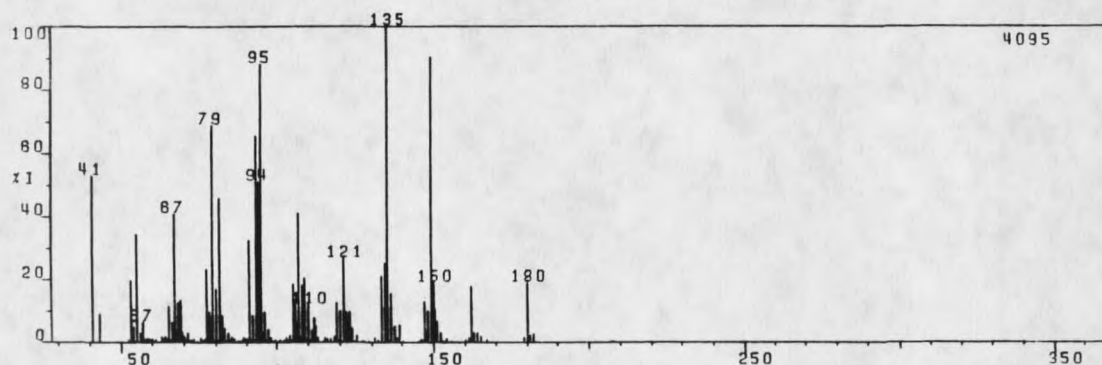


Figure 71. 70eV EI Mass Spectrum of Minor Isomer of [117].

The following mechanism appears to account for the processes of the loss of water for [117]-minor isomer (Figure 72). This is consistent with our other detailed MS conclusions and is a second piece of evidence pointing to the structure of the reduction products.

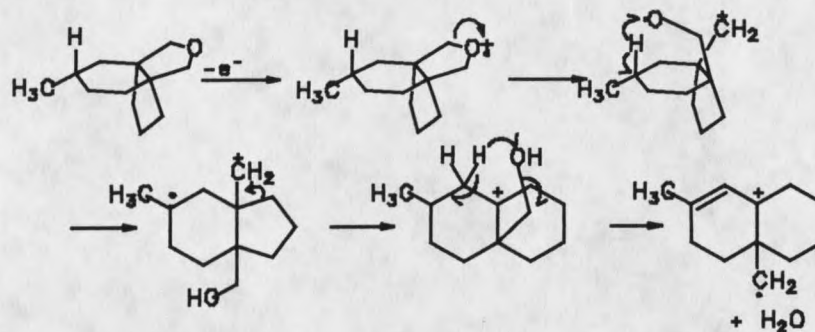


Figure 72. Loss of Water from [117]-Minor Isomer.

These two investigations suggested that catalytic hydrogenation of [112] produced one isomer by reduction from less hindered face without any interaction between diester group and catalyst.

CHAPTER 4

CONCLUSIONS

Synthesis Study

1. We prepared four kinds of different ring size propellanes using dianion ring annulation method.
2. We also prepared dioxapropellanes using Diels-Alder reaction and dianion chemistry.
3. A formal synthesis of maleimycin, an antibiotic natural product, was completed by dianion annulation and F.V.T.
4. Using F.V.T. condition, we made 1,2-dicarbomethoxycyclopentene in nearly 100% yield. This compound is the key intermediate of cyclopentanoids such as the antibiotic sarkomycin.
5. After hydroboration, alcohol mixtures were converted to para-nitrobenzoates. We used different solvent systems for flash separation and prepared the isomerically pure syn- and anti-tricyclic para-nitrobenzoates. X-ray structures of para-nitrobenzoates confirmed the relative stereochemistry.

Hydroboration Study

1. Competitive Hydroboration

The reactivities of different ring size would seem to be dependent on the atomic coefficient of olefin (Pz

orbital) based on FMO theory. There was no contribution by oxygen (which could possibly complex with borane) in their HOMO. The calculational studies have not provided a definitive answer as to why the reactivities are observed in the different ring size. Examination of the conformations might be helpful to understand these reactivity differences. From MNDO calculation, we see an interesting correlation between the reactivity and the interatomic distance of heteroatom and the olefinic carbon atom, which is steric effect. In dioxapropellanes, [28] and [34] the reactivities of these series depended on its HOMO energies and the atomic coefficient of olefin (Pz orbital). Again, there was no contribution by oxygen. In thiapropellane, the 0.623% difference of the Pzi, Pzj contribution to MO and complex between sulfur and borane caused to retard the reactivity.

2. Hydroboration

The results (Table 17) of hydroboration study suggested that the stereoisomer ratio of electrophilic additions to olefins depended on steric hinderance.

Solvolysis Study

1. To test new MSU-developed interfaces, we have reinvestigated H.C. Brown's solvolysis experiment.
2. The rate enhancement (1.6 times) was observed for the anti-tosylate of [10] relative to the syn-tosylate.

Also, the large rate enhancement (70 times) was observed for the *anti*-tosylate of [30] relative to the *syn*- isomer. The rate enhancement of *anti*-tosylate over *syn*-tosylate is due to oxygen and sulfur participation. Also, the distance between the heteroatom and the carbon atom which was connected to leaving group was corresponded to reactivity of solvolysis.

3. In examining the solvolysis of the different ring size analogue of [10], it appears that the reaction rate constant depends on steric hinderance.
4. From an examination of the tosylates of dioxapropellane, [28] and [34], we observed a rate retarding effect by transannular dipole affect of the second oxygen.

Mass Spectrum Fragmentation Study

The oxygen atom's role in a number of fragmentation processes has been studied. The major ions in the (EI) mass spectrum of [2] and propellanes have been determined and mechanisms investigated, to illustrate the oxygen atom's role in the fragmentation process.

Stereoselective Hydrogenation

Stereospecific hydrogenation was observed in the catalytic hydrogenation of [112], and modest stereoselectivity was observed in the catalytic hydrogenation of [113] and [114]. The NOE experiment and

(EI) mass spectroscopy fragmentation of major isomer of [117] suggested that catalytic hydrogenation of [112] produced only one isomer by reduction from less hindered face without any interaction between oxygen and catalyst.

CHAPTER 5

EXPERIMENTAL

General Procedure for Solvolysis

20 mL of the standard 50% aqueous methanol solution were added to the oven-dried cell, which was placed in a constant temperature bath and allowed to equilibrate. Approximately 1 mg of the substrate (tosylate) was added to the cell. The substrate was allowed to dissolve and the temperature to equilibrate (3 minutes). Upon temperature equilibration, the solvolysis reactions were followed for 3-5 half-lives, and after 15 half-lives an infinity conductance value (C_{∞}) was measured. The conductance and temperature measurements were recorded with a Laboratory Interface⁴³. This digital to analog converter interfaced the conductivity cell and thermistor to a PC, allowing for simultaneous acquisition of conductance, temperature, and time measurements. Rate constants were calculated by a least-squares method of $\ln (C_{\infty}-C_x)$ vs. time (seconds). Activation parameters were calculated by least squares method of $\ln(k)$ vs. $1/T$ ($^{\circ}\text{K}$)⁻¹. All kinetic experiments were completed using the same conductance cell. Rate measurements were made at three different temperatures for each tosylate, usually over a range of 40°C. The

temperature was controlled $\pm 0.05^\circ$. Product analysis and peak integrations were obtained by GC-MS and ^1H NMR.

Examples of plot of $\ln(C_\infty - C_x)$ vs. time (seconds) for the 50% aqueous methanolysis for each tosylate at three different temperatures are illustrated in Appendix A.

General Comments

Melting points were determined on a Fisher-Johns melting point apparatus and are uncorrected. ^1H spectra (300.133 MHz) and ^{13}C spectra (75.4 MHz) were obtained on a Bruker AC-300 300 MHz spectrometer using a 5-mm $^1\text{H}/^{13}\text{C}$ switchable probe. Samples were dissolved in CDCl_3 . All spectra were obtained at 293K. Chemical shifts are reported in parts per million (ppm) relative to tetramethylsilane. Splitting patterns are designated as follows: s, singlet; d, doublet; t, triplet; p, pentet; m, multiplet. Infrared spectra were recorded on a Nicolet DX FT-IR spectrometer. Low-resolution mass spectra were obtained on a VG-MM16 instrument. High-resolution and chemical ionization(CI) mass spectra were completed on the VG-7070E-HF mass spectrometer. To obtain HREI on those samples which gave no observed M^+ , larger sample quantities and greater detection sensitivity were used. X-ray crystallographic data were obtained with a Nicolet R3ME diffractometer. Analytical thin-layer chromatography (TLC) was performed on aluminum backed silica gel plates (Whatman ALSIL G/UV), and flash chromatography was completed using 500 mL flash column

packed with 40 μ M diameter silica gel and equipped with a UV absorbance monitor. MgSO_4 was used for drying organic solvents unless noted otherwise. THF and diethyl ether were freshly distilled from sodium / benzophenone. Diisopropyl amine and pyridine and dimethylsulfoxide (DMSO) were distilled from calcium hydride. All other reagents were used as received. All reactions involving moisture-sensitive reagents were carried out in oven or a flame-dried apparatus under argon.

Bromination of ethyl malonate⁴⁴

A mixture of ethyl malonate (112 g, 0.700 mol), N-bromosuccinimide (150 g, 0.843 mol), and 200 mL of CCl_4 was refluxed with benzoyl peroxide (2 g). After overnight reflux the solid succinimide was filtered off and the solvent was removed from the filtrate by rotary evaporation to yield a yellow-colored liquid. GC analysis showed ethyl monobromomalonate (80%) and ethyl dibromomalonate (18%), starting material (2%). The yellow liquid was distilled to yield ethyl monobromomalonate as a pale yellow oil (115 g, 0.481 mol) (69% yield).

Diethyl monobromomalonate, [35]

IR (neat, cm^{-1}): 2984, 1742, 1469, 1370, 1303, 1250, 1151,

1031, 865, 646

^1H NMR (300.133 MHz, CDCl_3): δ 1.26 (6H, t, $J=7.1\text{Hz}$), 4.24

(4H, q, $J=7.1\text{Hz}$), 4.79 (1H, s)

$^{13}\text{CNMR}$ (75.4 MHz, CDCl_3): δ 13.78 (q), 42.29 (d), 63.09 (t),
164.50 (s)

LRMS (EI) m/e (%abundance): 238 (M^+ , 3), 193 (19), 166 (35),
138 (100), 122 (26), 87 (12), 69 (28), 45 (22), 39 (12)

HRMS (EI) m/e calculated for $\text{C}_7\text{H}_{11}\text{O}_4\text{Br}$ = 237.9841 ; found =
237.9836

Preparation of tetraethylethylene tetracarboxylate¹⁶, [32]

A solution of diethylmonobromo malonate (17.8 g, 0.075 mol) and sodium trichloroacetate (13.9 g, 0.075 mol) in 50 mL of 1,2-dimethoxyethane was refluxed under a nitrogen atmosphere for 5 hours. The precipitated salt was filtered from the hot solution and washed with ether. The solvent was removed by rotary evaporation and ethanol:hexane (1:1) mixture was added to the resultant red oil. After standing in the freezer overnight, pale yellow crystals separated. Recrystallization from ethanol/hexane yield pure product as white feathery solid (15.2 g, 0.048 mol) (64% yield)

Tetraethylethylene tetracarboxylate, [32]

mp = 51-52°C (Ref¹⁶ 52-53°C)

IR (Nujol, cm^{-1}): 2935, 1735, 1457, 1371, 1254, 1025

$^1\text{HNMR}$ (300.133 MHz, CDCl_3): δ 1.29 (12H, t, $J=7.2\text{Hz}$) 4.29
(8H, q, $J=7.2\text{Hz}$)

$^{13}\text{CNMR}$ (75.4 MHz, CDCl_3): δ 13.78 (q), 62.47 (t), 135.43 (s),
162.32 (s)

LRMS (EI) m/e: 271, 243, 226, 215, 187, 169, 152, 143, 97,
44 (base)

LRMS (CI) (Methane) m/e (%abundance): 317 ($M+H^+$, 7), 271 (100), 243 (13)

Preparation of cyclohex-4-ene-(1,1,2,2)-tetraethylester,
[33]

Tetraethylethylene tetracarboxylate (5.00 g, 0.016 mol) was mixed with butadiene (5 mL) in bomb at 180°C. After heating 8 hours, a brown colored liquid was obtained. The liquid was distilled in high vacuum to yield pure product (5.70 g, 0.015 mol) as a pale yellow oil (96% yield).

Cyclohex-4-ene-[1,1,2,2)-tetraethylester⁴⁵, [33]

IR (neat, cm^{-1}): 3072, 2980, 2935, 1736, 1442, 1391, 1365, 1264, 1198, 1040, 863

¹HNMR (300.133 MHz, CDCl_3): δ 1.23 (12H, t, $J=7.2\text{Hz}$), 2.79 (4H, s), 4.18 (8H, q, $J=7.2\text{Hz}$), 5.67 (2H, t, $J=1.4\text{Hz}$)

¹³CNMR (75.4 MHz, CDCl_3): δ 13.78 (q), 31.28 (t), 56.87 (s), 61.58 (t), 124.05 (d), 167.01 (s)

LRMS (EI) m/e: 370 (M^+) 325, 297, 251, 223, 177 (base), 149, 105, 79, 44

HRMS (EI) m/e calculated for $\text{C}_{18}\text{H}_{26}\text{O}_8$ = 370.1628 ; found = 370.1630

Preparation of (1,1,2,2)-tetrahydroxymethylcyclohex-4-ene

A solution of LiAlH_4 (1.20 g, 0.032 mol) in 27 mL of THF was placed in a 250 mL three necked flask equipped with reflux condenser, dropping funnel and stirrer and protected from moisture until completion of the reaction by CaCl_2 tube attached to opening. Through the dropping funnel, the tetra

ester compound (4.10 g, 0.011 mol) was introduced at a rate such as to produce gentle reflux. Reflux was maintained for 20 hours with continuous stirring, after which time water was added dropwise and cautiously. The resulting solid was filtered off and the solvent was removed by rotary evaporation to yield white solid. Continuous extraction with ether yield pure product as a white powder (0.80 g, 0.004 mol) (36% yield).

[1,1,2,2]-Tetrahydroxymethylcyclohex-4-ene

mp = 220-225°C (Ref⁴⁵ mp = 220°C)

IR (Nujol, cm⁻¹): 3369, 3049, 2927, 2853, 1651, 1460, 1379,
1114, 1066, 897

Preparation of 8,11-dioxatricyclo[4,3,3,0]dodec-3-ene, [34]

[1,1,2,2]-Tetrahydroxymethylcyclohex-4-ene (3.00 g, 0.015 mol) was mixed with KHSO₄ (3.00 g, 0.022 mol) and heated to 190 - 200 °C in an oil bath. After 15 minutes, foaming was nearly finished. The reaction mixture became solid at a room temperature. The resulting solid was extracted with ether. The combined extracts were dried over MgSO₄ and the solvent removed at reduced pressure to yield product as a colorless oil (1.73 g, 0.010 mol) (70% yield). Florisil separation was employed to cleanly separate the pure compound. A solvent system of ethylacetate:hexane in the relative ratio 2:8 was used in this separation.

8,11-Dioxatricyclo[4,3,3,0]dodec-3-ene, [34]

IR (neat, cm^{-1}): 3038, 2925, 2853, 1646, 1460, 1377, 1096,
1054, 940, 719

^1H NMR (300.133 MHz, CDCl_3): δ 2.08 (4H, d, $J=3.1\text{Hz}$), 3.65
(4H, d, $J=8.9\text{Hz}$), 3.58 (4H, d, $J=8.9\text{Hz}$), 5.84 (2H, t,
 $J=3.1\text{Hz}$)

^{13}C NMR (75.4 MHz, CDCl_3): δ 29.76 (t), 57.67 (s), 79.42 (t),
128.22 (d)

LRMS (EI) m/e (%abundance): 166 (M^+ , 14), 148 (31), 135 (30),
121 (25), 112 (39), 105 (49), 99 (33), 91 (100), 79
(69), 67 (29), 53 (25), 39 (55)

HRMS (EI) m/e calculated for $\text{C}_{10}\text{H}_{14}\text{O}_2$ = 166.0994 ; found =
166.0990

Hydroboration of [34]

The alkene, [34] (0.830 g, 0.005 mol) was dissolved in 50 mL of dry THF to which was added NaBH_4 (0.190 g). An argon atmosphere was created and the reaction mixture was cooled to 0°C . Then $\text{BF}_3\text{O}(\text{C}_2\text{H}_5)_2$ (0.620 mL, 0.005 mol) was syringed into system. The reaction mixture was warmed to room temperature and stirred overnight. Excess NaBH_4 was quenched with H_2O and followed by 3mL of NaOH , 3 mL of H_2O_2 and stirred overnight. The reaction mixture was then neutralized with dilute HCl followed by extraction with dichloromethane. The extracts were dried over MgSO_4 and the solvent removed at reduced pressure to yield product as a colorless oil (0.900 g, 0.005 mol) (98% yield).

8,11-Dioxatricyclo[4,3,3,0]dodec-3-01, [66]

IR (neat, cm^{-1}): 3426, 2968, 2927, 2866, 1653, 1458, 1060, 912, 730.

^1H NMR (300.133 MHz, CDCl_3): δ 1.33-1.93 (6H, m), 2.25 (1H, br s), 3.65-3.86 (9H, m)

^{13}C NMR (75.4 MHz, CDCl_3): δ 26.84 (t), 30.41 (t), 37.01 (t), 51.82 (s), 53.79 (s), 66.24 (d), 75.59 (t), 75.75 (t), 79.02 (t), 79.57 (t)

LRMS (EI) m/e (%abundance): 166 (39), 153 (13), 139 (100), 131 (13), 121 (42), 105 (19), 91 (42), 79 (53), 67 (52), 55 (81), 41 (97)

LRMS (CI) (NH_3) m/e (%abundance): 185 ($\text{M}+\text{H}^+$, 100)

HRMS (CI) m/e calculated for $\text{C}_{10}\text{H}_{17}\text{O}_3$ = 185.1178; found = 185.1196

Preparation of tosylate derivatives of [66]

Alcohol, [66] (1.19 g, 6.47 mmol) was dissolved in 3 mL of dry pyridine under argon atmosphere in ice bath. Then TsCl (1.90 g, 9.97 mmol) in pyridine was added dropwise to the stirring solution. The reaction mixture was stirred at room temperature overnight. The reaction mixture was poured over conc. HCl on ice. The resulting acidic solution was extracted three times with dichloromethane. The extracts were combined and washed with sodium bicarbonate solution followed by an aqueous wash. After drying over MgSO_4 , removal of solvent by rotary evaporation yielded product. Flash separation was employed to cleanly separate the

product [88] (1.50 g, 4.44 mmol) (68% yield). A solvent system of ethylacetate:hexane in the relative ratio 1:1 was used in this separation.

3-Tosyl-8,11-dioxatricyclo[4,3,3,0]dodecane, [88]

mp = 68-70°C

IR (neat, cm^{-1}): 2935, 2869, 1735, 1598, 1448, 1359, 1246, 1174, 1096, 1066, 1049, 935, 917, 868, 816, 673

^1H NMR (300.133 MHz, CDCl_3): δ 1.48-1.92 (6H, m), 2.43 (3H, s), 3.59-3.78 (8H, m), 4.61-4.70 (1H, m), 7.31 (2H, d, $J=8.3\text{Hz}$), 7.75 (2H, d, $J=8.3\text{Hz}$)

^{13}C NMR (75.4 MHz, CDCl_3): δ 21.53 (q), 25.94 (t), 26.83 (t), 33.80 (t), 51.78 (s), 53.51 (s), 76.58 (t), 76.66 (t), 77.34 (d), 78.16 (t), 78.30 (t), 127.56 (d), 129.81 (d), 134.46 (s), 144.64 (S)

LRMS (EI) m/e (%abundance): 166 (15), 148 (8), 135 (24), 121 (37), 106 (58), 91 (100), 79 (48), 65 (14), 53 (13), 39 (30)

HRMS (EI) m/e calculated for $\text{C}_{17}\text{H}_{22}\text{O}_5\text{S}_1$ = 338.1188; found = 338.1197

Preparation of para-nitrobenzoate derivatives of [66]

Alcohol, [66] (0.199 g, 1.08 mmol) was dissolved in 3 mL of dry pyridine under argon atmosphere in an ice bath. Then PNBCL (0.306 g, 1.65 mmol) was added dropwise to the stirring solution. The reaction mixture was stirred at room temperature overnight. The reaction mixture was poured over conc. HCl on ice. The resulting acidic solution was

extracted three times with dichloromethane. The extracts were combined and washed with sodium bicarbonate solution followed by an aqueous wash. After drying over MgSO_4 and the removal of solvent by rotary evaporation to yield product. Flash separation was employed to cleanly separate the product, [40] (0.32 g, 0.961 mmol) (87% yield). A solvent system of ethylacetate:hexane in the relative ratio 1:1 was used in this separation.

para-Nitrobenzoate-8,11-dioxatricyclo[4,3,3,0]dodecane, [40]

mp = 78-80°C

^1H NMR (300.133 MHz, CDCl_3): δ 1.62-2.09 (6H, m), 3.67-3.82 (8H, m), 5.16-5.24 (1H, m), 8.11-8.23 (4H, m)

^{13}C NMR (75.4 MHz, CDCl_3): δ 26.16 (t), 32.90 (t), (two carbon overlap), 52.00 (s), 53.36 (s), 70.72 (d), 76.15 (t), 76.55 (t), 78.13 (t), 78.59 (t), 123.41 (d), 130.50 (d), 135.68 (s), 150.54 (s), 163.92 (s)

LRMS (EI) m/e (%abundance): 333 (M^+ , 1), 303 (12), 183 (6), 166 (76), 150 (72), 136 (92), 120 (100), 104 (60), 91 (60), 79 (48), 67 (26), 55 (18), 41 (38)

HRMS (EI) m/e calculated for $\text{C}_{17}\text{H}_{19}\text{O}_6\text{N}_1$ = 333.1212; found = 333.1212

Preparation of 4-biphenyl carboxylate derivatives of [66]

Alcohol, [66] (0.115 g, 0.623 mmol) was dissolved in 5 mL of dry pyridine under argon atmosphere in ice bath. Then 4-biphenyl carbonyl chloride (0.202 g 0.935 mmol) was added dropwise to the stirring solution. The reaction mixture was

stirred at room temperature overnight. The reaction mixture was poured over conc. HCl on ice. The resulting acidic solution was extracted three times with dichloromethane. The extracts were combined and washed with sodium bicarbonate solution followed by an aqueous wash. After drying over MgSO_4 , solvent was removed by rotary evaporation to yield the product (0.203 g, 0.558 mmol) (90% yield). Flash separation was employed to cleanly separate the pure product [95-OBP]. A solvent system of ethylacetate:hexane in the relative ratio 1:1 was used in this separation. Crystallization of the product was accomplished in hexane:dichloromethane in a relative ratio of 10:1, respectively.

4-Biphenyl carboxylate-8,11-dioxatricyclo[4,3,3,0]dodecane,
[95-OBP]

mp = 108-110°C

^1H NMR (300.133 MHz, CDCl_3): δ 1.62-2.09 (6H, m), 3.75-3.86 (8H, m), 5.19-5.27 (1H, m), 7.32-8.09 (9H, m)

^{13}C NMR (75.4 MHz, CDCl_3): δ 26.03 (t), 26.21 (t), 32.87 (t), 51.87 (s), 53.20 (s), 69.35 (d), 76.42 (t), 76.71 (t), 78.05 (t), 78.47 (t), 126.87 (d), 127.06 (d), 127.98 (d), 128.75 (d), 129.04 (s), 129.88 (d), 139.77 (s), 145.51 (s), 165.58 (s)

LRMS (EI) m/e (%abundance): 364 (M^+ , 15), 198 (44), 181 (100), 166 (69), 152 (41), 136 (72), 121 (21), 107 (18), 91 (22), 79 (19), 41 (15)

HRMS (EI) m/e calculated for $C_{23}H_{24}O_4$ = 364.1675; found = 364.1675

Crystallization of the product, [95-OBP] was accomplished in dichloromethane:hexane in a relative ratio of 10:1.

X-ray analysis:

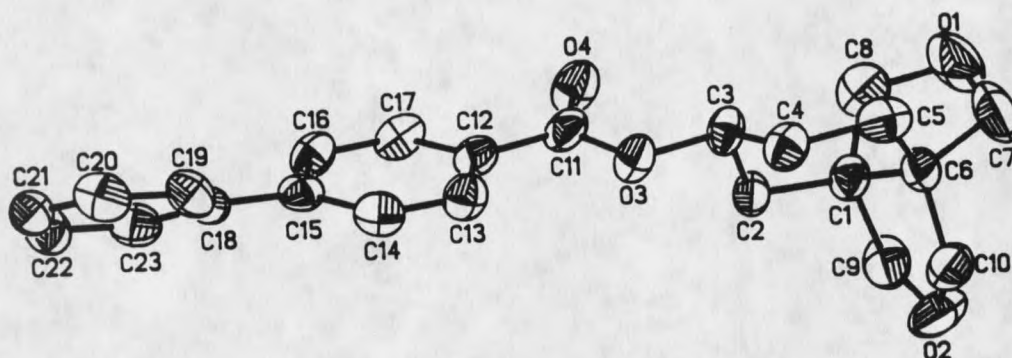


Figure 73. ORTEP Drawing of [95-OBP].

Table 40. Bond Lengths (Å) of [95-OBP].

C(1)-C(2)	1.532(4)	C(1)-C(6)	1.536(4)
C(1)-C(8)	1.510(5)	C(1)-C(9)	1.530(4)
C(2)-C(3)	1.515(4)	C(3)-C(4)	1.502(4)
C(3)-O(3)	1.465(4)	C(4)-C(5)	1.512(5)
C(5)-C(6)	1.527(4)	C(6)-C(7)	1.522(5)
C(6)-C(10)	1.512(5)	C(7)-O(1)	1.396(5)
O(1)-C(8)	1.412(5)	C(9)-O(2)	1.406(4)
O(2)-C(10)	1.413(4)	O(3)-C(11)	1.343(4)
C(11)-O(4)	1.206(4)	C(11)-C(12)	1.479(4)
C(12)-C(13)	1.382(4)	C(12)-C(17)	1.387(4)
C(13)-C(14)	1.389(4)	C(14)-C(15)	1.386(4)
C(15)-C(16)	1.395(4)	C(15)-C(18)	1.480(4)
C(16)-C(17)	1.382(4)	C(18)-C(19)	1.390(4)
C(18)-C(23)	1.390(4)	C(19)-C(20)	1.391(5)
C(20)-C(21)	1.382(5)	C(21)-C(22)	1.370(5)
C(22)-C(23)	1.385(5)		

Table 41. Bond Angles (°) of [95-OBP].

C(2)-C(1)-C(6)	114.6(2)	C(2)-C(1)-C(8)	114.1(3)
C(6)-C(1)-C(8)	102.9(3)	C(2)-C(1)-C(9)	110.7(3)
C(6)-C(1)-C(9)	100.9(2)	C(8)-C(1)-C(9)	112.8(3)
C(1)-C(2)-C(3)	112.9(3)	C(2)-C(3)-C(4)	110.7(2)
C(2)-C(3)-O(3)	109.6(2)	C(4)-C(3)-O(3)	106.7(2)
C(3)-C(4)-C(5)	109.6(3)	C(4)-C(5)-C(6)	114.6(3)

(Table 41. Continued)

C(1)-C(6)-C(5)	114.3(3)	C(1)-C(6)-C(7)	101.0(3)
C(5)-C(6)-C(7)	110.6(3)	C(1)-C(6)-C(10)	103.4(2)
C(5)-C(6)-C(10)	114.3(3)	C(7)-C(6)-C(10)	112.2(3)
C(6)-C(7)-O(1)	108.5(3)	C(7)-O(1)-C(8)	110.2(3)
C(1)-C(8)-O(1)	107.3(3)	C(1)-C(9)-O(2)	108.6(3)
C(9)-O(2)-C(10)	110.1(3)	C(6)-C(10)-O(2)	107.1(3)
C(3)-O(3)-C(11)	116.7(2)	O(3)-C(11)-O(4)	123.2(3)
O(3)-C(11)-C(12)	112.9(3)	O(4)-C(11)-C(12)	123.9(3)
C(11)-C(12)-C(13)	123.7(3)	C(11)-C(12)-C(17)	117.8(3)
C(13)-C(12)-C(17)	118.5(3)	C(12)-C(13)-C(14)	120.7(3)
C(13)-C(14)-C(15)	121.1(3)	C(14)-C(15)-C(16)	117.9(3)
C(14)-C(15)-C(18)	122.2(3)	C(16)-C(15)-C(18)	119.9(3)
C(15)-C(16)-C(17)	120.9(3)	C(12)-C(17)-C(16)	120.9(3)
C(15)-C(18)-C(19)	121.1(3)	C(15)-C(18)-C(23)	121.6(3)
C(19)-C(18)-C(23)	117.2(3)	C(18)-C(19)-C(20)	121.6(3)
C(19)-C(20)-C(21)	119.5(3)	C(20)-C(21)-C(22)	119.9(3)
C(21)-C(22)-C(23)	120.3(3)	C(18)-C(23)-C(22)	121.5(3)

Preparation of 1,5-dibromoethyl ether, [24]

1,5-Dihydroxyethyl ether (24.0 g, 0.226 mol) was placed in a 100 mL flask under argon. PBr_3 (20.0 mL, 0.211 mol) was added dropwise. The reaction mixture was refluxed overnight, after the solution was poured over ice water. The resulting solution was extracted three times with dichloromethane. The combined extracts were dried over

MgSO₄ and the solvent was removed by rotary evaporation to yield product as a colorless oil. (46.6 g, 0.201 mol) (89% yield)

1,5-Dibromoethyl ether, [24]

IR (neat, cm⁻¹): 2964, 2880, 2852, 1419, 1357, 1279, 1223, 1190, 1117, 1038, 949, 663

¹HNMR (300.133 MHz, CDCl₃): δ 3.44 (4H, t, J=6.2Hz), 3.79 (4H, t, J=6.2Hz)

¹³CNMR (75.4 MHz, CDCl₃): δ 29.97 (t), 70.94 (t)

LRMS (EI) m/e: 232, 231, 230, 139, 137, 109, 107, 95, 93, 43

Preparation of cis-1,6-dicarbomethoxy-9-oxa-bicyclo

[5,4,0]undec-3-ene, [23]

A solution of 100 mL of dry THF, 70 mL of 2.5 M n-BuLi (0.175 mol) and 25 mL of diisopropylamine (0.180 mol) was stirred under argon at -10°C for 30 minutes. The temperature was taken down to -78°C and *cis*-3,4-dicarbomethoxycyclohexene (14.0 g, 0.071 mol) was added dropwise, creating a bright red solution. After addition was completed the solution was allowed to stir for 15 minutes. 1,5-dibromoethyl ether (9 mL, 0.085 mol) was added dropwise. The solution was allowed to warm to room temperature and stirred overnight. The reaction mixture was then neutralized with dilute HCl. The resulting phases were separated and the remaining solution was extracted with dichloromethane. The combined extracts were dried over MgSO₄ and the solvent removed by rotary evaporation. The

resulting liquid was distilled to yield a product as a yellow, viscous oil (11.8 g, 0.044 mol) (62% yield).

cis-1,6-Dicarbomethoxy-9-oxa-bicyclo[5,4,0]undec-3-ene, [23]

IR (neat, cm^{-1}): 3028, 2948, 1734, 1434, 1280, 1200, 1145, 753, 673

^1H NMR (300.133 MHz, CDCl_3): δ 2.02-2.28 (4H, m), 2.39 (2H, d, $J=17.4\text{Hz}$), 2.66 (2H, d, $J=17.4\text{Hz}$), 3.65 (6H, s), 3.72-3.77 (4H, m), 5.56 (2H, s)

^{13}C NMR (75.4 MHz, CDCl_3): δ 34.00 (t), 36.72 (t), 49.10 (s), 51.71 (q), 65.88 (t), 124.10 (d), 175.64 (s)

LRMS (EI) m/e: 268, 236, 224, 208, 178, 163 (base), 150, 131, 118, 91, 77, 59, 41

HRMS (EI) m/e calculated for $\text{C}_{14}\text{H}_{20}\text{O}_5$ = 268.1311 ; found = 268.1301

Preparation of cis-1,6-dihydroxymethyl-9-oxabicyclo[5,4,0]undec-3-ene

A solution of [23] (3.30 g, 0.0123 mol) in 10 mL of dry THF was added dropwise at 0°C to a stirring solution of LAH (0.700 g, 0.0185 mol) in 100 mL of dry THF. The reaction mixture was stirred overnight at a room temperature and then hydrolyzed with wet ether. The white lithium salts were filtered off and the solvent removed by rotary evaporation to yield (1.50 g, 7.10 mmol) product as a white solid. (58% yield)

cis-1,6-Dihydroxymethyl-9-oxabicyclo[5,4,0]undec-3-ene

IR (Nujol, cm^{-1}): 3215, 3012, 2862, 1458, 1374, 1122, 1026,
666

^1H NMR (300.133 MHz, CDCl_3): δ 1.79 (4H, t, $J=6.5\text{Hz}$), 2.01
(2H, d), 2.10 (2H, d), 3.67 (4H, s), 3.65-3.80 (4H, m),
5.56 (2H, t, $J=1.3\text{Hz}$)

^{13}C NMR (75.4 MHz, CDCl_3): δ 33.18 (t), 35.75 (t), 42.00 (s),
64.44 (t), 67.39 (t), 124.27 (d)

LRMS (EI) m/e: 176, 148, 117, 91 (base), 77, 65, 44

LRMS (CI) (Methane) m/e (%abundance): 213 ($\text{M}+\text{H}^+$, 7), 195
(100), 177 (27), 165 (26), 159 (18), 149 (21), 133
(32), 121 (19), 107 (21)

HRMS (CI) m/e calculated for $\text{C}_{12}\text{H}_{21}\text{O}_3$ = 213.1491; found =
213.1462

Preparation of 8,12-dioxatricyclo[5,4,3,0]tetradec-3-ene,
[28]

cis-1,6-Dihydroxymethyl-9-oxabicyclo[5,4,0]undec-3-ene
(1.22 g, 5.76 mmol) was dissolved in 5 mL of dry pyridine
and then 0.45 mL of MsCl (0.660 g, 5.76 mmol) were added
dropwise to the stirring solution under argon in an ice
bath. The reaction mixture was stirred at room temperature
overnight. The reaction mixture was then poured over
concentrated HCl on ice to acidify. Extraction with
dichloromethane yielded the desired product as a colorless
oil (1.03 g, 5.30 mmol) (92% yield). Florisil separation
was employed to cleanly separate the pure product. A

solvent system of ethylacetate:hexane in the relative ratio 3:7 was used in this separation.

8,12-Dioxatricyclo[5,4,3,0]tetradec-3-ene, [28]

IR (neat, cm^{-1}): 3036, 2922, 2860, 1460, 1273, 1126, 1047,
950, 993, 814, 712, 661

^1H NMR (300.133 MHz, CDCl_3): δ 1.67-2.05 (8H, m), 3.55 (2H, d, $J=8.5\text{Hz}$), 3.68 (2H, d, $J=8.5\text{Hz}$), 3.64-3.81 (4H, m), 5.78-5.80 (2H, m)

^{13}C NMR (75.4 MHz, CDCl_3): δ 32.73 (t), 40.15 (t), 47.58 (s), 65.83 (t), 80.20 (t), 127.09 (d)

LRMS (EI) m/e (%abundance): 194 (M^+ , 2), 176 (7), 166 (61), 139(44), 131(38), 119(49), 105(72), 91(100), 79(68), 67(35), 53(28), 41(59)

HRMS (EI) m/e calculated for $\text{C}_{12}\text{H}_{18}\text{O}_2$ = 194.1307 ; found = 194.1306

Hydroboration of 8,12-dioxatricyclo[5,4,3,0]tetradec-3-ene, [28]

The propellane, [28] (0.260 g, 1.340 mmol) was dissolved in 5 mL of dry THF and then 2 mL of $\text{BH}_3\text{:THF}$ (0.0312 g, 2.26 mmol) were added dropwise to the stirring solution under argon at 0°C . The solution was warmed to room temperature and stirred overnight. The reaction mixture was quenched with a small amount of water followed by the slow addition of 1 mL of 3N-NaOH and 1 mL 30% H_2O_2 . After the addition was complete, the solution was stirred for overnight. The reaction mixture was then neutralized

with dilute HCl followed by extraction with dichloromethane. The solvent was dried over MgSO_4 and the solvent removed by rotary evaporation to yield alcohol mixture (0.284 g, 1.34 mmol) (99% yield). Capillary GC analysis showed the *syn*- and *anti*- alcohol in the ratio of 26:74.

syn-8,12-Dioxatricyclo[5,4,3,0]tetradec-3-ol, [67-*syn*]

IR (neat, cm^{-1}): 3421, 2930, 2868, 1714, 1456, 1358, 1260, 1118, 1051, 946, 922

^1H NMR (300.133 MHz, CDCl_3): δ 1.32-2.37 (10H, m), 3.47 (1H, d, $J=8.4\text{Hz}$), 3.60 (1H, d, $J=8.1\text{Hz}$), 3.90 (1H, d, $J=8.3\text{Hz}$), 4.09 (1H, d, $J=8.4\text{Hz}$), 3.59-4.01 (4H, m)

^{13}C NMR (75.4 MHz, CDCl_3): δ 25.78 (t), 30.74 (t), 35.95 (t), 36.40 (t), 43.05 (t), 45.18 (s), 46.00 (s), 62.65 (t), 64.38 (t), 66.78 (d), 78.22 (t), 78.41 (t)

LRMS (EI) m/e (%abundance): 194 (7), 166 (24), 149 (10), 139 (100), 131 (14), 121 (56), 105 (34), 91 (70), 79 (74), 67 (51), 55 (59), 41 (80)

LRMS (CI) (Methane) m/e (%abundance): 213 ($\text{M}+\text{H}^+$, 13), 211 (34), 195 (100), 177 (17), 165 (19), 159 (14), 151 (22), 139 (19), 133 (25), 121 (26), 107 (20), 97 (13), 93 (16)

HRMS (CI) m/e calculated for $\text{C}_{12}\text{H}_{21}\text{O}_3$ = 213.1491; found = 213.1487

anti-8,12-Dioxatricyclo[5,4,3,0]tetradec-3-ol, [67-*anti*]

IR (neat, cm^{-1}): 3421, 2930, 2868, 1714, 1456, 1358, 1260, 1118, 1051, 946, 922

^1H NMR (300.133 MHz, CDCl_3): δ 1.27-2.04 (10H, m), 3.46 (1H, d, $J=8.4\text{Hz}$), 3.49 (1H, d, $J=8.3\text{Hz}$), 3.91 (1H, d, $J=8.4\text{Hz}$), 3.99 (1H, d, $J=8.4\text{Hz}$), 3.58-3.95 (4H, m)

^{13}C NMR (75.4 MHz, CDCl_3): δ 31.18 (t), 33.41 (t), 35.14 (t), 36.04 (t), 37.14 (t), 44.00 (s), 47.44 (s), 62.53 (t), 64.51 (t), 66.95 (t), 77.33 (t), 79.00 (t)

LRMS (EI) m/e (%abundance): 212 (M^+ , 2), 194 (7), 166 (45), 149 (16), 139 (97), 131 (22), 121 (55), 105 (44), 91 (92), 79 (100), 67 (60), 55 (60), 41 (84)

LRMS (CI) (Methane) m/e (%abundance): 213 ($\text{M}+\text{H}^+$, 13), 211 (20), 195 (100), 177 (23), 165 (17), 159 (13), 151 (23), 139 (19), 133 (27), 121 (25), 107 (15), 93 (13)

HRMS (CI) m/e calculated for $\text{C}_{12}\text{H}_{21}\text{O}_3$ = 213.1491; found = 213.1488

Preparation of para-nitrobenzoate derivatives of 8,12-dioxatricyclo[5,4,3,0]tetradec-3-ene, [28]

The mixture of *syn*- and *anti*- alcohols derived from the hydroboration of [28] (0.284g, 1.11 mmol) was dissolved in 10 mL of dry pyridine and an argon atmosphere was created. Then PNB Cl (0.310g, 1.67 mmol) was dissolved in dry pyridine and added dropwise to the stirring solution at 0°C . The reaction was stirred at room temperature overnight. The reaction mixture was poured over ice water and neutralized with HCl . A white solid, (pyridine hydrochloride) formed which was filtered off and the resulting solution was extracted three times with dichloromethane. The extracts

were combined and washed with sodium bicarbonate solution followed by an aqueous wash. After drying over MgSO_4 and the solvent was removed by rotary evaporation to yield the product as a white solid. Flash chromatography was employed to cleanly isolate the isomers (0.313 g, 0.867 mmol) (78% yield). A solvent system of ethylacetate:hexane in the relative ratio 1:1 was used in this separation.

syn-3-para-Nitrobenzoate-8,12-dioxatricyclo[5,4,3,0]

tetradecane, [41-syn]

$^1\text{H NMR}$ (300.133 MHz, CDCl_3): δ 1.45-2.30 (10H, m), 3.61 (1H, d, $J=8.4\text{Hz}$), 3.71 (1H, d, $J=8.4\text{Hz}$), 3.91 (1H, d, $J=8.4\text{Hz}$), 4.07 (1H, d, $J=8.4\text{Hz}$), 3.67-3.86 (4H, m), 5.21-5.30 (1H, m), 8.14-8.28 (4H, m)

$^{13}\text{C NMR}$ (75.4 MHz, CDCl_3): δ 26.18 (t), 26.67 (t), 35.76 (t), 36.17 (t), 38.02 (t), 45.07 (s), 46.04 (s), 62.82 (t), 64.10 (t), 71.65 (d), 78.16 (t) (2 carbon), 123.49 (d), 130.61 (d), 135.90 (s), 150.52 (s), 164.05 (s)

LRMS (EI) m/e (%abundance): 210 (9), 164 (13), 151 (100), 136 (28), 121 (29), 109 (31), 91 (31), 79 (34), 67 (24), 55 (21)

LRMS (HPEC) (NH_3) m/e (%abundance): 361 (M^+ , 100), 345 (4), 329 (5), 148 (2), 127 (1)

HRMS (HPEC) (NH_3) m/e calculated for $\text{C}_{19}\text{H}_{23}\text{O}_6\text{N}_1 = 361.1525$;
found = 361.1529

anti-3-para-Nitrobenzoate-8,12-dioxatricyclo[5,4,3,0]
tetradecane, [41-anti]

$^1\text{H NMR}$ (300.133 MHz, CDCl_3): δ 1.36-2.42 (10H, m), 3.55 (1H, d, $J=8.3\text{Hz}$), 3.58 (1H, d, $J=8\text{Hz}$), 3.91 (1H, d, $J=8.3\text{Hz}$), 4.09 (1H, d, $J=8.5\text{Hz}$), 3.68-3.86 (4H, m), 5.25-5.35 (1H, m), 8.16-8.28 (4H, m)

$^{13}\text{C NMR}$ (75.4 MHz, CDCl_3): δ 26.98 (t), 32.40 (t), 32.53 (t), 35.47 (t), 36.89 (t), 44.19 (s), 47.24 (s), 62.87 (t), 64.70 (t), 71.85 (d), 77.50 (t), 78.88 (t), 123.48 (d), 130.65 (d), 135.95 (s), 150.59 (s), 164.14 (s)

LRMS (EI) m/e (%abundance): 196 (10), 165 (47), 151 (24), 137 (61), 123 (100), 107 (30), 93 (58), 79 (7), 67 (54), 55 (37)

LRMS (HPEC) (NH_3) m/e (%abundance): 361 (M^+ , 100), 148 (30)

HRMS (HPEC) (NH_3) m/e calculated for $\text{C}_{19}\text{H}_{23}\text{O}_6\text{N}_1$ = 361.1525;

found = 361.1511

Crystallization of the product, [41-anti] was accomplished in dichloromethane:hexane in a relative ratio of 1:20 respectively.

X-ray analysis:

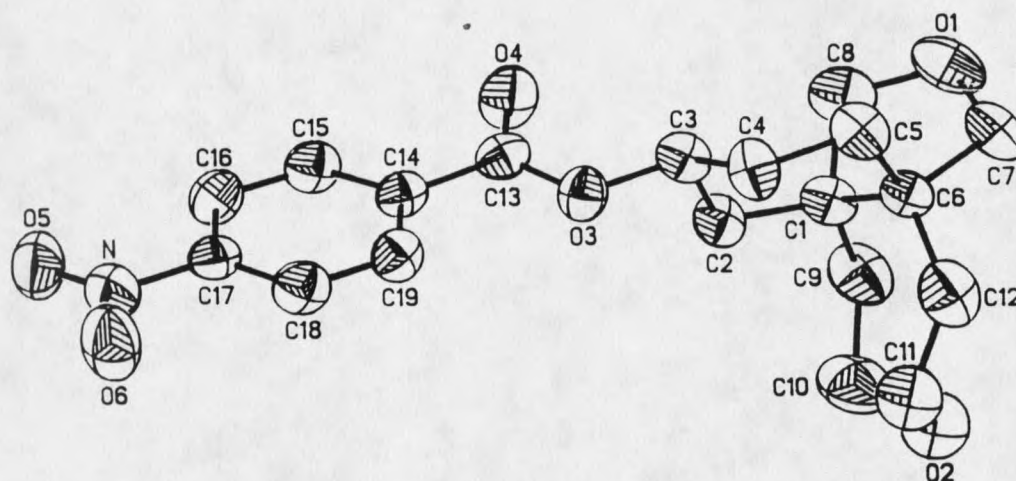


Figure 74. ORTEP Drawing of [41-anti].

Table 42. Bond Lengths (Å) of [41-anti].

C (1) - C (2)	1.537 (9)	C (1) - C (6)	1.563 (7)
C (1) - C (8)	1.534 (11)	C (1) - C (9)	1.508 (8)
C (2) - C (3)	1.504 (7)	C (3) - C (4)	1.504 (7)
C (3) - O (3)	1.463 (8)	C (4) - C (5)	1.527 (9)
C (5) - C (6)	1.543 (8)	C (6) - C (7)	1.543 (11)
C (6) - C (12)	1.524 (11)	C (7) - O (1)	1.411 (9)
O (1) - C (8)	1.423 (9)	C (9) - C (10)	1.489 (13)
C (10) - H (10a)	0.960 (1)	C (10) - H (10b)	0.960 (1)
C (10) - H (10c)	0.960 (1)	C (10) - H (10d)	0.960 (1)
C (10) - O (2)	1.430 (11)	C (10) - O (2')	1.430 (11)

(Table 42. Continued)

O(2)-C(11)	1.430 (12)	O(2')-C(11')	1.430 (18)
C(11)-H(11a)	0.960 (1)	C(11)-H(11b)	0.960 (1)
C(11)-C(12)	1.540 (13)	C(11')-H(11c)	0.960 (1)
C(11')-H(11d)	0.960 (1)	C(11')-C(12)	1.540 (12)
C(12)-H(12a)	0.960 (1)	C(12)-H(12b)	0.960 (1)
C(12)-H(12c)	0.960 (1)	C(12)-H(12d)	0.960 (1)
O(3)-C(13)	1.328 (7)	C(13)-O(4)	1.189 (9)
C(13)-C(14)	1.514 (9)	C(14)-C(15)	1.364 (8)
C(14)-C(19)	1.385 (9)	C(15)-C(16)	1.391 (10)
C(16)-C(17)	1.382 (10)	C(17)-C(18)	1.373 (8)
C(17)-N	1.493 (10)	C(18)-C(19)	1.380 (9)
N-O(5)	1.201 (8)	N-O(6)	1.200 (10)

Table 43. Bond Angles (°) of [41-anti].

C(2)-C(1)-C(6)	113.0 (4)	C(2)-C(1)-C(8)	111.2 (6)
C(6)-C(1)-C(8)	100.4 (5)	C(2)-C(1)-C(9)	110.1 (5)
C(6)-C(1)-C(9)	114.9 (5)	C(8)-C(1)-C(9)	106.7 (5)
C(1)-C(2)-C(3)	115.0 (5)	C(2)-C(3)-C(4)	110.6 (5)
C(2)-C(3)-O(3)	109.4 (5)	C(4)-C(3)-O(3)	107.4 (4)
C(3)-C(4)-C(5)	108.2 (5)	C(4)-C(5)-C(6)	112.2 (5)
C(1)-C(6)-C(5)	110.3 (5)	C(1)-C(6)-C(7)	99.5 (4)
C(5)-C(6)-C(7)	107.7 (6)	C(1)-C(6)-C(12)	117.3 (6)
C(5)-C(6)-C(12)	109.7 (5)	C(7)-C(6)-C(12)	111.7 (5)
C(6)-C(7)-O(1)	107.3 (5)	C(7)-O(1)-C(8)	109.8 (6)

(Table 43. Continued)

C(1)-C(8)-O(1)	106.9(5)	C(1)-C(9)-C(10)	120.0(6)
C(9)-C(10)-H(10a)	107.9(1)	C(9)-C(10)-H(10b)	108.2(1)
H(10a)-C(10)-H(10b)	109.7(1)	C(9)-C(10)-C(10c)	106.6(1)
C(9)-C(10)-H(10d)	107.0(1)	H(10c)-C(10)-H(10d)	109.5(1)
C(9)-C(10)-O(2)	114.7(8)	H(10a)-C(10)-O(2)	107.9(1)
H(10b)-C(10)-O(2)	108.2(1)	C(9)-C(10)-O(2')	119.6(8)
H(10c)-C(10)-O(2')	106.6(1)	H(10d)-C(10)-O(2')	107.3(1)
C(10)-O(2)-C(11)	107.5(8)	C(10)-O(2')-C(11')	107.8(12)
O(2)-C(11)-H(11a)	108.2(1)	O(2)-C(11)-H(11b)	108.6(1)
H(11a)-C(11)-H(11b)	109.4(1)	O(2)-C(11)-C(12)	113.8(10)
H(11a)-C(11)-C(12)	108.3(1)	H(11b)-C(11)-C(12)	108.4(1)
O(2')-C(11')-H(11c)	110.0(1)	O(2')-C(11')-H(11d)	110.5(1)
H(11c)-C(11')-H(11d)	110.0(1)	O(2')-C(11')-C(12)	104.9(10)
H(11c)-C(11')-C(12)	110.3(1)	H(11d)-C(11')-C(12)	111.0(1)
C(6)-C(12)-C(11)	124.(7)	C(6)-C(12)-C(11')	121.7(8)
C(6)-C(12)-H(12a)	105.6(1)	C(11)-C(12)-H(12a)	105.7(1)
C(6)-C(12)-H(12b)	105.6(1)	C(11)-C(12)-H(12b)	105.7(1)
H(12a)-C(12)-H(12b)	109.6(1)	C(6)-C(12)-H(12c)	106.3(1)
C(11')-C(12)-H(12c)	106.2(1)	C(6)-C(12)-H(12d)	106.2(1)
C(11')-C(12)-H(12d)	106.6(1)	H(12c)-C(12)-H(12d)	109.6(1)
C(3)-O(3)-C(13)	116.1(5)	O(3)-C(13)-O(4)	125.2(6)
O(3)-C(13)-C(14)	111.7(6)	O(4)-C(13)-C(14)	123.1(5)
C(13)-C(14)-C(15)	117.4(6)	C(13)-C(14)-C(19)	122.1(5)
C(15)-C(14)-C(19)	120.5(6)	C(14)-C(15)-C(16)	121.6(6)
C(15)-C(16)-C(17)	116.3(6)	C(16)-C(17)-C(18)	123.5(6)

(Table 43. Continued)

C(16)-C(17)-N	117.3(6)	C(18)-C(17)-N	119.2(6)
C(17)-C(18)-C(19)	118.6(6)	C(14)-C(19)-C(18)	119.6(5)
C(17)-N-O(5)	118.5(7)	C(17)-N-O(6)	117.7(6)
O(5)-N-O(6)	123.8(7)		

Preparation of syn-tosylate derivative of [28]

The *syn*-para-nitrobenzoate derivative of [28] (33.0 mg, 0.0914 mmol) was dissolved in 0.2 mL dichloromethane and then added to a 80% aqueous ethanol solution that was 0.5% by weight in KOH. The reaction was stirred overnight. Most of the solvent was removed by rotary evaporation, then 5 mL of water was added to the residue. The solution was extracted with dichloromethane. The combined extracts were dried over MgSO₄ and the solvent was removed by rotary evaporation to give *syn*-alcohol (17.8 mg, 0.0841 mmol) (92% yield). The *syn*-alcohol (12.7 mg, 0.0599 mmol) was dissolved in 0.2 mL of dichloromethane to which was added 1 mL of pyridine. The solution was cooled to 0°C and TsCl (45.8mg, 0.240 mmol) was added dropwise. The reaction was warmed to room temperature and stirred overnight. The solution was poured over ice water to neutralize with HCl and the solution was extracted with dichloromethane. The extracts were combined and washed with sodium bicarbonate solution followed by an aqueous wash. After drying over MgSO₄ the solvent was removed by rotary evaporation to yield

syn-tosylate as a white solid . Flash chromatography was employed to cleanly isolate the pure *syn*-tosylate (13.59 mg, 0.0371 mmol) (62% yield). A solvent system of ethylacetate:hexane in the relative ration 1:1 was used in this separation.

Preparation of anti-tosylate derivative of [28]

In a similar fashion, saponification of the *anti*-para-nitrobenzoate derivative of [28] (38.8 mg, 0.107 mmol) afforded 17.7 mg (0.0834 mmol) of the *anti*-alcohol (78% yield). Using the identical workup as reported above, the *anti*-alcohol (17.7 mg, 0.0834 mmol) were dissolved in 0.2 mL of dichloromethane to which was added 1 mL of pyridine and TSCl (24.0 mg, 0.16 mmol). The *anti*-tosylate was cleanly separated as a white solid 14.04 mg (0.0384 mmol) (46% yield).

anti-Tosyl-8,12-dioxatricyclo[5.4.3.0]tetradecane, [89]

$^1\text{H NMR}$ (300.133 MHz, CDCl_3): δ 1.32-2.29 (10H, m), 2.43 (3H, s), 3.46 (1H, d, $J=8.7\text{Hz}$), 3.50 (1H, d, $J=8.5\text{ Hz}$), 3.80 (1H, d, $J=8.5\text{Hz}$), 3.84 (1H, d, $J=8.6\text{Hz}$), 3.62-3.80 (4H, m), 4.71-4.81 (1H, m), 7.32 (2H, d, $J=8.3\text{Hz}$), 7.77 (2H, d, $J=8.3\text{Hz}$)

$^{13}\text{CNMR}$ (75.4 MHz, CDCl_3): δ 21.61 (g), 27.61 (t), 32.07 (t), 34.04 (t), 35.77 (t), 37.09 (t), 44.03 (s), 47.35 (s), 63.02 (t), 64.67 (t), 77.66 (t), 78.56 (d), 78.86 (t), 127.62 (d), 129.80 (d), 134.68 (s), 144.55 (s)

LRMS (EI) m/e (%abundance): 212 (1), 194 (18), 166 (23), 139 (19), 119 (22), 105 (29), 91 (100), 79 (54), 65 (28), 55 (17), 41 (20)

LRMS (CI) (NH₃) m/e (%abundance): 384 (M+NH₄⁺, 9), 212 (69), 195 (100)

HRMS (EI) m/e calculated for C₂₃H₂₆O₁S₂ = 366.1501; found = 366.1502

Preparation of *cis*-1,6-dicarbomethoxybicyclo[4,2,0]oct-3-ene, [20]

A solution of 200 mL of dry THF, 140 mL of 2.5 M n-BuLi (0.350 mol) and 50 mL of diisopropylamine (0.360 mol) was stirred under argon at -10°C for 30 minutes. The temperature was taken down to -78°C and *cis*-3,4-dicarbomethoxy cyclohexene 28 g (0.141 mol) was added dropwise, creating a bright red solution. After addition was completed, the solution was allowed to stir for 15 minutes and 14.56 mL of 1,2-dibromo ethane (0.169 mol) were added dropwise. The solution was allowed to warm to room temperature and stirred overnight. Identical workup (page 120) and distillation yielded product as a colorless oil (15.8 g, 0.071 mol) (50% yield).

cis-1,6-Dicarbomethoxybicyclo[4,2,0]oct-3-ene, [20]

IR (neat, cm⁻¹): 3037, 2997, 2950, 2844, 1735, 1436, 1277, 1237, 1118, 1011

¹HNMR (300.133 MHz, CDCl₃): δ 1.59-2.42 (8H, m), 3.62 (6H, s), 5.99 (2H, t, J=1.4Hz)

$^{13}\text{CNMR}$ (75.4 MHz, CDCl_3): δ 26.02 (t), 31.62 (t), 50.14 (s),
51.67 (q), 127.15 (d), 176.05 (s)

LRMS (EI) m/e: 192, 164, 133, 105 (base), 91, 77, 59, 51,
41

LRMS (CI) (Methane) m/e (%abundance): 225 ($\text{M}+\text{H}^+$, 39), 193
(100), 165 (18), 105 (14)

HRMS (CI) m/e calculated for $\text{C}_{12}\text{H}_{17}\text{O}_4$ = 225.1127; found =
225.1149

Preparation of *cis*-1,6-dihydroxymethylbicyclo[4,2,0] oct-3-ene

A solution of [20] (8.60 g, 0.0384 mol) in 20 mL of dry THF was added dropwise at 0°C to a stirring solution of LAH (2.20 g, 0.0576 mol) in 250 mL of dry THF. The reaction mixture was stirred overnight at a room temperature. An identical workup (page 121) yielded a product as a white solid (5.40 g, 0.032 mol) (84% yield).

cis-1,6-Dihydroxymethylbicyclo[4,2,0]oct-3-ene

mp = 112-114°C

IR (nujol, cm^{-1}): 3256, 3023, 2964, 2897, 2837, 1642, 1483,
1430, 1317, 1184, 1038, 865, 686

$^1\text{HNMR}$ (300.133 MHz, CDCl_3): δ 1.35-1.50 (4H, m), 1.68-1.75
(2H, m), 2.37 (2H, d, $J=14.9\text{Hz}$), 3.23 (2H, d,
 $J=11.4\text{Hz}$), 4.01 (2H, d, $J=11.4\text{Hz}$), 5.97 (2H, t,
 $J=3.2\text{Hz}$)

$^{13}\text{CNMR}$ (75.4 MHz, CDCl_3): δ 24.88 (t), 32.78 (t), 44.07 (s),
68.01 (t), 128.01 (d)

LRMS (EI) m/e: 150, 132, 117, 91 (base), 79, 65, 51, 41

LRMS (CI) (Methane) m/e (%abundance): 169 ($M+H^+$, 19), 151 (20), 133 (100), 121 (21), 105 (17)

HRMS (CI) m/e calculated for $C_{10}H_{17}O_2$ = 169.1129; found = 169.1237

Preparation of 8-oxatricyclo[4,3,2,0]undec-3-ene, [25]

cis-1,6-Dihydroxymethylbicyclo[4,2,0]oct-3-ene (2.92 g, 0.0174 mol) was dissolved in 5 mL of dry pyridine and then 1.35 mL of $MsCl$ (1.99 g, 0.0174 mol) were added dropwise to the stirring solution under argon in ice bath. The reaction mixture was stirred at room temperature overnight.

Identical workup (page 122) and florisil separation (hexane:ethylacetate, 19:1) yield a product as a pale yellow oil (1.88 g, 0.0125 mol) (72% yield).

8-Oxatricyclo[4,3,2,0]undec-3-ene, [25]

IR (neat, cm^{-1}): 3030, 2964, 2924, 2837, 1642, 1436, 1084, 1038, 932, 905

1H NMR (300.133 MHz, $CDCl_3$): δ 1.62-2.13 (8H, m), 3.29 (2H, d, $J=8.8$ Hz), 3.88 (2H, d, $J=8.8$ Hz), 5.93 (2H, m)

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 28.50 (t), 30.78 (t), 47.05 (s), 80.41 (t), 127.39 (d)

LRMS (EI) m/e (%abundance): 150 (M^+ , 27), 122 (18), 107 (11), 93 (100), 79 (39), 65 (13), 53 (12), 39 (34)

HRMS (EI) m/e calculated for $C_{10}H_{14}O_1$ = 150.1045; found = 150.1045

Hydroboration of 8-oxatricyclo[4,3,2,0]undec-3-ene, [25]

The propellane, [25], (0.104 g, 0.693 mmol) was dissolved in 10 mL of dry THF to which was added NaBH₄ (26.2 mg, 0.693 mmol). An argon atmosphere was created and the reaction was cooled to 0°C. Then BF₃O(C₂H₅)₂ (0.085 mL, 0.693 mmol) were syringed into system. The solution was warmed to room temperature and stirred overnight. The reaction was quenched with a small amount of water followed by the slow addition of 0.5 mL of 3N-NaOH and 0.5 mL of 30% H₂O₂. After the addition was complete, the solution was stirred overnight. The reaction mixture was then neutralized. Identical workup (page 123) yielded 57:43 mixture of *syn*-OH and *anti*-OH as a colorless oil (0.093 g, 0.554 mmol) (80% yield).

syn-8-Oxatricyclo[4,3,2,0]undec-3-ol, [62-*syn*]

IR (neat, cm⁻¹): 3428, 2930, 2857, 1775, 1456, 1363, 1171, 1038, 925, 732, 666

¹HNMR (300.133 MHz, CDCl₃): δ 1.21-1.95 (10H, m), 3.36 (1H, d, J=8.9Hz), 3.49 (1H, d, J=8.9Hz), 3.74 (1H, d, J=8.9Hz), 3.90 (1H, d, J=8.9Hz), 3.93-4.02 (1H, m)

¹³CNMR (75.4 MHz, CDCl₃): δ 26.89 (t), 28.38 (t), 28.56 (t), 30.37 (t), 40.42 (t), 45.20 (s), 46.57 (s), 67.59 (d), 79.15 (t), 82.75 (t)

LRMS (EI) m/e (%abundance): 168 (M⁺, 1), 150 (26), 140 (37), 122 (67), 106 (19), 93 (100), 79 (96), 67 (31), 55 (26)

LRMS (CI) (Methane) m/e (%abundance): 169 ($M+H^+$, 26), 151

(80), 133 (100), 121 (29), 107 (42), 95 (16)

HRMS (CI) m/e calculated for $C_{10}H_{17}O_2$ = 169.1129; found =

169.1263

anti-8-Oxatricyclo[4,3,2,0]undec-3-ol, [62-anti]

IR (neat, cm^{-1}): 3428, 2930, 2857, 1775, 1456, 1363, 1171,

1038, 925, 732, 666

1H NMR (300.133 MHz, $CDCl_3$): δ 1.32-2.03 (10H, m), 2.14 (1H,

s), 3.32 (1H, d, $J=8.9$ Hz), 3.42 (1H, d, $J=9$ Hz), 3.60-

3.69 (1H, m), 3.71 (1H, d, $J=8.9$ Hz), 3.91 (1H, d,

$J=9.0$ Hz)

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 25.69 (t), 29.81 (t), 29.86 (t),

30.89 (t), 39.80 (t), 44.75 (s), 47.30 (s), 67.14 (d),

79.11 (t), 82.07 (t)

LRMS (EI) m/e (%abundance): 168 (M^+ , 1), 150 (14), 140 (61),

122 (86), 107 (16), 93 (100), 79 (88), 67 (27), 55 (23)

LRMS (CI) (Methane) m/e (%abundance): 169 ($M+H^+$, 4), 167 ($M-$

H^+ , 14), 151 (60), 133 (100), 121 (19), 107 (46), 95

(13)

HRMS (CI) m/e calculated for $C_{10}H_{17}O_2$ = 169.1229; found =

169.1278

Preparation of para-nitrobenzoate derivatives of 8-

oxatricyclo[4,3,2,0]undec-3-ene, [25]

The mixture of *syn*- and *anti*-alcohol derived from the hydroboration of [25] (0.370 g, 2.20 mmol) was dissolved in 5 mL of dry pyridine and an argon atmosphere was created.

Then PNBCl (0.612 g, 3.30 mmol) was dissolved in dry pyridine and added dropwise to the stirring solution at 0°C. The reaction was allowed to stir at room temperature overnight. Identical workup (page 125) and flash chromatography (dichloromethane:ethylacetate:hexane, 10:1:1) isolated the isomers as a white powder (0.411 g, 1.30 mmol) (50% yield).

syn-3-para-Nitrobenzoate-8-oxatricyclo[4,3,2,0]undec-3-ene,
[36-syn]

mp = 73-74°C

¹HNMR (300.133 MHz, CDCl₃): δ 1.70-2.10 (10H, m), 3.47 (1H, d, J=8.9Hz), 3.51 (1H, d, J=8.9Hz), 3.89 (1H, d, J=8.7Hz), 3.92 (1H, d, J=8.7Hz), 5.34-5.42 (1H, m), 8.14-8.29 (4H, m)

¹³CNMR (75.4 MHz, CDCl₃): δ 26.36 (t), 27.60 (t) (two carbon), 27.83 (t), 35.96 (t), 45.17 (s), 45.62 (s), 71.92 (d), 80.12 (t), 81.83 (t), 123.56 (d), 130.62 (d), 136.04 (s), 151.00 (s), 164.14 (s)

LRMS (EI) m/e (%abundance): 150 (47), 122 (69), 104 (28), 93 (100), 79 (25), 41 (16)

HRMS (HPEC) (NH₃) m/e calculated for C₁₇H₁₉O₅N₁ = 317.1263;
found = 317.1257

anti-3-para-Nitrobenzoate-8-oxatricyclo[4,3,2,0] undecane,
[36-anti]

mp = 113-115°C

¹HNMR (300.133 MHz, CDCl₃): δ 1.54-2.05 (10H, m), 3.43 (1H, d, J=8.4Hz), 3.46 (1H, d, J=8.1Hz), 3.86 (1H, d, J=9.0Hz), 3.94 (1H, d, J=9.0Hz), 5.13-5.21 (1H, m), 8.18-8.30 (4H, m),

¹³CNMR (75.4 MHz, CDCl₃): δ 26.54 (t), 26.91 (t), 28.29 (t), 29.23 (t), 35.67 (t), 44.93 (s), 45.86 (s), 71.79 (d), 80.17 (t), 80.94 (t), 123.56 (d), 130.61 (d), 136.11 (s), 151.00 (s), 164.14 (s)

LRMS (EI) m/e (%abundance): 150 (31), 122 (83), 104 (30), 93 (100), 79 (23), 41 (15)

HRMS (HPEC) (NH₃) m/e calculated for C₁₇H₁₉O₅N₁ = 317.1263;
found = 317.1255

Crystallization of the product, [36-*syn*] was accomplished in dichloromethane:methanol in a relative ratio of 1:10, respectively. The product, [36-*anti*] was recrystallized from dichloromethane:hexane in a relative ratio of 1:5, respectively.

X ray analysis:

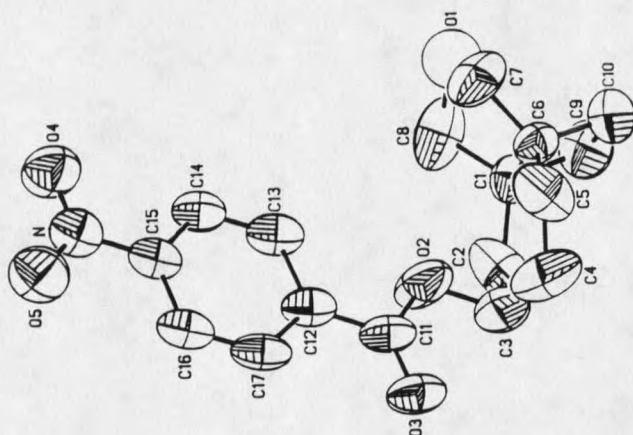


Figure 75. ORTEP Drawing of [36-*syn*].

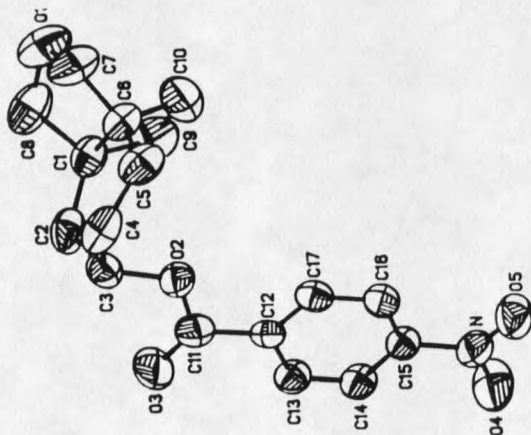


Figure 76. ORTEP Drawing of [36-*anti*].

Table 44. Bond Lengths (Å) of [36-anti].

C(1)-C(2)	1.524(7)	C(1)-C(6)	1.561(8)
C(1)-C(8)	1.525(7)	C(1)-C(9)	1.541(9)
C(2)-C(3)	1.517(6)	C(3)-C(4)	1.502(9)
C(3)-O(2)	1.462(6)	C(4)-C(5)	1.512(8)
C(5)-C(6)	1.494(7)	C(6)-C(7)	1.508(7)
C(6)-C(10)	1.556(9)	C(7)-O(1)	1.416(8)
O(1)-C(8)	1.405(8)	C(9)-C(10)	1.499(9)
O(2)-C(11)	1.330(6)	C(11)-O(3)	1.213(7)
C(11)-C(12)	1.454(7)	C(12)-C(13)	1.686(8)
C(12)-C(17)	1.400(7)	C(13)-C(14)	1.349(7)
C(14)-C(15)	1.388(7)	C(15)-C(16)	1.381(8)
C(15)-N	1.465(6)	C(16)-C(17)	1.367(7)
N-O(4)	1.216(7)	N-O(5)	1.218(5)

Table 45. Bond Angles (°) of [36-anti].

C(2)-C(1)-C(6)	117.7(4)	C(2)-C(1)-C(8)	113.6(4)
C(6)-C(1)-C(8)	101.4(4)	C(2)-C(1)-C(9)	117.8(5)
C(6)-C(1)-C(9)	89.1(4)	C(8)-C(1)-C(9)	113.9(4)
C(1)-C(2)-C(3)	113.9(4)	C(2)-C(3)-C(4)	111.4(4)
C(2)-C(3)-O(2)	111.3(4)	C(4)-C(3)-O(2)	105.9(4)
C(3)-C(4)-C(5)	112.2(5)	C(4)-C(5)-C(6)	112.5(5)
C(1)-C(6)-C(5)	120.3(4)	C(1)-C(6)-C(7)	102.8(4)
C(5)-C(6)-C(7)	114.6(5)	C(1)-C(6)-C(10)	88.3(4)
C(5)-C(6)-C(10)	115.3(4)	C(7)-C(6)-C(10)	112.4(4)

(Table 45. Continued)

C(6)-C(7)-O(1)	106.5(5)	C(7)-O(1)-C(8)	102.5(4)
C(1)-C(8)-O(1)	108.2(5)	C(1)-C(9)-C(10)	91.2(5)
C(6)-C(10)-C(9)	90.8(5)	C(3)-O(2)-C(11)	118.4(4)
O(2)-C(11)-O(3)	123.3(5)	O(2)-C(11)-C(12)	113.2(4)
O(3)-C(11)-C(12)	123.5(5)	C(11)-C(12)-C(13)	119.9(4)
C(11)-C(12)-C(17)	122.7(5)	C(13)-C(12)-C(17)	117.4(4)
C(12)-C(13)-C(14)	122.5(5)	C(13)-C(14)-C(15)	118.6(5)
C(14)-C(15)-C(16)	121.3(4)	C(14)-C(15)-N	119.4(5)
C(16)-C(15)-N	119.2(4)	C(15)-C(16)-C(17)	118.6(5)
C(12)-C(17)-C(16)	121.5(5)	C(15)-N-O(4)	117.8(4)
C(15)-N-O(5)	118.8(4)	O(4)-N-O(5)	123.3(4)

Preparation of syn-tosylate derivative of [25]

The *syn*-para-nitrobenzoate derivative of [25] (70.0 mg, 0.220 mmol) was dissolved in 0.2 mL of dichloromethane and then added to a 80% aqueous ethanol solution that was 0.5% by weight in KOH. The reaction was stirred overnight. Workup yielded a *syn*-alcohol as a colorless oil (34.7 mg, 0.210 mmol) (94% yield). The *syn*-alcohol (34.7 mg, 0.210 mmol) was dissolved in 2 mL of dichloromethane to which was added 0.1 mL of pyridine. The solution was cooled to 0°C and TsCl (57.2 mg, 0.300 mmol) was added in small portions. The reaction was warmed to room temperature and stirred overnight. Workup (page 131) and flash chromatography

(Hexane:ethylacetate, 1:1) yielded a *syn*-tosylate as colorless oil. (30.0 mg, 0.093 mol) (46% yield)

syn-3-Tosyl-8-oxatricyclo[4,3,2,0]undecane, [82]

¹HNMR (300.133 MHz, CDCl₃): δ 1.53-1.88 (10H, m), 2.43 (3H, s), 3.34 (1H, d, J=9Hz), 3.39 (1H, d, J=9.0Hz), 3.80 (2H, d, J=9.0Hz), 4.80-4.89 (1H, m), 7.32 (2H, d, J=8.3Hz)

¹³CNMR (75.4 MHz, CDCl₃): δ 21.58 (q), 27.02 (t), 27.10 (t), 27.55 (t), 27.62 (t), 36.67 (t), 44.72 (s), 45.35 (s), 78.80 (d), 79.83 (t), 81.34 (t), 127.56 (d), 129.79 (d), 134.71 (s), 144.52 (s)

LRMS (EI) m/e (%abundance): 277 (5), 172 (8), 167 (5), 155 (12), 150 (89), 135 (14), 122 (100), 107 (30), 93 (99), 79 (60), 65 (35), 55 (27), 41 (36)

LRMS (CI) (NH₃) m/e (%abundance): 340 (M+NH₄⁺, 100), 195 (24), 186 (14), 168 (79), 151 (32), 122 (13), 108 (29)

HRMS (EI) m/e calculated for C₁₇H₂₂O₄S₁ = 322.1239; found = 322.1236

Preparation of *anti*-tosylate derivative of [25]

In a similar fashion, saponification of the *anti*-para-nitrobenzoate derivative of [25] (84.5 mg, 0.270 mmol) afforded 40.0 mg (0.240 mmol) of the *anti*-alcohol (88% yield). Again, with identical workup (page 131), the *anti*-alcohol (40.0 mg, 0.240 mmol) were dissolved in 2 mL of dichloromethane to which was added pyridine (0.1 mL, 1.24 mmol) and TsCl (69.0 mg, 0.360 mmol). The *anti*-tosylate was

cleanly separated as a colorless oil 49.1 mg (0.150 mmol) (64% yield).

anti-3-Tosyl-8-oxatricyclo[4,3,2,0]undecane, [83]

$^1\text{H NMR}$ (300.133 MHz, CDCl_3): δ 1.40-1.91 (10H, m), 2.42 (3H, s), 3.25 (1H, d, $J=9.0\text{Hz}$), 3.34 (1H, d, $J=9.0\text{Hz}$), 3.75 (1H, d, $J=9.0\text{ Hz}$), 3.83 (1H, d, $J=9.0\text{Hz}$), 4.55-4.63 (1H, m), 7.31 (2H, d, $J=8.3\text{Hz}$), 7.77 (2H, d, $J=8.3\text{Hz}$)

$^{13}\text{C NMR}$ (75.4 MHz, CDCl_3): δ 21.56 (q), 26.73 (t), 27.08 (t), 27.78 (t), 28.73 (t), 36.29 (t), 44.61 (s), 45.67 (s), 78.61 (d), 80.16 (t), 80.60 (t), 127.58 (d), 129.78 (d), 134.59 (s), 144.52 (s)

LRMS (EI) m/e (%abundance): 172 (7), 150 (16), 122 (100), 107 (16), 93 (48), 79 (25), 65 (13), 55 (11), 41 (19)

LRMS (CI) (NH_3) m/e (%abundance): 340 ($\text{M}+\text{NH}_4^+$, 0.2), 184 (100), 108 (15).

HRMS (EI) m/e calculated for $\text{C}_{17}\text{H}_{22}\text{O}_4\text{S}_1 = 322.1239$; found = 322.1241

Preparation of cis-1,6-dicarbomethoxybicyclo[4,3,0]non-3-ene, [17]

A solution of 200 mL of dry THF, 140 mL of 2.5 M n-BuLi (0.350 mol) and 50 mL of diisopropylamine (0.360 mol) was stirred under argon at -10°C for 30 minutes. The temperature was taken down to -78°C and cis-3,4-dicarbomethoxy cyclohexene (28.0 g, 0.141 mol) was added dropwise, creating a bright red solution. After addition was completed, the solution was allowed to stir for 15

minutes, then 1,3-dibromopropane (17.2 mL, 0.169 mol) was added dropwise. The solution was allowed to warm to room temperature and stirred overnight. Workup (page 120) and distillation yielded a product as a pale yellow oil (23.0 g, 0.097 mol) (68% yield)

cis-1,6-Dicarbomethoxybicyclo[4,3,0]non-3-ene, [17]

IR (neat, cm^{-1}): 3030, 2953, 2846, 1733, 1626, 1597, 1436, 1382, 1293, 1210, 1097, 1043, 1002, 942, 764, 656

^1H NMR (300.133 MHz, CDCl_3): δ 1.61-1.80 (4H, m), 2.11-2.49 (6H, m), 3.63 (6H, s), 5.60 (2H, t, $J=1.5\text{Hz}$)

^{13}C NMR (75.4 MHz, CDCl_3): δ 18.73 (t), 31.74 (t), 34.63 (t), 51.70 (q), 52.22 (s), 123.32 (d), 176.45 (s)

LRMS (EI) m/e: 206, 178, 119 (base), 91, 77, 59, 41

LRMS (CI) (Methane) m/e (%abundance): 239 ($\text{M}+\text{H}^+$, 2), 207 (100), 179 (28), 119 (35)

HRMS (CI) m/e calculated for $\text{C}_{13}\text{H}_{19}\text{O}_4 = 239.1283$; found = 239.1280

Preparation of cis-1,6-dihydroxymethylbicyclo[4,3,0]non-3-ene, [31]

A solution of [17] (14.0 g, 0.059 mol) in 20 mL of dry THF was added dropwise at 0°C to a stirring solution LAH (3.00 g, 0.080 mol) in 350 mL of dry THF. The reaction mixture was stirred overnight at a room temperature. Workup (page 121) yielded a product as a white solid (9.00 g, 0.049 mol) (84% yield).

cis-1,6-Dihydroxymethylbicyclo[4,3,0]non-3-ene, [31]

mp = 152-153°C

IR (nujol, cm^{-1}): 3321, 3022, 2946, 2882, 1664, 1465, 1430,
1201, 1049, 915, 879 ^1H NMR (300.133 MHz, CDCl_3): δ 1.44-1.74 (6H, m), 1.90 (2H, d, $J=16.6\text{Hz}$), 2.11 (2H, d, $J=16.8\text{Hz}$), 3.43 (2H, d, $J=11.5\text{Hz}$), 3.61 (2H, d, $J=11.5\text{Hz}$), 5.58 (2H, s) ^{13}C NMR (75.4 MHz, CDCl_3): δ 18.54 (t), 31.46 (t), 33.58 (t),
46.46 (s), 67.29 (t), 124.60 (d)

LRMS (EI) m/e: 164, 133, 117, 106, 91 (base), 77, 65, 41

LRMS (CI) (Methane) m/e (%abundance): 183 ($\text{M}+\text{H}^+$, 1), 181
(3), 165 (20), 147 (100), 135 (38), 119 (27), 105 (14)HRMS (CI) m/e calculated for $\text{C}_{11}\text{H}_{19}\text{O}_2$ = 183.1385; found =
183.1385Preparation of 8-oxatricyclo[4,3,3,0]dodec-3-ene, [10]

The diol [31] (1.00 g, 5.49 mmol) was dissolved in 5 mL of dry pyridine and then 0.43 mL of MsCl (0.630 g, 5.50 mmol) was added dropwise to the stirring solution under argon in ice bath. The reaction mixture was stirred at room temperature overnight. Workup (page 122) and florisil separation (hexane:ethylacetate, 9:1) yielded a product as a colorless oil (0.730 g, 4.45 mmol) (81% yield)

8-Oxatricyclo[4,3,3,0]dodec-3-ene, [10]IR (neat, cm^{-1}): 3037, 2930, 2835, 1651, 1544, 1449, 1385,
1175, 1066, 943, 842, 711

$^1\text{H NMR}$ (300.133 MHz, CDCl_3): δ 1.46-1.67 (6H, m), 2.00 (2H, d, $J=3.0\text{Hz}$), 1.99 (2H, d, $J=3.0\text{Hz}$), 3.54 (4H, d, $J=1.3\text{Hz}$), 5.82 (2H, t, $J=3.0\text{Hz}$)

$^{13}\text{C NMR}$ (75.4 MHz, CDCl_3): δ 23.96 (t), 32.68 (t), 40.19 (t), 55.30 (s), 81.38 (t), 128.63 (d)

LRMS (EI) m/e (%abundance): 164 (M^+ , 18), 146 (11), 133 (31), 119 (32), 109 (26), 104 (14), 95 (31), 91 (100), 79 (39), 67 (25), 53 (16), 41 (33)

HRMS (EI) m/e calculated for $\text{C}_{11}\text{H}_{16}\text{O}_1 = 164.1202$; found = 164.1205

Hydroboration of 8-oxatricyclo[4,3,3,0]dodec-3-ene, [10]

The propellane, [10] (0.450 g, 2.74 mmol) was dissolved in 10 mL of dry THF and then 4 mL of $\text{BH}_3\cdot\text{THF}$ (62.4 mg, 4.52 mmol) were added dropwise to the stirring solution under argon at 0°C . The solution was warmed to room temperature and stirred overnight. Workup (page 123) yielded a 51:49 mixture of *syn*-OH and *anti*-OH as a colorless oil (0.443 g, 2.43 mmol) (89% yield).

syn-8-Oxatricyclo[4,3,3,0]dodec-3-ol, [63-*syn*]

$^1\text{H NMR}$ (300.133 MHz, CDCl_3): δ 1.34-1.89 (12H, m), 3.58 (1H, d, $J=8.5\text{Hz}$), 3.66 (1H, d, $J=8.4\text{Hz}$), 3.68 (1H, d, $J=8.4\text{Hz}$), 3.73-3.82 (1H, m), 3.84 (1H, d, 8.5Hz).

$^{13}\text{C NMR}$ (75.4 MHz, CDCl_3): δ 21.98 (t), 28.34 (t), 31.11 (t), 33.37 (t), 38.20 (t), 40.27 (t), 51.06 (s), 53.24 (s), 67.20 (d), 77.22 (t), 80.98 (t)

LRMS (EI) m/e (%abundance): 182 (M^+ , 1), 164 (49), 146 (13),
133 (35), 119 (55), 109 (100), 91 (67), 79 (43), 67
(25), 55 (15)

LRMS (CI) (Methane) m/e (%abundance): 183 ($M+H^+$, 11), 181
(15), 165 (100), 147 (44), 135 (24), 121 (16)

HRMS (CI) m/e calculated for $C_{11}H_{19}O_2$ = 183.1385; found =
183.1386

anti-8-Oxatricyclo[4,3,3,0]dodec-3-ol, [63-anti]

1H NMR (300.133 MHz, $CDCl_3$): δ 1.27-1.89 (12H, m), 3.60 (1H,
d, $J=8.9$ Hz), 3.63 (1H, d, $J=8.9$ Hz), 3.70 (1H, d,
 $J=8.2$ Hz), 3.75 (1H, d, $J=8.2$ Hz), 3.75-3.84 (1H, m)

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 22.11 (t), 29.83 (t), 31.14 (t),
32.65 (t), 38.47 (t), 39.53 (t), 51.18 (s), 53.42 (s),
67.29 (d), 77.20 (t), 80.22 (t)

LRMS (EI) m/e (%abundance): 182 (M^+ , 3), 164 (23), 151 (18),
133 (48), 119 (100), 105 (37), 91 (96), 86 (15), 79
(47), 67 (27), 55 (17)

LRMS (CI) (Methane) m/e (%abundance): 183 ($M+H^+$, 5), 181
(26), 165 (100), 147 (79), 135 (41), 121 (13)

HRMS (CI) m/e calculated for $C_{11}H_{19}O_2$ = 183.1385; found =
183.1385

Preparation of para-nitrobenzoate derivatives of 8-
oxatricyclo[4,3,3,0]dodec-3-ene, [10]

The mixture of syn-and anti-alcohols derived from the
hydroboration of [10] (0.560 g, 3.08 mmol) was dissolved in
5 mL of dry pyridine and an argon atmosphere was created.

Then PNBCL (0.820 g, 4.42 mmol) was dissolved in dry pyridine and added dropwise to the stirring solution at 0°C. The reaction was stirred at room temperature overnight.

Workup (page 125) and flash chromatography

(dichloromethane:ethylacetate:hexane, 10:1:1) isolated the isomers as a pale yellow solid (0.810 g, 2.45 mmol) (80 % yield).

syn-3-para-Nitrobenzoate-8-oxatricyclo[4,3,3,0] dodecane,
[37-syn]

mp = 115-117°C

^1H NMR (300.133 MHz, CDCl_3): δ 1.51-2.01 (12H, m), 3.63 (1H, d, $J=8.5\text{Hz}$), 3.72 (1H, d, $J=8.5\text{Hz}$), 3.73 (1H, d, $J=8.5\text{Hz}$), 3.85 (1H, d, $J=8.5\text{Hz}$), 5.13-5.22 (1H, m), 8.15-8.29 (4H, m)

^{13}C NMR (75.4 MHz, CDCl_3): δ 22.19 (t), 26.90 (t), 27.95 (t), 34.17 (t), 35.74 (t), 37.28 (t), 51.20 (s), 52.84 (s), 71.91 (d), 78.18 (t), 80.67 (t), 123.51 (d), 130.64 (d), 136.11 (s), 150.65 (s), 164.23 (s)

LRMS (EI) m/e (%abundance): 181 (7), 164 (82), 150 (31), 135 (33), 119 (54), 109 (100), 91 (52), 79 (29), 67 (21), 55 (15), 41 (28)

HRMS (EI) m/e calculated for $\text{C}_{18}\text{H}_{21}\text{O}_5\text{N}_1$ = 331.1420 ; found = 331.1426

anti-3-para-Nitrobenzoate-8-oxatricyclo[4,3,3,0] dodecane,
[37-anti]

mp = 115-116°C

¹HNMR (300.133 MHz, CDCl₃): δ 1.57-2.06 (12H, m), 3.65 (1H, d, J=8.6Hz), 3.70 (1H, d, 8.6Hz), 3.71 (1H, d, 8.6Hz), 3.83 (1H, d, 8.6Hz), 5.15-5.24 (1H, m), 8.15-8.29 (4H, m)

¹³CNMR (75.4 MHz, CDCl₃): δ 22.46 (t), 26.88 (t), 29.09 (t), 34.38 (t), 34.77 (t), 38.84 (t), 51.27 (s), 52.85 (s), 72.03 (d), 77.97 (t), 79.92 (t), 123.51 (d), 130.61 (d), 136.15 (s), 150.63 (s), 164.14 (s)

LRMS (EI) m/e (%abundance): 331 (M⁺, 1), 181 (39), 164 (50), 151 (72), 137 (82), 119 (100), 104 (37), 91 (70), 79 (33), 67 (21), 55 (15), 41 (27)

HRMS (EI) m/e calculated for C₁₈H₂₁O₅N₁ = 331.1420 ; found = 331.1432

Crystallization of the product, [37-syn] was accomplished in dichloromethane:hexane in a relative ratio of 1:5 respectively and the product, [37-anti] was accomplished in dichloromethane:methanol in a relative ratio of 1:10, respectively.

X-ray analysis:

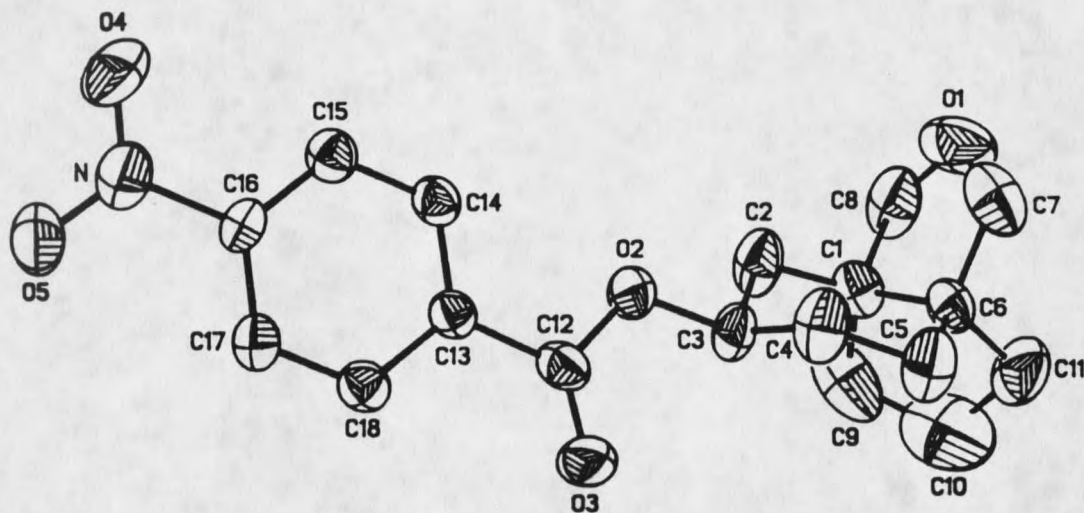


Figure 77. ORTEP Drawing of [37-syn].

Table 46. Bond Lengths (Å) of [37-syn].

C(1)-C(2)	1.556(17)	C(1)-C(6)	1.510(19)
C(1)-C(8)	1.568(19)	C(1)-C(9)	1.495(22)
C(2)-C(3)	1.472(18)	C(3)-C(4)	1.484(18)
C(3)-O(2)	1.457(14)	C(4)-C(5)	1.557(18)
C(5)-C(6)	1.526(19)	C(6)-C(7)	1.517(20)
C(6)-C(11)	1.567(20)	C(7)-O(1)	1.388(19)
O(1)-C(8)	1.354(19)	C(9)-C(10)	1.512(28)

(Table 46. Continued)

C(10)-C(11)	1.449(26)	O(2)-C(12)	1.325(15)
C(12)-O(3)	1.209(16)	C(12)-C(13)	1.464(17)
C(13)-C(14)	1.385(16)	C(13)-C(18)	1.400(16)
C(14)-C(15)	1.369(16)	C(15)-C(16)	1.380(16)
C(16)-C(17)	1.373(16)	C(16)-N	1.475(16)
C(17)-C(18)	1.380(16)	N-O(4)	1.195(15)
N-O(5)	1.214(14)		

Table 47. Bond Angles (°) of [37-syn].

C(2)-C(1)-C(6)	111.6(11)	C(2)-C(1)-C(8)	109.3(11)
C(6)-C(1)-C(8)	100.2(10)	C(2)-C(1)-C(9)	113.1(12)
C(6)-C(1)-C(9)	107.2(12)	C(8)-C(1)-C(9)	114.7(12)
C(1)-C(2)-C(3)	113.3(11)	C(2)-C(3)-C(4)	108.9(10)
C(2)-C(3)-O(2)	106.6(10)	C(4)-C(3)-O(2)	110.0(10)
C(3)-C(4)-C(5)	110.2(11)	C(4)-C(5)-C(6)	111.4(11)
C(1)-C(6)-C(5)	115.6(11)	C(1)-C(6)-C(7)	104.4(11)
C(5)-C(6)-C(7)	115.1(12)	C(1)-C(6)-C(11)	101.2(11)
C(5)-C(6)-C(11)	108.2(11)	C(7)-C(6)-C(11)	111.5(11)
C(6)-C(7)-O(1)	106.2(12)	C(7)-O(1)-C(8)	113.5(12)
C(1)-C(8)-O(1)	105.7(12)	C(1)-C(9)-C(10)	105.0(14)
C(9)-C(10)-C(11)	109.2(17)	C(6)-C(11)-C(10)	104.3(13)
C(3)-O(2)-C(12)	118.9(9)	O(2)-C(12)-O(3)	122.5(11)
O(2)-C(12)-C(13)	112.7(11)	O(3)-C(12)-C(13)	124.7(11)
C(12)-C(13)-C(14)	122.5(10)	C(12)-C(13)-C(18)	118.7(11)

(Table 47. Continued)

C (14) -C (13) -C (18)	118.7 (10)	C (13) -C (14) -C (15)	120.0 (10)
C (14) -C (15) -C (16)	120.5 (11)	C (15) -C (16) -C (17)	121.1 (11)
C (15) -C (16) -N	120.1 (10)	C (17) -C (16) -N	118.8 (11)
C (16) -C (17) -C (18)	118.4 (11)	C (13) -C (18) -C (17)	121.3 (11)
C (16) -N-O (4)	117.6 (10)	C (16) -N-O (5)	115.6 (11)
O (4) -N-O (5)	126.8 (11)		

X-ray analysis:

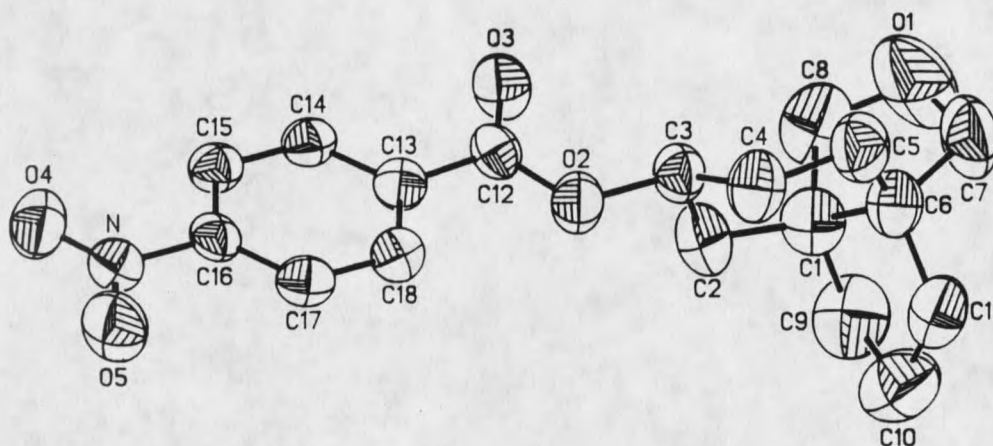


Figure 78. ORTEP Drawing of [37-anti].

Table 48. Bond Lengths (Å) of [37-anti].

C (1) -C (2)	1.565 (10)	C (1) -C (6)	1.546 (10)
C (1) -C (8)	1.506 (12)	C (1) -C (9)	1.526 (10)
C (2) -C (3)	1.460 (9)	C (3) -C (4)	1.521 (10)
C (3) -O (2)	1.472 (7)	C (4) -C (5)	1.539 (10)

(Table 48. Continued)

C(5)-C(6)	1.479(11)	C(6)-C(7)	1.551(12)
C(6)-C(11)	1.550(9)	C(7)-O(1)	1.380(13)
O(1)-C(8)	1.420(10)	C(9)-C(10)	1.524(15)
C(10)-C(11)	1.529(11)	O(2)-C(12)	1.324(7)
C(12)-O(3)	1.192(9)	C(12)-C(13)	1.486(9)
C(13)-C(14)	1.399(7)	C(13)-C(18)	1.396(9)
C(14)-C(15)	1.382(8)	C(15)-C(16)	1.369(9)
C(16)-C(17)	1.394(8)	C(16)-N	1.471(8)
C(17)-C(18)	1.375(8)	N-O(4)	1.209(6)
N-O(5)	1.213(8)		

Table 49. Bond Angles (°) of [37-anti].

C(2)-C(1)-C(6)	113.3(7)	C(2)-C(1)-C(8)	110.3(6)
C(6)-C(1)-C(8)	103.8(5)	C(2)-C(1)-C(9)	110.4(5)
C(6)-C(1)-C(9)	103.7(6)	C(8)-C(1)-C(9)	115.1(8)
C(1)-C(2)-C(3)	113.2(5)	C(2)-C(3)-C(4)	111.0(5)
C(2)-C(3)-O(2)	108.6(4)	C(4)-C(3)-O(2)	107.8(6)
C(3)-C(4)-C(5)	107.7(7)	C(4)-C(5)-C(6)	112.1(5)
C(1)-C(6)-C(5)	116.4(5)	C(1)-C(6)-C(7)	98.5(7)
C(5)-C(6)-C(7)	109.9(5)	C(1)-C(6)-C(11)	105.2(5)
C(5)-C(6)-C(11)	113.1(7)	C(7)-C(6)-C(11)	112.9(6)
C(6)-C(7)-O(1)	108.7(6)	C(7)-O(1)-C(8)	110.1(7)
C(1)-C(8)-O(1)	107.1(7)	C(1)-C(9)-C(10)	106.2(8)
C(9)-C(10)-C(11)	105.3(6)	C(6)-C(11)-C(10)	107.7(7)

(Table 49. Continued)

C(3)-O(2)-C(12)	116.7(5)	O(2)-C(12)-O(3)	123.9(6)
O(2)-C(12)-C(13)	111.7(6)	O(3)-C(12)-C(13)	124.3(5)
C(12)-C(13)-C(14)	117.5(6)	C(12)-C(13)-C(18)	122.6(5)
C(14)-C(13)-C(18)	119.9(5)	C(13)-C(14)-C(15)	120.6(6)
C(14)-C(15)-C(16)	118.3(5)	C(15)-C(16)-C(17)	122.5(6)
C(15)-C(16)-N	119.2(5)	C(17)-C(16)-N	118.3(6)
C(16)-C(17)-C(18)	119.2(6)	C(13)-C(18)-C(17)	119.5(5)
C(16)-N-O(4)	117.6(5)	C(16)-N-O(5)	119.7(5)
O(4)-N-O(5)	122.7(5)		

Preparation of syn-tosylate derivative of [10]

The *syn*-para-nitrobenzoate derivative of [10] (0.132 g, 0.400 mmol) was dissolved in 0.2 mL dichloromethane and then added to a 80% aqueous ethanol solution that was 0.5% by weight in KOH. The reaction was stirred overnight. Workup yielded a *syn*-alcohol as a colorless oil (68.8 mg, 0.378 mmol) (95% yield). The *syn*-alcohol (68.8 mg, 0.378 mmol) was dissolved in 3 mL of dichloromethane to which was added 0.2 mL of pyridine. The solution was cooled to 0°C and TsCl (176 mg, 0.920 mmol) was added dropwise. The reaction was warmed to room temperature and stirred overnight. Workup (page 131) and flash chromatography (hexane:ethylacetate, 1:1) yielded a *syn*-tosylate as a white powder (103 mg, 0.307 mmol) (81% yield).

syn-3-Tosyl-8-oxa-tricyclo[4,3,3,0]dodecane, [15]

mp = 85-87°C

¹HNMR (300.133 MHz, CDCl₃): δ 1.17-1.70 (12H, m), 2.42 (3H, s), 3.37 (1H, d, J=8.6Hz), 3.46 (1H, d, J=8.6Hz), 3.47 (1H, d, J=8.6Hz), 3.57 (1H, d, J=8.6Hz), 4.41-4.51 (1H, m), 7.15 (2H, d, J=8.3Hz), 7.60 (2H, d, J=8.3Hz)

¹³CNMR (75.4 MHz, CDCl₃): δ 21.60 (q), 21.99 (t), 27.63 (t), 27.68 (t), 33.73 (t), 36.68 (t), 37.14 (t), 50.81 (s), 52.99 (s), 77.76 (t), 78.78 (d), 80.33 (t), 127.59 (d), 129.77 (d), 134.86 (s), 144.47 (s)

LRMS (EI) m/e (%abundance): 172 (12), 164 (50), 146 (13), 133 (30), 119 (47), 109 (45), 91 (100), 79 (34), 65 (30), 55 (16), 41 (22)

LRMS (CI) (NH₃) m/e (%abundance): 354 (M+NH₄⁺, 76), 182 (100), 108 (18)

HRMS (EI) m/e calculated for C₁₈H₂₄O₄S₁ = 336.1395; found = 336.1393

Preparation of anti-tosylate derivative of [10]

In a similar fashion, saponification of the anti-para-nitrobenzoate derivative of [10] (0.113 g, 0.340 mmol) afforded 60.0 mg (0.330 mmol) of the anti-alcohol (97% yield). Again, using the identical workup (page 131), the anti-alcohol (77.6 mg, 0.426 mmol) was dissolved in 2 mL of dichloromethane to which was added pyridine (0.1 mL, 1.24 mmol) and TsCl (97.5 mg, 0.511 mmol). The anti-tosylate was

cleanly separated as a white powder 110 mg (0.327 mmol) (77% yield).

anti-3-Tosyl-8-oxatricyclo[4,3,3,0]dodecane, [16]

mp = 57-58°C

¹HNMR (300.133 MHz, CDCl₃): δ 1.41-1.84 (12H, m), 2.41 (3H, s), 3.52-3.90 (4H, m), 4.53-4.63 (1H, m), 7.30 (2H, d, J=8.2Hz), 7.74 (2H, d, J=8.2Hz)

¹³CNMR (75.4 MHz, CDCl₃): δ 21.53 (q), 22.23 (t), 27.34 (t), 28.74 (t), 34.16 (t), 35.49 (t), 38.30 (t), 50.84 (s), 52.82 (s), 77.76 (t), 78.75 (d), 79.61 (t), 127.55 (d), 129.73 (d), 134.48 (s), 144.45 (s)

LRMS (EI) m/e (%abundance): 181 (51), 164 (37), 145 (11), 133 (29), 119 (54), 105 (21), 91 (100), 79 (30), 65 (30), 55 (26), 41 (22)

LRMS (CI) (NH₃) m/e (%abundance): 354 (M+NH₄⁺, 12), 196 (35), 182 (100), 108 (15)

HRMS (CI) m/e calculated for C₁₈H₂₄O₄S₁ = 336.1395; found = 336.1402

Preparation of cis-1,6-dicarbomethoxybicyclo[4,4,0]dec-3-ene, [21]

A solution of 200 mL of dry THF, 140 mL of 2.5 M n-BuLi (0.350 mol) and 50 mL of diisopropylamine (0.360 mol) was stirred under argon at -10°C for 30 minutes. The temperature was taken down to -78°C and cis-3,4-dicarbomethoxy cyclohexene (28.0 g, 0.141 mol) was added dropwise, creating a bright red solution. After addition

was completed, the solution was allowed to stir for 15 minutes, then 1,4-dibromobutane (20.2 mL, 0.169 mol) was added dropwise. The solution was allowed to warm to room temperature and stirred overnight. Workup (page 120) and distillation yielded a product as a colorless oil (28.5 g, 0.113 mol) (80% yield)

cis-1,6-Dicarbomethoxybicyclo[4,4,0]dec-3-ene, [21]

IR (neat, cm^{-1}): 3026, 2946, 2860, 1731, 1460, 1429, 1294, 1238, 1201, 1140, 1072, 1023, 757

^1H NMR (300.133 MHz, CDCl_3): δ 1.38-2.47 (12H, m), 3.64 (6H, s), 5.57 (2H, s)

^{13}C NMR (75.4 MHz, CDCl_3): δ 22.05 (t), 31.62 (t), 33.15 (t), 45.94 (s), 51.56 (q), 123.27 (d), 176.58 (s)

LRMS (EI) m/e: 252, 220, 192, 133 (base), 91, 77, 59, 41

LRMS (CI) (Methane) m/e (%abundance): 253 ($\text{M}+\text{H}^+$, 5), 221 (100), 193 (58), 133 (86)

HRMS (CI) m/e calculated for $\text{C}_{14}\text{H}_{21}\text{O}_4$ = 253.1440; found = 253.1465

Preparation of cis-1,6-dihydroxymethylbicyclo[4,4,0]dec-3-ene

A solution of [21] (21.2 g, 0.084 mol) in 20 mL of dry THF was added dropwise at 0°C to a stirring solution of LAH (4.80 g, 0.130 mol) in 350 mL of dry THF. The reaction mixture was heated to a gentle reflux under argon overnight. Workup (page 121) yielded a product as a white powder (12.0 g, 0.061 mol) (73% yield).

cis-1,6-Dihydroxymethylbicyclo[4,4,0]dec-3-enemp = 145-147°C (Ref¹⁷ 143-145°C)IR (nujol, cm⁻¹): 3329, 3023, 2970, 2930, 1715, 1662, 1456,
1084, 1051, 878¹HNMR (300.133 MHz, CDCl₃): δ 1.35-1.52 (8H, methylene
envelope), 2.03 (4H, methylene envelope), 2.90 (2H, s),
3.55 (2H, d, J=11.5Hz), 3.67 (2H, d, J=11.5Hz), 5.55
(2H, d, J=1.3Hz)¹³CNMR (75.4 MHz, CDCl₃): δ 20.90 (t), 30.35 (t), 31.50 (t),
38.66 (s), 67.68 (t), 123.87 (d)LRMS (EI) m/e (%abundance): 178, 160, 147, 132, 117, 91
(base), 79, 67, 41LRMS (CI) (Methane) m/e (%abundance): 195 (M-H⁺, 4), 179
(34), 161 (100), 149 (24), 133 (26), 95 (23)Preparation of 8-oxatricyclo[4,4,3,0]tridec-3-ene, [26]

cis-1,6-Dihydroxymethylbicyclo[4,4,0]dec-3-ene (4.41 g, 0.0225 mol) was dissolved in 16 mL of dry pyridine and then 1.74 mL of MsCl (2.58 g, 0.0225 mol) were added dropwise to the stirring solution under argon in ice bath. The reaction mixture was stirred at room temperature overnight. Workup (page 122) and florisil separation (hexane:ethylacetate, 98:2) yielded a product as a pale yellow oil (3.40 g, 0.0191 mol) (85% yield).

8-Oxatricyclo[4,4,3,0]tridec-3-ene, [26]IR (neat, cm⁻¹): 3023, 2924, 2857, 1635, 1456, 1058, 1038,
912, 726, 659,

$^1\text{H NMR}$ (300.133 MHz, CDCl_3): δ 1.37-1.59 (8H, m), 1.89-2.06 (4H, m), 3.58 (2H, d, $J=7.6\text{Hz}$), 3.79 (2H, d, $J=7.6\text{Hz}$), 5.56 (2H, s)

$^{13}\text{C NMR}$ (75.4 MHz, CDCl_3): δ 22.15 (t), 30.79 (t), 31.30 (t), 40.62 (s), 77.42 (t), 123.69 (d)

LRMS (EI) m/e (%abundance): 178 (M^+ , 13), 160 (21), 147 (35), 132 (21), 123 (70), 117 (14), 105 (34), 95 (41), 91 (100), 79 (41), 67 (33), 55 (16), 51 (9), 41 (37)

HRMS (EI) m/e calculated for $\text{C}_{12}\text{H}_{18}\text{O}_1 = 178.1359$; found = 178.1355

Hydroboration of 8-oxatricyclo[4,4,3,0]tridec-3-ene, [26]

The propellane, [26] (0.480 g, 2.70 mmol) was dissolved in 10 mL of dry THF and then 4 mL of $\text{BH}_3\cdot\text{THF}$ (0.0624 g, 4.52 mmol) were added dropwise to the stirring solution under argon at 0°C . The solution was warmed to room temperature and stirred overnight. Workup (page 123) yielded 57:43 mixture of syn-OH and anti-OH as colorless oils (0.460 g, 2.35 mmol) (87% yield).

syn-8-Oxatricyclo[4,4,3,0]tridec-3-ol, [64-syn]

IR (neat, cm^{-1}): 3395, 2984, 2930, 2864, 1489, 1450, 1058, 918, 719, 666

$^1\text{H NMR}$ (300.133 MHz, CDCl_3): δ 1.26-1.84 (14H, m), 2.13 (1H, s), 3.39 (1H, d, $J=8.0\text{Hz}$), 3.45 (1H, d, $J=8.0\text{Hz}$), 3.69-3.79 (1H, m), 3.99 (1H, d, $J=7.9\text{Hz}$), 4.00 (1H, d, $J=7.9\text{Hz}$)

$^{13}\text{CNMR}$ (75.4 MHz, CDCl_3): δ 21.61 (t), 22.14 (t), 25.78 (t),
28.05 (t), 31.43 (t), 33.61 (t), 41.48 (s), 43.18 (t),
43.65 (s), 67.01 (d), 77.14 (t) (two carbon)

LRMS (EI) m/e (%abundance): 196 (M^+ , 1), 178 (28), 147 (20),
133 (31), 123 (100), 105 (22), 91 (53), 79 (28), 67
(26), 55 (13)

HRMS (EI) m/e calculated for $\text{C}_{12}\text{H}_{20}\text{O}_2$ = 196.1463 ; found =
196.1452

anti-8-Oxatricyclo[4,4,3,0]tridec-3-ol, [64-anti]

IR (neat, cm^{-1}): 3395, 2984, 2930, 2864, 1489, 1450, 1058,
918, 719, 666

$^1\text{HNMR}$ (300.133 MHz, CDCl_3): δ 1.20-1.80 (14H, m), 2.22 (1H,
s), 3.38 (1H, d, $J=7.9\text{Hz}$), 3.39 (1H, d, $J=7.9\text{Hz}$), 3.77-
3.89 (1H, m), 3.90 (1H, d, $J=8.0\text{Hz}$), 4.00 (1H, d,
 $J=8.0\text{Hz}$)

$^{13}\text{CNMR}$ (75.4 MHz, CDCl_3): δ 21.55 (t), 22.15 (t), 26.38 (t),
31.21 (t), 33.35 (t), 34.78 (t), 35.87 (t), 41.40 (s),
43.97 (s), 67.39 (d), 76.41 (t), 77.78 (t)

LRMS (EI) m/e (%abundance): 196 (M^+ , 13), 178 (30), 165
(21), 147 (50), 133 (100), 123 (28), 105 (39), 91 (82),
79 (44), 67 (36), 55 (22)

HRMS (EI) m/e calculated for $\text{C}_{12}\text{H}_{20}\text{O}_2$ = 196.1463 ; found =
196.1455

Preparation of para-nitrobenzoate derivatives of 8-oxatricyclo[4,4,3,0]tridec-3-ene, [26]

The mixture of *syn*-and *anti*-alcohols derived from the hydroboration of [26] (0.618 g, 3.15 mmol) was dissolved in 15 mL of dry pyridine and an argon atmosphere was created. Then PNBCl (0.878 g, 4.73 mmol) was dissolved in dry pyridine and added dropwise to the stirring solution at 0°C. The reaction was stirred at room temperature overnight.

Workup (page 125) and flash chromatography

(dichloromethane:ethylacetate:hexane, 10:1:1) isolated the isomers as white powders (0.569 g, 1.65 mmol) (52% yield).

syn-3-para-Nitrobenzoate-8-oxatricyclo[4,4,3,0]tridec-3-ene,

[38-*syn*]

mp = 172-173°C

¹HNMR (300.133 MHz, CDCl₃): δ 1.37-2.02 (14H, m), 3.57 (1H, d, J=8.1Hz), 3.61 (1H, d, J=8.1Hz), 4.00 (1H, d, J=8.3Hz), 4.03 (1H, d, J=8.3Hz), 5.16-5.25 (1H, d, J=4.9Hz), 8.17-8.28 (4H, m)

¹³CNMR (75.4 MHz, CDCl₃): δ 21.73 (t), 22.15 (t), 26.17 (t), 27.42 (t), 28.83 (t), 32.89 (t), 38.16 (t), 41.66 (s), 43.64 (s), 72.21 (d), 77.23 (t), 77.32 (t), 123.52 (d), 130.65 (d), 136.12 (s), 150.80 (s), 164.18 (s)

LRMS (EI) m/e (%abundance): 178 (64), 147 (25), 133 (39), 123 (100), 105 (23), 91 (43), 79 (21), 67 (20), 55 (15), 41 (21)

LRMS (HPEC) (NH₃) (Methane) m/e (%abundance): 345 (100), 314 (33), 136 (10)

HRMS (HPEC) (NH₃) m/e calculated for C₁₉H₂₃O₅N₁ = 345.1576 ;
found = 345.1579

anti-3-para-Nitrobenzoate-8-oxatricyclo[4,4,3,0] tridecane,
[38-anti]

mp = 144-145°C

¹HNMR (300.133 MHz, CDCl₃): δ 1.32-2.01 (14H, m), 3.49 (1H, d, J=8.1Hz), 3.53 (1H, d, J=8.2Hz), 4.04 (1H, d, J=8.2Hz), 4.05 (1H, d, J=8.1Hz), 5.19-5.29 (1H, d, J=5.1Hz), 8.17-8.28 (4H, m)

¹³CNMR (75.4 MHz, CDCl₃): δ 21.72 (t), 22.22 (t), 26.99 (t), 27.33 (t), 32.40 (t), 32.55 (t), 34.47 (t), 41.57 (s), 44.05 (s), 72.58 (d), 76.45 (t), 77.61 (t), 123.51 (d), 130.65 (d), 136.12 (s), 150.80 (s), 164.14 (s)

LRMS (EI) m/e (%abundance): 315 (10), 195 (14), 178 (50), 147 (54), 133 (100), 120 (36), 107 (45), 91 (60), 79 (32), 67 (28), 55 (22), 41 (28)

LRMS (HPEC) (NH₃) m/e (%abundance): 345 (100), 314 (27)

HRMS (HPEC) (NH₃) m/e calculated for C₁₉H₂₃O₅N₁ = 345.1576 ;
found = 345.1565

Crystallization of the product, [38-syn] was accomplished in dichloromethane:hexane in a relative ratio of 1:10 respectively and the product, [38-anti] was accomplished in dichloromethane:hexane in a relative ratio of 1:10, respectively.

X-ray analysis:

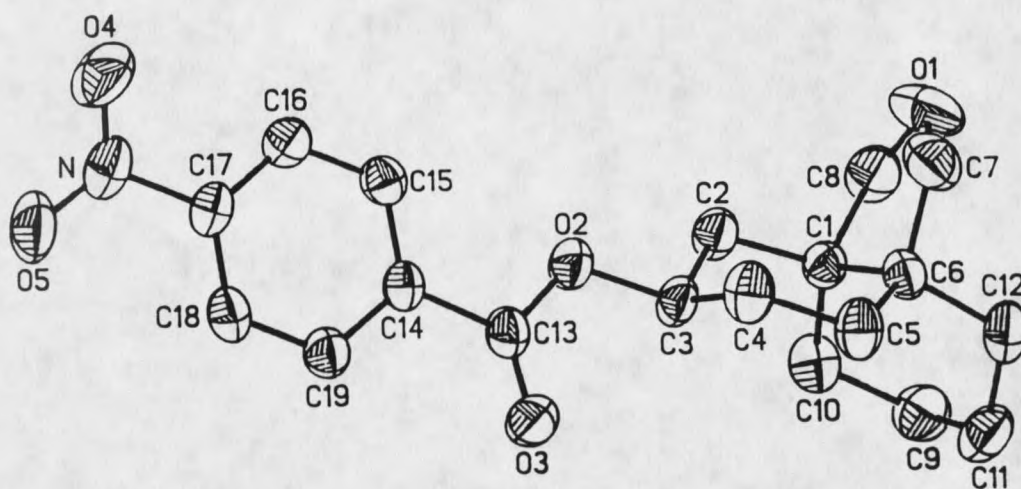


Figure 79. ORTEP Drawing of [38-syn].

Table 50. Bond Lengths (Å) of [38-syn].

C (1) - C (2)	1.546 (3)	C (1) - C (6)	1.557 (3)
C (1) - C (8)	1.535 (3)	C (1) - C (9)	1.533 (3)
C (2) - C (3)	1.506 (3)	C (3) - C (4)	1.508 (4)
C (3) - O (2)	1.470 (3)	C (4) - C (5)	1.531 (3)
C (5) - C (6)	1.529 (3)	C (6) - C (7)	1.528 (4)
C (6) - C (12)	1.546 (3)	C (7) - O (1)	1.419 (4)
O (1) - C (8)	1.415 (4)	C (9) - C (10)	1.532 (4)

(Table 50. Continued)

C(10)-C(11)	1.508(4)	C(11)-C(12)	1.519(4)
O(2)-C(13)	1.337(3)	C(13)-O(3)	1.201(3)
C(13)-C(14)	1.489(3)	C(14)-C(15)	1.397(3)
C(14)-C(19)	1.389(3)	C(15)-C(16)	1.378(3)
C(16)-C(17)	1.374(3)	C(17)-C(18)	1.379(3)
C(17)-N	1.474(3)	C(18)-C(19)	1.382(3)
N-O(4)	1.219(3)	N-O(5)	1.220(3)

Table 51. Bond Angles (°) of [38-syn].

C(2)-C(1)-C(6)	111.0(2)	C(2)-C(1)-C(8)	108.4(2)
C(6)-C(1)-C(8)	100.7(2)	C(2)-C(1)-C(9)	109.1(2)
C(6)-C(1)-C(9)	114.9(2)	C(8)-C(1)-C(9)	112.3(2)
C(1)-C(2)-C(3)	112.4(2)	C(2)-C(3)-C(4)	110.9(2)
C(2)-C(3)-O(2)	106.3(2)	C(4)-C(3)-O(2)	110.4(2)
C(3)-C(4)-C(5)	108.7(2)	C(4)-C(5)-C(6)	114.6(2)
C(1)-C(6)-C(5)	114.1(2)	C(1)-C(6)-C(7)	100.8(2)
C(5)-C(6)-C(7)	113.5(2)	C(1)-C(6)-C(12)	110.8(2)
C(5)-C(6)-C(12)	109.2(2)	C(7)-C(6)-C(12)	108.1(2)
C(6)-C(7)-O(1)	107.5(2)	C(7)-O(1)-C(8)	109.5(2)
C(1)-C(8)-O(1)	107.9(2)	C(1)-C(9)-C(10)	113.9(2)
C(9)-C(10)-C(11)	110.2(2)	C(10)-C(11)-C(12)	110.2(2)
C(6)-C(12)-C(11)	113.8(2)	C(3)-O(2)-C(13)	116.5(2)
O(2)-C(13)-O(3)	124.5(2)	O(2)-C(13)-C(14)	111.9(2)
O(3)-C(13)-C(14)	123.5(2)	C(13)-C(14)-C(15)	122.5(2)

(Table 51. Continued)

C(13)-C(14)-C(19)	117.7(2)	C(15)-C(14)-C(19)	119.8(2)
C(14)-C(15)-C(16)	119.6(2)	C(15)-C(16)-C(17)	119.3(2)
C(16)-C(17)-C(18)	122.5(2)	C(16)-C(17)-N	119.1(2)
C(18)-C(17)-N	118.4(2)	C(17)-C(18)-C(19)	118.0(2)
C(14)-C(19)-C(18)	120.7(2)	C(17)-N-O(4)	118.0(2)
C(17)-N-O(5)	117.7(2)	O(4)-N-O(5)	124.3(2)

X-ray analysis:

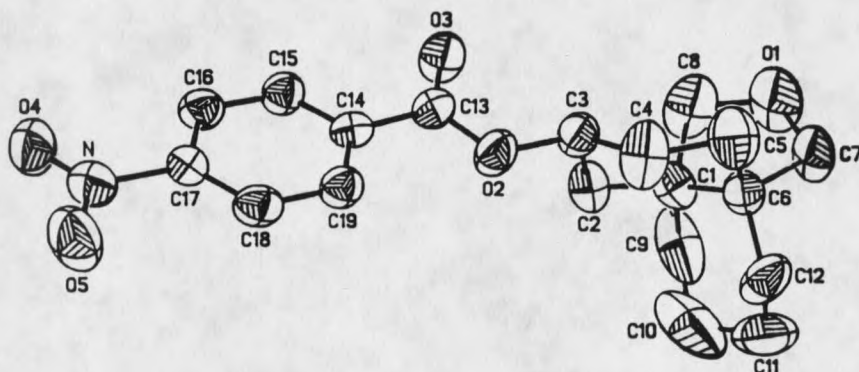


Figure 80. ORTEP Drawing of [38-anti].

Table 52. Bond Lengths (Å) of [38-anti].

C(1)-C(2)	1.561(7)	C(1)-C(6)	1.523(7)
C(1)-C(8)	1.522(8)	C(1)-C(9)	1.514(9)
C(2)-C(3)	1.475(7)	C(3)-C(4)	1.518(9)
C(3)-O(2)	1.464(5)	C(4)-C(5)	1.560(8)
C(5)-C(6)	1.502(8)	C(6)-C(7)	1.570(7)

(Table 52. Continued)

C(6)-C(12)	1.517(7)	C(7)-O(1)	1.380(8)
O(1)-C(8)	1.466(8)	C(9)-C(10)	1.473(16)
C(10)-C(11)	1.500(17)	C(11)-C(12)	1.504(16)
O(2)-C(13)	1.330(5)	C(13)-O(3)	1.198(7)
C(13)-C(14)	1.492(6)	C(14)-C(15)	1.393(6)
C(14)-C(19)	1.394(7)	C(15)-C(16)	1.373(6)
C(16)-C(17)	1.388(7)	C(17)-C(18)	1.378(6)
C(17)-N	1.470(6)	C(18)-C(19)	1.365(6)
N-O(4)	1.209(6)	N-O(5)	1.216(7)

Table 53. Bond Angles (°) of [38-anti].

C(2)-C(1)-C(6)	113.4(5)	C(2)-C(1)-C(8)	109.9(4)
C(6)-C(1)-C(8)	102.1(4)	C(2)-C(1)-C(9)	110.0(4)
C(6)-C(1)-C(9)	110.8(5)	C(8)-C(1)-C(9)	110.4(7)
C(1)-C(2)-C(3)	114.2(3)	C(2)-C(3)-C(4)	111.1(4)
C(2)-C(3)-O(2)	108.5(3)	C(4)-C(3)-O(2)	106.0(5)
C(3)-C(4)-C(5)	107.8(6)	C(4)-C(5)-C(6)	111.3(4)
C(1)-C(6)-C(5)	112.3(4)	C(1)-C(6)-C(7)	100.3(5)
C(5)-C(6)-C(7)	106.0(4)	C(1)-C(6)-C(12)	115.6(4)
C(5)-C(6)-C(12)	109.4(6)	C(7)-C(6)-C(12)	112.6(4)
C(6)-C(7)-O(1)	106.4(4)	C(7)-O(1)-C(8)	111.2(5)
C(1)-C(8)-O(1)	104.3(5)	C(1)-C(9)-C(10)	115.2(9)
C(9)-C(10)-C(11)	110.3(7)	C(10)-C(11)-C(12)	112.2(8)
C(6)-C(12)-C(11)	113.1(8)	C(3)-O(2)-C(13)	117.5(4)

(Table 53. Continued)

O(2)-C(13)-O(3)	124.0(4)	O(2)-C(13)-C(14)	111.6(4)
O(3)-C(13)-C(14)	124.3(4)	C(13)-C(14)-C(15)	117.5(4)
C(13)-C(14)-C(19)	122.6(4)	C(15)-C(14)-C(19)	119.8(4)
C(14)-C(15)-C(16)	120.3(5)	C(15)-C(16)-C(17)	118.2(4)
C(16)-C(17)-C(18)	122.4(4)	C(16)-C(17)-N	118.4(4)
C(18)-C(17)-N	119.1(4)	C(17)-C(18)-C(19)	118.8(5)
C(14)-C(19)-C(18)	120.3(4)	C(17)-N-O(4)	118.8(5)
C(17)-N-O(5)	118.5(4)	O(4)-N-O(5)	122.7(4)

Preparation of syn-tosylate derivative of [26]

The syn-para-nitrobenzoate derivative of [26] (0.107 g, 0.310 mmol) was dissolved in 0.2 mL dichloromethane and then added to a 80% aqueous ethanol solution that was 0.5% by weight in KOH. The reaction was stirred overnight. Workup yielded a syn-alcohol as a colorless oil (60.0 mg, 0.306 mmol) (99% yield). The syn-alcohol (60.0 mg, 0.306 mmol) was dissolved in 2 mL of dichloromethane to which was added 0.2 mL of pyridine. The solution was cooled to 0°C and TsCl (193 mg, 1.01 mmol) was added dropwise. The reaction was warmed to room temperature and stirred overnight. Workup (page 131) and flash chromatography (hexane:ethylacetate, 1:1) yielded a syn-tosylate as a white solid (104 mg, 0.297 mmol) (97% yield).

syn-3-Tosyl-8-oxatricyclo[4,4,3,0]tridecane, [84]

mp = 116-117°C

¹HNMR (300.133 MHz, CDCl₃): δ 1.25-1.79 (14H, m), 2.40 (3H, s), 3.45 (1H, d, J=8.0Hz), 3.48 (1H, d, J=8.0Hz), 3.86 (1H, d, J=8.1Hz), 3.87 (1H, d, J=8.1Hz), 4.57-4.67 (1H, m), 7.29 (2H, d, J=8.3Hz), 7.74 (2H, d, J=8.3Hz)

¹³CNMR (75.4 MHz, CDCl₃): δ 21.44 (t), 21.51 (q), 21.86 (t), 25.80 (t), 28.16 (t), 28.42 (t), 32.52 (t), 38.66 (t), 41.18 (s), 43.61 (s), 76.83 (t) (two carbon), 78.98 (d), 127.46 (d), 129.69 (d), 134.68 (s), 144.42 (s)

LRMS (EI) m/e (%abundance): 178 (73), 160 (13), 147 (23), 133 (27), 123 (91), 105 (23), 91 (100), 79 (44), 67 (43), 55 (26), 41 (20)

LRMS (CI) (NH₃) m/e (%abundance): 368 (M+NH₄⁺, 7), 196 (100)

HRMS (EI) m/e calculated for C₁₉H₂₆O₄S₁ = 350.1552; found = 350.1553

Preparation of anti-tosylate derivative of [26]

In a similar fashion, saponification of the anti-para-nitrobenzoate derivative of [26] (0.101 g, 0.293 mmol) afforded 53.4 mg (0.272 mmol) of the anti-alcohol (93% yield). Again, identical workup (page 131) gave the anti-alcohol (53.4 mg, 0.272 mmol). The alcohol was dissolved in 2 mL of dichloromethane to which was added pyridine (0.2 mL, 2.48 mmol) and TSCl (156 mg, 0.818 mmol). The anti-tosylate was cleanly separated as a white solid (94.0 mg, 0.269 mmol) (99% yield).

anti-3-Tosyl-8-oxatricyclo[4,4,3,0]tridecane, [85]

mp = 53-55°C

¹HNMR (300.133 MHz, CDCl₃): δ 1.22-1.81 (14H, m), 2.40 (3H, s), 3.37 (1H, d, J=8.1Hz), 3.41 (1H, d, J=8.2Hz), 3.74 (1H, d, J=8.2Hz), 3.92 (1H, d, J=8.1Hz), 4.56-4.66 (1H, m), 7.29 (2H, d, J=8.3Hz), 7.74 (2H, d, J=8.3Hz)

¹³CNMR (75.4 MHz, CDCl₃): δ 21.47 (t), 21.57 (q), 21.91 (t), 26.86 (t), 27.91 (t), 31.91 (t), 33.18 (t), 33.94 (t), 41.09 (s), 44.01 (s), 76.14 (t), 77.19 (t), 79.20 (d), 127.49 (d), 129.70 (d), 134.48 (s), 144.46 (s)

LRMS (EI) m/e (%abundance): 195 (37), 178 (37), 147 (40), 133 (92), 123 (33), 105 (36), 91 (100), 79 (32), 67 (24), 55 (28), 41 (66)

LRMS (CI) (NH₃) m/e (%abundance): 368 (M+NH₄⁺, 28), 196 (100), 108 (12)

HRMS (EI) m/e calculated for C₁₉H₂₆O₄S₁ = 350.1552; found = 350.1556

Preparation of cis-1,6-dicarbomethoxybicyclo[5,4,0]undec-3-ene, [22]

A solution of 100 mL of dry THF, 70 mL of 2.5 M n-BuLi (0.175 mol) and 25 mL of diisopropylamine (0.180 mol) was stirred under argon at -10°C for 30 minutes, The temperature was taken down to -78°C and cis-3,4-dicarbomethoxycyclohexene (14.0 g, 0.070 mol) was added dropwise, creating a bright red solution. After addition was completed the solution was allowed to stir for 15

minutes, then 1,5-dibromopentane (11.6 mL, 0.085 mol) was added dropwise. The solution was allowed to warm to room temperature and stirred overnight. Workup (page 120) and distillation yielded a product as a yellow oil (5.21 g, 0.020 mol) (29% yield).

cis-1,6-Dicarbomethoxybicyclo[5,4,0]undec-3-ene, [22]

LRMS (EI) m/e: 234, 206, 147, 131, 91 (base), 77, 59, 41

HRMS (CI) m/e calculated for $C_{15}H_{22}O_4$ = 266.1518 ; found = 266.1510

Preparation of cis-1,6-dihydroxymethylbicyclo [5,4,0]undec-3-ene

A solution of [22] (2.70 g, 10.2 mmol) in 5 mL of dry THF was added dropwise at 0°C to a stirring solution of LAH (0.58 g, 0.015 mol) in 5 mL of dry THF. The reaction mixture was stirred overnight at a room temperature. Workup (page 121) yielded a product as a white powder (1.70 g, 8.10 mmol) (79% yield).

cis-1,6-Dihydroxymethylbicyclo[5,4,0]undec-3-ene

mp = 152-153°C

LRMS (EI) m/e: 192 ($-H_2O$), 179, 174 ($-H_2O$), 161, 137, 121, 106, 91 (base), 79, 67, 41

LRMS (CI) (Methane) m/e (%abundance): 211 ($M+H^+$, 3), 209 (5), 193 (23), 175 (100), 163 (22), 147 (14), 133 (15), 119 (11), 109 (27), 95 (49)

HRMS (CI) m/e calculated for $C_{13}H_{23}O_2$ = 211.1698; found = 211.1687

Preparation of 8-oxatricyclo[5,4,3,0]tetradec-3-ene, [27]

cis-1,6-Dihydroxymethylbicyclo[5,4,0]undec-3-ene (1.7 g, 8.10 mmol) was dissolved in 7 mL of dry pyridine and then 0.63 mL of MsCl (0.928 g, 8.10 mmol) were added dropwise to the stirring solution under argon in ice bath. The reaction mixture was stirred at room temperature overnight. Workup (page 122) and flash chromatography (hexane:ethylacetate, 1:1) yield a product as a colorless oil (1.02 g, 5.31 mmol) (66% yield)

8-Oxatricyclo[5,4,3,0]tetradec-3-ene, [27]

¹HNMR (300.133 MHz, CDCl₃): δ 1.39-1.97 (14H, m), 3.48 (2H, d, J=8.7Hz), 3.63 (2H, d, J=8.7Hz), 5.84-5.86 (2H, m)

¹³CNMR (75.4 MHz, CDCl₃): δ 24.61 (t), 30.97 (t), 34.34 (t), 39.41 (t), 49.55 (s), 81.68 (t), 128.59 (d)

LRMS (EI) m/e: 192 (M⁺), 161, 136, 123, 109, 91 (base), 82, 67, 41

HRMS (EI) m/e calculated for C₁₃H₂₀O₁ = 192.1514; found = 192.1516

Hydroboration of 8-oxatricyclo[5,4,3,0]tetradec-3-ene, [27]

The propellane, [27] (0.044 g, 0.228 mmol) was dissolved in 2 mL of dry THF and then 1 mL of BH₃.THF (15.6 mg, 1.13 mmol) were added dropwise to the stirring solution under argon at 0°C. The solution was warmed to room temperature and stirred overnight. Workup (page 123) yielded a 59:41 mixture of *syn*-OH and *anti*-OH as colorless oils (38.9 mg, 0.185 mmol) (81% yield).

syn-8-Oxatricyclo[5,4,3,0]tetradec-3-ol, [65-syn]

¹HNMR (300.133 MHz, CDCl₃): δ 1.28-2.06 (16H, m), 3.43 (1H, d, J=8.7Hz), 3.59 (1H, d, J=8.5Hz), 3.80 (1H, d, J=8.5Hz), 3.83-3.92 (1H, m), 4.00 (1H, d, J=8.7Hz)

¹³CNMR (75.4 MHz, CDCl₃): δ 22.49 (t), 22.61 (t), 28.32 (t), 29.03 (t), 30.76 (t), 35.42 (t), 37.01 (t), 44.26 (t), 45.59 (s), 46.98 (s), 66.68 (d), 79.89 (t), 80.09 (t)

LRMS (EI) m/e (%abundance): 192 (13), 147 (17), 137 (100), 119 (12), 105 (20), 91 (50), 79 (47), 67 (44), 55 (35), 41 (46)

HRMS (CI) m/e calculated for C₁₃H₂₃O₂ = 211.1698; found = 211.1693

anti-8-Oxatricyclo[5,4,3,0]tetradec-3-ol, [65-anti]

¹HNMR (300.133 MHz, CDCl₃): δ 1.30-1.97 (16H, m), 3.42 (1H, d, J=8.3Hz), 3.50 (1H, d, J=8.3Hz), 3.82 (1H, d, J=8.3Hz), 3.90 (1H, d, J=8.3Hz), 3.93-4.03 (1H, m)

¹³CNMR (75.4 MHz, CDCl₃): δ 22.25 (t), 22.36 (t), 28.42 (t), 30.91 (t), 34.04 (t), 34.82 (t), 37.22 (t), 38.29 (t), 45.10 (s), 47.55 (s), 67.07 (d), 78.98 (t), 80.47 (t)

LRMS (EI) m/e (%abundance): 210 (M⁺, 2), 192 (11), 179 (13), 161 (17), 147 (53), 137 (18), 119 (29), 105 (47), 91 (100), 79 (88), 67 (66), 55 (66), 41 (71)

HRMS (CI) m/e calculated for C₁₃H₂₃O₂ = 211.1698; found = 211.1698

Preparation of para-nitrobenzoate derivatives of 8-oxatricyclo[5,4,3,0]tetradec-3-ene, [27]

The mixture of *syn*- and *anti*- alcohols derived from the hydroboration of [27] (38.9 mg, 0.185 mmol) was dissolved in 5 mL of dry pyridine and an argon atmosphere was created. Then PNBCl (51.5 mg, 0.278 mmol) was dissolved in dry pyridine and added dropwise to the stirring solution at 0°C. The reaction was stirred at room temperature overnight. Workup (page 125) and flash chromatography (dichloromethane:ethylacetate:hexane, 10:1:1) isolated the isomers as white solids (0.036 g, 0.010 mmol) (55% yield). *syn*-3-para-Nitrobenzoate-8-oxatricyclo[5,4,3,0] tetradecane, [39-*syn*]

¹HNMR (300.133 MHz, CDCl₃): δ 1.40-2.10 (16H, m), 3.60 (1H, d, J=8.7Hz), 3.63 (1H, d, J=8.6Hz), 3.90 (1H, d, J=8.3Hz), 3.97 (1H, d, J=8.6Hz), 5.18-5.27 (1H, m), 8.15-8.19 (2H, m), 8.24-8.28 (2H, m)

¹³CNMR (75.4 MHz, CDCl₃): δ 22.33 (t), 22.48 (t), 26.89 (t), 28.55 (t), 28.64 (t), 35.56 (t), 36.66 (t), 40.04 (t), 45.70 (s), 47.14 (s), 72.02 (d), 79.33 (t), 79.60 (t), 123.50 (d), 130.63 (d), 136.17 (s), 150.65 (s), 164.23 (s)

LRMS (EI) m/e (%abundance): 192 (55), 161 (15), 147 (32), 137 (100), 120 (25), 104 (17), 91 (32), 81 (22), 67 (20), 55 (13), 41 (27)

LRMS (HPEC) (NH₃) m/e (%abundance): 359 (100), 328 (27), 136 (13)

HRMS (HPEC) (NH₃) m/e calculated for C₂₀H₂₅O₅N₁ = 359.1733;
found = 359.1725

anti-3-para-Nitrobenzoate-8-oxatricyclo

[5,4,3,0]tetradecane, [39-anti]

¹HNMR (300.133 MHz, CDCl₃): δ 1.41-2.26 (16H, m), 3.51 (1H, d, J=8.7Hz), 3.64 (1H, d, J=8.6Hz), 3.75 (1H, d, J=8.6Hz), 4.00 (1H, d, J=8.7Hz), 5.31-5.41 (1H, m), 8.17-8.21 (2H, m), 8.25-8.29 (2H, m)

¹³CNMR (75.4 MHz, CDCl₃): δ 22.87 (t), 22.91 (t), 26.77 (t), 29.26 (t), 32.75 (t), 35.46 (t), 35.68 (t), 37.33 (t), 45.46 (s), 34.36 (s), 72.28 (d), 79.69 (t), 80.58 (t), 123.46 (d), 130.62 (d), 136.26 (s), 150.61 (s), 164.22 (s),

LRMS (EI) m/e (%abundance): 359 (M⁺, 2), 209 (41), 192 (34), 174 (11), 161 (39), 147 (77), 137 (100), 120 (42), 105 (58), 91 (71), 81 (50), 67 (45), 55 (27), 41 (54)

LRMS (HPEC) (NH₃) m/e (%abundance): 359 (100), 328 (21)

HRMS (HPEC) (NH₃) m/e calculated for C₂₀H₂₅O₅N₁ = 359.1733;
found = 359.1728

Crystallization of the product, [39-anti] was accomplished in dichloromethane:hexane in a relative ratio of 1:10, respectively.

X-ray analysis:

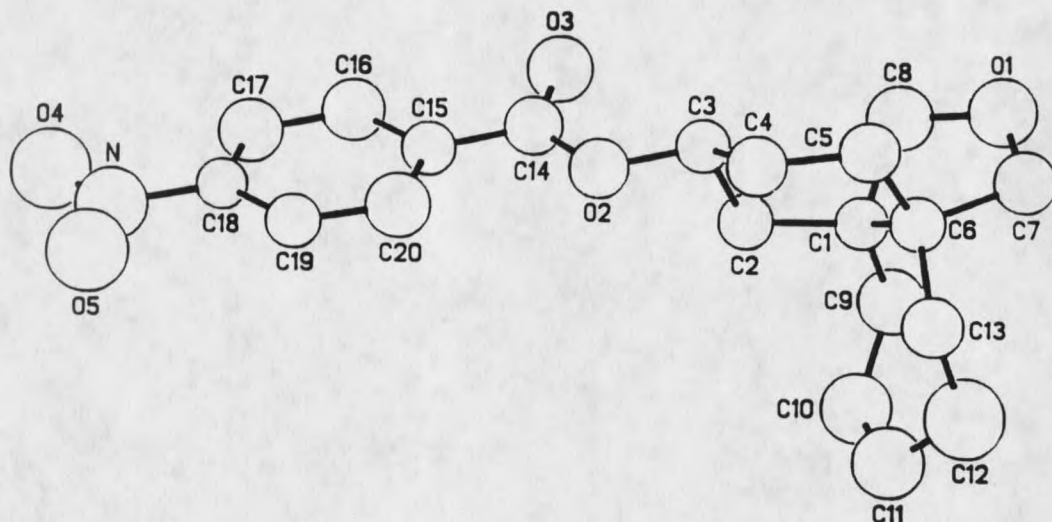


Figure 81. ORTEP Drawing of [39-anti].

Table 54. Bond Length (Å) of [39-anti].

C(1)-C(2)	1.524 (30)	C(1)-C(6)	1.558 (30)
C(1)-C(8)	1.588 (26)	C(1)-C(9)	1.499 (29)
C(2)-C(3)	1.555 (28)	C(3)-C(4)	1.519 (31)
C(3)-O(2)	1.422 (25)	C(4)-C(5)	1.493 (30)
C(5)-C(6)	1.505 (31)	C(6)-C(7)	1.579 (30)
C(6)-C(13)	1.560 (28)	C(7)-O(1)	1.405 (27)
O(1)-C(8)	1.427 (27)	C(9)-C(10)	1.507 (26)
C(10)-C(11)	1.461 (36)	C(11)-C(12)	1.459 (32)
C(12)-C(13)	1.497 (32)	O(2)-C(14)	1.316 (27)

(Table 54. Continued)

C(14)-O(3)	1.252(30)	C(14)-C(15)	1.444(32)
C(15)-C(16)	1.379(32)	C(15)-C(20)	1.376(33)
C(16)-C(17)	1.366(32)	C(17)-C(18)	1.351(33)
C(18)-C(19)	1.360(29)	C(18)-N	1.472(29)
C(19)-C(20)	1.390(32)	N-O(4)	1.184(30)
N-O(5)	1.215(33)		

Table 55. Bond Angles (°) of [39-anti].

C(2)-C(1)-C(6)	110.9(18)	C(2)-C(1)-C(8)	109.3(16)
C(6)-C(1)-C(8)	99.7(14)	C(2)-C(1)-C(9)	110.3(15)
C(6)-C(1)-C(9)	118.5(18)	C(8)-C(1)-C(9)	107.4(18)
C(1)-C(2)-C(3)	117.2(14)	C(2)-C(3)-C(4)	106.8(16)
C(2)-C(3)-O(2)	108.3(13)	C(4)-C(3)-O(2)	107.1(18)
C(3)-C(4)-C(5)	109.8(19)	C(4)-C(5)-C(6)	113.9(15)
C(1)-C(6)-C(5)	112.3(17)	C(1)-C(6)-C(7)	99.4(18)
C(5)-C(6)-C(7)	109.3(14)	C(1)-C(6)-C(13)	118.1(13)
C(5)-C(6)-C(13)	107.9(19)	C(7)-C(6)-C(13)	109.5(16)
C(6)-C(7)-O(1)	104.1(16)	C(7)-O(1)-C(8)	114.0(15)
C(1)-C(8)-O(1)	102.9(16)	C(1)-C(9)-C(10)	117.8(21)
C(9)-C(10)-C(11)	120.3(18)	C(10)-C(11)-C(12)	120.2(19)
C(11)-C(12)-C(13)	117.0(21)	C(6)-C(13)-C(12)	120.1(21)
C(3)-O(2)-C(14)	117.7(17)	O(2)-C(14)-O(3)	122.1(20)
O(2)-C(14)-C(15)	117.1(21)	O(3)-C(14)-C(15)	120.8(20)
C(14)-C(15)-C(16)	121.1(21)	C(14)-C(15)-C(20)	121.0(21)

(Table 55. Continued)

C(16)-C(15)-C(20)	117.8 (21)	C(15)-C(16)-C(17)	121.9 (22)
C(16)-C(17)-C(18)	119.0 (21)	C(17)-C(18)-C(19)	121.3 (20)
C(17)-C(18)-N	118.0 (19)	C(19)-C(18)-N	120.7 (20)
C(18)-C(19)-C(20)	119.4 (21)	C(15)-C(20)-C(19)	120.3 (21)
C(18)-N-O(4)	120.5 (22)	C(18)-N-O(5)	117.0 (19)
O(4)-N-O(5)	122.2 (22)		

Preparation of syn-tosylate derivative of [27]

The *syn*-para-nitrobenzoate derivative of [27] (10.0 mg, 0.025 mmol) was dissolved in 0.5 mL dichloromethane and then added to a 80% aqueous ethanol solution that was 0.5% by weight in KOH. The reaction was stirred overnight. Workup yielded a *syn*-alcohol as a colorless oil (5.00 mg, 0.024 mmol) (94% yield). The *syn*-alcohol (5.00 mg, 0.024 mmol) was dissolved in 0.5 mL of dichloromethane to which was added 1 mL of pyridine. The solution was cooled to 0°C and TsCl (5.40 mg, 0.029 mmol) was added dropwise. The reaction was warmed to room temperature and stirred overnight. Workup (page 131) and flash chromatography (hexane:ethylacetate, 7:3) yielded a *syn*-tosylate as a white solid (2.00 mg, 0.0055 mmol) (23% yield).

syn-3-Tosyl-8-oxatricyclo[5,4,3,0]tetradecane, [86]

¹HNMR (300.133 MHz, CDCl₃): δ 1.0-1.92 (16H, m), 2.43 (3H, s), 3.49 (1H, d, J=8.5Hz), 3.50 (1H, d, J=8.5Hz), 3.82

(1H, d, J=8.6Hz), 3.85 (1H, d, J=8.6Hz), 4.63-4.73 (1H, m), 7.32 (2H, d, J=8.3Hz), 7.77 (2H, d, J=8.3Hz)
¹³CNMR (75.4 MHz, CDCl₃): δ 21.63, 22.01, 22.19, 27.75, 28.10, 28.22, 35.08, 36.40, 40.84, 45.29, 47.29, 78.76, 78.92, 79.20, 127.60, 129.77, 134.75, 144.49

Preparation of anti-tosylate derivative of [27]

In a similar fashion, saponification of the anti-para-nitrobenzoate derivative of [27] (20.0 mg, 0.051 mmol) afforded 10.0 mg (0.048 mmol) of the anti-alcohol (93% yield). Again, using the identical workup (page 131), the anti-alcohol (10.0 mg, 0.048 mmol) was dissolved in 0.5 mL of dichloromethane to which was added 1 mL of pyridine and TsCl (10.8 mg, 0.057 mmol). The anti-tosylate was cleanly separated to give 3 mg (0.0082 mmol) of tosylate (17% yield) and starting material.

anti-3-Tosyl-8-oxatricyclo[5,4,3,0]tetradecane, [87]

¹HNMR (300.133 MHz, CDCl₃): δ 1.0-1.92 (16H, m), 2.43 (3H, s), 3.39 (1H, d, J=8.8Hz), 3.53 (1H, d, J=8.7Hz), 3.61 (1H, d, J=8.7Hz), 3.70 (1H, d, J=8.8Hz), 4.74-4.84 (1H, m), 7.32 (2H, d, J=8.3Hz), 7.77 (2H, d, J=8.3Hz)
¹³CNMR (75.4 MHz, CDCl₃): δ 21.64, 22.84 (2 carbons), 27.17, 29.28, 32.21, 35.60, 36.55, 36.88, 45.08, 47.44, 79.24, 79.83, 80.64, 127.70, 129.80, 134.79, 144.54

Preparation of cis-9,10-methanesulfonyloxymethylbicyclo
[4,3,0]non-3-ene, [29]

To an ice-cold stirred solution of methanesulfonyl chloride (10.0 mL, 0.130 mol) in 15 mL of pyridine was added dropwise to a solution of the diol [31] (6.75 mg, 0.037 mol) at 0°C. After an additional 2 hours stirring in the cold ice bath, workup (page 125) yielded a product as a white powder (9.80 g, 0.029 mol) (78% yield).

cis-9,10-Methanesulfonyloxymethylbicyclo[4,3,0]non-3-ene,
[29]

mp = 73-74°C

IR (nujol, cm^{-1}): 3030, 2951, 2857, 1456, 1337, 1171, 991,
 951, 839, 759, 679

^1H NMR (300.133 MHz, CDCl_3): δ 1.66- 1.87 (6H, m), 1.98-2.16
 (4H, m), 3.00 (6H, s), 4.08-4.17 (4H)

^{13}C NMR (75.4 MHz, CDCl_3): δ 18.39 (t), 30.35 (t), 33.44 (t),
 37.30 (q), 45.29 (s), 72.83 (t), 123.54 (d)

LRMS (EI) m/e: 146, 131 (base), 118, 104, 77, 63, 44

Preparation of 8-thiatricyclo[4,3,3,0]dodec-3-ene, [30]

The dimesylate, [29], (4.2 g, 0.012 mol) was mixed with sodium sulfide (3.43 g, 0.044 mol) (sodium sulfide.9 hydrate was treated with benzene azeotrope to remove water), and 50 mL of dry hexamethylphosphoramide, and heated to 120°C for 24 hours. The brownish colored contents were cooled to room temperature and treated with 50 mL of water, and extracted with ether. The ether layer was washed with water,

saturated brine, dried over MgSO_4 and reduced in volume to give the product as white powder (1.92 g, 0.0107 mol) (86% yield)

8-Thiatricyclo[4,3,3,0]dodec-3-ene, [30]

mp = 84-85°C

IR (nujol, cm^{-1}): 3025, 2967, 2902, 2855, 1460, 1214, 733, 663

^1H NMR (300.133 MHz, CDCl_3): δ 1.54-1.82 (6H, m), 1.97 (2H, d, $J=16.7\text{Hz}$), 2.13 (2H, d, $J=16.7\text{Hz}$), 2.69 (2H, d, $J=10.1\text{Hz}$), 2.81 (2H, d, $J=10.1\text{Hz}$), 5.56 (2H, t, $J=1.8\text{Hz}$)

^{13}C NMR (75.4 MHz, CDCl_3): δ 19.75 (t), 31.90 (t), 36.09 (t), 42.53 (t), 53.97 (s), 124.74 (d)

LRMS (EI) m/e (%abundance): 180 (M^+ , 61), 147 (8), 133 (37), 125 (15), 119 (98), 105 (28), 98 (12), 91 (100), 79 (25), 65 (12), 53 (12), 41 (21)

HRMS (EI) m/e calculated for $\text{C}_{11}\text{H}_{16}\text{S}_1$ = 180.0974; found = 180.0979

Hydroboration of 8-thiatricyclo[4,4,3,0]dodec-3-ene, [30]

The propellane, [30] (0.400 g, 2.22 mmol) was dissolved in 5 mL of dry THF and then 2 mL of $\text{BH}_3\cdot\text{THF}$ (0.031 mg, 2.26 mmol) were added dropwise to the stirring solution under argon at 0°C. The solution was warmed to room temperature and stirred overnight. Workup (page 123) yielded a 45:55 mixture of syn-OH and anti-OH as white solids (0.365 g, 1.84 mmol) (83% yield).

syn-8-Thiatricyclo[4,4,3,0]dodec-3-ol, [68-syn]

IR (neat, cm^{-1}): 3375, 2930, 2864, 1465, 1303, 1071, 1051,
998, 732, 666

^1H NMR (300.133 MHz, CDCl_3): δ 1.36-1.87 (12H, m), 2.55 (1H, d, $J=10.8\text{Hz}$), 2.69 (1H, d, $J=10.7\text{Hz}$), 2.89 (1H, d, $J=10.8\text{Hz}$), 3.02 (1H, d, $J=10.7\text{Hz}$), 3.70-3.80 (1H, m)

^{13}C NMR (75.4 MHz, CDCl_3): δ 19.49 (t), 29.61 (t), 31.45 (t), 33.00 (t), 36.78 (t), 38.53 (t), 38.93 (t), 44.50 (t), 54.16 (s), 57.07 (s), 67.48 (d)

LRMS (EI) m/e (%abundance): 198 (M^+ , 39), 180 (46), 133 (36), 125 (100), 119 (84), 105 (13), 97 (10), 91 (38), 79 (21), 67 (13), 53 (11)

HRMS (EI) m/e calculated for $\text{C}_{11}\text{H}_{18}\text{O}_1\text{S}_1 = 198.1078$; found = 198.1071

anti-8-Thiatricyclo[4,4,3,0]dodec-3-ol, [68-anti]

IR (neat, cm^{-1}): 3375, 2930, 2864, 1465, 1303, 1071, 1051,
998, 732, 666

^1H NMR (300.133 MHz, CDCl_3): δ 1.25-1.88 (12H, m), 2.51 (1H, d, $J=10.8\text{Hz}$), 2.72 (1H, d, $J=10.8\text{Hz}$), 2.89 (1H, d, $J=10.8\text{Hz}$), 2.91 (1H, d, $J=10.8\text{Hz}$), 3.70-3.79 (1H, m)

^{13}C NMR (75.4 MHz, CDCl_3): δ 19.54 (t), 28.50 (t), 31.27 (t), 31.95 (t), 37.99 (t), 39.25 (t), 39.61 (t), 43.32 (t), 54.70 (s), 56.52 (s), 67.24 (d)

LRMS (EI) m/e (%abundance): 198 (M^+ , 94), 180 (8), 151 (37), 133 (100), 119 (49), 109 (16), 93 (42), 79 (26), 67 (18), 60 (12), 53 (14), 45 (12)

HRMS (EI) m/e calculated for $C_{11}H_{18}O_1S_1 = 198.1078$; found = 198.1072

Preparation of para-nitrobenzoate derivatives of 8-thiatricyclo[4,3,3,0]dodec-3-ene, [30]

The mixture of *syn*- and *anti*-alcohol derived from the hydroboration of [30] (0.283 g, 1.43 mmol) was dissolved in 5 mL of dry pyridine and an argon atmosphere was created. Then PNBCl (0.398 g, 2.15 mmol) was dissolved in dry pyridine and added dropwise to the stirring solution at 0°C. The reaction was stirred at room temperature overnight.

Workup (page 125) and flash chromatography

(dichloromethane:ethylacetate:hexane, 25:1:1) isolated the isomers as white powders (0.288 g, 0.830 mmol) (58% yield).

syn-3-para-Nitrobenzoate-8-thiatricyclo[4,3,3,0] dodecane, [42-*syn*]

mp = 146-147°C

^1H NMR (300.133 MHz, CDCl_3): δ 1.52-1.98 (12H, m), 2.60 (1H, d, $J=11.0\text{Hz}$), 2.76 (1H, d, $J=10.8\text{Hz}$), 2.93 (1H, d, $J=11.0\text{Hz}$), 3.05 (1H, d, $J=10.8\text{Hz}$), 5.10-5.19 (1H, m), 8.13-8.25 (4H, m)

^{13}C NMR (75.4 MHz, CDCl_3): δ 19.48 (t), 27.31 (t), 28.98 (t), 33.13 (t), 34.71 (t), 36.46 (t), 38.77 (t), 44.13 (t), 54.18 (s), 56.77 (s), 72.13 (d), 123.40 (d), 130.56 (d), 135.95 (s), 150.48 (s), 164.06 (s)

LRMS (EI) m/e (%abundance): 347 (M^+ , 8), 317 (6), 180 (90),
150 (1), 125 (100), 104 (19), 91 (38), 79 (17), 65
(11), 41 (15)

HRMS (EI) m/e calculated for $C_{18}H_{21}O_4N_1S_1$ = 347.1191; found =
347.1191

anti-3-para-Nitrobenzoate-8-thiatricyclo[4,3,3,0] dodecane,
[42-anti]

mp = 123-124°C

^1H NMR (300.133 MHz, CDCl_3): δ 1.58-1.99 (12H, m), 2.61 (1H,
d, $J=10.9\text{Hz}$), 2.82 (1H, d, $J=10.9\text{Hz}$), 2.92 (1H, d,
 $J=10.9\text{Hz}$), 3.00 (1H, d, $J=10.9\text{Hz}$), 5.11-5.20 (1H, m),
8.14-8.26 (4H, m)

^{13}C NMR (75.4 MHz, CDCl_3): δ 19.63 (t), 27.18 (t), 28.04 (t),
32.53 (t), 35.47 (t), 37.63 (t), 39.53 (t), 42.75 (t),
54.65 (s), 56.31 (s), 72.12 (d), 123.45 (d), 130.58
(d), 136.00 (s), 150.51 (s), 164.03 (s)

LRMS (EI) m/e (%abundance): 347 (M^+ , 18), 317 (8), 180
(100), 150 (27), 125 (70), 104 (25), 91 (53), 79 (20),
67 (16), 60 (16), 41 (20)

HRMS (EI) m/e calculated for $C_{18}H_{21}O_4N_1S_1$ = 347.1191; found =
347.1185

Crystallization of the product, [42-syn] was accomplished in hexane:dichloromethane in a relative ratio of 10:1 respectively and the product, [42-anti] was accomplished in hexane:dichloromethane in a relative ratio of 10:1, respectively.

X-ray analysis:

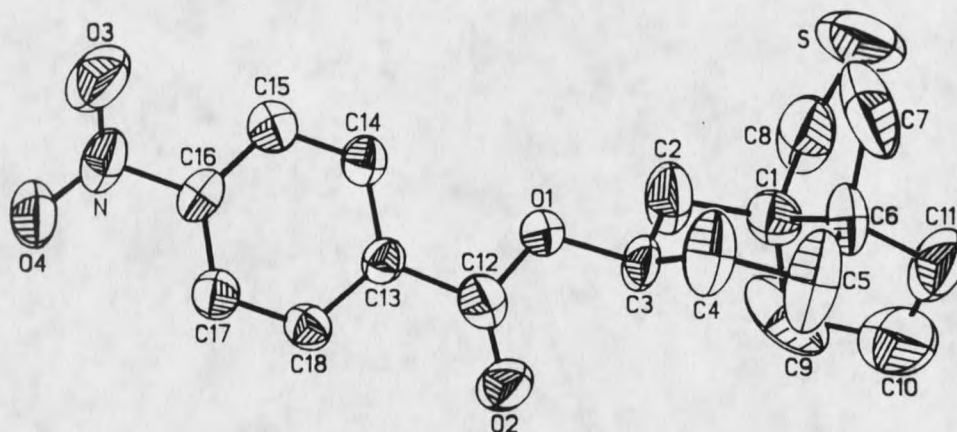


Figure 82. ORTEP Drawing of [42-syn].

Table 56. Bond Lengths (Å) of [42-syn].

C (1) -C (2)	1.570 (8)	C (1) -C (6)	1.493 (10)
C (1) -C (8)	1.516 (10)	C (1) -C (9)	1.534 (11)
C (2) -C (3)	1.478 (9)	C (3) -C (4)	1.505 (10)
C (3) -O (1)	1.466 (6)	C (4) -C (5)	1.554 (10)
C (5) -C (6)	1.522 (11)	C (6) -C (7)	1.573 (13)
C (6) -C (11)	1.526 (10)	C (7) -S	1.754 (11)
S -C (8)	1.751 (10)	C (9) -C (10)	1.572 (12)

(Table 56. Continued)

C(10)-C(11)	1.458 (13)	O(1)-C(12)	1.339 (7)
C(12)-O(2)	1.188 (7)	C(12)-C(13)	1.497 (8)
C(13)-C(14)	1.399 (8)	C(13)-C(18)	1.396 (7)
C(14)-C(15)	1.375 (8)	C(15)-C(16)	1.382 (8)
C(16)-C(17)	1.381 (8)	C(16)-N	1.475 (7)
C(17)-C(18)	1.380 (8)	N-O(3)	1.217 (7)
N-O(4)	1.225 (6)		

Table 57. Bond Angles (°) of [42-syn].

C(2)-C(1)-C(6)	112.4 (6)	C(2)-C(1)-C(8)	109.4 (5)
C(6)-C(1)-C(8)	106.0 (6)	C(2)-C(1)-C(9)	113.1 (5)
C(6)-C(1)-C(9)	104.7 (6)	C(8)-C(1)-C(9)	111.0 (6)
C(1)-C(2)-C(3)	112.4 (5)	C(2)-C(3)-C(4)	111.1 (5)
C(2)-C(3)-O(1)	106.2 (5)	C(4)-C(3)-O(1)	109.8 (5)
C(3)-C(4)-C(5)	108.2 (6)	C(4)-C(5)-C(6)	112.4 (7)
C(1)-C(6)-C(5)	112.3 (5)	C(1)-C(6)-C(7)	107.3 (6)
C(5)-C(6)-C(7)	114.1 (7)	C(1)-C(6)-C(11)	102.1 (6)
C(5)-C(6)-C(11)	110.3 (6)	C(7)-C(6)-C(11)	110.1 (5)
C(6)-C(7)-S	106.8 (7)	C(7)-S-C(8)	95.2 (5)
C(1)-C(8)-S	110.0 (6)	C(1)-C(9)-C(10)	102.4 (6)
C(9)-C(10)-C(11)	107.6 (7)	C(6)-C(11)-C(10)	105.1 (6)
C(3)-O(1)-C(12)	117.0 (1)	O(1)-C(12)-O(2)	125.2 (5)
O(1)-C(12)-C(13)	110.8 (5)	O(2)-C(12)-C(13)	124.0 (5)
C(12)-C(13)-C(14)	123.0 (5)	C(12)-C(13)-C(18)	117.1 (5)

(Table 57. Continued)

C(14)-C(13)-C(18)	119.9(5)	C(13)-C(14)-C(15)	120.3(5)
C(14)-C(15)-C(16)	118.0(5)	C(15)-C(16)-C(17)	123.5(5)
C(15)-C(16)-N	118.5(5)	C(17)-C(16)-N	118.0(5)
C(16)-C(17)-C(18)	117.9(5)	C(13)-C(18)-C(17)	120.3(5)
C(16)-N-O(3)	118.4(5)	C(16)-N-O(4)	118.0(5)
O(3)-N-O(4)	123.6(5)		

X-ray analysis:

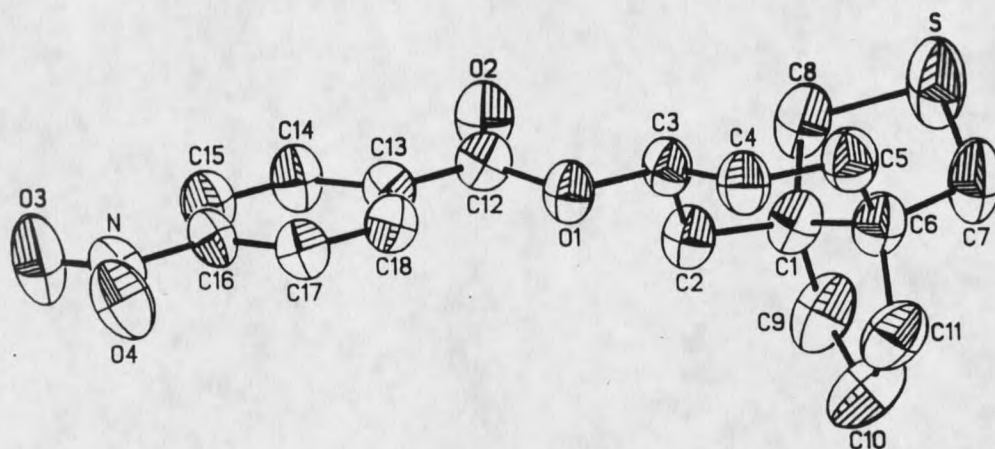


Figure 83. ORTEP Drawing of [42-anti].

Table 58. Bond Lengths (Å) of [42-anti].

C(1)-C(2)	1.553(6)	C(1)-C(6)	1.555(6)
C(1)-C(8)	1.531(6)	C(1)-C(9)	1.528(7)
C(2)-C(3)	1.511(6)	C(3)-C(4)	1.513(6)

(Table 58. Continued)

C(3)-O(1)	1.467(5)	C(4)-C(5)	1.527(6)
C(5)-C(6)	1.516(6)	C(6)-C(7)	1.536(6)
C(6)-C(11)	1.526(6)	C(7)-S	1.806(5)
S-C(8)	1.805(5)	C(9)-C(10)	1.527(7)
C(10)-C(11)	1.536(7)	O(1)-C(12)	1.337(5)
C(12)-O(2)	1.203(5)	C(12)-C(13)	1.489(5)
C(13)-C(14)	1.384(5)	C(13)-C(18)	1.400(5)
C(14)-C(15)	1.372(6)	C(15)-C(16)	1.374(6)
C(16)-C(17)	1.376(5)	C(16)-N	1.486(5)
C(17)-C(18)	1.370(5)	N-O(3)	1.218(5)
N-O(4)	1.212(5)		

Table 59. Bond Angles (°) of [42-anti].

C(2)-C(1)-C(6)	111.7(3)	C(2)-C(1)-C(8)	111.1(3)
C(6)-C(1)-C(8)	108.6(4)	C(2)-C(1)-C(9)	109.2(4)
C(6)-C(1)-C(9)	102.7(3)	C(8)-C(1)-C(9)	113.3(3)
C(1)-C(2)-C(3)	112.6(3)	C(2)-C(3)-C(4)	109.9(3)
C(2)-C(3)-O(1)	109.9(3)	C(4)-C(3)-O(1)	105.6(3)
C(3)-C(4)-C(5)	110.0(3)	C(4)-C(5)-C(6)	113.0(4)
C(1)-C(6)-C(5)	112.5(3)	C(1)-C(6)-C(7)	104.6(3)
C(5)-C(6)-C(7)	110.0(4)	C(1)-C(6)-C(11)	104.4(4)
C(5)-C(6)-C(11)	114.6(4)	C(7)-C(6)-C(11)	110.2(4)
C(6)-C(7)-S	108.7(3)	C(7)-S-C(8)	94.5(2)
C(1)-C(8)-S	107.6(3)	C(1)-C(9)-C(10)	105.6(4)

(Table 59. Continued)

C(9)-C(10)-C(11)	107.3(4)	C(6)-C(11)-C(10)	105.6(4)
C(3)-O(1)-C(12)	117.5(3)	O(1)-C(12)-O(2)	124.4(4)
O(1)-C(12)-C(13)	111.9(3)	O(2)-C(12)-C(13)	123.7(4)
C(12)-C(13)-C(14)	118.0(3)	C(12)-C(13)-C(18)	122.6(3)
C(14)-C(13)-C(18)	119.4(4)	C(13)-C(14)-C(15)	120.3(4)
C(14)-C(15)-C(16)	118.7(4)	C(15)-C(16)-C(17)	122.9(4)
C(15)-C(16)-N	118.5(4)	C(17)-C(16)-N	118.6(3)
C(16)-C(17)-C(18)	117.9(4)	C(13)-C(18)-C(17)	120.8(4)
C(16)-N-O(3)	118.2(3)	C(16)-N-O(4)	118.1(3)
O(3)-N-O(4)	123.7(4)		

Preparation of syn-tosylate derivative of [30]

The *syn*-*para*-nitrobenzoate derivative of [30] (47.7 mg, 0.137 mmol) was dissolved in 0.2 mL dichloromethane and then added to a 80% aqueous ethanol solution that was 0.5% by weight in KOH. The reaction was stirred overnight. Workup yielded a product as a white solid (24.8 mg, 0.125 mmol) (91% yield). The *syn*-alcohol (24.8 mg, 0.125 mmol) was dissolved in 0.2 mL of dichloromethane to which was added 0.1 mL of pyridine. The solution was cooled to 0°C and TsCl (71.5 mg, 0.375 mmol) was added dropwise. The reaction was warmed to room temperature and stirred overnight. Workup (page 131) and flash chromatography (hexane:ethylacetate, 1:1) yielded a product as a white solid (28.7 mg, 0.082 mmol) (65% yield).

syn-3-Tosyl-8-thiatricyclo[4,3,3,0]dodecane, [80]

mp = 77-79°C

¹HNMR (300.133 MHz, CDCl₃): δ 1.32-1.85 (12H, m), 2.43 (3H, s), 2.54 (1H, d, J=11.0Hz), 2.70 (1H, d, J=10.8Hz), 2.85 (1H, d, J=11.0Hz), 2.94 (1H, d, J=10.8Hz), 4.57-4.67 (1H, m), 7.31 (2H, d, J=7.9Hz), 7.77 (2H, d, J=8.3Hz)

¹³CNMR (75.4 MHz, CDCl₃): δ 19.44 (t), 21.58 (q), 28.29 (t), 28.94 (t), 33.12 (t), 35.55 (t), 36.30 (t), 38.68 (t), 43.91 (t), 53.92 (s), 56.95 (s), 79.02 (d), 127.55 (d), 129.75 (d), 134.89 (s), 144.44 (s)

LRMS (EI) m/e): 352 (M⁺), 180, 152, 125 (base), 105, 91, 79, 65, 55, 49, 41

LRMS (CI) (NH₃) m/e (%abundance): 370 (M+NH₄⁺, 99), 353 (6), 214 (22), 197 (26), 181 (100)

HRMS (EI) m/e calculated for C₁₈H₂₄O₃S₂ = 352.1167; found = 352.1163

Preparation of anti-tosylate derivative of [30]

In a similar fashion, saponification of the anti-para-nitrobenzoate derivative of [30] (67.0 mg, 0.193 mmol) afforded 38.2 mg (0.193 mmol) of the anti-alcohol (100% yield). Again, using the identical workup (page 131), the anti-alcohol (38.2 mg, 0.193 mmol) was dissolved in 0.5 mL of dichloromethane to which was added 0.1 mL of pyridine and TsCl (0.115 g, 0.579 mmol). The anti-tosylate was cleanly separated as white solid (53.6 mg, 0.152 mmol) (79% yield)

anti-3-Tosyl-8-thiatricyclo[4,3,3,0]dodecane, [81]

¹HNMR (300.133 MHz, CDCl₃): δ 1.52-1.82 (12H, m), 2.43 (3H, s), 2.53 (1H, d, J=10.9Hz), 2.73 (2H, s), 2.85 (1H, d, J=10.9Hz), 4.51-4.60 (1H, m), 7.32 (2H, d, J=8.1Hz), 7.77 (2H, d, J=8.3Hz)

¹³CNMR (75.4 MHz, CDCl₃): δ 19.54 (t), 21.60 (q), 27.89 (t), 27.99 (t), 32.61 (t), 36.19 (t), 37.38 (t), 39.58 (t), 42.50 (t), 54.37 (s), 56.45 (s), 78.98 (d), 127.64 (d), 129.81 (d), 134.95 (s), 144.50 (s)

LRMS (EI) m/e (%abundance): 352 (M⁺, 1), 307 (2), 197 (4), 180 (35), 149 (31), 119 (47), 105 (19), 97 (19), 91 (78), 81 (48), 69 (100), 57 (44), 40 (58)

LRMS (CI) (NH₃) m/e (%abundance): 370 (M+NH₄⁺, 1), 230 (7), 181 (100)

HRMS (EI) m/e calculated for C₁₈H₂₄O₃S₁ = 352.1167; found = 352.1168

Preparation of N-benzyloxymethyl-cis-1,2,3,6-tetrahydrophthalimide, [54]

A solution, prepared from *cis*-1,2,3,6-tetrahydrophthalimide (2.0 g, 0.013 mol), benzyl chloromethyl ether (2.2 mL, 0.016 mol), and K₂CO₃ (2.7 g, 0.02 mol), under argon atmosphere was refluxed overnight. After neutralization with HCl, the reaction mixture was extracted with dichloromethane. The combined extracts were washed with brine, dried over anhyd MgSO₄, filtered and reduced in volume by rotary evaporation. Flash

chromatography (silica gel, hexane:ethylacetate, 1:1) gave 2.6 g (91%) of the desired protected imide as a pale yellow oil.

N-benzyloxymethyl-*cis*-1,2,3,6-tetrahydrophthalimide, [54]

$^1\text{H NMR}$ (300.133 MHz, CDCl_3): δ 2.16-2.23 (2H, m), 2.53-2.60 (2H, m), 2.95-2.99 (2H, m), 4.53 (2H, s), 4.95 (2H, s), 5.86-5.88 (2H, m), 7.29 (5H, m)

$^{13}\text{C NMR}$ (75.4 MHz, CDCl_3): δ 23.36 (t), 39.08 (d), 67.77 (t), 71.97 (t), 126.96 (d), 127.61 (d), 127.68 (d), 128.35 (d), 128.54 (d), 137.57 (s), 179.70 (s)

LRMS (EI) m/e (%abundance): 271 (M^+ , 3), 165 (100), 136 (4), 111 (10), 91 (36), 79 (25), 65 (7), 41 (2)

HRMS (EI) m/e calculated for $\text{C}_{16}\text{H}_{17}\text{O}_3\text{N}$ = 271.1208; found = 271.1209

Preparation of N-benzyloxymethyl-7,9,-dioxo-8-azatricyclo [4,3,3,0]dodec-3-ene, [55]

A solution of 15 mL dry THF, 0.56 mL of 10M n-BuLi (0.0058 mol) and 0.83 mL of diisopropylamine (0.0059 mol) was stirred under argon at -78°C of 15 minutes. To this solution was slowly added 0.50 g of [54] (0.0023 mol), resulting in a red-colored solution of the dianion. After stirring of an additional 15 minutes, 1,3-dibromopropane (0.28 mL, 0.0028 mol) was added, dropwise. After the addition was completed the reaction mixture was allowed to warm to room temperature. After several more hours of stirring, the reaction mixture was neutralized with conc.

HCl. The salts were removed by filtration and excess solvent was removed from the filtrate by rotary evaporation. The residue was extracted with dichloromethane, and after drying the combined extracts over anhyd MgSO_4 , the excess solvent was removed by rotary evaporation. The crude residue was subjected to flash chromatography (silica gel, hexane:ethylacetate, 1:1) to give 0.36 g (61%) of product as a yellow oil.

N-benzyloxymethyl-7,9-dioxo-8-azatricyclo[4,3,3,0]dodec-3-ene, [55]

$^1\text{H NMR}$ (300.133 MHz, CDCl_3): δ 1.21-2.70 (10H, m), 4.50 (2H, s), 4.92 (2H, s), 5.88-5.90 (2H, m), 7.29 (5H, m)

$^{13}\text{C NMR}$ (75.4 MHz, CDCl_3): δ 24.46 (t), 31.12 (t), 38.18 (t), 56.05 (s), 67.72 (t), 71.76 (t), 127.69 (d), 127.78 (d), 127.94 (d), 128.34 (d), 128.50 (d), 131.86 (d), 137.46 (s), 182.32 (s)

LRMS (EI) m/e (%abundance): 311 (M^+), 205 (100), 176 (4), 148 (6), 119 (20), 91 (84), 65 (13), 41 (2)

HRMS (EI) m/e calculated for $\text{C}_{19}\text{H}_{21}\text{O}_3\text{N}$ = 311.1521; found = 311.1529

Preparation of 7,9-dioxo-8-azatricyclo[4,3,3,0]dodec-3-ene, [56]

A solution of [55] (33 mg, 0.13 mmol), BBr_3 (0.15 mL, 0.15 mmol) and 5 mL benzene was stirred at room temperature for 1 hour. Methanol (0.2 mL) was added to the reaction mixture and after 30 minutes the low-boiling solvents were

removed by rotary evaporation. The residue, in 4 mL water, was heated to boiling for 30 minutes. Water was removed by vacuum and the resulting solid was extracted with dichloromethane. The combined extracts were dried over anhyd MgSO_4 , and after removal of solvent the crude product was chromatographed (silica gel, hexane:ethylacetate, 1:1) to yield 20 mg (83%) of product as pale yellow powder.

7,9-Dioxo-8-azatricyclo[4,3,3,0]dodec-3-ene, [56]

mp = 162-163°C

^1H NMR (300.133 MHz, CDCl_3): δ 1.33-2.68 (10H, m), 5.90-5.92 (2H, m), 8.85 (1H, br)

^{13}C NMR (75.4 MHz, CDCl_3): δ 24.46 (t), 30.96 (t), 38.05 (t), 57.19 (s), 128.44 (d), 182.90 (s)

LRMS (EI) m/e (%abundance): 191 (M^+ , 100), 148 (42), 120 (47), 91 (61), 65 (9), 41 (5)

HRMS (EI) m/e calculated for $\text{C}_{11}\text{H}_{13}\text{O}_2\text{N}$ = 191.0946; found = 191.0938

Preparation of 2,4-dioxo-3-azabicyclo[3,3,0]oct- $\Delta^{1,5}$ -ene, [48]

The propellane [56] (20 mg, 0.11 mmol) was passed through a FVT apparatus at about 600 °C and under high vacuum. The products were collected in a trap cooled by dry ice, and consisted of 35% starting material, 60% product and 5% of an unidentified material. The product was purified by flash chromatography (silica gel, dichloromethane:hexane:ethylacetate, 20:1:1) to give a

crystalline sample, mp 178-179° (Ref²¹, 177-179°) as a white solid.

2,4-Dioxo-3-azabicyclo[3,3,0]oct- $\Delta^{1,5}$ -ene, [48]

¹HNMR (300.133 MHz, CDCl₃): δ 2.43 (2H, pentet, J=7.3Hz),
2.65 (4H, t, J=7.3Hz), 7.05 (1H, br)

¹³CNMR (75.4 MHz, CDCl₃): δ 26.40 (t), 27.55 (t), 154.61 (s),
166.66 (s)

LRMS (EI) m/e (%abundance): 137 (M⁺, 13), 94 (77), 66 (100),
52 (8), 41 (3)

HRMS (EI) m/e calculated for C₇H₇O₂N = 137.0477; found =
137.0474

Preparation of dimethyl-1,2-cyclopentene dicarboxylate, [18]

cis-1,6-Dicarbomethoxybicyclo[4,3,0]non-3-ene, [17]
(36.4 mg, 0.0153 mmol) was passed through a FVT apparatus at
about 600°C and under high vacuum. The products were
collected in a trap cooled by dry ice. Extraction with
dichloromethane yielded only product, [18] as a pale yellow
oil (28.0 mg, 0.152 mmol) (99% yield).

Dimethyl-1,2-cyclopentene dicarboxylate, [18]

¹HNMR (300.133 MHz, CDCl₃): δ 1.99 (2H, pentet, J=7.6Hz),
2.72 (4H, t, J=7.6Hz), 3.75 (6H, s)

¹³CNMR (75.4 MHz, CDCl₃): δ 22.27 (t), 34.60 (t), 51.90 (q),
140.11 (s), 166.09 (s)

LRMS (EI) m/e: 184 (M⁺), 152 (base), 124, 93, 79, 59, 41

HRMS (EI) m/e calculated for C₉H₁₂O₄ = 184.0736; found =
184.0740

Preparation of 3-methyl-cis-1,6-dicarbomethoxybicyclo
[4,3,0]non-3-ene, [112]

A solution of 20 mL of dry THF, 3.38 mL of 10M n-BuLi (0.0338 mol) and 4.38 mL of diisopropylamine (0.0341 mol) was stirred under argon at -10°C for 30 minutes. The temperature was taken down to -78°C and diester (2.89 g, 0.0136 mol) was added dropwise, creating a bright red solution. After addition was completed the solution was allowed to stir for 15 minutes, then 1,3-dibromo propane (1.67 mL, 0.0163 mol) was added dropwise. The solution was allowed to warm to room temperature and stirred overnight. Identical workup (page 120) and distillation yielded a product as a yellow oil (2.47 g, 9.80 mmol) (72% yield).

3-Methyl-cis-1,6-dicarbomethoxybicyclo [4,3,0]non-3-ene,
[112]

¹HNMR (300.133 MHz, CDCl₃): δ 1.65 (3H, d, J=1.5Hz), 1.61-2.88 (10H, m), 3.63 (3H, s), 3.64 (3H, s), 5.26-5.31 (1H, m)

¹³CNMR (75.4 MHz, CDCl₃): δ 18.92 (t), 23.15 (q), 32.45 (t), 34.63 (t), 34.89 (t), 36.40 (t), 51.66 (q) (two carbon), 51.96 (s), 53.23 (s), 117.25 (d), 130.42 (s), 176.55 (s)

LRMS (EI) m/e (%abundance): 252 (M⁺, 0.4), 220 (6), 192 (29), 133 (100), 105 (30), 91 (16)

LRMS (CI) (NH₃) m/e (%abundance): 270 (M+NH₄⁺, 10), 253 (M+H⁺, 100), 221 (24)

HRMS (CI) m/e calculated for $C_{14}H_{21}O_4$ = 253.1440; found =
253.1437

Preparation of 3-methyl-cis-1,6-dihydroxymethyl bicyclo
[4,3,0] non-3-ene, [113]

A solution of [112] (1.21 g, 4.80 mmol) in 2 mL of dry THF was added dropwise at 0°C to a stirring solution of LAH (0.40 g, 0.011 mol) in 10 mL of dry THF. The reaction mixture was stirred overnight at room temperature and then hydrolyzed. Workup (page 121) yielded a product as a pale yellow oil (0.771 g, 3.93 mmol) (82% yield).

3-Methyl-cis-1,6-dihydroxymethyl bicyclo [4,3,0] non-3-ene,
[113]

$^1\text{H NMR}$ (300.133 MHz, CDCl_3): δ 1.63 (3H, d, $J=1.2\text{Hz}$), 0.83-2.10 (10H, m), 3.40 (1H, d, $J=11.4\text{Hz}$), 3.45 (1H, d, $J=11.4\text{Hz}$), 3.58 (1H, d, $J=11.4\text{Hz}$), 3.61 (1H, d, $J=11.4\text{Hz}$), 5.27 (1H, m)

$^{13}\text{C NMR}$ (75.4 MHz, CDCl_3): δ 18.57 (t), 23.44 (q), 32.16 (t), 33.29 (t), 33.71 (t), 36.25 (t), 46.01 (s), 47.03 (s), 67.21 (t), 67.27 (t), 118.27 (d), 131.54 (s)

LRMS (EI) m/e (%abundance): 178 (7), 160 (11), 147 (26), 133 (19), 119 (22), 105 (100), 91 (74), 79 (37), 67 (22), 53 (21), 41 (32)

LRMS (CI) (Methane) m/e (%abundance): 197 ($\text{M}+\text{H}^+$, 20), 179 (42), 161 (100), 149 (28), 133 (21), 119 (20), 105 (41), 96 (33)

HRMS (CI) m/e calculated for $C_{12}H_{21}O_2$ = 197.1542; found =
197.1544

Preparation of 3-methyl-8-oxatricyclo[4,3,3,0]dodec-3-ene,
[114]

The diol, [113], (0.112 g, 0.571 mmol) was combined with 2 mL of dry pyridine under argon. Then TsCl (0.108 g, 0.571 mmol) dissolved in 2mL of dry pyridine was added dropwise to the stirring solution. The reaction was stirred overnight. Workup (page 122) and florisil separation (hexane:ethylacetate, 9:1) yielded a product as a pale yellow oil (87.4 mg, 0.491 mmol) (86% yield).

3-Methyl-8-oxatricyclo[4,3,3,0]dodec-3-ene, [114]

$^1\text{H NMR}$ (300.133 MHz, CDCl_3): δ 1.65-1.93 (10H, m), 2.21 (3H, s), 3.73-3.84 (4H, m), 5.74-5.78 (1H, m)

$^{13}\text{C NMR}$ (75.4 MHz, CDCl_3): δ 24.05 (q), 24.15 (t), 33.07 (t), 38.05 (t), 39.91 (t), 40.06 (t), 55.13 (s), 55.84 (s), 81.06 (t), 81.30 (t), 121.16 (d), 136.54 (s)

LRMS (EI) m/e (%abundance): 178 (M^+ , 29), 160 (33), 147 (46), 133 (34), 119 (26), 105 (92), 91 (100), 81 (50), 67 (18), 41 (37)

HRMS (EI) m/e calculated for $C_{12}H_{18}O_1$ = 178.1358; found =
178.1362

Hydrogenation of 3-methyl-cis-1,6-dicarbomethoxybicyclo
[4,3,0]non-3-ene, [112]

Diester, [112] (367 mg, 1.46 mmol) was combined with 20 mg of pt/c catalyst and 20 mL of absolute ethanol. The

reaction vessel was shaken under 20 psi of H₂ at room temperature for overnight. The catalyst was then filtered off and the ethanol was removed by rotary evaporation.

Extraction with dichloromethane yielded only one stereoisomer as an oil (317 mg, 1.25 mmol) (86% yield).

3-Methyl-cis-1,6-dicarbomethoxybicyclo[4,3,0]nonane, [115]

¹HNMR (300.133 MHz, CDCl₃): δ 0.90 (3H, d, J=6.4Hz), 1.38-1.86 (13H, m), 3.61 (3H, s), 3.62 (3H, s)

¹³CNMR (75.4 MHz, CDCl₃): δ 19.51 (t), 22.17 (q), 27.45 (d), 30.50 (t), 33.27 (t), 34.37 (t), 36.14 (t), 36.66 (t), 51.42 (q), 51.64 (q), 53.60 (s), 55.19 (s), 176.57 (s), 177.77 (s)

LRMS (EI) m/e (%abundance): 254 (M⁺, 1), 222 (8), 194 (40), 181 (7), 153 (8), 135 (100), 93 (13), 77 (6), 59 (7), 41 (8)

HRMS (EI) m/e calculated for C₁₄H₂₂O₄ = 254.1518; found = 254.1512

Hydrogenation of 3-methyl-cis-1,6-dihydroxymethylbicyclo[4,3,0]non-3-ene, [113]

In an identical procedure for [112], hydrogenation of the diol, [113] (159 mg, 0.820 mmol) afforded the reduced products in a ratio of 65:35, respectively.

3-Methyl-cis-1,6-dihydroxymethylbicyclo[4,3,0]nonane, [116]-major isomer

^1H NMR (300.133 MHz, CDCl_3): δ 0.86 (3H, d, $J=6.4\text{Hz}$), 1.11-2.07 (13H, m), 3.10 (1H, d, $J=11.26\text{Hz}$), 3.41 (1H, d, $J=11.59\text{Hz}$), 3.60 (1H, d, $J=11.32\text{Hz}$), 3.83 (1H, d, $J=11.47\text{Hz}$)

^{13}C NMR (75.4 MHz, CDCl_3): δ 18.78 (t), 22.62 (q), 27.61 (d), 31.33 (t), 32.26 (t), 33.04 (t), 34.22 (t), 36.74 (t), 46.48 (t), 48.48 (t), 66.02 (t), 69.08 (t)

LRMS (EI) m/e (%abundance): 180 (9), 162 (9), 149 (94), 135 (100), 119 (10), 107 (38), 93 (63), 79 (58), 67 (33), 55 (27), 41 (17)

Hydrogenation of 3-methyl-8-oxatricyclo[4,3,3,0]dodec-3-ene, [114]

In an identical procedure for [112], hydrogenation of the propellane, [114] (19.4 mg, 0.107 mmol) yielded the reduced products in a ratio of 3:1, respectively.

3-Methyl-8-oxatricyclo[4,3,3,0]dodecane, [117]-major isomer

^1H NMR (300.133 MHz, CDCl_3): δ 0.87 (3H, d, $J=6.1\text{Hz}$), 0.95-1.78 (13H, m), 3.52 (1H, d, $J=8.12\text{Hz}$), 3.61 (1H, d, $J=8.12\text{Hz}$), 3.66 (1H, d, $J=8.19\text{Hz}$), 3.78 (1H, d, $J=8.11\text{Hz}$)

^{13}C NMR (75.4 MHz, CDCl_3): δ 21.73 (t), 22.60 (q), 27.64 (d), 29.26 (t), 30.47 (t), 31.44 (t), 39.02 (t), 40.45 (t), 50.93 (s), 52.55 (s), 76.35 (t), 81.36 (t)

LRMS (EI) m/e (%abundance): 180 (M^+ , 6), 162 (1), 150 (21), 135 (100), 121 (9), 107 (18), 95 (37), 79 (31), 67 (19), 55 (14), 41 (23)

HRMS (EI) m/e calculated for $C_{12}H_{20}O_1$ = 180.1514; found =
180.1510

3-Methyl-8-oxatricyclo[4,3,3,0]dodecane, [117]-minor isomer

LRMS (EI) m/e (%abundance): 180 (M^+ , 19), 162 (18), 149
(90), 135 (100), 121 (27), 107 (41), 95 (88), 79 (69),
67 (41), 55 (34), 41 (53)

HRMS (EI) m/e calculated for $C_{12}H_{20}O_1$ = 180.1514; found =
180.1524

REFERENCES

1. R.D. Otzenberger, Pinacol-Tetrahydrophthalans-Frontalin, Ph.D. Thesis, Montana State University, (1971), P.49.
2. J.J. Theodore, Heteroatom Influences on Structure and Reactivity, Ph.D. Thesis, Montana State University, (1978).
3. D.K. Johnson, Ethereal Oxygen Effects on Structure and Reactivity, Ph.D. Thesis, Montana State University, (1988).
4. B. Capon and S.P. McManus, Neighboring Group Participation Vol.1, Plenum Press, New York, (1976).
5. P.V.R. Schleyer and C.T. Lancelot, J. Am. Chem. Soc., (1969), 91, 4297.
6. R.F. Gratz and P. Wilder, Jr., J. Chem. Soc., (1970), 1449.
7. G.T. Kwiatkowski, S.J. Kavarnos, and W.D. Closson, J. Hetero cyl. chem., (1965), 2, 11.
8. D.S. Tarbell and J.R. Hazen, J. Am. Chem. Soc., (1969), 91, 7657.
9. P.G. Gassman, J.G. Schaffhausen, and P.W. Raynolds, J. Am. Chem. Soc., (1982), 104, 6408.
10. L.A. Paquette and P.C. Storm, J. Am. Chem. Soc., (1970), 92, 4295.
11. R.D. Otzenberger, Op. Cit. P.69.
12. B.P. Mundy and D. Wilkenning, J. Org. Chem., (1984), 49, 8779.
13. a) R.N. McDonald and R.R. Reitz, J. Org. Chem., (1972), 2418-2422.
b) D.N. Harpp, L.O. Bao, C.J. Black, J.G. Gleason, and R.A. Smith, J. Org. Chem., (1975), 23, 3420.
14. J. Sauer, Angew. Chem. Inter. Ed., (1966), 5, 211, ibid., (1967), 6, 16.
15. L.A. Paquett, J. Am. Chem. Soc., (1971), 93(18), 4508.
16. A.P. Krapcho and P.S. Huyffer, J. Org. Chem., (1963), 28(10), 2904-2905.
17. J.G. Jun, New Approaches to Natural Products, Ph.D. Thesis, Montana State University, (1985).

18. D. Wilkening, A New Regiocontrolled and Stereospecific Total Synthesis of ($\pm$) Modhephene, Ph.D. Thesis, Montana State University, (1984).
19. E.F. Elstner, D.M. Carnes, R.J. Suhadolnik, G.P. Kreishman, M.P. Schweizer, and R.K. Robbins, Biochemistry, (1973), 12, 4992.
20. H. Kasugai, Japan Kokai, 75, 121, 433, (CI, AOIN, CO7D), 23, Sept. 1975.
21. P. Singh, M. Weinreb, Tetrahedron, (1976), 32, 2379.
22. a) K. Fukuta, A. Mizumi, A. Mori, N. Ikeda, H. Yamamoto, Tetrahedron Lett., (1984), 25, 669.
b) A. Misumi, K. Fukuta, H. Yamamoto, ibid., 671.
23. D. Wilkening, and B.P. Mundy, syn-Commun., (1984), 14(3), 227.
24. a) E.J. Barreiro, Tetrahedron Lett., (1982), 3605.
b) A.P. Kozikowski and P.D. Stein, J. Am. Chem. Soc., (1982), 104, 4023.
25. a) A.B. Smith, III, S.J. Branca, N.N. Pilla and M.A. Guaciaro, J. Org. Chem., (1982), 47, 1855.
b) A.B. Smith, III, S.J. Branca, J. Am. Chem. Soc., (1978), 100, 7767.
26. A.B. Smith, III, and D. Boschelli, J. Org. Chem., (1983), 48, 1217.
27. a) G.M. Strunz and G.S. Lal, Can. J. Chem., (1982), 60, 2528.
b) T. Siwapiyos and T. Thebtaranonth, J. Org. Chem., (1982), 47, 598.
28. R.G. Pearson, Hard Soft Acid and Base, (1973), Dowden, Hutchinson and Ross, Stroudberg PA.
29. S.E. Wood, B. Rickborn, J. Org. Chem., (1983), 48, 555.
30. H.C. Brown, J. Chandrasekharan, D.J. Nelson, J. Am. Chem. Soc., (1984), 106, 3768.
31. We greatly appreciate professor K.N. Houk at U.C.L.A. for providing advanced copy of this manuscript.
32. N.L. Allinger, M.T. Tribble, M.A. Miller, and D.H. Wertz, J. Am. Chem. Soc., (1971), 93, 1637.

33. D.B. Boyd and K.B. Lipkowitz, J. Chem. Ed., (1982), 59, 269.
34. a) W. Davidon, Comput. J., (1968), 10, 406.
b) R. Fletcher, ibid. (1963), 6, 163.
35. M.J.S. Dewar and W. Thiel, J. Am. Chem. Soc., (1977), 99, 4907.
36. H.C. Brown and G. Ham, J. Am. Chem. Soc., (1956), 78, 2735-2739.
37. T.H. Lowery and K.S. Richardson, Mechanisms and Theory in Organic Chemistry, Second edition, Harper and Row, New York, (1981), 374.
38. S.B. Glancy, Ethereal Oxygen Influences on Solvomercuration and Hydrogenation Reactions, Ph.D. Thesis, Montana State University, (1983).
39. D. Wilkening and B.P. Mundy, Tetrahedron Lett., (1984), 25, 4619.
40. B.P. Mundy, D. Wilkening, and K. Lipkowitz, J. Org. Chem., (1985), 50, 5727.
41. G.A. Kraus, J. Shi, J. Org. Chem., (1990), 55, 5423-5424.
42. J. Sanders and J.D. Merish, Prog. Nucl. Magn. Reson. Spec., (1983), 15, 353.
43. J.R. Amend, R.D. Briggs, R.P. Furstenau, K. Tucker, R.A. Howald, and B.E. Ivey, Journal of Computers in Mathematical and Science Teaching, (1989), 95-105.
44. N.P. Buu-Hoi and P. Demerseman, J. Org. Chem., (1953), 18, 649.
45. Von Emil Buchta, Siegfried Billenstein, Liebigs Ann. Chem., (1967), 702, 51-54.

APPENDICES

APPENDIX A

- Plot of $\ln (C_{\infty}-C_x)$ vs. time (seconds) for the Solvolysis of tosylates at three different temperatures.
- Plot of $\ln (k)$ vs. $1/T$ (K^{-1}) for tosylates.

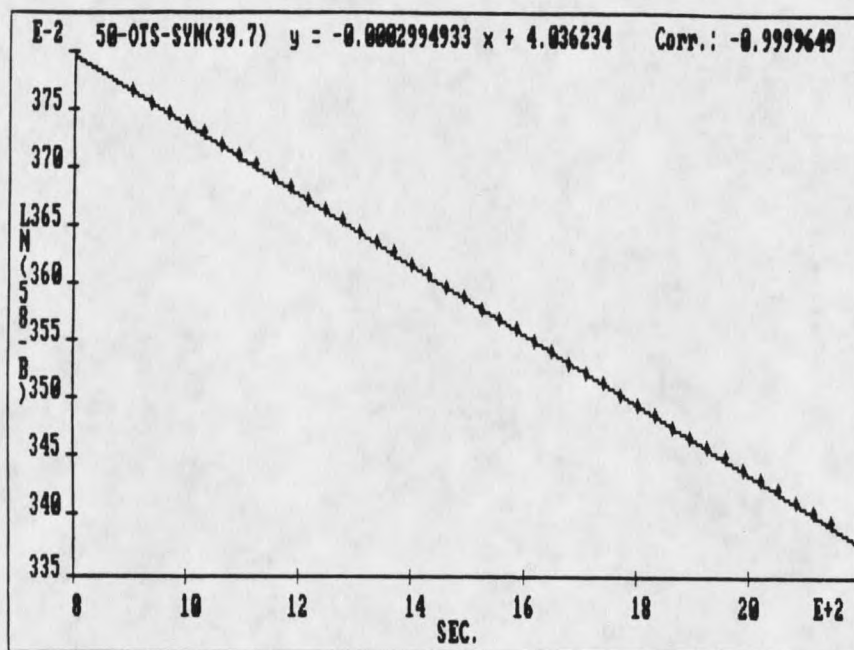


Figure 84. Plot of $\ln (C_{\infty} - C_t)$ vs. time (seconds) for the Solvolysis of [15] at 39.7°C.

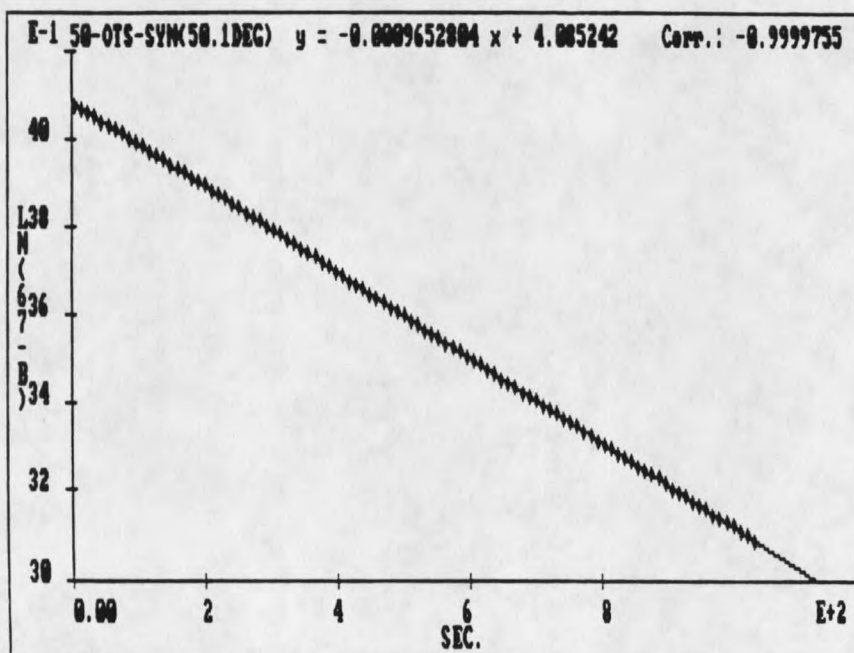


Figure 85. Plot of $\ln (C_{\infty} - C_t)$ vs. time (seconds) for the Solvolysis of [15] at 50.1°C.

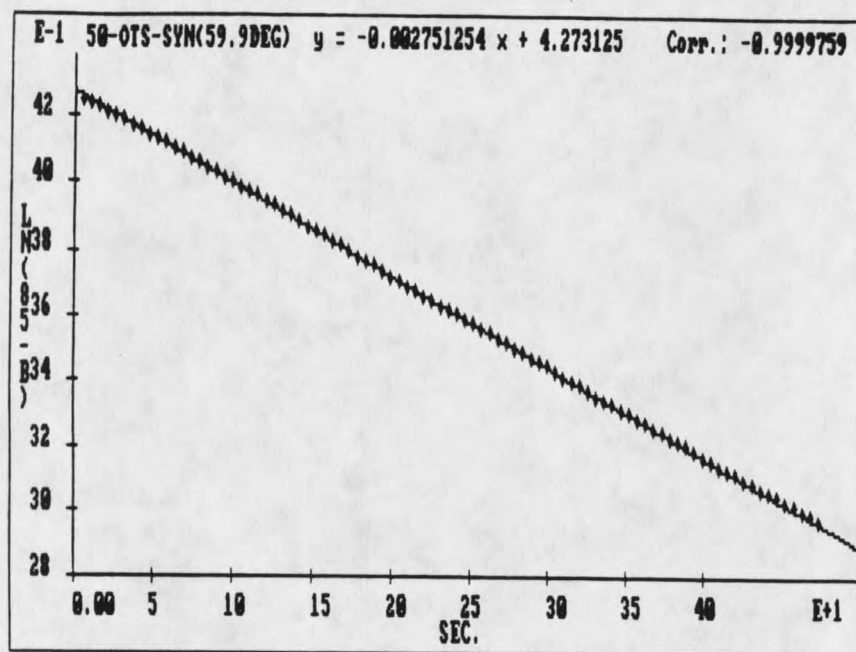


Figure 86. Plot of $\ln(C_\infty - C_x)$ vs. time (seconds) for the Solvolysis of [15] at 59.9°C.

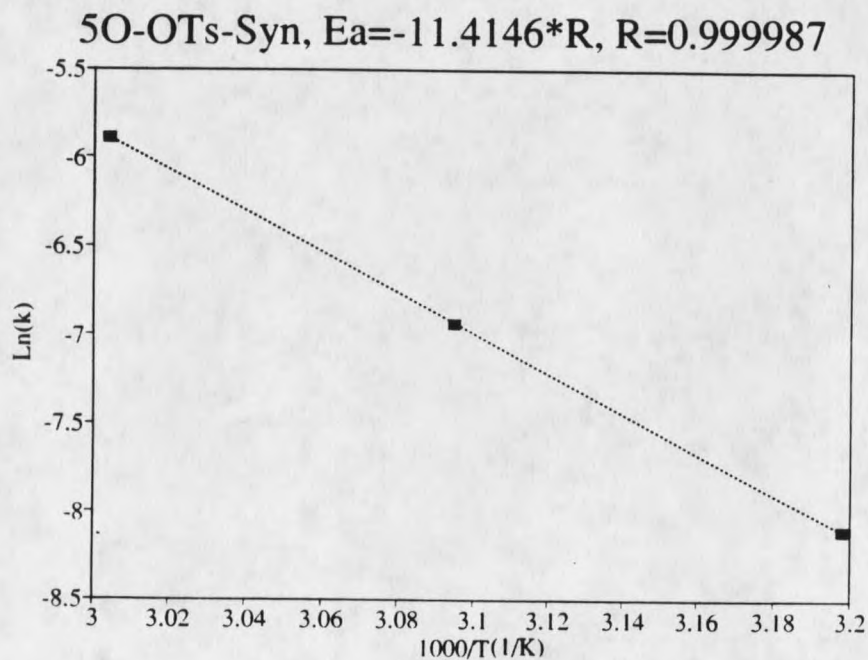


Figure 87. Plot of $\ln(k)$ vs. $1/T (K^{-1})$ for [15].

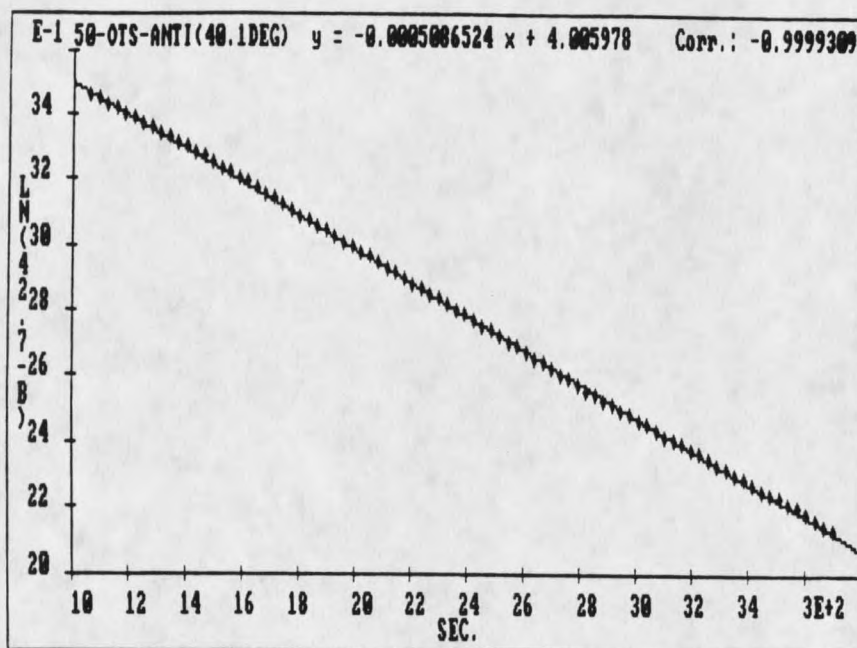


Figure 88. Plot of $\ln (C_{\infty} - C_x)$ vs. time (seconds) for the Solvolysis of [16] at 40.1°C.

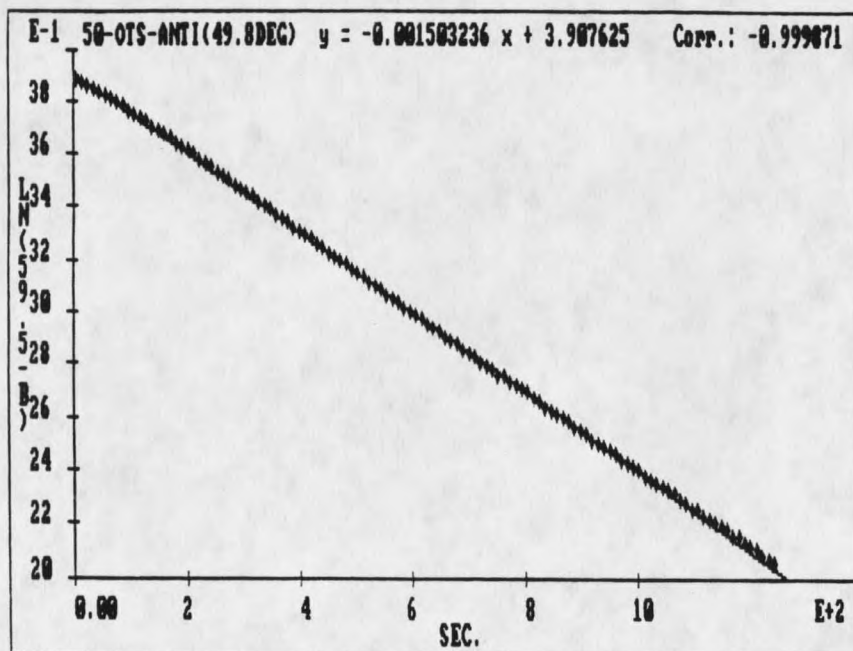


Figure 89. Plot of $\ln (C_{\infty} - C_x)$ vs. time (seconds) for the Solvolysis of [16] at 49.8°C.

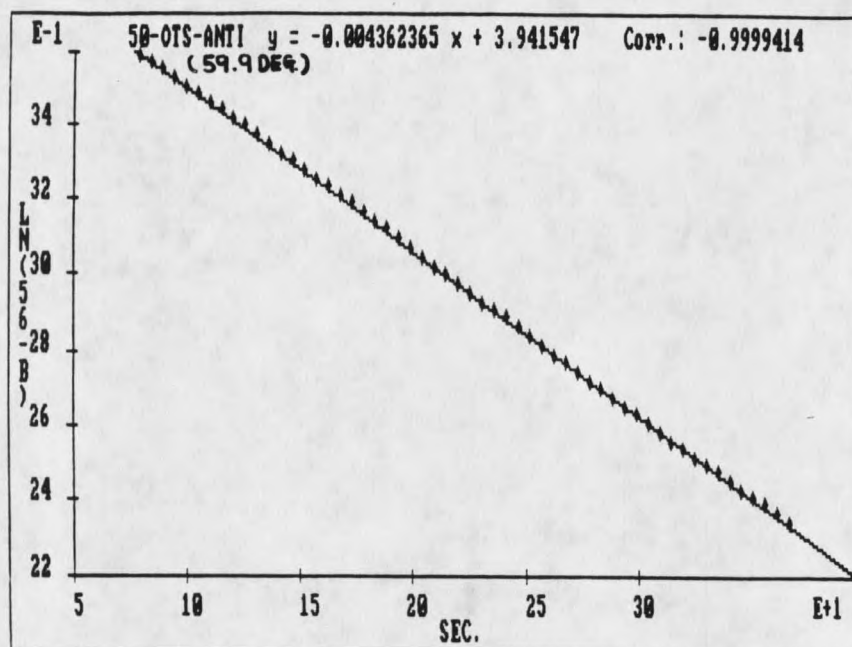


Figure 90. Plot of $\ln (C_{\infty} - C_x)$ vs. time (seconds) for the Solvolysis of [16] at 59.9°C.

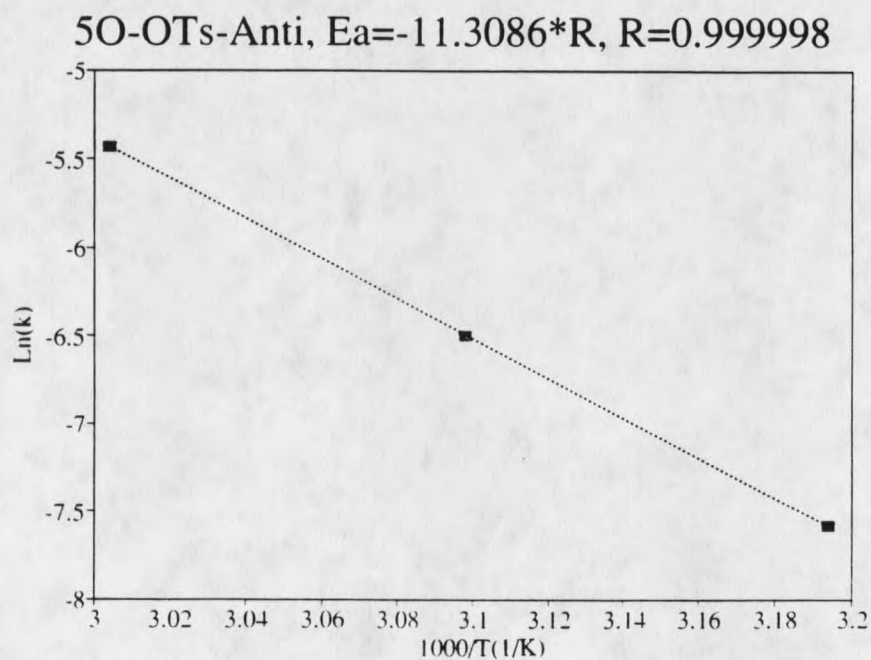


Figure 91. Plot of $\ln (k)$ vs. $1/T$ (K^{-1}) for [16].

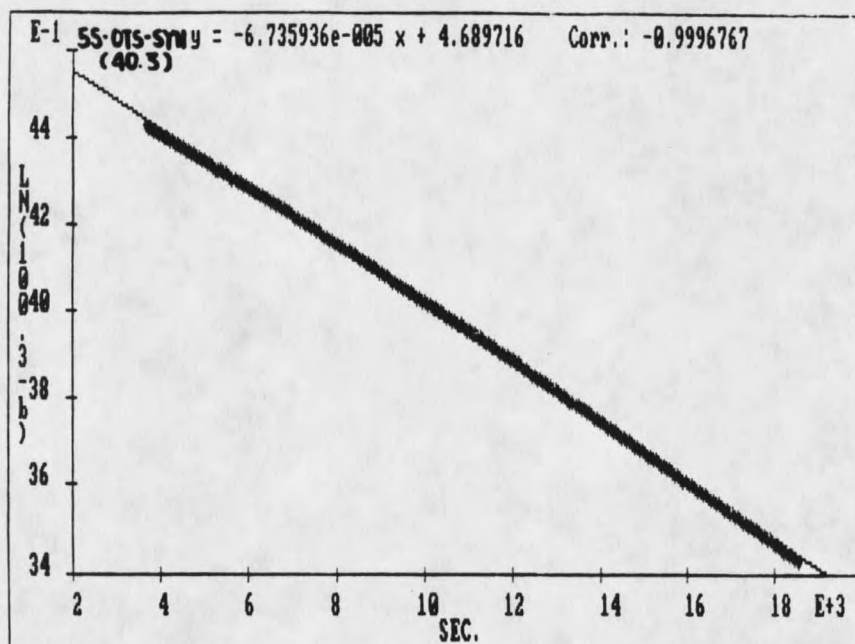


Figure 92. Plot of $\ln(C_{\infty} - C_x)$ vs. time (seconds) for the Solvolysis of [80] at 40.3°C.

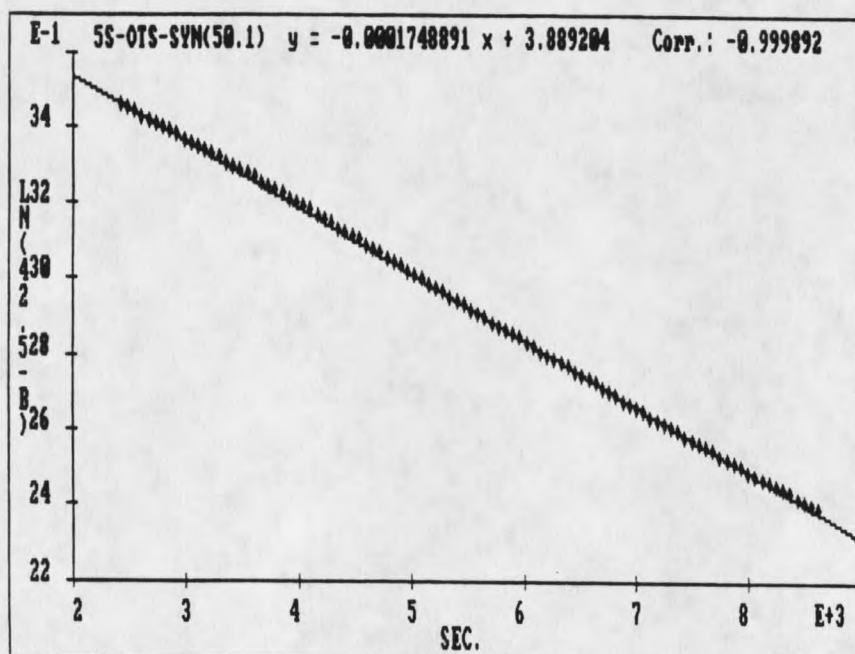


Figure 93. Plot of $\ln(C_{\infty} - C_x)$ vs. time (seconds) for the Solvolysis of [80] at 50.1°C.

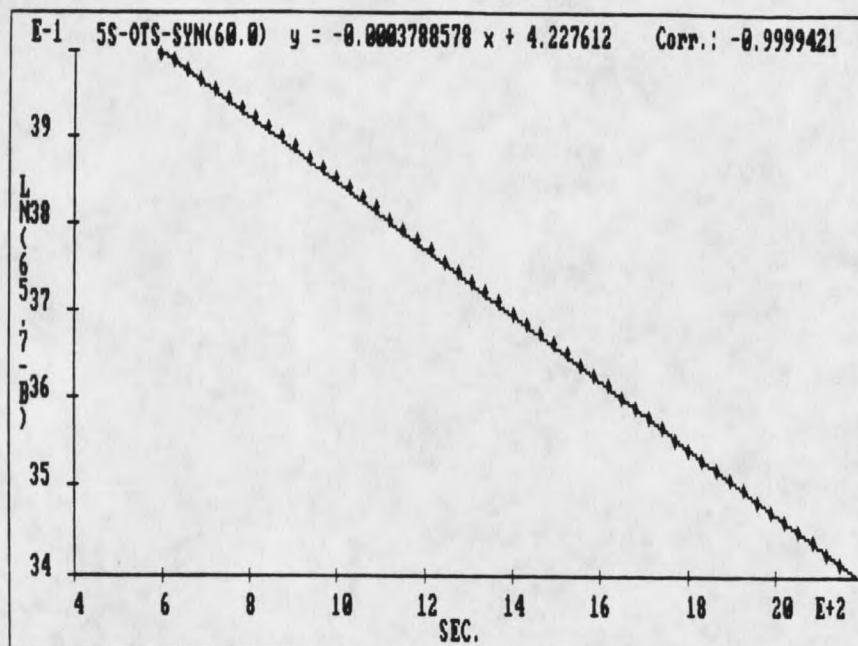


Figure 94. Plot of $\ln(C_{\infty} - C_x)$ vs. time (seconds) for the Solvolysis of [80] at 60.0°C.

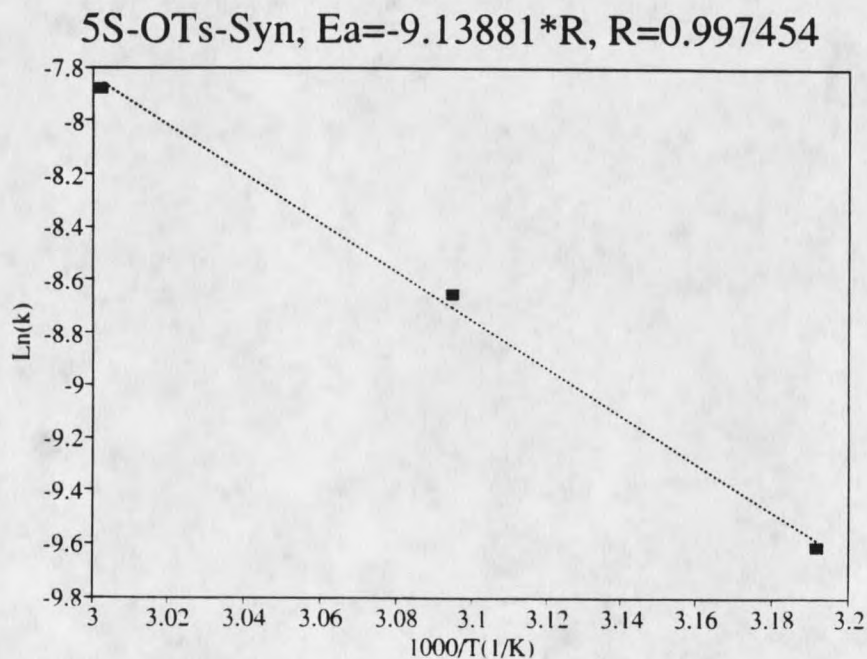


Figure 95. Plot of $\ln(k)$ vs. $1/T$ (K^{-1}) for [80].

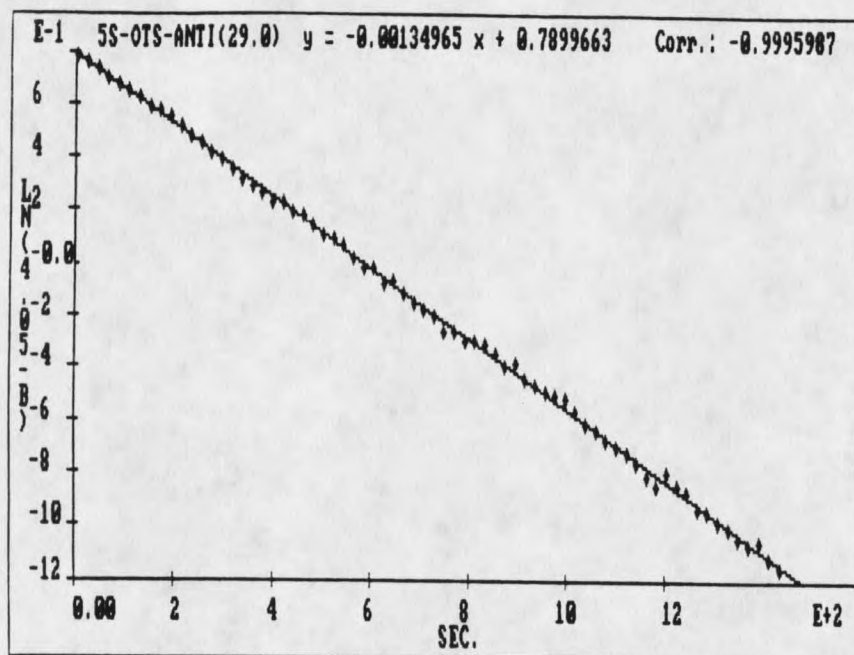


Figure 96. Plot of $\ln (C_{\infty} - C_x)$ vs. time (seconds) for the Solvolysis of [81] at 29.0°C.

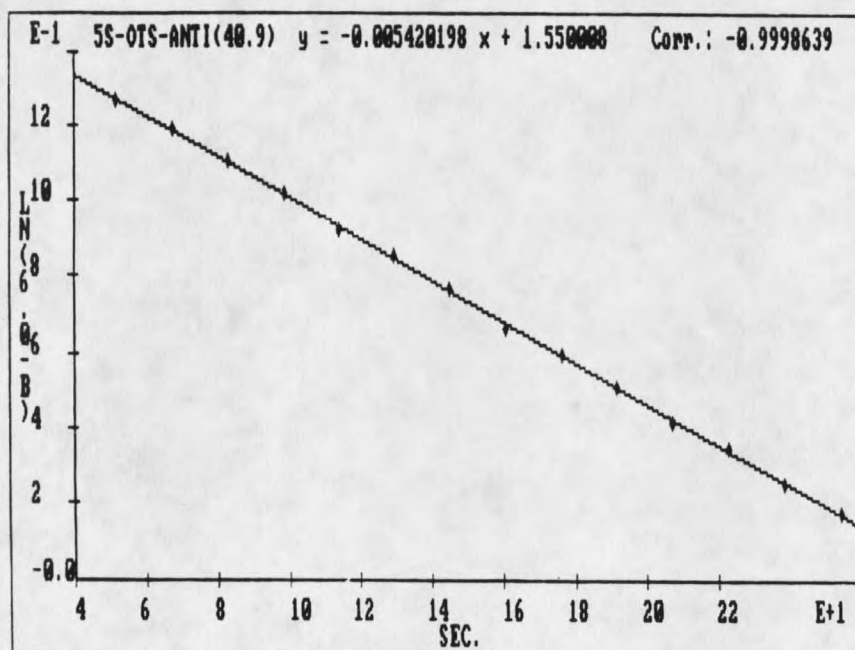


Figure 97. Plot of $\ln (C_{\infty} - C_x)$ vs. time (seconds) for the Solvolysis of [81] at 40.9°C.

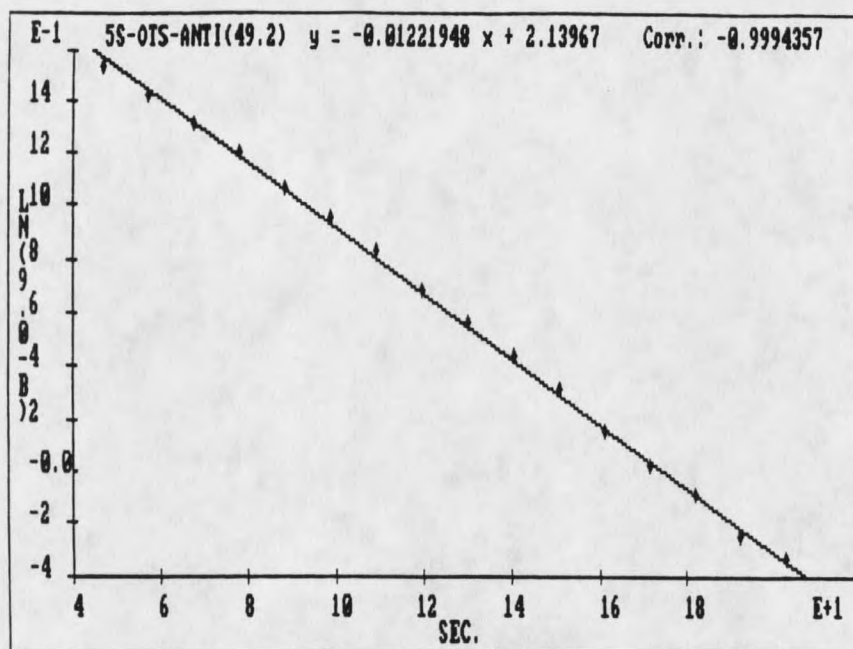


Figure 98. Plot of $\ln(C_\infty - C_x)$ vs. time (seconds) for the Solvolysis of [81] at 49.2°C.

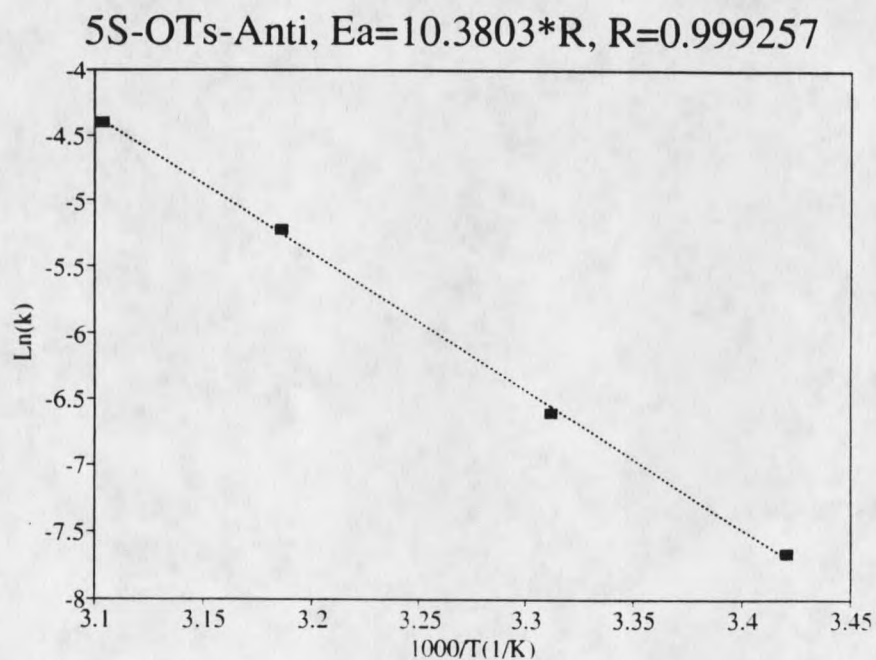


Figure 99. Plot of $\ln(k)$ vs. $1/T$ (K^{-1}) for [81].

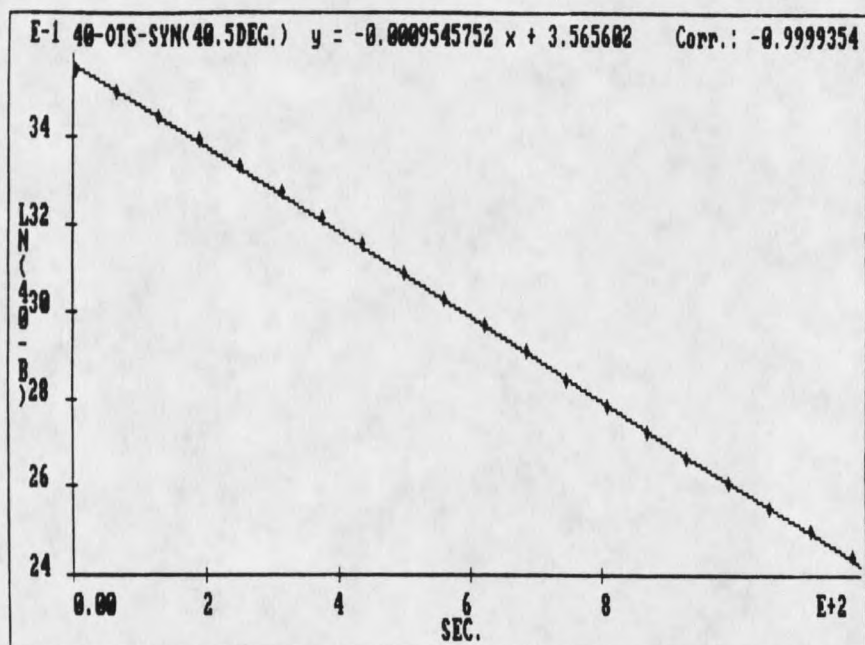


Figure 100. Plot of $\ln (C_{\infty} - C_x)$ vs. time (seconds) for the Solvolysis of [82] at 40.5°C.

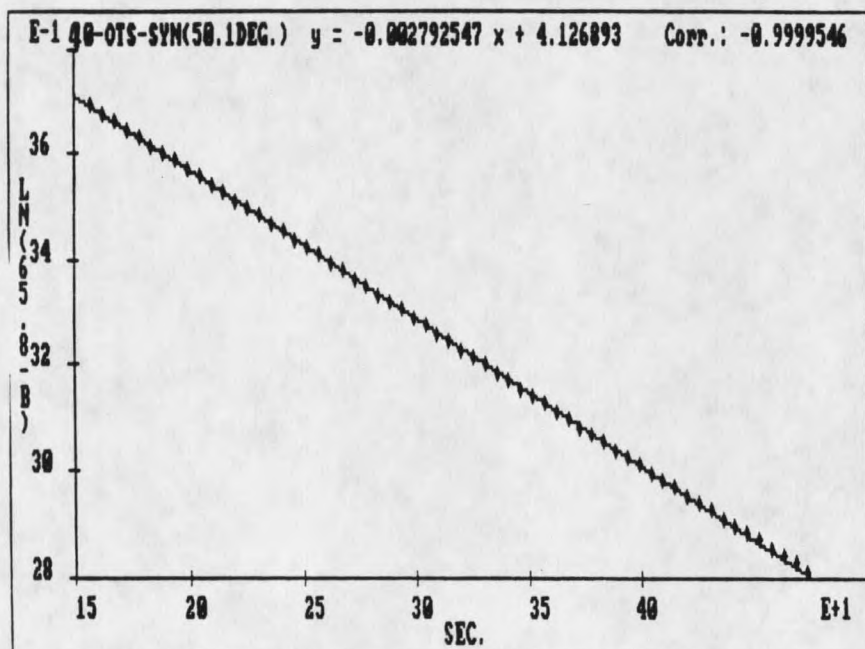


Figure 101. Plot of $\ln (C_{\infty} - C_x)$ vs. time (seconds) for the Solvolysis of [82] at 50.1°C.

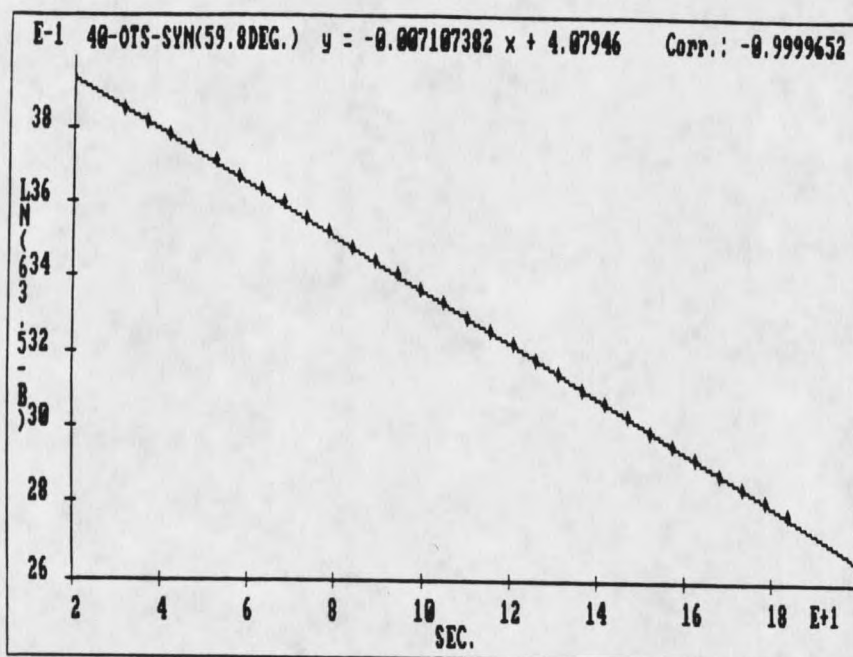


Figure 102. Plot of $\ln (C_{\infty} - C_x)$ vs. time (seconds) for the Solvolysis of [82] at 59.8°C.

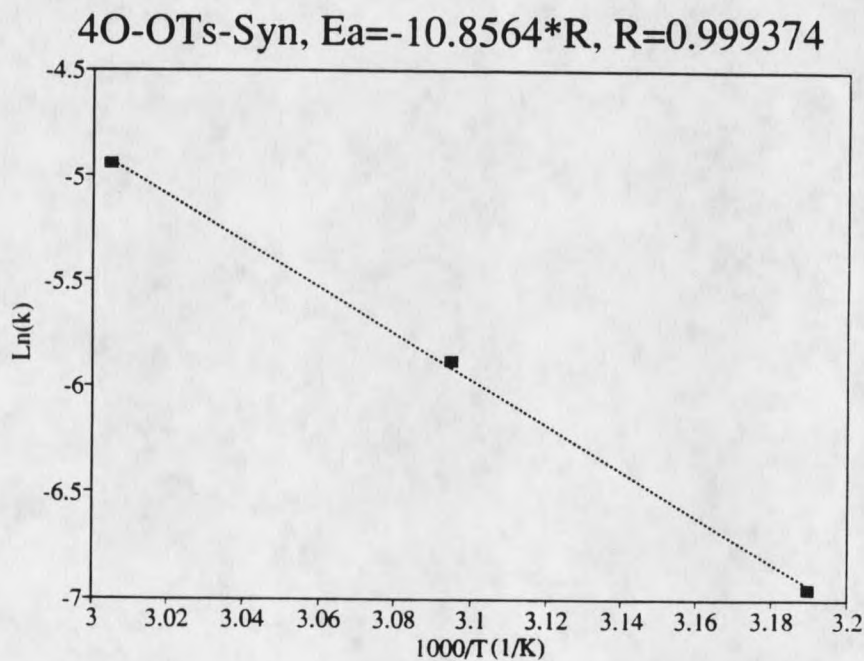


Figure 103. Plot of $\ln (k)$ vs. $1/T$ (K^{-1}) for [82].

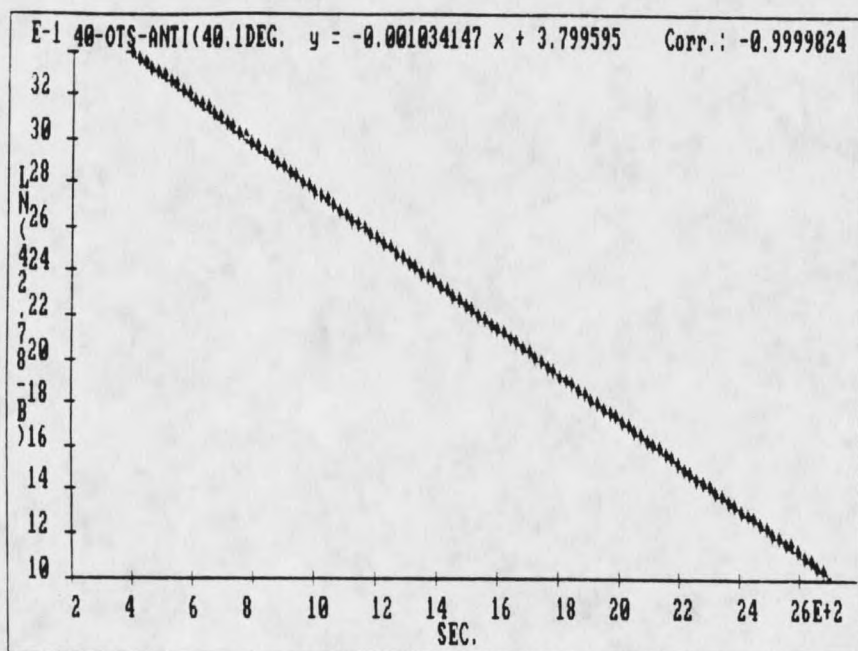


Figure 104. Plot of $\ln (C_{\infty}-C_x)$ vs. time (seconds) for the Solvolysis of [83] 40.1°C.

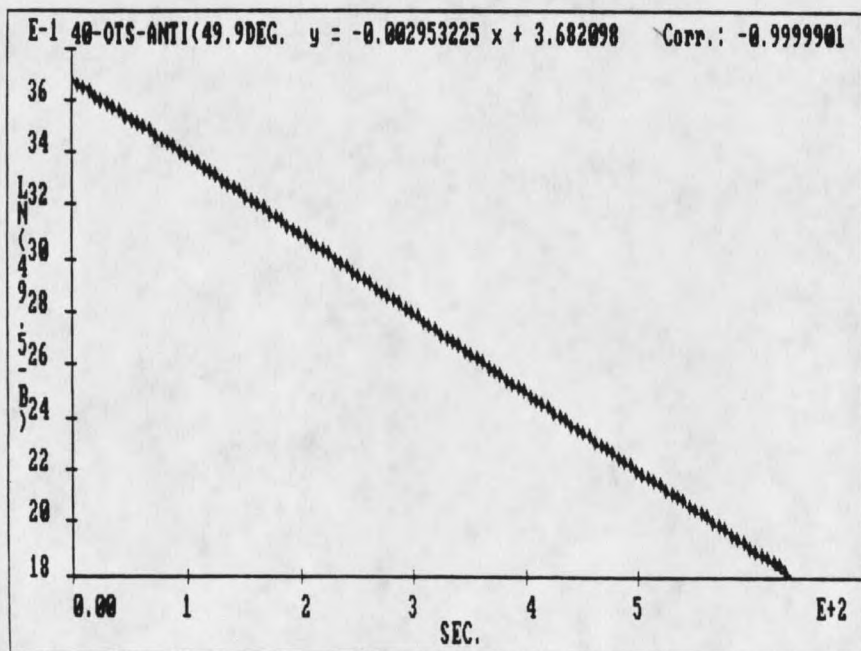


Figure 105. Plot of $\ln (C_{\infty}-C_x)$ vs. time (seconds) for the Solvolysis of [83] at 49.9°C.

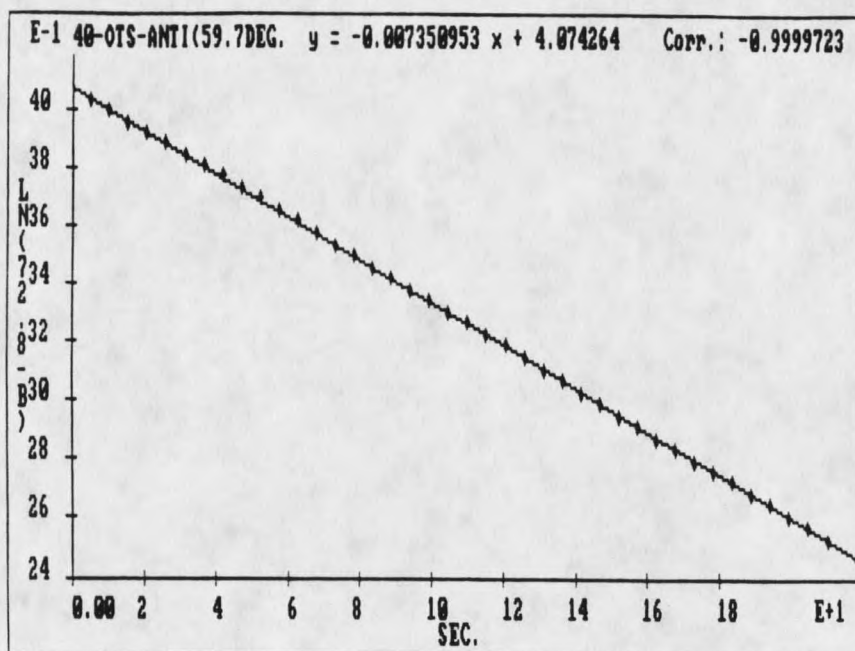


Figure 106. Plot of $\ln(C_{\infty} - C_x)$ vs. time (seconds) for the Solvolysis of [83] at 59.7°C.

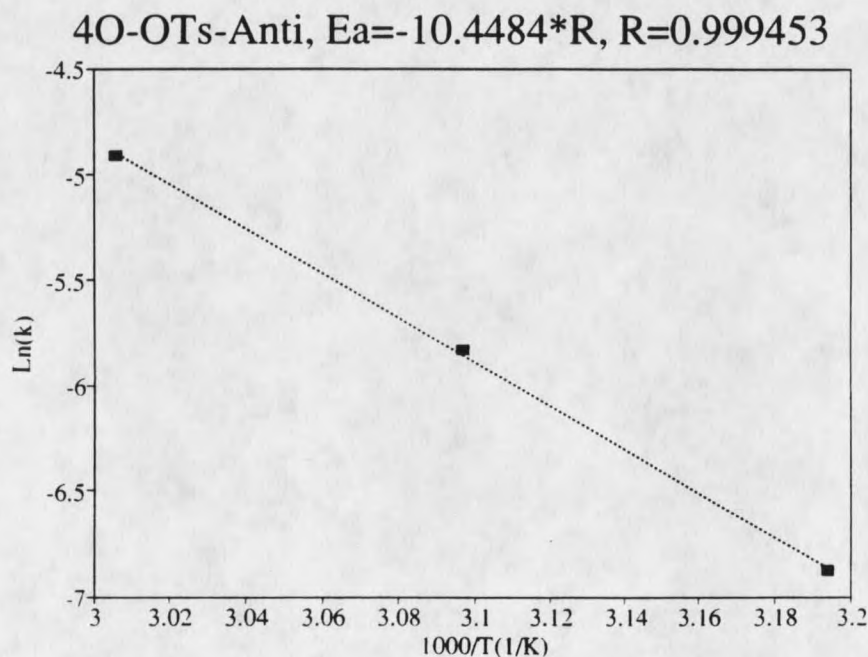


Figure 107. Plot of $\ln(k)$ vs. $1/T$ (K^{-1}) for [83].

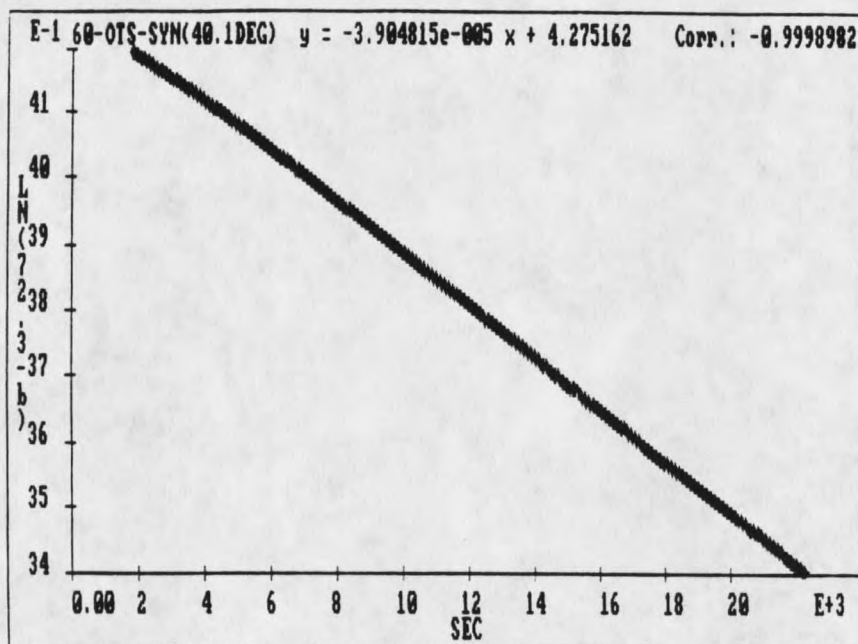


Figure 108. Plot of $\ln(C_{\infty} - C_x)$ vs. time (seconds) for the Solvolysis of [84] at 40.1°C.

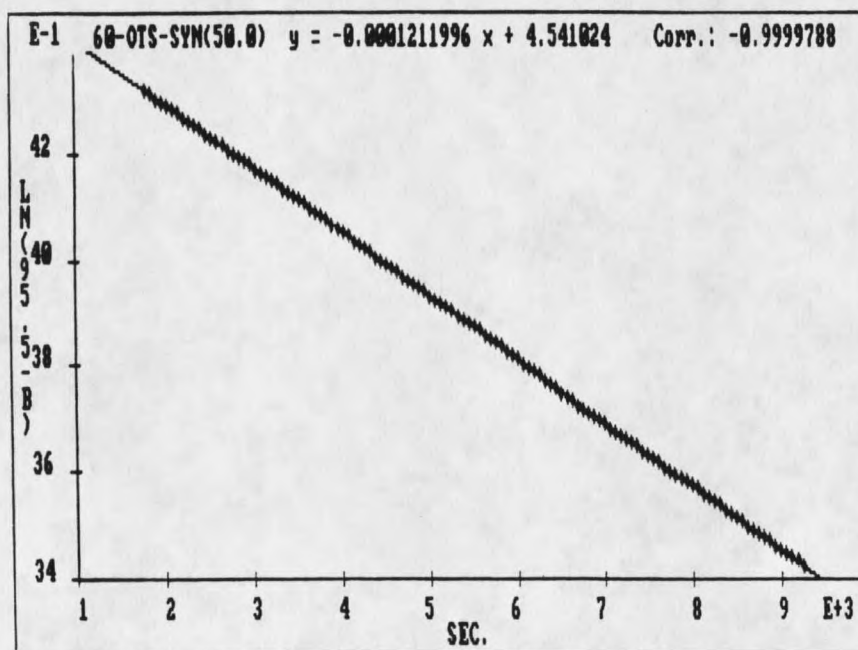


Figure 109. Plot of $\ln(C_{\infty} - C_x)$ vs. time (seconds) for the Solvolysis of [84] at 50.0°C.

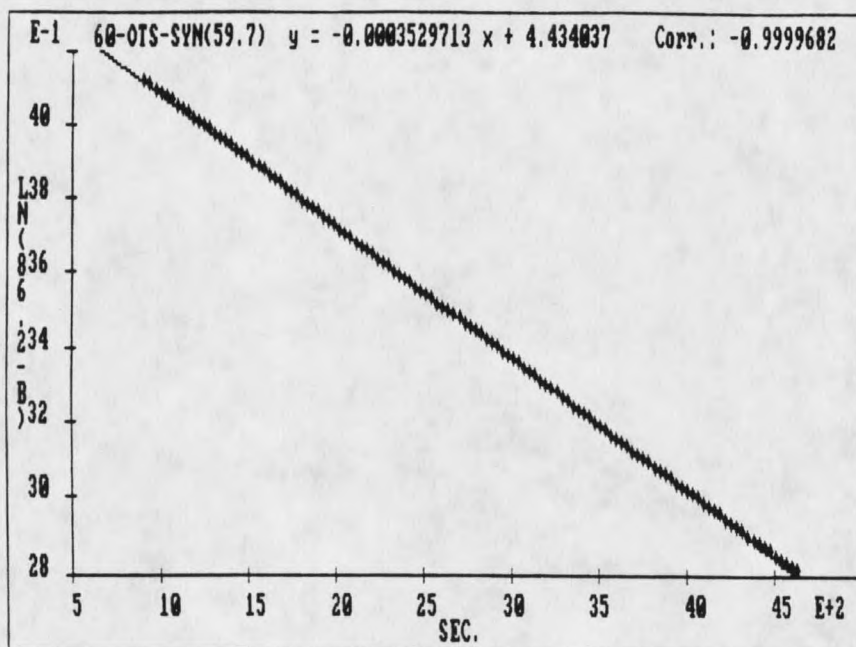


Figure 110. Plot of $\ln (C_{\infty} - C_x)$ vs. time (seconds) for the Solvolysis of [84] at 59.7°C.

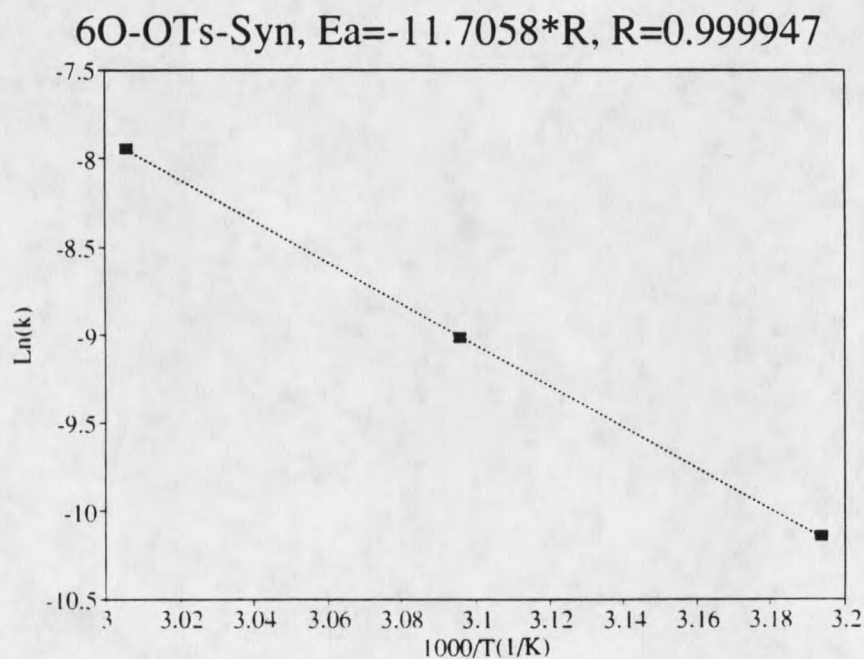


Figure 111. Plot of $\ln (k)$ vs. $1/T$ (K^{-1}) for [84].

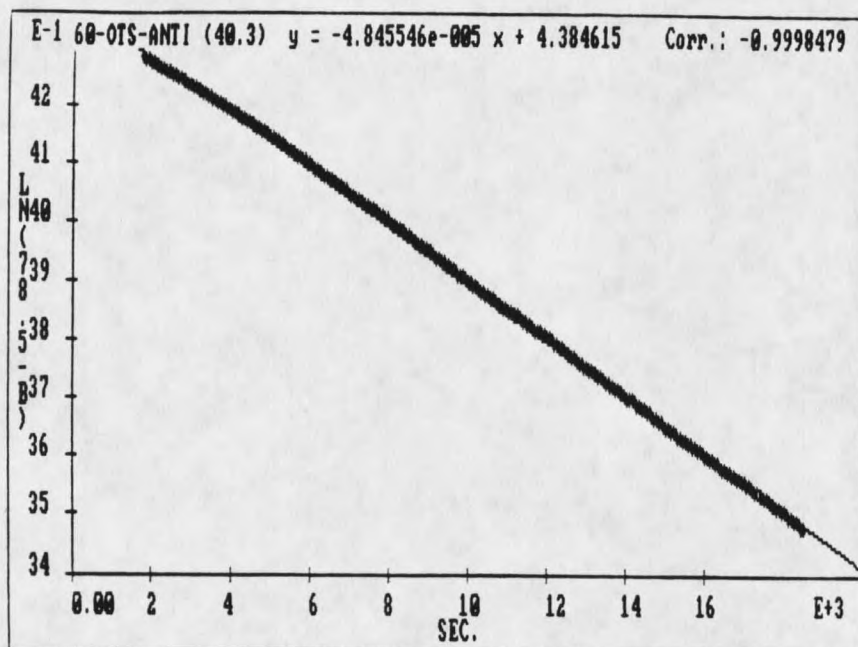


Figure 112. Plot of $\ln (C_{\infty} - C_x)$ vs. time (seconds) for the Solvolysis of [85] at 40.3°C.

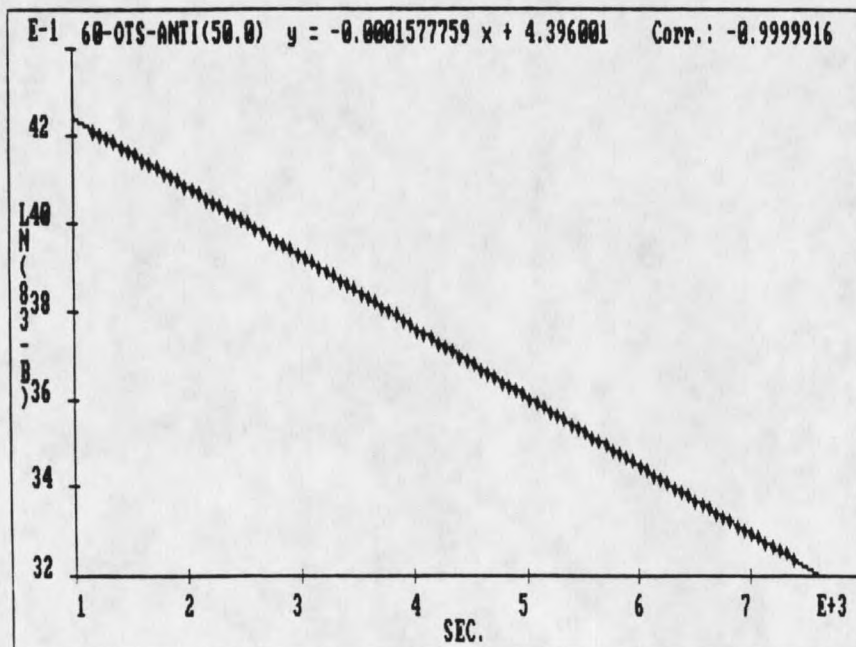


Figure 113. Plot of $\ln (C_{\infty} - C_x)$ vs. time (seconds) for the Solvolysis of [85] at 50.0°C.

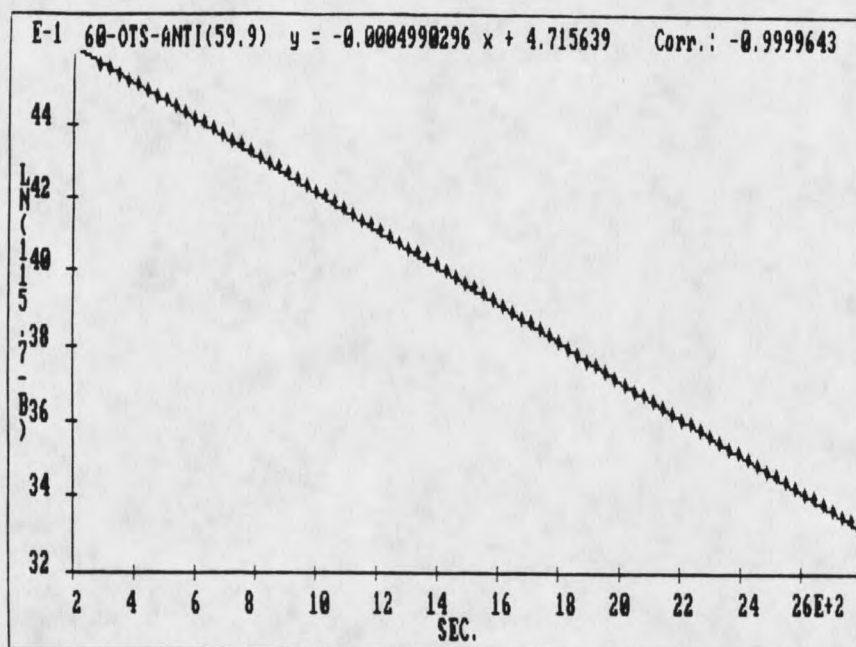


Figure 114. Plot of $\ln(C_{\infty} - C_x)$ vs. time (seconds) for the Solvolysis of [85] at 59.9°C.

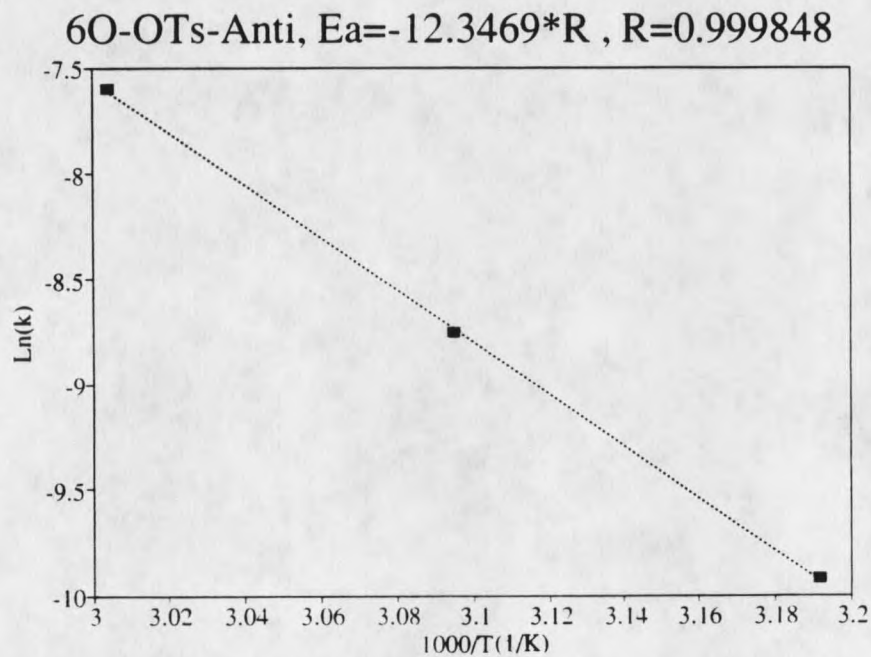


Figure 115. Plot of $\ln(k)$ vs. $1/T$ (K^{-1}) for [85].

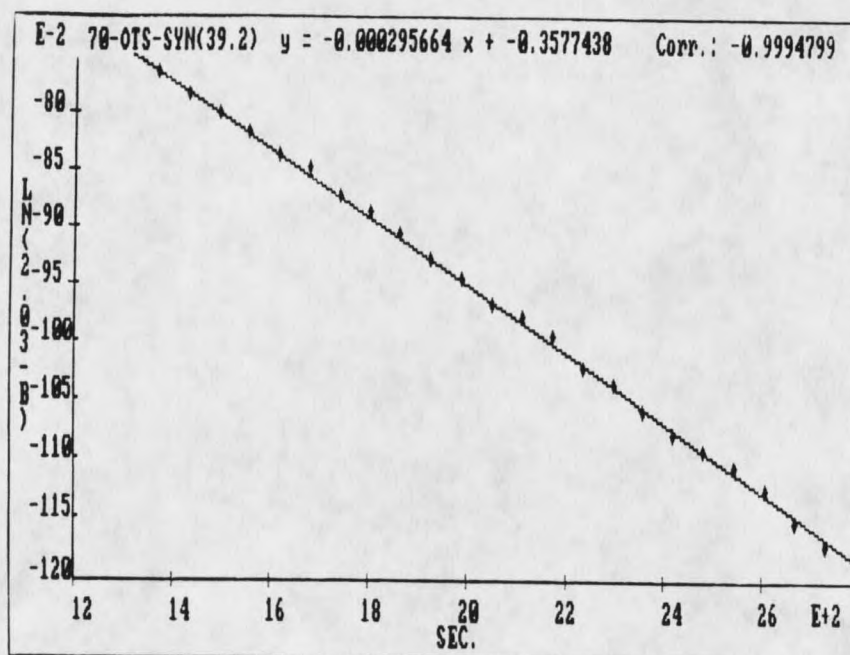


Figure 116. Plot of $\ln (C_{\infty} - C_x)$ vs. time (seconds) for the Solvolysis of [86] at 39.2°C.

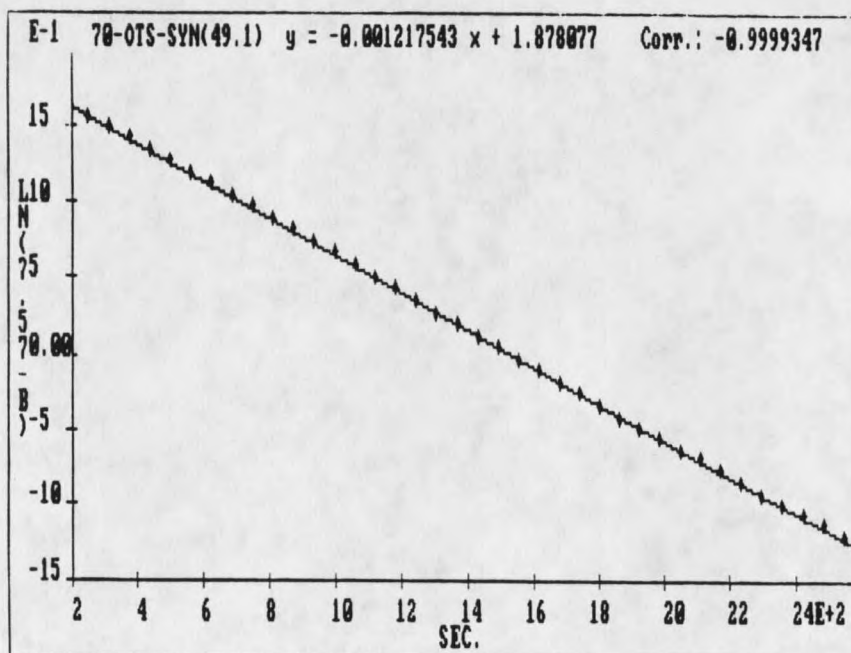


Figure 117. Plot of $\ln (C_{\infty} - C_x)$ vs. time (seconds) for the Solvolysis of [86] at 49.1°C.

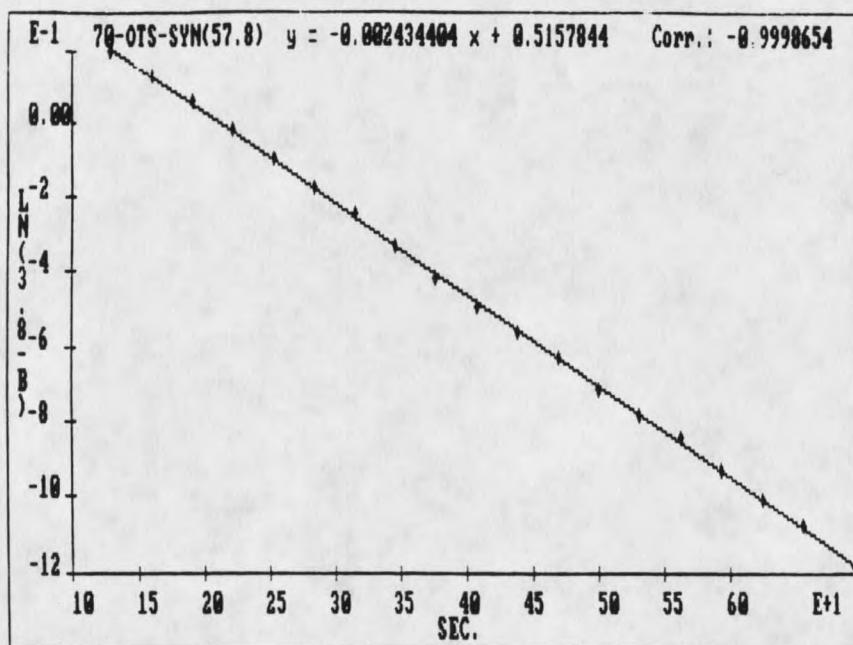


Figure 118. Plot of $\ln(C_{\infty} - C_x)$ vs. time (seconds) for the Solvolysis of [86] at 57.8°C.

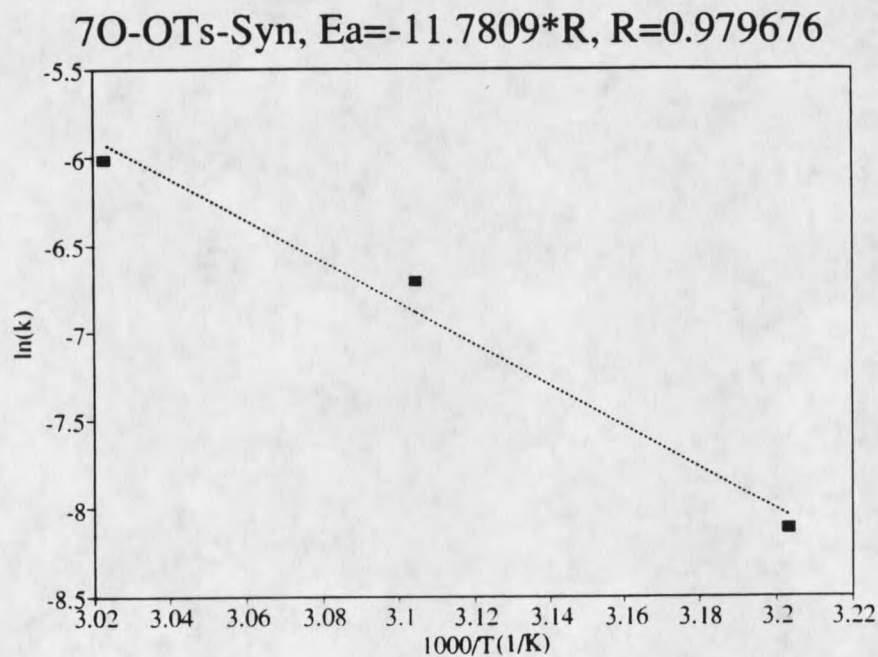


Figure 119. Plot of $\ln(k)$ vs. $1/T (K^{-1})$ for [86].

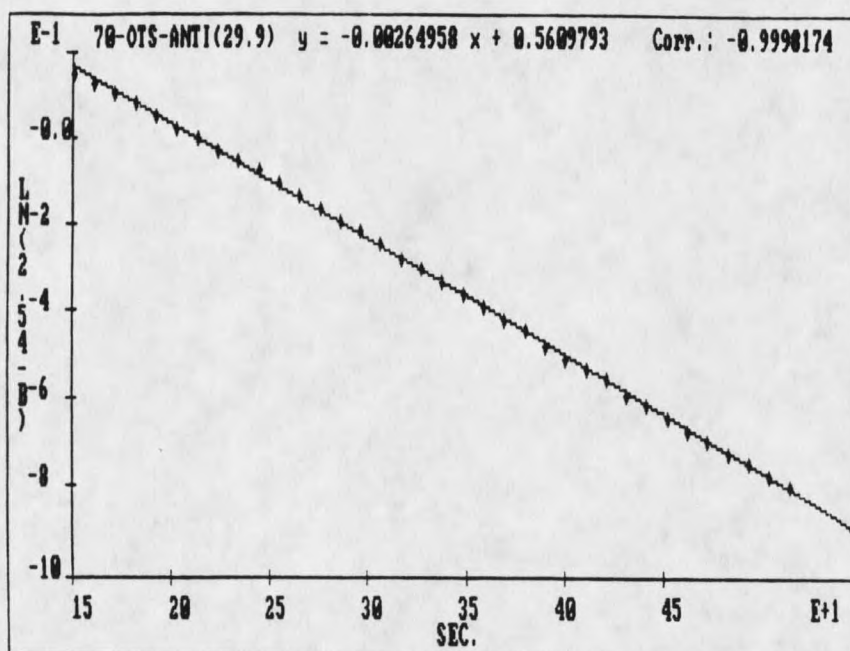


Figure 120. Plot of $\ln (C_{\infty} - C_x)$ vs. time (seconds) for the Solvolysis of [87] at 29.7°C.

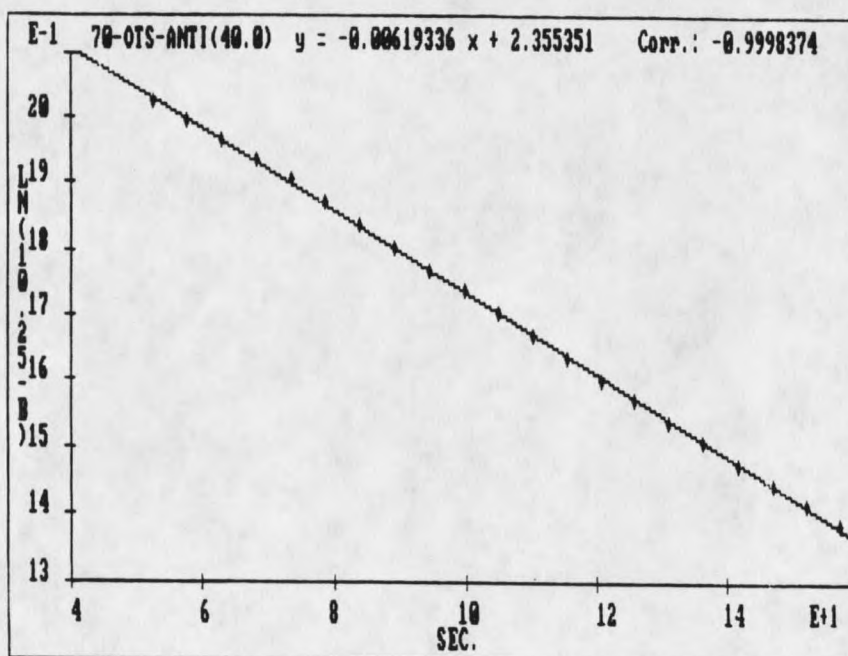


Figure 121. Plot of $\ln (C_{\infty} - C_x)$ vs. time (seconds) for the Solvolysis of [87] at 40.0°C.

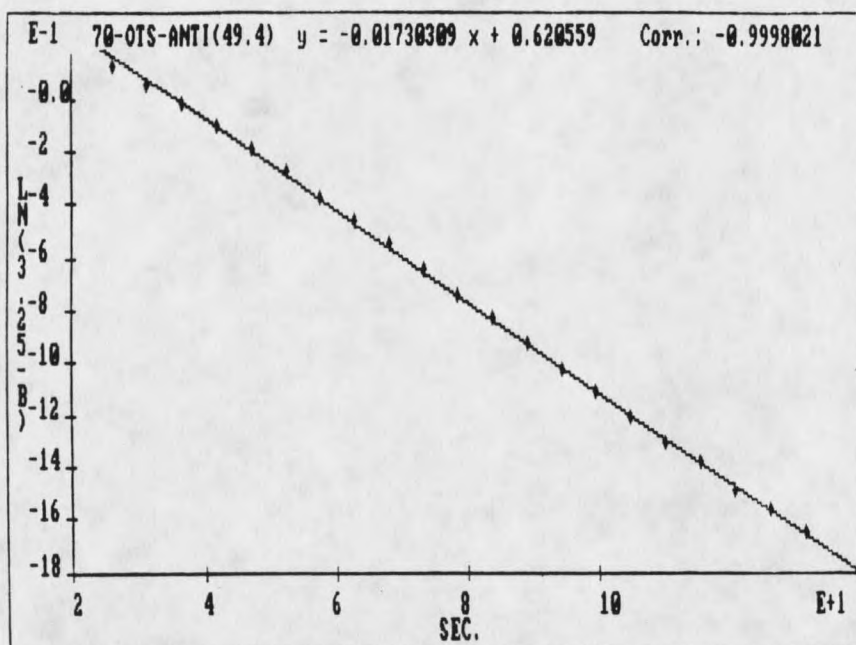


Figure 122. Plot of $\ln(C_{\infty} - C_x)$ vs. time (seconds) for the Solvolysis of [87] at 49.4°C.

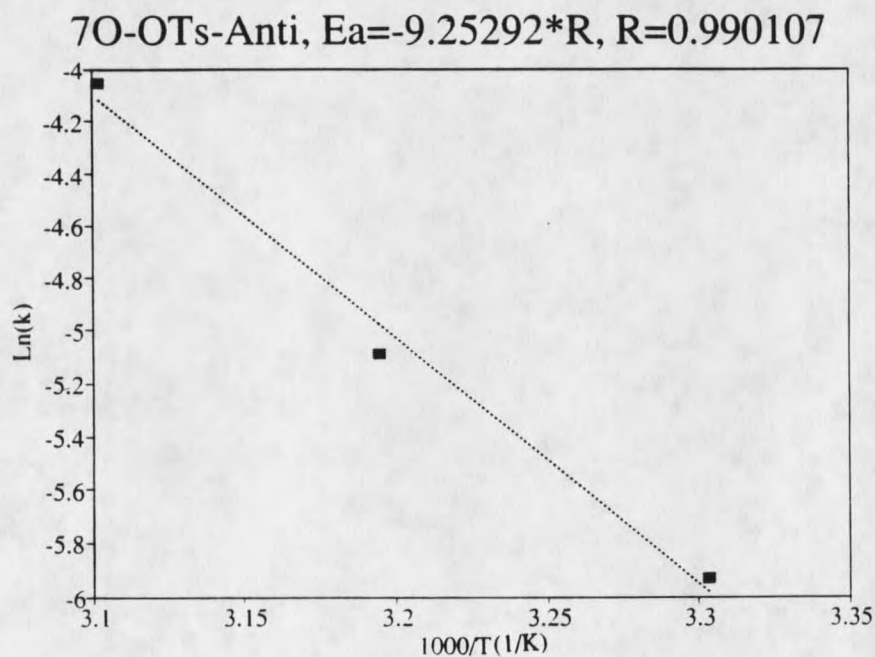


Figure 123. Plot of $\ln(k)$ vs. $1/T (K^{-1})$ for [87].

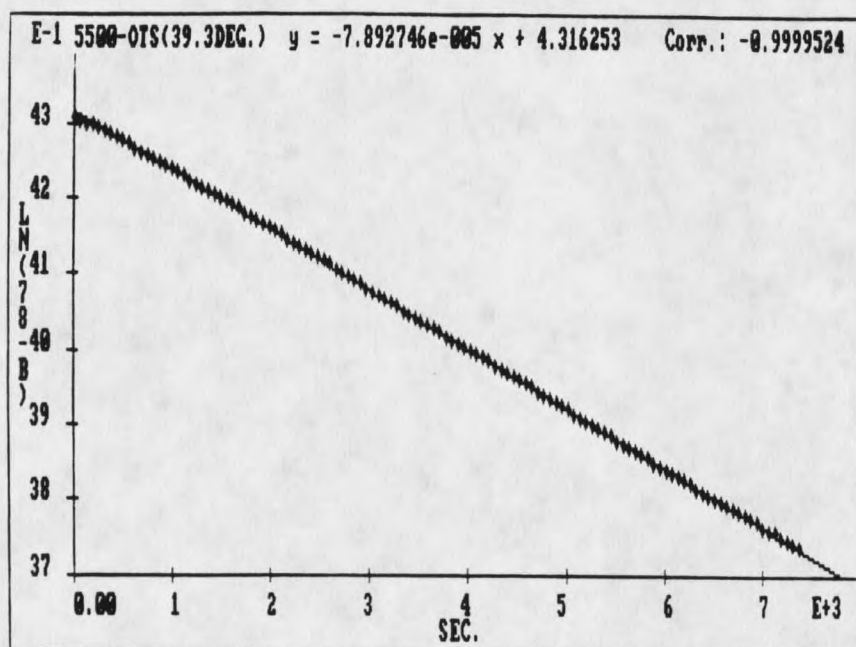


Figure 124. Plot of $\ln (C_{\infty} - C_x)$ vs. time (seconds) for the Solvolysis of [88] at 39.3°C.

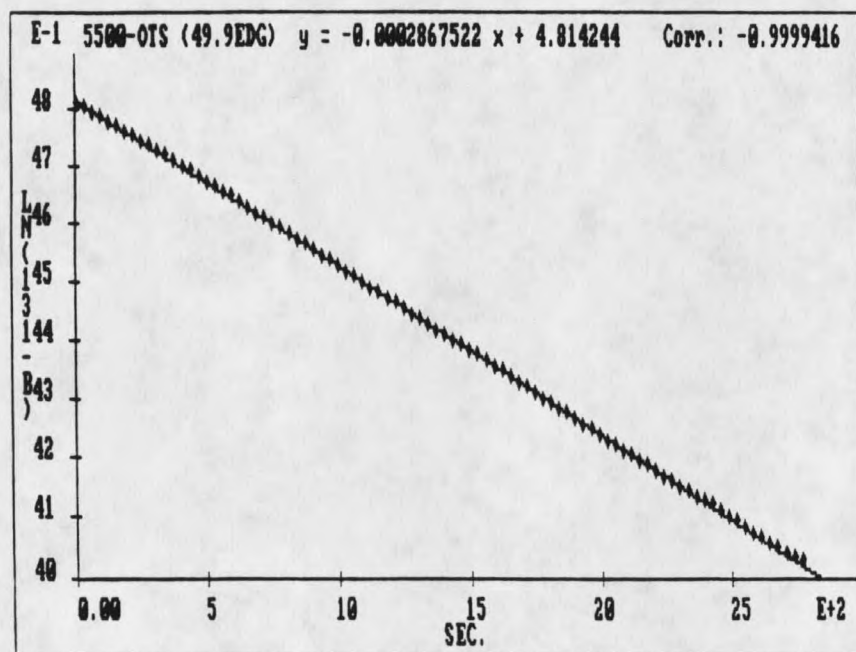


Figure 125. Plot of $\ln (C_{\infty} - C_x)$ vs. time (seconds) for the Solvolysis of [88] at 49.9°C.

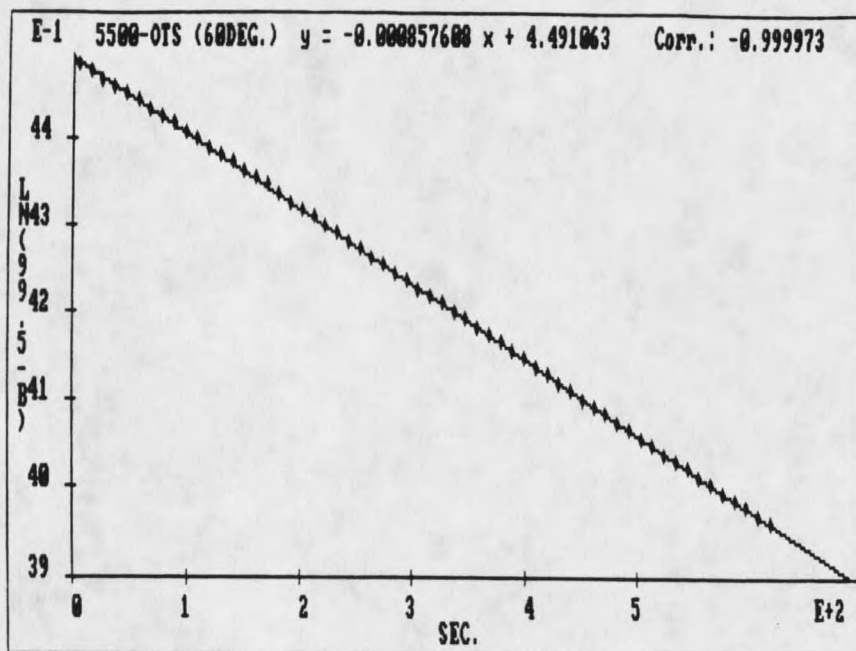


Figure 126. Plot of $\ln (C_{\infty} - C_x)$ vs. time (seconds) for the Solvolysis of [88] at 60.0°C.

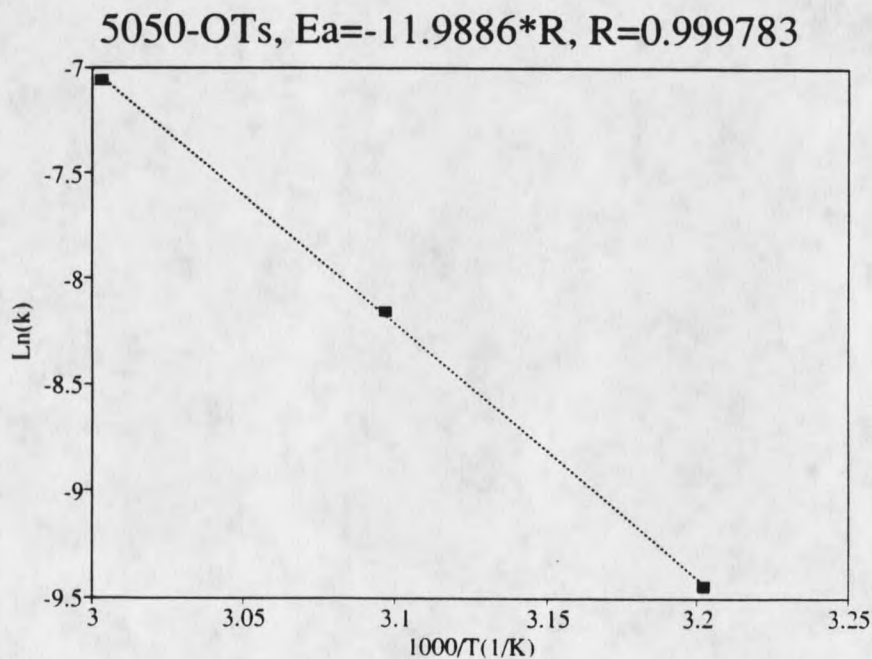


Figure 127. Plot of $\ln (k)$ vs. $1/T$ (K^{-1}) for [88].

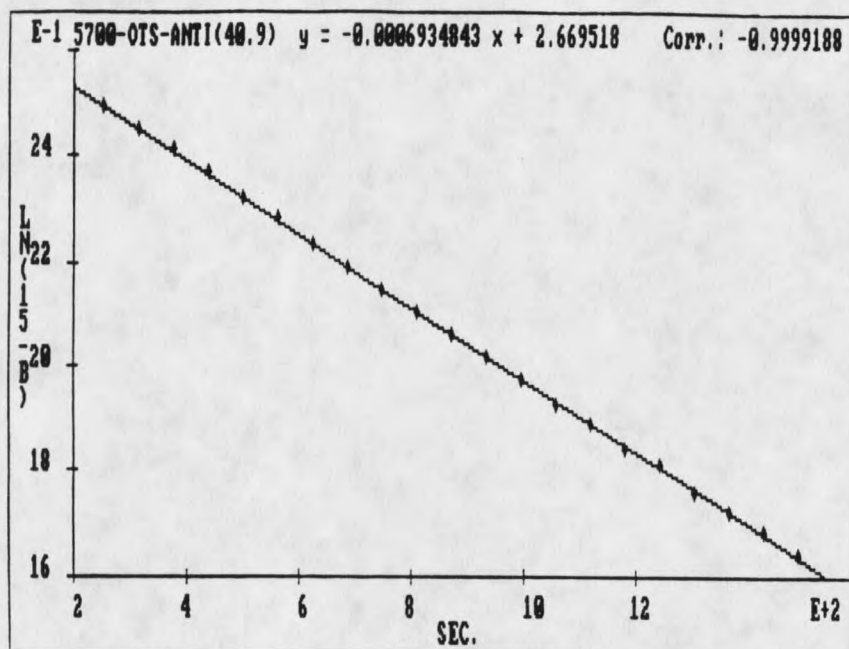


Figure 128. Plot of $\ln(C_{\infty} - C_x)$ vs. time (seconds) for the Solvolysis of [89] at 40.9°C.

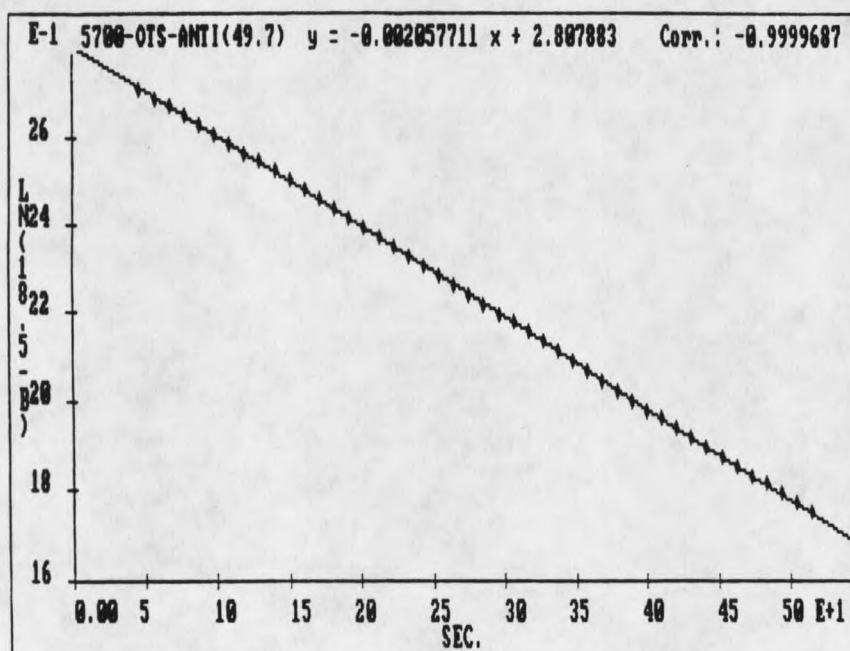


Figure 129. Plot of $\ln(C_{\infty} - C_x)$ vs. time (seconds) for the Solvolysis of [89] at 49.7°C.

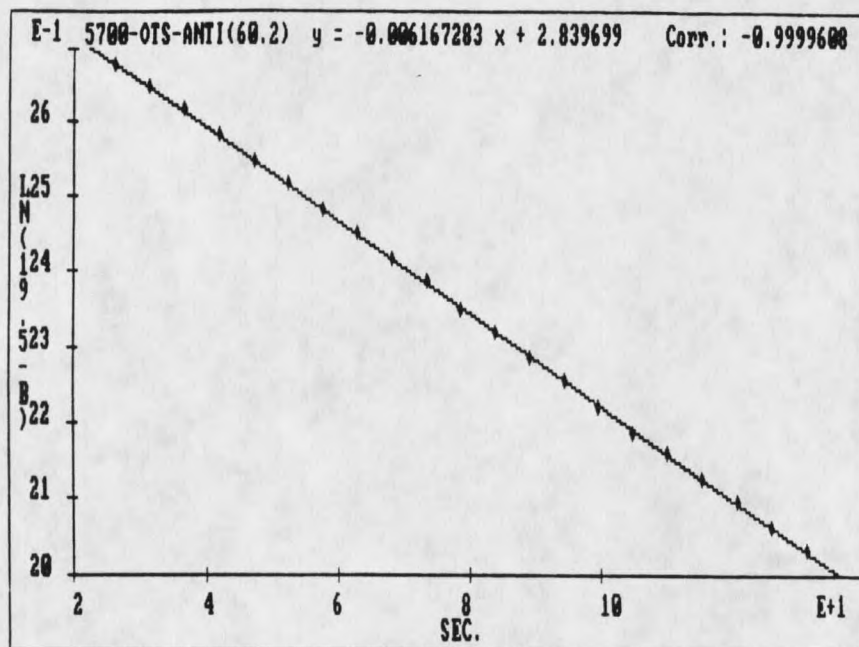


Figure 130. Plot of $\ln(C_{\infty} - C_x)$ vs. time (seconds) for the Solvolysis of [89] at 60.2°C.

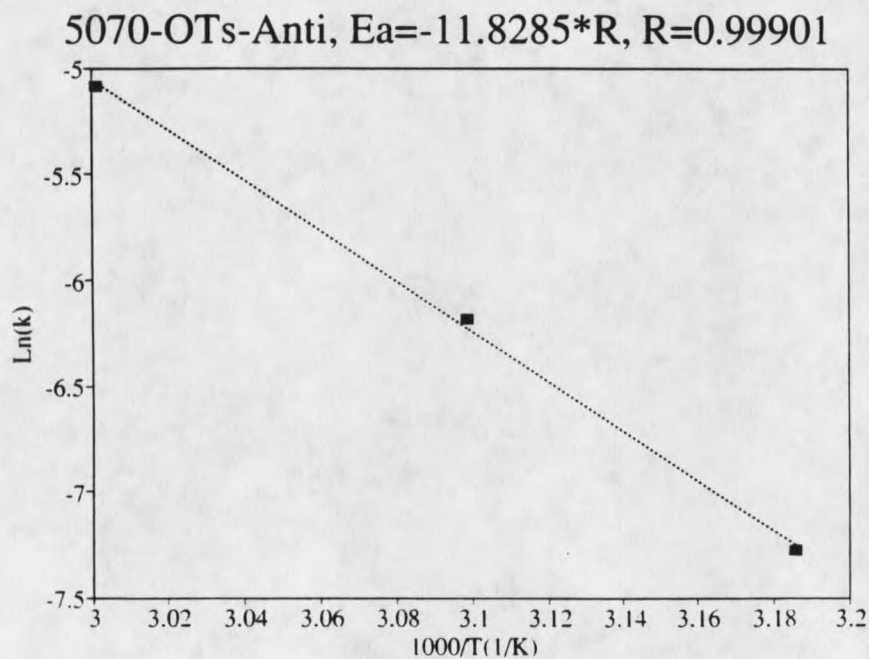


Figure 131. Plot of $\ln(k)$ vs. $1/T$ (K^{-1}) for [89].

APPENDIX B

- ¹HNMR spectra of *syn*- and *anti*-tosylates of propellanes.

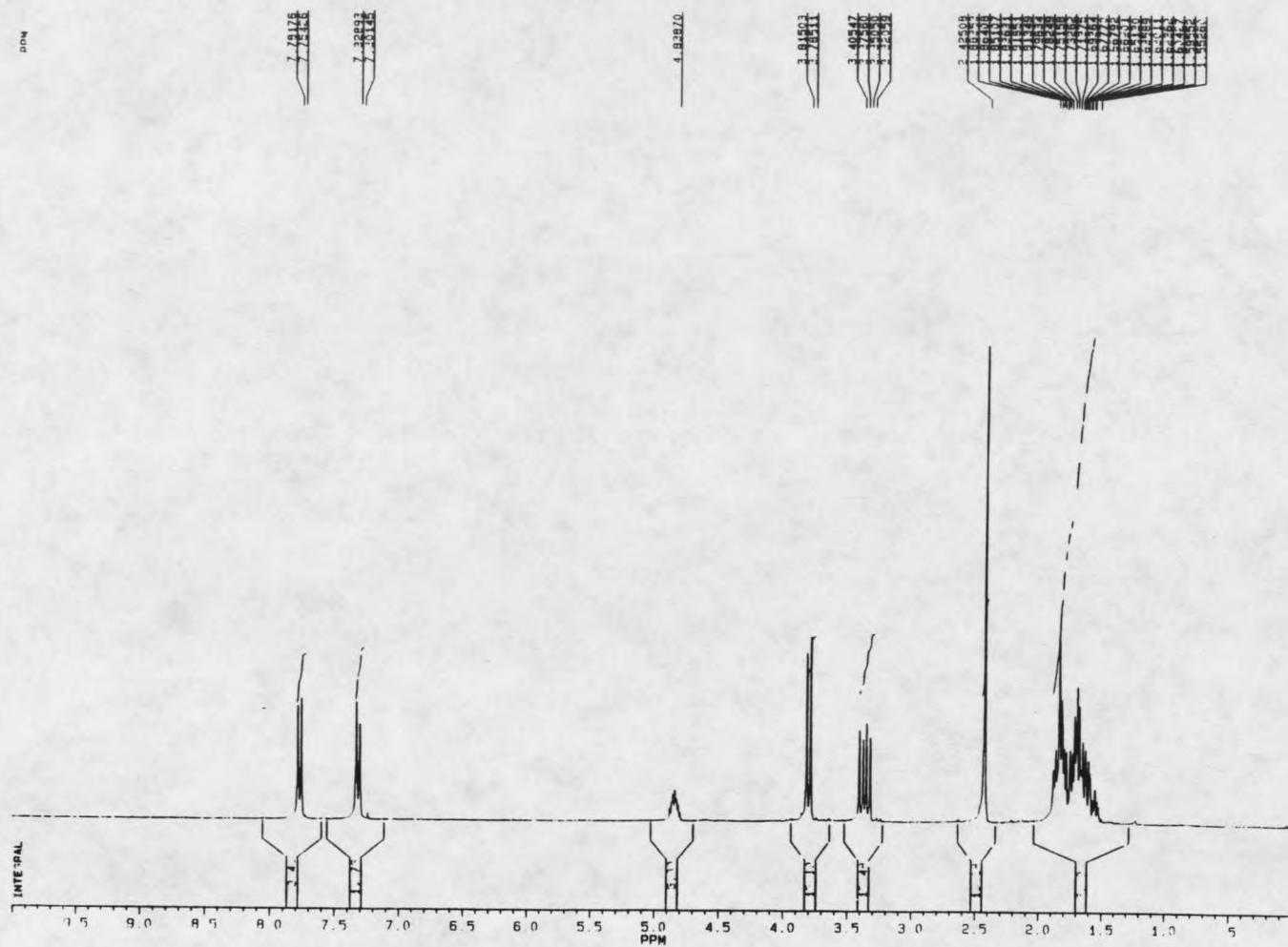


Figure 132. 300.133 MHz ^1H NMR: (syn)-3-Tosyl-8-oxatricyclo[4,3,2,0]undecane, [82].

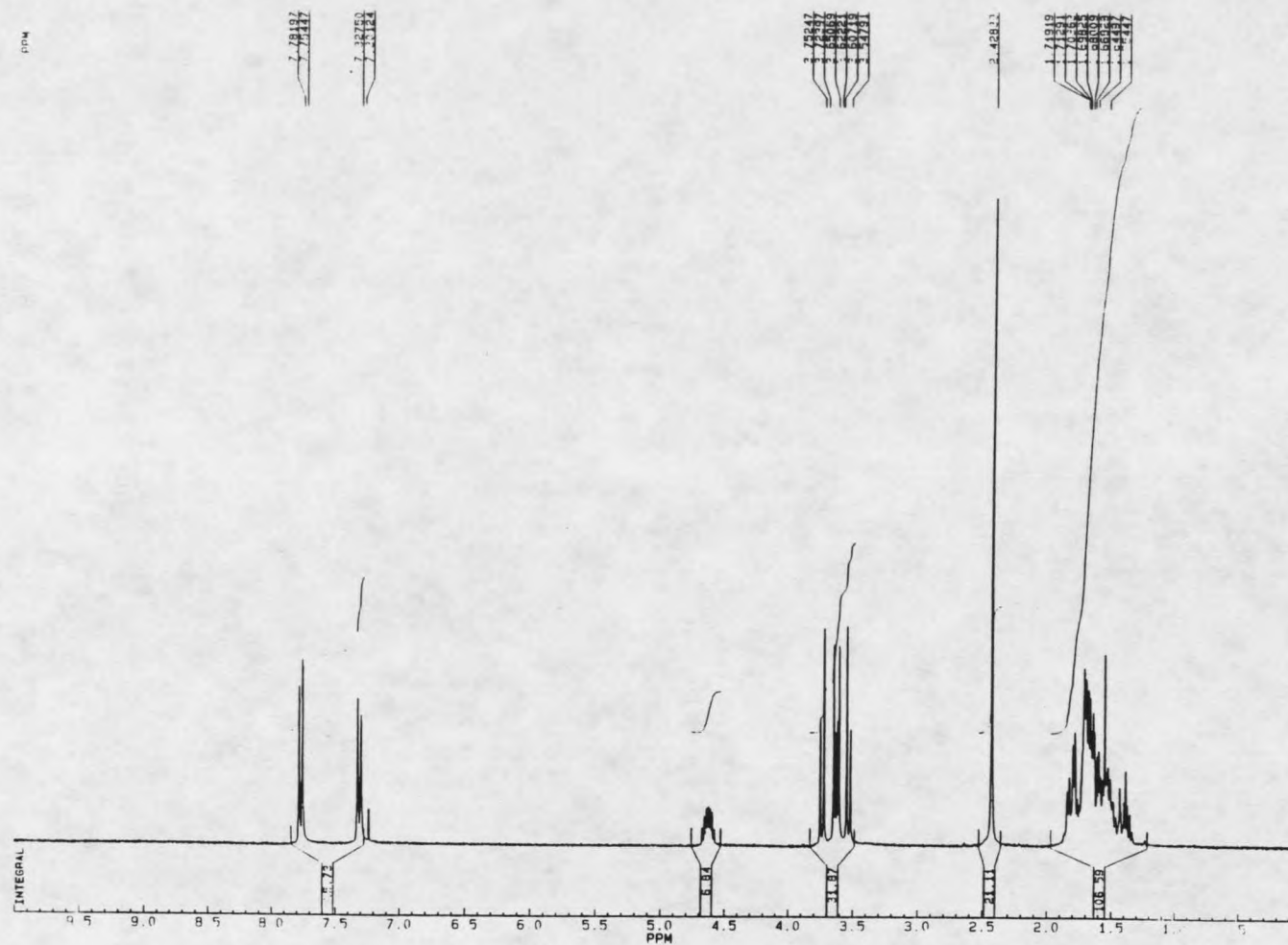


Figure 134. 300.133 MHz ^1H NMR: (syn)-3-Tosyl-8-oxatricyclo[4,3,3,0]dodecane, [15].

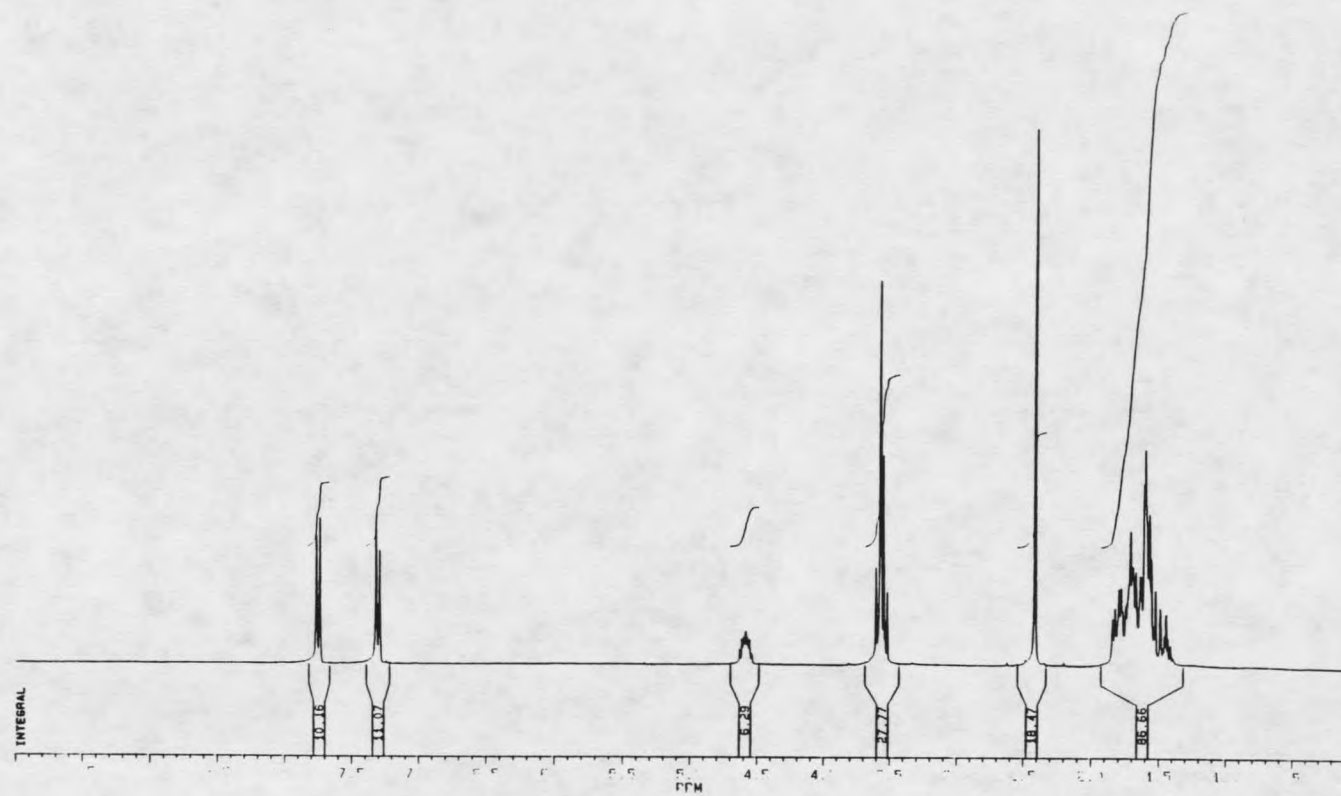


Figure 135. 300.133 MHz ^1H NMR: (anti)-3-Tosyl-8-oxatricyclo[4,3,3,0]dodecane, [16].

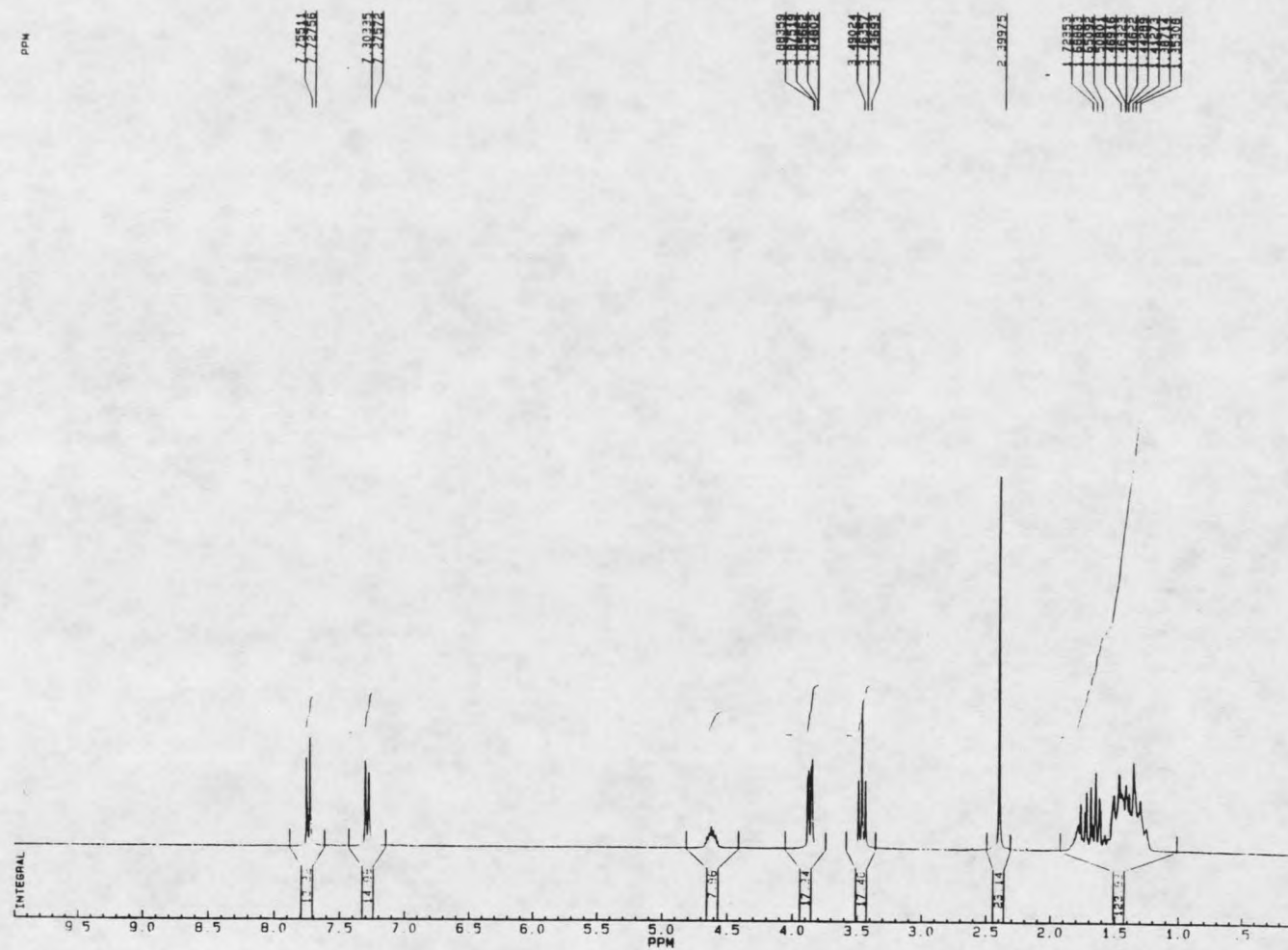


Figure 136. 300.133 MHz ^1H NMR: (syn)-3-Tosyl-8-oxatricyclo[4,4,3,0]tridecane, [84].

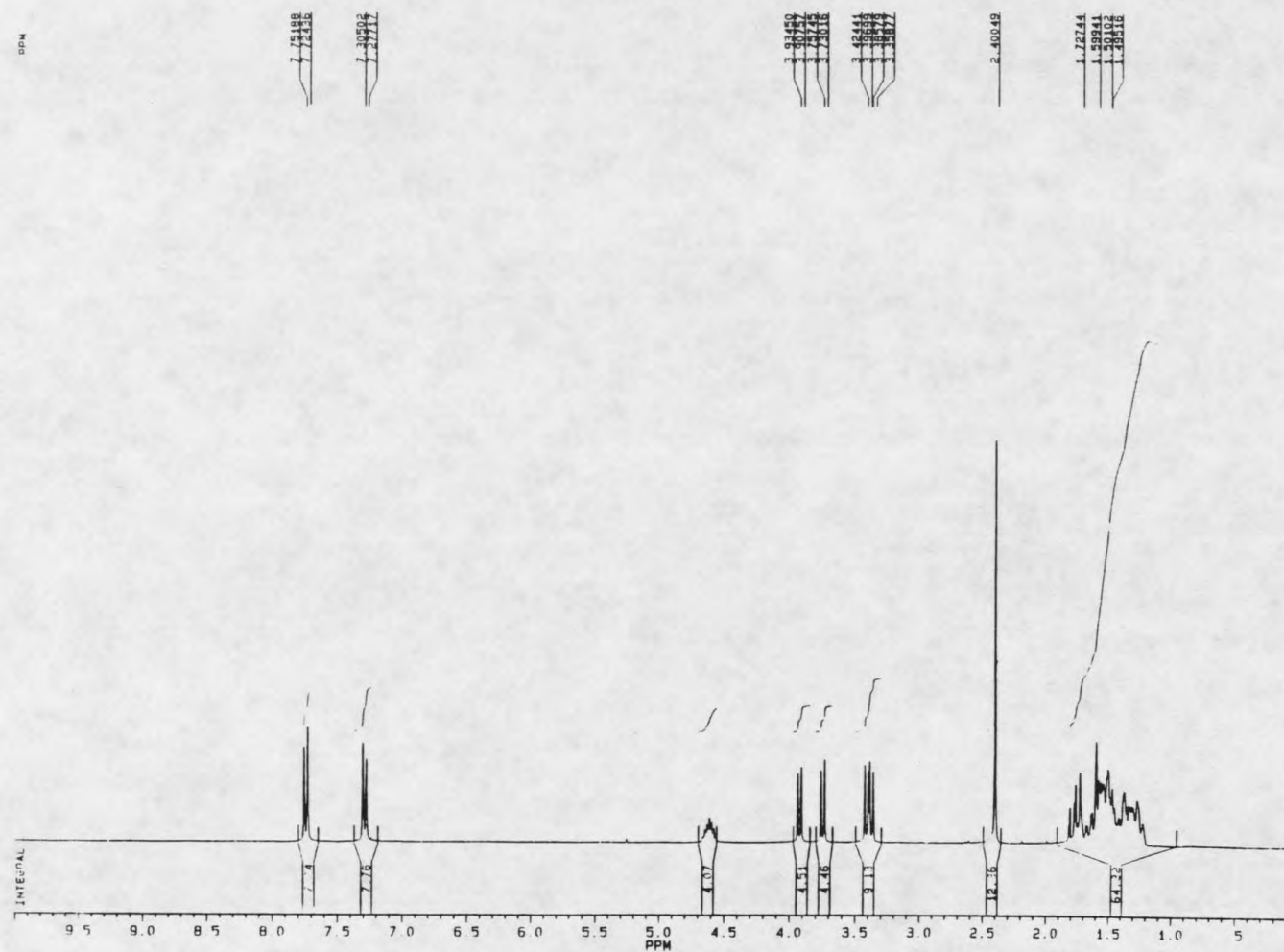


Figure 137. 300.133 MHz ^1H NMR: (anti)-3-Tosyl-8-oxatricyclo[4,4,3,0]tridecane, [85].

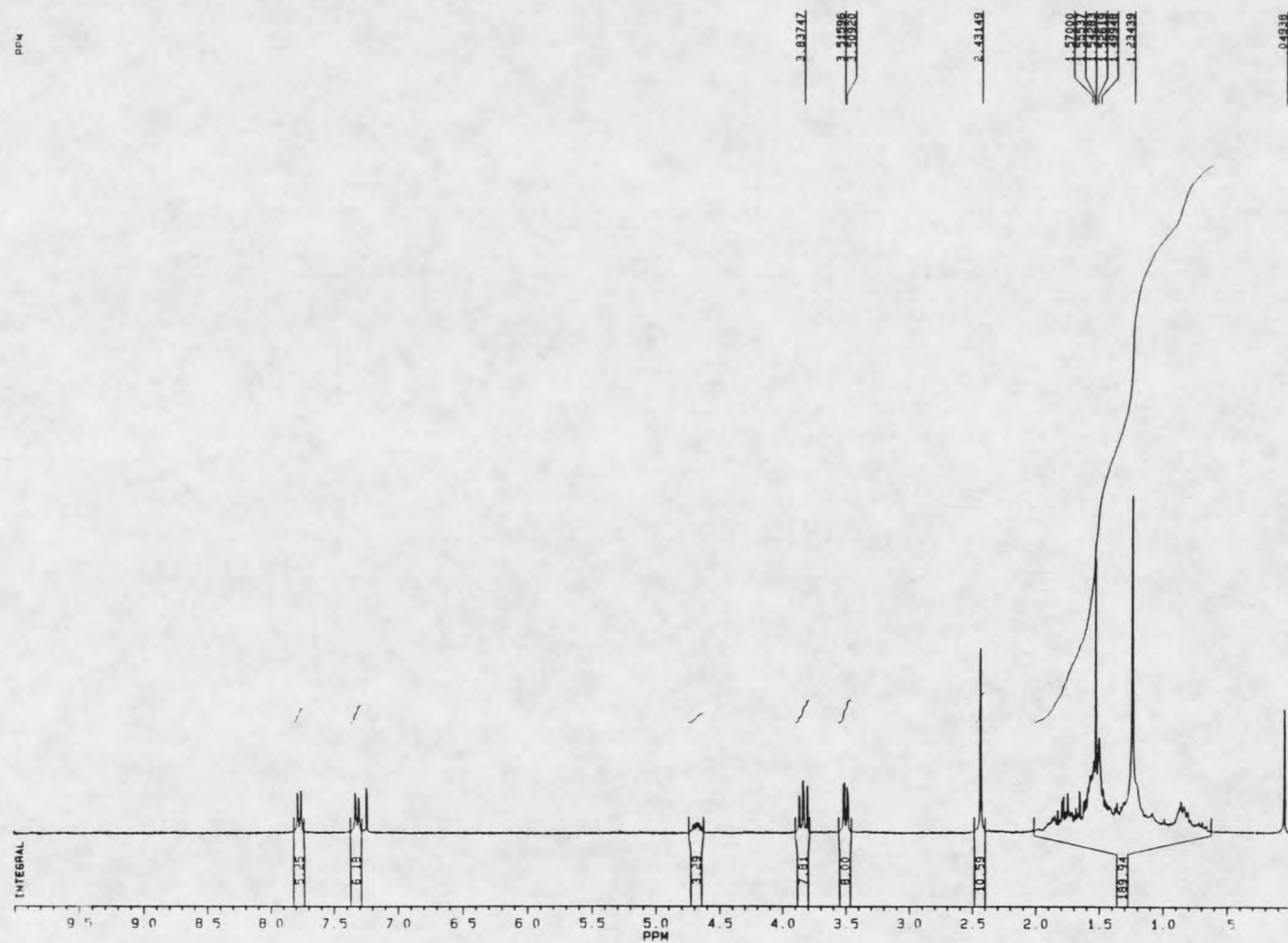


Figure 138. 300.133 MHz ^1H NMR: (syn)-3-Tosyl-8-oxatricyclo[5,4,3,0]tetradecane, [86].

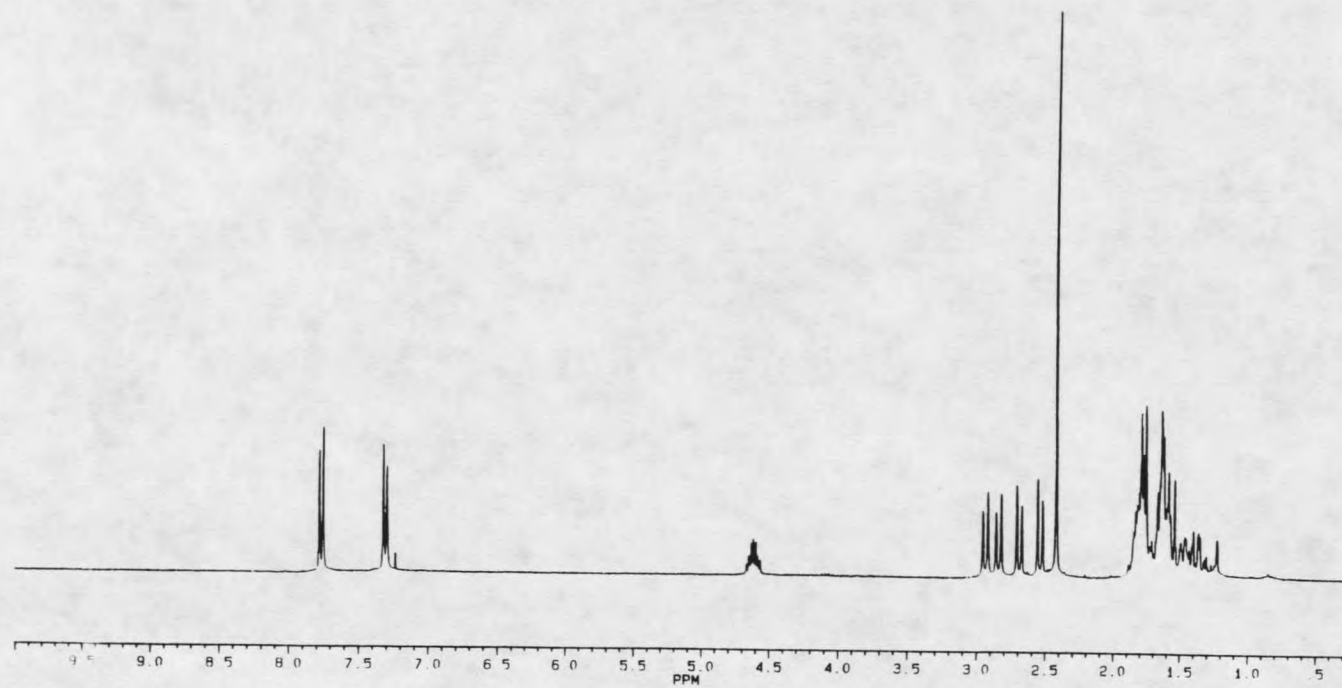
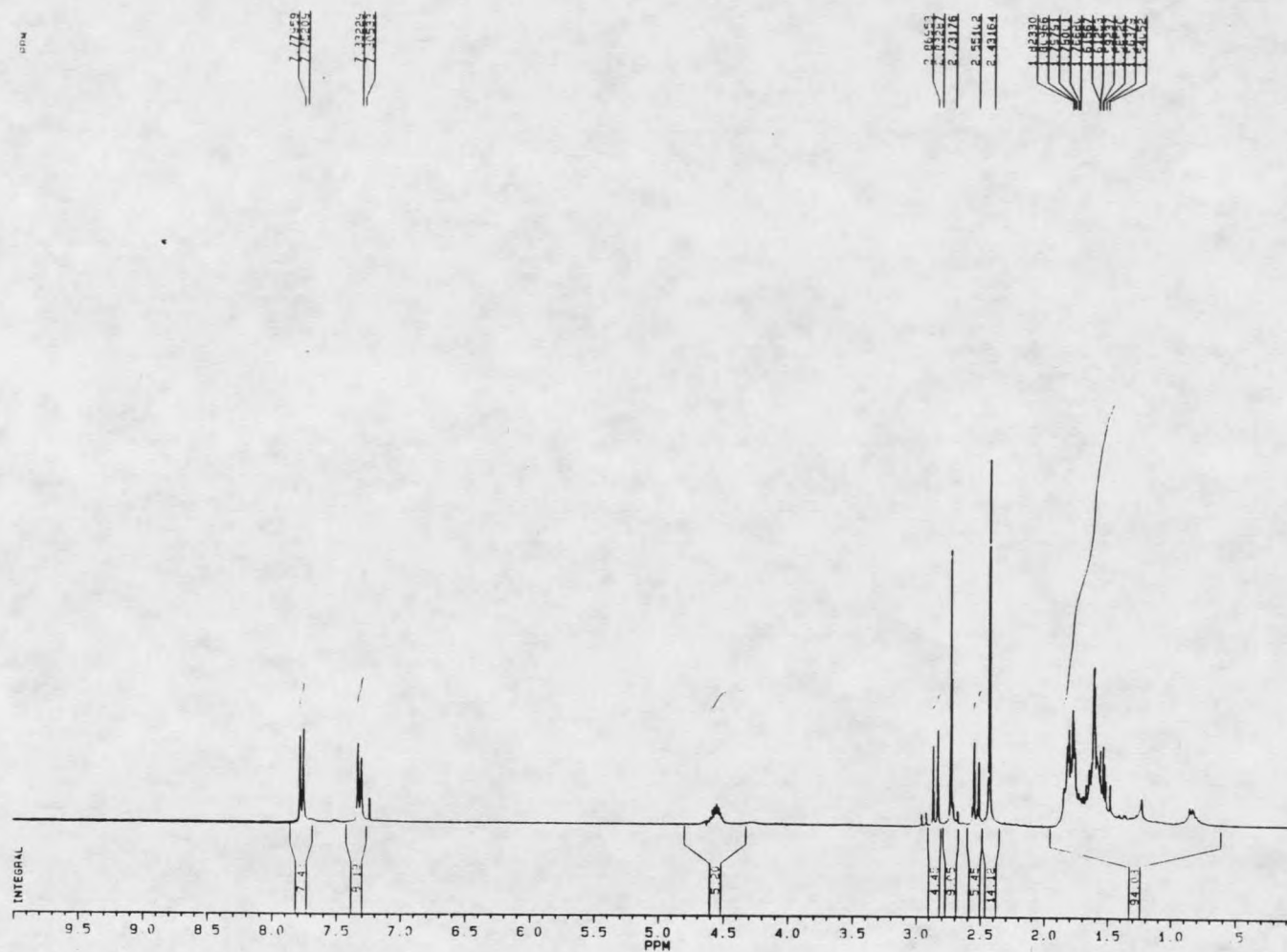


Figure 140. 300.133 MHz ^1H NMR: (syn)-3-Tosyl-8-thiatricyclo[4,3,3,0]dodecane, [80].



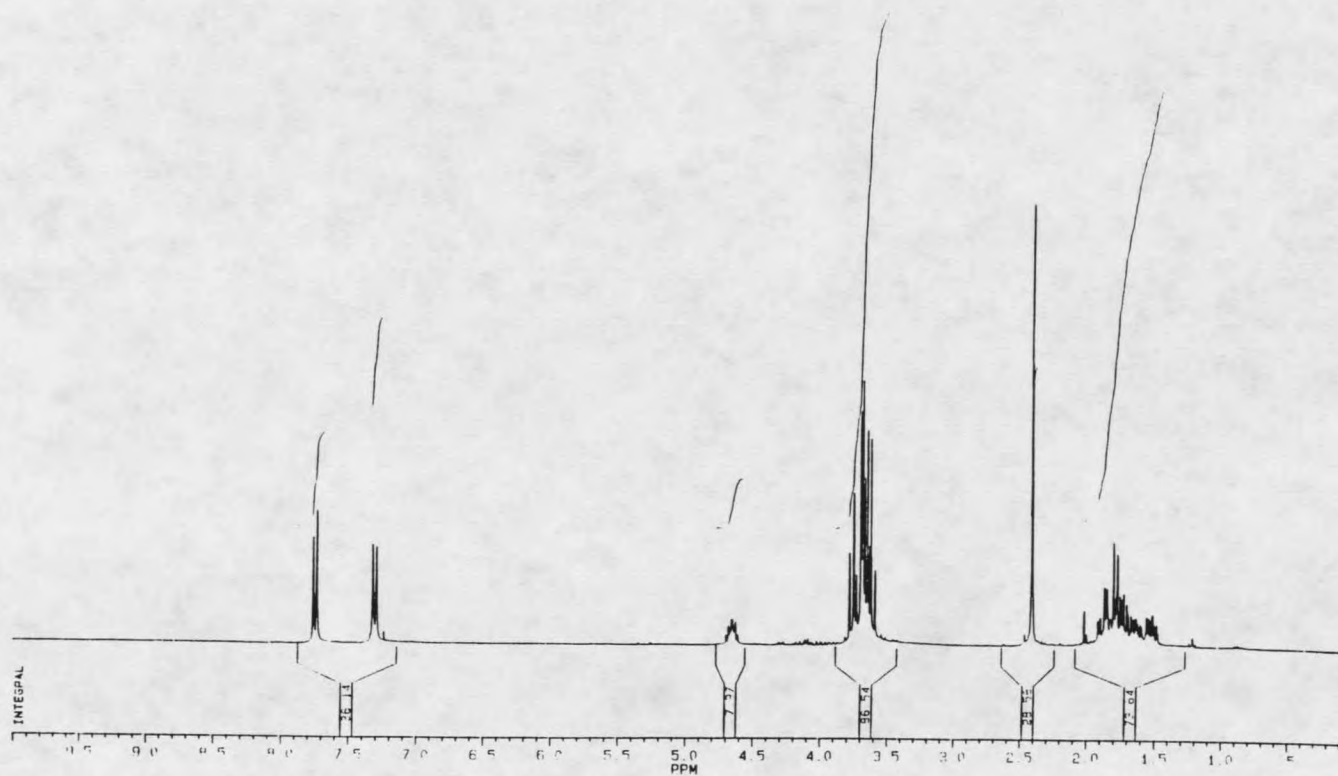


Figure 142. 300.133 MHz ^1H NMR: 3-Tosyl-8,11-dioxatricyclo[4,3,3,0]dodecane, [88].

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