I. SYNTHESIS OF ω-AMINO ALKYNES

II. THIOLS IN THE TANDEM MICHAEL REACTION

III. STRUCTURAL DETERMINATION OF [3a*S*-(3a*R**, 14b*R**, 14c*R**)]-(±)-2,3,9,10,14b,14c-HEXAHYDROBENZO[*a*.*e*]CYCLOPENTA-[1,3]CYCLOPROPA[1,2-*c*]-CYCLONONEN-1(8*H*)-ONE

By

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1980

Submitted to the Faculty of the Graduate College
of the Oklahoma State University
in partial fulfillment of the requirements
for the Degree of
MASTER OF SCIENCE
May, 1987

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ACKNOWLEDGMENTS

I wish to express my thanks and appreciation to my adviser, Dr. R. A. Bunce, for all his help. Gratitude is also expressed to my committee members, Dr. E. J. Eisenbraun, Dr. E. M. Holt, and Dr. A. J. Mort for their assistance.

I am grateful to the members of the support staff of O.S.U. and want to express my thanks to those who have made my graduate work easier. In particular, I am especially grateful to Mr. Stan Sigle, who has assisted me, on short notice on several occasions, in obtaining much needed NMR data. Also, I am grateful to Mr. Norman Perreira for providing mass spectral data.

Much would not have been possible without the financial, as well as moral, support of my wife's parents, Jimmie and Nadine Sallee. They have been more valuable than mere words can express. They have provided sound guidance and constant belief in my eventual success.

Finally, I thank my wife and son for their patience, understanding, and loving support in all my endeavors. I also gratefully thank my wife for typing this manuscript, and my wife's aunt, Janet Sallee, who typed the final draft.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

PART I

SYNTHESIS OF ω-AMINO-1-ALKYNES

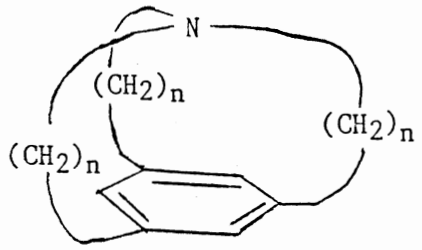
INTRODUCTION

This thesis is divided into three parts due to the difference in the major objective of the three investigations. Each part contains an Introduction and/or Historical, Results and Discussion, and Experimental Section. Part III encompasses all of these sections in one chapter. The Bibliography is combined.

CHAPTER I

INTRODUCTION AND HISTORICAL

Despite the myriad synthetic approaches to organic compounds bearing the amine functional group, there have been few syntheses of primary ω-alkynylamines reported.[1] The current project required two such compounds, e.g. 4-pentynylamine and 5-hexynylamine, for use in the development of a synthesis of the nitrogen-bridged 1,3,5-heterocyclophane 1. Scant literature precedent coupled with the lack of experimental detail, however, required that we first develop a reproducible, high-yield procedure for the acquisition of these compounds.

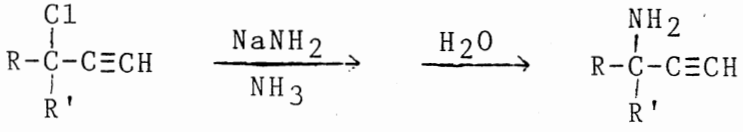


n = 3,4

1

The earliest synthesis of primary alkynyl amines was reported by G. F. Hennion in 1952 (see Figure 1).[2] His approach involved reacting secondary and tertiary propargyl chlorides with sodamide in liquid ammonia to produce primary alkynylamines in 41 - 76% yield. The method

affords only polymeric material, however, when one or both of the R groups are aryl.



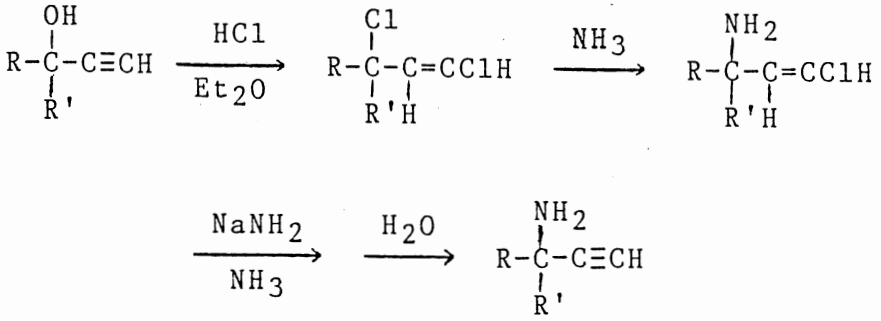
R = Aliphatic, R' = Aliphatic

Figure 1. Hennion Synthesis of Propargylic Amines

The Hennion synthesis of alkynyl amines was modified by N. R. Easton to include the synthesis of 1,1-diaryl or 1-alkyl-1-aryl propargylamines (see Figure 2).[3] The Easton approach begins with 1,3-dichloropropenes which were prepared by treatment of 2-alkyn-1-ols with dry ethereal hydrogen chloride. The 1,3-dichloropropene derivatives were reacted with an amine (NH_3 or RNH_2) to form 3-amino- or 3-alkylamino-1-chloro-1-propenes in 10 - 35% yield. Dehydrohalogenation with sodamide in liquid ammonia then gave the desired alkynylamine in 50 - 70% yield.

Neither Hennion's nor Easton's synthesis could be applied to the preparation of unbranched primary ω-alkynylamines. This is because carbocation stabilization as in the zwitterionic intermediate 2 is lacking. Whereas intermediates in the above reported synthesis incorporate a secondary or tertiary propargylic carbocationic center (R' and/or R' = alkyl), this stabilization of intermediates leading to the target compounds is absent.

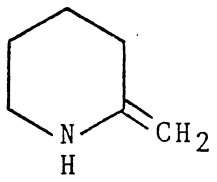
2



R = Aromatic, R' = Aliphatic or Aromatic

Figure 2. Easton Synthesis of Propargylic Amines

Dumont and Cadiot prepared ω-alkynylamines from 1-amino-ω-phenoxyalkanes by first converting these to ω-bromoalkylammonium bromides with dry hydrogen bromide (see Figure 3).[4,5] These salts were then reacted with sodium acetylide in 40% dimethylformamide/liquid ammonia solution to give the ω-alkynylamines. Yields were in the range of 50 - 90% except in the preparation of 1-amino-5-hexyne where the recovery was 5%. The low yield is due to the facile intramolecular addition of the amino group to C5, the internal alkynyl carbon. This initially generates the enamine 3 which rapidly tautomerizes to the more stable imine 4.



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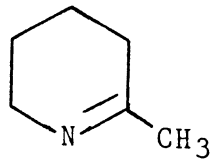

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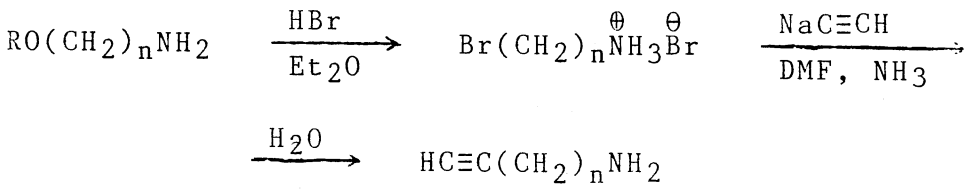


Figure 3. Dumont Approach to the Synthesis of Alkynylamines

In a synthesis of 1-amino-5-hexyne developed by Hebrand, guanidine was alkylated with 1-iodo-5-hexyne to form a guanidinium salt (see Figure 4).[6] Alkaline hydrolysis of this salt afforded 1-amino-5-hexyne in 35% yield. As in the Dumont synthesis, 2-methyl-3,4,5,6-tetrahydropicoline, 4, was the major product. Thus, while these methods seem to be adequate for the preparation of the majority of ω-alkynylamines, those which can readily cyclize to a five or six-membered ring pose a severe limitation.

Nitrile reduction constitutes another approach to terminal alkynylamines. Reduction of 1-cyano-10-undecyne using lithium aluminum hydride has been reported by Gauthier to yield 1-amino-11-dodecyne (see Figure 5).[7] No experimental conditions were given for this procedure, however,

and no attempt was made to prepare 5-hexynylamine by this route. A single attempt was made in our laboratory to reduce 1-cyano-5-hexyne; none of the desired product could be isolated.

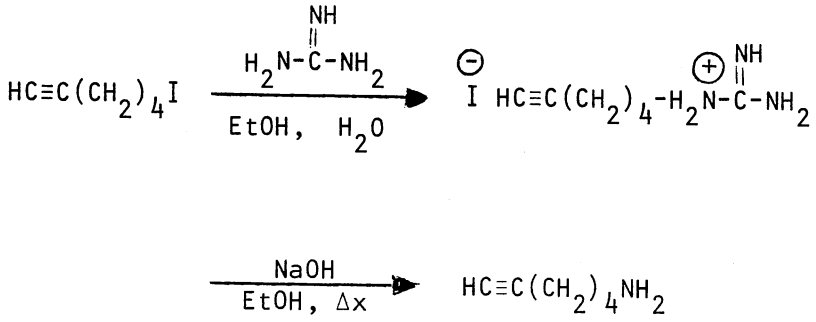


Figure 4. Hebrand Synthesis of 5-Hexynylamine

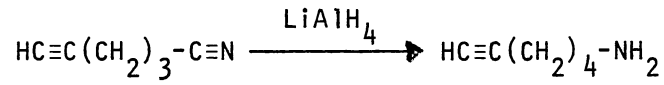
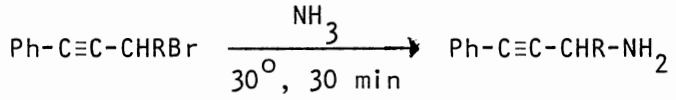


Figure 5. Gauthier Approach to 5-Hexynylamine

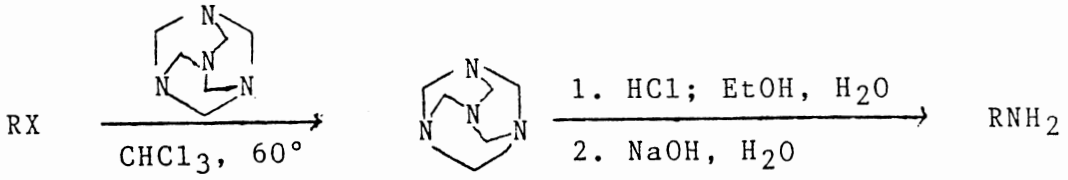
In a recent report, Simon prepared several 1-substituted 3-phenyl-propargylamines, similar to compounds which have shown activity against Tremorine tremors (see Figure 6).[8] Simon's method involves treating an alkyl bromide with ammonia or a volatile amine in a pressure reactor at 35°C for 30 minutes. The volatile amine is then vented and the mixture worked up. This method, though simple, requires the use of a dangerous and corrosive amine as well as an expensive pressure reactor and, thus, is not suitable in the current application.



R = H or Me

Figure 6. Simon Synthesis of Alkynylamines

The most convenient and least expensive method that has historically given the best results in all cases is the Delepine synthesis (see Figure 7).[9,10] Galat attempted to improve the Delepine synthesis by making it a one-pot procedure.[11] Following preparation of the quaternary hexamminium salt in ethanol, gaseous hydrogen chloride was bubbled directly into the crude reaction mixture. This modification, while slightly improving the yield, diminishes the efficiency of the synthesis by increasing the required reaction time by as much as a factor of ten.



R = Alkyl, X = TsO, MsO, $PhSO_3$, Br, Cl, I

Figure 7. Delepine Synthesis of Amines

Marszak and Marszak-Fleury have used the Delepine synthesis to prepare many primary alkynylamines using various solvents and leaving groups.[12,13,14,15] Experimental details in these reports are minimal

making their work marginal in utility. Based upon their work, we have developed improved and reproducible procedures for the preparation of both 4-pentynylamine and 5-hexynylamine, two of the more difficult cases. This work is detailed in the next chapter.

CHAPTER II

RESULTS AND DISCUSSION

It was planned that the synthesis of ω-amino-1-alkynes would proceed most logically through the corresponding halogen compound (see Figure 8). The initial target of our synthesis was, therefore, 1-bromo-5-hexyne. This compound was first prepared in 52% yield by treatment of 5-hexyn-1-ol with phosphorous tribromide according to the procedure of Keskin.[16] We later discovered a two-step method which affords the desired bromide in 73%. This approach involves preparation of the mesylate derivative of the alkynol followed by S_N2 displacement with bromide ion (see Figure 9). The mesylate is readily available using the method developed by Crossland.[17] Treatment of the mesylate with calcium bromide monohydrate in 2-(2-ethoxyethoxy)ethanol (carbitol) then afforded the bromide in high yield. The latter step is a modification of the procedure reported by Henbest for conversion of the tosylate to the bromide.[18] This sequence also proved useful in the preparation of 1-bromo-4-pentyne, though yields were slightly lower for this compound.

$$HC{\equiv}C(CH_2)_nNH_2 \longrightarrow HC{\equiv}C(CH_2)_nX \longrightarrow HC{\equiv}C(CH_2)_nOH$$

Figure 8. Retrosynthetic Analysis for 1-Amino-5-hexyne

$$HC\equiv C(CH_2)_4OH \xrightarrow[CHCl_3]{MsCl,\ Et_3N} HC\equiv C(CH_2)_4OMs$$

$$\xrightarrow[Carbitol]{CaBr_2\cdot H_2O} HC\equiv C(CH_2)_4Br$$

Figure 9. Synthesis of 1-Bromo-5-hexyne

Once adequate supplies of the bromide were available, attempts were made to generate the ω-aminoalkynes by use of the Gabriel synthesis, azide formation-reduction and the Delepine synthesis. These methods were chosen because of their demonstrated versatility in the synthesis of primary amines and the expected compatibility of required reagents with the alkyne functional group. Each approach will be discussed separately and evaluated in the current application.

The Gabriel synthesis was the first route investigated (see Figure 10). The phthalimide derivative was first prepared using a procedure described by Mitsunobu and coworkers.[19] Treatment of the 5-hexyn-1-ol with phthalimide in the presence of triphenylphosphine and diethyl azodicarboxylate afforded moderate yields of the 1-phthaloyl-5-hexyne. Further work, however, revealed that higher yields of this intermediate could be achieved using the procedure of Sheehan.[20] Reaction of 1-bromo-5-hexyne with potassium phthalimide in dimethylformamide gave the phthalimide derivative in 87% yield (65% overall from the alkynol).

Attempts to effect hydrazinolysis of the 1-phthaloyl-5-hexyne met with repeated failure, mostly due to problems with isolation of the amine from the crude reaction mixture (see Figure 10). Two procedures were investigated for the hydrazinolysis step. One, described by Sheehan,[20]

calls for refluxing the reaction in methanol while a second, reported by Danishefsky,[21] is performed in the same solvent at room temperature for longer periods of time. Neither produced the amine in acceptable yields (as judged by GC). The product isolation was difficult.

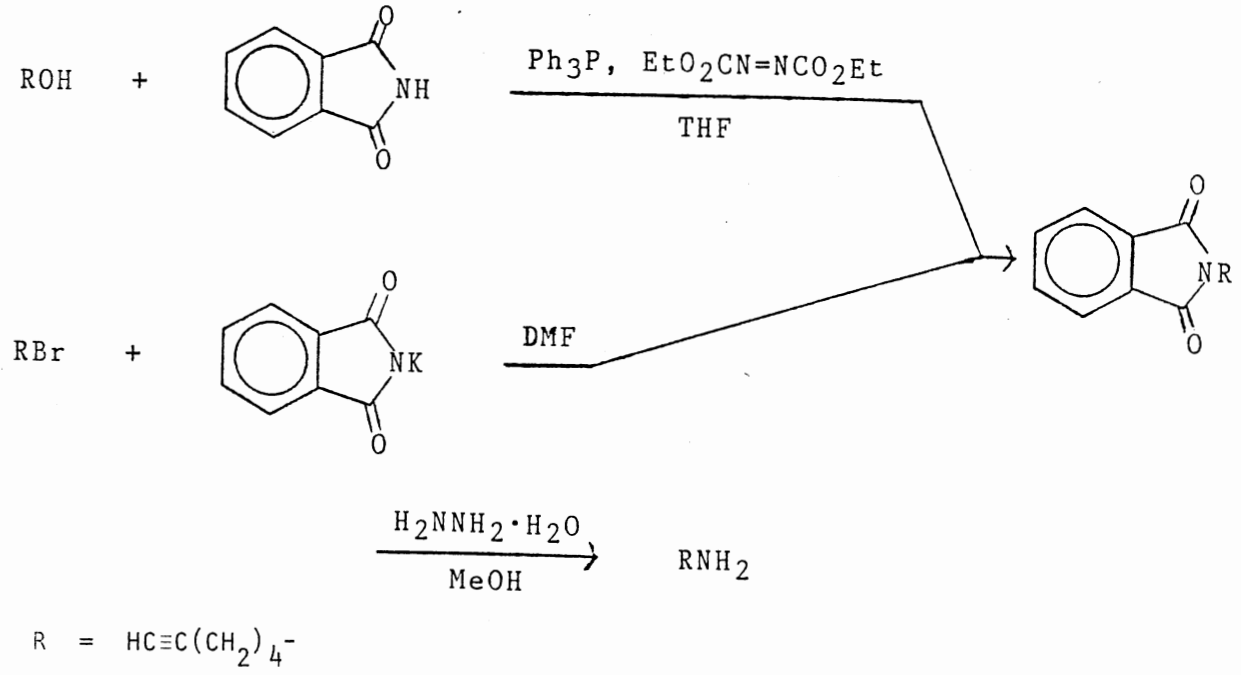


Figure 10. Gabriel Synthesis of 1-Amino-5-hexyne

The second approach explored the possibility of displacing the bromide of 1-bromo-5-hexyne with azide followed by reduction to the amine (see Figure 11). Our initial preparation of the azide revealed that it was best prepared under phase transfer conditions reported by Rolla and used without further purification.[22,23] All attempts to distill or chromatograph the azide resulted in significant decomposition. Azide

reductions have been reported in the literature using sodium borohydride[23] and 1,3-propanedithiol. All attempts to reduce the 5-hexynyl-azide with sodium borohydride gave unacceptably low yields. Reduction with 1,3-propanedithiol failed.

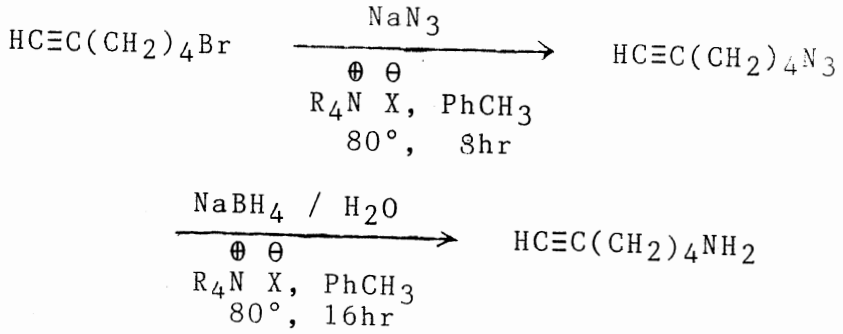


Figure 11. Synthesis of 1-Amino-5-hexyne by Azide Formation and Reduction

The successful route to the required ω-amino-1-alkynes was an adaptation of the Delepine synthesis (see Figure 12).[10] The quaternary hexamminium salts were readily produced from 1-bromo-5-hexyne and 1-bromo-4-pentyne by refluxing with hexamethylenetetramine in chloroform according to the modification of Marszak and Marszak-Fleury.[12,13,14,15] The resulting salts were then hydrolyzed in ethanolic hydrogen chloride to produce the ω-amino-1-alkynes in up to 43% yield from the starting alkynol.

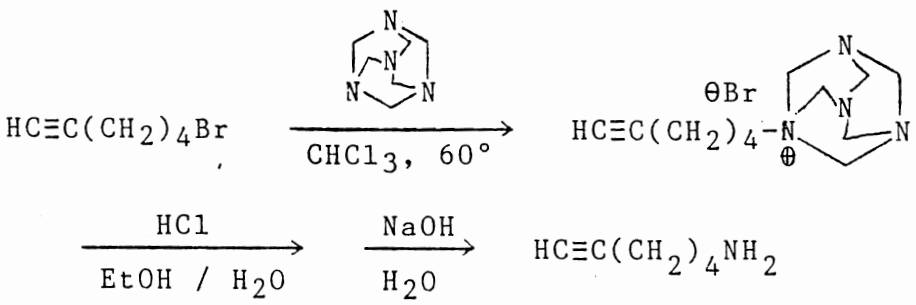


Figure 12. Delepine Synthesis of 1-Amino-5-hexyne

CHAPTER III

EXPERIMENTAL SECTION

All reagents and solvents were used as obtained from commercial suppliers. Melting points were obtained on a Fisher-Johns melting point apparatus and are uncorrected. Infrared spectra, reported in cm^{-1}, were recorded with a PE-681 instrument and are referenced to polystyrene. ^{1}H NMR and ^{13}C NMR spectra were measured in solution in the solvent indicated at 300 MHz, respectively, using a Varian XL-VXR-300 superconducting FT instrument. Spectra are referenced to internal Me_4Si for spectra run in $CDCl_3$ and 3-(trimethylsilyl)-1-propanesulfonic acid sodium salt (TSP) for spectra run in D_2O. Chemical shifts are reported in δ units for ^{1}H and in ppm for ^{13}C relative to these standards. NMR spectral data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant (Hz) and integration (nH). Mass spectra were recorded at 70 eV using a CEC 21-110B double-focusing mass spectrometer with a Data General Nova 3 data handling system. Analytical mass spectral data are reported as calculated, found. Reactions were monitored by TLC on silica gel GF (Analtech No. 02521) or using a Varian 3400 capillary GC (3 m SE-30 column) with FI detection.

1-Methanesulfonyloxy-5-hexyne. A solution of 5.00 g (51.0 mmol) of 5-hexyn-1-ol, 7.73 g (76.5 mmol) of triethylamine and 250 mL of methylene chloride was cooled to 0 ^{o}C and a 10 mL methylene chloride solution of 6.65 g (56.3 mmol) of methanesulfonyl chloride was added dropwise with

stirring. The mixture was allowed to gradually warm to room temperature overnight. The mixture was washed twice with 100 mL of saturated sodium bicarbonate and 100 mL of saturated sodium chloride. The solution was dried over anhydrous sodium sulfate and concentrated under vacuum to give 9.58 g (56.0 mmol, 109%) of the crude mesylate which was used without further purification. The spectral data were: IR (thin film) 3305, 2122, 1355, 1152 cm^{-1}; ^{1}H NMR ($CDCl_3$)δ, 4.32(t, J = 4 Hz, 2 H), 3.06 (s, 3 H), 2.31 (td, J = 6, 2 Hz, 2 H), 1.92 (m, 3 H), 1.69 (m, 2 H); ^{13}C NMR ($CDCl_3$) 83.3, 69.4, 69.0, 37.3, 27.9, 24.2, 17.7 ppm; MS, exact mass calculated for $C_7H_{12}O_3S$, m/e 176.0508, no M^+ was observed.

1-Bromo-5-hexyne. A solution of 8.10 g (40.5 mmol) of calcium bromide monohydrate and 9.50 g (54.0 mmol) of 1-methanesulfonyloxy-5-hexyne in 100 mL of 2-(2-ethoxyethoxy) ethanol was stirred at room temperature. The temperature was slowly increased and the crude product distilled directly from the reaction mixture through a 30 cm Vigreux column (bp 55 - 135 °C). The crude product was added to 10 mL of hexane and extracted three times with 100 mL of water. The organic layer was dried over anhydrous sodium sulfate and concentrated with rotary evaporation. Vacuum distillation afforded 6.96 g (39.3 mmol, 72.8%) of the purified bromide boiling at 63 - 64 °C (15 mm Hg). The spectral data were: IR (thin film) 3295, 2118, 1250 cm^{-1}; ^{1}H NMR ($CDCl_3$)δ, 3.46, (t, J = 6 Hz, 2 H), 2.25 (td, J = 6, 2 Hz, 2 H), 1.98 (m, 3 H), 1.69 (m, 2 H); ^{13}C NMR ($CDCl_3$) 83.5, 65.8, 33.1, 31.5, 26.7, 17.5 ppm; MS, exact mass calculated for C_6H_9Br, m/e 159.9888, found m/e 158.9822.

5-Hexynylhexamminium Bromide. A stirred 60-mL chloroform solution of 14.0 g (100 mmol) of hexamethylenetetramine was brought to reflux and 16.0 g (94.4 mmol) 1-bromo-5-hexyne was added dropwise. The mixture was

heated at reflux for 8 h, then cooled and filtered to give 20.7 g (68.7 mmol, 69.1%) of 5-hexynyl-hexamminium bromide as a white powder, mp. 161 - 163 °C (dec). The spectral data were: IR (nujol) 3330, 2140, 1010 cm^{-1}; ^{1}H NMR (D_2O) δ, 4.80 - 4.50 (m, 12 H), 2.97 (m, 2 H), 2.32 (t, J = 4 Hz, 2 H), 1.87 (m, 3 H), 1.59 (m, 2 H); ^{13}C NMR (D_2O) 84.9, 81.2, 74.6, 72.9, 58.9, 21.3, 18.0 ppm; MS, exact mass calculated for $C_{12}H_{21}BrN_4$, m/e 300.0951, no M^+ was observed.

1-Amino-5-hexyne. A mixture of 20.0 g (66.4 mmol) of 5-hexynylhexamminium bromide, 130 mL of 95% ethanol and 50 mL of concentrated hydrochloric acid was heated at reflux for 20 minutes, then cooled to 0 °C. The precipitated ammonium chloride was filtered and the solution was concentrated to a volume of 70 mL (diethoxymethane removed) under vacuum with rotary evaporation. The above procedure was then repeated using 50 mL of 95% ethanol and 20 mL of concentrated hydrochloride acid. The solution was cooled to 0 °C and carefully neutralized with 200 mL of ice cold 6 N sodium hydroxide keeping the temperature below 40 °C. The solution was then extracted six times with 50 mL of diethyl ether. The ethereal solution was dried over anhydrous sodium sulfate and concentrated under vacuum. The product was distilled at 28 - 29 °C (1 mm Hg) [lit.[13] bp. 50 °C (25 mm Hg)] to give 5.64 g (58.0 mmol, 84.5%) of 5-amino-1-hexyne. The spectral data were: IR (thin film) 3480, 3310, 3324, 2120, 1597, 1073, 885 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ, 2.71 (m, 4 H), 2.00 (d, J = 4 Hz, 2 H), 1.95 (t, J = 2 Hz, 1 H), 1.88 (, 2 H), 1.54 (m, 4 H); ^{13}C NMR ($CDCl_3$) 84.3, 68.5, 41.6, 32.7, 25.8, 18.3 ppm; MS, exact mass calculated for $C_6H_{11}N$, m/e 97,0892, found m/e 97.0888.

1-Methanesulfonyloxy-4-pentyne. A stirred solution of 25.0 g (0.297 mol) of 4-pentyn-1-ol, 45.1 g (0.446 mol) of triethylamine and 500 mL of

methylene chloride was cooled to 0 °C and 37.4 g (0.327 mol) of methanesulfonyl chloride was added. After the addition was complete, the mixture was allowed to stir for 8 h with gradual warming to 20 °C. The mixture was washed twice with 200 mL of ice water and successively with 50 mL of ice cold 10% hydrochloric acid, 200 mL of saturated sodium bicarbonate and 200 mL of saturated sodium chloride. The solution was dried with anhydrous sodium sulfate and concentrated to give 47.6 g (0.294 mol, 99.0%) of the crude mesylate which was used without further purification. The spectral data were: IR (thin film) 3295, 2118, 1355, 1175 cm^{-1}; ^{1}H NMR ($CDCl_3$)δ, 4.38 (t, J = 4 Hz, 2 H), 3.06 (s, 3 H), 2.39 (td, J = 4, 2 Hz, 2 H, 2.08 (t, J = 2 Hz, 1 H), 1.98 (m, 2 H); ^{13}C NMR ($CDCl_3$) 82.3, 69.9, 37.2, 27.8, 14.7 ppm; MS, exact mass calculated for $C_6H_{12}O_3S$, m/e 162.0351, no M^+ was observed.

1-Bromo-4-pentyne. A solution of 200 mL of 2-(2-ethoxyethoxy)ethanol and 65.4 g (0.300 mol) of calcium bromide monohydrate was heated to 110 °C at 16 mm Hg to remove water and volatiles. The solution was cooled to room temperature and 47.6 g (0.294 mol) of 1-methanesulfonyloxy-4-pentyne was added. The reaction mixture was slowly warmed under aspirator vacuum (ca. 20 mm Hg). The crude product distilled directly from the reaction mixture through a 30 cm Vigreux column between 80 - 115 °C. The bromide was purified by redistillation through a 60 cm Vigreux column at 44 - 46 °C (16 mm Hg) [lit. [25] bp. 82 °C (100 mm Hg)] to give 29.5 g (0.201 mol, 68.4%). The spectral data were: IR (thin film) 3296, 2110, 1245 cm^{-1}; ^{1}H NMR ($CDCl_3$)δ, 3.53 (t, J = 6 Hz, 2 H), 2.38 (m, 2 H), 2.02 (m, 3 H); ^{13}C NMR ($CDCL_3$) 82.4, 69.5, 32.2, 31.2, 17.1 ppm; MS exact mass calculated for C_5H_7Br, m/e 145.9731, no M^+ was observed.

4-Pentynylhexamminium Bromide. A stirred 60 mL chloroform solution of 14.0 g (99.9 mmol) of hexamethylenetetramine was brought to reflux

and 14.6 g (99.3 mmol) of 1-boromo-4-pentyne was added dropwise. The reaction mixture was refluxed for 8 h, then cooled to 0 °C and filtered to give 20.3 g (70.8 mmol, 71.3%) of 4-pentynylhexamminium bromide, mp, 161 - 163 °C (dec). The spectral data were: IR (thin film) 3170, 2095, 995 cm^{-1}; ^{1}H NMR (D_2O) δ, 4.80 - 4.50 (m, 12 H), 3.09 (t, J = 6 Hz, 2 H), 1.37 (t, J = 4 Hz, 2 H), 1.97 (m, 3 H); ^{13}C NMR (D_2O) 84.7, 81.1, 74.6, 72.9, 58.9, 18.0 ppm; MS, exact mass calculated for $C_{11}H_{19}BrN_4$, m/e 286.07047, no M^+ was observed.

1-Amino-4-pentyne. A mixture of 20.0 g (69.6 mmol) of 4-pentynylhexamminium bromide, 130 mL of 95% ethanol and 50 mL of concentrated hydrochloric acid was heated at reflux for 20 minutes, then cooled to 0 °C. The precipitated ammonium chloride was filtered and the solution was concentrated to a volume of 80 mL (diethoxymethane removed) under vacuum with rotary evaporation. The above procedure was then repeated using 50 mL of 95% ehtanol and 20 mL of concentrated hydrochloric acid. The solution was cooled to 0 °C and carefully neutralized with 6 N sodium hydroxide keeping the temperature below 40 °C and then extracted six times with 50 mL of diethyl ether. The ethereal solution was dried over anhydrous sodium sulfate and concentrated under vacuum. The product was distilled at 27 - 31 °C (1 mm Hg) [lit.[4,5] bp. 124 °C (760 mm Hg)] to afford 3.16 g (38.0 mmol, 54.6%) of 1-amino-4-pentyne. The spectral data were: IR (thin film) 3360, 3290, 2100, 1595, 1045 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ, 2.80 (t, J = 6 Hz, 2 H), 2.25 (m, 2 H), 1.98 (t, J = 2 Hz, 1 H), 1.79 (S, 2 H), 1.65 (m, 2 H); ^{13}C NMR ($CDCl_3$) 83.9, 68.7, 41.0, 32.1, 15.9 ppm; MS, exact mass calculated for C_5H_9N, m/e 83.0736, found, m/e 83.0735.

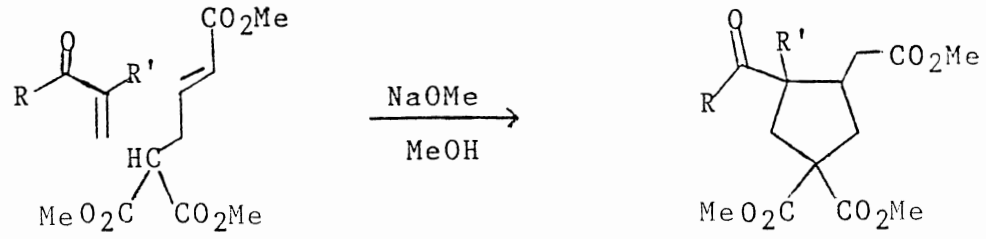
PART II

THIOLS IN THE TANDEM MICHAEL REACTION

CHAPTER IV

INTRODUCTION AND HISTORICAL

Substituted butenoic acids, esters and nitriles are important synthetic compounds due to their diverse functionality. Recently, a tandem Michael reaction has been reported for the synthesis of five-ring carbocycles.[26] The key reagents utilized in this process incorporate both a Michael donor and an acceptor moiety within the same compound. The reaction, formulated in Figure 13, involves deprotonation of the donor portion of the molecule, conjugate addition to an unsaturated carbonyl compound and intramolecular capture of the intermediate anion by the built-in acceptor.



R = Me, Ph; R' = H, Me

Figure 13. Tandem Michael Preparation of Carbocycles

In an attempt to extend this methodology to the synthesis of heterocyclic five-ring compounds, 4-hetero-2-butenoic esters and nitriles were

sought. Review of the literature, showed that the corresponding nitrogen[27] and oxygen[28] compounds were known, but the sulfur derivatives were conspicuously absent from the literature. Recently, two groups have independently reported the syntheses of 4-mercapto-2-butenoic esters.[29, 36,31] These systems are well suited to the tandem Michael process with the thiol as a Michael donor and the acrylate moiety as the acceptor.

Bunce and coworkers utilized a Wittig approach, reacting stabilized carbomethoxymethylene triphenylphosphoranes with 2,5-dihydroxy-1,4-dithiane, the dimer of 2-mercapto-acetaldehyde (see Figure 14).[29] It was previously reported that the monomeric aldehyde could be generated <u>in situ</u> by refluxing the dimer in benzene and utilized in a variety of transformations.[32] Cracking of the dimer in the presence of a stabilized slide affords the mercapto esters in high yield (80 - 85%). To date, this constitutes the most efficient preparation of these compounds. Development of methodology for employing these substrates in the tandem Michael process is the focus of the current study.

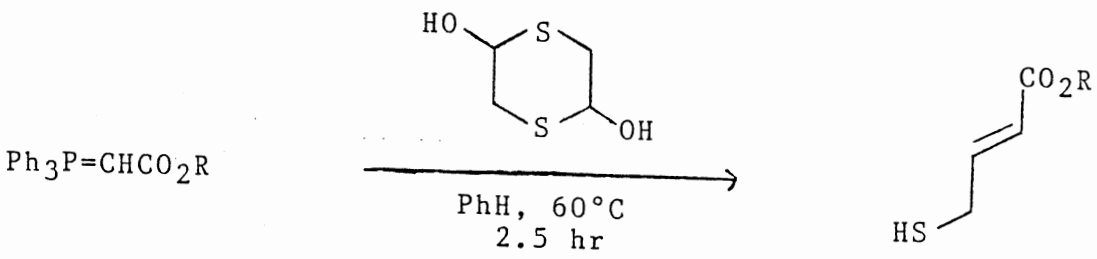


Figure 14. Bunce Synthesis of 4-Mercapto-2-butenoic Esters

Margaretha has prepared 4-mercapto-2-butenoic esters by irradiation of 2(5H)-thiophenone at $\lambda > 300$ nm in alcoholic solution (see Figure 15).[30,31] This method suffers from several disadvantages--the starting thiophenone must be synthesized (70% yield[33]), it requires long irradiation times (12 h) and the yields are generally lower (60 - 70%) than the Bunce procedure. An advantage of the photochemical approach is that a greater variety of mercaptocrotonic esters are accessible since the thiophenone synthesis[33] can be readily adapted to substrates bearing different substitution patterns.

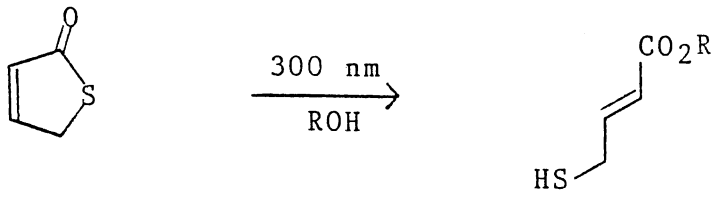


Figure 15. Margeretha Synthesis of 4-Mercapto-2-butenoic Esters

Margaretha has demonstrated that mercapto esters, generated by the photochemical route, can be isolated as pure compounds when they are prepared in alcohol solvents.[30,31] Further irradiation of these mercapto esters in the presence of alkenes results in consecutive photo-induced addition reactions affording tetrahydro-3-thienylacetic esters in a single operation (see Figure 16).[30,31,34,35] Margaretha also succeeded in preparing 2,3-dihydrothiophene-3-carboxylic esters photolytically from 2(5H)-thiophenone and alkynes.[34,35]

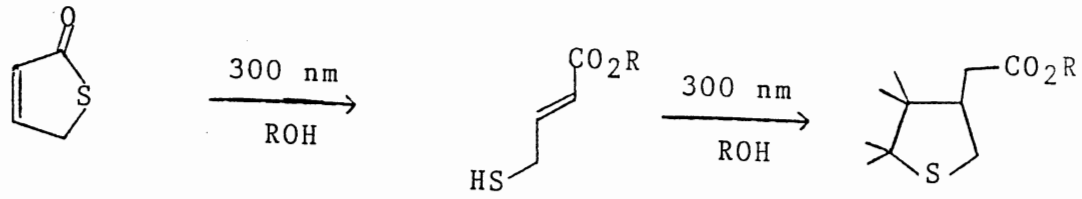


Figure 16. Formation of Tetrahydro-3-thienylacetic Esters by Photolysis of 2(5H)-Thiophenones

The proposed mechanism for the photochemical production of tetrahydrothiophene derivatives from 2(5H)-thiophenones and alkenes is illustrated in Figure 17.[31] Photo excitation of thiophenone 5 results in five membered ring opening to the thio acyl diradical 6. Reaction of this specie with a molecule of the alcohol solvent yields the 4-mercapto-crotonic ester 7. Further irradiation of this initial product generates the alkylthio radical 8 which adds to the alkene, present in the reaction mixture, to form 9. This intermediate then cyclizes on the activated acrylate double bond to afford the stabilized radical 10.[36] Abstraction of H from another molecule of 7 then gives the tetrahydro-3-thientylacetic ester 11.

Finally, Margaretha also explored the use of the Michael reaction for the preparation of tetrahydro-3-thienylacetic esters from the 4-mercapto-2-butenoic esters.[37] Acceptors, investigated with varying degrees of success, have included α,β-unsaturated esters, nitriles and ketones. While some substrates are observed to undergo tandem Michael reaction, most seem to require two steps. To date, there has been no reliable procedure developed to assure that the double Micahel reaction occurs. This will be the focus of future studies using ultrahigh pressure conditions.

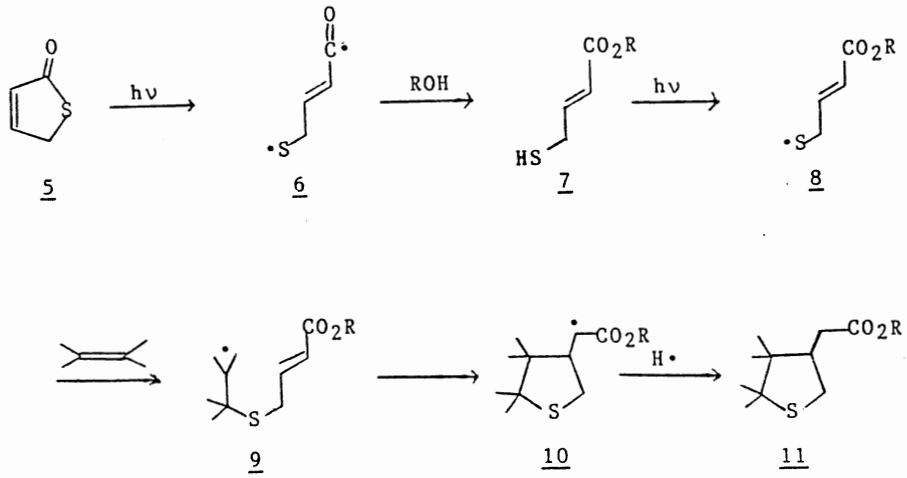


Figure 17. Mechanism for the Photochemical Production of Tetrahydrothiophene Derivatives

CHAPTER V

RESULTS AND DISCUSSION

The synthesis of 3-thienylacetic acid esters should proceed readily from 4-mercaptocrotonic esters and activated Michael acceptors using the tandem Michael procedure (see Figure 18). Margaretha has succeeded in preparing three thienylacetic esters by this route via photochemically generated 4-mercaptocrotonic esters. The process has been successful both as a one-pot and as a two-pot method though it is not easy to predict the success of the second ring-closing conjugate addition.[37]

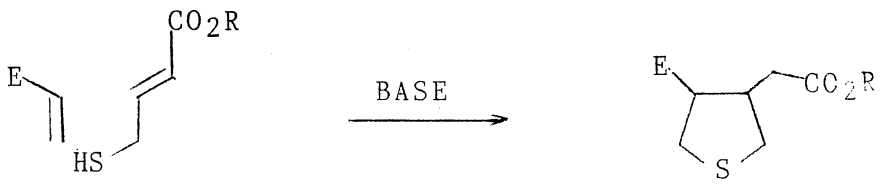


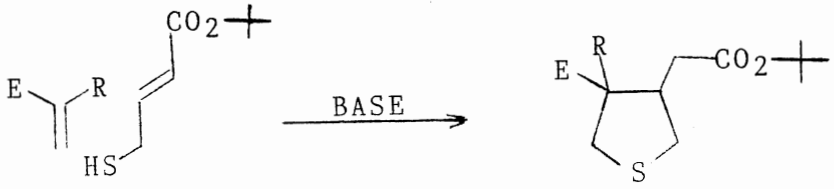
Figure 18. Proposed Reaction Scheme for Synthesis of 3-Thienylacetic Acid Esters

The first step in the preparation of substituted 3-thienylacetic esters from the mercaptocrotonic esters was expected to proceed without difficulty. Thioglycolic acid has been shown to add to α,β-unsaturated aldehydes at pH's as low as 1.5 to give the Michael addition product.[38] Additions promoted by catalytic base have also been demonstrated. It

has been suggested that two major effects govern the addition of the thiolate anion to the acceptor: (1) inhibition of solvation of the thiolate anion which increases its nucleophilicity and (2) steric interactions between the thiolate and the olefin in the transition state.[39] Inhibition of solvation is exploited by using less polar solvents such as benzene and steric hindrance can be minimized through the use of a primary mercaptan and a terminal olefinic Michael acceptor.

In the current work, attempts have been made to induce tandem Michael reactions of tert-butyl 4-mercapto-2-butenoate with several activated alkenes. A variety of bases (1,8-diazabicyclo[5.4.0] undecene-7, DBU; 1,5-diazabicyclo[3.4.0] nonene-5, DBN; tetramethylguanidine, TMG; triethylamine, Et_3N; potassium t - butoxide, KOt-Bu; lithium diisopropylamide, LDA) in several solvents (methanol, chloroform, benzene) were screened using methyl acrylate as the model acceptor system. Under these conditions, good to excellent yields of the Michael adduct were obtained, with DBU in benzene affording a quantitative yield. Other Michael acceptors gave lesser yields. The poorest acceptors proved to be phenyl vinyl ketone and phenyl isopropenyl ketones which gave yields well below 40% regardless of the base or solvent employed. None of the trials produced more than a trace of the desired ring-closed product even under the most stringent of conditions, e.g. lithium diisopropylamide (LDA) in ether at 20 ^{o}C for 14 h (see Figure 19).

Examination of Margaretha's substrates revealed one structural feature which appears to be critical to the success of the second Michael reaction. Acceptors possessing two activating groups on one end of the reacting alkene were observed to undergo successfully the second Michael reaction in a one-pot procedure. Upon initial addition, a highly stabilized carbanion is formed which can then undergo a Michael reaction with



E	R	BASE	SOLVENT	YIELD
MeO_2C	Me	NaOMe	MeOH	60
MeO_2C	H	DBU	PhH	100
MeCO	Me	DBU	PhH	40
MeCO	H	DBU	PhH	72

Figure 19. Michael Reactions With 4-Mercapto-2-butenoate

the built-in acceptor. Thus, it appears that the intermediate donor subunit must have approximately the same pK_a as the thiol (ca. 10-11)[40] for sequential Michael reactions to occur. The monoactivated acceptors utilized in this study yield much less stabilized anions following the initial addition and may pick up a proton (from solvent or the protonated base) faster than they can react. This contrasts with the earlier tandem Michael report.[26,37] An explanation for the failure of LDA to close the ring in a second step requires further control studies. One possible explanation would be that retro-Michael reaction occurs preferentially from the LDA-generated anion of the initial Michael adduct. This would regenerate the stabilized thiolate anion.

This reaction will, in the future, be explored further using ultra-high pressure (15 kilobars, 220,000 psi) conditions to drive the reaction. Pressure has shown great promise in promoting Michael type reactions of hindered substrates.[41] Adducts formed under these conditions have little tendency to undergo retro-Michael reaction since this process has a positive activation volume and would be disfavored at elevated pressures. Furthermore, it has been demonstrated that the addition products, once formed, are stable to purification conditions. Finally, since base strength seems to increase with pressure,[42] the tandem Michael process will likely proceed as a one-pot procedure at 15 Kbar.

CHAPTER VI

EXPERIMENTAL SECTION

All reagents and solvents were used as obtained from commercial suppliers. Synthetic reactions were performed under an atmosphere of dry nitrogen using tert-butyl 4-mercapto-2-butenoate prepared according to the procedure of Bunce.[29] Infrared spectra, reported in cm^{-1}, were recorded with a PE-681 instrument and are referenced to polystyrene. ^{1}H NMR and ^{13}C NMR spectra were measured as solutions in $CDCl_3$ at 300 MHz and 75 MHz, respectively, using a Varian XL-VXR-300 superconducting FT instrument. Chemical shifts are reported in δ units for ^{1}H and ^{13}C relative to internal Me_4Si. NMR spectral data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant (Hz) and integration (nH). Mass spectra were obtained at 70 eV using a CEC 21-110B double focusing mass spectrometer with a Data General Nova 3 data handling system. Analytical mass spectral data are reported as calculated, found. Reactions were monitored by thin layer chromatography on silica gel GF (Analtech No. 02521). Purification of products was carried out by preparative thick layer chromatography on silica gel GF (Analtech No. 02015) using the solvent mixtures noted in each case.

tert-Butyl E-8-Oxo-5-thio-2-nonenoate. A 15 mL benzene solution of 0.18 g (2.5 mmol) of methyl vinyl ketone and 0.47 g (2.5 mmol) of tert-butyl 4-mercapto-2-butenoate was treated with 0.01 g (0.07 mmol) of 1,8-diazabicyclo 5.4.0 undec-7-ene (DBU). The reaction was stirred for 2 h

at 20 °C, then added to 25 mL of water, and extracted three times with 15 mL of ether. The combined ether layers were washed with 15 mL of saturated sodium chloride and dried over anhydrous sodium sulfate, concentrated under vacuum and was purified by preparative thick layer chromatography using 25% ether in hexane as the eluent. The yield of tert-butyl 8-oxo-5-thio-2-nonenoate was 0.44 g (1.8 mmol, 72%). The spectral data were: IR (thin film) 1725, 1715, 1645, 1390, 1367, 1150, 665 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.06 (m, 1 H), 5.78 (m, 1 H), 3.23 - 2.65 (m, 6 H), 2.17 (s, 3 H), 1.48 (s, 5 H), 1.46 (s, 4 H); ^{13}C NMR ($CDCl_3$) 206.5, 165.3, 142.2, 124.8, 80.6, 43.4, 33.2, 30.1, 28.1, 28.1, 24.9 ppm; MS, exact mass calculated for $C_{12}H_{20}O_3S$, m/e 244.1134, found m/e 244.1151.

tert-Butyl 7-Methyl-8-oxo-5-thio-2-nonenoate. A 15 mL benzene solution of 0.21 g (2.5 mmol) of methyl isopropenyl ketone[43] and 0.47 g (2.5 mmol) of tert-butyl 4-mercapto-2-butenoate was treated with 0.01 g (0.07 mmol) of DBU. The reaction was stirred for 2 h at 20 °C, then added to 25 mL of water and extracted three times with 15 mL of ether. The combined ether layers were washed with 15 mL of saturated sodium chloride dried over anhydrous sodium sulfate, concentrated under vacuum and the remaining oil was purified by preparative thick layer chromatography using 25% ether in hexane to give 0.25 g (1.0 mmol, 40%) of tert-butyl 7-methyl-8-oxo-5-thio-2-nonenoate. The spectral data were: IR (thin film) 1727, 1713, 1647, 1393, 1368, 1145, 668 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.06 (m, 1 H), 5.77 (m, 1 H), 3.22-2.40 (m, 5 H), 2.09 (s, 3 H), 1.48 (s, 5 H), 1.46 (s, 4 H), 1.20 (m, 3 H); ^{13}C NMR ($CDCl_3$) 210.5, 165.5, 142.2, 124.9, 80.6, 47.0, 36.2, 35.5, 33.5, 28.1, 28.1, 16.4 ppm; MS, exact mass calculated for $C_{13}H_{22}O_3S$, m/e 258.1291, found m/e 258.1157.

tert-Butyl 7-Methoxycarbonyl-5-thio-2-heptenoate. A 5 mL benzene solution of 50 mg (0.5 mmol) of methyl acrylate and 90 mg (0.5 mmol) of tert-butyl 4-mercapto-2-butenoate was treated with 0.01 g (0.07 mmol) of DBU. The reaction was stirred for 24 h at 20 ^{o}C, then added to 10 mL of water and extracted three times with 10 mL of ether. The combined ether extracts were washed with 10 mL of saturated sodium chloride, dried over anhydrous sodium sulfate, concentrated under vacuum and the product pruified by preparative thick layer chromatography using 25% ether in hexane as the eluent. The yield of tert-butyl 7-methoxycarbonyl-5-thio-2-heptenoate was 0.13 g (0.5 mmol, 100%). The spectral data were: IR (thin film) 1732, 1715, 1645, 1390, 1368, 1145, 670 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.77 (dt, J = 12, 3 Hz, 1 H), 5.80 (d, J = 12 Hz, 1 H), 3.71 (s, 3 H), 3.23-2.55 (m, 6 H), 1.47 (s, 5 H), 1.45 (s, 4 H); ^{13}C NMR ($CDCl_3$) 172.1, 165.2, 142.0, 124.9, 80.6, 51.8, 34.3, 32.8, 28.1, 28.1, 26.0 ppm; MS, exact mass calculated for $C_{12}H_{20}O_4S$, m/e 260.1083, found m/e 260.1072.

tert-Butyl 7-Methoxycarbonyl-5-thio-2-octenoate. A mixture of 50 mg (0.5 mmol) of methyl methacrylate and 90 mg (0.5 mmol) of tert-butyl 4-mercapto-2-butenoate was treated with 1.5 mL of methanolic sodium methoxide prepared by dissolving 80 mg (3.5 mmol) of sodium metal in 100 mL of anhydrous methanol. The reaction was stirred for 3 h at 20 ^{o}C, then added to 15 mL of water and extracted three times with 10 mL of ether. The combined ether extracts were washed with brine, dried over anhydrous sodium sulfate, concentrated under vacuum, and the product was purified by preparative thick layer chromatography using 25% ether in hexane as the eluent. The yield of tert-butyl 7-methoxycarbonyl-5-thio-2-octenoate was 80 mg (0.3 mmol, 60%). The spectral data were: IR (thin film) 1730, 1715, 1645, 1393, 1368, 1145, 665 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ

6.73 (m, 1 H), 5.77 (m, 1 H), 3.68 (s, 3 H), 3.22-2.47 (m, 5 H), 1.48 (s, 2 H), 1.46 (s, 7 H), 1.23 (m, 3 H); ^{13}C NMR ($CDCl_3$) 175.4, 170.4, 170.4, 142.1, 124.9, 80.6, 51.9, 40.0, 43.4, 33.2, 28.1, 28.1, 16.8 ppm; MS, exact mass calculated for $C_{13}H_{22}O_4S$, m/e 274.1240, found m/e 274.1091.

PART III

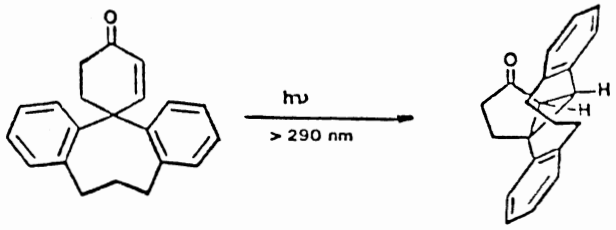
STRUCTURAL DETERMINATION OF [3a*S*-(3a*R**, 14b*R**, 14c*R**)]-(±)-2,3,9,10,14b,14c-HEXAHYDROBENZO[*a*.*e*]CYCLOPENTA[1,3]CYCLOPROPA[1,2-*c*]CYCLONONEN-1(8*H*)-ONE

CHAPTER VII

STRUCTURAL DETERMINATION OF [3a*S*-(3a*R**, 14b*R** 14c*R**)]- (±)-2,3,9,10,14b,14c-HEXAHYDROBENZO[*a*.*e*]CYCLOPENTA[1,3]CYCLOPROPA[1,2-*c*]CYCLONONEN-1(8*H*)-ONE

Introduction

The title compound, 13, was prepared by photolysis of 12 through Pyrex using a 450 W medium pressure Hanovia lamp with *tert*-butanol as the solvent (see Figure 19).[43] Bunce has shown that the C1-C2 bond of 13 (see Figure 20) is specifically cleaved in a lithium-liquid ammonia reduction. He offered this as proof that this is the most strained bond in the cyclopropyl ring of 13. In the following crystallographic study, additional supporting data for Bunce's hypothesis will be shown.



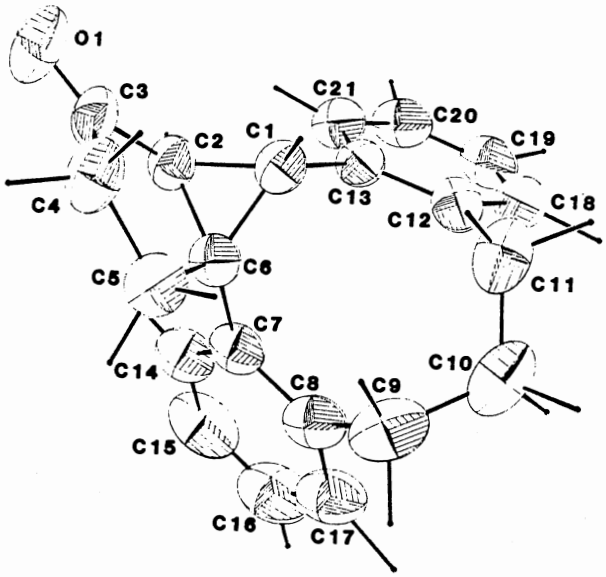


Figure 21. ORTEP Drawing of 13

Results and Conclusions

From the ORTEP drawing, it can be seen that the cyclopentanone ring is cis to the cyclopropane ring while the cyclononyl ring is joined trans to the cyclopropyl ring.[44] The cyclopropyl ring has an average bond angle of 60° (2) and an average bond distance of 1.55(1) which is longer than a C-C bond in cyclopropane[43] by 0.04 Å showing the whole ring is strained more than normal. The C1-C2 bond is 1.58(1) which is somewhat longer than an average cyclopropyl ring bond suggesting this bond is somewhat electron deficient making it much more susceptible to lithium-liquid ammonia reductions as Bunce found experimentally.[44]

Another interesting feature of this molecule is the C6-C7, C2-C3, and the C1-C13 bonds which are slightly shorter than an average carbon-carbon bond (observed 1.49(1) Å, expected 1.53(1) Å) possibly due to the increased 5 characters of these bonds by interaction with the cyclopropyl ring. This would shorten the C2-C3 and C1-C13 bonds by giving them some double bond character.

Crystallographic data including positional parameters anistropic thermal parameters, bond distances, and bond angles are presented in Tables I - V, respectively. There are two molecules of 13 in the asymmetric unit; one molecule is labeled O1, C1, C2 - C21, while the other molecule is labeled O91, C91, C92-C921.

Experimental

A crystal of $C_{21}H_{20}O$, 13, was mounted on a Syntex P3 automated diffractometer. Unit cell dimensions (Table I) were determined by least squares refinement of the best angular positions for fifteen independent reflections ($2\theta > 15^{o}$) during normal alignment procedures using molybdenum radiation ($\lambda = 0.71069\text{Å}$). Data, (8604 points), were collected at room temperature using a variable scan rate, a $\theta - 2\theta$ scan mode and a scan width of 1.2 below $K\alpha_1$ and 1.2 above $K\alpha_2$ to a maximum 2θ value of 60.0^{o}. Backgrounds were measured at each side of the scan for a combined time equal to the total scan time. The intensities of three standard reflections were remeasured after every 97 reflections and as the intensities of these reflections showed less than 6% variation, corrections for decomposition were deemed unnecessary. Data were corrected for Lorentz, polarization and background effects. After removal of redundant and space group forbidden data, 2113 points were considered observed, ($I > 3.0\ \sigma(I)$). The structure was solved using MULTAN to locate the atom positions.[45] Least squares refinement followed by a difference Fourier synthesis allowed location of the hydrogen atom positions.

Refinement of scale factor, positional and anisotropic thermal parameters for all non-hydrogen atoms was carried out to convergence. Hydrogen atom positions and assigned isotropic thermal parameters were included

in the final cycles of refinement but were held fixed.[47] Unit weights were used until the final cycles of refinement when a weight = $1/\sigma F$ was introduced. $R = 8.7\%$; $R_w = 10.7\%$. The final cycle of refinement - [function minimized, see Equation 1],

$$R_w = \Sigma(|F_o| - |F_c|)^2 \quad (1)$$

led to a final agreement factor of 8.7% [see Equation 2].

$$R = \Sigma(|F_o| - |F_c|)/\Sigma|F_o| \times 100 \quad (2)$$

TABLES OF CRYSTALLOGRAPHIC DATA

TABLE I

CRYSTAL DATA FOR [3aS-(3aR*, 14bR*, 14cR*)](±)2,3,9,10,14b,14c-HEXAHYDRODIBENZO[a.e]CYCLOPENTA[1,3]CYCLOPROPA-[1,2-c]CYCLONONEN-1(8H)-ONE (13)

Formula	$C_{21}H_{20}O$
MWT	288.4
a	20.679(8)Å
b	15.422(9)
c	9.777(2)
α	90°
β	91.15(3)
γ	90
V	3117.4(23)Å^3
F(000)	1232
μMoKα	0.685 cm^{-1}
λMoKα	0.71069Å
D_{calc}	1.229 g cm^{-3}
Z	8
Obs. refl.	2113
R/R_w	8.7/10.7%
Space group	$P2_1/c$

TABLE II

POSITIONAL PARAMETERS FOR [2aS-(3aR*, 14bR*, 14cR)](±)2,3,9,10, 14b, 14c-HEXAHYDRODIBENZO[a.e]CYCLOPENTA[1,3]CYCLOPROPA [1,2-c]CYCLONONEN-1(8H)-ONE (13)

ATOM	X(SIG(X))	Y(SIG(Y))	Z(SIG(Z))
O1	0.1253(3)	0.5663(4)	0.8221(8)
C1	0.1989(4)	0.3593(5)	0.9034(9)
C2	0.2032(4)	0.4616(5)	0.8933(9)
C3	0.1635(4)	0.5101(6)	0.7918(10)
C4	0.1805(4)	0.4826(6)	0.6473(9)
C5	0.2333(4)	0.4124(5)	0.6628(8)
C6	0.2498(4)	0.4016(5)	0.8162(8)
C7	0.3172(4)	0.3814(5)	0.8627(9)
C8	0.3446(4)	0.2979(6)	0.8361(9)
C9	0.3104(4)	0.2306(6)	0.7466(9)
C10	0.2817(4)	0.1553(6)	0.8253(11)
C11	0.2245(4)	0.1776(5)	0.9190(9)
C12	0.1633(4)	0.2118(6)	0.8461(8)
C13	0.1485(4)	0.3008(5)	0.8412(8)
C14	0.3533(4)	0.4427(6)	0.9376(9)
C15	0.4141(4)	0.4229(6)	0.9897(9)
C16	0.4399(4)	0.3411(7)	0.9850(10)
C17	0.4050(4)	0.2803(6)	0.8900(10)
C18	0.1197(4)	0.1516(6)	0.7868(10)
C19	0.0630(4)	0.1797(6)	0.7253(9)
C20	0.0465(4)	0.2658(6)	0.7233(9)
C21	0.0891(4)	0.3260(6)	0.7824(9)
O91	0.5511(4)	-0.0530(4)	0.3327(8)
C91	0.6031(4)	0.1619(5)	0.3970(8)
C92	0.5484(4)	0.0971(5)	0.3938(8)
C93	0.5512(4)	0.0217(6)	0.2976(11)
C94	0.5492(4)	0.0523(7)	0.1495(10)
C95	0.5466(5)	0.1528(6)	0.1532(9)
C96	0.5445(4)	0.1790(5)	0.3051(8)
C97	0.5068(4)	0.2590(6)	0.3415(9)
C98	0.5314(4)	0.3404(6)	0.3067(9)
C99	0.5916(4)	0.3536(5)	0.2246(9)
C910	0.6520(4)	0.3850(5)	0.3046(9)
C911	0.6805(4)	0.3215(5)	0.4085(8)
C912	0.7060(4)	0.2371(5)	0.3459(8)
C913	0.6707(4)	0.1585(5)	0.3410(7)
C914	0.4508(4)	0.2521(6)	0.4199(10)
C915	0.4188(4)	0.3254(8)	0.4605(11)
C916	0.4421(5)	0.4077(8)	0.4233(11)
C917	0.4969(5)	0.4140(6)	0.3462(10)
C918	0.7684(4)	0.2373(6)	0.2912(9)

TABLE II (Cont'd.)

ATOM	X(SIG(X))	Y(SIG(Y))	Z(SIG(Z))
C919	0.7955(4)	0.1630(6)	0.2389(9)
C920	0.7621(4)	0.0856(6)	0.2432(9)
C921	0.6991(4)	0.0849(5)	0.2914(8)
H1	0.2103	0.3316	0.9867
H2	0.2150	0.4820	1.0000
H3	0.1967	0.5318	0.5964
H4	0.1427	0.4591	0.6001
H5	0.2175	0.3571	0.6255
H6	0.2716	0.4301	0.6145
H7	0.2794	0.2665	0.6769
H8	0.3433	0.2136	0.6571
H9	0.2642	0.1116	0.7356
H10	0.3156	0.1039	0.8610
H11	0.2307	0.1858	1.0471
H12	0.2100	0.1100	0.9455
H13	0.3300	0.5132	0.9607
H14	0.4384	0.4653	1.0427
H15	0.4802	0.3337	1.0268
H16	0.4237	0.2235	0.8752
H17	0.1384	0.0828	0.7869
H18	0.0412	0.1379	0.6676
H19	0.0000	0.2868	0.6802
H20	0.0773	0.3869	0.7826
H91	0.6038	0.1936	0.5088
H92	0.5225	0.0780	0.4825
H93	0.5876	0.0331	0.1029
H94	0.5110	0.0295	0.1026
H95	0.5081	0.1736	0.1053
H96	0.5846	0.1770	0.1113
H97	0.6022	0.2986	0.1822
H98	0.5817	0.3961	0.1542
H99	0.6805	0.4046	0.2192
H910	0.6404	0.4382	0.3663
H911	0.6471	0.3066	0.4727
H912	0.7160	0.3499	0.4568
H913	0.4348	0.1954	0.4454
H914	0.3801	0.3205	0.5146
H915	0.4198	0.4597	0.4519
H916	0.5151	0.4897	0.3254
H917	0.7921	0.2996	0.2902
H918	0.8381	0.1651	0.1990
H919	0.7822	0.0327	0.1953
H920	0.6722	0.0240	0.2955

TABLE III

ANISOTROPIC THERMAL PARAMETERS FOR [3aS-(3aR*, 14bR*, 14cR*)]-(±)2,3,9,10,14b,14c-HEXAHYDRODIBENZO[a.e]CYCLOPENTA-[1,3]CYCLOPRPPA[1,2-c]CYCLONONEN-1(8H)-ONE (13)

ATOM	U11	U22	U33	U12	U13	U23
O1	82(5)	64(4)	122(6)	32(4)	-15(4)	- 5(4)
C1	38(4)	25(4)	54(5)	- 2(3)	0(4)	-12(4)
C2	38(5)	41(5)	53(5)	- 9(4)	- 3(4)	1(4)
C3	53(6)	39(5)	80(7)	- 2(4)	-21(5)	6(5)
C4	68(6)	55(6)	44(5)	4(5)	-20(4)	13(4)
C5	71(6)	34(5)	41(5)	0(4)	0(4)	6(4)
C6	39(4)	24(4)	44(5)	- 1(3)	- 5(4)	-10(4)
C7	42(5)	43(5)	44(5)	- 9(4)	4(4)	3(4)
C8	46(5)	42(5)	54(6)	5(4)	11(4)	9(4)
C9	61(6)	47(5)	54(6)	11(4)	10(4)	- 5(4)
C10	53(6)	34(5)	106(8)	0(4)	2(5)	- 5(5)
C11	59(6)	42(5)	61(6)	1(4)	3(4)	20(4)
C12	47(5)	51(5)	41(5)	- 7(4)	13(4)	2(4)
C13	55(5)	34(5)	28(4)	2(4)	4(4)	- 4(3)
C14	40(5)	46(5)	48(5)	-11(4)	3(4)	11(4)
C15	53(6)	63(6)	52(6)	- 7(5)	- 5(4)	12(5)
C16	42(5)	86(7)	60(6)	0(5)	-10(4)	13(5)
C17	40(5)	56(6)	81(7)	18(4)	13(5)	4(5)
C18	49(5)	50(6)	68(6)	- 4(4)	7(4)	- 4(5)
C19	55(5)	49(5)	65(6)	-27(4)	8(5)	-10(5)
C20	44(5)	76(7)	43(5)	-15(5)	- 4(4)	4(5)
C21	47(5)	55(6)	52(6)	15(4)	4(4)	- 3(4)
O91	121(6)	38(3)	105(6)	-17(4)	31(4)	-10(3)
C91	35(4)	45(5)	33(4)	2(4)	2(3)	- 1(4)
C92	46(5)	38(5)	51(5)	- 1(4)	10(4)	16(4)
C93	52(5)	39(5)	83(7)	-14(4)	17(5)	- 6(5)
C94	57(6)	68(7)	61(7)	-10(5)	-11(5)	-10(5)
C95	72(6)	54(6)	52(6)	-12(5)	- 3(5)	- 8(5)
C96	43(5)	41(5)	37(5)	-10(4)	8(4)	2(4)
C97	36(5)	47(5)	50(5)	- 6(4)	- 5(4)	1(4)
C98	50(6)	50(6)	60(6)	6(4)	-11(4)	- 1(5)
C99	60(6)	43(5)	56(6)	-12(4)	- 4(4)	11(4)
C910	62(6)	38(5)	53(6)	- 3(4)	6(4)	3(4)
C911	62(6)	42(5)	39(5)	-20(4)	3(4)	- 6(4)
C912	57(5)	48(5)	26(4)	3(4)	- 7(4)	- 3(4)
C913	44(4)	35(4)	22(4)	- 3(4)	- 2(3)	0(3)
C914	35(5)	63(6)	73(7)	2(5)	-12(5)	- 9(5)
C915	31(5)	94(8)	83(8)	18(6)	-21(5)	- 1(7)
C916	71(7)	85(8)	82(8)	25(7)	-12(6)	-27(7)
C917	72(6)	49(6)	68(7)	11(5)	-20(5)	- 6(5)
C918	40(5)	66(6)	48(5)	-11(5)	0(4)	- 4(5)
C919	51(5)	75(7)	39(5)	- 1(5)	0(4)	0(5)

TABLE III (Cont'd.)

ATOM	U11	U22	U33	U12	U13	U23
C920	42(5)	67(6)	54(6)	3(4)	0(4)	1(5)
C921	54(5)	44(5)	38(5)	0(4)	0(4)	- 9(4)

Anisotropic parameters are in the form:

$$\exp(-2\pi^2(U_{11}h^2a^{*2} + U_{22}k^2b^{*2} + U_{33}l^2c^{*2} + 2U_{12}hka^*b^*$$

$$+ 2U_{13}hla^*c^* + 2U_{23}klb^*c^*)) \times 10^3$$

TABLE IV

BONDING DISTANCES FOR [3a*S*-(3a*R**, 14b*R**, 14c*R**)](±)2,3,9,10, 14b, 14c-HEXAHYDRODIBENZO[*a*.*e*]CYCLOPENTA[1,3]CYCLOPROPA-[1,2-*c*]CYCLONONEN-1(8H)-ONE (13)

ATOM1	ATOM2	DISTANCE(SIG)
O1	C3	1.21(1)
C1	C2	1.58(1)
C1	C6	1.52(1)
C1	C13	1.50(1)
C2	C3	1.48(1)
C2	C6	1.54(1)
C3	C4	1.52(1)
C4	C5	1.54(1)
C5	C6	1.54(1)
C6	C7	1.49(1)
C7	C8	1.43(1)
C7	C14	1.40(1)
C8	C9	1.52(1)
C8	C17	1.37(1)
C9	C10	1.52(1)
C10	C11	1.55(1)
C11	C12	1.53(1)
C12	C13	1.41(1)
C12	C18	1.41(1)
C13	C21	1.40(1)
C14	C15	1.38(1)
C15	C16	1.39(1)
C16	C17	1.39(1)
C18	C19	1.38(1)
C19	C20	1.37(1)
C20	C21	1.40(1)
O91	C93	1.20(1)
C91	C92	1.51(1)
C91	C96	1.52(1)
C91	C913	1.51(1)
C92	C93	1.50(1)
C92	C96	1.53(1)
C93	C94	1.52(1)
C94	C95	1.55(1)
C95	C96	1.54(1)
C96	C97	1.51(1)
C97	C98	1.40(1)
C97	C914	1.41(1)
C98	C99	1.51(1)
C98	C917	1.40(1)
C99	C910	1.53(1)
C910	C911	1.52(1)

TABLE IV (Cont'd.)

ATOM1	ATOM2	DISTANCE(SIG)
C911	C912	1.54(1)
C912	C913	1.42(1)
C912	C918	1.41(1)
C913	C921	1.37(1)
C915	C915	1.37(2)
C915	C916	1.41(2)
C916	C917	1.38(2)
C918	C919	1.38(1)
C919	C920	1.38(1)
C920	C921	1.39(1)

TABLE V

BOND ANGLES FOR [3aS-(3aR*, 14bR*, 14cR*)](±)2,3,9,10,14b,14c-HEXAHYDRODIBENZO[a.e]CYCLOPENTA[1,3]CYCLOPROPA-[1,2-c]CYCLONONEN-1(8H)-ONE (13)

ATOM1	ATOM2	ATOM3	ANGLE
C2	C1	C6	59.7(5)
C2	C1	C13	128.0(7)
C6	C1	C13	121.1(7)
C1	C2	C3	121.0(7)
C1	C2	C6	58.0(5)
C3	C2	C6	108.6(7)
O1	C3	C2	123.5(9)
O1	C3	C4	126.1(9)
C2	C3	C4	110.3(7)
C3	C4	C5	106.3(7)
C4	C5	C6	108.3(7)
C1	C6	C2	62.3(5)
C1	C6	C5	116.9(7)
C1	C6	C7	113.2(7)
C2	C6	C5	106.5(6)
C2	C6	C7	124.4(7)
C5	C6	C7	120.4(7)
C6	C7	C8	120.2(7)
C6	C7	C14	120.3(7)
C8	C7	C14	119.5(7)
C7	C8	C9	122.3(7)
C7	C8	C17	118.0(8)
C9	C8	C17	119.6(8)
C8	C9	C10	114.3(8)
C9	C10	C11	116.2(7)
C10	C11	C12	115.7(7)
C11	C12	C13	121.9(7)
C11	C12	C18	118.6(8)
C13	C12	C18	119.4(7)
C1	C13	C12	115.2(7)
C1	C13	C21	126.5(7)
C12	C13	C21	118.3(7)
C7	C14	C15	121.0(8)
C14	C15	C16	119.1(8)
C15	C16	C17	120.5(8)
C8	C17	C16	122.0(8)
C12	C18	C19	120.3(8)
C18	C19	C20	121.4(8)
C19	C20	C21	118.9(8)
C13	C21	C20	121.7(8)
C92	C91	C96	60.9(5)

TABLE V (Cont'd.)

ATOM1	ATOM2	ATOM3	ANGLE
C92	C91	C913	131.9(7)
C96	C91	C913	121.6(6)
C91	C92	C93	119.2(7)
C91	C92	C96	59.8(5)
C93	C92	C96	106.8(7)
O91	C93	C92	124.4(9)
O91	C93	C94	124.6(9)
C92	C93	C94	110.8(7)
C93	C94	C95	106.7(8)
C94	C95	C96	106.6(7)
C91	C96	C92	59.3(5)
C91	C96	C95	119.2(7)
C91	C96	C97	114.5(7)
C92	C96	C95	109.1(7)
C92	C96	C97	124.2(7)
C95	C96	C97	117.8(7)
C96	C97	C98	119.0(7)
C96	C97	C914	120.2(8)
C98	C97	C914	120.6(8)
C97	C98	C99	124.0(8)
C97	C98	C917	118.1(8)
C99	C98	C917	117.9(8)
C98	C99	C910	116.2(8)
C99	C910	C911	115.8(7)
C910	C911	C912	114.3(7)
C911	C912	C913	123.9(7)
C911	C912	C918	117.8(8)
C913	C912	C918	118.4(8)
C91	C913	C912	116.0(7)
C91	C913	C921	124.2(7)
C912	C913	C921	119.8(7)
C97	C914	C915	120.2(9)
C914	C915	C916	119.8(9)
C915	C916	C917	119.6(10)
C98	C917	C916	121.6(9)
C912	C918	C919	121.5(8)
C918	C919	C920	120.0(8)
C919	C920	C921	119.2(8)
C913	C921	C920	121.6(8)

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