LONG-RANGE HYPERFINE SPLITTING IN BICYCLIC SEMIDIONES

by

George William Holland, Jr.

A Dissertation Submitted to the
Graduate Faculty in Partial Fulfillment of
The Requirements for the Degree of
DOCTOR OF PHILOSOPHY

Major Subject: Organic Chemistry

Approved:

Signature was redacted for privacy.

In Charge of Major Work

Signature was redacted for privacy.

Head of Major Department

Signature was redacted for privacy.

Dean of Graduate College

Iowa State University
Of Science and Technology
Ames, Iowa

1969

TABLE OF CONTENTS

INTRODUCTION

The Electron Spin Resonance Experiment

The net magnetic moment of most stable organic molecules is zero owing to the fact that the electrons in the molecule are aligned with their spins opposed to one another. A free radical has a net, measurable magnetic moment because of its unpaired electron. In the electron spin resonance (esr) experiment a powerful external magnetic field is applied and the energy change detected when the spin of the unpaired electron flips, i.e., changes from being "aligned with" to "opposed to" the applied magnetic field. This energy change is recorded as an absorption peak. All esr spectra of radicals would be very similar were it not for the interaction of the unpaired electron with nuclei within the molecule. Only those nuclei which possess a nuclear spin cause a visual change in the spectrum. This change comes in the form of additional absorption lines; a phenomenon known as hyperfine splitting.

At first glance the esr spectra obtained from many organic free radicals appear to be an uninterpretable jumble. However, after some basic principles are learned, the hours of frustration that plague the beginner mellow and the analysis becomes a continual source of entertainment. Perhaps the two most complicating factors are that esr spectra are recorded as a first derivative and that hyperfine splitting lines are symmetrically distributed about the center of the spectrum. Magnetically non-equivalent nuclei manifest themselves in the size of the hyperfine

splittings. The discussion that follows is strictly true only for first order esr spectra and second order effects will be neglected.

In the absence of interacting nuclei the esr spectrum of a radical appears as a single line with a Lorentzian lineshape. When interaction with nuclei possessing nuclear spin occurs, this single line splits into 2nI+1 lines where n is the number of magnetically equivalent nuclei of nuclear spin I. The most important nuclei associated with organic radicals are H, C^{13}, and F^{19} with I = 1/2, N and H^2 with I = 1, and O^{17} with I = 5/2. If, for example, the radical interacted with one nucleus of spin 1/2, then the single line (Figure 1-a) will be divided into a two line pattern (Figure 1-b). A three line spectrum is observed with interaction of two magnetically equivalent nuclei of spin 1/2 (Figure 1-c) or with one nucleus of spin 1 (Figure 1-d).

The splitting constant, a^n, is extracted by measuring the distance, in gauss, separating the neighboring lines of a related group and is a measure of the amount of interaction of the nucleus with the unpaired electron. A hydrogen atom (H·), where the unpaired electron can reside around only one nucleus, shows hyperfine splitting of 500 gauss while a methyl radical (CH_3·), where the electron can interact with four nuclei but resides mainly around the carbon nucleus, shows hyperfine splitting by hydrogen of only 23 gauss.

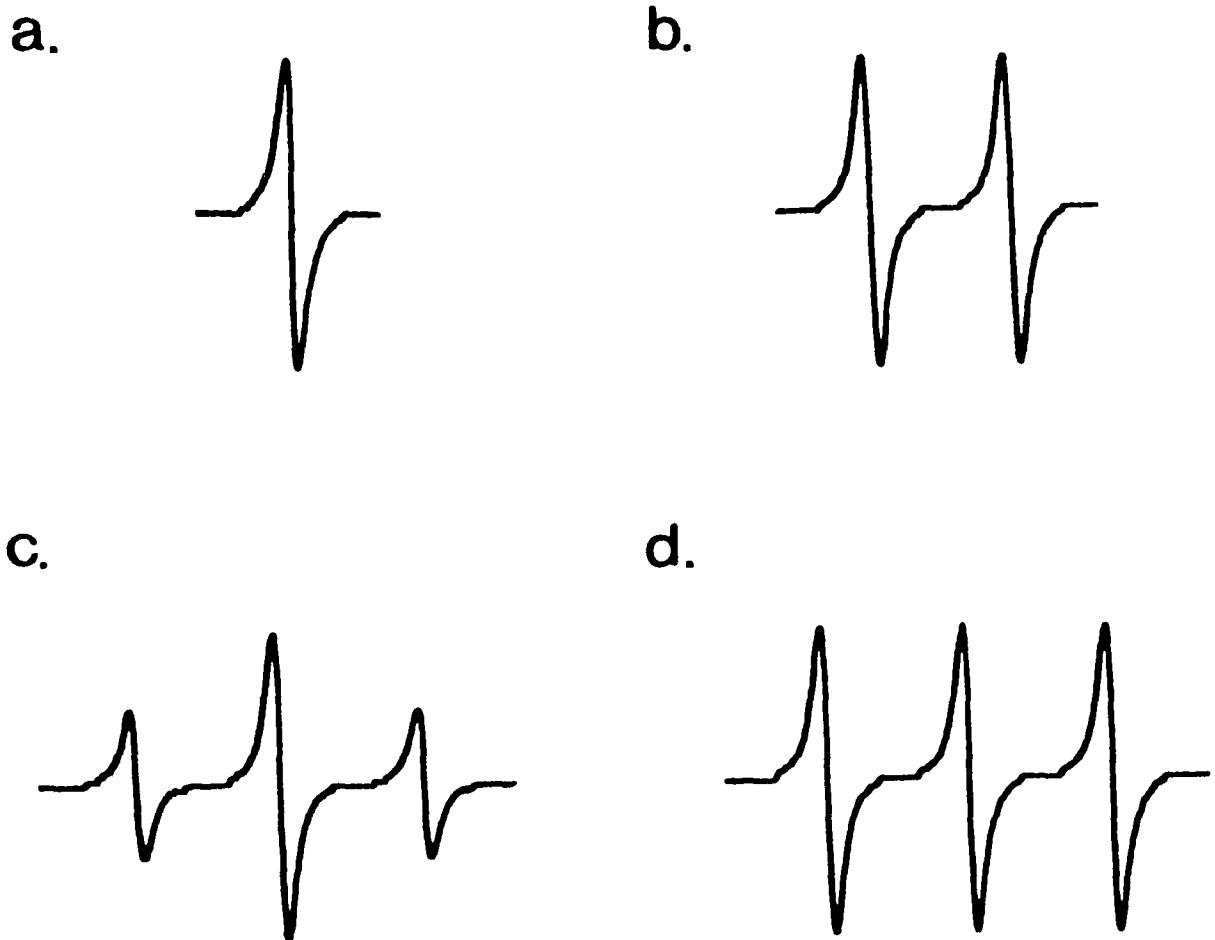


Figure 1. First derivative esr spectrum of a radical (a) in the absence of significant interaction with nuclei possessing a nuclear spin; (b) with interaction with one nucleus of spin 1/2; (c) with interaction with two magnetically equivalent nuclei of spin 1/2 and, (d) with interaction with one nucleus of spin 1.

A nucleus has 2I+1 possible orientations in a magnetic field. For a nucleus of spin 1/2 these spin states are referred to as α and β (+1/2 and -1/2), and since they are equally probable, give rise to the 1:1 doublet in Figure 1-b. The 1:1:1 triplet arises from three equally probable spin states for a nucleus of spin 1 (+1, 0, -1). Four combinations of spin states are possible ($\alpha\alpha$, $\alpha\beta$, $\beta\alpha$, $\beta\beta$) for the two spin systems of Figure 1-c. The $\alpha\beta$ and $\beta\alpha$ combinations are degenerate and thus give a 1:2:1 triplet. In general, the number of lines for a magnetically equivalent group of nuclei is given by 2nI+1. The intensities for nuclei of spin 1/2 vary as the coefficients of a binomial expansion. A more convenient approach is <u>via</u> the so-called "magic triangles" which are generated by adding neighboring numbers in a row and placing the sums in a row below those numbers (see Figure 2).

An esr spectrum is a composite of groups of lines from each magnetically nonequivalent group of nuclei with the maximum numbers of lines given by $\pi(2I+1)^n$. It often occurs that the theoretical number of lines is not realized due to fortuitous magnetic equivalence, but not always chemical equivalence, of interacting nuclei.

The total area under the absorption peak is dependent upon the radical concentration and perturbation by hyperfine splitting cannot alter this. Directly related to area is line height (intensity), and in the absence of line broadening or overlap

a.

n											
0						1					
1					1		1				
2				1		2		1			
3			1		3		3		1		
4		1		4		6		4		1	
5	1		5		10		10		5		1

b.

n								
0				1				
1			1	1	1			
2		1	2	3	2	1		
3	1	3	6	7	6	3	1	

Figure 2. Line intensities of groups of magnetically equivalent nuclei with (a) I=1/2, and (b) I=1.

with other peaks in the spectrum, its measurement provides an acceptable means to estimate the relative amounts of radicals present in a mixture.

Correlation diagrams are often employed to aid in the analysis of esr spectra. The diagram is constructed by systematically introducing the hyperfine splitting of the various nuclei, normally commencing with the largest and adding in descending order. The spectrum in Figure 3 is obtained by the oxidation of isophorone in basic dimethyl sulfoxide solution. Visual inspection of the spectrum reveals a 5.4 gauss quartet which is diagramed in Figure 3-a. The 4.75 gauss doublet is then added (Figure 3-b). Finally, a 1.75 gauss triplet completes the twenty-four line diagram in which each line corresponds to a line in the spectrum.

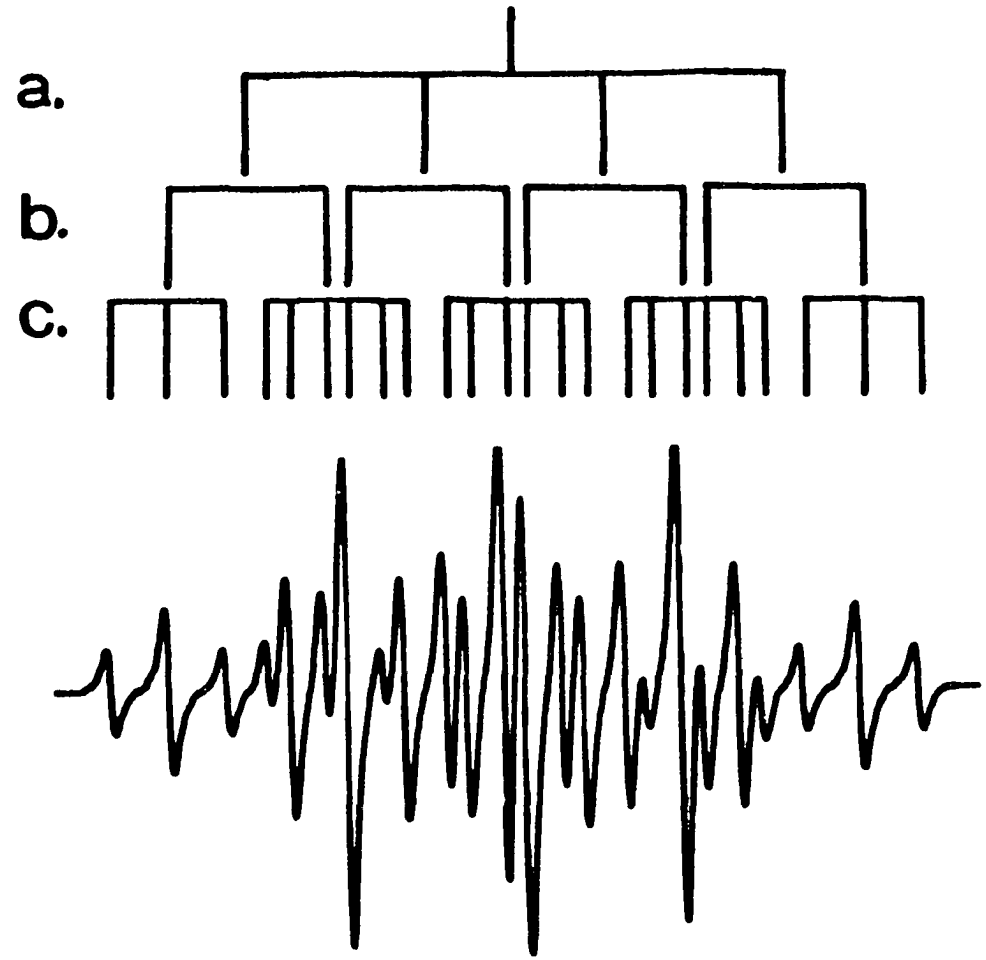
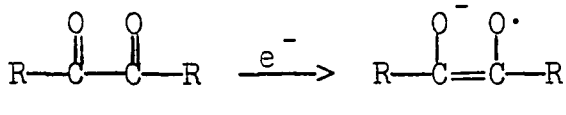
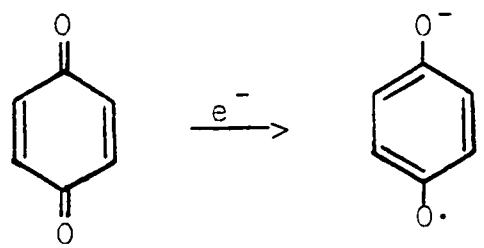


Figure 3. The construction of a correlation diagram in which a (a) 5.4 G quartet is added followed by (b) the 4.75 G doublet and finally (c) a 1.75 G triplet.

Brief Introduction to Semidiones

It has long been known that oxygen reacts at room temperature with some of the Group I and II metals to form dark-colored materials which contain the paramagnetic superoxide ion, $O_2^{\cdot -}$. The one electron reduction of an α-diketone produces the vinylog of the superoxide ion and is termed a semidione. Likewise, the one electron reduction of a quinone produces a semiquinone,



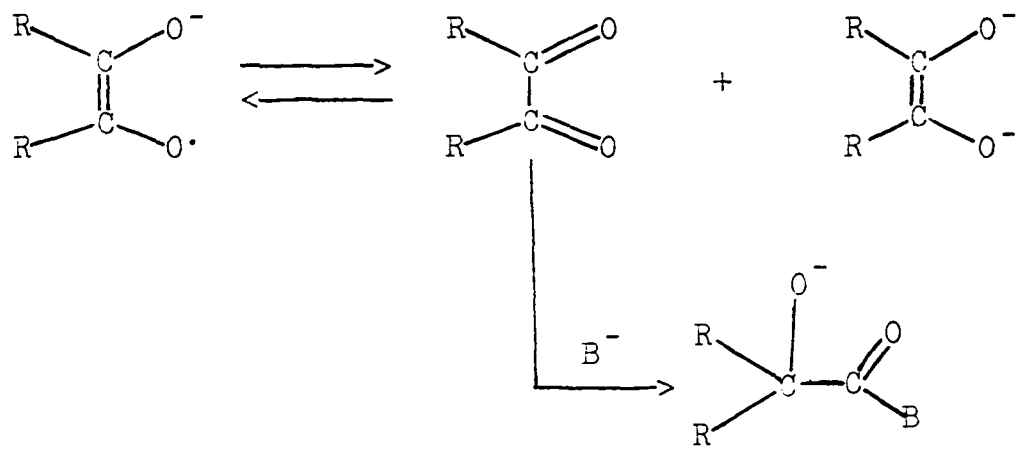


the phenylog. In view of the remarkable stability of the superoxide ion, it is not surprising that semiquinones and semidiones establish a stable class of organic radical anions.

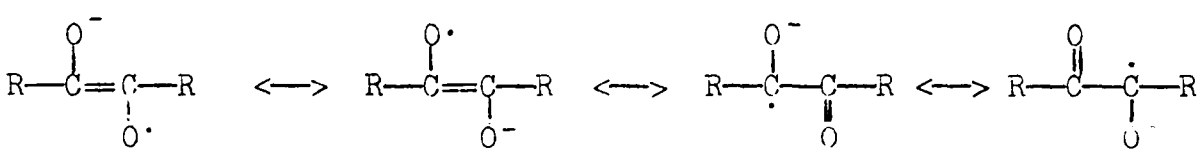
During the past decade a wealth of electron spin resonance information has been gathered from many structurally different and substituted semiquinones (1, 2, 3, 4, 5) and semidiones (3, 6, 7, 8, 9, 10, 11). Consequently, a great deal is known about the assignment of hyperfine splitting constants (hfsc), structure, conformation, and the distribution of spin and electron density in these radicals.

Semiquinones are commonly prepared by the electrolytic or chemical reduction of the quinone, or by the oxidation of the hydroquinone with oxygen in basic solution. Semidiones are generated by the basic oxidation of ketones containing an α-methylene group; chemical, photochemical, or electrolytic reduction of α-diketones; hydrolysis-oxidation of bis(trimethylsiloxy)alkenes; and oxidation of α-bromo or α-acetoxy ketones and enediol dianions. Semidiones also have been detected under the conditions of the acyloin condensation (12).

Once generated, semidiones are stable for hours at room temperature but do decompose in basic solution, probably by a benzilic acid type rearrangement (13, 14, 15).



The resonance forms of a semidione, a, imply that the



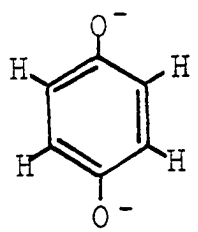
a

unpaired electron may be nearly equally shared among the four atoms of the semidione system. Carbon-13 and oxygen-17 esr studies of labeled semidiones, as well as Hückel molecular orbital calculations, support this conclusion (16, 17, 18).

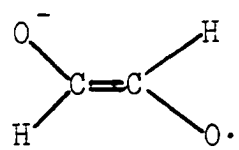
The splitting constants for the protons, a , of the parent semidione and semiquinone are given in b, and can be quantitatively described by the expression:

$$a^H = \rho_C{}^{\pi} Q$$

where Q is a constant of approximately -25 gauss (G) and $\rho_C{}^{\pi}$ is



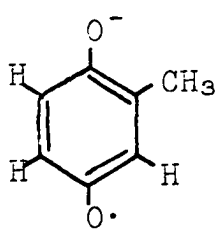
a^H = 2.34 G



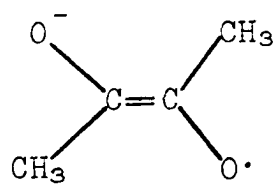
a^H = 7.7 G

b

the electron density at the carbon atom adjacent to the hydrogen atom (19). Replacing the hydrogens with methyl groups leads to



a^H = 2.78, 2.53, 1.82 (g)(3H)
= 2.16 G (3H,CH_3)



a^H = 5.7 G

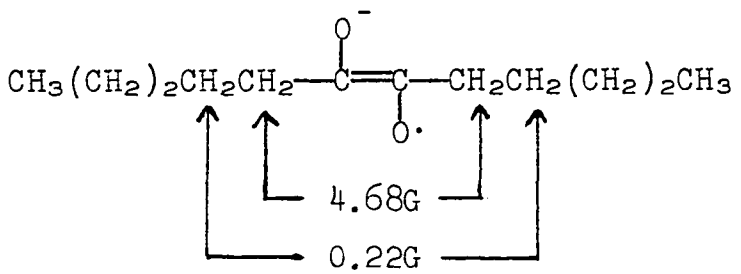
c

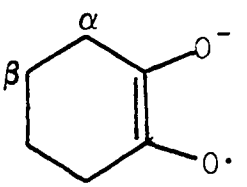
splitting constants listed for c.

Numerous splittings of this type adhere to the expression:

$$a^H = \rho_C{}^{\pi}(Bo + B\cos^2\theta)$$

where $\rho_C{}^{\pi}$ is the electron density in the adjacent carbon p orbital, Bo is a constant near zero, B is a constant of approximately 50 G, and θ is the dihedral angle between the p orbital and the carbon-hydrogen bond (20). Splitting by beta hydrogens are relatively small and are often not observable. Hydrogens,





a^H_α = 9.8 G

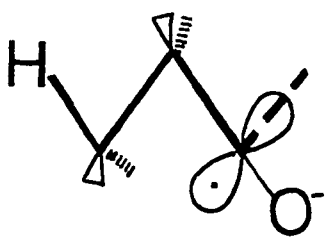
a^H_β = <0.1 G

d

on a gamma, or further removed carbons, are rarely seen. However, if the spin label is incorporated into a bridged bicyclic structure, extensive long-range hyperfine splittings is observed. The first reports of such compounds had the semidione spin label incorporated into the bicyclo[2.2.1]heptane, bicyclo[2.2.2]-octane, and bicyclo[3.2.1]nonane systems and dealt primarily with the assignment of hyperfine splittings to the various hydrogens in the radical (21, 22, 23). Since then a number of other

bridged bi- and tricyclic semidiones, including the [2.1.1]-hexane, [3.1.0]hexane, [4.1.0]heptane, [3.2.0]heptane, [4.2.1.-$0^{2,5}$]nonane, and [4.2.2.$0^{2,5}$]decane systems, have been studied in detail (24, 25). An additional report on the bicyclo[2.2.2]-octane (26) as well as semiquinones contained in the bicyclo-[2.2.1]heptane and bicyclo[2.2.2]octane systems have appeared (27, 28, 29, 30, 31).

In all of the rigid bicyclic molecules studied, the most prominent long-range splittings are those due to the hydrogens that lie in a coplanar, zigzag arrangement with the p orbital that contains the unpaired electron. This has been termed the "W-plan" or "V" arrangement (32) which is recognized in proton



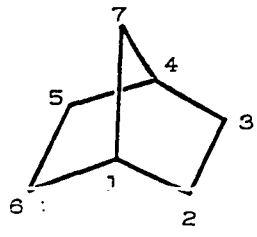
nuclear magnetic resonance (nmr) studies of bicyclic molecules (33, 34, 35).

This work was undertaken to assign and confirm some of the splitting assignments in the [2.2.1] and [2.2.2] semidiones and to obtain information on the nature of splitting mechanisms operating in these radicals. The problem of hfsc assignment was overcome through deuterium and methyl substitution. Splitting mechanisms were probed by methyl substitution and introduction of points of unsaturation, i.e., increased strain within the radical.

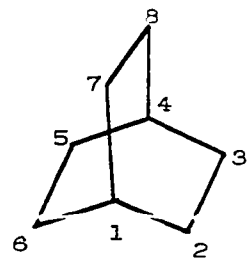
NOMENCLATURE

The Baeyer system of nomenclature is used throughout this manuscript. The steps followed in choosing a Baeyer name are: choose the largest possible ring as the main ring; find the longest chain of remaining atoms for the main bridge and, in the event of there being more than one choice, choose the chain that most equally divides the ring; denote subsidiary rings by the number of atoms in them along with the lowest possible value of superscripts giving their points of attachment.

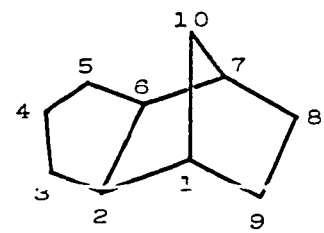
Numbering of the bicyclic structure is initiated at one main bridgehead atom and proceeds along the longer branch of the main ring to the second main bridgehead atom, continues along the shorter segment of the main ring back to the first main bridgehead atom; then proceeds along the main bridge to the second bridgehead atom. Subsidiary bridges are subsequently numbered. Baeyer names are written with the number of atoms in the bridges enclosed in brackets in descending order from the larger segment of the main ring. Thus, e-1 is bicyclo[2.2.1]-heptane, e-2 is bicyclo[2.2.2]octane, and e-3 is tricyclo-[5.2.1.$0^{2,6}$]decane.



e-1



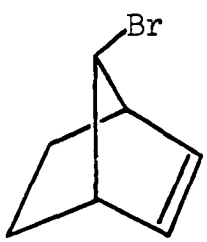
e-2



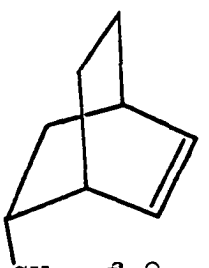
e-3

e

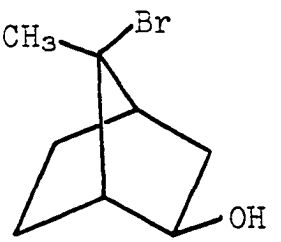
A substituent at C-7 of e-1 is designated as being <u>syn</u> if it is on the same side as the C-2, C-3 bridge, and as <u>anti</u> if it is on the side with the C-5, C-6 bridge. Substituents on carbons 2, 3, 5, and 6 of e-1 and carbons 2, 3, 5, and 6 of e-2 are designated <u>endo</u> if they are inside the cage formed by carbon atoms 2, 3, 5, and 6, and are <u>exo</u> if they lie outside this cage. Thus, f-1 is <u>syn</u>-7-bromobicyclo[2.2.1]heptene, and f-2 is endo-6-methylbicyclo[2.2.2]octene, and f-3 is anti-7-methyl-<u>syn</u>-7-bromobicyclo[2.2.1]heptan-<u>exo</u>-2-ol.



f-1



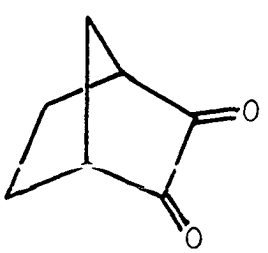
f-2



f-3

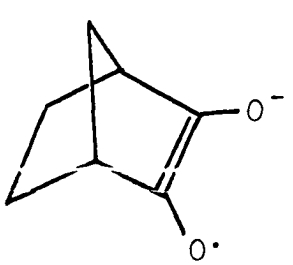
f

In this study the semidione spin label normally constitutes one of the main bridges and the radical is named in an analogous manner to the parent α-diketone. Thus, g-1 is bicyclo[2.2.1]-heptan-2,3-dione and g-2 is bicyclo[2.2.1]heptan-2,3-semidione.



g-1

g

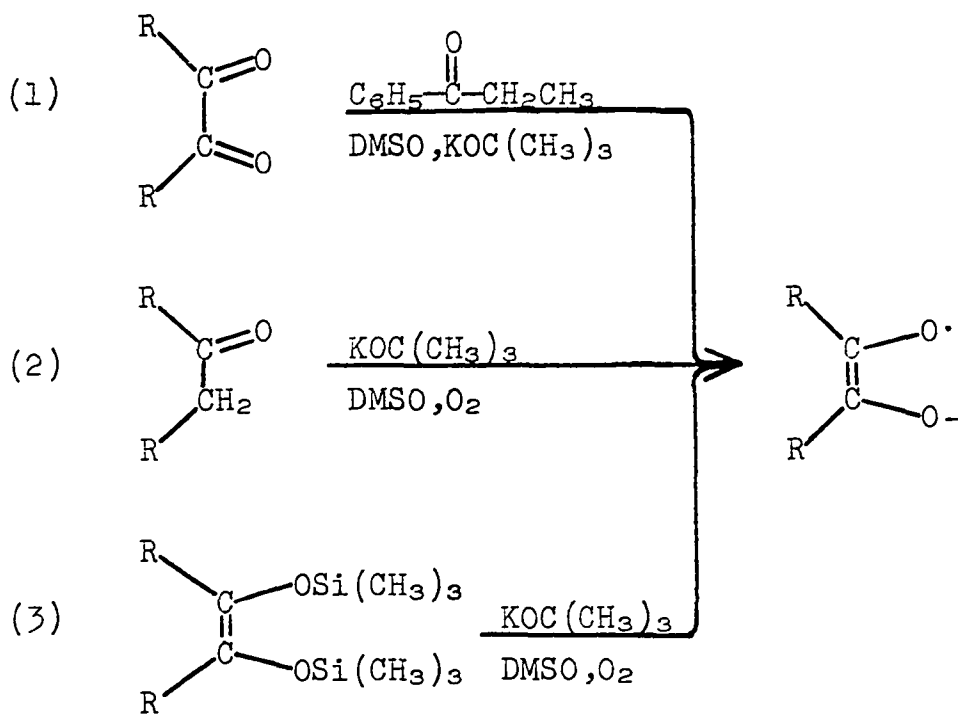


g-2

RESULTS AND DISCUSSION

Preparation of Semidiones

In general, the semidiones used in this study had the semidione spin label incorporated into a rigid bicyclic structure and were normally generated by one of three general methods: (1) reduction of an α-diketone by propiophenone enolate anion; (2) oxidation of a ketone in dimethyl sulfoxide (DMSO) solutions of potassium t-butoxide with air; and (3) by hydrolysis-oxidation of bis(trimethylsiloxy)alkenes in basic DMSO solutions.



Bicyclo[2.2.1]heptan-2,3-semidiones

Chang (23) observed that the selenium dioxide oxidation of bicyclo[2.2.1]heptan-2-one failed to yield a well defined α-diketone but instead gave a yellow-orange gum from which pure bicyclo[2.2.1]heptan-2,3-dione was never isolated. A well resolved esr spectrum, which could be interpreted in terms of the parent bicyclo[2.2.1]heptan-2,3-semidione (I), was however obtained by treatment of a dimethyl sulfoxide (DMSO) solution of this gum with propiophenone enolate anion. A much weaker but identical signal was obtained by mixing 3-bromobicyclo-[2.2.1]heptan-2-one with a DMSO solution of potassium t-butoxide and a trace of air. The generation of radicals from α-bromo ketones is thought to proceed via a Kornblum-type reaction.

Application of the reactions of Scheme I to bicyclo[2.2.1]-heptene produced bis(trimethylsiloxy)alkene I-a which, when treated with a DMSO solution of potassium t-butoxide and a trace of air, also yielded semidione I. The signal is very strong and gave a clean, well resolved spectrum (Figure 4). It consists of a 6.48 gauss (G) doublet assigned to the anti-7-proton, a 2.49 G quintet due to two bridgehead and the two exo-5,6-protons, and finally a 0.36 G doublet from the syn-7-proton.

Cohen and Tsuji (36, 37) reported a very interesting reaction in which epoxides are converted to α-hydroxy ketones simply by heating DMSO solutions of the epoxide with a catalytic amount of

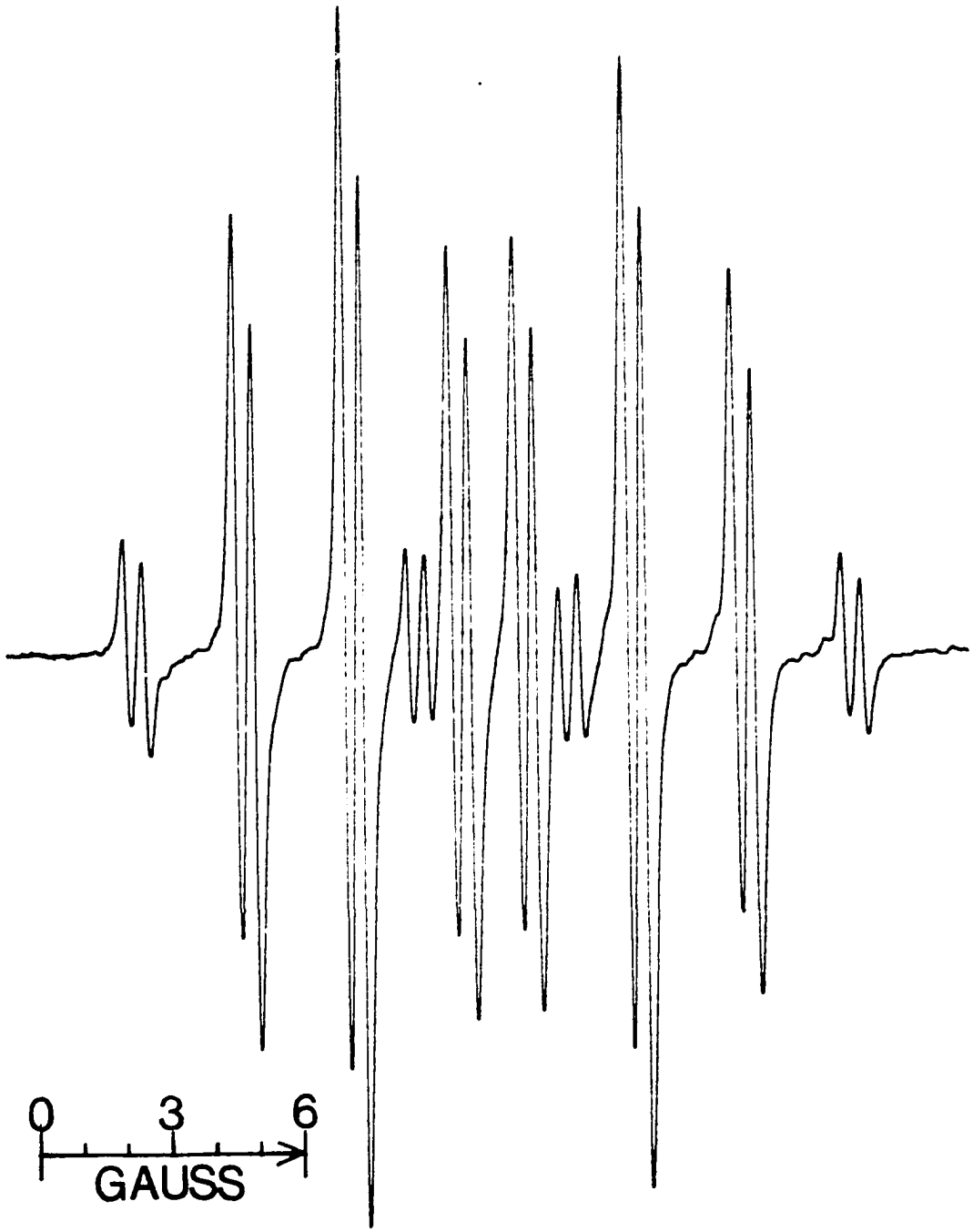
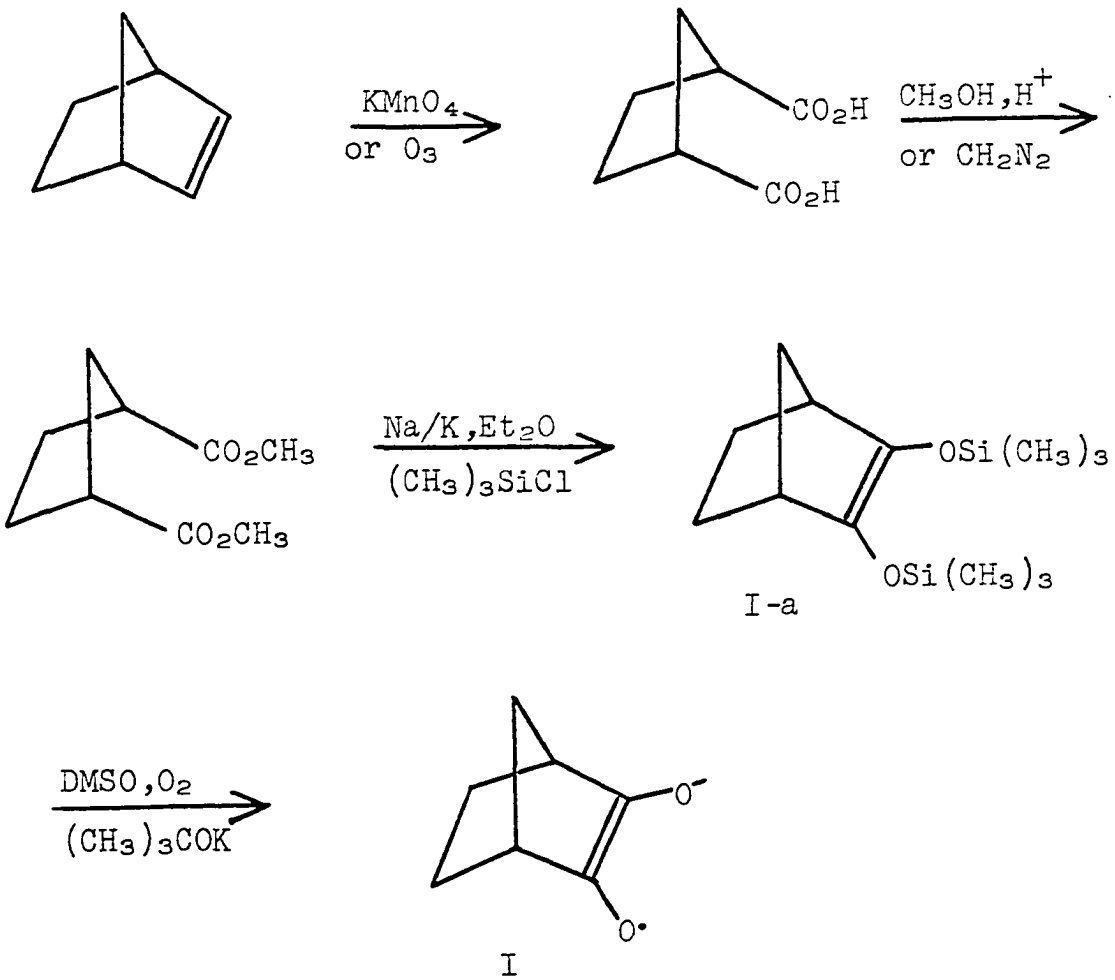
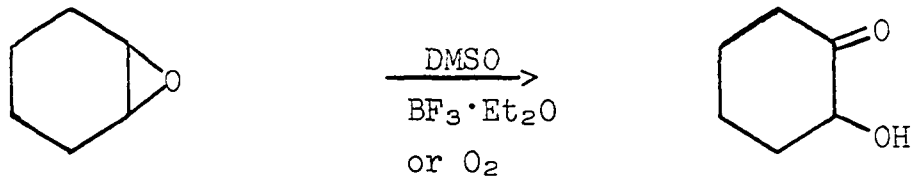


Figure 4. First-derivative esr spectrum of bicyclo[2.2.1]-heptan-2,3-semidione (I) generated in DMSO from bis(trimethylsiloxy)alkene I-a.

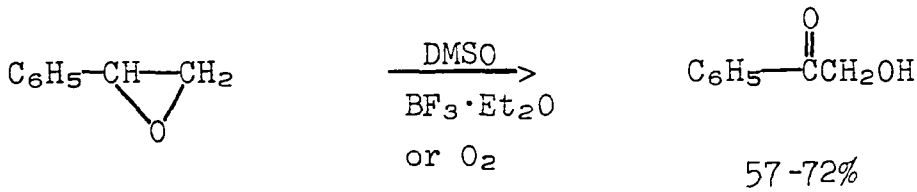
Scheme I



boron trifluoride etherate or oxygen. In a typical reaction, cyclohexene oxide was converted to α-hydroxycyclohexanone in 65-76% yield while styrene oxide gave 57-72% of phenacyl alcohol. In view of the fact that α-hydroxy ketones are among the most desirable precursors to semidiones, it was hoped that this reaction might provide an <u>in situ</u> route to some elusive bicyclic semidiones.



65-76%



57-72%

Heating a DMSO solution of cyclohexene oxide for 20-24 hours at 80°, in the absence of oxygen or boron trifluoride etherate, followed by mixing with a 0.1 M DMSO solution of potassium t-butoxide yielded no detectable radicals. When a catalytic amount of boron trifluoride or oxygen was employed, an esr signal was observed. The spectrum (Figure 5-a) is identical to that reported for cyclohexane semidione in pure DMSO (7) and consists of a 1:4:6:4:1 quintet separated by 9.82 gauss.

Treatment of styrene oxide in the same manner yielded the complex spectrum shown in Figure 5-b. The identity of this radical is not known. The spectrum width (8.80 G) and splitting patterns are different from those of the semidiones derived from either phenylglyoxal (12.6 G wide (38)) or propiophenone (16.4 G wide (17)).

Under these conditions, bicyclo[2.2.1]heptene oxide (I-b)

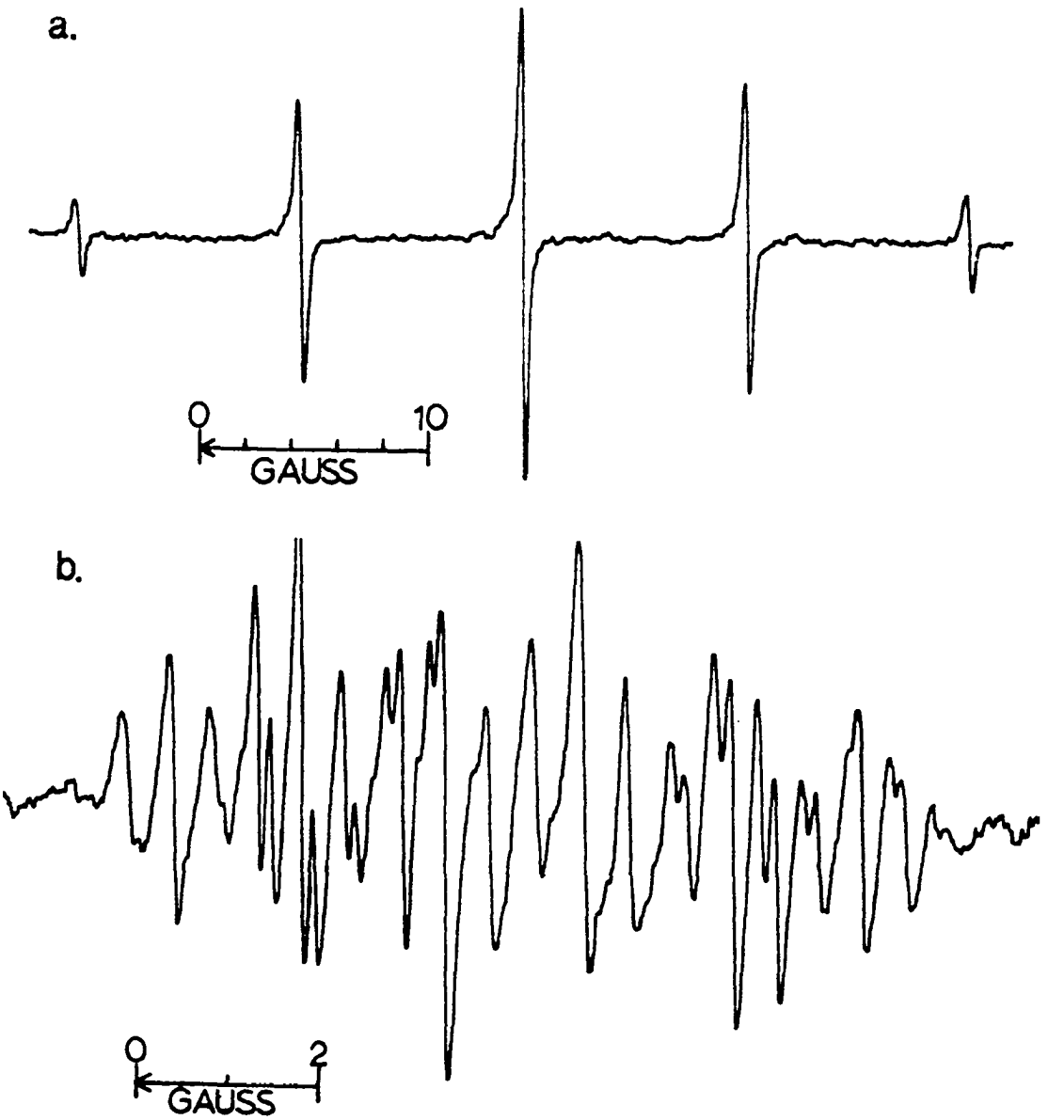
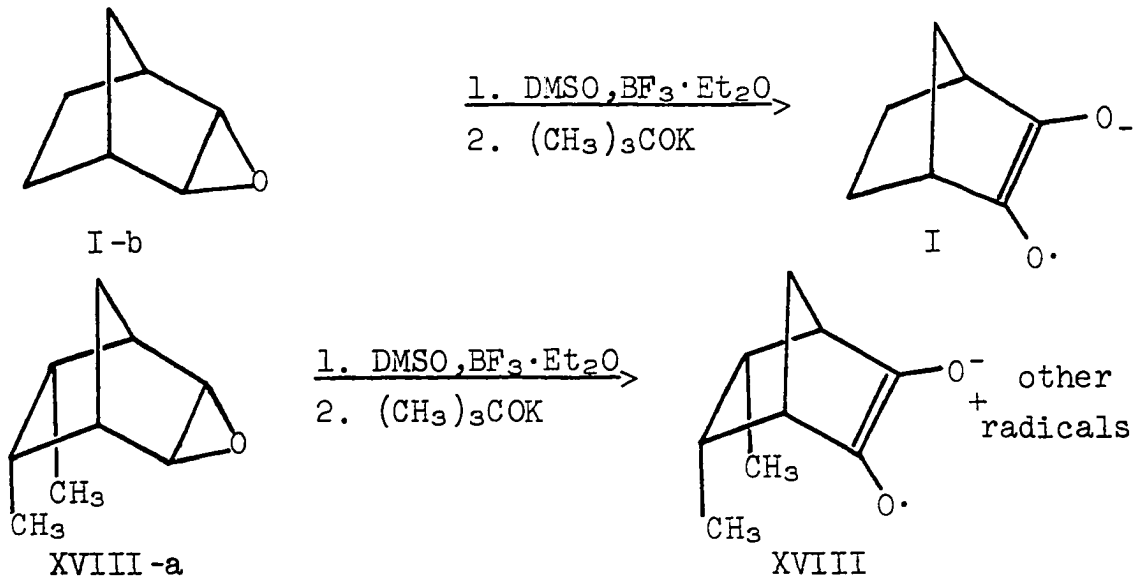


Figure 5. First-derivative esr spectrum of (a) cyclohexan-2,3-semidione generated from cyclohexene oxide with boron trifluoride etherate in DMSO and, (b) the radical obtained in the same manner from styrene oxide.

produced the same radical (Figure 6-a) as was obtained by the hydrolysis-oxidation of I-a and by the reduction of bicyclo-[2.2.1]heptan-2,3-dione. However, endo, endo-5,6-dimethyl-bicyclo[2.2.1]heptene oxide (XVIII-a) yielded a complex spectrum (Figure 6-b). The spectrum is largely due to unidentified radicals but some of the lines due to the expected semidione (XVIII) can be seen.



A series of methyl substituted bicyclo[2.2.1]heptan-2,3-semidiones were prepared by Chang (23) and they are listed in Chart I along with his assignment of splitting constants (a^H). The correct assignment of hyperfine splitting constants (hfsc) in semidione I was made on the basis of these semidiones. Methyl substitution, particularly in the endo-5,6 and syn- and anti-7 positions, significantly altered the size of some hyperfine splittings. A rigorous confirmation of hfsc in I was made

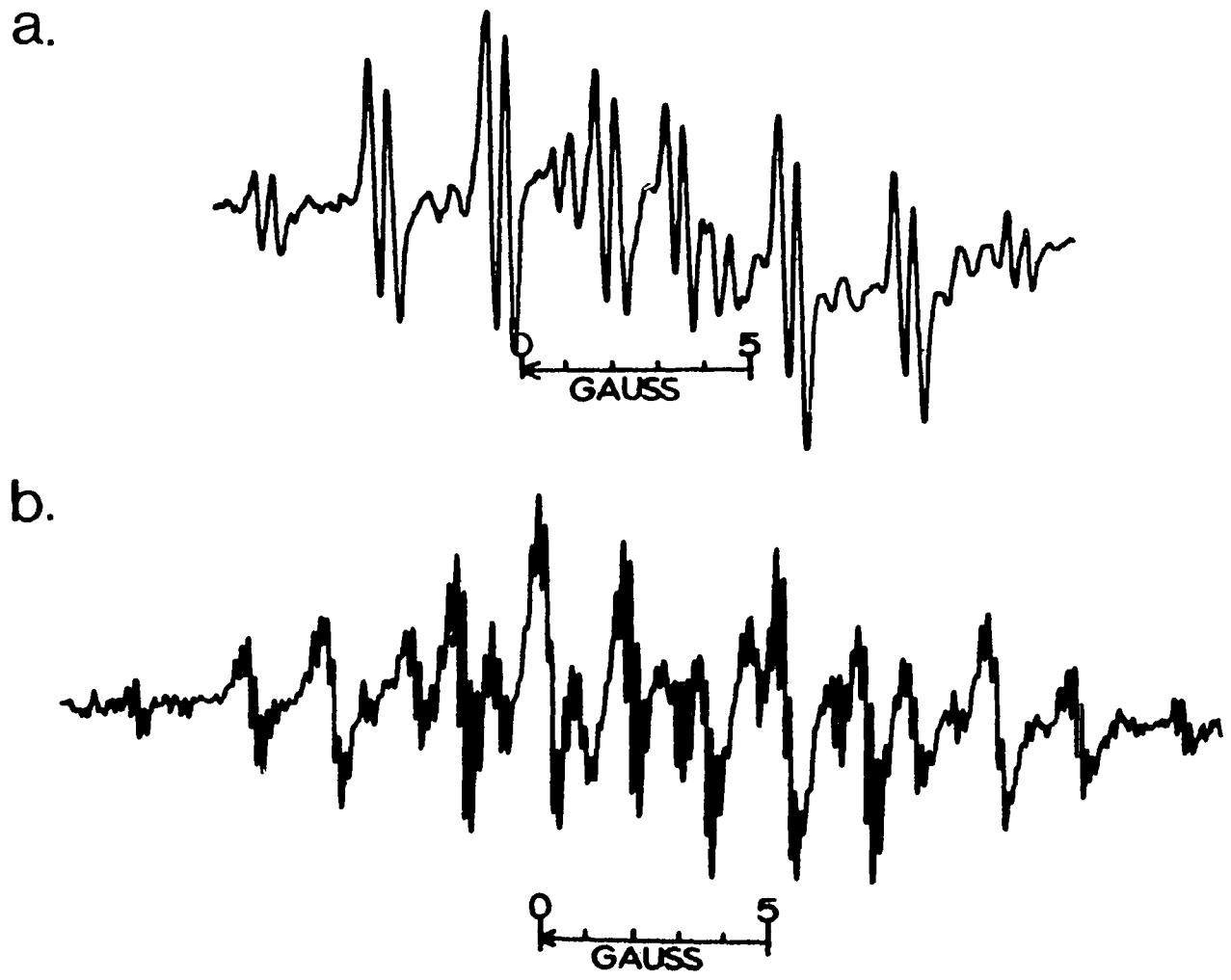
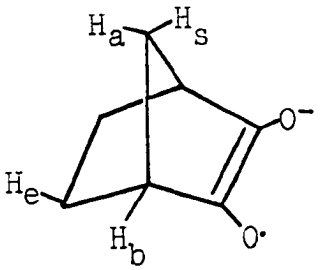


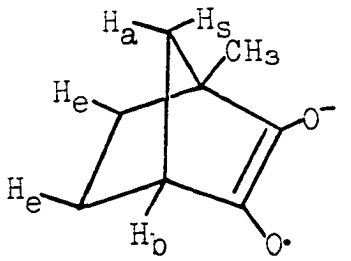
Figure 5. First-derivative esr spectrum of (a) I prepared from bicyclo[2.2.1]heptene oxide with boron trifluoride etherate in DMSO and, (b) the mixture of radicals obtained in the same manner from endo, endo-5,6-dimethylbicyclo-[2.2.1]heptene oxide.

Chart I



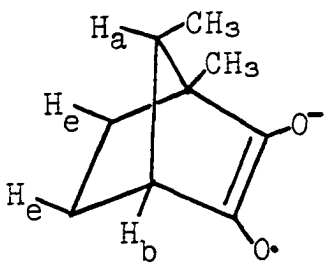
I

a^H= 6.54 (1H) H_a
2.43 (4H) H_b,H_e
0.41 (1H) H_s



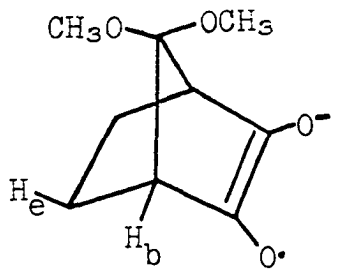
II

a^H= 6.29 (1H) H_a
2.51 (3H) H_b,H_e
0.46 (1H) H_s



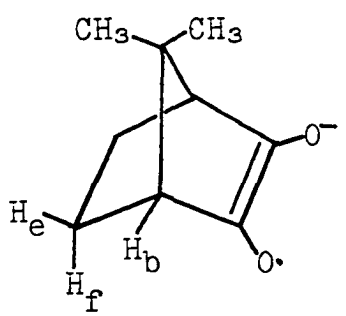
III

a^H= 3.05 (1H) H_a
2.55 (3H) H_b,H_e
0.18 (6H) 2 CH_3



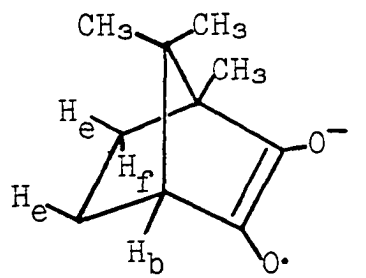
IV

a^H= 2.50 (2H) H_b,H_e
1.96 (2H)



V

a^H= 2.90 (2H) H_b,H_e
2.07 (2H)
0.53 (3H) anti-CH_3
0.26 (2H) H_f

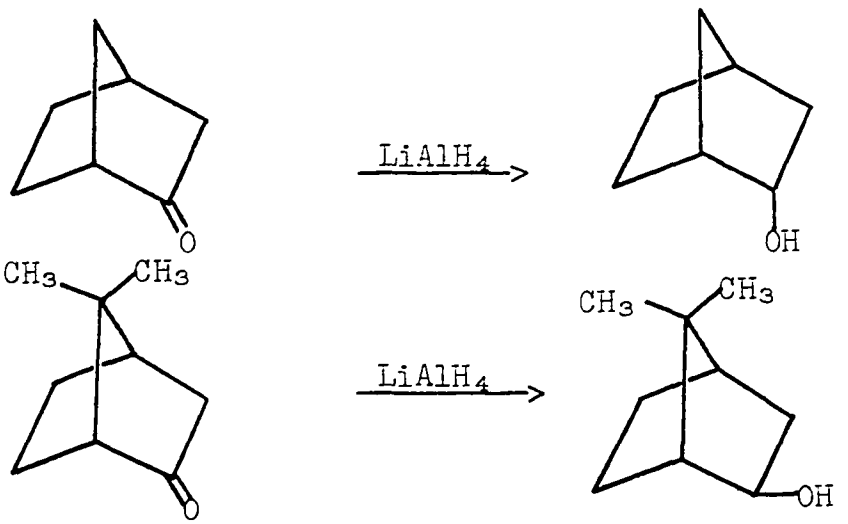


VI

a^H= 3.01 (2H) H_e
2.08 (1H) H_b
0.55 (3H) anti-CH_3
0.22 (1H) H_f
0.15 (3H) C_f-1 CH_3

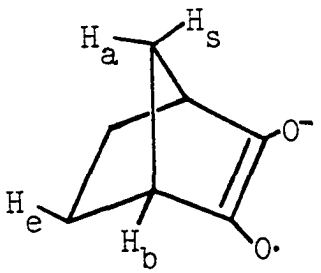
via the series of specifically deuterated semidiones shown in Chart II. The results obtained from these semidiones are only consistent with the assignments listed for semidione I. Deuterium substitution has an advantage over methyl substitution in that it normally does not alter the geometry from that of the undeuterated semidione. Underwood and Givens (39) have shown that the relative magnitude of hfsc in semidiones can be anticipated by extended Hückel calculations and that a slight alteration in the geometry of the semidione is reflected by large changes in the calculated hfsc.

Reactions such as hydroboration (40), nitrosyl halide addition (41, 42), and lithium aluminum hydride reductions (43) on the C-2, C-3 bridge of the bicyclo[2.2.1]heptane system have all been observed to proceed by attack from the least hindered exo side, unless the exo side is blocked by a syn-7 substituent.



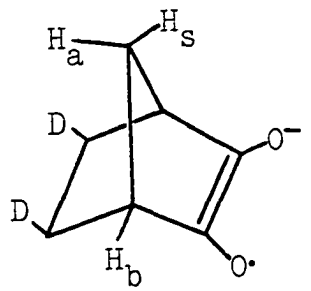
It was therefore reasoned that alcohol VII-a would be reduced in an analogous exo manner and that α-diketone VII-c

Chart II



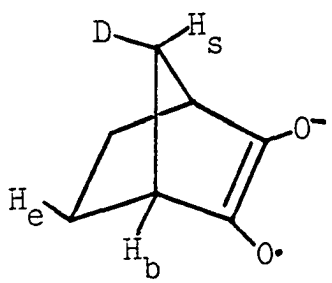
I

a^H= 6.48 (1H) H_a
2.49 (4H) H_b,H_e
0.36 (1H) H_s



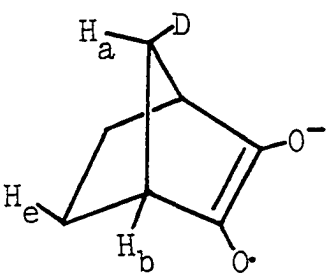
VII

a^H= 6.48 (1H) H_a
2.50 (2H) H_b
0.40 (1H) H_s
a^D= 0.40 (2D)
a^H/a^D= 5.22



IX

a^H= 2.50 (4H) H_b,H_e
0.40 (1H) H_s
a^D= 1.0 (1D)
a^H/a^D= 6.50

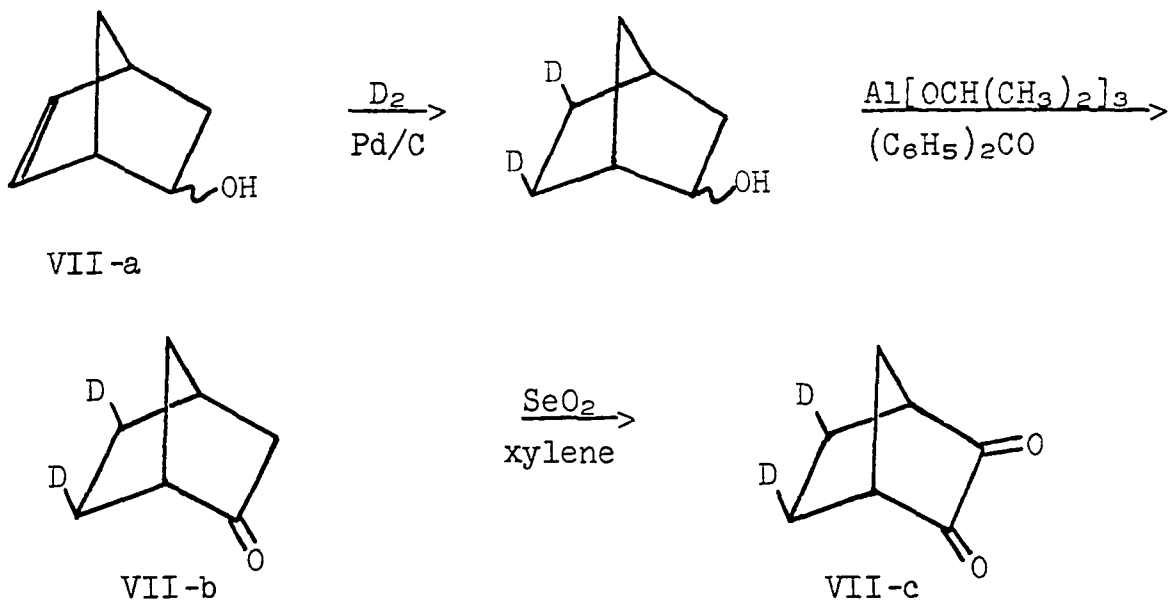


XI

a^H= 6.50 (1H) H_a
2.50 (4H) H_b,H_e
a^D<0.1

could be prepared by the reactions outlined in Scheme II. The reactions all proceeded as anticipated, except for the selenium dioxide oxidation of monoketone VII-b.

Scheme II



A yellow-orange gum, from which pure α-diketone VII-c could not be isolated, was obtained from this reaction. Treatment of a DMSO solution of this gum with propiophenone enolate anion did generate semidione VII. Its esr spectrum (Figure 7-a) displays identical proton hyperfine splittings as semidione I except that the 2.49 G quintet of I has been reduced to a 1:2:1 triplet. A 1:2:3:2:1 quintet of 0.4 G, due to two magnetically equivalent deuterium atoms, has been added. The hyperfine splittings of this semidione were verified by simulation (Figure 7-b).

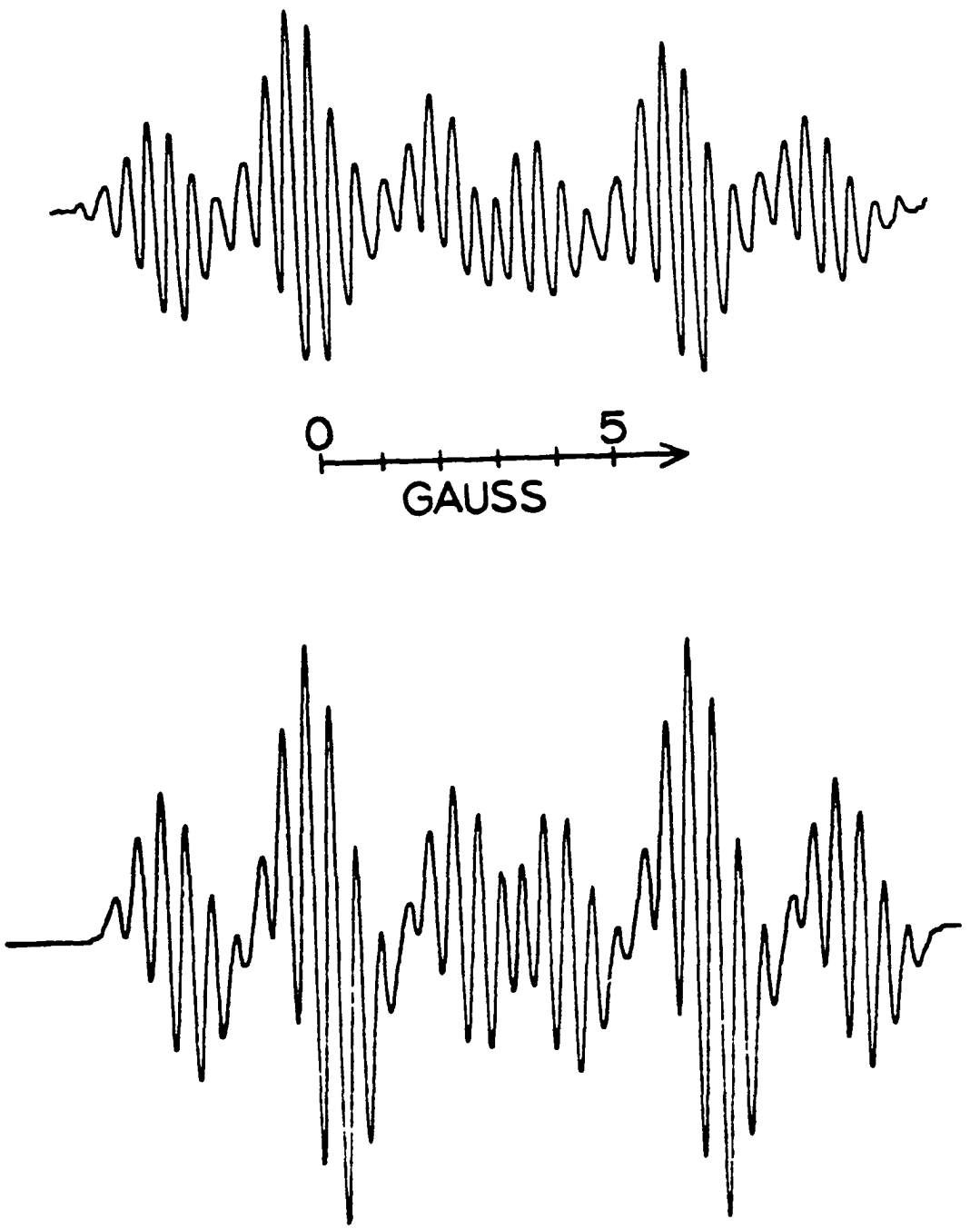
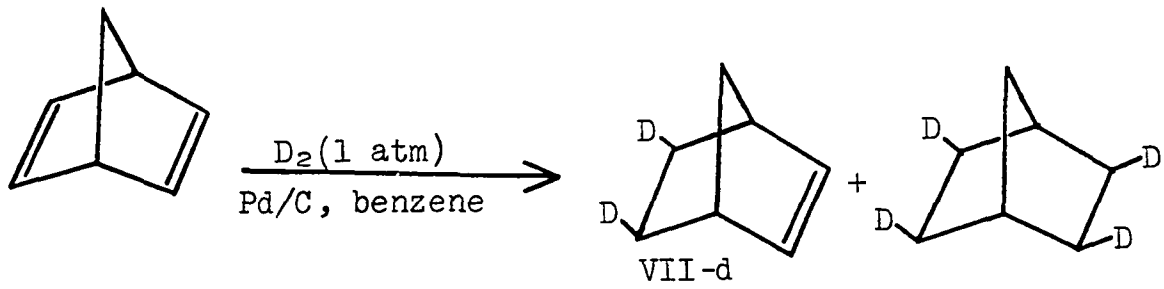


Figure 7. First-derivative esr spectrum of (a) exo, exo-5,6-dideuterobicyclo[2.2.1]heptan-2,3-semidione (VII) prepared by reduction of α-diketone VII-c and, (b) the simulated spectrum using the hfsc of the text.

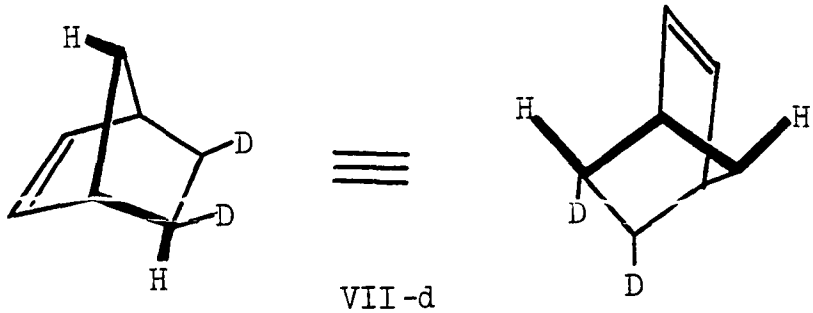
Mass spectral analysis of ketone VII-b indicated 97% deuterium incorporation with only 2.1% of d_3 or higher deuterated species. The exo-cis stereochemistry of the deuterium atoms in VII was confirmed by its preparation by another route.

Arnold, Trecker, and Whipple (44) have claimed that deuterium added to bicyclo[2.2.1]heptadiene (Pd/C catalyst in benzene) in an exo-cis fashion. The claim was substantiated by Baird, Franzus, et al. (45, 46) through proton magnetic resonance studies on VII-d. The complete absence of absorptions for the exo protons at 2 ppm (parts per million) and a syn-7-endo-5 coupling of 2.0-2.5 Hz (hertz) was overwhelming evidence in favor of exo-cis deuterium incorporation.*



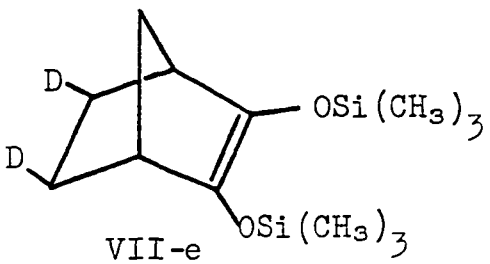
VII-d

*The usefulness of the syn-7—endo-5 long-range coupling in compound VII-d should be noted. This coupling is between two protons that lie in a zig-zag or "W-plan" arrangement of atoms. The same stereochemistry is observed to be necessary for the major long-range hyperfine splittings in bicyclic semidiones.

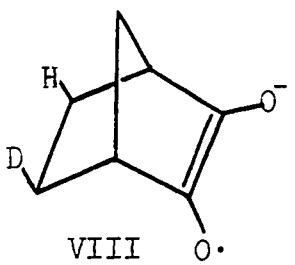


VII-d

Bis(trimethylsiloxy)alkene VII-e was prepared by subjecting the products of the reaction of bicyclo[2.2.1]heptadiene and 1.2 mole-equivalent of deuterium to the reactions of Scheme I.

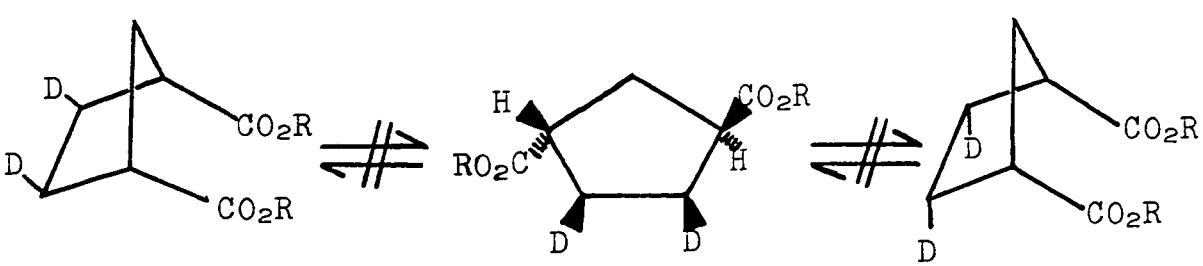


VII-e



VIII

A strong esr signal due to semidione VII was obtained from VII-e upon mixing with a DMSO solution of potassium t-butoxide. The wing peaks of the spectrum (Figure 8) are slightly complicated by lines due to several percent of monodeuterated semidione VIII. If the conditions of Scheme I were equilibrating the diacid intermediates, some deuterium atoms would be placed in the endo-5,6 position of VII-e and a spectrum identical to semidione I would be observed. No such spectrum has ever been detected.



R = H, CH_3

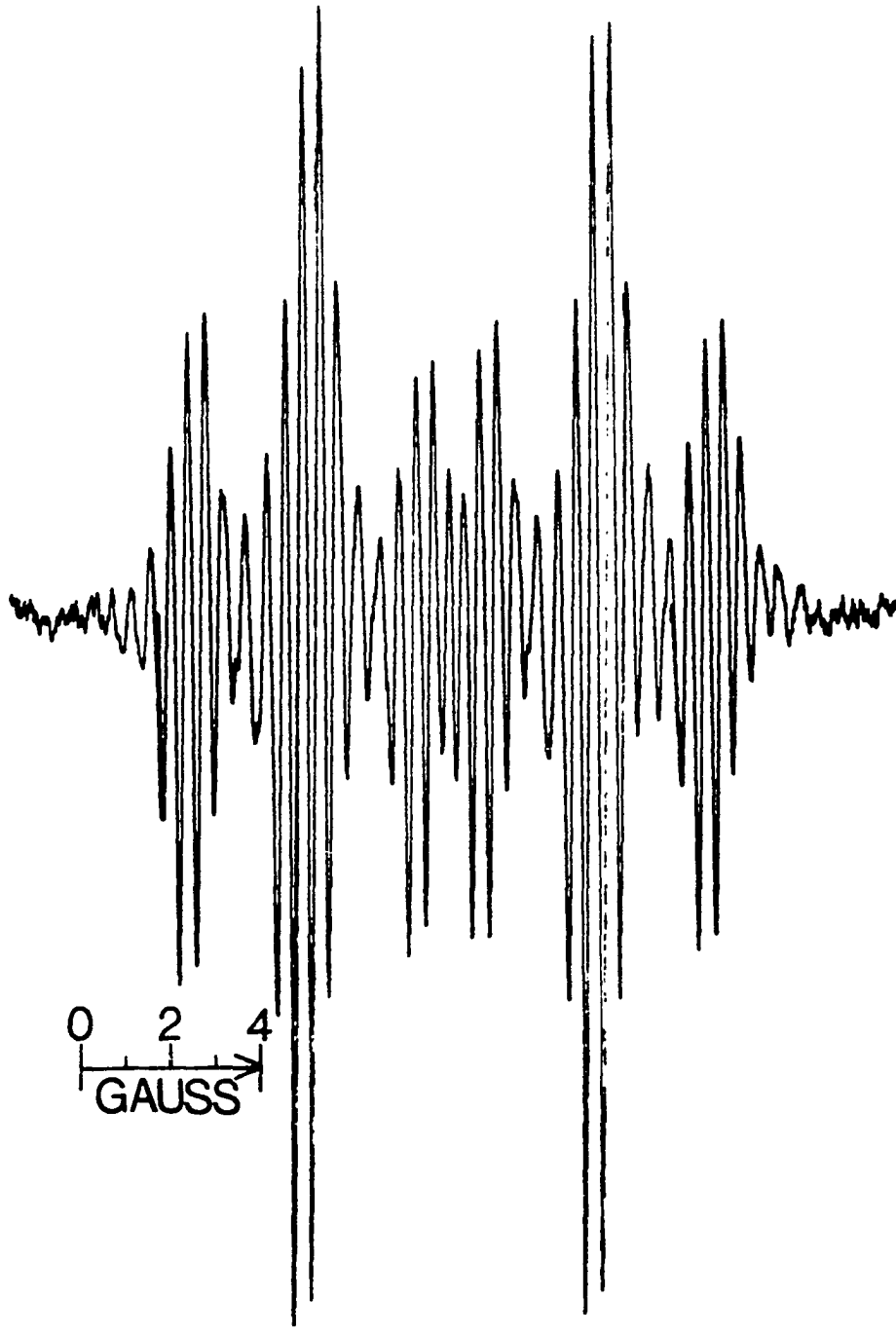
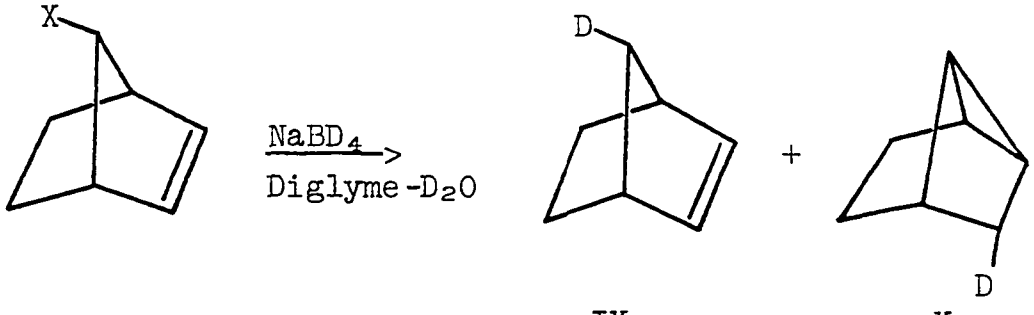


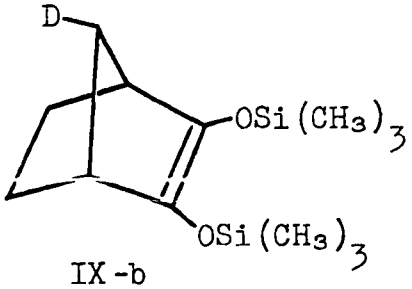
Figure 8. First-derivative esr spectrum of semidione VII generated in DMSO from bis(trimethylsiloxy)alkene VII-e.

Brown (47) and Winstein (48) have shown that the solvolysis of anti-7-chloro and anti-7-tosyloxybicyclo[2.2.1]heptene in the presence of sodium borodeuteride yields anti-7-deutero-bicyclo[2.2.1]heptene (IX-a) and 5-deuterotricyclo[4.1.0.$0^{4,7}$]-heptane (X). The ratio of the two products is solvent dependent.

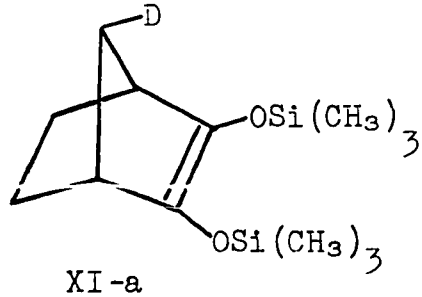


X= Cl, OTs IX-a X

Analogously, anti-7-bromobicyclo[2.2.1]heptene was solvolyzed, but under the conditions described by Marchand and Rose (65% diglyme-35% D_2O, 1.5 M $NaBD_4$, 50°) (49), to yield IX-a, which was converted to bis(trimethylsiloxy)alkene IX-b by the reactions of Scheme I. Compound IX-b generated semidione IX upon mixing with a DMSO solution of potassium t-butoxide. The esr spectrum (Figure 9) consists of a 2.50 G quintet (1:4:6:4:1), a 0.4 G doublet, and a 1.0 G triplet (1:1:1) due to one deuterium atom.



IX-b



XI-a

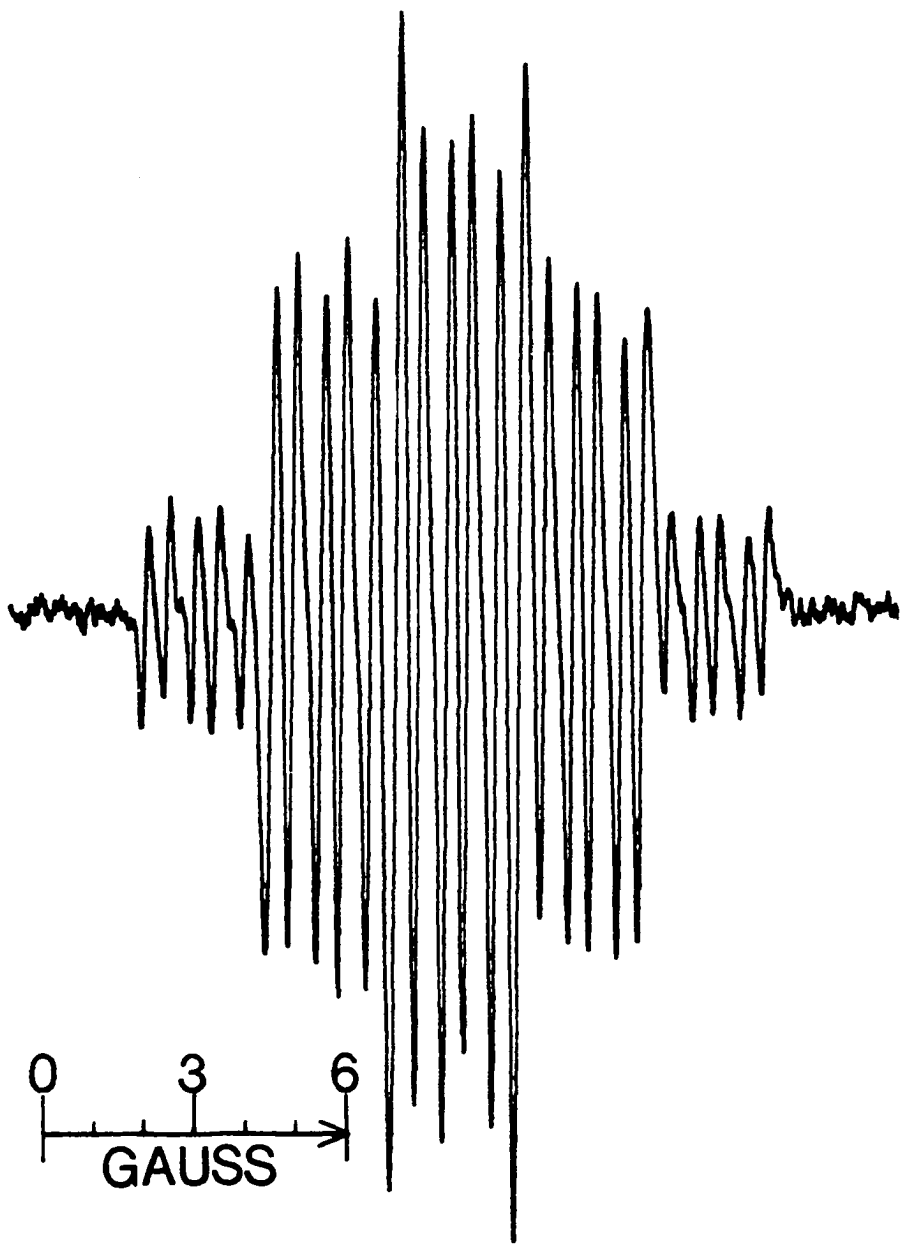
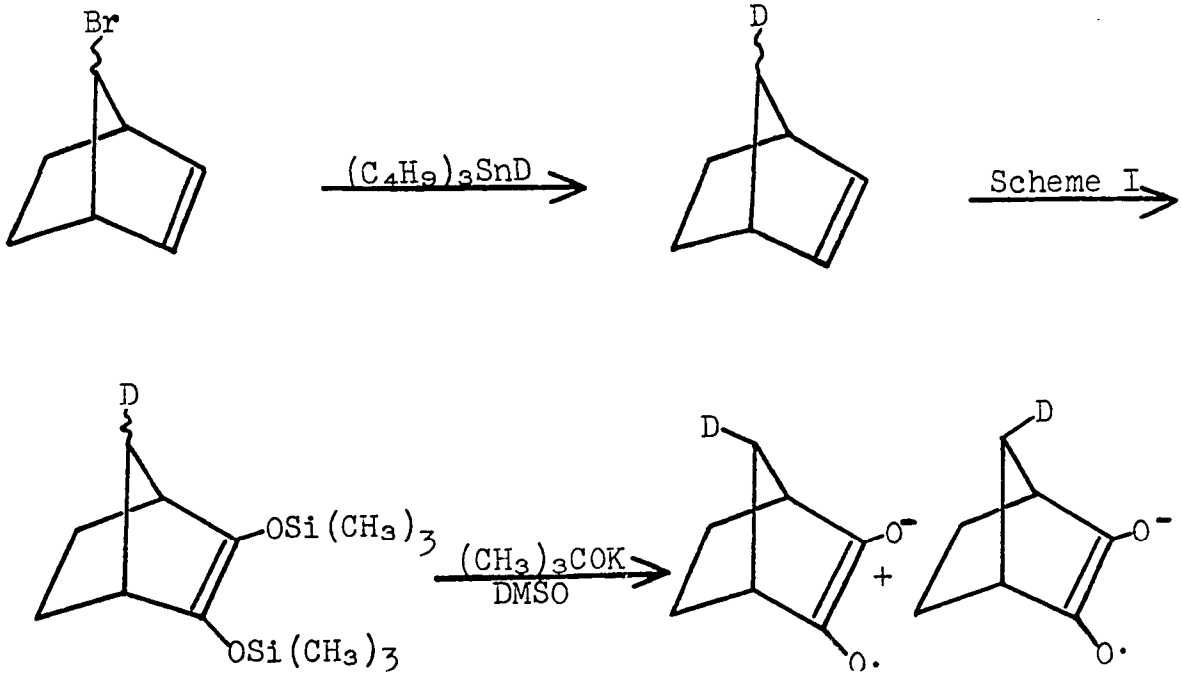


Figure 9. First-derivative esr spectrum of anti-7-deuterobicyclo[2.2.1]heptan-2,3-semidione (IX) generated in DMSO from bis(trimethylsiloxy)alkene IX-b.

Trialkyl- and triaryltin hydrides are known to reduce alkyl halides to alkanes (50). Hence, deuterium can be specifically introduced into a molecule by reduction of the appropriately substituted alkyl halide with a trialkyl- or triaryltin deuteride. Reduction of 7-bromobicyclo[2.2.1]heptene with tri-n-butyltin deuteride yielded 7-deuterobicyclo[2.2.1]heptene which was converted (via Scheme I) to bis(trimethylsiloxy)-alkenes, IX-b and XI-a. An identical mixture of semidiones IX and XI (84% IX, 16% XI) was obtained from the bis(trimethyl-siloxy)alkenes (prepared from either syn or anti-7-bromo-bicyclo[2.2.1]heptene) upon reaction with potassium t-butoxide in DMSO.



IX-b and XI-a

IX 84%

XI 16%

Figure 10 shows the esr spectrum of the mixture. The lines for XI are clearly visible and consist of a 6.50 G doublet and a 2.50 G quintet. No deuterium splittings are observed since the expected hfsc for a syn deuterium is only 0.05-0.06 G*, which is too small to have been resolved.

The reaction of tri-n-butyltin deuteride with either syn- or anti-7-bromobicyclo[2.2.1]heptene has been reported to yield only anti-7-deuterobicyclo[2.2.1]heptene (51). Since we have already shown (via semidione VII) that the reactions of Scheme I proceed with complete preservation of the stereochemistry of the initial olefin, this account cannot be accurate. Cristol and Noreen (52) have verified this conclusion and presented proton nmr data confirming the presence of the syn-7-deutero olefin. A discussion of the important implications of this reaction, in regard to the nature of the intermediate C-7 radical, is presented in the Appendices.

The methyl splittings observed in semidiones II, III, V, and VI (Chart III) were best interpreted by assigning the 0.5 G splitting to the anti-7-methyls and the lesser, 0.1-0.2 G, splittings to bridgehead and syn-7-methyls (21, 23). In view of the results obtained for semidiones XIII-XVI (listed in Chart IV) these assignments must be revised so that the 0.5 G splitting

---

* The expected deuterium hfsc can be calculated from the ratio of nuclear moments of hydrogen and deuterium, i.e.,

$$a^H/a^D = 6.514$$

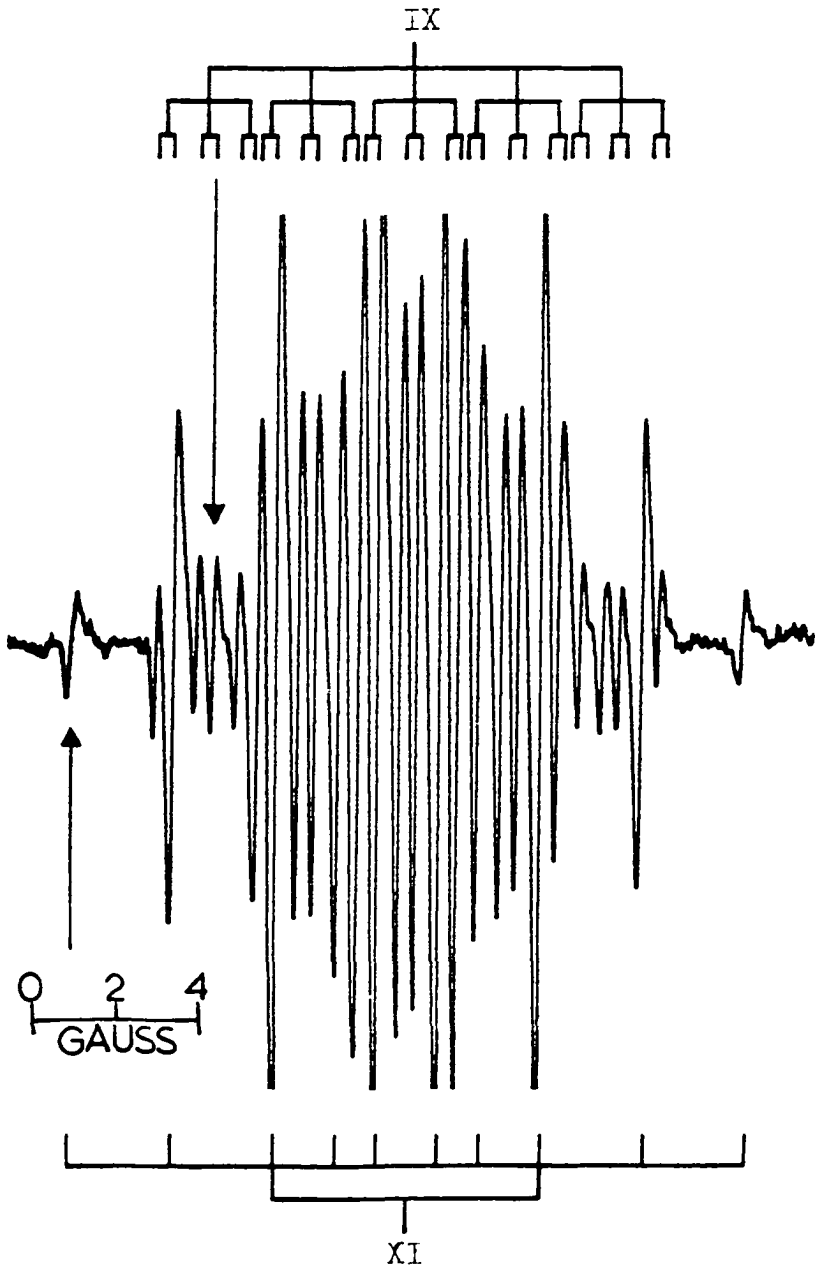
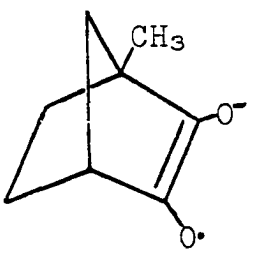


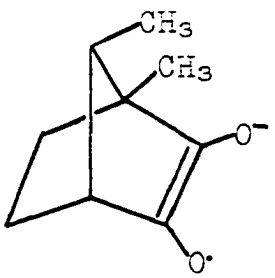
Figure 10. First-derivative esr spectrum of the mixture of 7-deuterobicyclo[2.2.1]heptan-2,3-semidiones (IX and XI) obtained from the 7-deuterobicyclo[2.2.1]-heptene produced by the reaction of tri-n-butyltin deuteride with syn or anti-7-bromobicyclo[2.2.1]-heptene.

Chart III



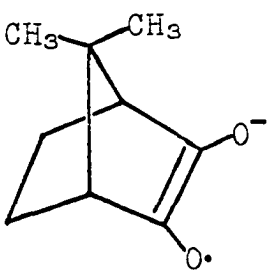
II

$a^{H}_{CH_3}$ = 0.14 (3H)



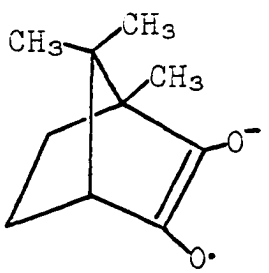
III

$a^{H}_{CH_3}$ = 0.18 (6H)



V

$a^{H}_{CH_3}$ = 0.53 anti-CH_3*



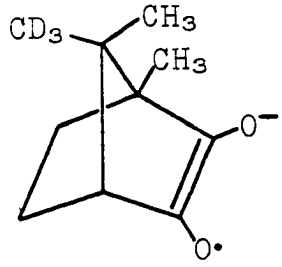
VI

$a^{H}_{CH_3}$ = 0.55 anti-CH_3*
0.15 C-1 CH_3

---

*Revised to syn-CH_3.

Chart IV

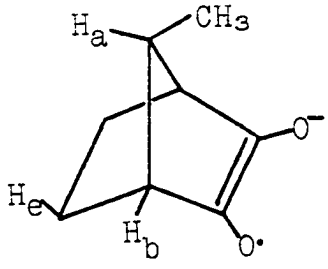


XIII

a^H = same as VI

$a^H_{CH_3}$ = 0.55 (3H) syn-CH_3

0.15 (3H) C-1 CH_3

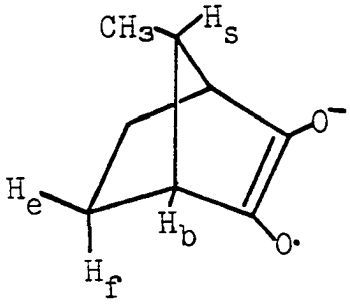


XIV

a^H = 3.11 (1H) H_a

2.52 (4H) H_b, H_e

0.18 (3H) syn-CH_3



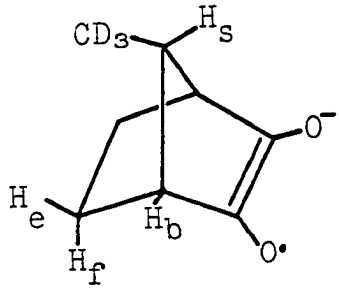
XV

a^H = 2.37 (4H) H_b, H_e

0.49 (1H) H_s

0.19 (3H) anti-CH_3

0.09 (2H) H_f



XVI

a^H = 2.38 (4H) H_b, H_e

0.50 (1H) H_s

$a^D_{CD_3}$ and $a^H_{H_f}$ unresolved

is assigned to the syn-7-methyl position. With this revision, methyl splittings for all of the semidiones are consistent.

Hence, semidiones possessing a syn-7-methyl as part of a gem-dimethyl system display a 0.5-0.55 G methyl splitting, otherwise $a^{H}_{\underline{syn}\text{-}CH_3}$ is 0.18 G. An anti-7-methyl shows a 0.2 G interaction unless there is a syn-7-methyl group, in which case $a^{H}_{\underline{anti}\text{-}CH_3}$ is reduced to less than 0.1 G and is not detected. Bridgehead methyl splittings are 0.15-0.2 G and appear to be unaffected by substitution in other parts of the molecule. Finally, an anti-7-methyl group is apparently necessary to observe splitting from endo-5,6-protons.

These variations of hfsc are perhaps best rationalized by envisioning small, but important, geometry changes in the semidione upon methyl substitution. Just how big of a change is necessary for it to be noticeable is not known. For example, semidiones VI and XIII have identical hfsc (compare Figures 11 and 12). Some difference might have been anticipated due to a geometry change in the ring upon deuterium substitution in a position where the relatively smaller trideuteromethyl group could decrease some of the nonbonded interactions in the molecule. When compared to its protio counterpart, D-(+)-camphor-9,9,9-d_3 (XIII-a) displays a larger than normal decrease in its molecular rotations (ORD). A conformational difference in the two ketones was suggested as a possible explanation for this observation (53).

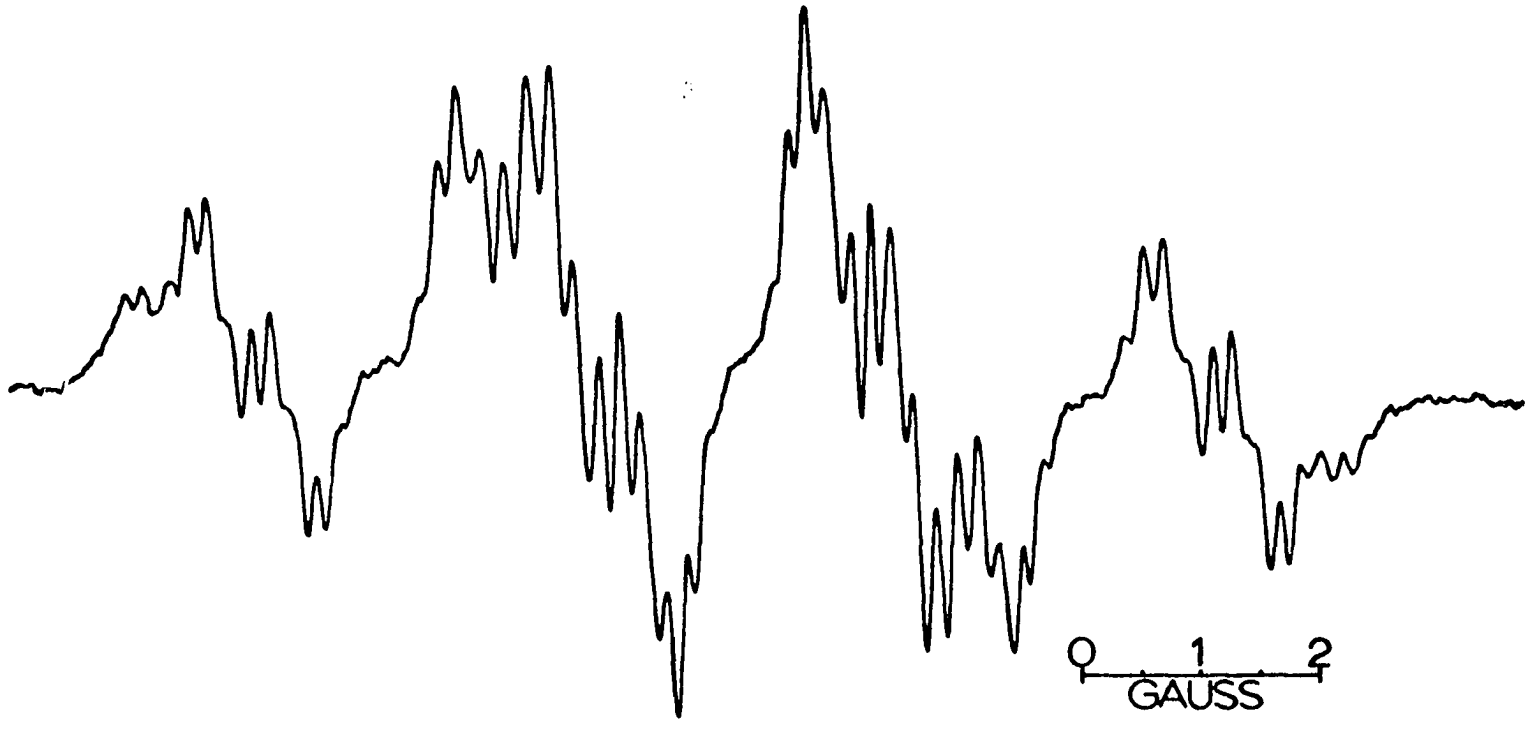


Figure 11. First-derivative esr spectrum of semidione VI obtained by Dr. K.-Y. Chang by the reduction of camphor quinone with the enolate anion of propiophenone in DMSO.

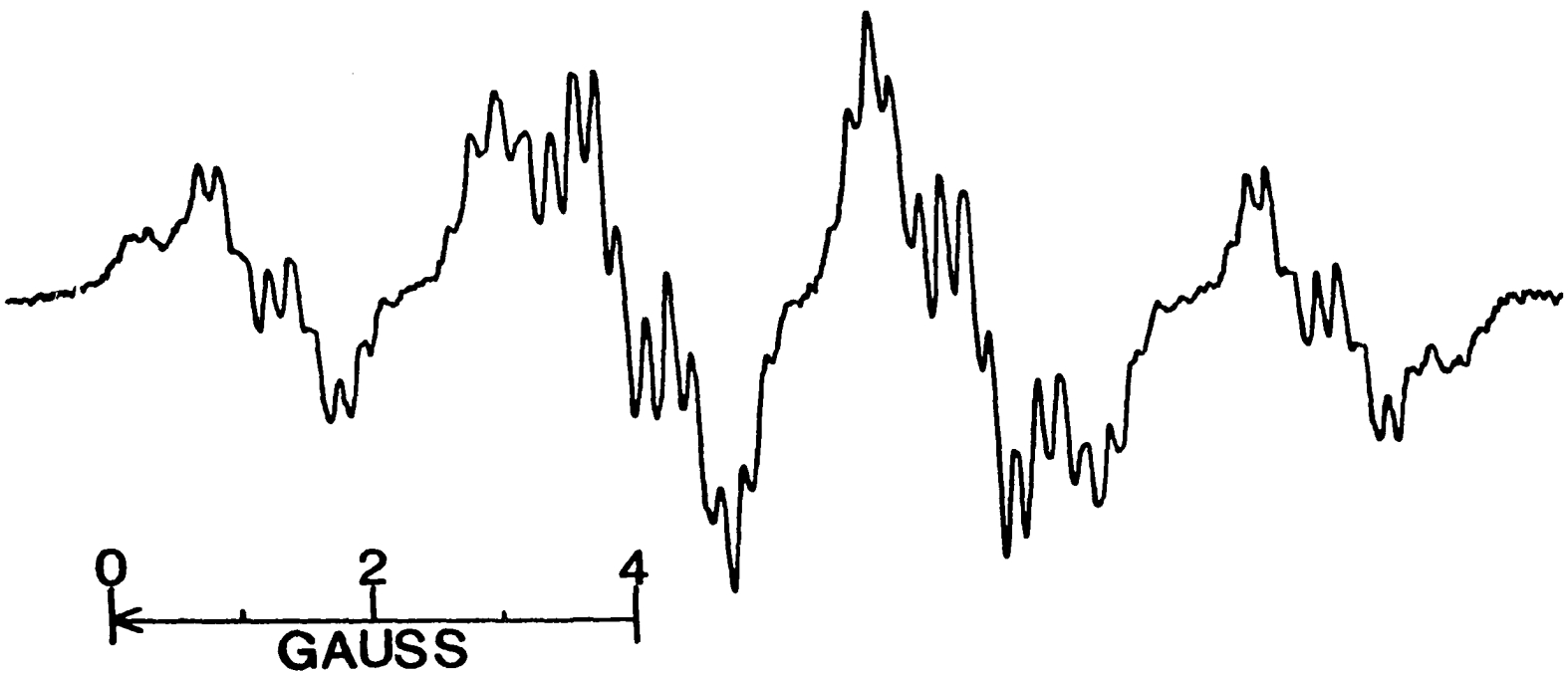
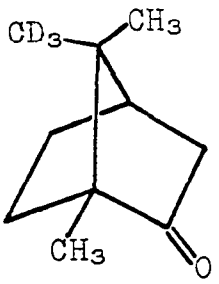
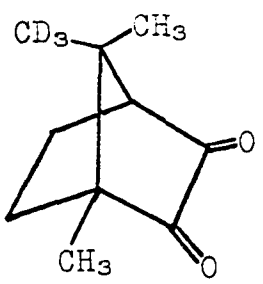


Figure 12. First-derivative esr spectrum of anti-7-trideuteromethyl semidione XIII prepared by reduction of α-diketone XIII-b with the enolate anion of propiophenone in DMSO.

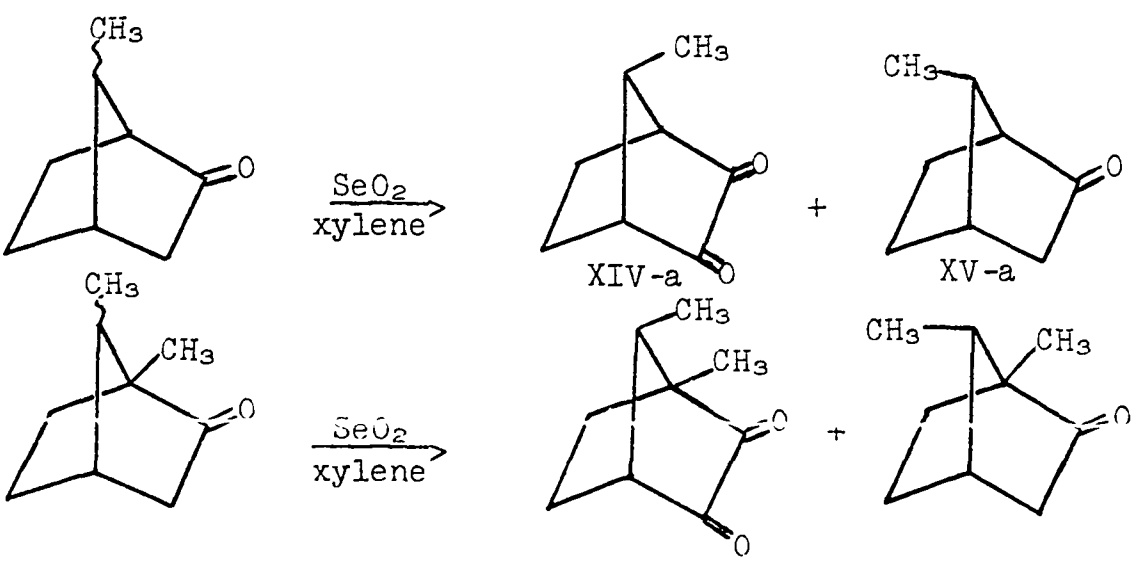


XIII-a



XIII-b

Semidione XIII was prepared by reduction of α-diketone XIII-b with the enolate anion of propiophenone. Likewise, semidione XIV (Figure 13) was generated from α-diketone XIV-a, which was obtained by the selenium dioxide oxidation of a mixture of <u>syn</u> and <u>anti</u>-7-methylbicyclo[2.2.1]heptan-2-ones. Only α-diketone XIV-a, the <u>syn</u> isomer, was formed. The <u>anti</u>-7-methyl monoketone (XV-a) could be partially recovered from the reaction mixture. This is analogous to the observations of Chang (23) who obtained only the <u>syn</u>-methyl α-diketone upon selenium dioxide oxidation of a mixture of <u>syn</u> and <u>anti</u>-1,7-dimethylbicyclo[2.2.1]heptan-2-ones.



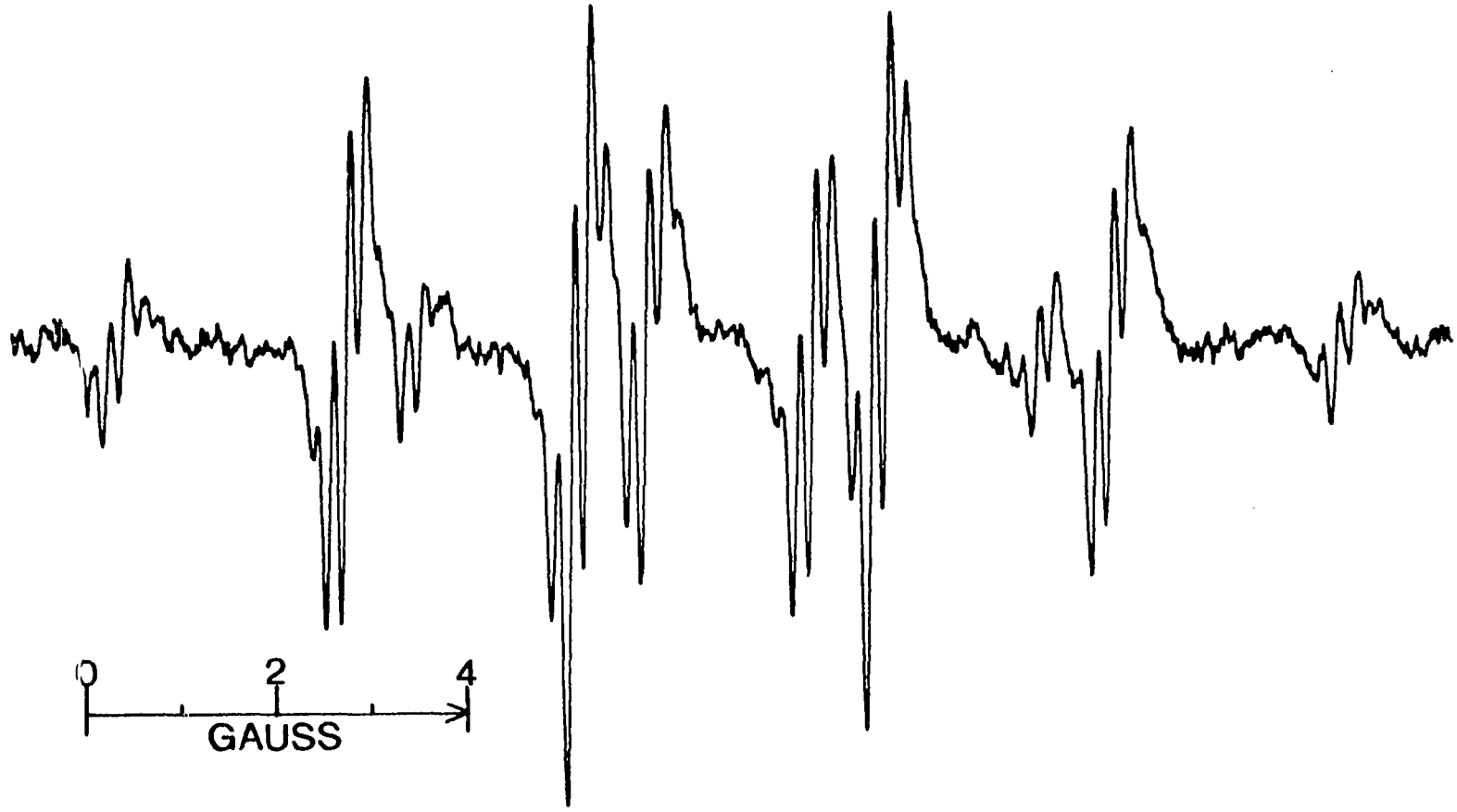
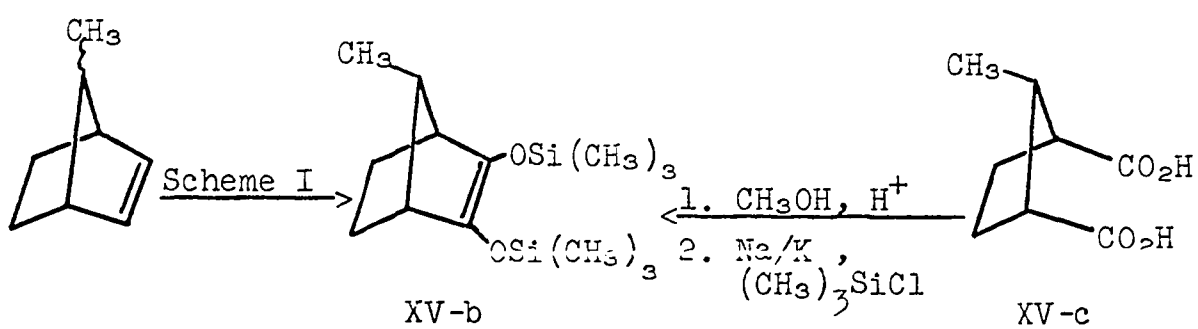


Figure 13. First-derivative esr spectrum of syn-7-methylbicyclo[2.2.1]heptan-2,3-semidione (XIV) generated by reduction of α-diketone XIV-a with the enolate anion of propiophenone in DMSO.

Preferential oxidation of the syn ketone is possibly due to the relief of nonbonded interactions between the syn-7-substituent and the C-2,3 bridge. This could occur through an increased rate of enolization, compared to the anti isomer. Selenium dioxide would be expected to attack from the unhindered exo side for the anti isomer and from the endo side for the syn isomer. The activation energy for the decomposition of the intermediate selenium complex may be significantly different for the two isomers, with the endo complex requiring less energy than the exo, since the endo complex experiences nonbonded interactions from the endo C-5,6 protons.

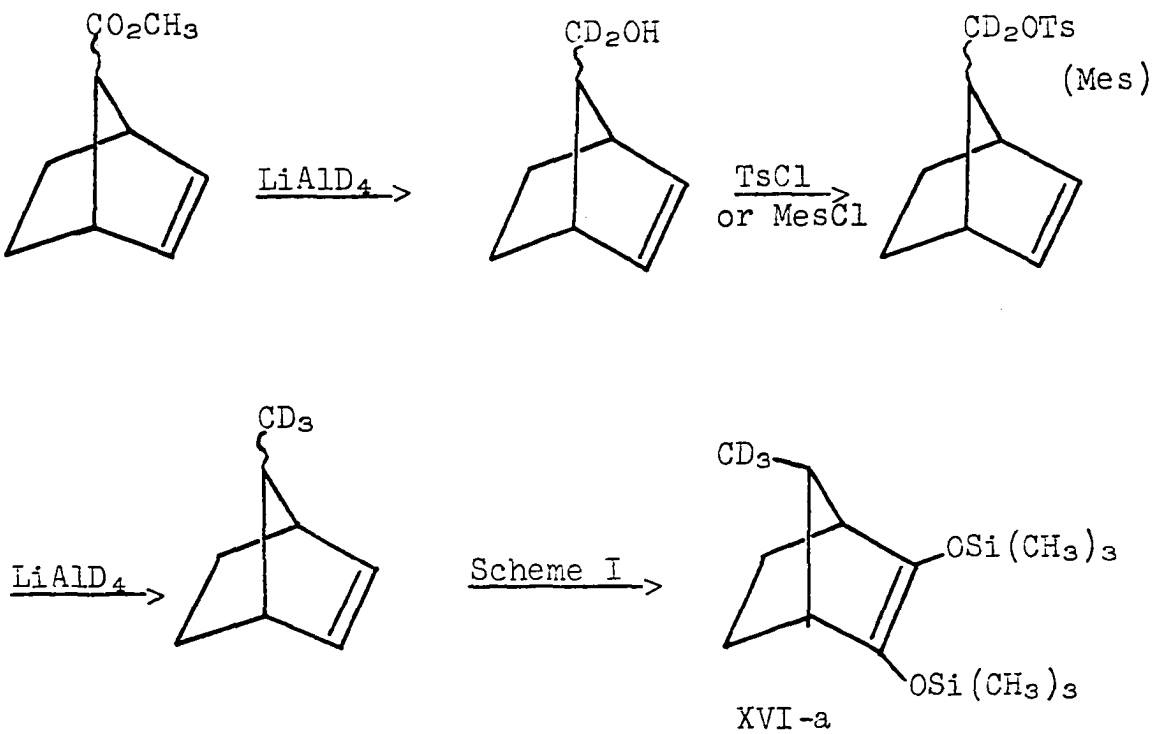
When a mixture of syn and anti-7-methylbicyclo[2.2.1]-heptenes was subjected to the reactions of Scheme I, only bis-(trimethylsiloxy)alkene XV-b was produced. XV-b was also prepared from a pure sample of trans-2-methylcyclopentane-cis-1,3-dicarboxylic acid (XV-c). Apparently the reactions of Scheme I do not preserve the stereochemistry of the initial olefin when the C-7 substituent is other than hydrogen or deuterium.



XV-b XV-c

Bis(trimethylsiloxy)alkenes XV-b and XVI-a generated the corresponding semidiones XV (Figure 14) and XVI (Figure 15) upon mixing with a DMSO solution of potassium t-butoxide. The trideuteromethyl group of XVI-a was introduced by employing lithium aluminum deuteride in the reactions outlined in Scheme III.

Scheme III



XVI-a

The effect of alkyl substitution on the C-5,6 bridge was investigated through semidiones XVII-XX, which are listed in Chart V.

The Diels-Alder adduct of maleic anhydride and cyclopentadiene can be thermally equilibrated to a mixture of exo and endo adducts and separated by fractional crystallization (54).

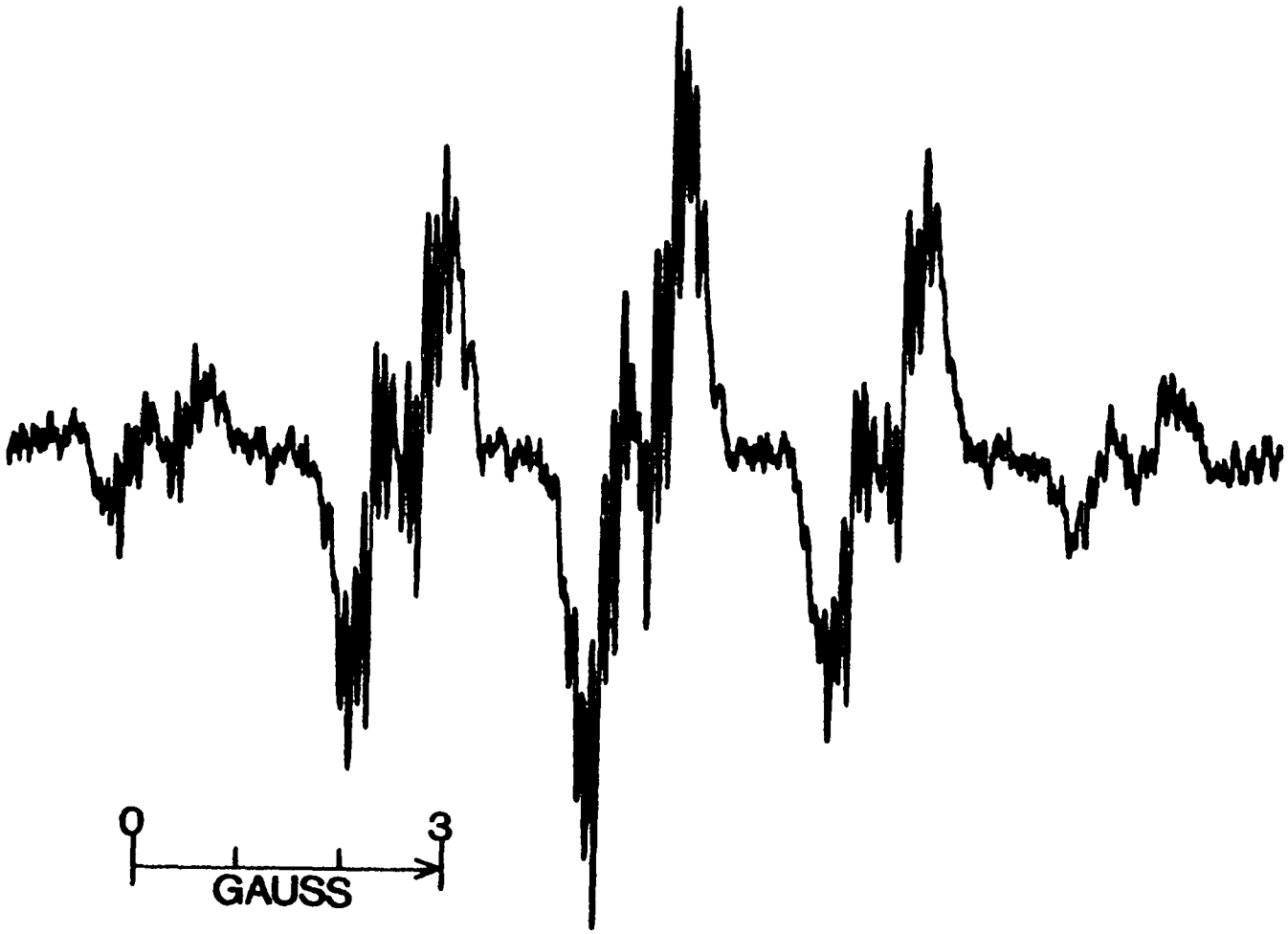


Figure 14. First-derivative esr spectrum of anti-7-methylbicyclo[2.2.1]heptan-2,3-semidione (XV) generated from bis(trimethylsiloxy)alkene XV-b in DMSO.

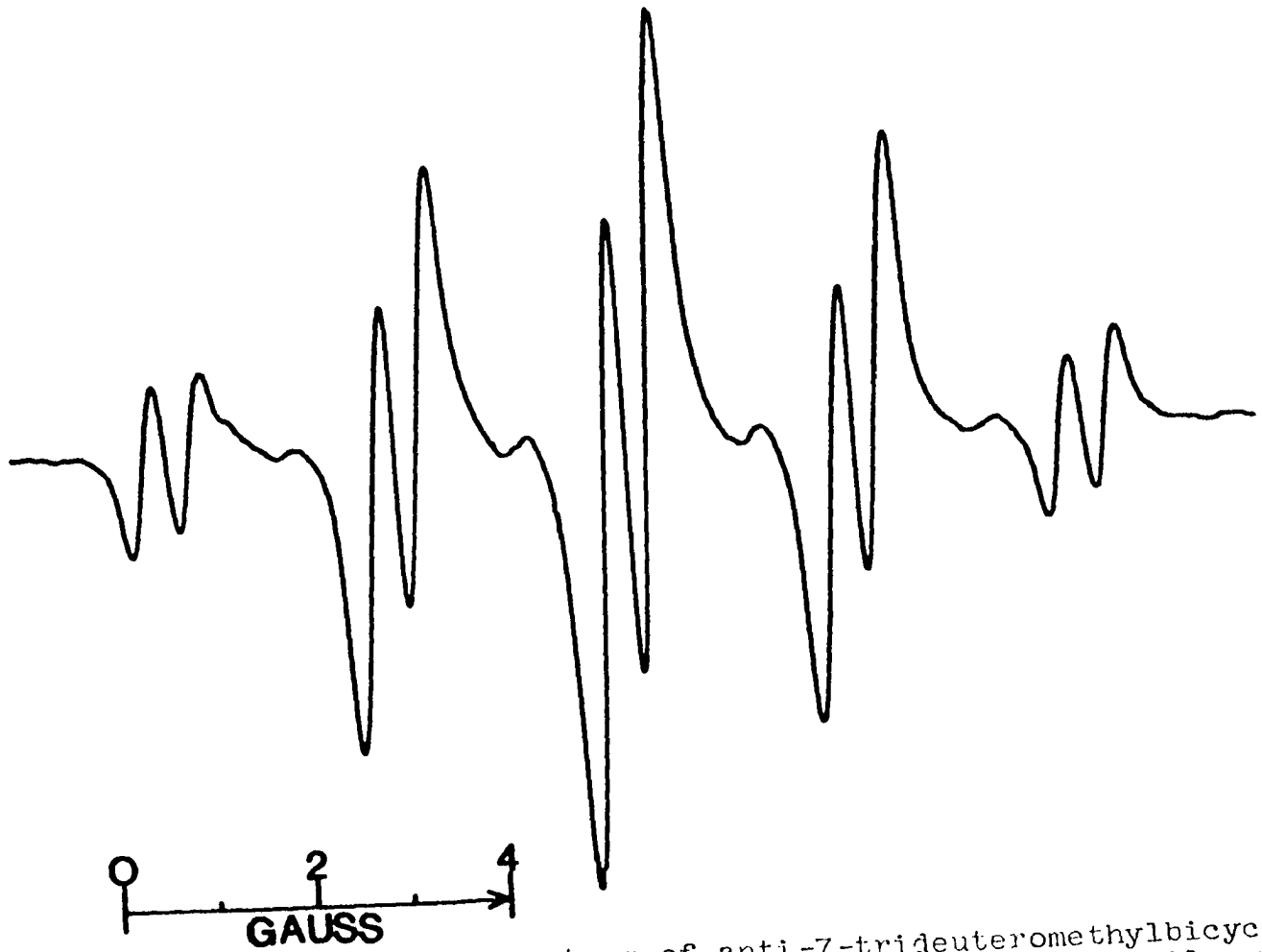
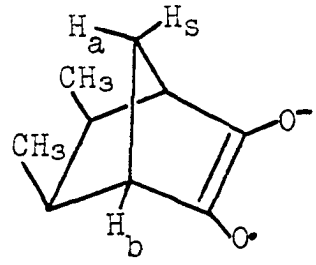


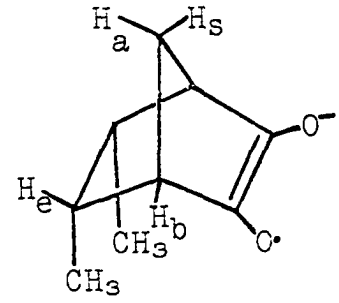
Figure 15. First-derivative esr spectrum of anti-7-trideuteromethylbicyclo[2.2.1]-heptan-2,3-semidione (XVI) generated from bis(trimethylsiloxy)alkene XVI-a in DMSO.

Chart V



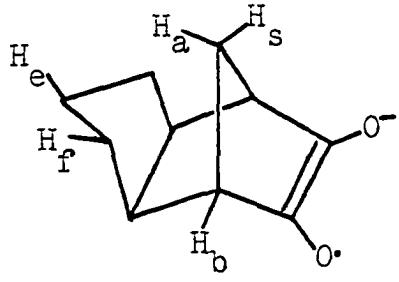
XVII

a^H= 6.19 (1H) H_a
2.59 (2H) H_b
0.40 (1H) H_s
0.18 (6H) CH_3



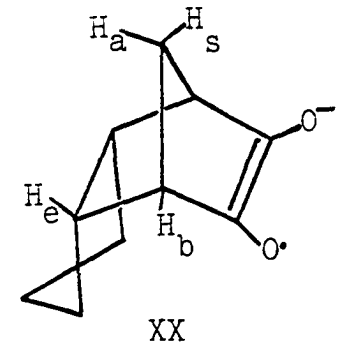
XVIII

a^H= 6.97 (1H) H_a
2.33 (2H) H_b
1.84 (2H) H_e
0.40 (1H) H_s
0.2 (6H) CH_3



XIX

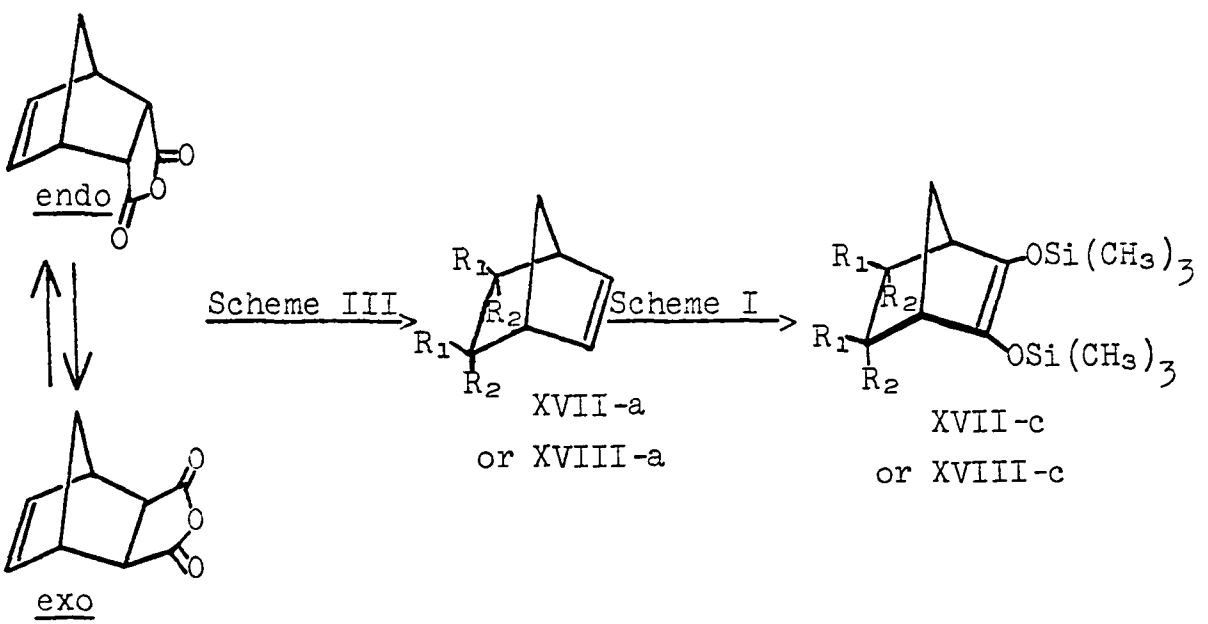
a^H= 6.42 (1H) H_a
2.34 (2H) H_b
1.31 (1H) H_e
0.42 (1H) H_s
0.10 (2H) H_f



XX

a^H= 6.96 (1H) H_a
2.68 (2H) H_b
1.68 (2H) H_e
0.88 (1H)
0.38 (1H) H_s
0.17 (2H)

This isomerization provided a convenient route to symmetrical C-5,6 methyl substituted semidiones. The exo and endo adducts were transformed to bis(trimethylsiloxy)alkenes XVII-c and XVIII-c by the reactions of Schemes III and I. Hydrolysis-oxidation of these compounds in a basic DMSO solution produced



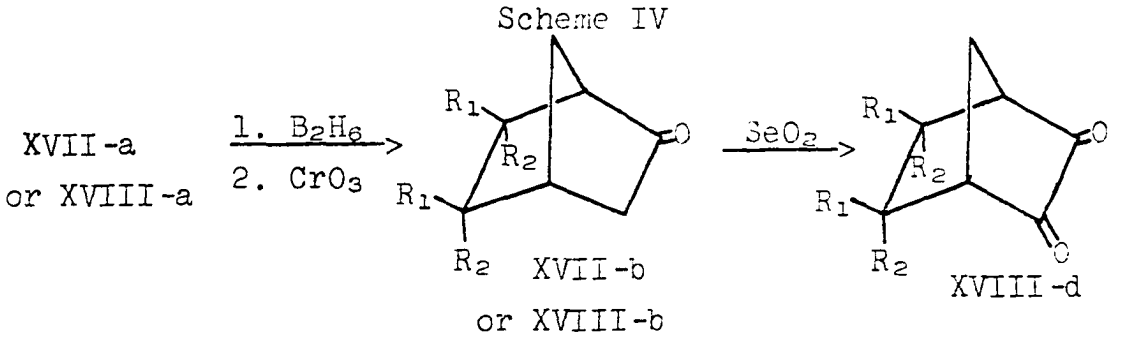
XVII- $R_1=CH_3$, $R_2=H$

XVIII- $R_1=H$, $R_2=CH_3$

strong radical concentrations. The stereochemistry was shown to have been preserved throughout the sequence of reactions by conversion of the intermediate olefins XVII-a and XVIII-a to the corresponding ketones XVII-b and XVIII-b. Neither ketone produced detectable concentrations of semidiones upon oxidation in a DMSO solution of potassium t-butoxide and a trace of air.

Only ketone XVIII-b yielded an α-diketone (XVIII-d) upon oxidation with selenium dioxide. Reduction of XVIII-d with propiophenone enolate anion yielded the same radical as bis(trimethylsiloxy)alkene XVIII-c.

Scheme IV



XVII-b $R_1 = CH_3$, $R_2 = H$

XVIII-b $R_1 = H$, $R_2 = CH_3$

Ketones XIX-a and XX-a also failed to yield a detectable semidione concentration upon oxidation with air and were remarkably resistant to oxidation by selenium dioxide. However, they could be converted to the corresponding bis(trimethylsiloxy)-alkenes XIX-b and XX-b by the reactions of Scheme V. XIX-b and XX-b generated semidiones XIX and XX when mixed with a DMSO solution of potassium t-butoxide. The esr spectra of semidiones XVII-XX (Figures 16-19) all show extensive long-range interactions as well as some curious changes in hfsc.

It was noted earlier that an anti-7-methyl group induced endo-5,6 hyperfine splittings (see semidiones V, VI, and XV); perhaps by pushing the endo-5,6 bridge toward the dicarbonyl

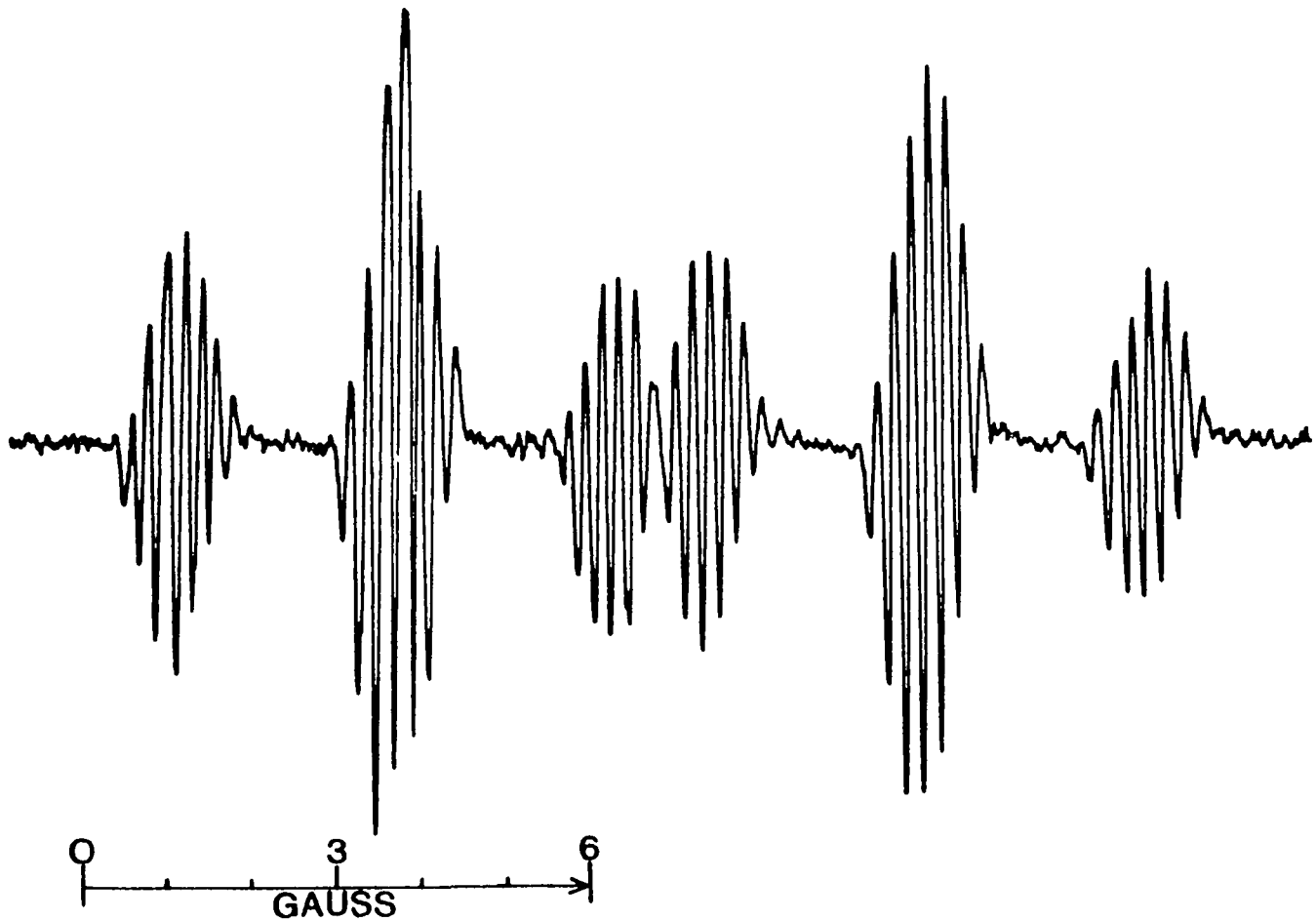


Figure 16. First-derivative esr spectrum of exo, exo-5,6-dimethylbicyclo[2.2.1]heptan-2,3-semidione (XVII) generated from bis(trimethylsiloxy)alkene XVII-c in DMSO.

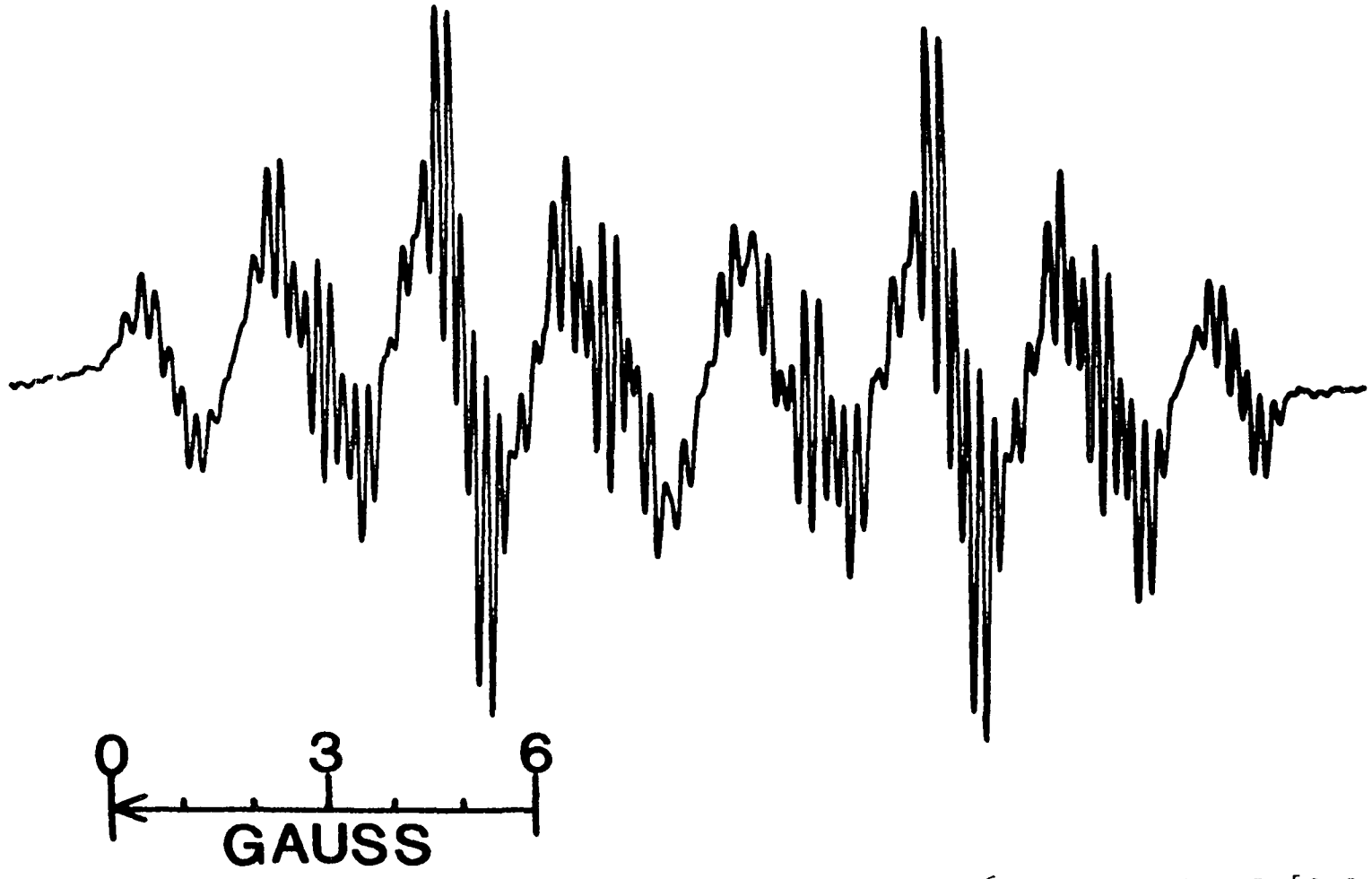


Figure 17. First-derivative esr spectrum of endo, endo-5,6-dimethylbicyclo[2.2.1]-heptan-2,3-semidione (XVIII) generated from bis(trimethylsiloxy)alkene XVIII-d in DMSO.

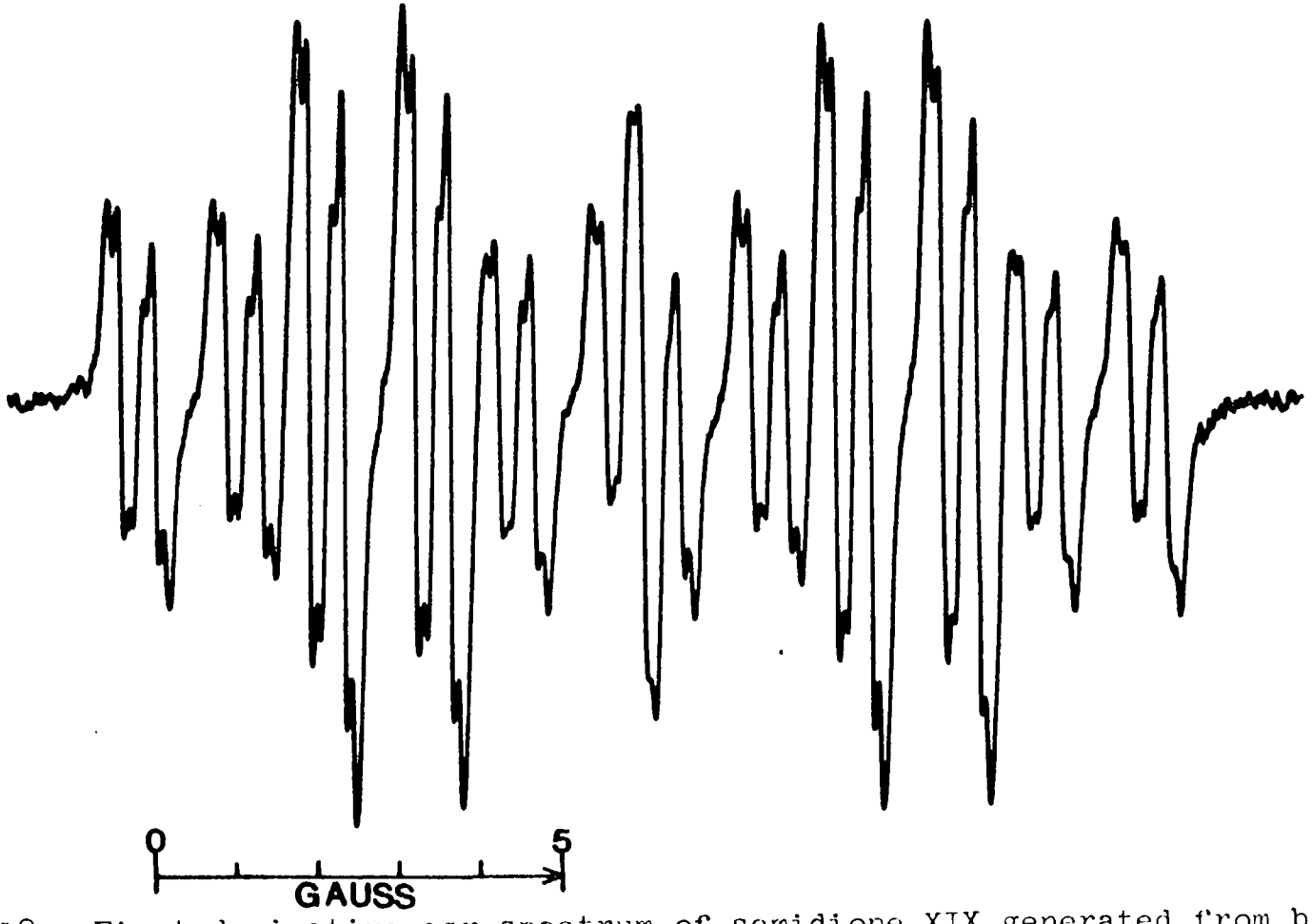


Figure 18. First-derivative esr spectrum of semidione XIX generated from bis(trimethylsiloxy)alkene XIX-b in DMSO.

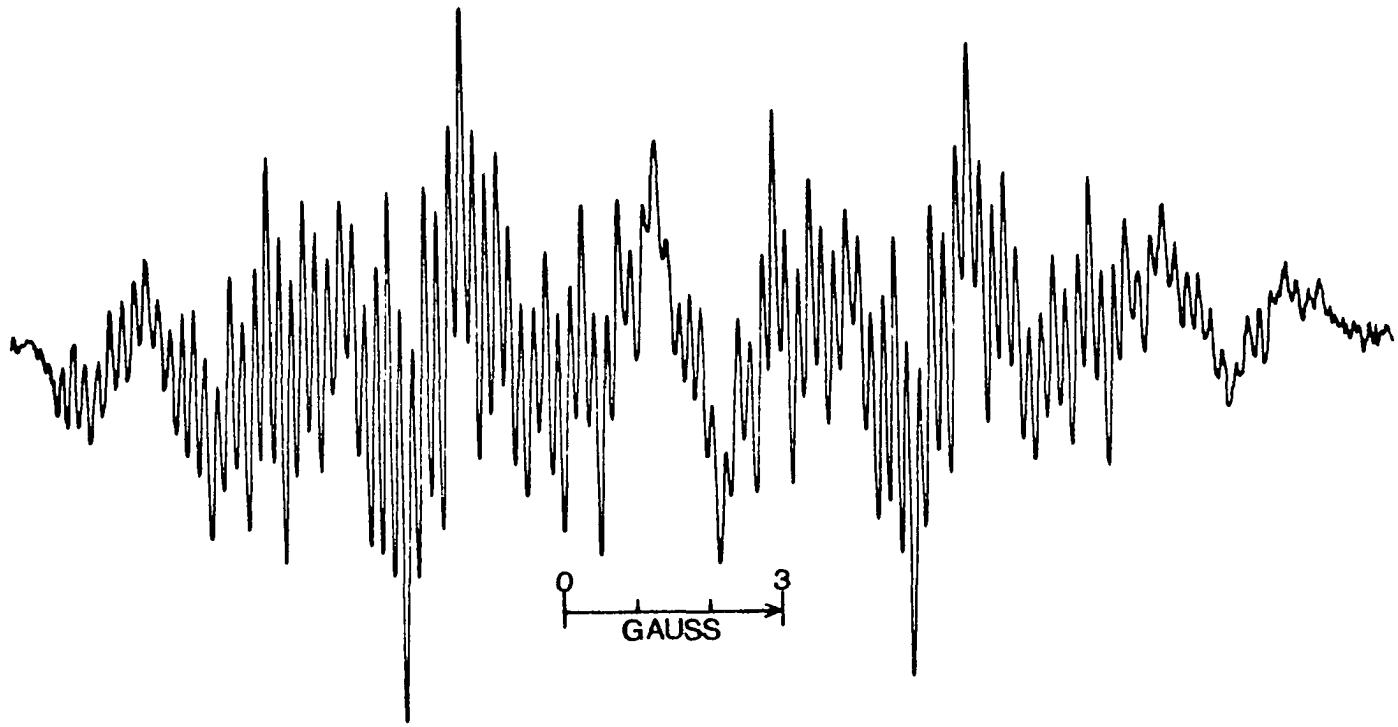
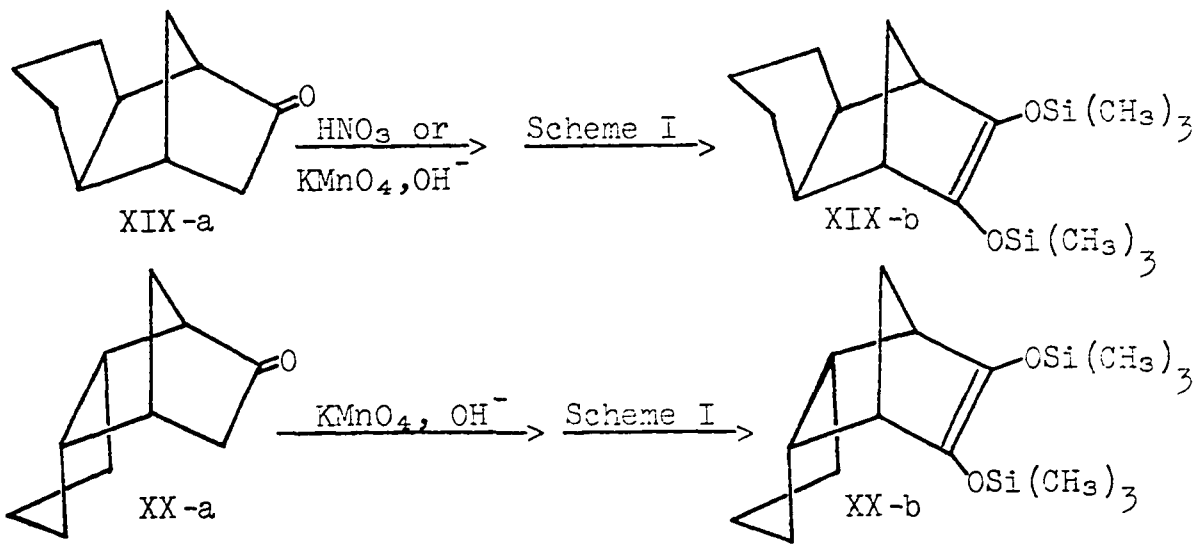


Figure 19. First-derivative esr spectrum of semidione XX generated from bis(trimethylsiloxy)alkene XX-b in DMSO.

Scheme V



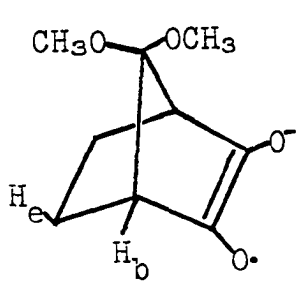
system. An exo-5,6 substituent should produce the same effect since it will experience nonbonded interactions similar to that of an anti-7 group. However, no endo-5,6 splittings are detected in the spectra of semidiones XVII and XIX. It would seem that geometry changes are not responsible for the introduction of endo splittings.

Comparison of semidiones (Charts I, IV, and V) which have either syn or endo alkyl groups reveals that substitution in these positions significantly reduces the anti or exo hyperfine splitting, often by as much as one-half. Again geometry changes cannot account for this decrease since other hfsc in these semidiones are comparable to those of the parent semidione I.

In semidiones IV and V (Chart VI) the bridgehead and exo-5,6 protons are no longer magnetically equivalent. Data were insufficient to make a positive assignment of hfsc to these

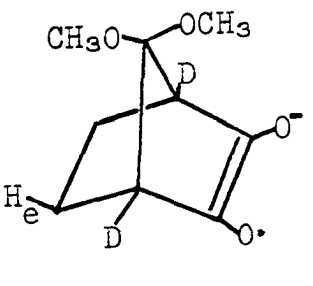
positions. This problem was surmounted by incorporating deuterium (via the reactions outlined in Scheme VI) into the bridgehead positions of semidione IV. Semidione XXI was obtained by oxidation of ketone XXI-a with a trace of air in a DMSO solution of potassium t-butoxide. Its esr spectrum (Figure 20) is not well-resolved and consists of a 2.0 G triplet. The lines are broadened due to unresolved deuterium splittings. The 2.0 G splittings of semidiones IV, V, and XXI can now be assigned to the exo-5,6 position and the larger, 2.5-2.9 G, splittings of IV and V to the bridgehead position.

Chart VI



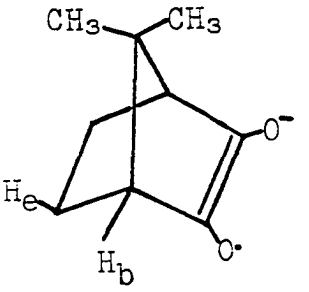
IV

a^H = 2.50 (2H) H_b
1.96 (2H) H_e



XXI

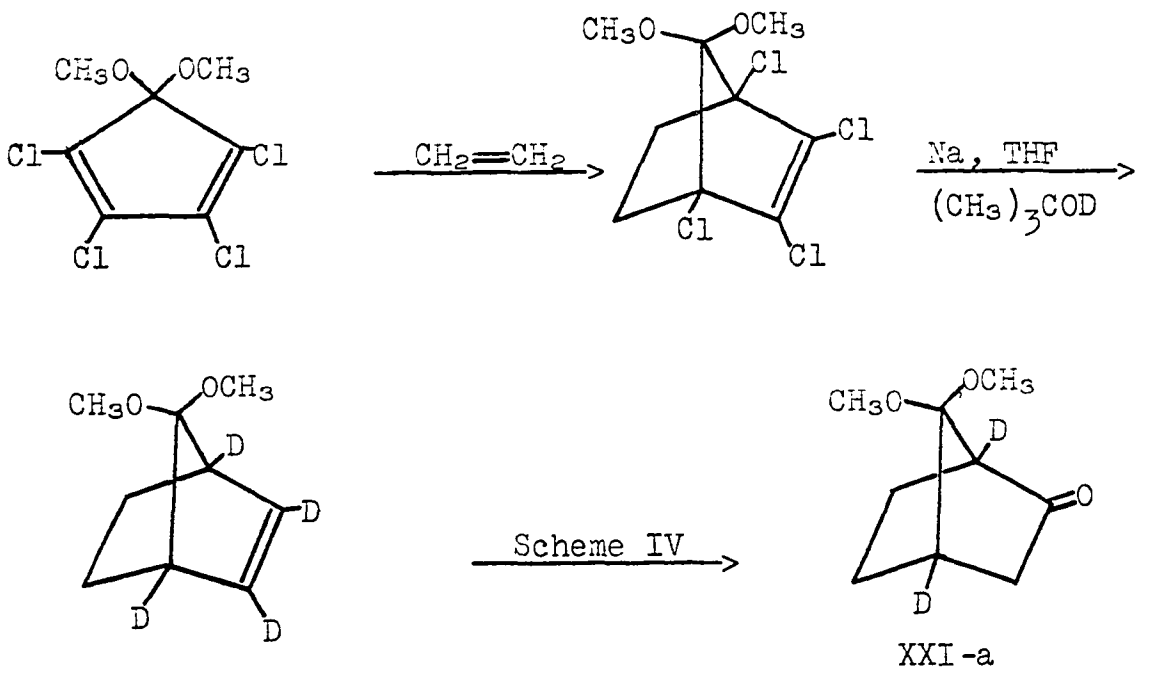
a^H = 2.0 (2H) H_e



V

a^H = 2.90 (2H) H_b
2.07 (2H) H_e

Scheme VI



XXI-a

α-Diketone XXIII can be prepared by the acidic or basic hydrolysis of the Diels-Alder adduct of cycloheptatriene and dichlorovinylene carbonate (XXII) (13). This α-diketone failed to yield detectable concentrations of radicals upon reduction with propiophenone enolate anion. In an attempt to prepare diacid XXIV, a complex mixture of acidic materials was obtained from the hydrolysis of the adduct with basic hydrogen peroxide. An in situ hydrolysis of the adduct within the esr sample cell failed to produce any observable radicals.

Oxidation of monoketones XXVI-XXX with air in DMSO and potassium t-butoxide failed to produce any stable radical species. Selenium dioxide oxidation of these ketones yielded complex

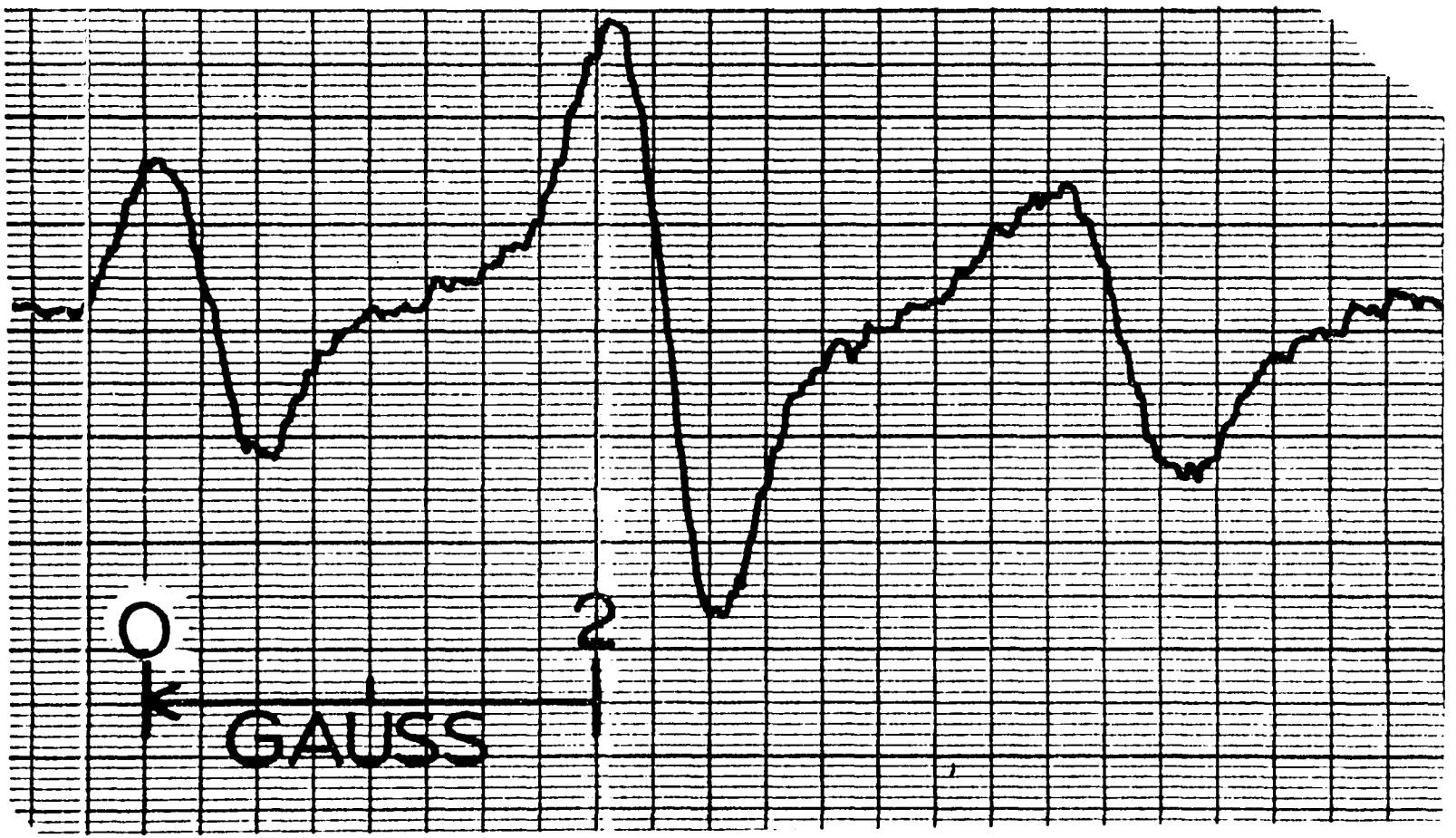
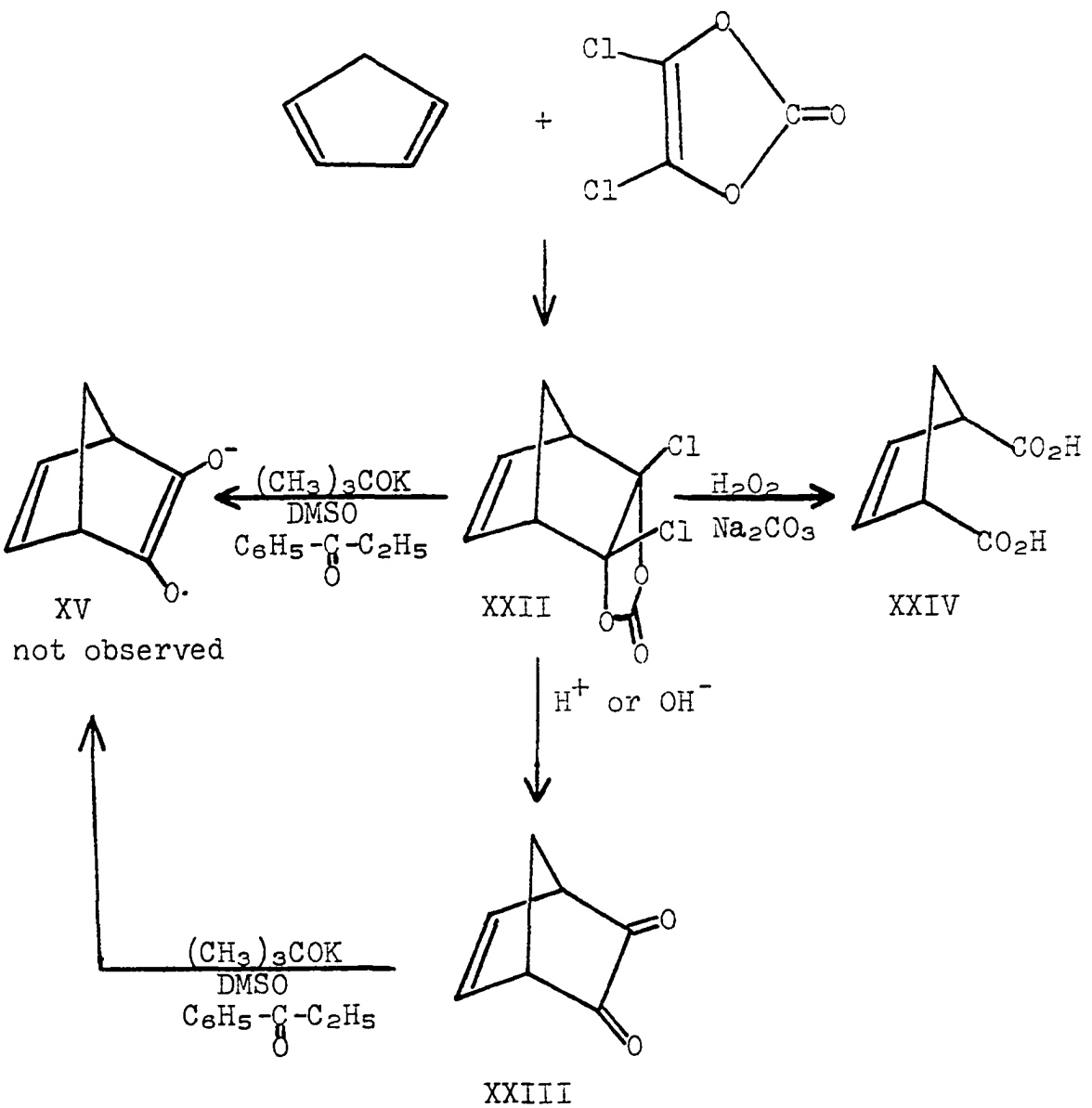
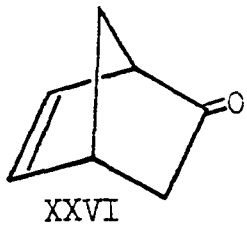


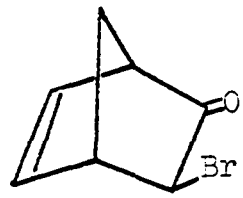
Figure 20. First-derivative esr spectrum of semidione XXI generated by air oxidation of monoketone XXI-a in DMSO and potassium t-butoxide.



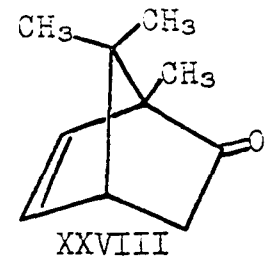
reaction mixtures which also failed to produce stable radicals upon reduction with the enolate anion of propiophenone.



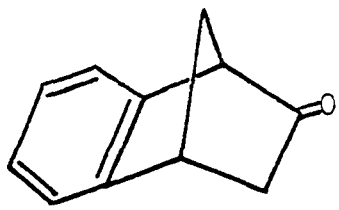
XXVI



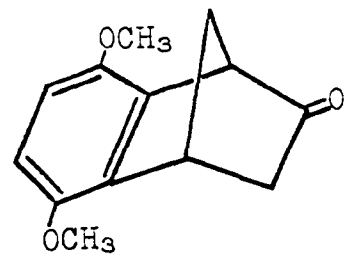
XXVII



XXVIII

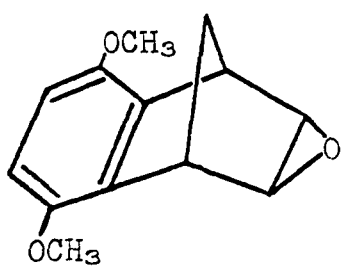


XXIX



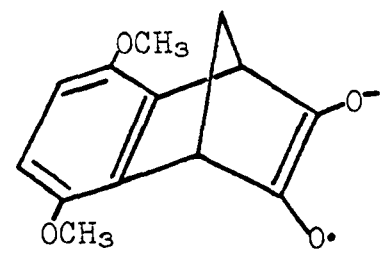
XXX

Heating a DMSO solution of epoxide XXXI-a with a small amount of boron trifluoride etherate, followed by mixing with potassium t-butoxide, failed to generate semidione XXXI.



XXXI-a

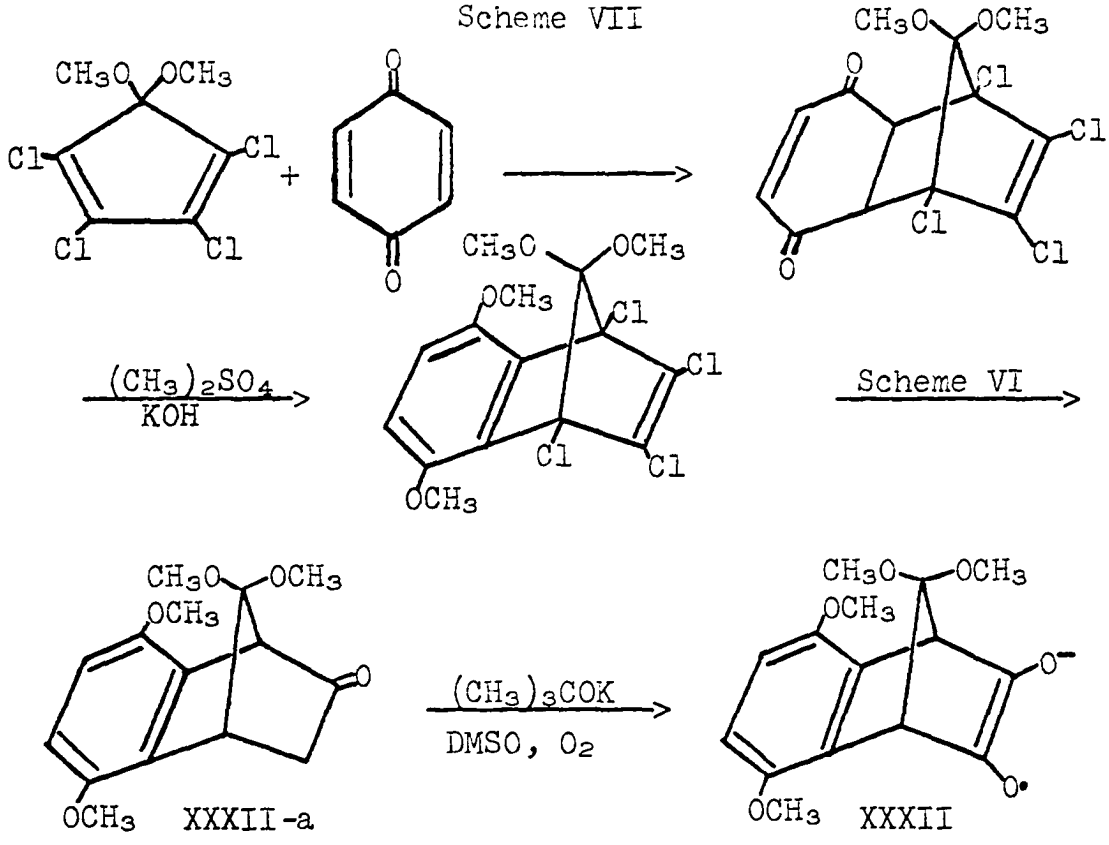
1. DMSO, $BF_3 \cdot Et_2O$
2. $(CH_3)_3COK$



XXXI
not observed

Oxidation of monoketone XXXII-a yielded a stable radical. Its esr spectrum (Figure 21) consists of two triplet splittings (a^H = 3.51, 2.52 G) and a quartet (a^H = 0.65 G). The hfsc can not easily be reconciled with the structure of the expected semidione XXXII. Monoketone XXXII-a was prepared by the reactions outlined in Scheme VII.

Scheme VII



Only one unsaturated bicyclo[2.2.1]heptan-2,3-semidione has been observed. Semidione XXXIII (Figure 22-a) was generated by reduction of benzobicyclo[2.2.1]heptene-2,3-dione with propiophenone enolate anion. The radical decomposes very rapidly (life time of about six minutes at 25° in DMSO). The increased strain in the molecule, due to the benzo group, appears to

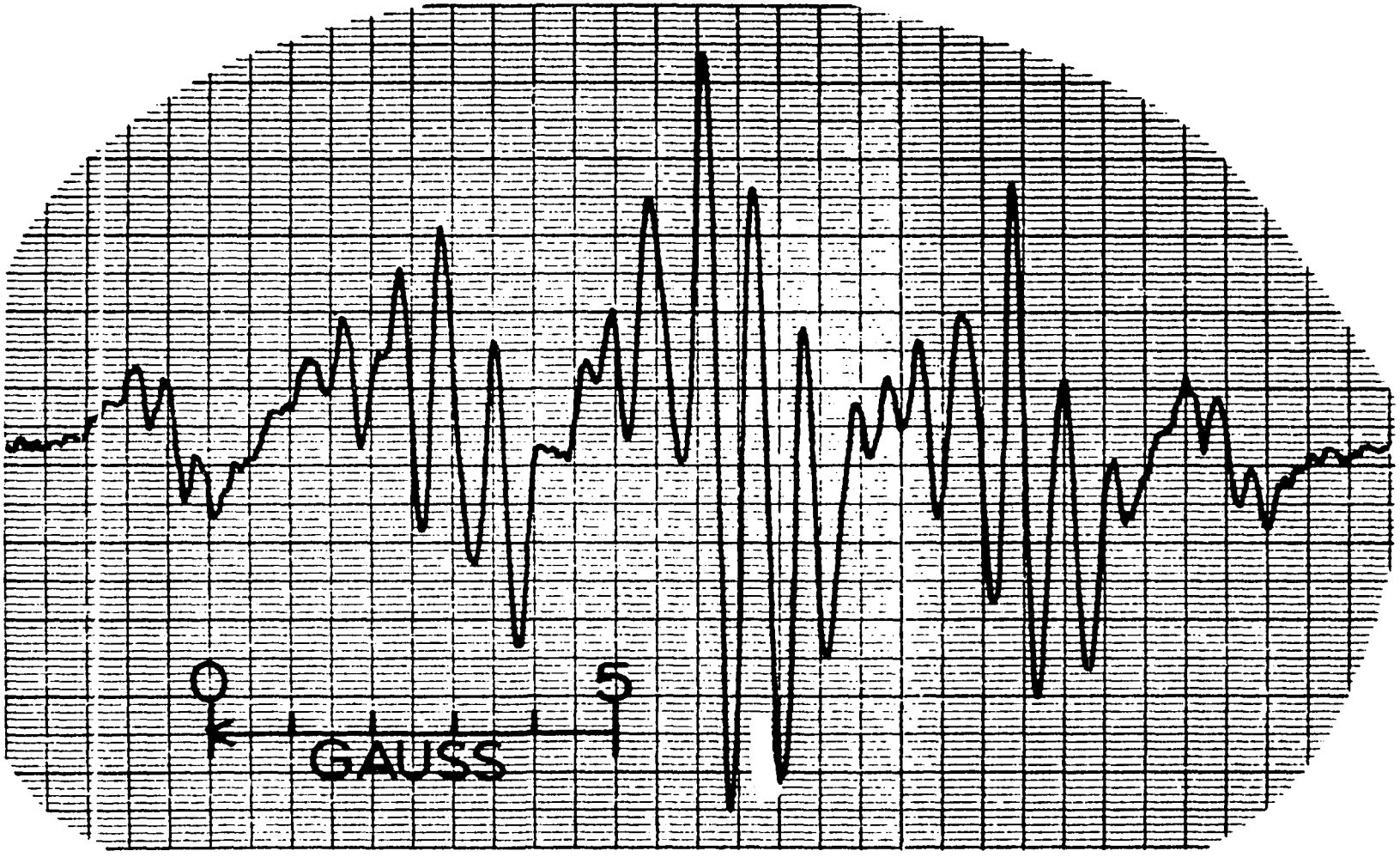


Figure 21. First-derivative esr spectrum of the radical obtained by air oxidation of monoketone XXXIII-a in DMSO and potassium t-butoxide.

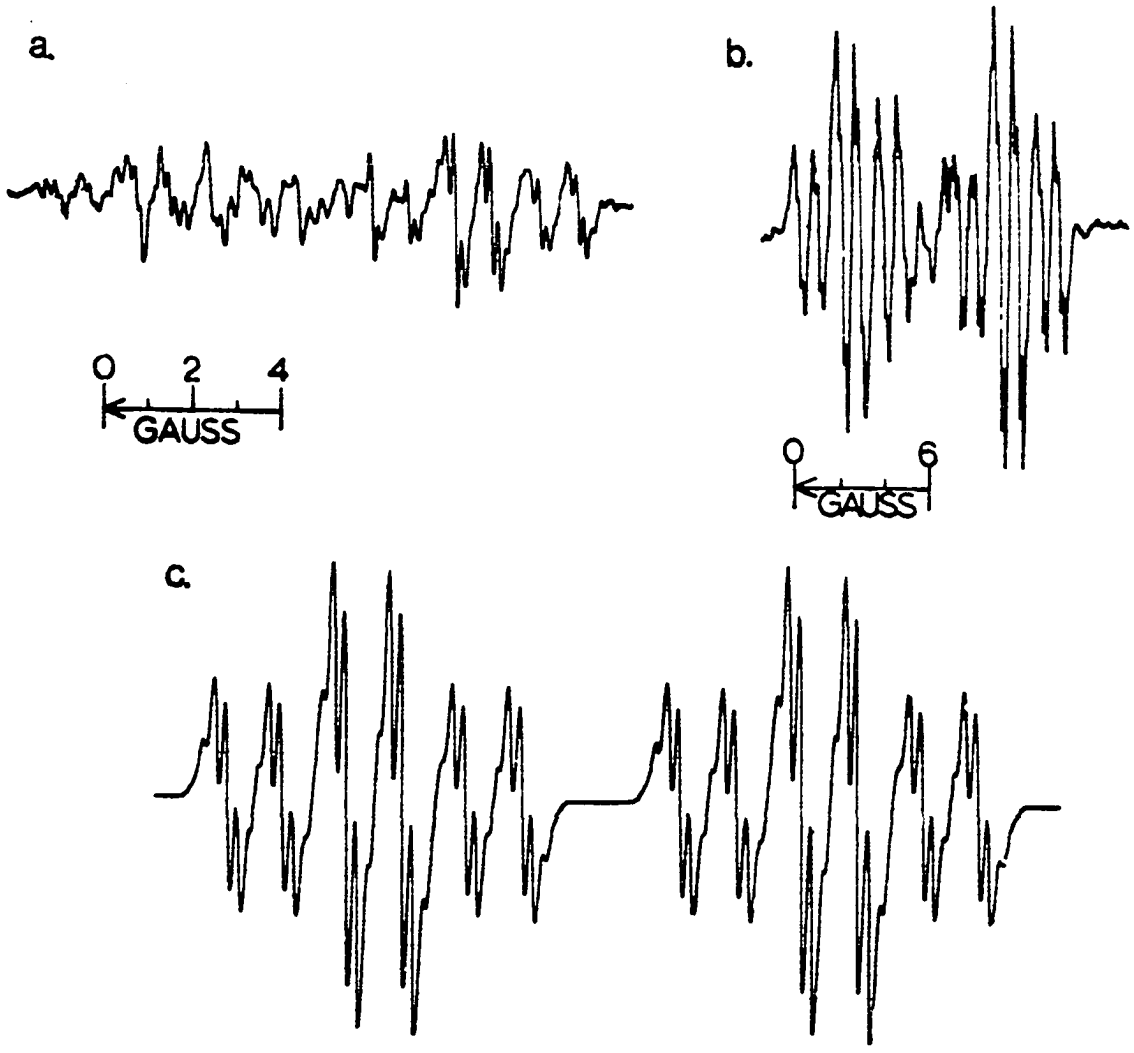
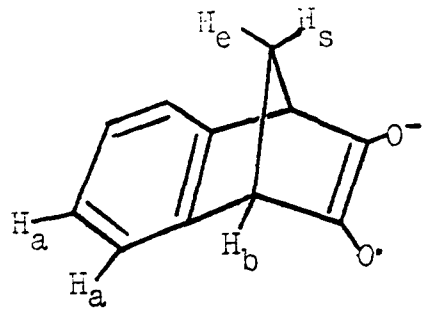
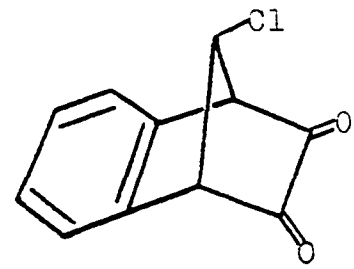


Figure 22. First-derivative esr spectrum of benzobicyclo-[2.2.1]hepten-2,3-semidione (XXXIII) in DMSO; (a) 10 min scan, (b) 5 min scan and, (c) simulated using the hfsc in the text.



XXXIII



XXXIV

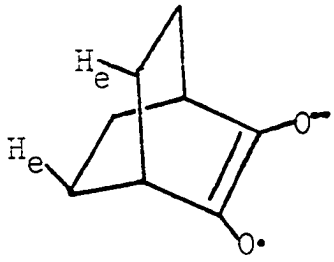
a^H = 7.06 (1H) H_e
1.86 (2H) H_b
0.87 (1H) H_s
0.18 (4H) H_a

accelerate the benzilic acid-type rearrangement of this type of α-diketones in basic DMSO solution, and perhaps explains why this group of semidiones is so elusive. Subjection of α-diketone XXXIV to the same conditions produced a radical that gave an eight-line esr spectrum (12.8 G wide), which could not be interpreted in terms of the expected semidione. The lifetime of this radical was 4-6 minutes.

Bicyclo[2.2.2]octan-2,3-semidiones

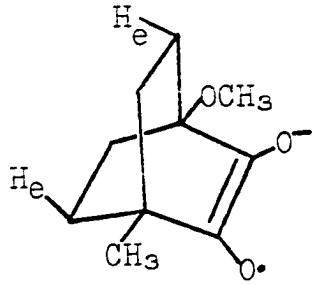
The results of Chang (23) for the bicyclo[2.2.2]octane system are listed in Chart VII. It is noted that only one hyperfine interaction is observed for the parent semidione, XXXV. A comparison of the data compels that the hyperfine splitting be assigned to the four equivalent exo protons (H_e). Bridgehead, endo, and methyl splittings are all normally less

Chart VII



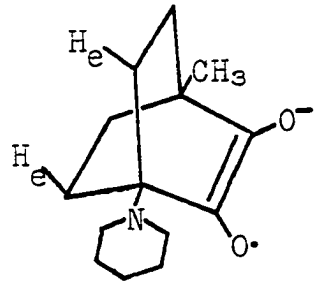
XXXV

a^H= 2.09 (4H) H_e



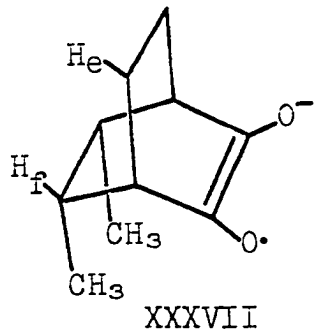
XXXVI

a^H= 2.14 (4H) H_e



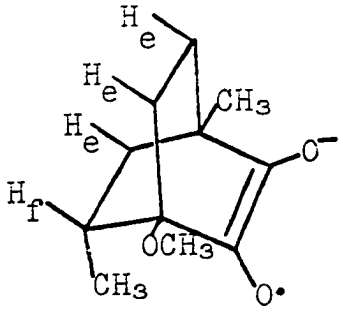
XXXVIII

a^H= 2.21 (4H) H_e



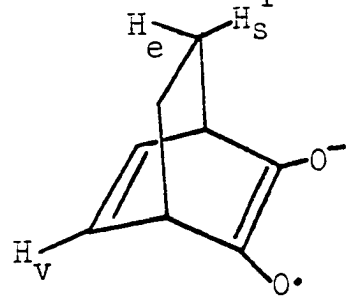
XXXVII

a^H= 2.12 (2H) H_e
1.34 (2H) H_f



XXXIX

a^H= 2.10 (3H) H_e
0.93 (1H) H_f

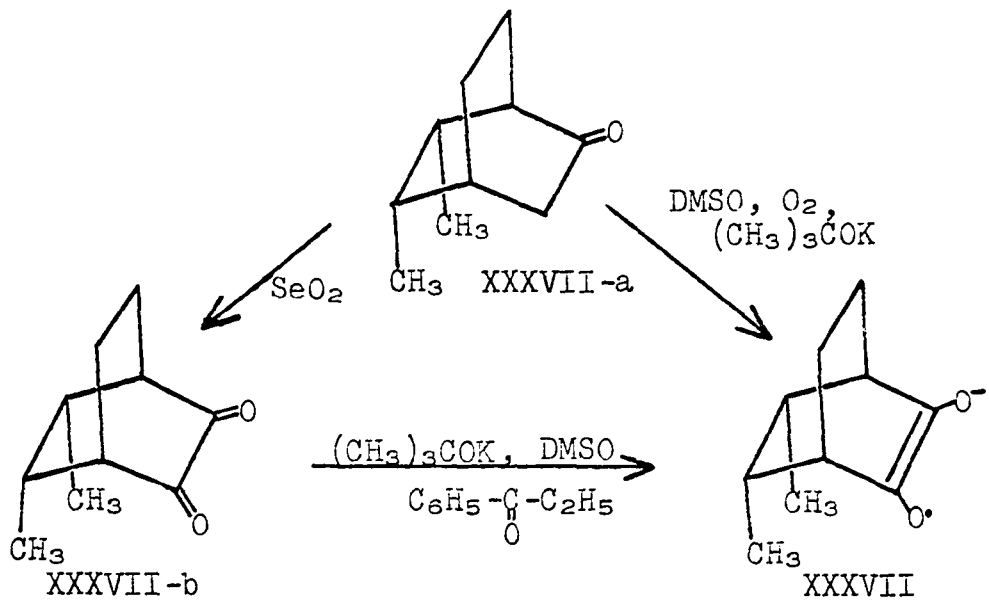


XL

a^H= 2.60 (2H) H_e
0.41 (4H) H_s, H_v

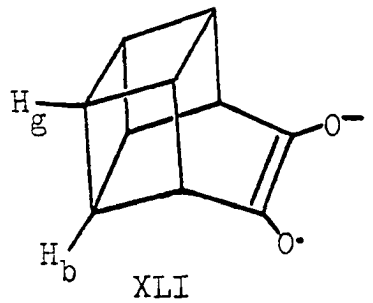
than 0.1 G and thus are not resolved. As was observed in the bicyclo[2.2.1]heptane systems, *endo* alkyl substitution decreases the *exo* hfsc of that bridge. The introduction of a double bond into the molecule causes an additional 0.41 G quintet which is assigned to two vinyl and the two *endo* protons.

The only additional work done in this area was the confirmation of XXXVII *via* its preparation from α-diketone XXXVII-b. An esr spectrum identical in every respect to that obtained by the oxidation of monoketone XXXVII-a (23) was obtained.



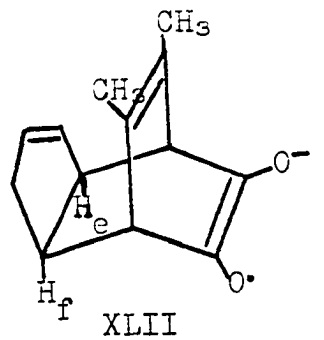
With the exception of XL, these semidiones are (due to their lack of hyperfine interactions) not very exciting but are valuable in that they established the long-range *exo* splitting as the major interaction of this system. Due to the intense interest in long-range interactions and splitting mechanisms in bicyclic semidiones, a number of additional

Chart VIII



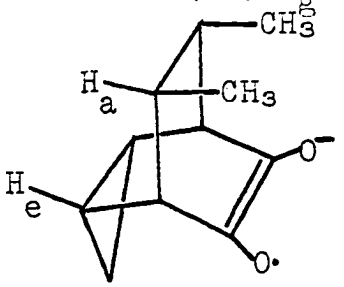
XLI

a^H= 0.53 (4H) H_b
0.09 (2H) H_g



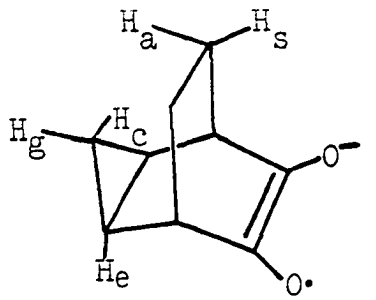
XLII

a^H= 0.48 (8H) CH_3, H_e, H_f



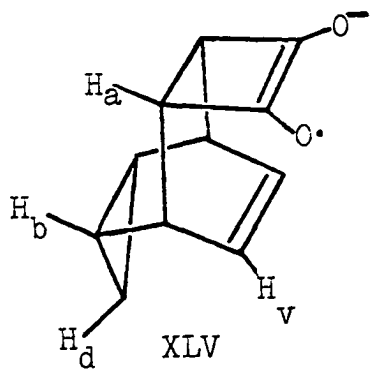
XLIII

a^H= 1.55 (2H) H_a
0.44 (2H) H_e



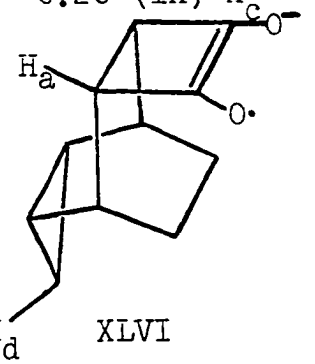
XLIV

a^H= 2.21 (2H) H_a
1.98 (1H) H_a
0.65 (2H) H_s^g or H_e
0.32 (2H) H_e or H_s
0.20 (1H) H_c



XLV

a^H= 11.00 (2H) H_a
1.06 (1H) H_d
0.45 (2H) H_v
0.15 (2H) H_b



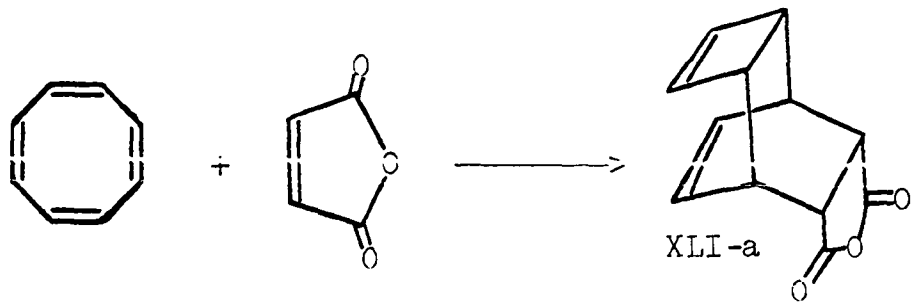
XLVI

a^H= 11.50 (2H) H_a
0.68 (1H) H_d

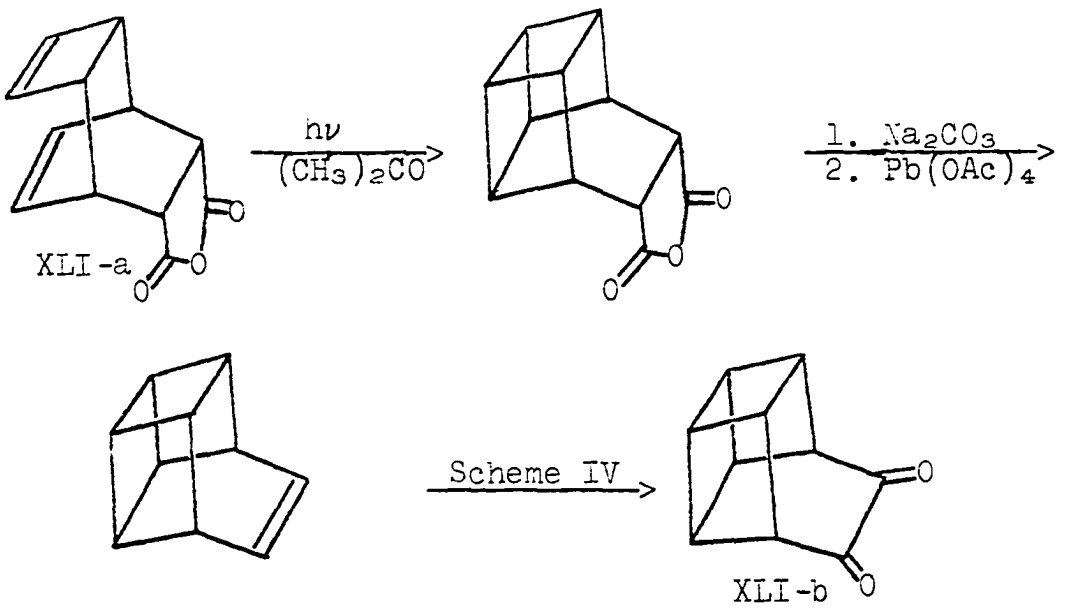
semidiones and semiquinones containing the bicyclo[2.2.2]octane nucleus and rich in long-range hyperfine interactions were prepared. In some instances, unexpectedly large hyperfine splittings are observed for protons five bonds removed from the carbonyl carbon of the semidione system. The results are listed in Charts VIII and IX.

Semidiones XLI, XLII, and XLVII-LI were prepared as DMSO solutions by the reduction of the corresponding α-diketones with the enolate anion of propiophenone. Semidiones XLIV-XLVI were prepared from the appropriate bis(trimethylsiloxy)alkene and semiquinones LII-LV were generated by the air oxidation of hydroquinones in DMSO and potassium t-butoxide.

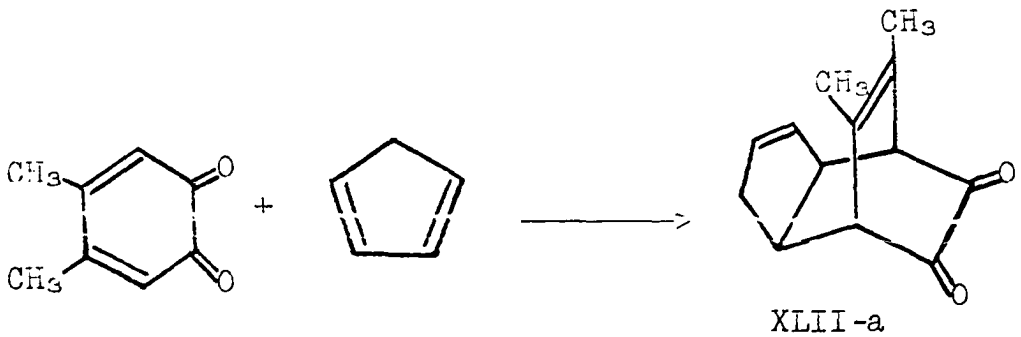
Figure 23 shows the esr spectrum of semidione XLI. It consists of a 0.53 G quintet (1:4:6:4:1) which must be due to the four equivalent beta protons (H_b). The remaining 0.9 G triplet is assigned to the two gamma (H_g) protons since bridgehead splitting has never been observed in bicyclo[2.2.2]-octane semidiones. The precursor to this semidione, XLI-b, was prepared by another research group (55) (see also Dauben and Whalen (56)) starting from the Diels-Alder adduct (XLI-a) of maleic anhydride and cyclooctratetraene.



XLI-a



Semidione XLII displays a nine-line pattern in its esr spectrum (Figure 24). The lines are separated by 0.48 G and must be due to eight nearly magnetically equivalent protons. At least six of these must be from the two vinyl methyl groups. The remaining two are most likely the <u>endo</u> protons (H_e and H_f in Chart VIII) as the hfsc are comparable to known <u>endo</u> splitting in similar semidiones; e.g., semidione XL. α-Diketone XLII-a was prepared by another research group by the Diels-Alder reaction of cyclopentadiene and 4,5-dimethyl-o-quinone (57).



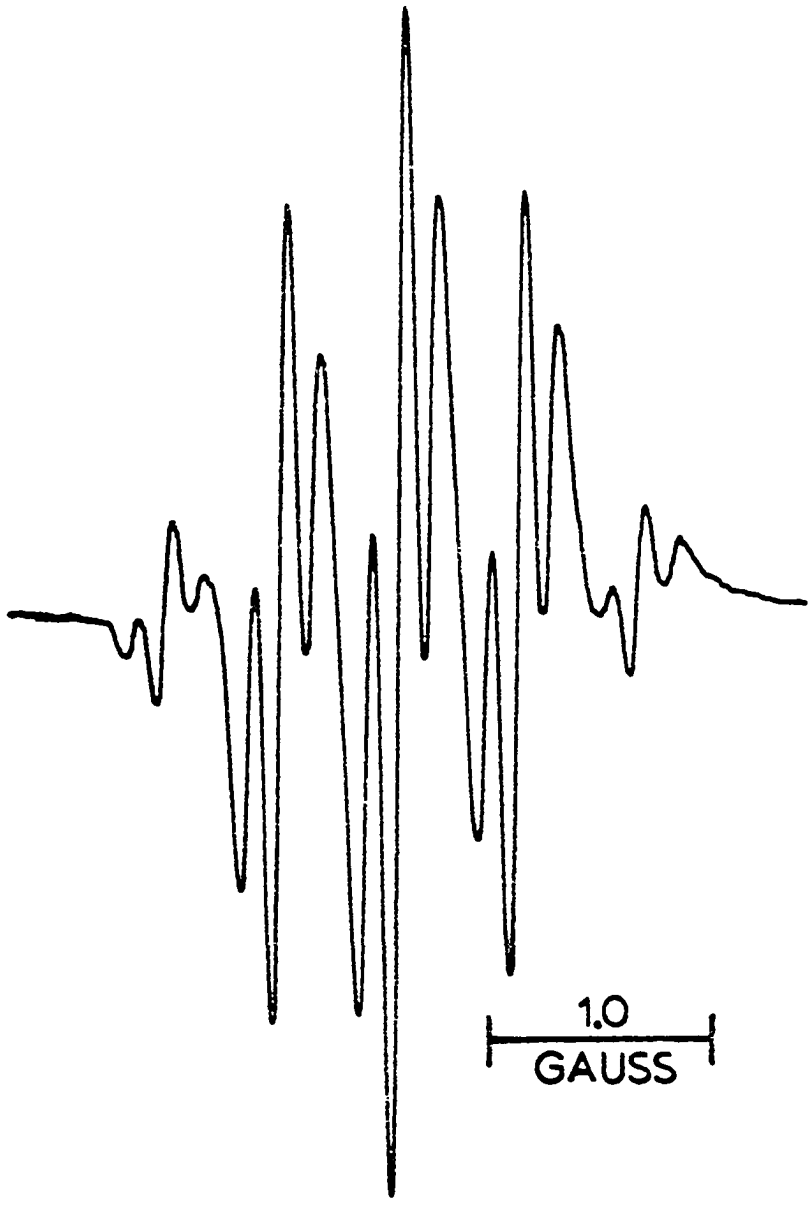


Figure 23. First-derivative esr spectrum of semidione XLI generated by reduction of α-diketone XLI-b with the enolate anion of propiophenone in DMSO.

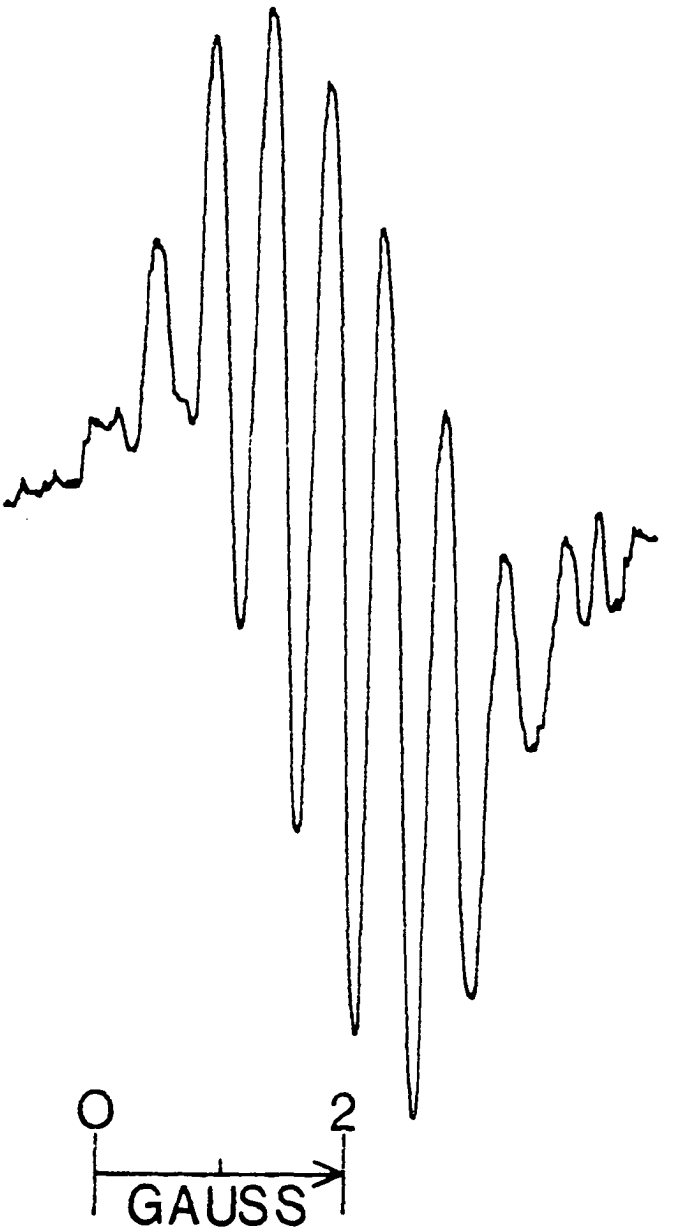
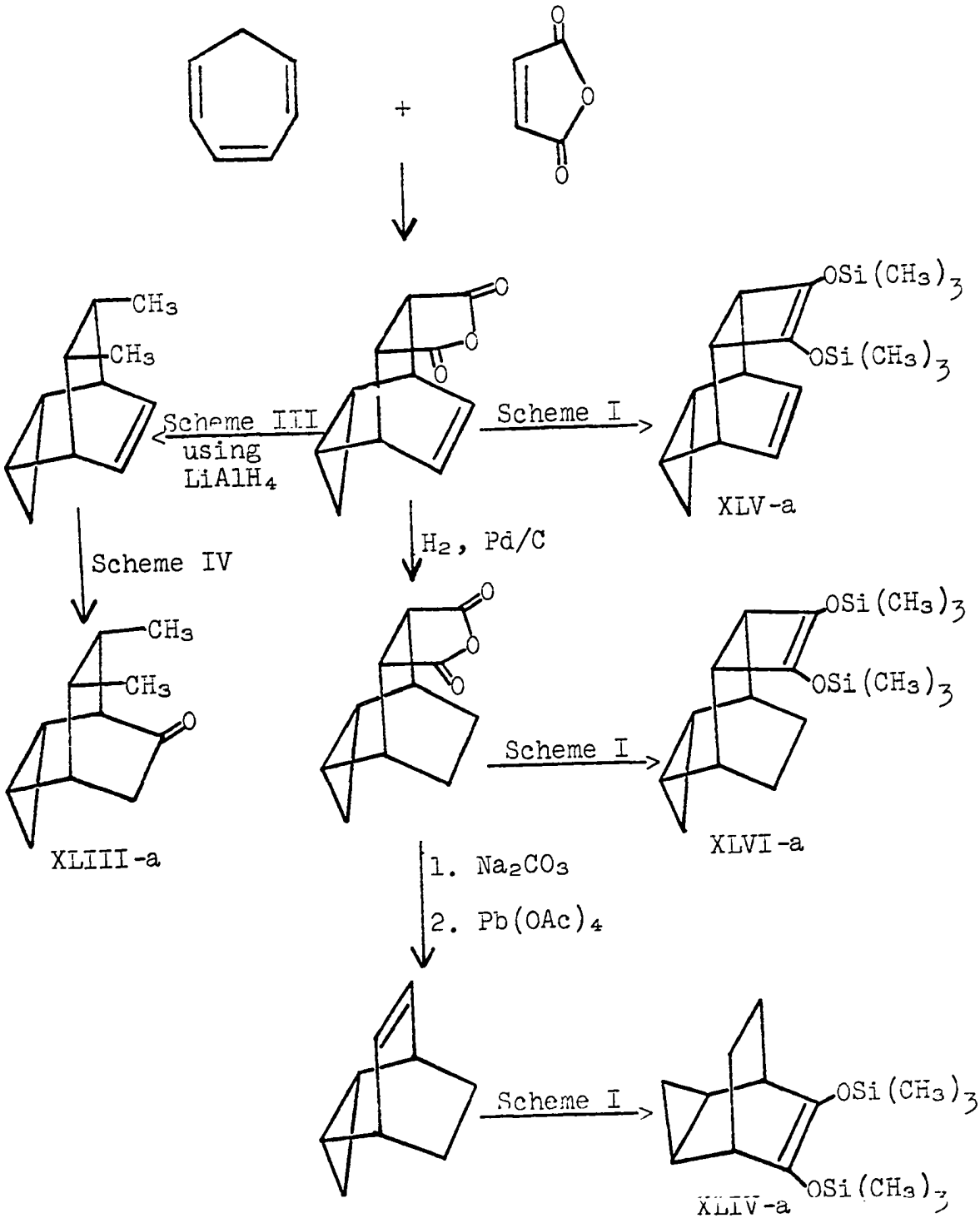


Figure 24. First-derivative esr spectrum of semidione XLII generated by reduction of α-diketone XLII-a with the enolate anion of propiophenone in DMSO.

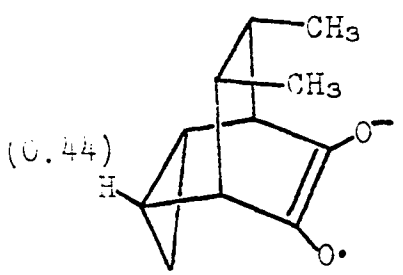
Semidiones exceedingly rich in long-range hyperfine interactions were obtained by incorporating cyclopropane and cyclobutane rings as main bridges into the bicyclo[2.2.2]octane system. The carbon skeleton for these semidiones (XLIII-XLVI in Chart VIII) was obtained from the Diels-Alder adduct of cycloheptatriene and maleic anhydride. The reactions for the transformations of this adduct into the various radical precursors (XLII-a - XLVI-a) are outlined in Scheme VIII.

Semidiones XLIII and XLIV possess endo and exo cyclopropane rings. The esr spectrum of the exo semidione XLIV (Figure 26) displays hyperfine splitting from every position in the molecule, except the bridgehead. Unfortunately, the spectrum of XLIII (Figure 25) is not well resolved but does show the expected triplet of 1.55 G for two exo protons on a bridge with endo methyl substituents. A 0.44 G triplet is observed for XLIII which must be assigned to the two exo protons on the cyclopropane bridge (assuming that the two methylene protons of the cyclopropane ring are not fortuitously magnetically equivalent and that bridgehead protons are not interacting with the unpaired electron). The magnitude of hfsc for endo and exo cyclopropane is curiously constant at 0.32-0.44 G, nearly equivalent to one another, and of comparable magnitude to splittings of vinyl protons in the same position. The exo protons might have been expected to show a larger interaction than the endo since they lie in a zig-zag arrangement with the

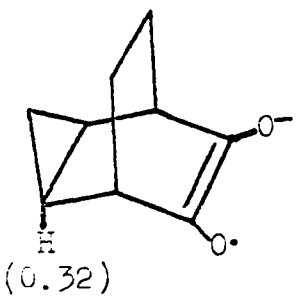
Scheme VIII


CH3
CH3
Scheme III
using
LiAlH4
Scheme I
OSi(CH3)3
OSi(CH3)3
XLV-a
Scheme IV
H2, Pd/C
CH3
CH3
XLIII-a
Scheme I
OSi(CH3)3
OSi(CH3)3
XLVI-a
1. Na2CO3
2. Pb(OAc)4
Scheme I
OSi(CH3)3
OSi(CH3)3
XLIV-a

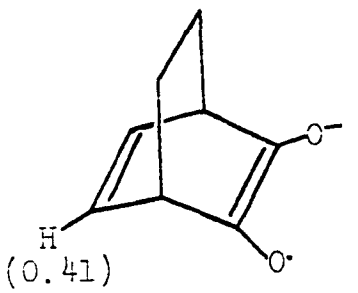
p_z orbital of the carbonyl carbon.* The exo hfsc of XLIV (2.21 G) is slightly enhanced as compared to the parent



XLIII



XLIV

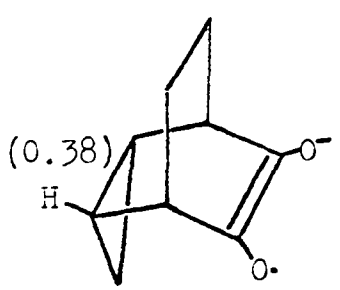


XL

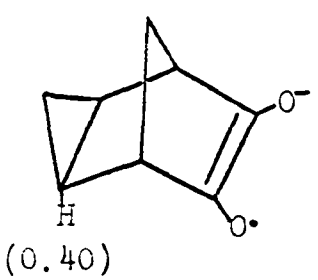
semidione XXXV (a^H = 2.09 G) and the gamma proton (H_g) that lies in a zig-zag arrangement of bonds with the p_z orbital of the carbonyl carbon of the semidione spin label displays a

---

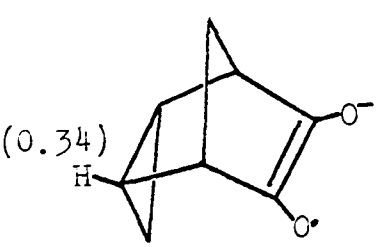
*Mr. Robert G. Keske (of the Iowa State University of Science and Technology) has prepared semidiones LVI-LVIII for the purpose of testing predictions for hfsc by extended Hückel calculations. In all cases, a comparable interaction is predicted for the exo and endo cyclopropane protons and a 0.34-0.4 G triplet is observed in their esr spectra.



LVI



LVII



LVIII

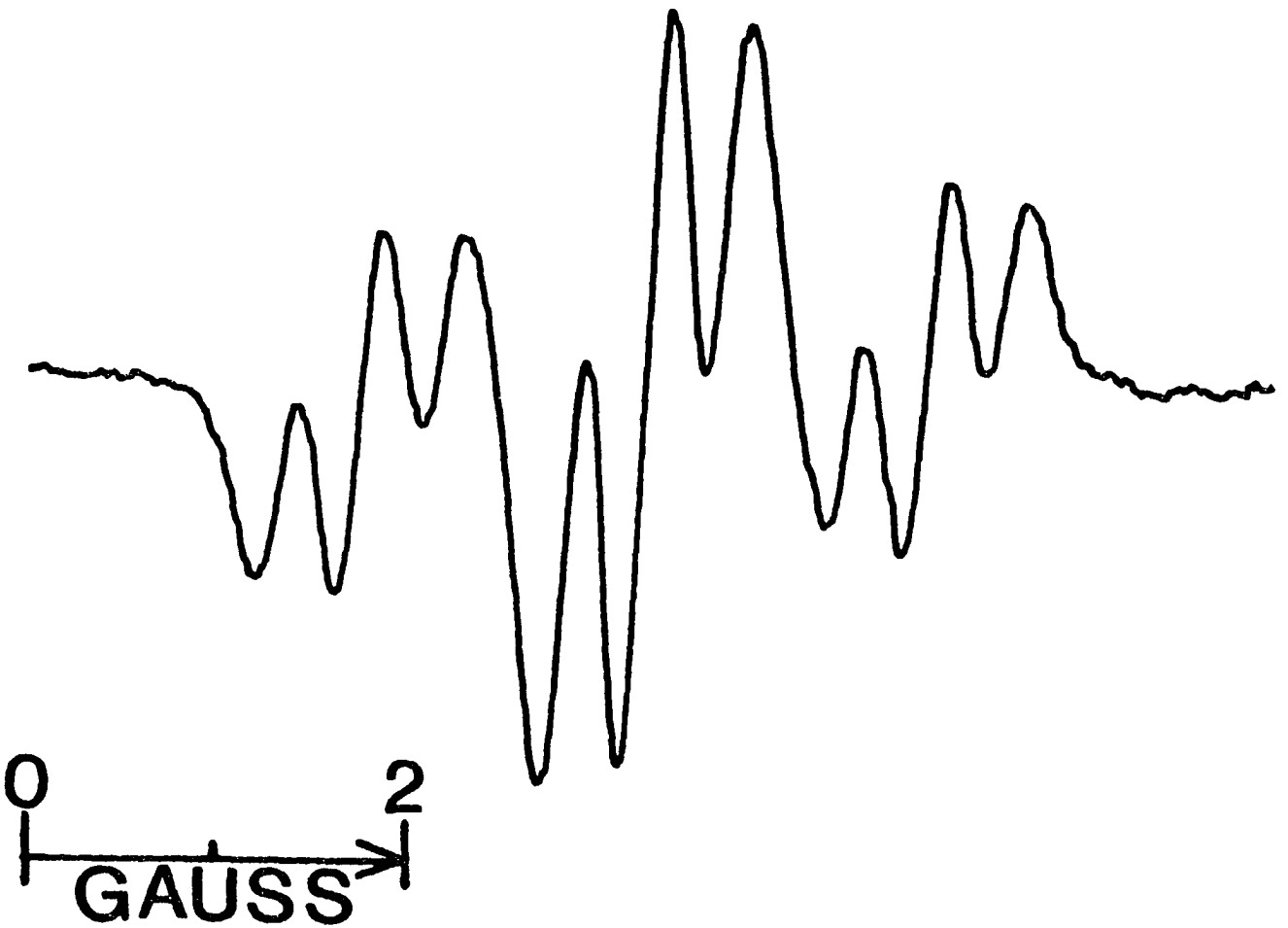


Figure 25. First-derivative esr spectrum of semidione XLIII generated by air oxidation of monoketone XLIII-a in DMSO and potassium t-butoxide.

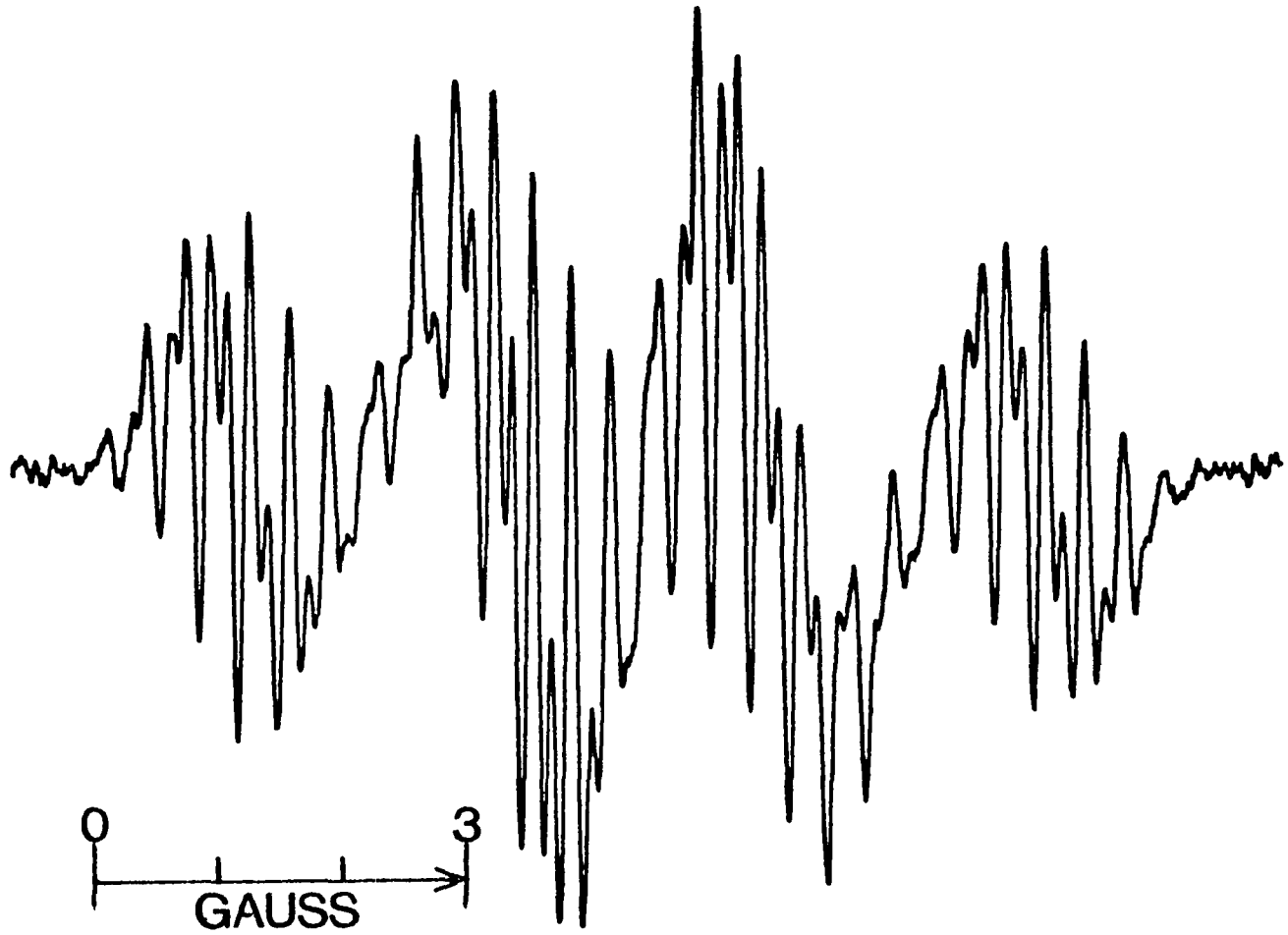
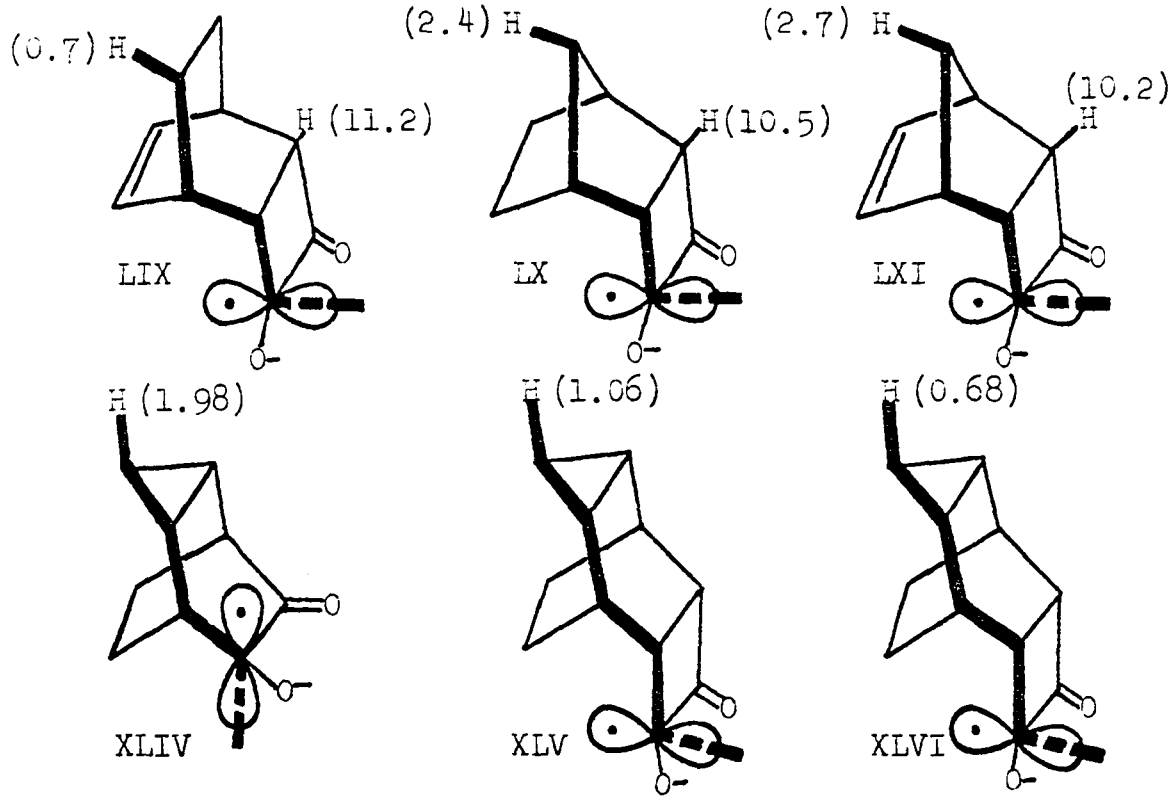


Figure 26. First-derivative esr spectrum of semidione XLIV generated from bis(trimethylsiloxy)alkene XLIV-a in DMSO.

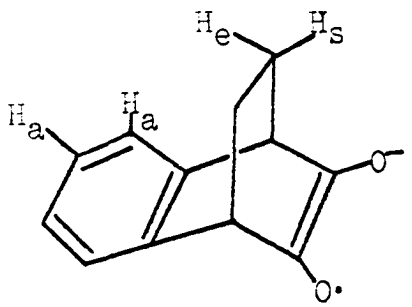
surprisingly large interaction of 1.98 G. This assignment is made by analogy to semidiones LIX-LXI (25).



Semidiones XLV and XLVI show a similar, but one additional bond removed, interaction. The esr spectra (Figures 27 and 28) are well resolved so that the additional small hyperfine splitting created by the presence of a double bond (semidione XLV) is observed and known to be absent in the saturated case (semidione XLVI). The large triplet is assigned to the cyclobutane protons in analogy to LIX-LXI and cyclobutan-1,2-semidione (a^H = 13.55 G) (25).

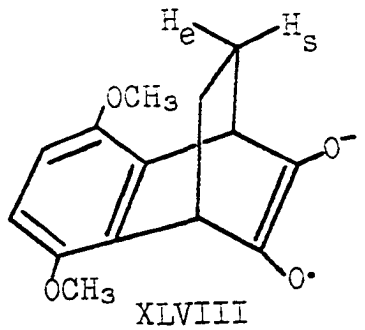
The results of some benzo- semidiones and semiquinones are listed in Chart IX. The esr spectrum of the parent benzobicyclo[2.2.2]octen-2,3-semidione, XLVII, (Figure 29) shows

Chart IX



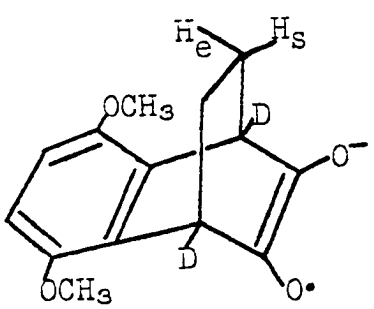
XLVII

a^H= 2.35 (2H) H_e
0.20 (2H) H_s
0.09 (4H) H_a



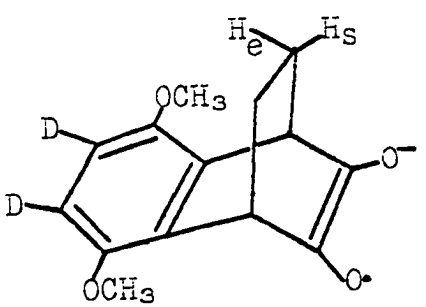
XLVIII

a^H= 2.28 (2H) H_e
00.29 (2H) H_s



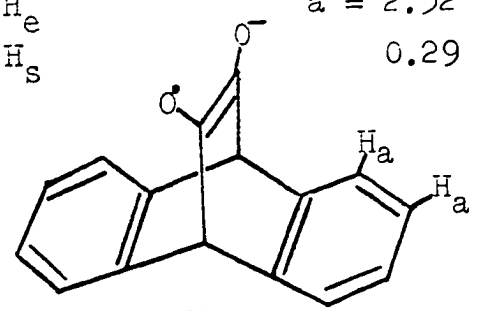
XLIX

a^H= 2.39 (2H) H_e
0.29 (2H) H_s



L

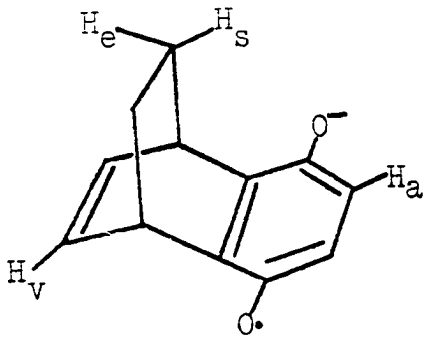
a^H= 2.32 (2H) H_e
0.29 (2H) H_s



LI

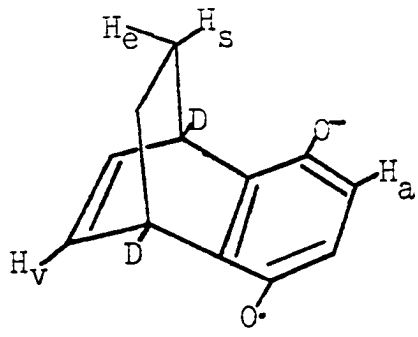
a^H= 0.15 (8H) H_a

Chart IX continued



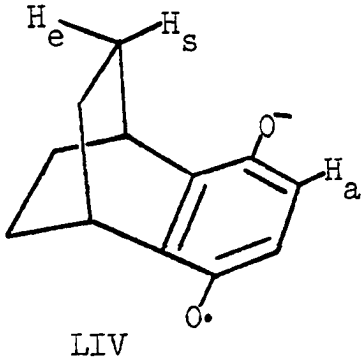
LII

a^H= 2.62 (2H) H_a
0.49 (4H) H_e, H_v
0.18 (2H) H_s



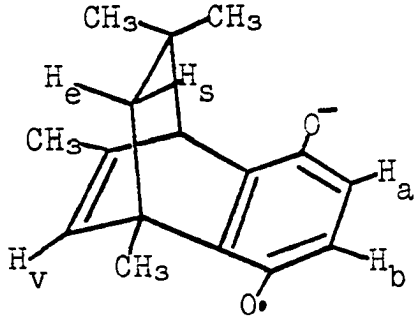
LIII

a^H= 2.62 (2H) H_a
0.49 (4H) H_e, H_v
0.18 (2H) H_s



LIV

a^H= 2.67 (2H) H_a
0.39 (4H) H_e
0.08 (4H) H_s



LV

a^H= 2.82 (1H) H_a, H_b
2.39 (1H)
0.43 (2H) H_e, H_v
H_s is not resolved

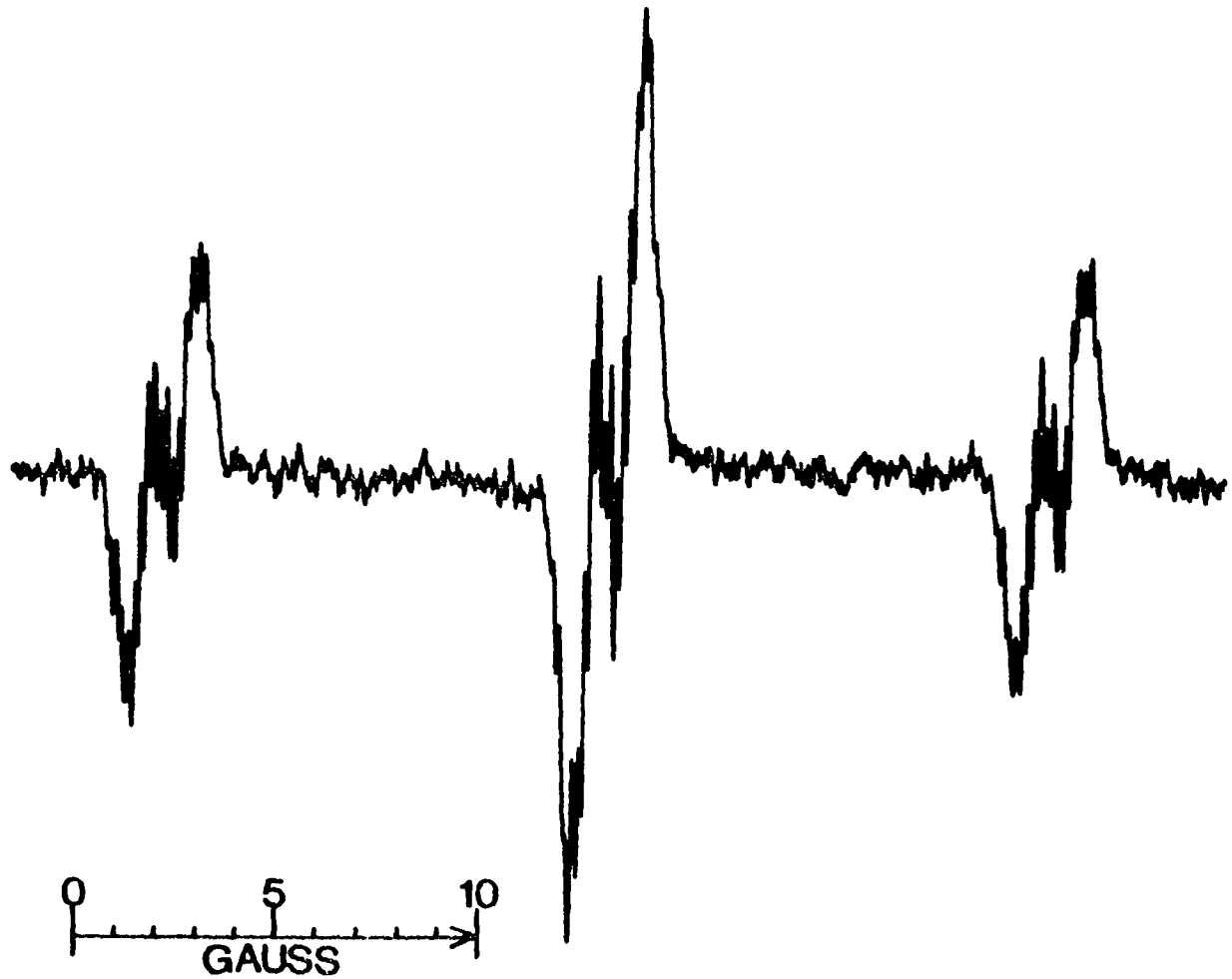


Figure 27. First-derivative esr spectrum of semidione XLV generated from bis(trimethylsiloxy)alkene XLV-a in DMSO.

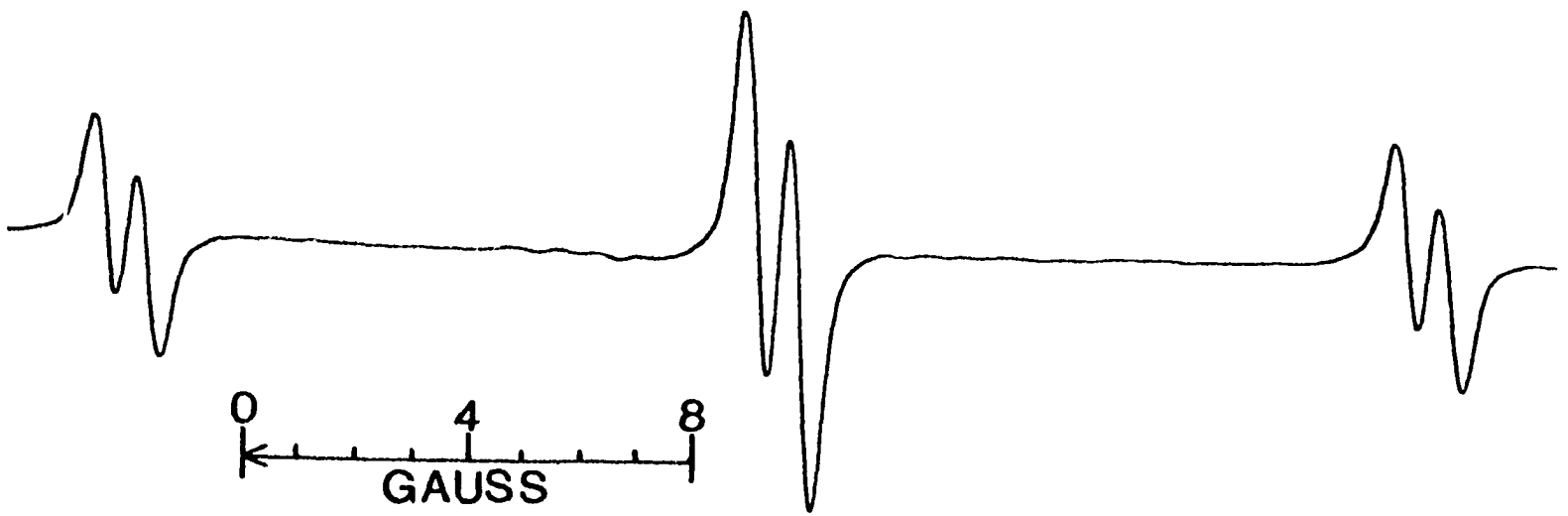


Figure 28. First-derivative esr spectrum of semidione XLVI generated from bis(trimethylsiloxy)alkene XLVI-a in DMSO.

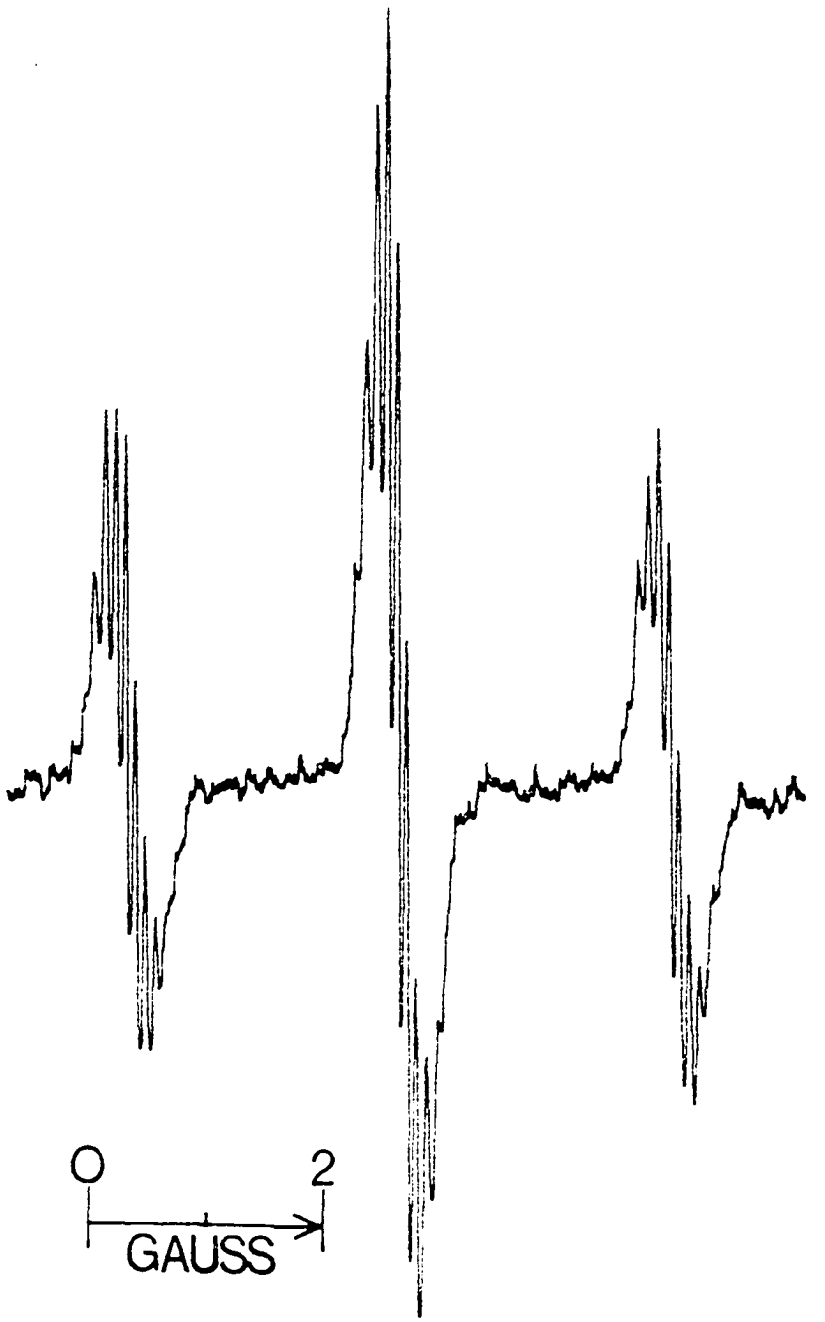
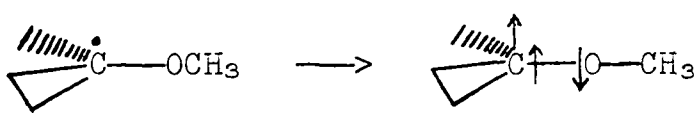


Figure 29. First-derivative esr spectrum of benzobicyclo[2.2.2]-octen-2,3-semidione (XLVII) in DMSO.

hyperfine splitting by all of the protons in the molecule except the bridgehead. The 2.35 G triplet is assigned to the exo protons and the 0.25 G triplet to the endo protons of the ethano bridge. A 0.09 G quintet is observed due to four fortuitously magnetically equivalent aromatic protons. These assignments are based on a series of deuterated semidiones XLVIII-L and semidione XL.

Only four protons of semidione XLIII interact with the unpaired electron and, thus, its esr spectrum (Figure 30-a) is extremely simple consisting of a well resolved triplet of triplets (a^H = 2.28, 0.29 G). Deuterium substitution at the bridgehead (XLIX, Figure 30-b) and in the aromatic ring (L, Figure 30-c) failed to alter the spectrum, thus revealing that the four protons of the ethano bridge are responsible for the observed hyperfine interactions. Apparently a methoxy substituent on the aromatic ring draws sufficient spin density out of ring to reduce the aromatic hyperfine constants to much less than 0.09 gauss.



The carbon skeleton of semidiones XLVIII-L and semiquinones LII-LV were obtained via the Diels-Alder reaction of p-benzoquinone and the appropriate 1,3-cyclohexadiene. Deuterium was introduced into the bridgehead position by employing 1,4-dideutero-1,3-cyclohexadiene in these reactions.

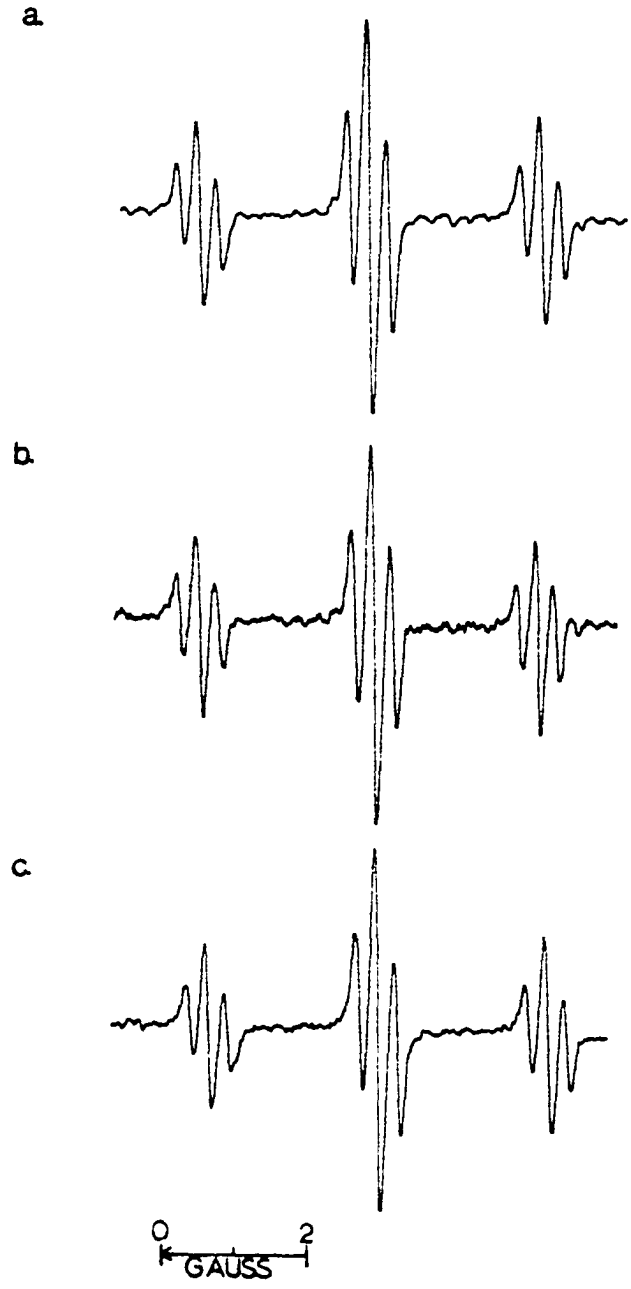
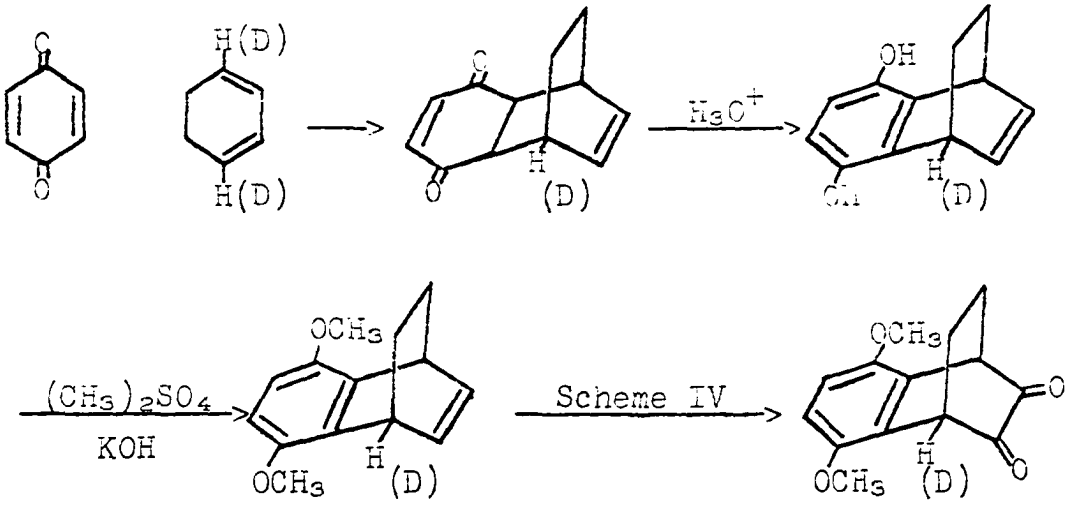
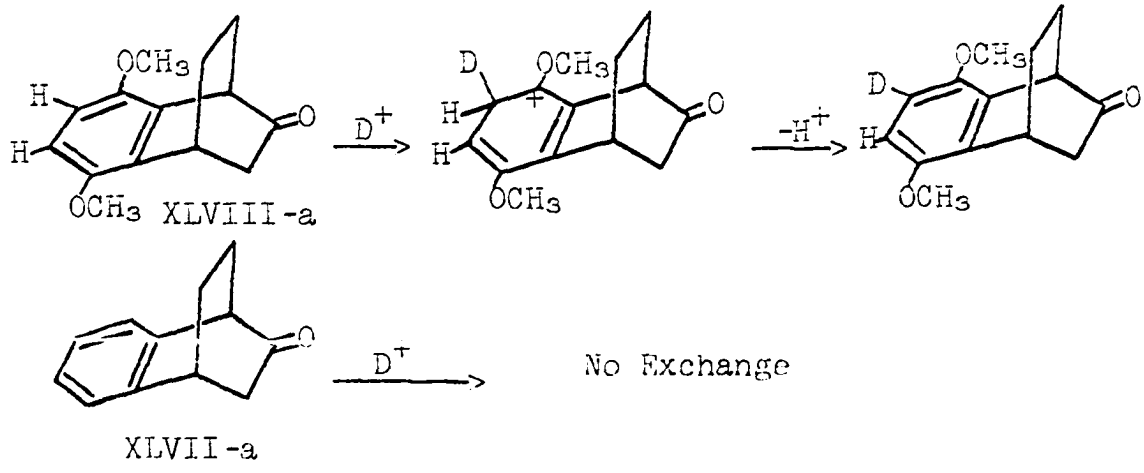


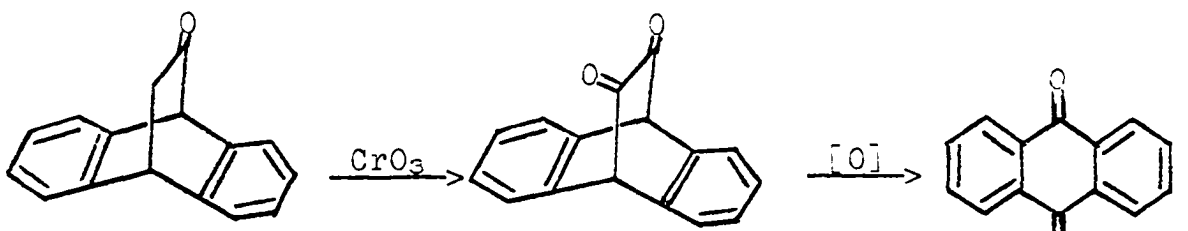
Figure 30. First-derivative esr spectrum of (a) 5,8-dimethoxybenzobicyclo[2.2.2]octen-2,3-semidione (XLVIII), (b) 1,4-dideutero- (XLIX) and (c) 6,7-dideutero- (L); all prepared by reduction of the appropriate α-diketone with the enolate anion of propiophenone in DMSO.



The aromatic protons of monoketone XLVIII-a were exchanged for deuterium by heating XLVIII-a in a mixture of o-deutero-acetic acid, deuterium oxide, and a catalytic amount of sulfuric acid. The reaction owes its success to activation of the aromatic ring by the two methoxy groups as a similar attempt to exchange the aromatic protons of benzobicyclo[2.2.2]octen-2-one (XLVII-a) failed.

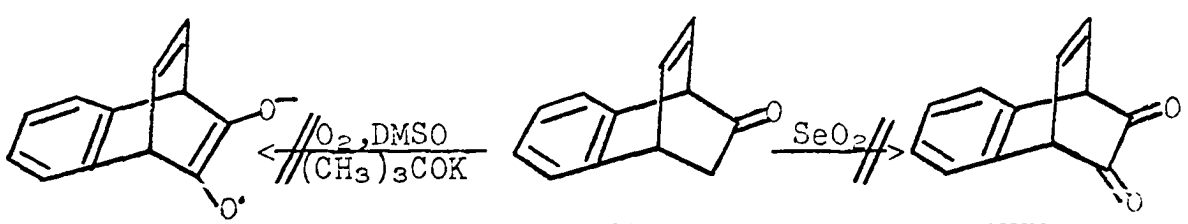


The reported esr spectrum of semidione LI was composed of overlapping quintets (a^H = 0.96, 0.30 G) (7, 23). A purified sample of the precursor, dibenzobicyclo[2.2.2]octadiene-2,3-dione (LI-a) gave a nine line esr spectrum (Figure 31) consistent with eight magnetically equivalent protons of semidione LI (a^H = 0.15 G). It is now realized that the overlapping quintet spectrum is due to antharaquinone, an oxidation product LI-a. Semidione LI has also been generated from bis(trimethylsiloxy)alkene and the same spectrum is obtained when the bridgehead positions contain deuterium (25).



LI-a

It would be interesting to compare the aromatic and vinyl splitting of semidione LXII. Oxidation of monoketone LXII-a with air in basic DMSO solution or with selenium dioxide to α-diketone LXII-b was unsuccessful.



LXII
not observed

LXII-a

LXII-b

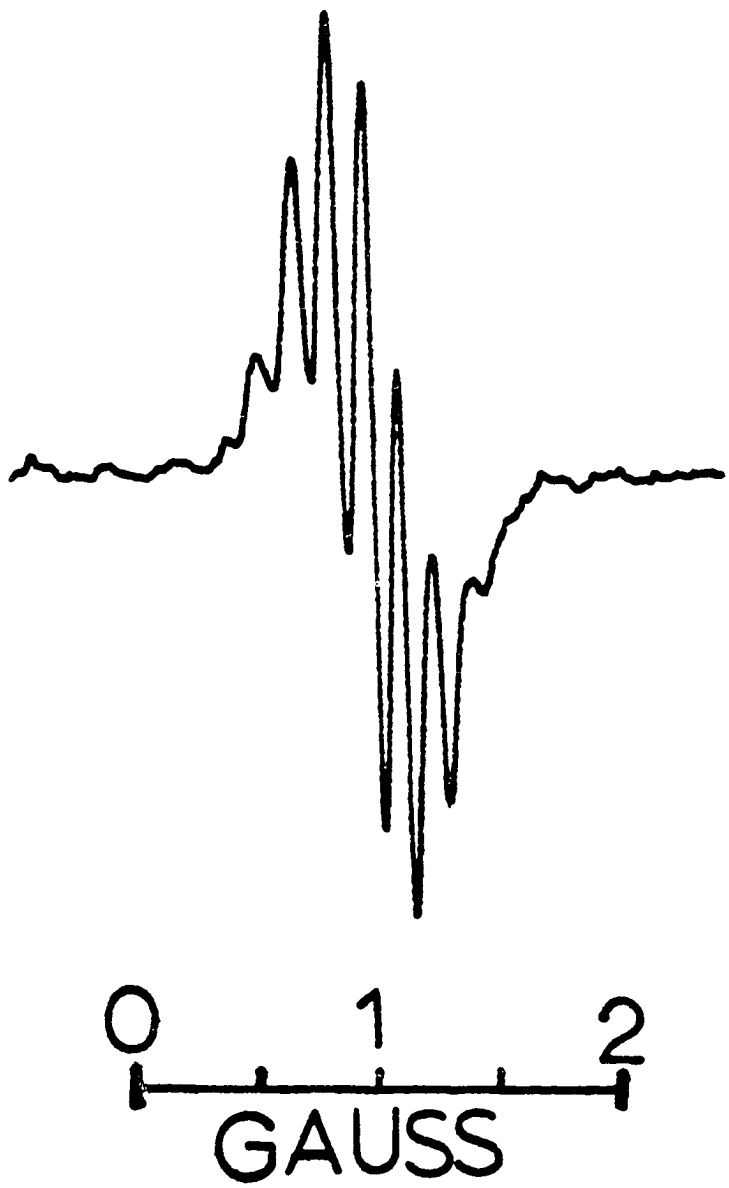
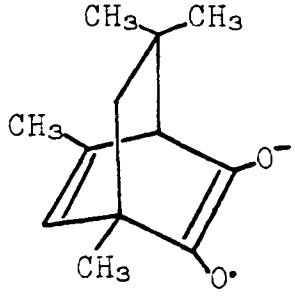


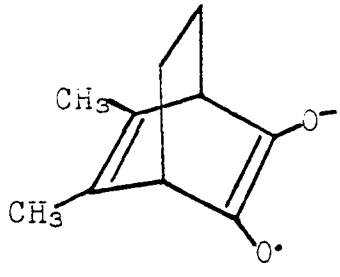
Figure 31. First-derivative esr spectrum of dibenzobicyclo-[2.2.2]oct-5,7-diene-2,3-semidione (LI) generated by reduction of α-diketone LI-a with the enolate anion of propiophenone.

Semiquinones LII-LV were prepared for comparison to their corresponding semidiones and were not studied extensively as active investigations involving this class of radicals were in progress in other research groups (27-31). Incorporation of deuterium into the bridgehead (LIII) does not alter the esr spectrum from that of LII (compare Figures 32 and 33). Hyperfine interactions can be detected from all positions in these radicals, except the bridgehead and methyl.

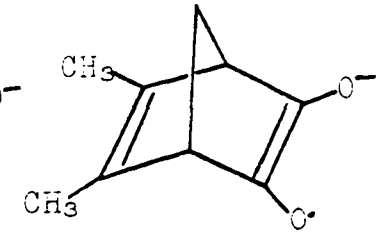
Several additional semidiones (LXIII-LXV)possessing allylic methyl groups were desired for comparison of a^{H} and $a^{H}_{CH_3}$. Two general approaches to appropriate precursors were unsuccessful.



LXIII



LXIV



LXV

The first, via the reactions of Scheme IV on the maleic anhydride adduct of a substituted diene, is illustrated above for LXIII. This sequence failed with the bisdecarboxylation of the intermediate diacid LXIII-b with lead tetraacetate in a variety of solvents. The product was predominantly the

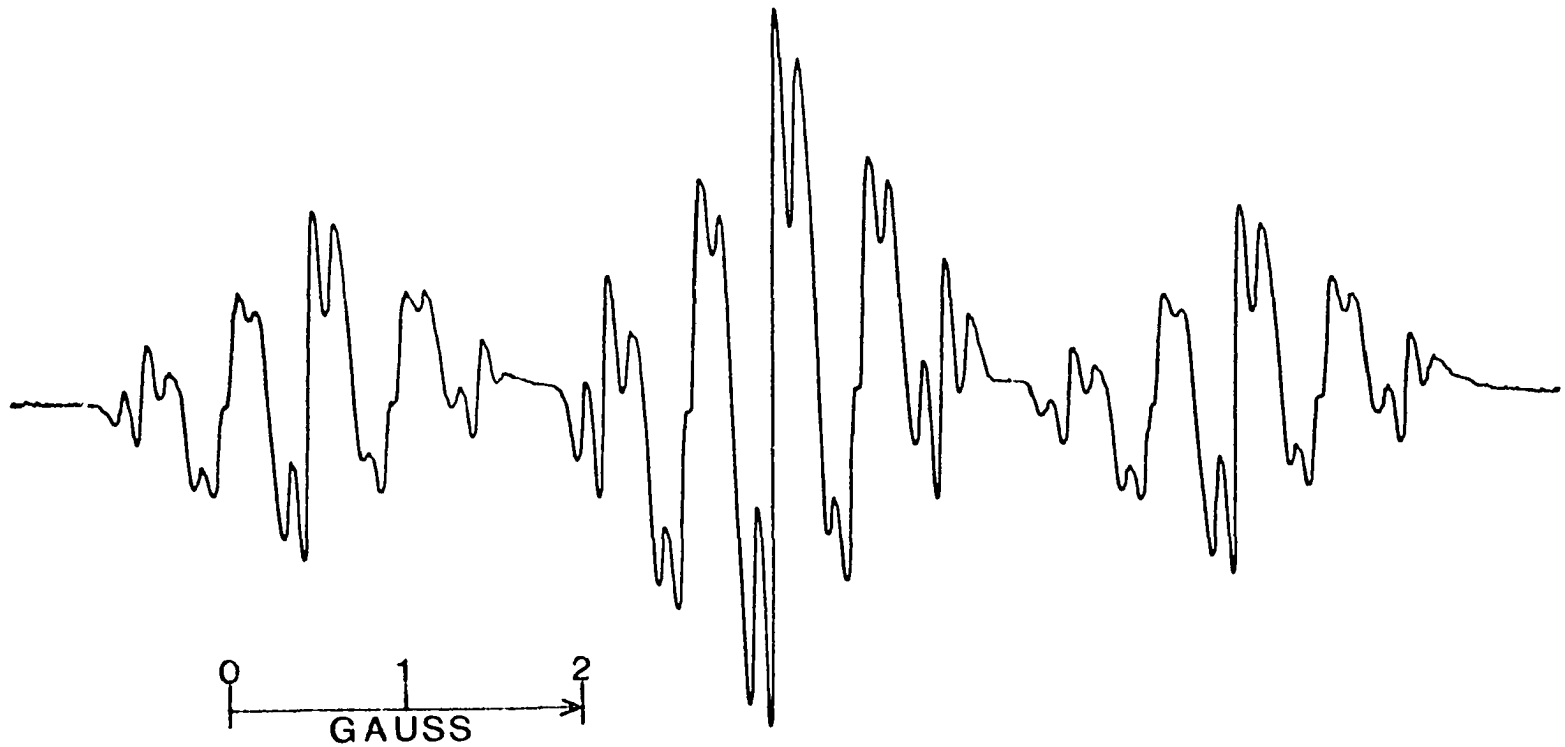


Figure 32. First-derivative esr spectrum of semiquinone LII in DMSO.

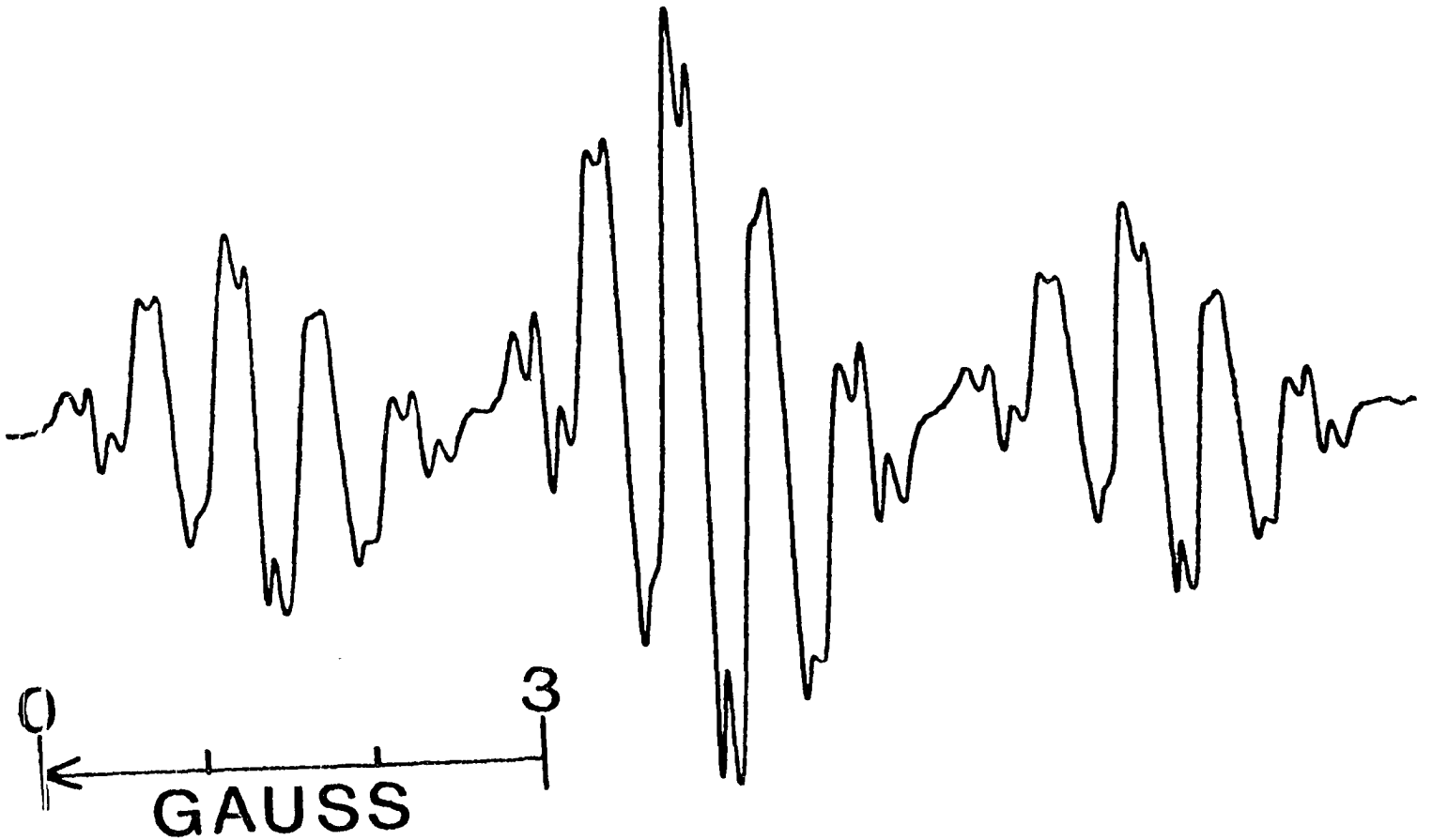


Figure 33. First-derivative esr spectrum of semiquinone LIII in DMSO.

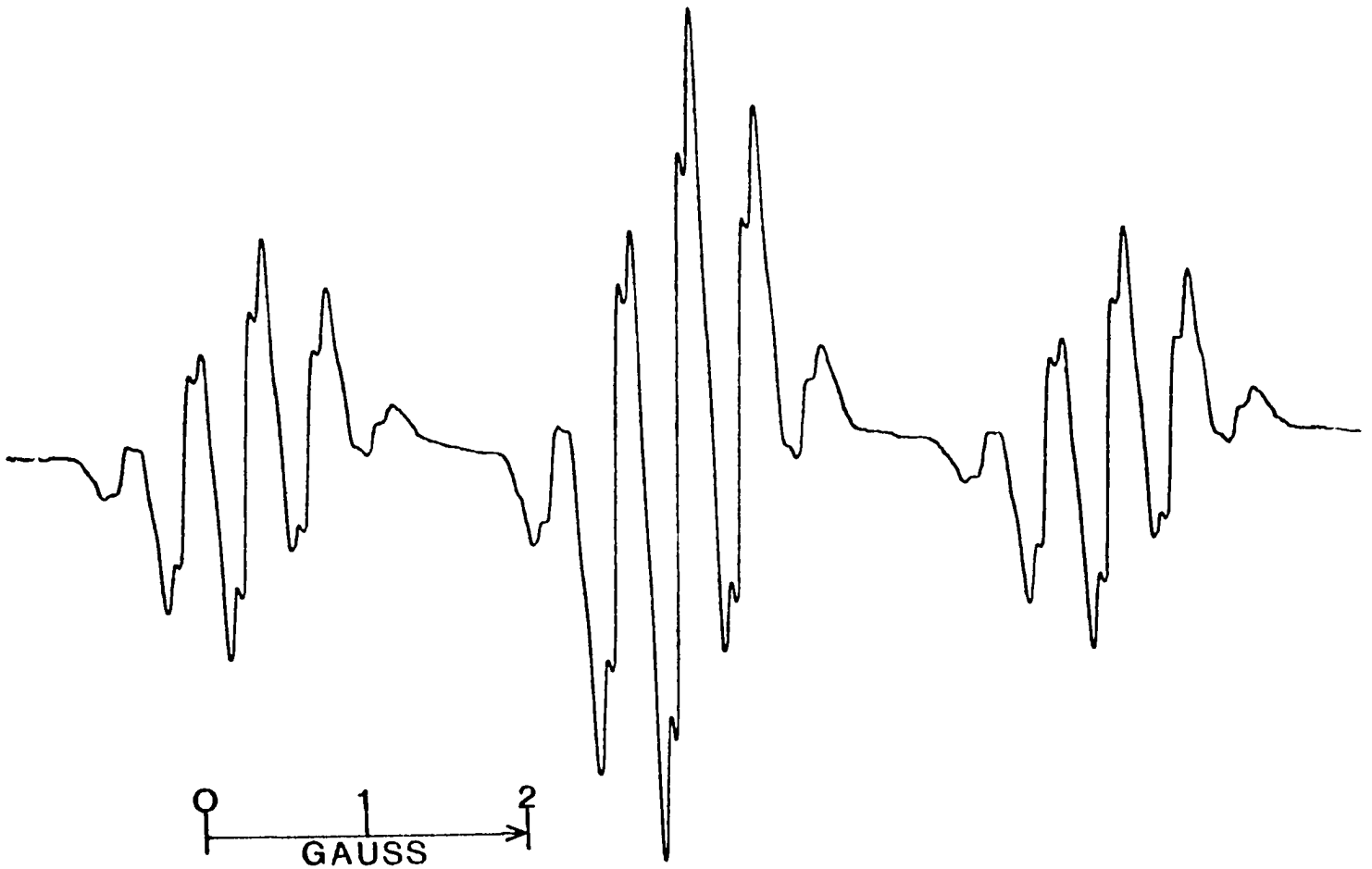


Figure 34. First-derivative esr spectrum of semiquinone LIV in DMSO.

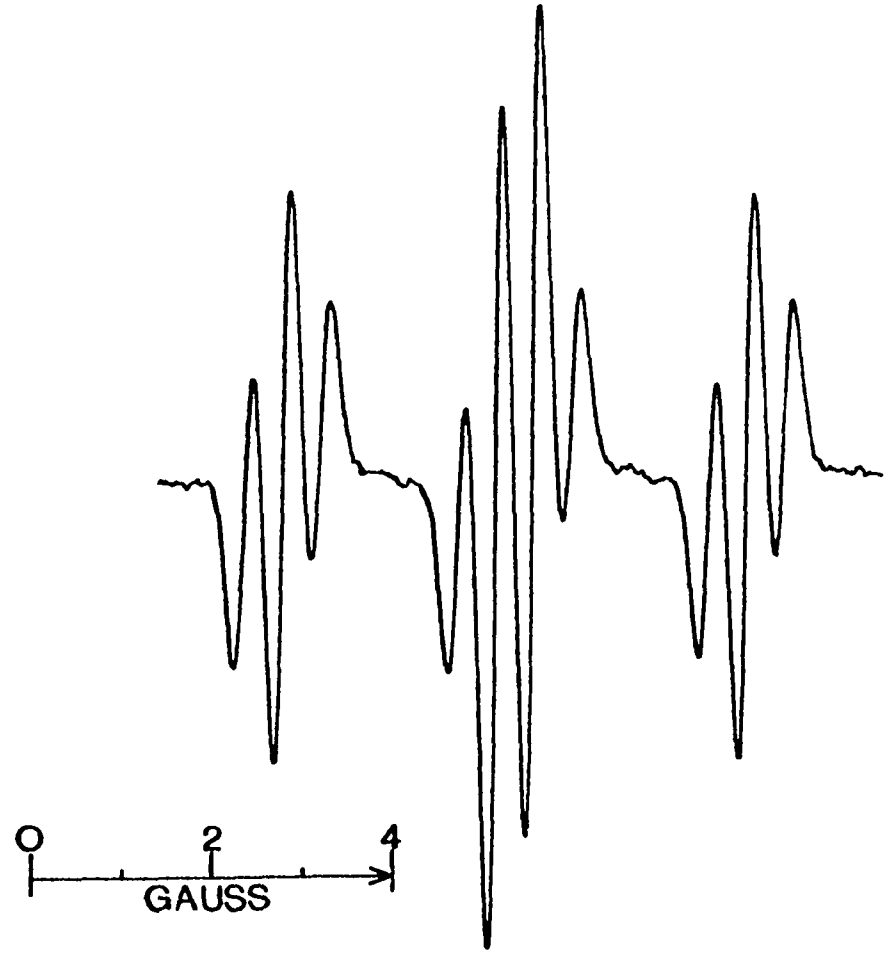
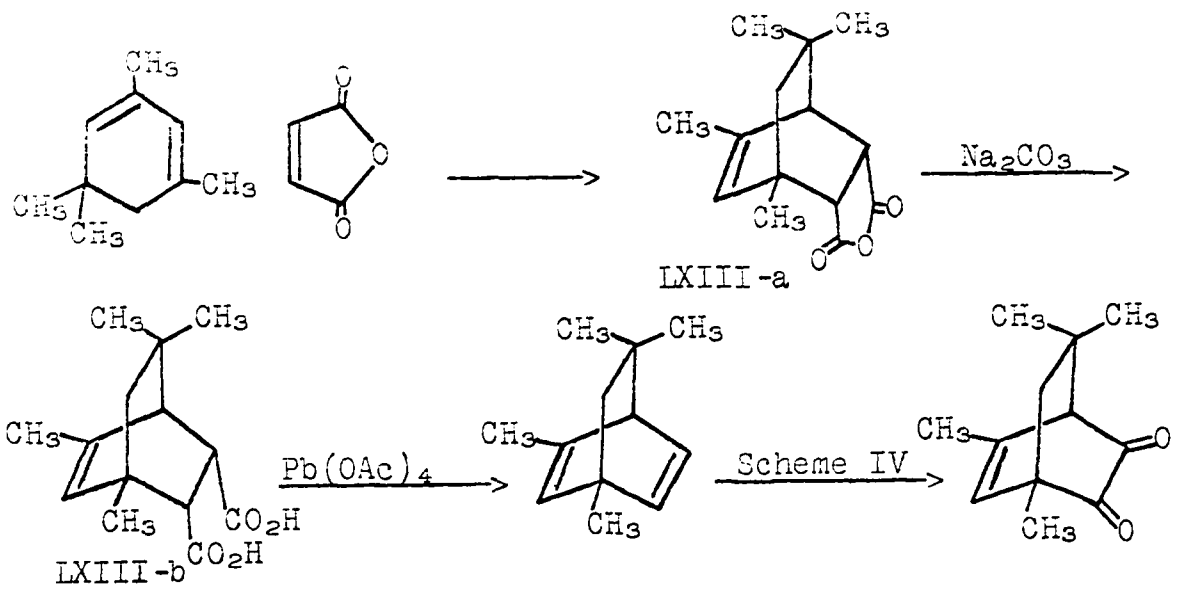
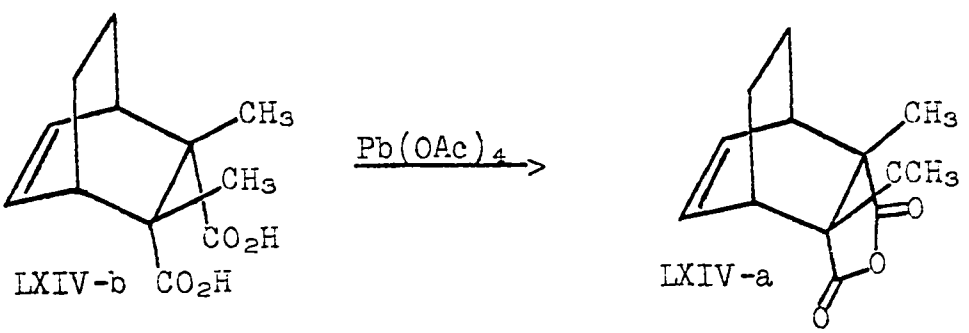


Figure 35. First-derivative esr spectrum of semiquinone LV in DMSO.

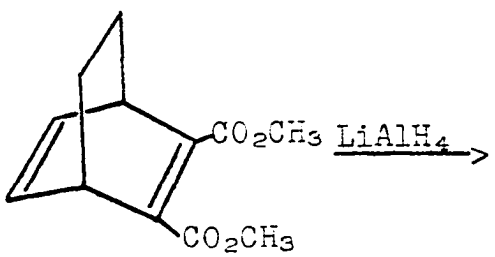
starting dicarboxylic anhydride LXIII-a.

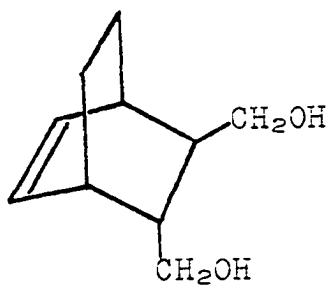


The same result was observed with diacid LXIV-b.

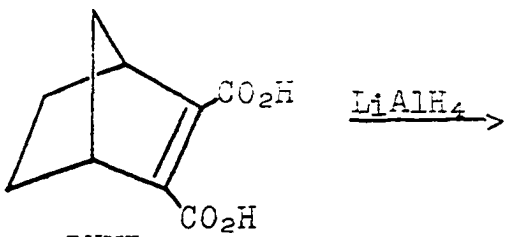


The second approach involved the application of the reactions of Scheme I and III to the Diels-Alder adducts of dimethyl acetylenedicarboxylate. However, lithium aluminum hydride reduction of the conjugated diesters LXIV-c and LXV resulted in reduction of the double bond as well as the carbonyl functions and gave the <u>trans</u> dimethanol compounds.

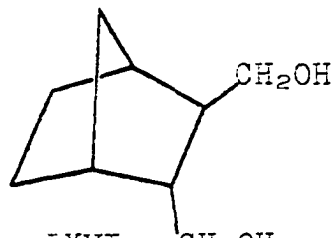




LXIV-c

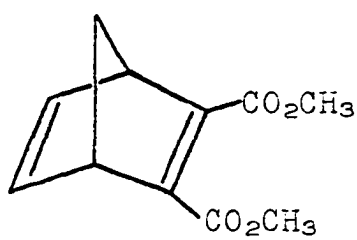


LXVI



LXVI-a

This result was unfortunately anticipated due to the close analogy to the reported reduction of diacid LXVI to the <u>trans</u> dimethanol compound LXVI-a (58).

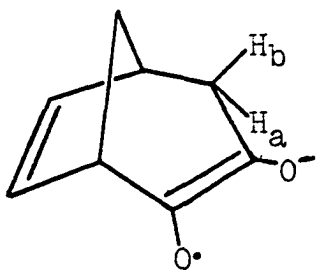


LXV

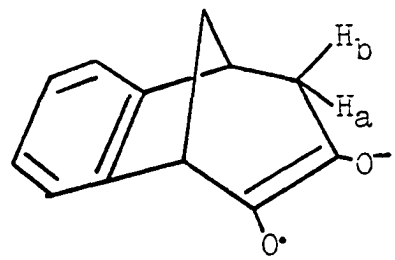
Unsaturated Bicyclo[3.2.1]oct-6-en-2,3-semidiones

Chang (23) reported hyperfine splitting for all eight protons of semidione LXVII(a^H = 8.74, 7.70, 2.66, 1.20, 0.71, 0.49, 0.14, and 0.14). In this work, semidione LXVIII, the corresponding benzo analog, was prepared.

A comparison of the esr spectra of LXVII and LXVIII (Figures 36 and 37) reveals that the hfsc for each must be very similar. An analysis of these spectra leads to the hfsc listed beneath structures LXVII and LXVIII.



LXVII



LXVIII

a^H = 8.74 (1H) H_a	a^H = 10.56 (1H) H_a
7.70 (1H) H_b	7.54 (1H) H_b
2.66 (1H)	2.20 (1H)
1.01 (1H)	1.03 (1H)
0.70 (1H)	0.52 (1H)
0.35 (1H)	0.32 (1H)
0.17 (1H)	0.19 (1H)

These values for hfsc were obtained by simulation of the spectra but, due to the complexity of the spectra, there still exists some uncertainty in hfsc <0.5 gauss. The only splittings

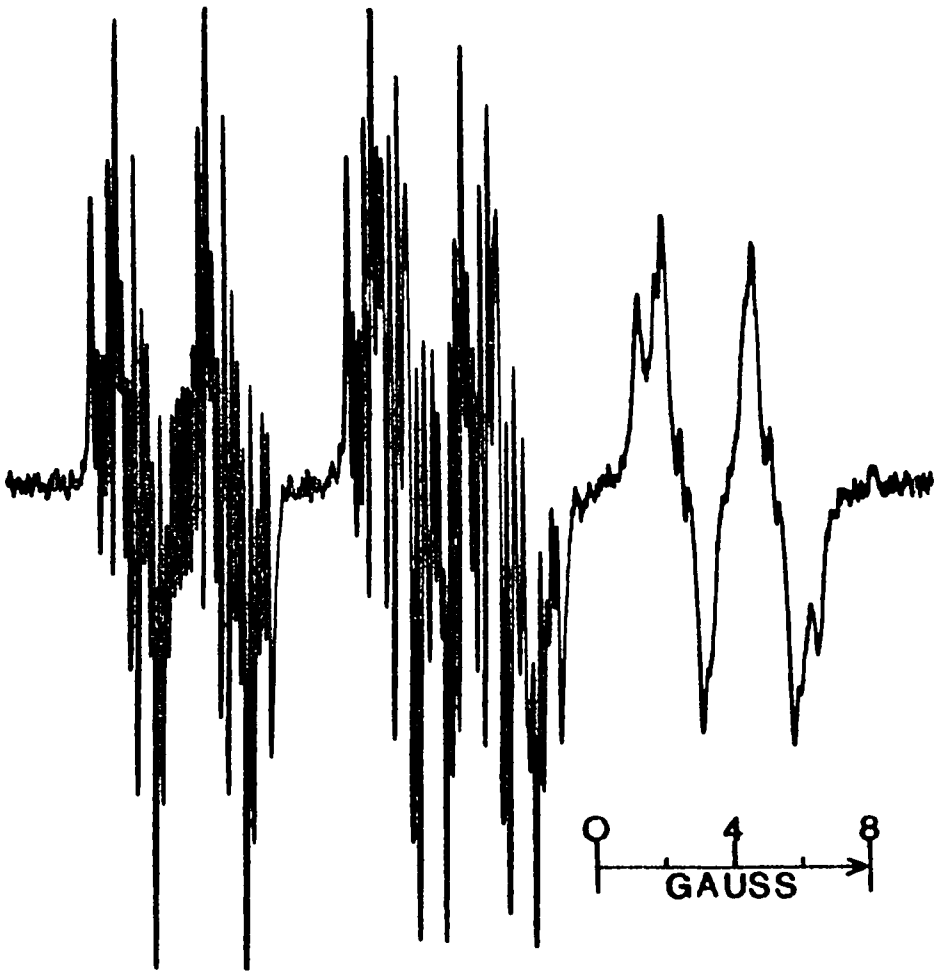


Figure 36. First-derivative esr spectrum of bicyclo[3.2.1]oct-6-en-2,3-semidione (LXVI) prepared by air oxidation of monoketone LXVI-a in DMSO and Potassium t-butoxide.

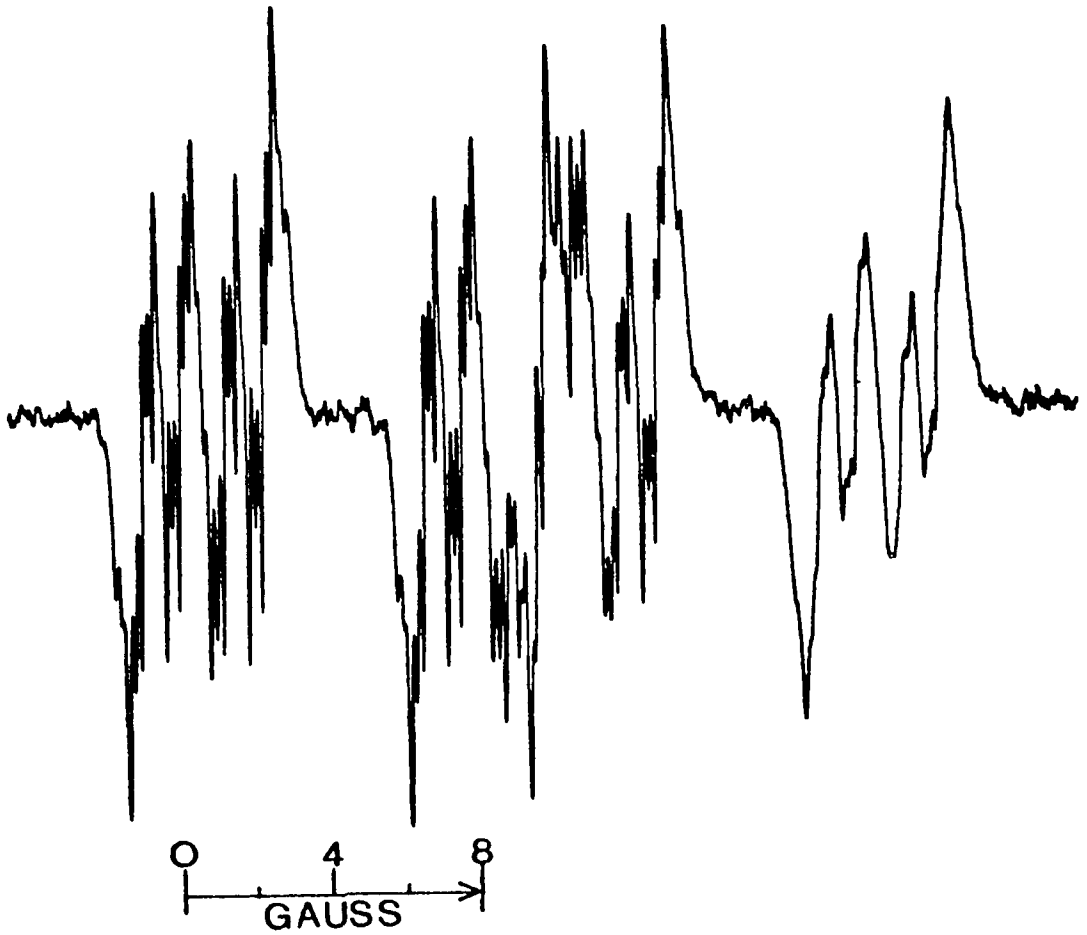
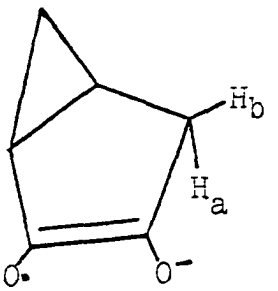


Figure 37. First-derivative esr spectrum of benzobicyclo[3.2.1]oct-6-en-2,3-semidione (LXVII) prepared by air oxidation of monoketone LXVII-a In DMSO and potassium t-butoxide.

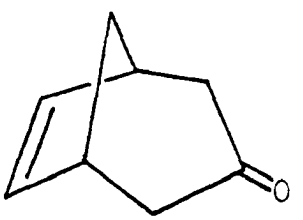
that can be assigned with any certainty are the two largest and are assigned to the two α-methylene protons (H_a and H_b) in analogy to bicyclo[3.1.0]hexan-2,3-semidione (LXIX) (24, 25).



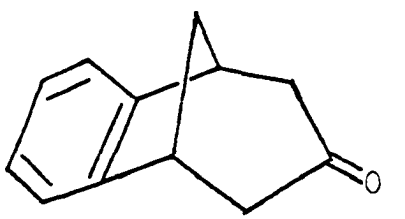
LXIX

a^H = 14.9 (H_a)
7.9 (H_b)

Both semidiones LXVII and LXVIII were prepared by air oxidation of the corresponding monoketones, LXVII-a and LXVIII-a, in DMSO and potassium t-butoxide.



LXVII-a



LXVIII-a

g-Values of Semidiones and Semiquinones

The g-values of several bicyclic semidiones and semiquinones were measured by the method of Norman and Pritchett (59) and are listed in Table 1. g-Values are not of special importance to a discussion of hyperfine splitting but are listed here mainly as a convenience to other researchers who may wish a knowledge of them for other purposes.

Table 1. g-Values for bicyclic semidiones and semiquinones in DMSO and potassium t-butoxide at room temperature

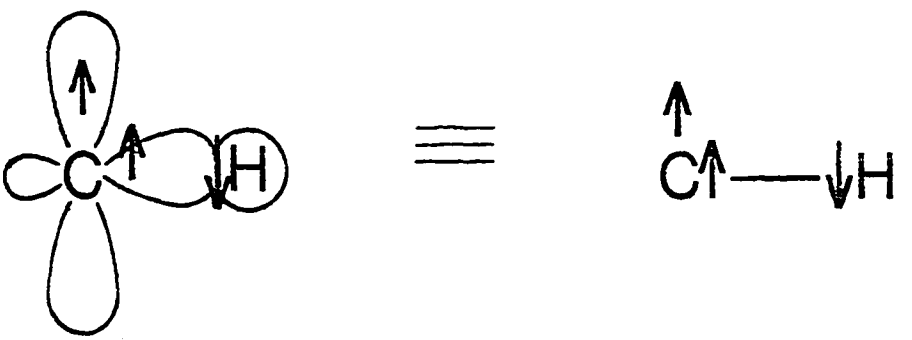
Radical	g-Value ± 0.00005
LIV	2.00496
LII	2.00493
LV	2.00498
XVI	2.00497
XIV	2.00483
L	2.00465
LI	2.00451

Discussion of Hyperfine Splittings

The Fermi contact mechanism (60) has long been used to explain the coupling of nuclei observed in nuclear magnetic resonance studies. The salient feature of this mechanism is that, if an electron possesses a probability of being right at the nucleus, then the nuclear spin can couple with the electron spin. Likewise, a nucleus can couple with an unpaired electron in a radical, if unpaired spin density can come into intimate contact with the nucleus. Since the 1S atomic orbital of carbon or hydrogen is the only low-lying orbital that does not have a node at the nucleus, spin density must reach this orbital if a hyperfine interaction is to be observed from these nuclei.

In many organic radicals the unpaired electron formally resides either in a carbon $2p_z$ atomic orbital or a molecular π orbital delocalized over a carbon atom framework. In both instances, the hydrogens lie in a plane perpendicular to the p_z atomic orbital on carbon and (due to the node of the $2p_z$ orbital at the carbon nucleus) are not in a position to have overlap of their 1S atomic orbital with the carbon $2p_z$ orbital. For organic radicals, an understanding of hyperfine interactions is then highly dependent upon an understanding of how spin density reaches the S atomic orbital of the interacting nuclei. Two basic mechanisms to accomplish this have been generally accepted (61 , 62).

The first of these covers splitting by protons directly bonded to the radical center and involves an indirect coupling through the C-H bond (spin polarization). Exchange forces between the electrons couple the spins of the σ electrons in the C-H bond with the spin of the unpaired electron in the p_z orbital. A valence bond approach concludes that the spin density so polarized into the hydrogen 1S atomic orbital is of opposite sign to that in the carbon $2p_z$ orbital (63). This is a consequence of Hund's rule which predicts that the electron



spins on an atom will be in a parallel alignment. The same conclusions are reached from a molecular orbital viewpoint.

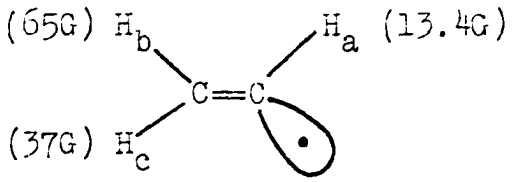
McConnell (19) observed that splitting by protons of this type (α-protons) can be described by the empirical expression

$$a_{\alpha}^{H} = \rho_C^{\pi} Q \qquad (1)$$

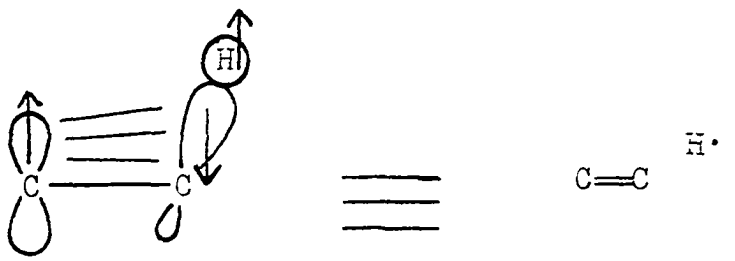
where Q is a constant of around -25 gauss for planar sp^2 carbon and ρ_C^{π} is the π electron spin density in the carbon $2p_z$ orbital.

The second mechanism involves hyperconjugation and is the major mechanism associated with splitting by β-protons. The results from esr studies of the vinyl radical (specifically,

the trans-hydrogen (H_b) is believed to show a stronger hyperfine interaction than the eclipsed cis-hydrogen (H_c)), and



observations with bicyclic semidiones, indicate that the maximum interaction occurs when the C-H bond and the $2p_z$ orbital are in a trans-coplanar arrangement. This is contrary to the normal description of hyperconjugation in which the interaction is thought to occur via overlap of the eclipsed C-H bond and p_z orbital. As is seen, a positive coupling is predicted (i.e.,

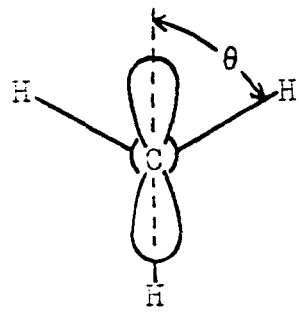


the spin of the unpaired electron in the carbon $2p_z$ atomic orbital is in a parallel alignment with the electron in the hydrogen 1S atomic orbital).

The magnitude of hyperfine interactions can be anticipated by the expression

$$a_\beta^H = \rho_C^\pi (B_o + B \cos^2\theta) \qquad (2)$$

where θ is the dihedral angle between the axis of the p_z orbital and the C-H bond. B_o is a constant associated with the indirect



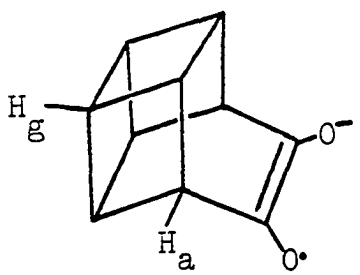
spin polarization mechanism. Its contribution to a^H is small owing to the fact that spin polarization is not normally substained through σ-bonds. The $B\cos^2\theta$ portions deal with the hyperconjugation contribution to a^H.

As previously stated, splitting by gamma or further removed hydrogens are encountered only in special cases. Several reasonable mechanisms can be envisioned to account for these long-range splittings but, in general, such interactions are not well understood.

The closest protons to the spin label in bicyclic semidiones are the bridgehead (beta) protons. To consider the hyperconjugation mechanism as an explanation for the splitting by bridgehead in bicyclo[2.2.1]heptane semidione is seemingly a violation of Bredt's rule. However, this objection can be minimized by realizing that little change in the geometry of the radical is involved and that there is, of course, no actual double bond formed as implied by valence bond representations of this mechanism. Support for the hyperconjugation mechanism

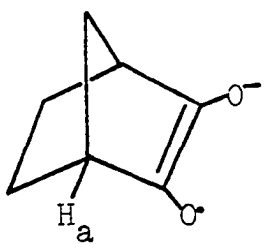
is found in the observation that $a^{H}_{bridgehead}$ does indeed show the expected angular dependence (i.e., $a^{H} << 0.1G$ for [2.2.2] systems where $\theta = 90°$ while $a^{H} \simeq 2.5$ G for [2.2.1] systems where $\theta < 90°$).

An estimate of the maximum possible value for B_o of the Heller-McConnell expression (equation 2) can be made via the data for semidione XLI; the only bicyclo[2.2.2]octan-2,3-semidione displaying a hyperfine interaction that could possibly be



XLI

$a^{H} = 0.09$ (H_g or H_a)



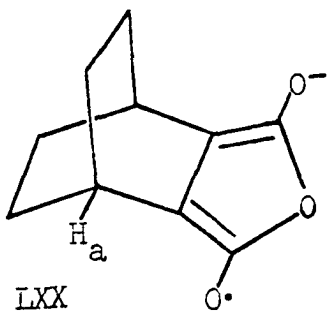
I

$a^{H} = 2.50$ (H_a)

due to a bridgehead proton . Using $\rho_C^{\pi} \simeq 0.25$ (17), $a^{H}_{Ha} = 0.09$ and, $\theta = 90°$ in equation 2 leads to a value of B_o of 0.36. Since it is felt that the 0.09G splitting is actually due to H_g, B_o is probably much less than 0.36 for these systems. Other estimates of B_o range from 1.1 - 4.5 gauss (64-67).

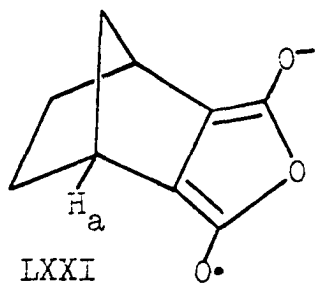
Hyperfine splitting by bridgehead protons in semifuraquinones LXX and LXXI (68) follows the same pattern as semidiones. The corresponding semiquinones LIV and LXXII(30) do not display

hyperfine splitting in either case while similar dicyanoethylene radical anions LXXIII and LXXIV (69) possess a 0.15-0.22G bridgehead splitting. It would thus appear that spin polarization is more important in dicyanoethylene radical anions and that is can not be an important mechanism in long-range interactions in semidiones, semifuraquinones, or semiquinones. Variation of the spin density at C-2 has been suggested as a possible cause for these differences (30).



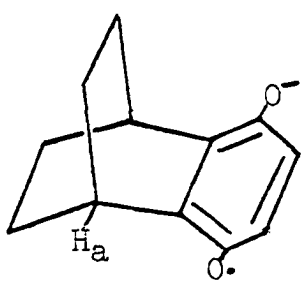
LXX

$a^{H}_{H_a}$ < 0.1



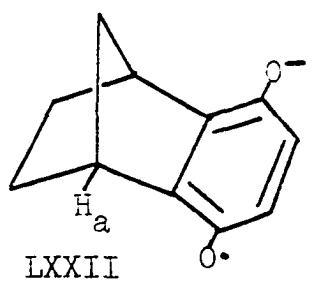
LXXI

$a^{H}_{H_a}$ = 0.27 or 0.37



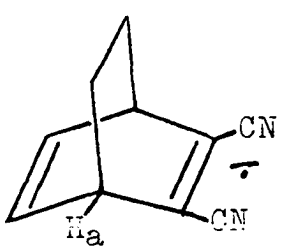
LIV

$a^{H}_{H_a}$ < 0.1



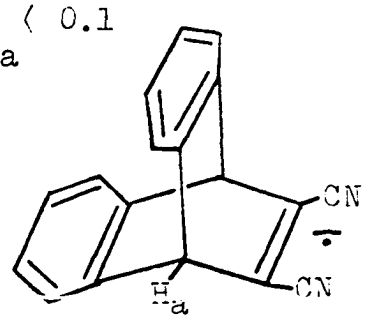
LXXII

$a^{H}_{H_a}$ < 0.1



LXXIII

$a^{H}_{H_a}$ = 0.225



LXXIV

$a^{H}_{H_a}$ = 0.15

An estimate of the extent of delocalization of unpaired spin density into the bridgehead hydrogen 1S atomic orbital of I can be made by comparing the observed hfsc to that of a free hydrogen atom ($a^H_{H\cdot} = 507G$).*

$$a^H_{obs}/a^H_{H\cdot} = 2.5/507 = 0.0049$$

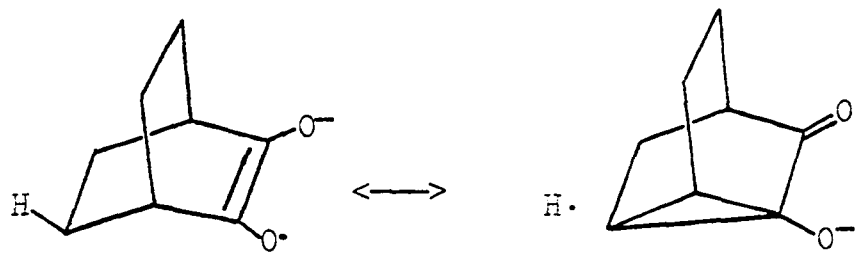
The bridgehead hydrogen 1S orbital of I thus contains 0.0049 of an unpaired spin. Taking the unpaired spin density of a carbonyl carbon in a semidione to be about 0.25, this represents a 2% delocalization of the carbonyl spin density.

The comparatively large splitting from <u>exo</u> and <u>anti</u> protons and the small to nonexistent interaction by <u>syn</u> and <u>endo</u> protons demand a highly stereospecific splitting mechanism for their explanation. Many such gamma hyperfine splittings can be explained by a 1,3-σ,π interaction which has been termed homohyperconjugation (26, 70) in analogy to homoenolization (71) and is depicted by structures XXXV-a and I-c.

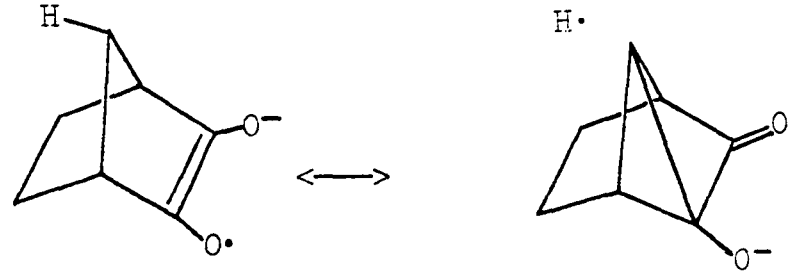
The homohyperconjugation mechanism is preferred over a through bond spin polarization mechanism on the basis of the observed value of B_o in equation 2 and since it offers a

---

*Bonding of a hydrogen atom to carbon distorts the hydrogen 1S orbital from that in a free hydrogen atom. A value of a^H (in gauss) as high as 1000 x ρ_H has been estimated empirically (72).



XXXV XXXV-a



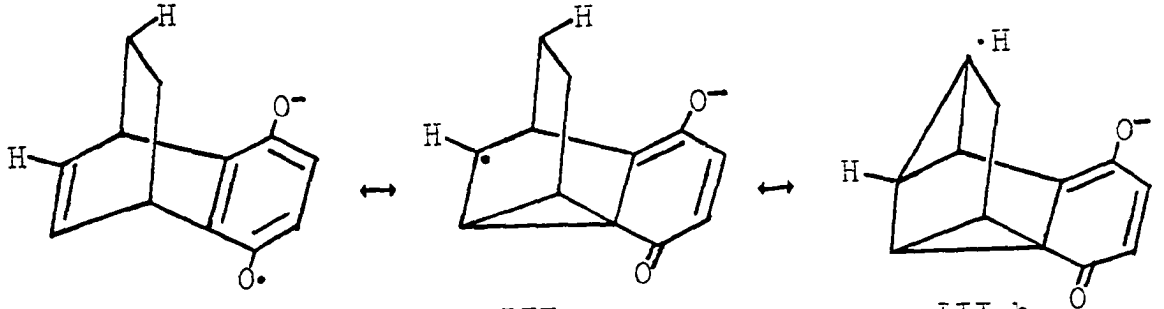
I I-c

explanation for the stereospecificity of the hyperfine interaction.

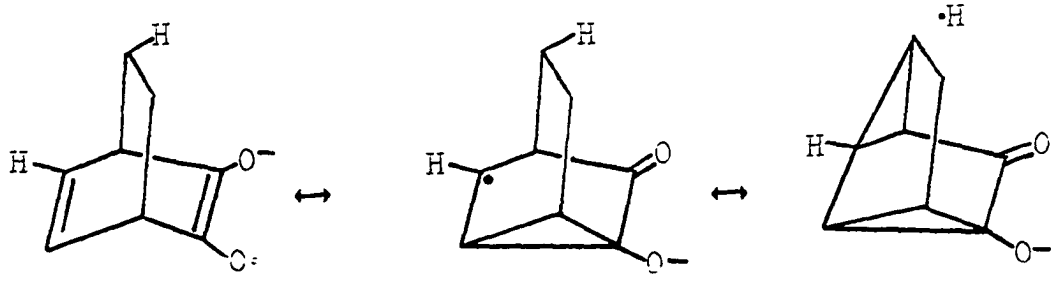
The spin densities acquired in the hydrogen 1S atomic orbital by such a mechanism can be estimated from the $a^{H}_{obs}/a^{H}_{H\cdot}$ ratio. Thus, the <u>exo</u> protons of XXXV acquire 0.004 of an unpaired spin which represents 1.6% delocalization. The total delocalization of the spin on the carbonyl carbon by the two equivalent hydrogens is 3.2%. For semidione I, $\rho_{H_{exo}}$ is estimated at 0.0040 (2% delocalization). The exceptionally large splitting by the <u>anti</u>-7 proton in I is anticipated since

there are two equivalent resonance forms contributing to $a^{H}_{\underline{anti}}$. 6.5G represents 0.013 of an unpaired spin or a total delocalization of carbonyl spin density of 2.6% [(0.013/2 x 0.25) (100)].

Inspection of the various hfsc for syn and anti protons reveals that an increase in $a^{H}_{\underline{syn}}$ is accompanied by a comparable increase in $a^{H}_{\underline{anti}}$. $a^{H}_{\underline{syn}}$ is made to increase by introducing points of unsaturation into the bicyclic nucleus. Structures such as LII-a and LII-b have been proposed to explain vinyl and syn hyperfine splittings in semiquinones (28, 31) but analogous structures XL-a and XL-b are unable to account for the increase in $a^{H}_{\underline{anti}}$ for semidiones.

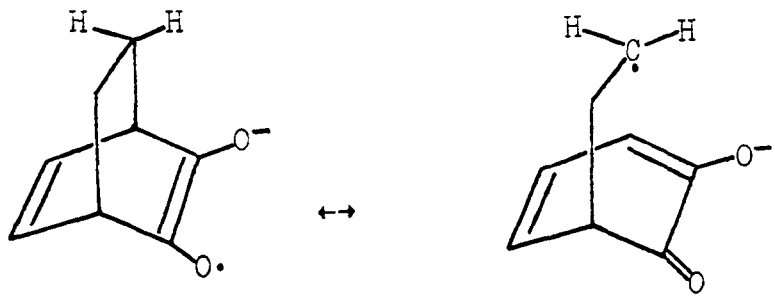


LII LII-a LII-b



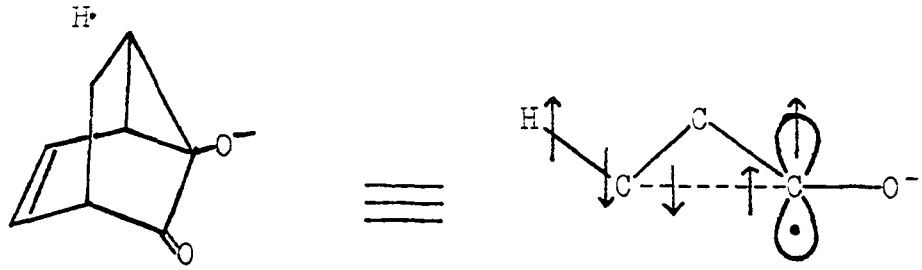
XL XL-a XL-b

Perhaps the increased strain in bicyclic semidiones created by the introduction of a double bond provides the driving force for carbon-carbon hyperconjugation (i.e., structure XL-c) and provides a mechanism to explain the variation of $a^{H}_{\underline{syn}}$ and $a^{H}_{\underline{anti}}$.



XL XL-c

In structure XL-c, the methylene spin density would be expected to be transmitted (via spin polarization) about equally to the syn and anti hydrogen atoms. It was noted earlier that the sign of the hfsc for a proton alpha to the radical center is negative. This arises from the value of Q (~ -23G) used in equation 1. The homohyperconjugation mechanism (represented by structure XL-d) predicts a positive sign for $a^{H}_{\underline{anti}}$. An increase in $a^{H}_{\underline{syn}}$ should be accompanied by a decrease in $a^{H}_{\underline{anti}}$ upon introduction of a double bond into the molecule; a prediction contrary to the experimental observations.



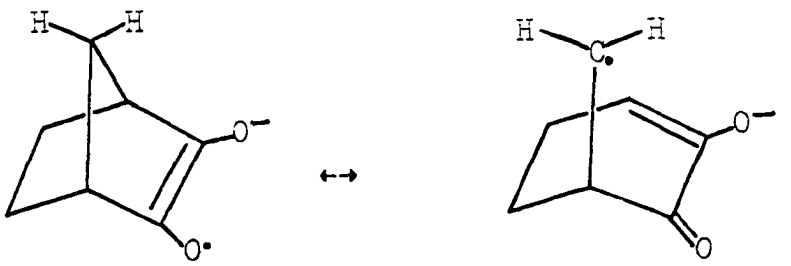
XL-d

This difficulty is circumvented by recalling that the value of Q used in this discussion applies to a planar radical in which the carbon bearing the unpaired electronis sp^2 hybridized The methylene carbon of XL-c is more nearly sp^3 than sp^2 hybridized. Q for a sp^3 carbon atom is not known but has been calculated to be around +15 gauss (73). Using this value of Q, the prediction becomes that $a^H_{\underline{syn}}$ and $a^H_{\underline{anti}}$ will show comparable increases; a conclusion compatible with the experimental data.

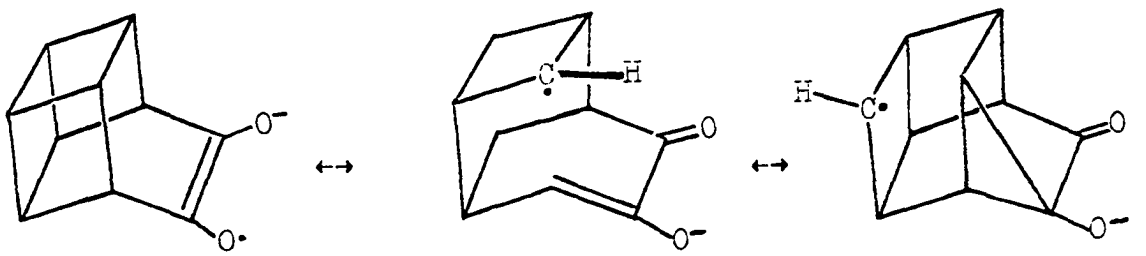
For unsaturated bicyclo[2.2.2]octan semidiones, such as XL, the increase in spin density experienced through structure XL-c is about 0.0008 of an unpaired spin per hydrogen or a total delocalization of about 0.6%. Thus, carbon-carbon hyperconjugation is an important splitting mechanism but contributes very little to the total resonance description of semidiones.

Carbon-carbon hyperconjugation also provides an explanation of why <u>syn</u>-7 interactions, but not <u>endo</u>-5,6, are observed in bicyclo[2.2.1] semidiones. The <u>syn</u>-7 proton is on a bridge that is more highly strained than the C-5,6 bridge. This inherent strain in the methylene bridge causes sufficient carbon-carbon

hyperconjugation to make $a^{H}_{\underline{syn}}$ observable; even in the absence of a double bond. Introduction of a benzo- group (see semidione XXXIII) increases both $a^{H}_{\underline{syn}}$ and $a^{H}_{\underline{anti}}$ by the same amount.



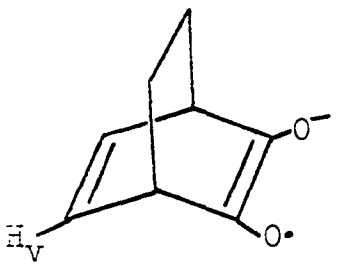
Carbon-carbon hyperconjugation also provides a mechanism for splitting in the highly strained semidione XLI.



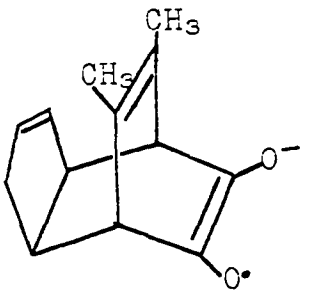
XLI

Attention is now drawn to splitting by vinyl and benzo-protons. A comparison of the data for semidiones XL and XLII indicates that the ratio of hfsc for a vinyl proton and a corresponding allylic methyl approaches unity. This is predicted by equations 1 and 2 if electron as well as spin density

reaches the double bond.



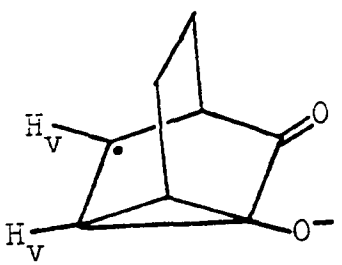
XL



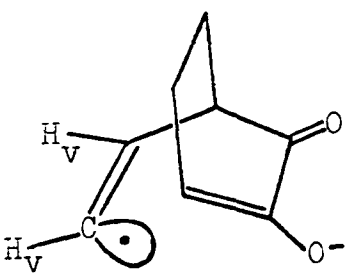
XLII

$$a^{H}_{CH_3} / a^{H}_{H_V} = \frac{0.48}{0.41} \simeq 1.2$$

This ratio is taken as strong evidence in support for a mechanism for vinyl splittings which involves electron transfer. A 1,3-π,π overlap mechanism (structure XL-a) appears very attractive. Carbon-carbon hyperconjugation (structure XL-d) is much less appealing in view of the $a^{H}_{CH_3}/a^{H}_{H_V}$ ratio. Spin



XL-a

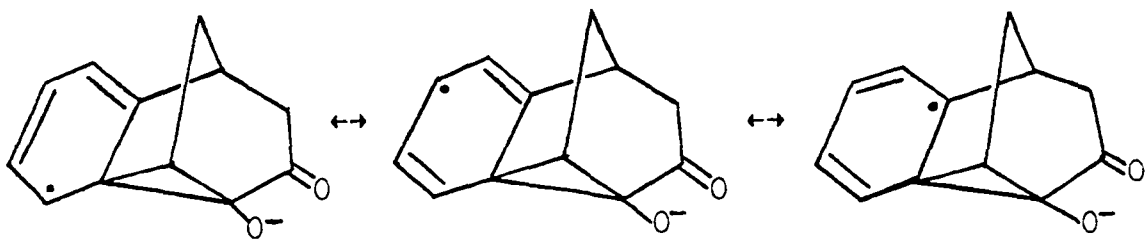


XL-d

polarization is not seriously considered as it would not place spin density into the $2p_z$ orbital of the vinyl carbons. Due to a fall-off factor of around 3 for spin polarization interactions, the $a^{H}_{CH_3}/a^{H}_{H}$ would be expected to be much less than unity. The

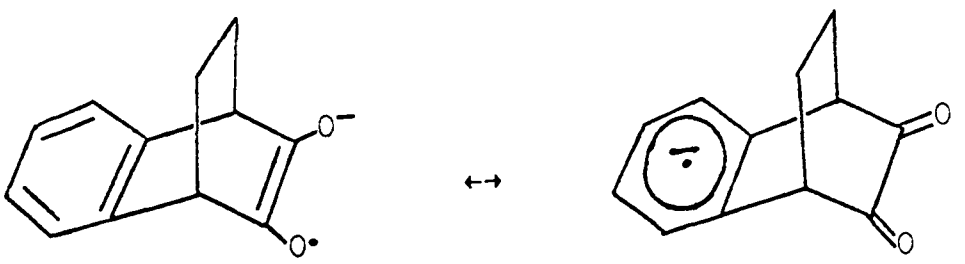
hfsc of semidione LXVII lend support to the 1,3-π,π overlap mechanism.

Semidione LXVIII is unsymmetrical and as such constrains the 1,3-π,π mechanism to placing spin density into only three positions in the aromatic ring. Only two of these positions have hydrogens alpha to the carbon bearing unpaired spin density and only a maximum of two aromatic splittings are observed in the esr spectrum of LXVIII.



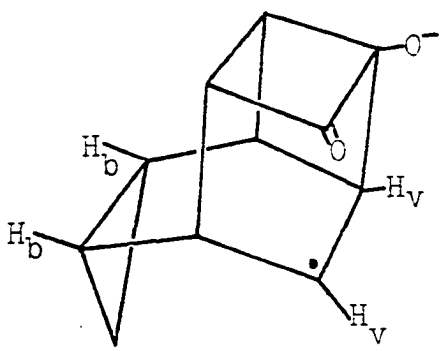
LXVIII

The data for symmetrical benzobicyclosemidiones (i.e., XXXIII, and XLVII-LI) are in contrast to that of LXVIII in that all aromatic protons are observed and are "fortuitously" magnetically equivalent. In these systems the π-system of the spin label is not angled away from the aromatic π-system by an additional methylene group as in LXVIII. It seems plausible that there could be a rapid exchange of the unpaired electron between the dicarbonyl system and the aromatic ring. With such a mechanism for aromatic splittings, the aromatic hydrogens feel a more even distribution of spin density. Weak support



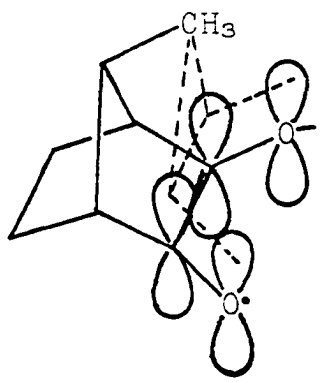
for this view is found in a comparison of g-values for radical anions. The g-value for benzene radical anion [(g = 2.00276) (74)] is lower than the g-value obtained for saturated aliphatic semidiones in DMSO (g = 2.00490). The g-values for some semidiones was presented in Table 1. Of the semidiones examined, those containing an aromatic ring have slightly lower g-values. A rapid electron transfer would introduce some benzene radical anion character into the semidione; a result that would be reflected in a relatively lower g-value. Since the g-values were determined under identical conditions, solvent effects on the g-value should be absent.

A 1,4-π,π-interaction is observed for semidione XLV. The photochemical 2 + 2 cycloaddition observed in this system (55, 56) indicates that the π-bonds are close enough to one another that valence bond structures, such as XLV-b, are not unreasonable. Spin density so introduced into this double bond is not only sufficient to produce observable vinyl splittings (0.45G) but also induce splitting by the two corresponding <u>exo</u> protons (H_b). Saturation of this position removes both splittings.



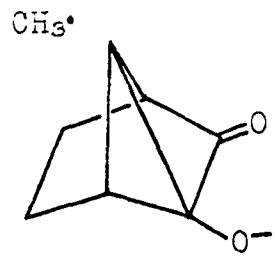
XLV-b

Due to their proximity in relation to the semidione spin label, endo and syn methyl splittings probably arise via a through space interaction.

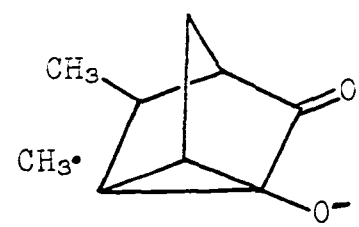


The decrease in a^H_{anti} and a^H_{exo} with corresponding syn and endo alkyl substitution is in better agreement with a homo-hyperconjugation mechanism than a spin polarization one since a syn or endo alkyl group may sterically inhibit the through space interactions inherent in this mechanism whereas the through bond spin polarization should be relatively unaffected by alkyl substitution.

Predictions for $a^{H}_{CH_3}$ *via* the homohyperconjugation mechanism are encouraging. For example, if homohyperconjugation is responsible for methyl splittings, it must be through structures involving carbon-carbon hyperconjugation (such as XV-d and XVII-d).



XV-d

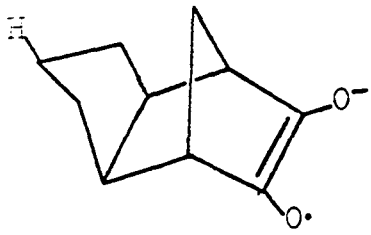


XVII-d

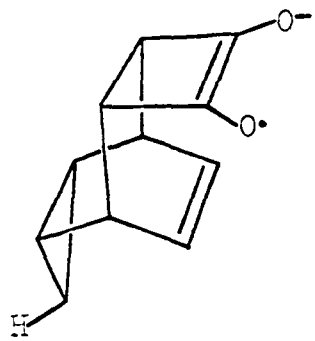
It has already been estimated that an *anti*-7 hydrogen can obtain around 0.013 of unpaired spin density via homohyperconjugation. If this value is taken as the largest possible value of ρ_C that a *anti*-7 methyl group could obtain, then $a^{H}_{CH_3}$ is predicted to be 0.19 gauss (using Q = +15 in equation 1). This prediction agrees extremely well with the experimental data (e.g., semidione XV, $a^{H}_{\underline{anti}\text{-}CH_3}$ = 0.19G). A similar prediction for $a^{H}_{\underline{exo}\text{-}CH_3}$ of 0.07 G is also in agreement with the experimental data (e.g., semidione XVII, $a^{H}_{\underline{anti}\text{-}CH_3}$ = 0.18 G).

The valence bond structures used thus far to aid in the explanation of homohyperconjugation and other mechanisms fail to account for the surprisingly large long-range interactions

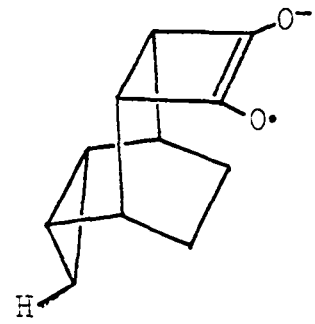
of semidiones XIX, XLV and XLVI. Inspection of the data for all



XIX
$a^H = 1.31$

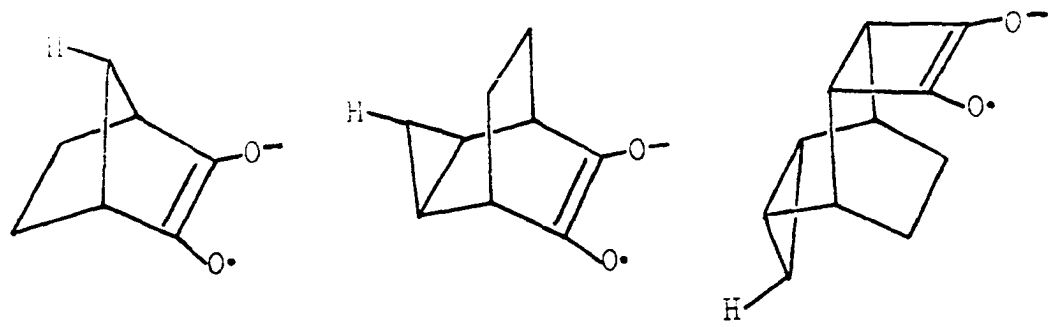


XLV
$a^H = 1.06$



XLVI
$a^H = 0.68$

bicyclic semidiones reveals that the major splittings are by protons that lie in a coplanar zig-zag arrangement of atoms with the $2p_z$ carbonyl orbital. This has been termed the "W-plan" or "V" arrangement (7, 23-25). In this notation, hydrogens alpha to the radical center are in a V arrangement, β-hydrogens are 1 1/2V, exo and anti a 2V, exo and anti methyl group protons a 2 1/2V, and the long-range interacting protons of XIX, XLV and XLVI a 3V. The observation of 3V splittings casts serious doubt upon the validity of using a homohyperconjugation mechanism to explain 2V and 2 1/2V interactions since it would be expected that the same mechanism should explain all "V" interactions beyond 1 1/2V. A comparison of a series of semidiones reveals that the interactions are related since a steady fall-off factor of about 3 per 1/2V is observed in going from the 2V to 3V arrangements. Perhaps the best overall explanation is not in terms of homohyperconjugation as it has been presented but in terms of the unconventional trans



2V 2 1/2V 3V

hyperconjugation mentioned earlier for the vinyl radical. From this point of view, all long-range "V" interactions result from a highly stereospecific through bond mechanism but is, in some as yet unexplained manner, fundamentally different from spin polarization. It follows a $\cos^2\theta$ relationship through bonds achieving maximum interaction in a coplanar trans arrangement of bonds. This change of point of view only challenges the validity of the name homohyperconjugation and not its conclusions since the same stereochemistry is required for both 2 and 2 1/2V splittings.

Kosman and Stock have recently presented an excellent discussion of hyperfine splitting in bicyclic semiquinones (30). Among the differences noted between semidiones and semiquinones is the exceedingly small $a^H_{CH_3}/a^H_{H_V}$ ratio.(<0.1) for vinyl interactions and a failure of a^H_{anti} to vary with a^H_{syn}. These differences, as well as differences for other bicyclic radicals, may be related to the symmetry of the highest occupied molecular orbital of the spin label. For a semiquinone, the unpaired

electron resides in a molecular orbital which is antisymmetric with respect to a plane bisecting the quinone nucleus and the bicyclic structure. The unpaired electron of a semidione is in an orbital which is symmetric with respect to a plane bisecting the dicarbonyl fragment and the bicyclic structure. In spite of the fact that highly stereospecific hfs are observed for semiquinones, they conclude that a spin polarization is the fundamental mechanism in their system.

Although the exact nature of the splitting mechanism responsible for long-range interactions in bicyclic semidiones cannot as yet be unequivocally stated, it surely must be the highly rigid carbon framework and strained bonds in the bicyclo[2.2.1]heptane and bicyclo[2.2.2]octane systems that enhance this mechanism for spin propagation throughout the semidione molecule.

EXPERIMENTAL

Reagents

Common solvents and chemicals were obtained from commercial sources and were used without purification. If purification was required, it is so stated where pertinent. Dimethyl sulfoxide was distilled at reduced pressure from calcium hydride and stored under nitrogen over 4A molecular sieves. Sodium-potassium alloy was prepared by mixing the desired amounts of each metal in refluxing dimethoxymethane under nitrogen.

Preparation of Solutions of Radicals

Solutions of radicals were prepared in an apparatus (Figure 38) consisting of an H-cell connected to a flat fused-silica cell (Varian V-4548 aqueous solution sample cell).

Sufficient radical precursor, 5-10 mg for α-diketones, was placed in one half of the H-cell while an equivalent amount of potassium t-butoxide was placed in the other half. DMSO (1 ml) was equally divided between the two sides to give 0.5-0.1 M solutions of each reactant. Propiophenone (8 μl) was added to the side containing the diketone and the two solutions were degassed for 30 min with prepurified nitrogen. After this time, the nitrogen inlets were removed from the cell and the cell sealed with a glass stopper. The apparatus was inverted and the solutions mixed and shaken into the flat fused-silica cell. This procedure is standard for the preparation of semidiones (75).

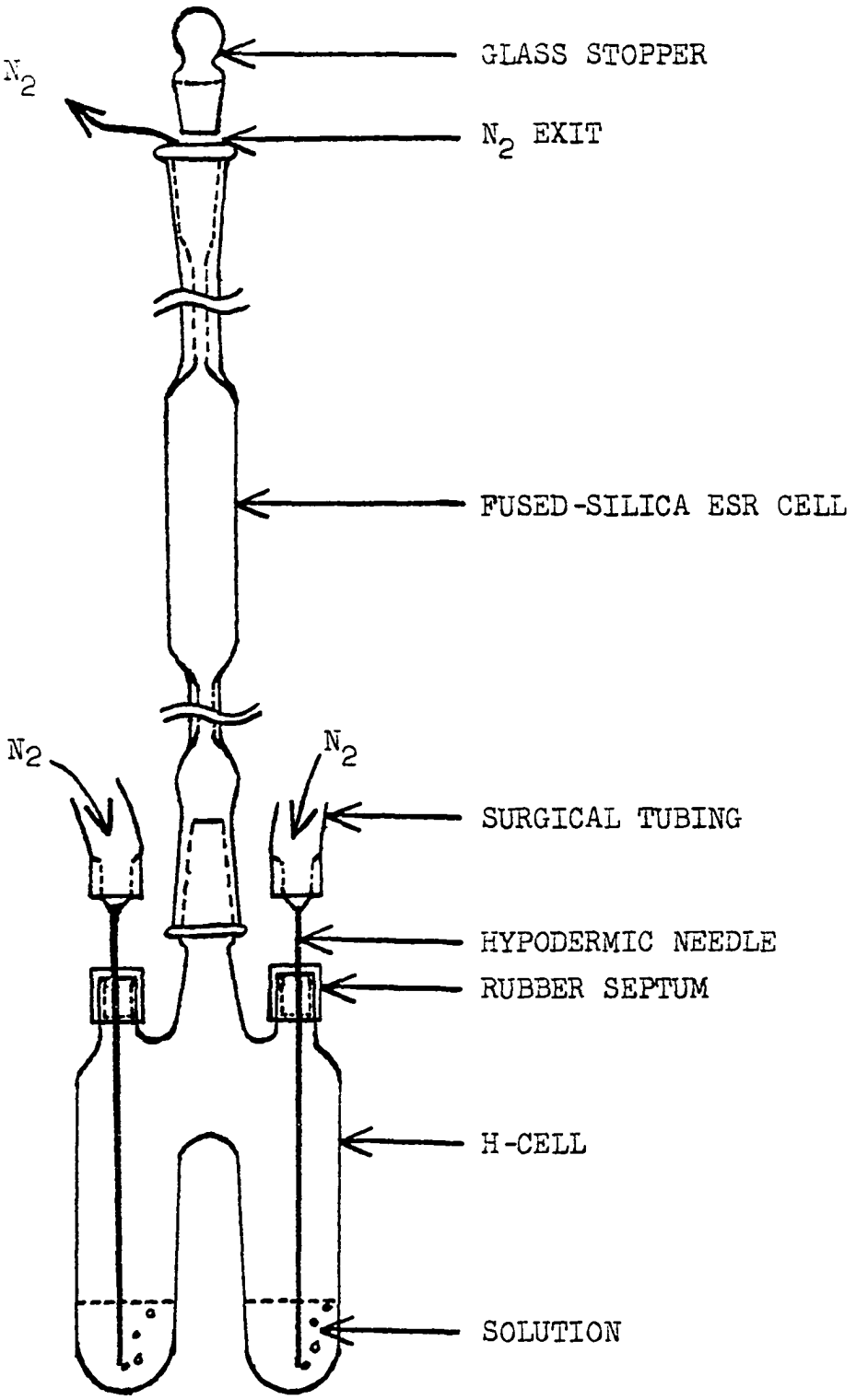


Figure 38. Apparatus for the preparation of solutions of stable radicals.

Oxidation of mono ketones containing an α-methylene group required initial DMSO solutions of 0.1-0.2 M in both ketone and potassium t-butoxide and a degassing period of 10-15 minutes. If additional oxygen was desired, the glass stopper and one rubber septum were removed for a 5-10 sec period.

Solutions of bis(trimethylsiloxy)alkenes (5 μl in 0.5 ml DMSO) and potassium t-butoxide (0.1 M in DMSO, 0.5 ml) were degassed for 10 min. No additional oxygen was ever needed with this procedure.

Hydroquinones (1-3 mg) and potassium t-butoxide (5 mg) in 0.5 ml DMSO each, degassed 10-15 min, and mixed afforded workable concentrations of semiquinones.

Recording of ESR Spectra

The esr spectra were obtained from either a Varian E-3 spectrometer employing a 4 inch magnet and 100 KHz field modulation or a Varian V-4500 spectrometer with a 9 inch magnet and 100 KHz field modulation.

Synthesis of ESR Spectra

A JEOLCO (Japan Electron Optics Laboratory Co.) JNM-RA-1 spectrum accumulator was employed for the synthesis of esr spectrum. The instrument was programed to fit a Lorentzian linewidth (variable) to a line diagram computed from the number of groups of magnetically equivalent nuclei, the number of nuclei in each group, their spin, and their splitting constant.

Measurement of g-Values

Spectroscopic splitting factors, g-values, were determined by measuring the difference, in gauss, between the center of the spectrum of the radical under investigation and the center of the spectrum of a standard, Fremy's salt [$(KSO_3)_2NO$], whose g-value was taken as 2.0055 ± 0.00005 (59). The esr spectra of both radicals were recorded simultaneously by taping a capillary tube containing a degassed aqueous solution of Fremy's sale to the flat portion of the esr cell. The g-value of the unknown was calculated from the expression $g = g_S(1-\Delta H/H_O)$ where g_S is the g-value of the standard, H_O is the magnetic field (in gauss), and ΔH is the difference between the centers of the two spectra. If the center of the spectrum of the unknown was upfield from that of Fremy's salt, ΔH was taken as a positive number.

Characterization of Compounds

Nmr spectra were recorded at room temperature on a Varian A-60 spectrometer. Chemical shifts of resonances were measured in parts per million relative to tetramethylsilane taken as zero. Resonances upfield from tetramethylsilane are denoted by a preceding minus sign. Infrared spectra were recorded on a Perkin-Elmer Model 21 Double Beam Spectrometer. All mass spectra were obtained with an Atlas CH4 spectrometer. Gas chromatography analysis and purifications were achieved with an Aerograph model A-90-P gas chromatograph. Melting points are uncorrected and were determined with a Thomas Hoover capillary melting point

apparatus. C and H analyses were preformed by the commercial analyst whose name appears with the analysis.

Preparation of Compounds

Bis(trimethylsiloxy)alkenes

Providing that pure diesters are employed, the bis(trimethylsiloxy)alkenes prepared by the acyloin condensation can be used as radical precursors without purification (25). The alkenes were generally prepared by stirring 10-50 mg of diester with 0.5 g of sodium-potassium alloy (1:1 by weight), chlorotrimethylsilane (5 ml), and diethyl ether (25 ml) at 0-25° for one hour. The ether solution was decanted and condensed at reduced pressure to yield the bis(trimethylsiloxy)alkene as an oil.

Bicyclo[2.2.1]hept-2-ene oxide (I-b)

Bicyclo[2.2.1]hept-2-ene oxide was prepared as described by Walborsky and Loncrini (76). Thus, 9.4 g (0.10 mole) of norbornylene (Aldrich), 5.0 g of sodium acetate, and chloroform (10 ml) were mixed and cooled to 0° in an ice bath. 40% peracetic acid (25 ml, Aceto) was slowly added. The mixture was stirred at 0° for an additional hour, neutralized with 30% sodium hydroxide, and extracted with chloroform (3 x 40 ml). The combined chloroform extracts were dried (Na_2SO_4), filtered, and condensed *in vacuo* to yield an oil. The oil was distilled to yield 7.1 g (64%) of a fragrant, waxy solid: bp 153-157° [lit (76) bp 155-158°]; nmr (CCl_4) δ0.64 (d, 1H, J = 9.8 Hz),

0.9-1.7 (overlapping multiplets, 5H), 2.41 (broad singlet, 2H), and 2.90 (s, 2H).

Endo, endo-5,6-dimethylbicyclo[2.2.1]hept-2-ene oxide (XVIII-a)

Endo, endo-5,6-dimethylbicyclo[2.2.1]hept-2-ene oxide was prepared by the same procedure already described for bicyclo-[2.2.1]hept-2-ene oxide. 3.8 g (0.031 mole) of olefin mixed with sodium acetate (1.2 g) in chloroform (5 ml) was reacted with 40% peracetic acid (8 ml) to yield 1.85 g (43%) of the solid oxide: bp 115-120° (50 mm); nmr (CCl_4) δ0.67 (d, 1H, J = 9.4 Hz), 0.94 (d, 6H, J = 6.9 Hz, $-CH_3$), 1.30 (d, 1H, J = 9.4 Hz), 2.13 (multiplet, 2H, C-5,6 H), 2.32 (multiplet, 2H, C-1,4 H), and 3.12 (s, 2H, epoxide H).

5,8-Dimethoxybenzobicyclo[2.2.1]hept-2-ene oxide

The title compound was prepared in 49% yield by the same procedure used for XVIII-a: nmr (CCl_4) δ1.1-2.1 (multiplets, 2H, C-7 H), 3.2 (broad singlet, 2H, epoxide H), 3.54 (multiplet, 2H, C-1,4 H), 3.70 (s, 6H, $-OCH_3$), and 6.43 (s, 2H, aromatic H).

Exo, exo-5,6-dideuterobicyclo[2.2.1]heptan-2-ol (exo and endo)

7.5 g (0.068 mole) of 5-norbornen-2-ol (mixture of exo and endo, Aldrich Chemical Co.) was mixed with ethyl acetate (75 ml) and 0.25 g of 10% palladium on powdered charcoal (Matheson Coleman and Bell) and stirred under an atmosphere of deuterium gas (Matheson) until deuterium was no longer absorbed. The mixture was filtered and the ethyl acetate removed at reduced pressure to yield 5.63 g (72%) of alcohol after recrystallization from pentane: mp 97-107°; ir (CCl_4) 3650 and 3500 (-OH), 2180

(C-D), and 1056 cm^{-1} (C-O); nmr (CCl_4) δ0.6-2.4 (overlapping multiplets, 8H), 3.63 (s, 1H, -OH, removed by added D_2O), and 3.9-4.3 (overlapping multiplets, 1H, -CH-O); mass spectrum (70 eV) M^+ = 114, prominent peaks at 112 (m-2), 96(18),81(M-33), 69 (M-45) and 68 (M-46).

Anal. Calcd for $C_7H_{10}OD_2$: C, 73.63; H, 10.79. Found, (Spang): C, 73.92; H, 10.73.

Exo, exo-5,6-dideuterobicyclo[2.2.1]heptan-2-one (VII-b)

3.0 g (0.026 mole) of exo, exo-5,6-dideuterobicyclo[2.2.1]-heptan-2-ol, 0.5 g of aluminum isopropoxide, and 10 g of benzophenone were mixed and heated to 150°. The isopropyl alcohol that formed was removed at reduced pressure (35 mm). The temperature was slowly raised from 150° to 190° while the pressure was held at 50 mm. The ketone collected as a waxy solid in the condenser of the distillation apparatus. 2.50 g (85%) of ketone was collected and purified by sublimation at 70°(1 atm):mp 92.5-94° [lit (77) mp 96.5-97.5°]; ir (CCl_4) 2180 (C-D), and 1648 cm^{-1} (C=O); nmr (CCl_4) δ0.8-2.3 (overlapping multiplets,6H),and 2.4-2.8 (overlapping multiplets, 2H); mass spectrum (70 eV) M^+ = 112, major peaks at 96 (M-16), 83 (M-29), 68 (M-44),55(M-57), and 42 (M-70), calcd isotopic purity of 99.99%.

Anal. Calcd for $C_7H_8OD_2$: C, 74.95; H, 9.19. Found,(Spang): C, 74.93; H, 9.54.

Exo, exo-5,6-dideuterobicyclo[2.2.1]heptan-2,3-dione (VII-c)

1.0 g (8.9 mmole) of exo, exo-5,6-dideuterobicyclo[2.2.1]-heptan-2-one, 1.0 g (8.9 mmole)of selenium dioxide,and xylene

(5 ml) were mixed and refluxed at 140° for 4 hours. The mixture was filtered and the filtrate condensed *in vacuo* to yield a brown paste from which 0.42 g (41%) of a yellow semisolid was isolated by repeated sublimation at 80° (13 mm). Attempted purification by recrystallization or column chromatography over silica gel failed to yield a well defined solid as reported, [lit (78) mp 112-113°], and in agreement with the observations of Chang (23). The carbonyl region of the deuterated and undeuterated α-diketones were superimposable: ir (CCl_4)2198 (C-D), 1782 and 1762 cm^{-1} (C=O).

Endo, endo-bicyclo[2.2.1]hept-2-ene-5,6-dicarboxylic anhydride

The anhydride was obtained from the reaction of equimolar amounts of cyclopentadiene and maleic anhydride in benzene at room temperature (79). Commercial samples were obtained from the Velsical Chemical Corp. (mp 153-156°) and from Aldrich Chemical Company (mp 141-146°). The anhydride was purified by recrystallization from benzene to a constant melting point of 162-164°: [lit (54) mp 165°].

Exo, exo-bicyclo[2.2.1]hept-2-ene-5,6-dicarboxylic anhydride

The *exo* anhydride was prepared in a manner similar to that described by Craig (54). Thus, 35.0 g of *endo* anhydride was heated for 1.5 hours at 190°, warmed on a steam bath for 0.5 hour with an equal volume of benzene and 5 g of activated charcoal, filtered, and cooled to room temperature. The white crystals (mp 105-110°) that formed were collected by filtration

and recrystallized from benzene until a constant melting point of 141-143° was obtained: [lit (54) mp 142°]. The mother liquors were combined, the benzene evaporated and the solid thus obtained treated as described above until 25.7 g (73.5%) of pure exo anhydride was obtained.

Endo, endo-5,6-dicarbomethoxybicyclo[2.2.1]hept-2-ene

Endo, endo-5,6-dicarbomethoxybicyclo[2.2.1]hept-2-ene was prepared by the reaction of endo, endo-bicyclo[2.2.1]hept-2-ene-5,6-dicarboxylic anhydride and methanol with a trace of acid. A typical conversion involved refluxing 82.0 g (0.50 mole) of anhydride, 1.0 g of p-toluenesulfonic acid or 1 ml of sulfuric acid (~96%), and 180 ml of anhydrous methanol for ten hours. The excess methanol was removed by distillation at reduced pressure (15 mm) to yield a light yellow oil. This oil was combined with diethyl ether (200 ml), washed with 5% sodium bicarbonate solution (2 x 200 ml) and water (1 x 100 ml). The ether solution was dried (Na_2SO_4), filtered, concentrated at reduced pressure, and distilled to yield 88.8 g (84.6%) of diester: bp 131-139° (10 mm) [lit (80) bp 129-130°]; ir (neat) 1724 (C=O), 1428, 1186, 1160 cm^{-1} (ester); nmr (CCl_4) δ1.35 (multiplet, 2H, C-7 syn and anti), 3.09 (multiplet, 2H, C-1,4 bridgehead), 3.21 (multiplet, 2H, C-5,6 exo), 3.50 (s, 6H, $-CH_3$), and 6.12 (multiplet, 2H, vinyl).

Endo, endo-5,6-dimethanolbicyclo[2.2.1]hept-2-ene

Endo, endo-5,6-dimethanolbicyclo[2.2.1]hept-2-ene was prepared by the lithium aluminum hydride reduction of either

endo, *endo*-5,6-dicarbomethoxybicyclo[2.2.1]hept-2-ene or *endo*, endo-bicyclo[2.2.1]hept-2-ene-5,6-dicarboxylic anhydride

Preparation from the dimethyl ester (81)

73.3 g (0.35 mole) of dimethyl ester in 100 ml of diethyl ether was added over a two hour period to a mixture of 13.9 g (0.37 mole) of lithium aluminum hydride in 500 ml of diethyl ether. Cooling with an ice bath was required during the addition. The reaction mixture was refluxed for two days, hydrolyzed with 10% hydrochloric acid (600 ml), and the organic phase dried (Na_2SO_4), filtered, and concentrated at reduced pressure to yield a viscous oil which solidified upon cooling to -15° (methanol-ice). The solid was recrystallized from an equal volume of diethyl ether at -78° (dry ice-acetone) giving 41.6 g (77.4%) of white, crystalline diol: mp 74-76° [lit (82) 82-83°, lit (83) mp 62°]; ir 3290 (OH); nmr δ1.41 (broad singlet, 2H, C-7 *syn* and *anti*), 2.52 (multiplet, 2H), 2.79 (multiplet, 2H), 3.5 (multiplet, 4H, $-CH_2O-$), 4.68 (broad singlet removed by added D_2O, 2H, -OH), and 6.04 (multiplet, 2H, vinyl).

Preparation from the anhydride (82)

65.0 g (0.398 mole) of *endo*, *endo*-bicyclo[2.2.1]hept-2-ene-5,6-dicarboxylic anhydride was extracted *via* a Soxhlet extraction apparatus in a refluxing mixture of 15.2 g (0.40 mole) of lithium aluminum hydride in 500 ml of diethyl ether. The reaction mixture was refluxed for an additional 5 hours, then hydrolyzed with 10% hydrochloric acid (125 ml). Water (250 ml)

was added, the ether layer separated, dried (Na_2SO_4), filtered, and condensed at reduced pressure (~15 mm) to yield 20.1 g (32.9%) of diol possessing the same properties as the diol obtained from the diester.

Endo, endo-5,6-dimethanolbicyclo[2.2.1]hept-2-ene ditosylate

54.7 g (0.355 mole) of endo, endo-5,6-dimethanolbicyclo-[2.2.1]hept-2-ene was mixed with 15 g (2.0 mole) of pyridine (freshly distilled from barium oxide). This solution was cooled in an ice bath and 157 g (0.825 mole) of p-toluene-sulfonyl chloride (mp 66-67° from pentane) was added at such a rate that the temperature did not rise above 20°. This mixture was stirred at 10-20° for three hours, then mixed with 900 ml of 10% hydrochloric acid. A heavy, dark oil separated which was dissolved in hot methanol. The methanol solution deposited a crystalline solid (mp ~95°) upon cooling to -21°. This solid was recrystallized from methanol to yield 111.9 g (68%) of the white crystalline ditosylate: mp 103-104°: [lit (83) mp 90-91°]; nmr ($CDCl_3$) δ1.37 (multiplet, 2H, C-7 syn and anti), 2.44 (s, 3H, Ar-CH_3), 2.5 (multiplet, 2H, C-5,6 exo), 2.89 (multiplet, 2H, C-1, 4 bridgehead), 3.68 multiplet, 4H, CH_2-O-), 5.90 (multiplet, 2H, vinyl), 7.32 (d, 2H, J = 8.4 Hz, m-aromatic), and 7.74 (d, 2H, J = 8.4 Hz, o-aromatic).

Endo, endo-5,6-dimethylbicyclo[2.2.1]hept-2-ene (XVIII-a)

23.9 g (0.05 mole) of endo, endo-5,6-dimethanolbicyclo-[2.2.1]hept-2-ene ditosylate was placed in a Soxhlet extraction apparatus and extracted into a mixture of 10.0 g (0.26 mole) of

lithium aluminum hydride in 750 ml of diethyl ether. The mixture was refluxed for an additional 16 hours, hydrolyzed with 10% hydrochloric acid (300 ml), and the ether layer separated from the water. The ether solution was washed with 5% sodium hydroxide (50 ml), water (50 ml), dried (Na_2SO_4), filtered, and the ether carefully removed by distillation to yield an oil which was distilled to yield 4.1 g (63%) of the dimethyl olefin: bp 73-76° (79 mm) [lit (58) 61.5° (10 mm)]; ir (CCl_4) 3075 (-$\overset{H}{C}$=$\overset{H}{C}$-), 1652 (C=C), 1468 and 1450 cm^{-1} (C—CH_3); nmr (CCl_4) δ0.7 (d, 2H, J = 6.6 Hz, -CH_3), 1.35 (multiplet, 2H, C-7 syn and anti), 2.14 (multiplet, 2H, C-5,6 exo), 2.62 (multiplet, 2H, C-1,4 bridgehead), and 6.08 (multiplet, 2H, vinyl).

Endo, endo-5,6-dimethylbicyclo[2.2.1]heptan-2-ol (exo)

The alcohol was prepared utilizing the hydroboration reaction as described by Brown and Rao (84). Thus, a solution of 1.8 g (13 mmole) of boron trifluoride etherate (freshly distilled, bp 65°/33mm) in 5 ml of diglyme (distilled from calcium hydride, bp 66-67°/20 mm) was added over a one hour period to a solution of 1.2 g (8.6 mmole) of endo, endo-5,6-dimethylbicyclo-[2.2.1]hept-2-ene and 0.4 g (10 mmole) of sodium borohydride in 15 ml of diglyme. The reaction mixture was stirred at room temperature for 2 hours and then the excess diborane was decomposed by the careful addition of 2 ml of water. Sodium hydoxide (3N, 5 ml) was added followed by hydrogen peroxide (30%, 5 ml). This mixture was stirred for 15 minutes, mixed with ice water

(250 ml) and the alcohol extracted from the aqueous mixture with diethyl ether (2 x 50 ml). The combined ether extracts were washed with water (10 cc), dried (Na_2SO_4), filtered, and the ether removed at reduced pressure to give an oil that yielded 1.7 g (83%) of alcohol upon distillation: bp 130-138° (55 mm); ir 3620 and 3390 (-OH), 1465 and 1443 (C-CH_3), and 1021 cm^{-1} (C-O); nmr (CCl_4) δ0.76 and 0.80 (overlapping doublets, 6H, J = 6 Hz, -CH_3), 0.8-1.4 (overlapping multiplets, 2H, C-7 syn and anti), 1.5-2.2 (overlapping multiplets, 6H), 3.94 (multiplet, 1H, C$\underline{H}$-O), and 4.0 (s, 1H, -O$\underline{H}$, removed by added D_2O).

Anal. Calcd for $C_9H_{16}O$: C, 77.09; H, 11.50. Found (Spang): C, 77.20; H, 11.64.

Endo, endo-5,6-dimethylbicyclo[2.2.1]heptan-2-one (XVIII-b)

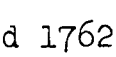
A solution of 1.7 g (17 mmole) of chromium trioxide, water (3 ml), and glacial acetic acid (15 ml) was added dropwise over a one hour period to a solution of 4.90 g (35 mmole) of endo, endo-5,6-dimethylbicyclo[2.2.1]heptan-2-ol in glacial acetic acid (15 ml). This mixture was stirred for 8 hours at room temperature, diluted with ice water (300 ml), and extracted with diethyl ether (5 x 70 ml). The combined ether extracts were washed with 5% sodium bicarbonate (100 ml), dried (Na_2SO_4), filtered, and concentrated at reduced pressure to a sweet-smelling oil. The oil yielded 3.20 g (66%) of a colorless, waxy solid upon distillation: bp 103-106° (13 mm); ir (CCl_4) 1744

cm^{-1} (C=O); nmr (CCl_4) δ0.79 and 0.90 (overlapping doublets, 6H, J = 6.2 Hz, -CH_3), 0.8-1.37 (overlapping multiplets, 2H, C-7 *syn* and *anti*), and 1.5-2.6 (overlapping multiplets, 6H).

Anal. Calcd for $C_9H_{24}O$: C, 78.21; H, 10.21. Found (Spang): C, 78.15; H, 10.31.

Endo, endo-5,6-dimethylbicyclo[2.2.1]heptan-2,3-dione (XVIII-d)

3.20 g (23 mmole) of *endo*, *endo*-5,6-dimethylbicyclo[2.2.1]-heptan-2-one, 2.9 g (24 mmole) of selenium dioxide, and xylene (15 ml) were mixed and strongly refluxed for 4 hours. The reaction mixture was allowed to stand overnight, filtered, and the filtrate distilled to yield 1.62 g (46%) of a yellow oil that solidified to a bright yellow solid (bp 135/35 mm). The yellow solid was purified by sublimation at 75° (5 mm) to yield crystals melting at 87-91°.

An alternate purification procedure involved column chromatography of the filtered reaction mixture over silica gel (20 mesh) and developing first with pentane (200 ml) followed by benzene-pentane (1:1 by volume) until a yellow fraction was collected. Removal of the solvent *in vacuo* yielded the α-diketone as a yellow solid which was recrystallized from hexane: mp 101-102°; ir (CCl_4) 1781 and 1762 cm^{-1} (); nmr (CCl_4) δ0.88 (d, 6H, J = 6.9 Hz, -CH_3), 2.11 (multiplet, 2H, C-7 *syn* and *anti*), 2.67 (multiplet, 2H, C-5,6 *exo*), and 2.85 (multiplet, 2H, C-1,4 bridgehead); mass spectrum (70 eV) M^+ = 152, prominent peaks at 124 (M-28), 95 (M-57), 81 (M-71), and 69 (M-83).

Anal. Calcd for $C_9H_{12}O_2$: C, 71.03; H, 7.95. Found (Spang): C, 70.55; H, 7.95.

Exo, exo-5,6-dicarbomethoxybicyclo[2.2.1]hept-2-ene (XVII-a)

Exo, exo-5,6-dicarbomethoxybicyclo[2.2.1]hept-2-ene was prepared from exo, exo-bicyclo[2.2.1]hept-2-ene-5,6-dicarboxylic anhydride by the same procedure already described for endo,endo-dicarbomethoxybicyclo[2.2.1]hept-2-ene. Thus 46.5g (0.284 mole) of exo anhydride yielded 54.5 g (91%) of the exo diester: bp 101-105° (1 mm) [lit (83) mp 52°]; ir (neat) 1732 (C=O), and 1197 cm^{-1} (C–O–C); nmr (CCl_4) δ1.42 (complex doublet, 1H, J= 9.0Hz), 2.08 (complex doublet, 1H, J = 9.0 Hz), 2.53 (d, 2H, J=1.9Hz, C-5,6 endo), 3.03 (multiplet, 2H, C-1,4 bridgehead), 3.59 (s, 6H, $-OCH_3$), and 6.18 (multiplet, 2H, vinyl).

Exo, exo-5,6-dimethanolbicyclo[2.2.1]hept-2-ene

Exo, exo-5,6-dimethanolbicyclo[2.2.1]hept-2-ene was prepared by the lithium aluminum hydride reduction of either exo, exo-5,6-dicarbomethoxybicyclo[2.2.1]hept-2-ene or exo, exo-bicyclo[2.2.1]hept-2-ene dicarboxylic anhydride in a manner already described for endo, endo-5,6-dimethanolbicyclo[2.2.1]-hept-2-ene. Thus, 54.5 g (0.258 mole) of diester yielded 30.2g (76%) of diol while 20.8 g (0.127 mole) of exo-anhydride yielded 13.5 g (69%) of the diol: bp 120-130 (2 mm) [lit (83) bp 95° (0.035 mm)]; ir 3330 (-OH) and 1036 cm^{-1} (C-O); nmr (CCl_4) δ1.0-1.4 (multiplet, 1H), 1.5-1.9 (multiplet, 1H), 2.55 (d, 2H, J = 1.2 Hz, C-5,6 endo), 3.04 (multiplet, 2H, C-1,4 bridgehead),

3.63 (multiplet, 4H, -CH_2-O-), 4.88 (broad singlet removed by added D_2O, 2H, -O<u>H</u>), and 6.13 (multiplet, 2H, vinyl).

Exo, exo-5,6-dimethanolbicyclo[2.2.1]hept-2-ene ditosylate

Exo, exo-5,6-dimethanolbicyclo[2.2.1]hept-2-ene ditosylate was prepared from the corresponding diol by the same procedure already described for the preparation of endo, endo-5,6-dimethanolbicyclo[2.2.1]hept-2-ene ditosylate. Hence, 27.9 g (0.18 mole) of diol yielded 37.1 g (44%) of exo ditosylate: mp 168-170°, [lit (83) mp 173°]; nmr ($CDCl_3$) δ1.29 (multiplet, 2H, C-7 syn and anti), 1.82 (multiplet, 2H, C-5,6 endo), 2.45 (s, 6H, Ar-CH_3), 2.69 (multiplet, 2H, C-1,4 bridgehead), 4.0 (multiplet, 4H, -CH_2-O-), 6.09 (multiplet, 2H, vinyl), 7.35 (d,2H, J= 7.6 Hz, m-aromatic), and 7.78 (d, 2H, J = 7.6 Hz, o-aromatic).

Exo,exo-5,6-dimethanolbicyclo[2.2.1]hept-2-ene dimethanesulfonate

The preparation of exo, exo-5,6-dimethanolbicyclo[2.2.1]hept-2-ene was patterned after that described by Wilder and Feliu-Otero (85). 38.0 g (0.332 mole) of methane-sulfonyl chloride was slowly added to 50 ml of pyridine (distilled from barium oxide) at 0°. A solution of 18.8 g (0.122 mole) of diol in pyridine (80 ml) was added at such a rate that the temperature did not rise above 5°. This mixture was stirred for 6 hours at 0°, stored overnight at 0°, and then mixed with 10% hydrochloric acid (400 ml) at 0°. This mixture was added to ice (1000 ml). The solid that formed was removed by suction filtration, air dried, and recrystallized from absolute ethanol to yield 18.9 g

(50%) of white, crystalline dimesylate: mp 119-120° [lit (85) mp 120°]; nmr ($CDCl_3$) δ1.49 (multiplet, 2H, C-7 syn and anti), 2.01 (multiplet, 2H, C-5,6 endo), 2.83 (multiplet, 2H, C-1,4 bridgehead), 3.0 (s, 6H, $-CH_3$), 4.30 (multiplet, 4H, $-CH_2O-$), and 6.23 (multiplet, 2H, vinyl).

Exo, exo-5,6-dimethylbicyclo[2.2.1]hept-2-ene (XVII-a)

Exo, exo-5,6-dimethylbicyclo[2.2.1]hept-2-ene was prepared by the action of lithium aluminum hydride on the corresponding dimethanesulfonate. The same procedure as was used to prepare endo, endo-5,6-dimethylbicyclo[2.2.1]hept-2-ene from the ditosylate was employed. 40.4 g (0.13 mole) of dimesylate extracted via a Soxhlet extraction apparatus into a solution of 10.0 g (0.26 mole) of lithium aluminum hydride in diethyl ether (700 cc) yielded 9.05 g (57%) of the olefin: bp 72-74° (75 mm), [lit (83) bp 53° (25 mm)]; ir (CCl_4) 3080 ($-\overset{H}{\underset{|}{C}}=\overset{H}{\underset{|}{C}}-$), 1652 (C=C), 1469 and 1452 cm^{-1} ($C-CH_3$); nmr (CCl_4) δ0.71-1.90 (overlapping multiplets, 6H), 0.92 (d, 6H, J = 7.2 Hz, $-CH_3$), 2.32 (multiplet, 2H, C-1,4 bridgehead), and 6.02 (multiplet, 2H vinyl).

Exo, exo-5,6-dimethylbicyclo[2.2.1]heptan-2-ol (exo)

Exo, exo-5,6-dimethylbicyclo[2.2.1]heptan-2-ol was prepared by the hydroboration-oxidation reaction of exo, exo-5,6-dimethylbicyclo[2.2.1]hept-2-ene by the same procedure already described for the preparation of the endo, endo-5,6-dimethyl isomer. 6.0 g (0.049 mole) of olefin yielded 2.8 g (41%) of exo alcohol: bp 85-87° (5 mm); ir (CCl_4) 3630 and 3480 (-OH), and 1112 cm^{-1} C-O-); nmr (CCl_4) δ0.80 and 0.83 (overlapping doublets, 6H, J =

6.2 Hz, -C$\underline{H}_3$), 0.8-1.9 (overlapping multiplets, 8H), 3.69 (d of d, 1H, J = 6.5, 3.0 Hz, -C$\underline{H}$OH), and 3.97 (s, 1H, -O$\underline{H}$, removed by added D_2O).

Exo, exo-5,6-dimethylbicyclo[2.2.1]heptan-2-one (XVII-b)

Exo, exo-5,6-dimethylbicyclo[2.2.1]heptan-2-one was prepared by the chromium trioxide oxidation of the corresponding alcohol in acetic acid as already described for endo, endo-5,6-dimethylbicyclo[2.2.1]heptan-2-ol. 2.69 g (0.0192 mole) of alcohol yielded 2.06 g (78%) of ketone: bp 90-95° (13 mm); ir (CCl_4) 1652 cm^{-1} (C=O); nmr (CCl_4) δ0.7-2.3 (overlapping multiplets).

Cis-1,3-cyclopentanedicarboxylic acid

Bicyclo[2.2.1]heptene was oxidized to cis-cyclopentan-1,3-dicarboxylic acid with either ozone or potassium permanganate.

Oxidation with ozone

A procedure similar to that of Bailey (86) was used. 2.3 g (25 mmole) of olefin was dissolved in absolute methanol (75 ml), cooled to -78° (dry ice-acetone), and treated with 25 mmole of ozone (produced in a Welsbach ozone generator). The methanol was removed at reduced pressure and the residual oil mixed with 90% formic acid (15 ml) and 30% hydrogen peroxide (8 ml). After warming to reflux (30 min) on a steam bath, the mixture was condensed at reduced pressure to an oil (1.9 g, 49%) which crystallized upon cooling: mp 113-116°.

Oxidation with potassium permanganate in water

3.0 g (32 mmole) of bicyclo[2.2.1]heptene in hexane (200 ml) was stirred at room temperature for 4 hours with a solution of 13.5 g of potassium permanganate, 20 g of sodium bicarbonate and 600 ml of water. The layers were separated and the water mixture treated with sulfur dioxide until a clear solution was obtained. The clear solution was acidified with sulfuric acid, condensed at reduced pressure to a white paste, and the paste thoroughly washed with diethyl ether. The combined ether washings were dried (Na_2SO_4), filtered, and evaporated to yield 4.15 g (82%) of diacid: mp 115-117°.

Oxidation with potassium permanganate in acetone

2.4 g (25.6 mmole) of bicyclo[2.2.1]heptene, 5 g of sodium bicarbonate, and 200 ml of acetone were stirred at 0° while solid potassium permanganate was added in small portions until a purple color persisted for greater than 0.5 hour. The mixture was filtered by suction. The brown solid thus obtained was mixed with water (100 ml) and treated with sulfur dioxide until a clear solution was obtained. The clear solution was processed as described above for the oxidation in water and yielded 2.67 g (66%) of diacid: mp 114-117°. Recrystallization from water yielded a solid melting at 117-119° [lit (87) 121.5°].

Dimethyl cis-1,3-cyclopentanedicarboxylate

Treatment of cis-1,3-cyclopentanedicarboxylic acid with methanol and a trace of acid as described for the preparation

of endo, endo-bicyclo[2.2.1]hept-5,6-dicarboxylic anhydride led to the preparation of the diester in yields of 96%: bp 95-97° (1 mm) [lit (88) bp 138-138.5 (25 mm)]; ir (neat) 1726 (C=O), 1365 ($-CH_3$), 1198 and 1159 cm^{-1} (C—O—C); nmr (CCl_4) δ1.8-3.0 (overlapping multiplets, 8H), and 3.60 (s, 6H, $-OCH_3$).

Dimethyl trans,trans-4,5-dideuterocyclopentane-cis-1,3-dicarboxylate

3.0 g (32.6 mmole) of bicyclo[2.2.1]heptadiene, benzene (50 ml), 0.3 g of 10% palladium on powdered charcoal, and 1.0 g (0.04 g-atom) of magnesium were stirred in a closed container while o-deuterated acetic acid (>97% deuterated) was added over a 15 hour period. The mixture was filtered, washed with water (20 ml), and dried ($MgSO_4$). Acetone (200 ml) and 3.0 g of sodium bicarbonate were added to the benzene solution. This solution was treated with potassium permanganate as described for the oxidation of bicyclo[2.2.1]heptene in acetone.

The crude diacid, upon refluxing with methanol and a trace of acid, yielded 1.45 g (24% based on 3.0 g of bicyclo[2.2.1]-heptadiene) of the diester which was purified by vpc (15% Carbowax 20 M, 140°).

Dimethyl trans, trans-4,5-dimethylcyclopentane-cis-1,3-dicarboxylate

3.0 g (25 mmole) of exo, exo-5,6-dimethylbicyclo[2.2.1]-hept-2-ene was oxidized with ozone in the manner described for bicyclo[2.2.1]heptene. The crude oxidation product yielded 2.8 g

(53%) of the diester upon refluxing with methanol and a trace of acid. The diester was purified by vpc (15% Carbowax 20 M, 160°): nmr (CCl_4) δ0.93 (d, 6H, J = 6.0 Hz, C–CH_3), 1.9-2.6 (overlapping multiplets, 6H), and 3.62 (s, 6H, O–CH_3).

Dimethyl cis, cis-4,5-dimethylcyclopentane-cis-1,3-dicarboxylate

1.28 g (10.5 mmole)of endo,endo-5,6-dimethylbicyclo[2.2.1]-hept-2-ene was oxidized with ozone as described for bicyclo-[2.2.1]heptene to yield 0.90 g (40%) of the diester after refluxing in methanol and a trace of acid. The diester was purified by vpc (15% Carbowax 20 M, 170°).

Dimethyl octahydro-cis-pentalene-trans-1-trans-3-dicarboxylate

8.2 g (55 mmole) of exo-8-ketotricyclo[5.2.1.$0^{2,6}$]decane (Aldrich) was mixed with conc nitric acid (75 ml) and vigorously heated on a steam bath for 3 hours. The mixture was diluted with water (150 ml) and cooled to 0°. 2.4 g (22%) of white, crystalline diacid (mp 173-175°) was obtained. Recrystallization from ethyl acetate-hexane raised the melting point to 180-181° [lit (89) mp 182.5-183°]. The same diacid was obtained by oxidizing the tricyclic ketone with potassium permanganate in the presence of potassium hydroxide. Thus, 7.0 g (47 mmole) of ketone was stirred at room temperature for two days with a solution of 28 g (0.177 mole) of potassium permanganate, 7.0 g (0.125 mole) of potassium hydroxide, and water (700 ml). The reaction mixture was processed in the same manner as described for the oxidation of bicyclo[2.2.1]heptene in water and yielded

2.1 g (23%) of the diacid.

The diacid yielded the dimethyl ester upon refluxing with methanol and a trace of acid. Purification was achieved by vpc (15% Carbowax 20M, 180°): nmr (CCl_4) δ1.57 (multiplet, 6H), 1.7-2.9 (overlapping multiplets, 6H), and 3.62 (s, 6H, $-OCH_3$).

Dimethyl octahydro-cis-pentalene-cis-1-cis-3-dicarboxylate

3.55 g (23.6 mmole) of endo-8-ketotricyclo[5.2.1.$0^{2,6}$]-decane was stirred with 7.5 g (47.5 mmole) of potassium permanganate, 2.0 g (36 mmole) of potassium hydroxide for two days at room temperature. Isolation of the diacid (100 mg, 2.1%) was accomplished as described for the oxidation of bicyclo-[2.2.1]heptene: mp 227-229° [lit (90) mp 231.5-232°]. Refluxing the diacid (100 mg) in methanol and a trace of acid yielded 85 mg (74%) of the dimethyl ester: nmr (CCl_4) δ1.2-2.9 (overlapping multiplets, 12H), and 3.62 (s, 6H, $-OCH_3$); mass spectrum (70 eV) M^+ = 226 major peaks at 195 (M-31), 194 (M-32), 166 (M-60), 155 (M-71), 126 (M-100), and 67 (M-159).

Endo-tricyclo[5.2.1.$0^{2,6}$]dec-3-ene-exo-8-ol and endo-tricyclo-[5.2.1.$0^{2,6}$]dec-3-ene-exo-9-ol

The mixture of alcohols was prepared via the hydroboration reaction. 42 g (0.318 mole) of dicyclopentadiene (bp 70-73°/40 mm), 5.7 g (0.15 mole) of sodium borohydride, and 7.1 g (0.05 mole) of boron trifluoride etherate yielded 13.0 g (27%) of alcohol: bp 103-110° (6 mm); ir (CCl_4) 3680 and 3400 (-OH), and 1053 cm^{-1} (C-O-).

Endo-tricyclo[5.2.1.$0^{2,6}$]decan-exo-8-ol

9.7 g (64.6 mmole) of a mixture of endo-tricyclo[5.2.1.$0^{2,6}$]-dec-3-ene-exo-8-ol and -exo-9-ol, benzene (50 ml), and 0.5 g of 10% palladium on charcoal were stirred under a hydrogen (1 atm) for 36 hours. The mixture was filtered and distilled to yield 8.5 g (86%) of the saturated alcohol which solidified to a waxy solid: bp 94-97° (1 mm), mp 41-42° [lit (90) mp 81.5-82.5°].

The exo configuration is expected from what is known of the course of the hydroboration reaction with bicyclic molecules (91). The low melting point suggests that several percent of the endo isomer is present. Cristol et al. (90) have observed very large cryoscopic constants for both the endo and exo alcohols in that 4.7% of exo alcohol mixed with 95.3% of endo (mp 54°) melts at 41-43° while 8.7% of exo with 91.3% of endo is an oil at room temperature.

Endo-tricyclo[5.2.1.$0^{2,6}$]decan-8-one

3.6 g (0.036 mole) of chromium trioxide was cautiously added in small portions to pyridine (80 ml). A solution of 7.5 g (49.4 mmole) of endo-tricyclo[5.2.1.$0^{2,6}$]decan-8-ol (exo and endo) in pyridine (50 ml) was added and stirred overnight at room temperature. The mixture was poured into 6N hydrochloric acid (200 ml), filtered and ether extracted (5 x 50 ml). The combined ether extracts were dried (Na_2SO_4), filtered, condensed at reduced pressure, and the residual oil distilled to

yield 2.1 g (59%) of a waxy solid possessing a camphor-like odor: bp 110-118° (2 mm), mp 103-104° [lit (92) mp 109-110°]; ir (CCl_4) 1750 cm^{-1} (C=O) [lit (90) 1751 cm^{-1}].

Exo-2-syn-7-dibromobicyclo[2.2.1]heptane

Bicyclo[2.2.1]heptene (163.4 g, 1.74 mole) was brominated with 285 g (1.78 mole) of bromine in carbon tetrachloride-pyridine (930 ml/160 ml) at 0° as described by Kwart and Kaplan (93). Fractionation of the bromides using a 12 inch vacuum-jacketed column topped with a 6 inch vacuum-jacketed distillation head yielded four fractions as follows:

Fraction I	bp 27-80° (4 mm), mono bromides, 50.3 g	
Fraction II	bp 80-100° (4 mm), 2,3 and 2,7 dibromides	93.2 g
Fraction III	bp 100-103° (4 mm), 2,3 and 2,7 dibromides	
Fraction IV	bp 103-107° (4 mm), 2,7 dibromide	161.4 g (47%)

Syn-7-bromobicyclo[2.2.1]hept-2-ene

Syn-7-bromobicyclo[2.2.1]hept-2-ene was prepared in 49% yield by the dehydrobromination of exo-2-syn-7-dibromobicyclo-[2.2.1]heptane with potassium t-butoxide in t-butyl alcohol at 60° for 12 hours as described by Kwart and Kaplan (93). Yields were increased by using a mixture of t-butyl alcohol and dimethyl sulfoxide as the solvent. In a typical preparation 161 g (0.63 mole) of dibromide in dimethyl sulfoxide (220 ml) was rapidly added to a solution of potassium t-butoxide (prepared from 25.7 g; 0.66 g-atom of potassium metal) t-butyl alcohol (500 ml).

After stirring at 60-70° for 12 hours, the mixture yielded 106 g (78%) of syn-7-bromobicyclo[2.2.1]hept-2-ene: bp 85-90° (30 mm) [lit (93) bp 68-70° (13 mm)]; nmr (CCl_4) δ0.7-2.1 (overlapping multiplets, 4H, CH_2-CH_2), 2.95 (multiplet, 2H, C-1,4 bridgehead), 3.8 (multiplet, 1H, =CHBr), and 5.94 (multiplet, 2H, vinyl).

Syn and anti-7-deuterobicyclo[2.2.1]hept-2-ene

Tri-n-butyltin deuteride was prepared according to the procedure of Kuivila and Beumel (94) and reacted with syn or anti-7-bromobicyclo[2.2.1]hept-2-ene as described by Warkentin and Sanford (51). In a typical reaction 7.0 g (21.6 mmole) of tri-n-butyltin chloride (Columbia) was reacted for 3 hours at room temperature under a nitrogen atmosphere with 0.5 g (15.6 mmole) of lithium aluminum deuteride (Metal Hydrides) in diethyl ether (70 ml). The reaction was hydrolyzed with water, the layers separated, the ether layer dried ($MgSO_4$), and condensed at reduced pressure to yield 6.0 g of a colorless oil which was not further purified. A solution of 2.4 g (13.9 mmole) of bromide in hexane (10 ml, washed with conc sulfuric acid) was added and the resulting solution allowed to stand at room temperature under a nitrogen atmosphere. The course of the reaction could be followed via nmr by observing changes in the vinyl resonances of the reaction mixture. After 24 hours the hexane was carefully distilled at atmospheric pressure and the residual 7-deuterobicyclo[2.2.1]heptene collected in a cold trap (-78°) while heating the residue at 150° (1 mm) for one hour.

Pure olefin (~80 mg) was obtained by preparative vpc (20% TCEP, 40°). Later experiments revealed that the hexane distillate contained large quantities of 7-deuterobicyclo[2.2.1]heptene: nmr (CCl_4) δ0.97 (multiplet, 2H), 1.30 (multiplet, 1H), 1.61 (multiplet, 2H), 2.80 (multiplet, 2H), and 5.93 (t, 2H, J = 2 Hz). [lit (49) nmr (CCl_4) δ 0.96 (5,6 endo), 1.06 (7 anti), 1.33 (7 syn), 1.59 (5,6 exo), 2.82 (1,4 bridgehead), and 5.93 (2,3 vinyl)].

Dimethyl cis and trans-2-deutero-cis-1,3-cyclopentanedicarboxylate

Oxidation of pure 7-deuterobicyclo[2.2.1]hept-2-ene (as isolated by vpc), the hexane distillate from the reaction mixture of tri-n-butyltin deuteride and 7-bromobicyclo[2.2.1]hept-2-ene, or of the crude reaction mixture with potassium permanganate in acetone as already described for bicyclo[2.2.1]hept-2-ene yielded 2-deutero-cis-1,3-cyclopentanedicarboxylic acid. Treatment of the diacid with methanol and a trace of acid or with diazomethane in ether yielded the same trans, cis (trans/cis = 4.9) mixture of diesters. Purification was achieved by vpc (15% Carbowax 20 M, 140°).

Anti-7-hydroxybicyclo[2.2.1]hept-2-ene

Anti-7-hydroxybicyclo[2.2.1]hept-2-ene was prepared by the method of Story (95). 12 g (73 mmole) of 7-t-butoxybicyclo-[2.2.1]heptene (Frinton) was mixed with glacial acetic acid (100 ml), acetic anhydride (24 ml), and 17.0g of 70-72% perchloric

acid to yield 11.0 g (94%) of 7-acetoxybicyclo[2.2.1]heptene: bp 70-74° (10 mm); nmr (CCl_4) δ1.84 (s, 3H, $-CH_3$), 3.55 (multiplet, 2H, C-1,4 bridgehead), 4.46 (multiplet, 1H, C<u>H</u>—C), 6.48 (multiplet, 2H), and 6.66 (t, 2H, J = 2 Hz). 10.4 g (69 mmole) of acetate was reduced with 3.7 g (97 mmole) of lithium aluminum hydride in diethyl ether (250 ml). The crude alcohol was shaken for 10 min with pentane (50 ml) and 47-49% hydrobromic acid (100 ml). The layers were separated, the pentane solution washed with water (15 ml), dried ($MgSO_4$), and the pentane removed at reduced pressure to give an oil which was distilled to yield 5.5 g (46%, based on 10.4 g of acetate): bp 63-65° (20 mm); nmr (neat) δ1.04 (multiplet, 2H, C-5,6 <u>endo</u>), 2.04 (multiplet, 2H, C-5,6 <u>exo</u>), 2.75 (multiplet, 2H, C-1,4 bridgehead), 3.74 (multiplet, 1H, C-7), and 6.03 (t, 2H, J = 2.2 Hz, vinyl).

<u>Dimethyl trans-2-deutero-cis-1,3-cyclopentanedicarboxylate</u>

Solvolysis of <u>anti</u>-7-bromobicyclo[2.2.1]hept-2-ene in the presence of sodium borodeuteride in a manner analogous to the reported solvolysis of <u>anti</u>-7-tosyloxybicyclo[2.2.1]hept-2-ene (47,96) and the corresponding <u>anti</u>-7-chloro compound (48) gave only <u>anti</u>-7-deuterobicyclo[2.2.1]hept-2-ene. 3.0 g (17.3 mmole) of <u>anti</u>-7-bromide was mixed with diglyme-D_2O (32 ml, 65% digylme-35% D_2O), 2.0 g (47.8 mmole) sodium borodeuteride (Merck, Sharp and Dohme of Canada Limited), and 0.163 g (4 mmole) of sodium hydroxide and stirred at 50° for 2 hours under a nitrogen atmosphere. The mixture was diluted with water (100 ml), pentane

extracted (3 x 40 ml), the combined pentane extracts were dried ($MgSO_4$), filtered, and mixed with acetone (250 ml). The acetone pentane solution was oxidized with potassium permanganate as already described for bicyclo[2.2.1]hept-2-ene. The crude oxidation product was converted to dimethyl trans-2-deutero-cis-1,3-cyclopentanedicarboxylate by refluxing with methanol and a trace of acid. The diester, 1.15 g (35%, based on 3.0 g of bromide), was purified by vpc (15% Carbowax 20 M, 160°): nmr (CCl_4) δ1.7-2.2 (overlapping multiplets, 4H), 2.4-3.1(multiplet, 1H), and 3.61 (s, 6H, $-OCH_3$).

7,7-Dibromobicyclo[4.1.0]hept-2-ene

22.9 g (0.587 g atom) of potassium was dissolved under nitrogen in t-butyl alcohol (350 ml) and the excess alcohol removed at reduced pressure to yield a white paste. Pentane (300 ml) was added and this mixture cooled to 0°. 35 g (0.438 mole) of 1,3-cyclohexadiene in pentane (100 ml) was added with stirring followed by the slow (5 hours) addition of 100 g (0.392 mole) of bromoform in pentane (70 ml). The mixture was stirred an additional 2 hours after the addition was complete, then diluted with ice water (2000 ml) and the layers separated. The water layer was extracted with pentane (2 x 70 ml). The combined pentane layers were washed with water (1 x 70 ml), dried ($NaSO_4$), filtered, and the pentane removed at reduced pressure to yield an oil which was distilled to give 76.2 g (77%) of the bicyclic dibromide: bp 69-73° (1 mm); nmr (CCl_4) δ2.0 (broad singlet, 6H), and 5.9 (overlapping multiplets, 2H).

Syn-7-bromo-anti-7-methylbicyclo[2.2.1]hept-2-ene

74.6 g (0.296 mole) of 7,7-dibromobicyclo[4.1.0]hept-2-ene and ethyl ether (75 ml) were mixed and cooled to -78° under a nitrogen atmosphere. Methyl lithium in ethyl ether (0.340 mole, i.e., 140 ml of 2.43 M from Alfa Inorganics) was added from a dropping funnel over a 75 min period. The mixture was stirred under nitrogen at -78° for 2 hours, then allowed to warm to ice bath temperature. Water (100 ml) was cautiously added, the layers separated, the ether layer dried (Na_2SO_4), filtered, and the ether removed at reduced pressure to yield an oil which was distilled to yield 42 g (76%) of bicyclic bromide which froze in the condensor of the distillation apparatus but was a liquid at room temperature: bp 75-85° (15 mm); nmr (CCl_4) δ1.02 (multiplet, 2H, C-5,6 endo), 1.71 (s, 3H, $-CH_3$), 1.82 (multiplet, 2H, C-5,6 exo), 2.82 (multiplet, 2H, C-1,4 bridgehead), 6.07 (t, J = 2 Hz, 2H, vinyl).

7-Methylbicyclo[2.2.1]hept-2-ene (syn and anti)

52 g (0.16 mole) of tri-n-butyltin chloride in ethyl ether (30 ml) was added to a solution of 3.0 g (0.079 mole) of lithium aluminum hydride in ether (180 ml). After 2 hours the mixture was hydrolyzed with water (50 ml), the ether decanted, dried (Na_2SO_4), filtered, and removed at reduced pressure to yield an oil which was not further purified. 40.75 g (0.218 mole) of syn-7-bromo-anti-7-methylbicyclo[2.2.1]hept-2-ene was mixed with this oil. The reaction became very exothermic after several minutes. Tri-n-butyltin hydride prepared as described above

from an additional 26 g (0.08 mole) of tri-n-butyltin chloride was added after 15 hours. After a second 15 hour period, the mixture was distilled to yield 19.5 g (83%) of olefin: bp 27-60° (50 mm); nmr (CCl_4) δ0.69 (d, J = 6.9 Hz, $-CH_3$), 0.8 (d, J = 6.2 Hz, $-CH_3$), 0.7-1.9 (overlapping multiplets, 5H), 2.38 (multiplet, 1.1 H, C-1,4 bridgehead of anti isomer), 2.49 (multiplet, 0.9 H, C-1,4 bridgehead of syn isomer), 5.80 (multiplet, 0.9 H, vinyl of syn isomer), and 5.99 (t, J = 2 Hz, 1.1H, vinyl of anti isomer).

Trans-2-methylcyclopentane-cis-1,3-dicarboxylic acid

3.0 g (27.8 mmole) of 7-methylbicyclo[2.2.1]hept-2-ene (syn, anti mixture) was oxidized with potassium permanganate in acetone (250 ml) as described for the oxidation of bicyclo[2.2.1]hept-2-ene to yield 2.75 g (57%) of a mixture of diacids.

606 mg of the diacid mixture was refluxed with 50% sulfuric acid (10 ml) for 8 hours. The solution was extracted with diethyl ether (5 x 10 ml), the combined extracts dried ($MgSO_4$), filtered, and the ether removed at reduced pressure to yield a white solid. The solid was recrystallized from ethyl acetate at -21° to yield 273 mg (45%) of trans diacid: mp 152-153° [lit (97) mp 154-155°].

Dimethyl trans-2-methylcyclopentane-cis-1,3-dicarboxylate

2.75 g (16 mmole) of the mixture of diacids obtained from the oxidation of syn and anti-7-methylbicyclo[2.2.1]hept-2-ene was refluxed for 8 hours with methanol (150 ml) and conc sulfuric

acid (8 drops) to yield 2.40 g (75%) of the trans diester.

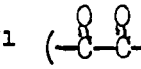
The same procedure using pure trans-2-methylcyclopentane-cis-1,3-dicarboxylic acid yielded the trans diester in 77% yield: ir (neat) 1730 (C=O), 1432 ($-CH_3$), and 1158 cm^{-1} (C—O—C); nmr (CCl_4) δ1.03-1.19 (complex, 3H, $-CH_3$), 1.78-2.50 (overlapping multiplets, 7H), and 3.63 (s, 6H, $-OCH_3$); mass spectrum (20 eV) M^+ = 200, major peaks at 185 (M-15), 169 (M-31), 140 (M-60), 81 (M-119), 75 (m-125), 59 (M-141), and 55 (M-145).

7-Methylbicyclo[2.2.1]heptan-2-one (syn and anti)

The ketone was prepared in a manner analogous to the general procedure described by Brown and Garg (98). 0.9 g (24 mmole) of sodium borohydride, 0.2 g of anhydrous zinc chloride and ethyl ether (30 ml) were stirred under nitrogen for 12 hours. 5.0 g (46.3 mmole) of 7-methylbicyclo[2.2.1]hept-2-ene in ether (10 ml) was added followed by the slow addition (1 hour) of 4.25 g (0.03 mole) of boron trifluoride etherate. After 6 hours the excess diborane was decomposed with water (5 ml) and the mixture oxidized with 11.0 g (36.9 mmole) of sodium dichromate dihydrate in 96% sulfuric acid (8.25 ml, 147.4 mmole) and water (30 ml). This mixture was refluxed for 2 hours, the layers separated, the water ether extracted with diethyl ether (3 x 50 ml), the combined ether solutions were dried ($MgSO_4$), filtered, and the ether removed at reduced pressure to yield an oil which was distilled to yield 2.75 g (48%) of a mixture of syn and anti ketone: bp 95-105° (45 mm); ir (neat) 1740 cm^{-1} (C=O); nmr (CCl_4)

δ1.94 (d, J = 6.6 Hz, $-CH_3$), 1.95 (d, J = 7 Hz, $-CH_3$), and 1.1-2.4 (overlapping multiplets).

Syn-7-methylbicyclo[2.2.1]heptan-2,3-dione (XIV-a)

0.8 g (6.5 mmole) of a mixture of syn and anti-7-methylbicyclo[2.2.1]heptan-2-one, 0.8 g (7.2 mmole) of selenium dioxide, and xylene (10 ml) was vigorously refluxed for 6 hours. The mixture was filtered and the filtrate chromatographed over silica gel using pentane-benzene (7:3, 250 ml), then pentane-chloroform (8:2, 250 ml), and finally methanol as eluants. A 70 ml fraction of the methanol eluant containing the yellow α-diketone was condensed to 10 ml at reduced pressure, diluted with pentane (50 ml) and water (50 ml). The layers were separated, the pentane layer dried ($MgSO_4$), filtered, and condensed to a yellow oil at reduced pressure. The oil solidified upon standing and cooling to -21°. The solid was recrystallized from benzene-hexane (1:1) to yield 118 mg (26%) of α-diketone: mp 73-74°; ir (KBr) 1778 and 1754 cm^{-1} (); nmr ($CDCl_3$) δ1.10 (d, 3H, J = 7.5 Hz, $-CH_3$), 1.5-2.8 (overlapping multiplets, 5H), and 2.89 (multiplet, 2H, C-1,4 bridgehead); mass spectrum (70 eV) M^+ = 138, major peak at 110 (M-28), 89 (M-49), 82 (M-56), 67 (M-71), and 55 (M-83).

Anal. Calcd for $C_8H_{10}O_2$: C, 69.55; H, 7.30. Found (Ilse Beetz): C, 69.48; H, 7.26.

7-Carbomethoxybicyclo[2.2.1]hept-2-ene (syn and anti)

100 g (0.532 mole) of ethylene bromide was added over a 5 hour period to a mixture of 53.2g (0.308 mole) of syn-7-bromo-

bicyclo[2.2.1]hept-2-ene, 20.2 g (0.84 g-atom), of magnesium, and ethyl ether (450 ml). The mixture was stirred at room temperature under a nitrogen atmosphere for 5 days. Dry carbon dioxide gas was then vigorously bubbled through the mixture for one hour. This mixture was hydrolyzed with 6N hydrochloric acid (300 ml), ether extracted, the combined ether extracts were dried (Na_2SO_4), filtered, and condensed at reduced pressure to yield 29.6 g (44%) of crude acid. The crude acid (29.6 g) was converted to the methyl ester by refluxing in methanol (150 ml) and sulfuric acid (2 ml) to give 21.7 g (67%) of ester: bp 68-75° (5 mm) [lit (99) *syn* 95.5° (25 mm); *anti* 93-93.5° (30 mm)] nmr (CCl_4) δ *anti isomer* 0.96 (multiplet, 2H, C-5,6 *endo*), 1.81 (multiplet, 2H, C-5,6 *exo*), 2.31 (multiplet, 1H, *syn* C-7), 2.98 (multiplet, 2H, C-1,4 bridgehead), 3.57 (s, 3H, $-OCH_3$), and 6.01 (t, 2H, J = 2Hz, vinyl); *syn isomer*, 1.01 (multiplet, 2H, C-5,6 *endo*), 1.75 (multiplet, 2H, C-5,6 *exo*), 2.29 (multiplet, 1H, *anti* C-7), 3.11 (multiplet, 2H, C-1,4 bridgehead), 3.51 (s, 3H, $-OCH_3$), and 5.93 (t, 2H, J = 1.8 Hz, vinyl).

7-α,α-Dideuteromethanolbicyclo[2.2.1]hept-2-ene (syn and anti)

8.0 g (52 mmole) of 7-carbomethoxybicyclo[2.2.1]hept-2-ene (~1:1 *syn*/*anti* mixture) in diethyl ether was added over a one hour period to a solution of 1.3 g (31.8 mmole) of lithium aluminum deuteride in ether (90 ml). The mixture was refluxed 2 hours, hydrolyzed with saturated ammonium chloride, the ether decanted, dried ($MgSO_4$), and removed at reduced pressure to yield 6.05 g (91%) of crude alcohol: nmr (CCl_4) δ0.77-1.96 (overlapping

multiplets, 2H, C-1,4 bridgehead), 3.97 (broad singlet, 1H, -OH, removed by added D_2O), 5.84 (t, J = 1.9 Hz, 0.9 H, vinyl of syn isomer), and 6.06 (t, J = 2Hz, 1.1H, vinyl of anti isomer).

7-α,α-Dideuteromethanolbicyclo[2.2.1]hept-2-ene tosylate

6.05 g (48 mmole) of 7-α,α-dideuteromethanolbicyclo[2.2.1]-hept-2-ene was reacted with 10.0 g (53 mmole) of p-toluene-sulfonyl chloride in pyridine (35 ml) at 0° for 24 hours. This mixture yielded 10.9 g (75%) of tosylate upon dilution with 6N hydrochloric acid (200 ml): mp 45-48° [lit (99) syn mp 38.5-39.5°; anti mp 60-61°]; nmr ($CDCl_3$) δ1.73-1.97 (overlapping multiplets, 5H), 2.44 (s, 3H, Ar-CH_3), 2.66 (overlapping multi-plets, 2H, C-1,4 bridgehead), 5.76 (t, J = 1.6 Hz, 0.9 H, vinyl of syn isomer), 6.02 (t, J = 2 Hz, 1.1 H, vinyl of anti isomer), 7.33 (d, J = 8.5 Hz, 2H, m-aromatic), and 7.77 (d, J = 8.5 Hz, 2H, o-aromatic).

7-Trideuteromethylbicyclo[2.2.1]hept-2-ene

10.9 g (0.039 mole) of 7-α,α-dideuteromethanolbicyclo[2.2.1]-hept-2-ene tosylate in ethyl ether (60 ml) was added over a 0.5 hour period to a solution of 0.7 g (16.7 mmole) of lithium aluminum deuteride in ether (140 ml). The mixture was refluxed 2 days, hydrolyzed with saturated sodium chloride solution, the ether decanted, dried ($MgSO_4$), filtered, and the ether carefully removed at reduced pressure. The olefin was collected in a cold trap (-78°) while heating the residue at 100° (1 mm): nmr (CCl_4) δ0.7-1.3 (overlapping multiplets, 2H, C-5,6 endo), 1.43-1.83 (overlapping multiplets, 3H, C-5,6 exo and C-7), 2.38 (multiplet,

1.2 H C-1,4 bridgehead of anti isomer), 2.50 (multiplet, 0.8 H, C-1,4 bridgehead of syn isomer), 5.79 (multiplet, 0.8 H, vinyl of syn isomer), and 5.98 (t, J = 2 Hz, 1.2 H, vinyl of anti isomer).

2-Trideuteromethylcyclopentane-cis-1,3-dicarboxylic acid

All of the crude 7-trideuterome hylbicyclo[2.2.1]hept-2-ene was oxidized with potassium permanganate in acetone as described for the oxidation of bicyclo[2.2.1]hept-2-ene to yield 0.76 g of white, crystalline diacid: mp 137-142°.

Dimethyl trans-2-trideuteromethylcyclopentane-cis-1,3-dicarboxylate

0.76 g (43.5 mmole) of 2-trideuteromethylcyclopentane-cis-1,3-dicarboxylic acid was refluxed 15 hours with methanol (40 ml) and conc sulfuric acid (8 drops) to yield 0.62 g (70%) of diester: ir (neat) 2210 (C-D), 1728 (C=O), 1436 ($-CH_3$), and 1154 cm^{-1} (C—O—C); nmr (CCl_4) δ1.8-2.5 (overlapping multiplets, 7H), and 3.64 (s, 6H, $-OCH_3$); mass spectrum (70 eV) M^+ = 203, major peaks at 185 (M-15), 172 (M-31), 143 (M-60), 84 (M-119), 83 (M-118), 72 (M-131), 59 (M-144), and 55 (M-148).

Tetrachloroethylene carbonate

30 g of ethylene carbonate (Aldrich) was stirred with carbon tetrachloride (400 ml) and benzoylperoxide (0.5 g). The mixture was irradiated with two sun lamps while the mixture was kept saturated with a stream of chlorine gas. After 14 hours, the mixture possessed no visible nmr resonances and was condensed

at reduced pressure to yield 65.5 g (85%) of tetrachloroethylene carbonate.

Dichlorovinylene carbonate

55 g (0.24 mole) of tetrachloroethylene carbonate in diethyl ether (100 ml) was stirred for 24 hours with 30 g (~0.46 g-atom) of zinc-copper couple (prepared by mixing 30 g zinc and 0.8 g of copper(II) acetate in hot glacial acetic acid followed by diethyl ether wash) and dimethyl formamide (5 ml). The ether was decanted, rapidly washed with water (20 ml), dried ($MgSO_4$), and the ether removed at reduced pressure. The residual oil was distilled at reduced pressure to yield 34.5 g (90%) of carbonate: bp 65-70° (35 mm).

Exo, exo-5,6-dichlorobicyclo[2.2.1]hept-2-ene-endo, endo-5,6-carbonate (XXII)

5.0 g (32 mmole) of dichlorovinylene carbonate and 6.6 g (100 mmole) of cyclopentadiene were refluxed for 24 hours. Evaporation of the reaction in a crystallization dish yielded 1.2 g of a black solid from which 0.72 g (10%) of adduct sublimed (50°, 10 mm): mp 146-147° [lit(100) mp 147°]; nmr (CCl_4) δ2.04 (t, J = 1.8 Hz, 2H, C-7), 3.49 (quintet, 2H, C-1,4 bridgehead), and 6.22 (t, J = 2.1 Hz, 2H, vinyl).

Bicyclo[2.2.1]hept-5-ene-2,3-dione (XXIII)

Hydrolysis of exo, exo-5,6-dichlorobicyclo[2.2.1]hept-2-ene-endo, endo-5,6-carbonate (0.72 g) in water (40 ml) and potassium hydroxide (0.54 g) for 24 hours at room temperature yielded the α-diketone. The crude α-diketone was isolated by continuous

ether extraction of the hydrolysis mixture. Evaporation of the ether yielded a yellow solid that was shown by nmr to be a complex mixture of products. No suitable purification procedure was found.

Bicyclo[2.2.1]hept-5-ene-2-one (XXVI)

0.3 g (31%) of the unsaturated ketone was obtained by distillation of a mixture of bicyclo[2.2.1]hept-5-ene-2-ol (endo and exo mixture, Aldrich) (1.0 g), aluminum isopropoxide (1.2 g) and benzophenone (3.6 g) as described by Toivonen and Kaila (77).

3-Bromo-2-nitrosobicyclo[2.2.1]hept-5-ene

A mixture of bicyclo[2.2.1]heptadiene (20 g), glacial acetic acid (40 ml), 95% ethyl alcohol (40 ml), and n-butyl nitrite (36 g) were stirred at 0° while a mixture of 48% hydrobromic acid (40 g) and 95% ethyl alcohol (100 ml) was added over a 10 min period. The white adduct was collected by suction filtration and air dried to yield 13.7 g (57%) of product: mp 151-152°.

3-Bromobicyclo[2.2.1]hept-5-ene-2-one (XXVII)

13.7 g of 3-bromo-2-nitrosobicyclo[2.2.1]hept-5-ene was mixed with levulinic acid (300 g) and 2 N hydrochloric acid (25 ml) and heated for 4 hours at 75°. The dark mixture was diluted with water (1000 ml) and extracted with diethyl ether (3 x 100 ml). The combined ether extracts were washed with 5% sodium bicarbonate solution until neutral, dried ($MgSO_4$), and condensed at reduced pressure to yield a dark mass. About 0.1 g

of ketone was obtained by distillation of the dark material at 80-100° (1 mm).

5,8-Diacetoxybenzobicyclo[2.2.1]heptadiene

22.4 g (0.12 mole) of the Diels-Alder adduct of p-benzoquinone and cyclopentadiene [(101) (mp 71-72°)] was mixed with 52.6 g (0.51 mole) acetic anhydride and glacial acetic acid (35 ml). Concentrated hydrochloric acid (50 drops, ~2.5 ml) was added and the mixture was allowed to stand at room temperature for 24 hours. Water (300 ml) was added. The white crystals that formed upon cooling to 0° were collected by suction filtration and recrystallized from hexane to yield 9.6 g (28%) of diacetate: mp 102-103° [lit(101) mp 105-106°].

5,8-Dimethoxybenzobicyclo[2.2.1]heptadiene

10.0 g (39 mmole) of 5,8-diacetoxybenzobicyclo[2.2.1]heptadiene, water (200 ml), sodium hydroxide (28 g, 0.7 mole) were stirred under a nitrogen atmosphere while 35 g (0.28 mole) of dimethyl sulfate was added over a 1.5 hour period. After 4 additional hours, the solid that had formed was taken up in diethyl ether, dried ($MgSO_4$), and the ether removed at reduced pressure to yield a solid (5.0 g, 64%) which was recrystallized from hexane: mp 74-75° [lit (102) mp 78.5-79°].

5,8-Dimethoxybenzobicyclo[2.2.1]heptene-2-one (XXX)

10 g (49 mmole) of 5,8-dimethoxybenzobicyclo[2.2.1]heptadiene was converted to the alcohol by the hydroboration reaction using 2.0 g (52 mmole) of sodium borohydride and 7.2 g (53 mmole) of boron trifluoride etherate and oxidizing with 30% hydrogen

peroxide (12 ml). The crude alcohol (9.8 g, 90%) was mixed with 8.25 g (82.5 mmole) of chromium trioxide in pyridine (50 ml). After 20 hours, the mixture was diluted with 5% hydrochloric acid (200 ml) and extracted with ethyl ether (3 x 60 ml). The combined ether extracts were washed with 5% hydrochloric acid (20 ml), water (20 ml), dried ($MgSO_4$), filtered, and condensed at reduced pressure to yield 6.8 g (64% overall) of ketone: mp 92-93°; ir (CCl_4) 1730 cm^{-1} (C=O); nmr ($CDCl_3$) δ1.50-2.66 (overlapping multiplets, 2H, C-2,7), 3.8 (multiplet, 2H, C-1,4 bridgehead), 3.73 and 3.76 (s, 6H, $-OCH_3$), and 6.60 (s, 2H, aromatic).

Benzobicyclo[2.2.1]heptadiene

A mixture of 25 g (0.143 mole, Aldrich) of 2-bromofluorobenzene, cyclopentadiene (10 g, 0.16 mole) and tetrahydrofuran (90 ml, distilled from lithium aluminum hydride) was slowly dropped into a refluxing mixture of 4.5 g (0.19 g-atom) of magnesium and tetrahydrofuran (10 ml) under nitrogen. After refluxing for 30 min, the mixture was poured into saturated ammonium chloride solution (300 ml) and the olefin extracted with ethyl ether (3 x 70 ml). The combined ether extracts were washed with water (50 ml), dried (Na_2SO_4), and distilled to yield 13.4 g (66%) of olefin: bp 69-70° (8 mm) [lit(103) bp 82.5-83.0 (12 mm)]; nmr (CCl_4 δ2.19 (multiplet, 2H, C-7), 3.73 (multiplet, 2H, C-1,4 bridgehead), and 6.5-7.2 (multiplet, 4H, aromatic).

Benzobicyclo[2.2.1]heptene-2-ol

13.0 g (91 mmole) of benzobicyclo[2.2.1]heptadiene was converted to the -2-ol *via* hydroboration using 2.1 g (55 mmole) of sodium borohydride, 8.0 g (58 mmole) of boron trifluoride etherate in diglyme (40 ml) and oxidizing with 30% hydrogen peroxide (15 ml) to yield 11.4 g (78%) of alcohol: mp 67-69° [lit (104) mp 74.1-75.4°].

Benzobicyclo[2.2.1]heptene-2-one (XXIX)

7.0 g (44 mmole) of benzobicyclo[2.2.1]heptene-2-ol was stirred for 9 hours with a mixture of 3.3 g (33 mmole) of chromium trioxide, glacial acetic acid (15 ml) and water (5 ml). This mixture was diluted with water (200 ml), ethyl ether extracted (4 x 50 ml) and the combined ether extracts were washed until neutral with 5% sodium bicarbonate solution, dried (Na_2SO_4), and condensed at reduced pressure to yield an oil, which was purified by column chromatography over silica gel to yield 4.10 g (59%) of ketone: ir ($CHCl_3$) 1748 cm^{-1} (C=O).

o-Deutero-t-butyl alcohol

50 g of t-butyl alcohol was mixed with 65 g of deuterium oxide in a separatory funnel. The solution was saturated with sodium chloride and the layers separated. The t-butyl alcohol and 25 g of deuterium oxide was treated in the same manner and finally with a third 25 g portion of deuterium oxide. The t-butyl alcohol was dried over calcium hydride and distilled to give 41.2 g of anhydrous o-deuterated t-butyl alcohol (96.6% deuterium incorporation by nmr).

5,5-Dimethoxy-1,2,3,4-tetrachlorocyclopentadiene

A solution of 112 g (2 mole) of potassium hydroxide in methanol (500 ml) was added over a 4 hour period to a mixture of 210 g (0.77 mole) of hexachlorocyclopentadiene in methanol (200 ml). The majority of the methanol was removed at reduced pressure, the residue washed with water, dried (Na_2SO_4), filtered, and distilled to yield 186 g (92%) of the diene: bp 97-105° (4 mm), [lit(105) bp 108-110° (11 mm)].

7,7-Dimethoxy-1,2,3,4-tetrachlorobicyclo[2.2.1]hept-2-ene

A mixture of ethylene and nitrogen (1:1) was bubbled into 20.7 g of 5,5-dimethoxy-1,2,3,4-tetrachlorocyclopentadiene at 190°. Distillation of the reaction mixture yielded 12.0 g (52%) of adduct: bp 99-104° (2 mm) [lit (106) bp 72-81° (0.1 mm)]; nmr (CCl_4) δ1.5-2.5 (overlapping multiplet, 4H, CH_2CH_2) and 3.50 and 3.58 (s, 6H, $-OCH_3$).

1,2,3,4-Tetradeutero-7,7-dimethoxybicyclo[2.2.1]hept-2-ene

A mixture of 11.9 g (40 mmole) of 7,7-dimethoxy-1,2,3,4-tetrachlorobicyclo[2.2.1]hept-2-ene, 19.1 g (0.83 g-atom) of finely divided sodium metal, 31.9 g of O-deuterated t-butyl alcohol, and tetrahydrofuran (140 ml) were rapidly stirred and gently refluxed under nitrogen for 10 hours. The excess sodium was destroyed with methanol. The mixture was diluted with water (500 ml) and extracted with diethyl ether (5 x 50 ml). The combined ether extracts were dried (Na_2SO_4), filtered, and distilled to yield 2.2 g (34%) of dechlorinated product: bp 75-80°

(40 mm) [lit (106) bp 74-78° (30 mm)]; nmr (CCl_4) δ0.7-1.0 (multiplet, 2H, C-5,6 endo), 1.7-2.0 (multiplet, 2H, C-5,6 exo), and 3.01 and 3.10 (s, 6H, $-OCH_3$).

1,4-Dideutero-7,7-dimethoxybicyclo[2.2.1]heptan-2-one (XXI-a)

2.2 g (14 mmole) of 1,2,3,4-tetradeutero-7,7-dimethoxybicyclo[2.2.1]hept-2-ene was converted to the -2-ol via hydroboration using 0.9 g (23 mmole) of sodium borohydride, 2.0 g (14 mmole) of boron trifluoride etherate in tetrahydrofuran (45 ml) and oxidizing with 30% hydrogen peroxide (10 ml) to yield 1.76 g (71%) of alcohol, which was not further purified. The crude alcohol was oxidized with 0.67 g (6.7 mmole) of chromium trioxide in pyridine (20 ml) to yield 0.3 g (17%) of ketone as an oil: [lit (107) mp 33-35°]; nmr (CCl_4) δ0.8-2.0 (overlapping multiplets, 6H) and 3.20 and 3.23 (s, 6H, $-OCH_3$).

1,2,3,4-Tetrachloro-5,8-diacetoxy-9,9-dimethoxybenzobicyclo-[2.2.1]heptadiene

18 g of the Diels-Alder adduct (mp 160-161°)of 5,5-dimethoxy-1,2,3,4-tetrachlorocyclopentadiene and p-benzoquinone, acetic anhydride (20 ml), glacial acetic acid (10 ml), and conc hydrochloric acid (5 ml) were heated on a steambath for 12 hours. The mixture was poured into ice-water (200 ml) and the solid that formed was collected by suction filtration: nmr (CCl_4)δ2.20 (s, 6H, $-CH_3$), 3.36 (s, 3H, $-OCH_3$), 3.57 (s, 3H, $-OCH_3$), and 6.88 (s, 2H, aromatic).

1,2,3,4-Tetrachloro-5,8,9,9-tetramethoxybenzobicyclo[2.2.1]-heptadiene

17.7 g (38 mmole) of 1,2,3,4-tetrachloro-5,8-diacetoxy-9,9-dimethoxybenzobicyclo[2.2.1]heptadiene, 16 g (400 mmole) of sodium hydroxide, and 12.6 g (100 mmole) of dimethylsulfate stirred together under nitrogen in water (200 ml) yielded 8.7 g (56%) of tetramethoxy compound: mp 148-149°; nmr (CCl_4) δ3.45 (s, 3H, $-OCH_3$), 3.63 (s, 3H, $-OCH_3$), 3.75 (s, 6H, aromatic-CH_3), and 6.73 (s, 2H, aromatic).

5,8,9,9-Tetramethoxybenzobicyclo[2.2.1]heptadiene

9.3 g (23.4 mmole) of 1,2,3,4-tetrachloro-5,8,9,9-tetramrthoxy-benzobicyclo[2.2.1]heptadiene, 20 g (270 mmole) of t-butyl alcohol, 13 g (0.56 g-atom) of finely divided sodium metal, and tetrahydrofuran (100 ml) was vigorously stirred and refluxed under nitrogen for 8 hours. The excess sodium was destroyed with methanol. Water (300 ml) was added and the olefin isolated by ether extraction to yield 1.2 g (20%): mp 89-90° (from hexane); nmr (CCl_4) δ2.93 (s, 3H, $-OCH_3$), 3.09 (s, 3H, $-OCH_3$), 3.65 (s, 3H, aromatic $-OCH_3$), 4.10 (t, J = 2.4 Hz, 2H, C-1,4 bridgehead), 6.37 (s, 2H, aromatic), and 6.57 (t, J = 214 Hz, 2H, vinyl).

Anal. Calcd for $C_{15}H_{18}O_4$: C, 68.68; H, 6.92. Found (Spang): C, 68.78; H, 6.79.

5,8,9,9-Tetramethoxybenzobicyclo[2.2.1]hepten-2-ol

900 mg of 5,8,9,9-Tetramethoxybenzobicyclo[2.2.1]hepta-diene, 100 mg of sodium borohydride, 130 mg of boron trifluoride etherate, and diglyme (20 ml) were reacted and oxidized with 30%

hydrogen peroxide (7 ml) to yield 930 mg (96%) of alcohol: mp 109-110°; nmr ($CDCl_3$) δ0.66 and 0.87 (d of d, J = 21, 2.8 Hz, 1H, endo C-3), 2.2-2.7 (multiplet, 1H), 3.0 (s, 3H, $-OCH_3$), 3.2 (s, 3H, $-OCH_3$), 3.36-3.54 (overlapping multiplets, 2H), 3.71 (s, 6H, aromatic $-OCH_3$), 3.6-3.8 (overlapping multiplet, 2H) and 6.58 (s, 2H, aromatic).

5,8,9,9-Tetramethoxybenzobicyclo[2.2.1]hepten-2-one (XXXII-a)

900 mg of 5,8,9,9-Tetramethoxybenzobicyclo[2.2.1]hepten-2-ol was oxidized for 12 hours with 250 mg of chromium trioxide in pyridine (10 ml) to yield 558 mg (63%) of ketone: mp 124-125°; nmr ($CDCl_3$) δ1.84 (d, J = 28 Hz, 1H, C-3 endo), 2.52 (complex d, J = 28 Hz, 1H, C-3 exo), 3.10 (s, 3H, $-OCH_3$), 3.28 (s, 3H, $-OCH_3$), 3.74 (s, 6H, aromatic $-OCH_3$), 3.84 (multiplet, 2H, C-1,4 bridgehead), and 6.60 (s, 2H, aromatic).

Endo, endo-5,6-dimethylbicyclo[2.2.2]octan-2,3-dione (XXXVII-b)

476 mg (28.7 mmole) of endo, endo-5,6-dimethylbicyclo[2.2.2]-octan-2-one, 400 mg of selenium dioxide, and xylene (4 ml) were mixed and vigorously refluxed for 4 hours. The mixture was filtered and the xylene evaporated in the open air to yield an orange-yellow residue which was crystallized from carbon tetrachloride-pentane (1:1) yielding yellow crystals (mp 82-84°). These crystals were further purified by sublimation at 70° (2 mm): mp 86-87°; ir ($CHCl_3$) 1726 and 1691 cm^{-1} (); nmr (CCl_4) δ0.88 (d, 6H, J = 6.4 Hz, $-CH_3$), 1.97 (multiplet, 4H, $-CH_2-CH_2-$), and 2.46 (overlapping multiplets, 4H, C-1,4 bridgehead, C-5,6-exo); mass spectrum (70 eV) M^+ = 166, prominent peaks at 138

(M-28), 110 (M-56), 95 (M-71), 81 (M-85), and 56 (M-110).

Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found(Spang): C, 72.29; H, 8.48.

Endo-1,4,11,12-tetrahydro-1,4-ethanonaphthalene-5,8-dione

Endo-1,4,11,12-tetrahydro-1,4-ethanonaphthalene-5,8-dione was prepared as described by Diels and Alder (108). 37.5 g (0.47 mole) of 1,3-cyclohexadiene, 48.6 g (0.45 mole) of p-benzoquinone, and benzene (150 ml) were mixed and allowed to stand at room temperature for 4 days. Removal of the benzene yielded a solid which was recrystallized from hexane to yield 72.6 g (86%) of the yellow adduct: mp 93-95° [lit (108) 98°]; nmr (CCl_4) δ1.55 (multiplet, 4H, $-CH_2CH_2-$), 292 (multiplet, 2H, C-11,12 exo), 3.19 (multiplet, 2H, C-1,4 bridgehead), 6.19 (multiplet, 2H, C-2,3 vinyl), and 6.53 (s, 2H, C-6,7 vinyl).

5,8-Dihydroxybenzobicyclo[2.2.2]octadiene

The title compound was prepared similar to the procedure described by Diels and Alder (108). 33.6 g (0.179 mole) of endo-1,4,11,12-tetrahydro-1,4-ethanonaphthalene-5,8-dione, glacial acetic acid (50 ml), and 38% hydrochloric acid (1 ml) were mixed and warmed on a steam bath for 15 minutes and then allowed to stand at room temperature for 6 hours. Water (100 ml)was added,the precipitated solid filtered and recrystallized from glacial acetic acid to yield 30.2 g (93%) of diol: mp 175-177° [lit (108) mp 178°].

5,8-Dihydroxybenzobicyclo[2.2.2]octene

100 mg of 5,8-dihydroxybenzobicyclo[2.2.2]octadiene, 15 ml of benzene, and 50 mg of 10% palladium on powdered charcoal were mixed and stirred under hydrogen (1 atm) for 10 hours. The mixture was filtered and the benzene removed at reduced pressure to yield 94 mg (93%) of reduced diol: mp 204-206° [lit (109) mp 201-206°].

5,8-Dimethoxybenzobicyclo[2.2.2]octadiene

44 g (1 mole) of sodium hydroxide was dissolved in water (250 ml) and the solution degassed with nitrogen (prepurified) for 20 minutes. 33.1 g (176 mmole) of 5,8-dihydroxybenzobicyclo[2.2.2]octadiene was added, the solution cooled to 0°, 139 g (1.1 mole) of dimethyl sulfate (Mallinckrodt) added over a 25 min period, and stirred for 4 hours. The mixture was now acidic. An additional 25 g (0.62 mole) of sodium hydroxide followed by 70 g (0.55 mole) of dimethyl sulfate was added. The mixture was stirred for one hour, an additional 20 g (0.5 mole) of sodium hydroxide added and stirring continued for 4 hours. The solid that had formed was taken up in diethyl ether, the ether solution dried (Na_2SO_4), condensed at reduced pressure to an oil and the oil was mixed with an equal volume of hexane. 31.6 g (75%) of the dimethoxy olefin was collected from this solution upon cooling to -10°: mp 56-57°; nmr ($CDCl_3$) δ1.45 (multiplet, 4H, $-CH_2CH_2-$), 3.77 (s, 6H, $-OCH_3$), 4.42 (multiplet, 2H, C-1,4 bridgehead), 6.50 (multiplet, 2H, vinyl), and 6.58

(s, 2H, aromatic H).

5,8-Dimethoxybenzobicyclo[2.2.2]octen-2-ol (exo and endo)

The title compound was prepared *via* the hydroboration reaction. Thus, a solution of 10.5 g (70 mmole) of boron trifluoride etherate in diglyme (15 ml) was added over a 2 hour period to a solution of 20 g (93 mmole) of 5,8-dimethoxybenzobicyclo[2.2.2]octadiene, 2.6 g (68 mmole) of sodium borohydride, and diglyme (55 ml) at 0°. After one hour, water (8 ml) was added followed by 3 M sodium hydroxide (20 ml), then 40% hydrogen peroxide (20 ml). Dilution with water (600 ml) yielded 21 g (97%) of alcohol: mp 85-87°; ir (CCl_4) 3620 (-OH), 1252 (=C-O-C), and 1032 cm^{-1} (C-O); nmr (CCl_4) δ0.7-2.3 (overlapping multiplets, 7H, one hydrogen removed by added D_2O), 3.44 (overlapping multiplets, 2H, C-1,4 bridgehead), 3.4-4.1 (overlapping multiplets, 1H, =C<u>H</u>-O), 3.66 and 3.68 (s, 6H, $-OCH_3$ of two isomeric alcohols), and 6.49 and 6.51 (s, 2H, aromatic H's of two isomeric alcohols).

Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found (Spang): C, 71.53; H, 7.88.

5,8-Dimethoxybenzobicyclo[2.2.2]octen-2-one (XLVIII-a)

A solution of 0.7 g (3.0 mmole) of 5,8-dimethoxybenzobicyclo[2.2.2]octen-2-ol (exo and endo mixture) and pyridine (10 ml) was added to a mixture of 0.8 g of chromium trioxide in pyridine (15 ml). After 15 hours at 27° the mixture was poured into water (300 ml) and the ketone extracted with pentane (3 x

15 ml). Removal of the pentane at reduced pressure yielded a solid which was sublimed at 80° (4 mm) to yield 0.6 g (86%) of white, crystalline ketone: mp 84.5-86°; mp of 2,4-dinitrophenylhydrazone 187-188°; ir (CCl_4) 1729 (C=O), and 1253 cm^{-1} (=C–O–C); nmr (CCl_4) δ1.3-2.0 (overlapping multiplets, 4H, CH_2CH_2), 2.04 (t, 2H, J = 2.2 Hz, $CH_2\overset{O}{C}$), 3.70 (s, 6H, $-OCH_3$), 3.7-4.0 (overlapping multiplets, 2H, C-1,4 bridgehead), and 6.57 (s, 2H, aromatic H's).

Anal. Calcd for $C_{14}H_{18}O_3$: C, 72.39; H, 6.94. Found (Spang): C, 72.21; H, 6.83.

5,8-Dimethoxybenzobicyclo[2.2.2]octen-2,3-dione

2.0 g (8.6 mmole) of 5,8-dimethoxybenzobicyclo[2.2.2]octen-2-one, 1.0 g of selenium dioxide, and xylene (15 ml) were mixed and vigorously refluxed for 4 hours. The mixture was filtered while hot. The filtrate deposited 1.69 g (79%) of the diketone (mp 205-208°) upon cooling. Further purification was achieved by sublimation at 140° (2 mm) to give a solid (mp 210-211°) which was recrystallized from benzene yielding the pure diketone mp 211-212°; ir ($CHCl_3$) 1753 and 1736 cm^{-1} ($-\overset{O}{\overset{\|}{C}}-\overset{O}{\overset{\|}{C}}-$); nmr ($CDCl_3$) δ1.8-2.4 (overlapping multiplets, 4H, $-CH_2-CH_2-$), 3.78 (s, 6H, $-OCH_3$), 4.40 (t, 2H, C-1,4 bridgehead), and 6.80 (s,2H,aromatic H's); mass spectrum (70 eV) M^+ = 246, major peaks at 190 (M-56), 175 (M-71), 159 (M-87), 147 (M-99), 131 (M-115), 115 (M-131), 103 (M-143), small peak at 218 (M-28).

Anal. Calcd for $C_{14}H_{14}O_4$: C, 68.28; H, 5.73. Found(Spang): C, 68.10; H, 5.89. Found (Schwarzkopf): C, 68.09; H, 6.00.

1,4-Dideutero-5,8-dimethoxybenzobicyclo[2.2.2]octen-2,3-dione

1,4-Dideutero-5,8-dimethoxybenzobicyclo[2.2.2]octen-2,3-dione was prepared starting with 1,4-dideutero-1,3-cyclohexadiene and p-benzoquinone using the same series of reactions already described for the undeuterated dione. 1,4-Dideutero-1,3-cyclohexadiene was prepared by the method of Franzus (110) but without isolation of purified intermediates. Thus, 5.0 g (45 mmole) of 1,4-cyclohexadione (Aldrich) in tetrahydrofuran (60 ml) was reacted with 1.1 g (29 mmole) of lithium aluminum deuteride (Metal Hydrides) in tetrahydrofuran (20 ml). After 3 hours diethyl ether (80 ml) was added and the reaction hydrolyzed with saturated ammonium chloride solution, the ether decanted, dried (Na_2SO_4), and removed at reduced pressure to yield 4.5 g (85%) of the diol: ir (neat) 3610 and 3430 (-OH), and 2115 cm^{-1} (C-D). The diol (4.5 g) was dissolved in pyridine (50 ml) and reacted at 0° with 16.5 g of p-toluenesulfonyl chloride. After 48 hours at room temperature the pyridine solution was poured into 2N hydrochloric acid (400 ml) at 0°. The ditosylate (11.9 g, 73%) was isolated by suction filtraction and recrystallized from ethanol-water to give white plates: mp 145-147°. A mixture of the ditosylate (11.9 g), sodium hydroxide (2.5 g), and n-propyl alcohol (75 ml) was heated to reflux and 70 ml of distillate (bp <97°) collected. 1.5 g of p-benzoquinone was dissolved in the distillate. After 3 days at room temperature it was poured into water (400 ml) and the adduct (1.57 g, mp 85-87°) was

isolated by suction filtration and air dried: nmr ($CDCl_3$) δ1.55 (multiplet, 4H, $-CH_2CH_2-$), 3.0 (s, 2H, C-11,12 exo), 6.20 (s, 2H, C-2,3 vinyl), and 6.64 (s, 2H, C-6,7 vinyl). The adduct (1.57 g) isomerized to 1,4-dideutero-5,8-dihydroxybenzobicyclo[2.2.2]-octadiene in glacial acetic acid (5 ml) and concentrated hydrochloric acid (3 drops). The diol was converted with dimethyl sulfate to 1,4-dideutero-5,8-dimethoxybenzobicyclo[2.2.2]octadiene: nmr (CCl_4) δ1.38 (multiplet, 4H, $-CH_2CH_2-$), 3.63 (s, 6H, $-OCH_3$), and 6.39 (s, 2H, aromatic). Hydroboration using 0.3 g of sodium borohydride, 0.4 g of borontrifluoride etherate, and 5 ml of 30% hydrogen peroxide yielded the alcohol which yielded 1.37 g of 1,4-dideutero-5,8-dimethoxybenzobicyclo[2.2.2]octen-2-one upon oxidation with chromium trioxide (1.75 g) in pyridine (40 ml). 0.7 g (3.0 mmole) of ketone reacted with selenium dioxide (0.5 g, 4.4 mmole) in xylene (5 ml) to yield 0.37 g (50%) of the α-diketone: mp 211-212°; ir ($CHCl_3$) 2195 (C-D), and 1758 and 1730 cm^{-1} ($-\overset{O}{\overset{\|}{C}}-\overset{O}{\overset{\|}{C}}-$); nmr ($CDCl_3$) δ2.05 (multiplet, 4H, $-CH_2CH_2-$), 3.79 (s, 6H, $-OCH_3$), and 6.80 (s, 2H, aromatic H's); mass spectrum (70 eV) $M^+ = 248$, major peaks at 192 (M-56), 177 (M-71), 161 (M-87), 149 (M-99), 133 (M-115), 117 (M-131), 105 (M-143), small peak at 220 (M-28), calcd isotopic purity of 98.48%.

6,7-Dideutero-5,8-dimethoxybenzobicyclo[2.2.2]octen-2-one

5,8-Dimethoxybenzobicyclo[2.2.2]octen-2-one (0.27 g), 99% o-deuteroacetic acid (10 ml), 99.5% deuterium oxide (2 ml), and

concentrated sulfuric acid (6 drops) were mixed and heated at 90° for 10 days. The mixture was poured into water (120 ml) and the ketone extracted with diethyl ether (3 x 30 ml). The combined ether extracts were washed with 5% sodium bicarbonate (20 ml), dried (Na_2SO_4), and removed at reduced pressure to yield 0.25 g (92%) of 6,7,3,3-tetradeutero-5,8-dimethoxybenzobicyclo-[2.2.2]octen-2-one: nmr (CCl_4) δ1.3-2.2 (overlapping multiplets, 4H, CH_2CH_2), 3.69 (s, 6H, $-OCH_3$), and 3.7-4.0 (overlapping multiplets, 2H, C-1,4 bridgehead). Treatment of this ketone with potassium hydroxide (0.4 g) in methanol (30 ml) and water (15 ml) at room temperature for 2 hours yielded 6,7-dideutero-5,8-dimethoxybenzobicyclo[2.2.2]octen-2-one: mp 84-86°; nmr (CCl_4) δ1.3-2.2 (overlapping multiplets, 4H, $-CH_2CH_2-$), 2.04 (t, 2H, J = 2.2 Hz, $CH_2\overset{O}{C}$), 3.70 (s, 6H, $-OCH_3$), and 3.7-4.0 (overlapping multiplets, 2H, C-1,4 bridgehead).

6,7-Dideutero-5,8-dimethoxybenzobicyclo[2.2.2]octen-2,3-dione

Refluxing of 565 mg of 6,7-dideutero-5,8-dimethoxybenzobicyclo[2.2.2]octen-2-one with selenium dioxide (0.35 g) and xylene (6 ml) for 8 hours yielded the α-diketone (472 g , 79%): mp 211-212°; ir ($CHCl_3$) 2320 (C-D), and 1754 and 1736 cm^{-1} ($-\overset{O}{\overset{\|}{C}}-\overset{O}{\overset{\|}{C}}-$); nmr ($CDCl_3$) δ1.8-2.4 (overlapping multiplets, 4H, $-CH_2CH_2-$), 3.77 (s, 6H, $-OCH_3$), and 4.39 (multiplet, 2H, C-1,4 bridgehead); mass spectrum (70 eV) M^+ = 248, major peak at 192 (M-56), 177 (M-71), 161 (M-87), 149 (M-99), 133 (M-115), 117 (M-131), 105 (M-143), and 101 (M-147), small peak at 220 (M-28),

calcd isotopic purity of 90.57%.

Benzobicyclo[2.2.2]oct-5,7-diene-2-one (LXII-a)

Benzobicyclo[2.2.2]oct-5,7-dien-2-one was prepared by the method of Kitahonoki and Takana (111). 144 g (1.0 mole) of β-naphthol and 98 g (1.0 mole) of maleic anhydride were heated at 220° for 30 min. The reaction mixture was dissolved in the minimum amount of hot ethyl acetate. Upon cooling the ethyl acetate solution deposited 37.2 g (15%) of adduct: mp 193-195° [lit (112) mp 194-195°]. The adduct (37.2 g, 0.154 mole) was heated with 35 g of sodium carbonate in 250 ml of water until all of the adduct had dissolved. The resulting solution was acidified with 6 N hydrochloric acid and upon standing deposited 32.9 g (82%) of the diacid: mp 176-178° (with loss of H_2O) [lit (113) mp 173-180° (d)]. Pyridine (30 ml) was cautiously added to a solution of 32.9 g (0.128 mole) of the diacid, 66.5 g (0.15 mole) of lead tetraacetate, and benzene (250 ml). After 20 min the mixture was slowly warmed to reflux and held there for 3 hours. It was then filtered and the filtrate washed with 6 N hydrochloric acid (2 x 50 ml), 5% sodium bicarbonate (50 ml), dried (Na_2SO_4) and condensed at reduced pressure to yield a dark colored oil. The oil was purified by chromatography over silica gel using benzene-diethyl ether (9:1) as the eluant to yield 16.8 g (17%) of benzobicyclo[2.2.2]oct-5,7-dien-2-one: mp 56-58° [lit (111) mp 56.5-58°]; nmr (CCl_4) δ1.88 (multiplet, 2H, $-CH_2\overset{O}{\overset{\|}{C}}-$), 4.01 (multiplet,

1H, C-1 bridgehead), 4.27 (multiplet, 1H, C-4 bridgehead), 6.50 (overlapping multiplets, 2H, CH=CH), and 7.09 (multiplet, 4H, aromatic H's).

Benzobicyclo[2.2.2]oct-5-ene-2-one (XLVII-a)

10 g (59 mmole) of benzobicyclo[2.2.2]oct-5,7-dien-2-one, 0.2 g of 10% palladium on powdered charcoal, and benzene (50 ml) was stirred under hydrogen (1 atm) for 12 hours. The mixture was filtered and condensed at reduced pressure to give 9.8 g (97%) of benzobicyclo[2.2.2]oct-5-en-2-one: ir (CCl_4) 1739 cm^{-1} (C=O); nmr (CCl_4) δ1.2-2.1 (overlapping multiplets, 4H, CH_2CH_2), 2.04 (t, 2H, J = 2.2 Hz, $CH_2\overset{O}{\overset{\|}{C}}$), 3.22 (multiplet, 1H, C-1 bridgehead), 3.47 (multiplet, 1H, C-4 bridgehead), and 7.06 (s, 4H, aromatic H's).

Benzobicyclo[2.2.2]oct-5-ene-2,3-dione

Benzobicyclo[2.2.2]oct-5-ene-2-one (1.4 g, 8.1 mmole) was mixed with 0.9 g (8.2 mmole) of selenium dioxide and vigorously refluxed in xylene (6 ml) for 17 hours. The solution was filtered, evaporated, and the residue crystallized from hexane-benzene (1:1) to give the α-diketone (0.6 g, 40%): mp 123-124°; ir (CCl_4) 1757 and 1736 cm^{-1} ($-\overset{O}{\overset{\|}{C}}-\overset{O}{\overset{\|}{C}}-$); nmr ($CDCl_3$) δ2.10 (multiplet, 4H, CH_2CH_2), 3.96 (multiplet, 2H, C-1,4 bridgehead), and 7.31 (s, 4H, aromatic H's); mass spectrum (70 eV) M^+ = 186, major peaks at 130 (M-56), 115 (M-71), and 102 (M-84).

Anal. Calcd for $C_{12}H_{10}O_2$: C, 77.40; H, 5.41. Found (Spang): C, 77.19; H, 5.49.

Dibenzobicyclo[2.2.2]octa-2,5,7-triene

Maleic anhydride and anthracene were reacted under the conditions described by Diels and Alder (114) but the adduct was not isolated. Thus, 72 g (0.40 mole) of anthracene and 48 g (0.49 mole) of maleic anhydride were heated to 220° for 20 min. The reaction mixture was treated with potassium hydroxide and hot water until it had all dissolved. The solution was treated with 5 g of activated charcoal, filtered, and acidified with hydrochloric acid. Upon standing, it deposited 91.6 g (77%) of cis-dibenzobicyclo[2.2.2]oct-5,7-diene-2,3-dicarboxylic acid: mp 258-260° [lit(114) mp 251-253°]. 91 g (0.31 mole) of the diacid was reacted with 170 g (0.38 mole) of lead tetraacetate in a solution of 60 ml of pyridine and 600 ml of benzene. The procedure was the same as already described for the preparation of benzobicyclo[2.2.2]oct-5,7-diene-2-one and yielded 11.2 g (18%) of pure dibenzobicyclo-[2.2.2]oct-2,5,7-triene: mp 115-117° [lit (115) mp 119-120.5°]; nmr (CCl_4) δ4.94 (multiplet, 2H, C-1,4 bridgehead), and 6.63-7.33 (overlapping multiplets, 10H, vinyl and aromatic).

Dibenzobicyclo[2.2.2]oct-5,7-diene-2-ol

Hydroboration of 11.0 g (54 mmole) of dibenzobicyclo[2.2.2]-oct-2,5,7-triene using 1.6 g (42 mmole) of sodium borohydride and 2.2 g (15.5 mmole) of boron trifluoride etherate in diglyme (45 ml) followed by oxidation with 25 ml of 30% hydrogen peroxide gave 9.6 g (80%) of the alcohol: mp 141-142° [lit(116) mp 142-143°]; nmr ($CDCl_3$) δ1.0-1.6 (overlapping peaks, 2H,

one hydrogen removed by added D_2O, 1.9-2.5 (multiplet, 1H), 3.8-4.4 (overlapping multiplets, 3H, C-1,4 bridgehead and -C<u>H</u>-O), and 7.13 (multiplet, 8H, aromatic).

<u>Dibenzobicyclo[2.2.2]oct-5,7-diene-2-one</u>

Oxidation of 15.5 g (70 mmole) of dibenzobicyclo[2.2.2]-oct-5,7-diene-2-ol with 3.2 g (32 mmole) of chromium trioxide in glacial acetic acid (200 ml) as described by Wawzonek and Hallum (116) gave 0.8 g (8.3%) of dibenzobicyclo[2.2.2]oct-5,7-diene-2-one: mp 150-151° [lit (116) mp 152.5-153°]; nmr (CCl_4) δ2.26 (d, 2H, J = 2.4 Hz, CH_2C(=O)), 4.48 (t, 1H, J = 2.4 Hz, C-4 bridgehead), 4.75 (s, 1H, C-1 bridgehead), and 7.22 (multiplet, 8H, aromatic). The major product of the oxidation was anthraquinone (mp 280-282°) and the desired ketone was isolated (anthraquinone free) by repeated chromatography over silica gel with hexane-benzene (1:1) as the eluant and by recrystallization from hexane.

<u>Dibenzobicyclo[2.2.2]oct-5,7-diene-2,3-dione (LI-a)</u>

Oxidation of 127 mg (54 mmole) of dibenzobicyclo[2.2.2]oct-5,7-diene-2-one with 123 mg (110 mmole) of selenium dioxide in refluxing xylene (2 ml) for 3 hours led to the production of 95 mg (70%) of the α-diketone: mp 199.5-201° [lit (117) mp 199-201.5°]; ir ($CHCl_3$) 1754 and 1738 cm^{-1} (C(=O)–C(=O)); nmr ($CDCl_3$) δ4.0 (s, 2H, C-1,4 bridgehead), and 7.41 (multiplet, 8H, aromatic); mass spectrum (70 eV) M^+ = 234, major peaks at 178 (M-56), 150 (M-84), 89 (M-145), and 76 (M-158).

Endo-tricyclo[3.2.2.$0^{2,4}$]non-6-ene-endo, cis-8,9-dicarboxylic anhydride

Refluxing 19.0 g (0.206 mole) of cycloheptatriene (Aldrich), 22.0 g (0.224 mole) of maleic anhydride, and xylene (70 ml) for 5 hours yielded 29.2 g (74%) of adduct: mp 100-101° [lit (118)mp 101°]; nmr ($CDCl_3$) δ0.17-0.58 (overlapping multiplets, 2H, cyclopropyl CH_2), 0.98-1.34 (overlapping multiplet, 2H, C-2,4), 3.28 (multiplet, 2H, C-8,9), 3.40 (multiplet, 2H, C-1, 5), and 5.86 (multiplet, 2H, vinyl).

Endo-tricyclo[3.2.2.$0^{2,4}$]nonane-endo, cis-6,7-dicarboxylic anhydride

29.4 g (0.155 mole) of endo-tricyclo[3.2.2.$0^{2,4}$]non-6-ene-endo, cis-8,9-dicarboxylic anhydride was dissolved in benzene (200 ml) and stirred under hydrogen (1 atm) with 0.3 g of 10% palladium on charcoal until hydrogen was no longer absorbed to yield 27.0 g (91%) of the saturated anhydride: mp 139-140° [lit(119) mp 140°]; nmr ($CDCl_3$) δ0.4-1.0 (overlapping multiplets, 2H, cyclopropyl CH_2), 0.97-1.28 (overlapping multiplets, 2H, C-2,4 cyclopropyl), 1.33 (broad singlet, 4H, CH_2CH_2), 2.57 (multiplet, 2H, C-1,5 bridgehead), and 3.30 (multiplet, 2H, C-8,9).

Endo-tricyclo[3.2.2.$0^{2,4}$]nonane-endo, cis-6,7-dicarboxylic acid

45.6 g (0.238 mole) of anhydride was heated at 70° with a solution of excess sodium bicarbonate in water until all of the anhydride had dissolved. The solution was condensed at reduced

pressure, acidified with 6N hydrochloric acid, cooled, and the white crystals filtered and air dried: mp 185-186° with evolution of a gas.

Exo-tricyclo[3.2.2.$0^{2,4}$]non-6-ene

60 g (0.286 mole) of endo-tricyclo[3.2.2.$0^{2,4}$]nonane-endo, cis-6,7-dicarboxylic acid was decarboxylated with 160 g (0.362 mole) of lead tetraacetate in a solution of benzene (550 ml) and pyridine (65 ml). The procedure was the same as described for the preparation of benzobicyclo[2.2.2]oct-5,7-diene-2-one. The desired olefin was sublimed (100°/2 mm) from the reaction products to yield 7.6 g (22%) of a waxy solid: nmr (CCl_4) δ0.3-1.6 (overlapping multiplets, 8H), 2.58 (multiplet, 2H, C-1,5 bridgehead), and 6.40 (multiplet, 2H, vinyl).

Exo-tricyclo[3.2.2.$0^{2,4}$]nonan-6-ol (exo and endo)

4.0 g (33.4 mmole) of exo-tricyclo[3.2.2.$0^{2,4}$]non-6-ene was reacted with 0.95 g (25 mmole) of sodium borohydride and 4.5 g (31.6 mmole)of boron trifluoride etherate in diglyme (25 ml). Oxidation of the reaction mixture with 30% hydrogen peroxide (20 ml) led to 3.6 g (78%) of tricyclic alcohol which was recrystallized from pentane: mp 163-164°; ir (CCl_4) 3610 and 3400 cm^{-1} (-OH); nmr (CCl_4) δ0.0-2.3 (overlapping multiplets, 10H), 3.9-4.3 (overlapping multiplets, 1H), and 4.04 (s, 1H, -OH, removed by added D_2O).

Exo-tricyclo[3.2.2.$0^{2,4}$]nonan-6-one

Stirring 1.7 g (12.3 mmole) of exo-tricyclo[3.2.2.$0^{2,4}$]-nonan-6-ol in a mixture of 0.83 g (83 mmole) of chromium

trioxide in pyridine (15 ml) to yield 0.9 g (54%) of ketone: mp 149-150°; ir (CCl_4) 1722 cm^{-1} (C=O); nmr (CCl_4) δ0.0-2.5 (overlapping multiplets).

Trans-bicyclo[4.1.0]heptane-cis-2,5-dicarboxylic acid

2.60 g (21.6 mmole) of exo-tricyclo[3.2.2.$0^{2,4}$]non-6-ene was oxidized with potassium permanganate in acetone (250 ml) by the same procedure described for the oxidation of bicyclo-[2.2.1]hept-2-ene. 2.62 g (66%) of diacid was obtained: mp 165-166° from ethyl acetate; mass spectrum M^+ = 184, major peaks at 166 (M-18), 138 (M-46), and 93 (M-91).

Refluxing of 1.14 g (62 mmole) of diacid with methanol (75 ml) and a trace of acid yielded 1.20 (91%) of the dimethyl ester: nmr (CCl_4)δ-0.14 (multiplet, 1H), 0.34-0.73 (multiplet, 1H), 0.97-1.46 (overlapping multiplets, 6H), 2.35 (multiplet, 2H), and 3.43 (s, 6H,-OCH_3).

Endo-tricyclo[3.2.2.$0^{2,4}$]non-6-ene-endo, cis-8,9-dimethanol

28.0 g (147 mmole) of endo-tricyclo[3.2.2.$0^{2,4}$]non-6-ene-endo, cis-8,9-dicarboxylic anhydride was extracted via a Soxhlet extraction apparatus into a mixture of 11.0 g (0.29 mole) of lithium aluminum hydride in diethyl ether (500 ml). After refluxing for 30 hours, the mixture was hydrolyzed with saturated ammonium chloride, the ether decanted, dried (Na_2SO_4), filtered, and the ether removed at reduced pressure to yield 22.7 g (86%) of diol which was recrystallized from benzene: mp 113-114°; nmr ($CDCl_3$) δ-0.18-0.16 (multiplet, 2H, cyclopropyl CH_2), 0.93

(multiplet, 2H, C-2,4), 2.22 (multiplet, 2H), 2.65 (multiplet, 2H), 3.50 (multiplet, 4H, CH_2O-), 4.57 (broad singlet, 2H, -OH, removed by added D_2O), and 5.61 (multiplet, 2H, vinyl).

Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found (Spang): C, 73.25; H, 8.95.

Endo-tricyclo[3.2.2.$0^{2,4}$]non-6-ene-endo, cis-8,9-dimethanol ditosylate

14.9 g (83 mmole) of endo-tricyclo[3.2.2.$0^{2,4}$]non-6-ene-endo, cis-8,9-dimethanol was reacted with 35 g (184 mmole) of p-toluenesulfonyl chloride in pyridine (110 ml) at 0° for 24 hours. The mixture was diluted with 6N hydrochloric acid (300 ml) at 0° and the crude ditosylate isolated by suction filtration. Recrystallization from absolute methanol yielded 22.3 g (55%) of pure ditosylate: mp 93.5-94.5°; nmr ($CDCl_3$) δ-0.14-0.3 (overlapping multiplets, 2H, cyclopropyl CH_2), 0.87 (multiplet, 2H, C-2,4), 2.33 (multiplet, 2H), 2.43 (s, 3H, Ar-CH_3), 2.80 (multiplet, 2H), 3.79 (multiplet, 4H, CH_2-O-), 5.54 (multiplet, 2H, vinyl), 7.34 (d, 4H, J = 8 Hz, m-aromatic), and 7.78 (d, 4H, J = 8 Hz, o-aromatic).

Endo, cis-8,9-dimethyl-endo-tricyclo[3.2.20^{2,4}]non-6-ene

22.2 g (45.5 mmole) of endo-tricyclo[3.2.20^{2,4}]non-6-ene-endo, cis-8,9-dimethanol ditosylate was extracted via a Soxhlet extraction apparatus into a solution of 6.0 g (158 mmole) of lithium aluminum hydride in diethyl ether (700 ml). After 70 hours of refluxing, the mixture was hydrolyzed with saturated

ammonium chloride solution, the ether decanted, dried (Na_2SO_4), filtered, and the ether removed at reduced pressure to yield an oil. Distillation of the oil yielded 6.74 g (54%) of tricyclic olefin: bp 85-87° (15 mm); nmr (CCl_4) δ-0.24-0.33 (overlapping multiplets, 2H, cyclopropyl CH_2), 0.6-1.16 (overlapping multiplets, 2H, C-2,4), 0.81 (d, 6H, J = 7 Hz, $-CH_3$), 1.98 (multiplet, 2H), 2.52 (multiplet, 2H), and 5.71 (multiplet,2H,vinyl).

Anal. Calcd for $C_{11}H_{16}$: C, 89.12; H, 10.88. Found (Spang): C, 84.80; H, 9.96; C, 84.85; H, 10.08.

Endo, cis-8,9-dimethyl-endo-tricyclo[3.2.2.$0^{2,4}$]nonan-6-ol

Hydroboration of 3.6 g (24.3 mmole) of endo, cis-8,9-dimethyl-endo-tricyclo[3.2.2.$0^{2,4}$]non-6-ene using 0.8g(21 mmole) of sodium borohydride and 3.6 g (25.4 mmole)of boron trifluoride etherate in diglyme (30 ml) and oxidizing with 30% hydrogen peroxide (12 ml) yielded 2.86 g (71%) of the tricyclic alcohol. The alcohol was purified by recrystallization from hexane and sublimation at 65° (2 mm): mp 74-75°; ir (CCl_4) 3430 cm^{-1}(-OH); nmr (CCl_4) δ-0.7-0.54 (overlapping multiplets, 2H, cyclopropyl CH_2), 0.65-2.37 (overlapping multiplets, 15H), and 3.60 (multiplet, 1H, C<u>H</u>-O-).

Anal. Calcd for $C_{11}H_{18}O$: C, 79.46; H, 10.91. Found (Spang): C, 79.64; H, 10.86.

Endo, cis-8,9-dimethyl-endo-tricyclo[3.2.2.$0^{2,4}$]nonan-6-one (XLIII-a)

2.21 g (13.3 mmole)of endo,cis-8,9-dimethyl-endo-tricyclo-

[3.2.2.$0^{2,4}$]nonan-6-ol was added to a mixture of 1.0 g (10 mmole) of chromium trioxide in pyridine (30 ml) and this mixture stirred for 9 hours at room temperature. The mixture was diluted with 6N hydrochloric acid (100 ml), ether extracted, the combined ether extracts were dried (Na_2SO_4), filtered, and the ether removed at reduced pressure to yield 0.68 g (31%) of ketone which was purified by preparative vpc (15% Carbowax 20 M, 164°); ir (neat) 1718 cm^{-1} (C=O); nmr (CCl_4) δ0.0-2.5 (overlapping multiplets); mass spectrum (20 eV) M^+ = 164, major peaks at 149 (M-15), 136 (M-28), 131 (M-33), 115 (M-49), 107 (M-57), and 92 (M-72).

Dimethyl endo-tricyclo[3.2.2.$0^{2,4}$]non-6-ene-endo, cis-8,9-dicarboxylate

68.6 g (0.36 mole) of endo-tricyclo[3.2.2.$0^{2,4}$]non-6-ene endo, cis-8,9-dicarboxylic anhydride upon refluxing with methanol (500 ml) and 2.0 g of p-toluenesulfonic acid yielded 76.2 g (89%) of the diester which was purified by distillation and recrystallization from hexane: bp 135-140° (2 mm), mp 66-67°; nmr (CCl_4) δ-0.41-0.20 (overlapping multiplets, 2H, cyclopropyl CH_2), 0.64 (multiplet, 2H, C-2,4), 2.72 (overlapping multiplets, 4H), 3.19 (s, 6H, $-OCH_3$), and 5.46 (multiplet, 2H, vinyl).

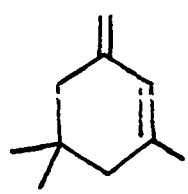
Dimethyl endo-tricyclo[3.2.2.$0^{2,4}$]nonane-endo, cis-6,7-dicarboxylate

1.54 g (8 mmole) of endo-tricyclo[3.2.2.$0^{2,4}$]nonane-endo, cis-6,7-dicarboxylic anhydride was refluxed with methanol

(50 ml) and 0.05 g of p-toluenesulfonic acid for 24 hours yielded 1.24 g (65%) of white, crystalline diester after recrystallization from hexane: mp 58-59°; nmr (CCl_4) δ0.2-1.9 (overlapping multiplets, 8H), 2.23 (multiplet, 2H), 2.94 (broad singlet, 2H), and 3.58 (s, 6H, $-OCH_3$).

1,3,5,5-Tetramethyl-1,3-cyclohexadiene

55 g (0.35 mole) of methyl iodide in diethyl ether (100 ml) was reacted with 8.4 g (0.35 g-atom) of magnesium in diethyl ether (400 ml). A solution of 41 g (0.297 mole) of isophrone (Aldrich) in ether (150 ml) was added over a one hour period. This mixture was refluxed for 2 hours, hydrolyzed with saturated sodium chloride (50 ml), the ether decanted, dried ($MgSO_4$), filtered, and distilled with a trace of sulfuric acid to yield 32.0 g (79%) of olefin bp 69-85° (70 mm) [lit (120) bp 24-25° (7 mm)]. The nmr spectrum (CCl_4) shows resonances at δ0.89 (s, 3H, $-CH_3$), 0.91 (s, 3H, CH_3), 1.6-2.1 (overlapping multiplets, 7.3H), and 4.62, 4.97, 5.42, and 5.87 (multiplets, 2.3H, vinyl). The lack of area in the 1.6-2.1 region (only 7.3H, 8.0 expected) and excess resonances in the vinyl region suggest the presence of a minor olefin, perhaps the exo methylene isomer (LXXV). None of the resonances were removed by added D_2O.



LXXV

1,5,8,8-Tetramethylbicyclo[2.2.2]oct-5-en-endo, endo-2,3-dicarboxylic anhydride (LXIII-a)

13.6 g (0.1 mole) of 1,3,5,5-tetramethyl-1,3-cyclohexadiene, 9.8 g (0.1 mole) of maleic anhydride, and benzene (11 ml) were mixed and refluxed for one hour to yield 17.3 g (74%) of adduct: mp 97-99° from benzene-pentane (1:1) [lit (120) mp 98-99°]; nmr ($CDCl_3$) δ0.89 (s, 3H, $-CH_3$), 1.10 (s, 5H, CH_3 and CH_2), 1.36 (s, 3H, $-CH_3$), 1.78 (d, J = 1.2 Hz, 3H, allylic CH_3), 2.49 (d of d, J = 3.6, 1.2 Hz, 1H), 2.75 (d, J = 8.4 Hz, 1H), 3.56 (d of d, J = 8.4, 3.6 Hz, 1H), and 5.51 (multiplet, 1H, vinyl).

1,5,8,8-Dimethylbicyclo[2.2.2]oct-5-ene-endo, endo-2,3-dicarboxylic acid (LXIII-b)

81.8 g of 1,5,8,8-tetramethylbicyclo[2.2.2]oct-5-en-endo, endo-2,3-dicarboxylic anhydride was stirred with water (200 ml) and excess sodium carbonate at 50° for 24 hours. The mixture was acidified with 5N hydrochloric acid, cooled to 0°, and the white diacid isolated by suction filtration and air dried: mp 151-153° [lit (120) mp 154-155°].

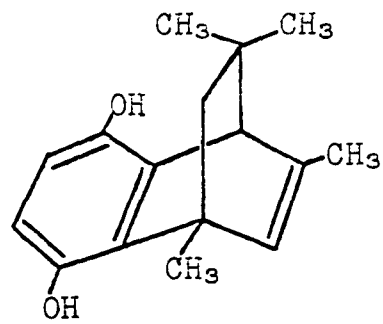
Endo-1,4,11,12-tetrahydro-1,3,10,10-tetramethyl-1,4-ethano-naphthalene-5,8-dione

5.4 g (50 mmole) of p-benzoquinone, 6.8 g (50 mmole) of 1,3,5,5-tetramethyl-1,3-cyclohexadiene, and benzene (20 ml) were mixed and refluxed for 5 hours. The reaction mixture was chromatographed over silica gel (hexane-3% ethyl ether) to

yield 9.8 g of adduct: mp 57-58° (from hexane); nmr (CCl_4) δ0.85 (s, 3H, CH_3), 1.05 (s, 3H, $-CH_3$), 1.13 (s, 3H, $-CH_3$), 1.2 (multiplet, 2H, CH_2), 2.61 (d, J = 8 Hz, 1H), 3.25 (d of d, J = 8, 3.1 Hz, 1H), 5.40 (multiplet, 1H, C-2 vinyl), and 6.48 (s, 2H, vinyl).

Anal. Calcd for $C_{16}H_{20}O_2$: C, 78.65; H, 8.25. Found (Ilse Beetz): C, 78.62; H, 8.10.

The diketone isomerized upon standing to the isomeric hydroquinone LXXVI: mp 140-141°.



LXXVI

Exo, exo-2,3-dimethylbicyclo[2.2.2]oct-5-ene-endo, endo-dicarboxylic anhydride (LXIV-a)

12.6 g (0.1 mole) of dimethyl maleic anhydride (Aldrich) and 14.5 g (0.18 mole) of 1,3-cyclohexadiene was sealed in an autoclave and heated at 155-160° for 84 hours. The solid mass was washed with benzene to yield 13.0 g (63%) of adduct: mp 259-261° [lit (121) mp 263.5°].

Exo, exo-2,3-dimethylbicyclo[2.2.2]oct-5-ene-endo, endo-2,3-dicarboxylic acid (LXIV-b)

13.0 g of exo, exo-2,3-dimethylbicyclo[2.2.2]oct-5-ene-

endo, endo-2,3-dicarboxylic anhydride was stirred for 50 hours at 50° with water (200 ml) and excess sodium carbonate. The mixture was acidified with dil hydrochloric acid, cooled to 0°, and the diacid isolated by suction filtration and air dried to yield 13.3 g (94%) of diacid: mp 258-269°.

Dimethyl bicyclo[2.2.2]octadiene-2,3-dicarboxylate (LXIV-c)

The title compound was prepared similar to the procedure described by Diels and Alder (122). Thus, 8.0 g (0.1 mole) of 1,3-cyclohexadiene and 14.2 g (0.1 mole) of dimethyl acetylenedicarboxylate were heated at 80° for 24 hours to give a quantitative yield of adduct not requiring further purification: nmr (CCl_4) δ1.40 (multiplet, 4H, CH_2CH_2), 3.68 (s, 6H, $-CH_3$), 3.97 (multiplet, 2H, C-1,4 bridgehead), and 6.63 (multiplet, 2H, vinyl).

Heating the adduct above 80° decomposes it to ethylene and dimethyl phthalate in quantitative yields.

Dimethyl bicyclo[2.2.1]heptadiene-2,3-dicarboxylate (LXV)

A quantitative yield of adduct, not requiring purification, was obtained by mixing 14.2 g (0.1 mole) of dimethyl acetylenedicarboxylate and 6.6 g (0.1 mole) of cyclopentadiene. The reaction is very exothermic and requires cooling in an ice bath: nmr (CCl_4) δ2.14 (multiplet, 2H, C-7), 3.69 (s, 6H, $-CH_3$), 3.88 (multiplet, 2H, C-1,4 bridgehead), and 6.88 (multiplet, 2H, vinyl).

The adduct, unlike the cyclohexadiene adduct, was stable towards heat.

Trans-5,6-dimethanolbicyclo[2.2.2]oct-2-ene ditosylate

33.3 g (0.15 mole) of diester was reduced with 6.8 g (0.18 mole) of lithium aluminum hydride in ethyl ether (700 ml). The reaction was refluxed for one hour, hydrolyzed with saturated sodium chloride, the ether decanted and removed at reduced pressure to yield 23.2 g (81%) of diol. The diol was converted to the ditosylate by treatment with p-toluenesulfonyl chloride (60 g) in pyridine (150 ml) at 0° for 24 hours. The pyridine solution was mixed with dilute hydrochloric acid (700 ml) at 0° to yield 34.8 g (52%) of ditosylate: mp 125-126°.

Isosteviol

1450 mg of steviolside was dissolved in 48% hydrobromic acid (22 ml) and allowed to stand at room temperature for 20 hours. The white solid that had formed was filtered, washed with water, and air dried to yield 512 mg (89%) of isosteviol: mp 226-227° [lit (123) mp 226-228°].

Isisteviol diketone

470 mg (1.48 mmole) of isosteviol, 200 mg (1.8 mmole) of selenium dioxide, and xylene (5 ml) were mixed and vigorously refluxed for 5 hours. The mixture was filtered and the filtrate evaporated to a yellow solid in the hood. The solid was recrystallized from carbon tetrachloride-chloroform to yield yellow crystals (260 mg, 53%): mp 285-287° [lit (124) mp 272-274°]; mass spectrum (70 eV) M^+ = 332.

Sources of Chemicals

Chemical	Source
Dimethyl maleic anhydride	Aldrich
Sodium borodeuteride	Merck, Sharp and Dohme of Canada Limited
Sodium borohydride	Metal Hydrides
Boron trifluoride etherate	Eastman Organic
Lithium aluminum deuteride	Metal Hydrides
Methyl lithium	Alfa Inorganics
Tri-n-butyltin chloride	Columbia Organic
Deuterium oxide	Columbia Organic
Chloroform-D_1 ($CDCl_3$)	Columbia Organic
Potassium t-butoxide	MSA Research Corp.
Deuterium	Matheson
Silica gel (M-5)	Davis
Propiophenone	Aldrich
Selenium dioxide	Dr. H. L. Malkus
1,7,7-Trimethylbicyclo[2.2.1]heptan-2,3-dione	Aldrich
Anti-7-trideuteromethyl-1,7-dimethylbicyclo[2.2.1]hepta-2,3-dione	Dr. W. L. Meyer
Pentacyclo[4.2.$0^{2,5}$.$0^{3,8}$.$0^{4,7}$]decane-9,10-dione	Dr. S. Masamune
Diketone XLII-a	Dr. J.W. Gates,Jr.

Chemical	Source
Gibberic acid	Abbott
Gibberellic acid	Aldrich
7-*t*-Butoxybicyclo[2.2.1]heptadiene	Frinton
Benzobicyclo[2.2.1]hepten-2,3-dione	Dr. H. Tanida
syn-9-Chlorobenzobicyclo[2.2.1]hepten-2,3-dione	Dr. H. Tanida
1,7,7-Trimethylbicyclo[2.2.1]hept-5-en-2-one	Dr. P. Mälkönen Dr. R. S. Givens
Endo, *endo*-5,6-dimethylbicyclo-[2.2.2]octan-2-one	Dr. K.-Y. Chang
Steviolside	Drs. H.G.Fletcher, Jr. and J. A. Waters
α-Acetoxyketone for LXXXIII	Dr. S. Masamune
α-Acetoxyketone for LXXXII	Dr. D.E.U.Ekong
Benzobicyclo[3.2.1]oct-6-en-3-one	Dr. P.T.Lansbury
Bicyclo[3.2.1]oct-6-en-3-one	Dr. N. Lebel

APPENDICES

The 7-Bicyclo[2.2.1]heptenyl Radical

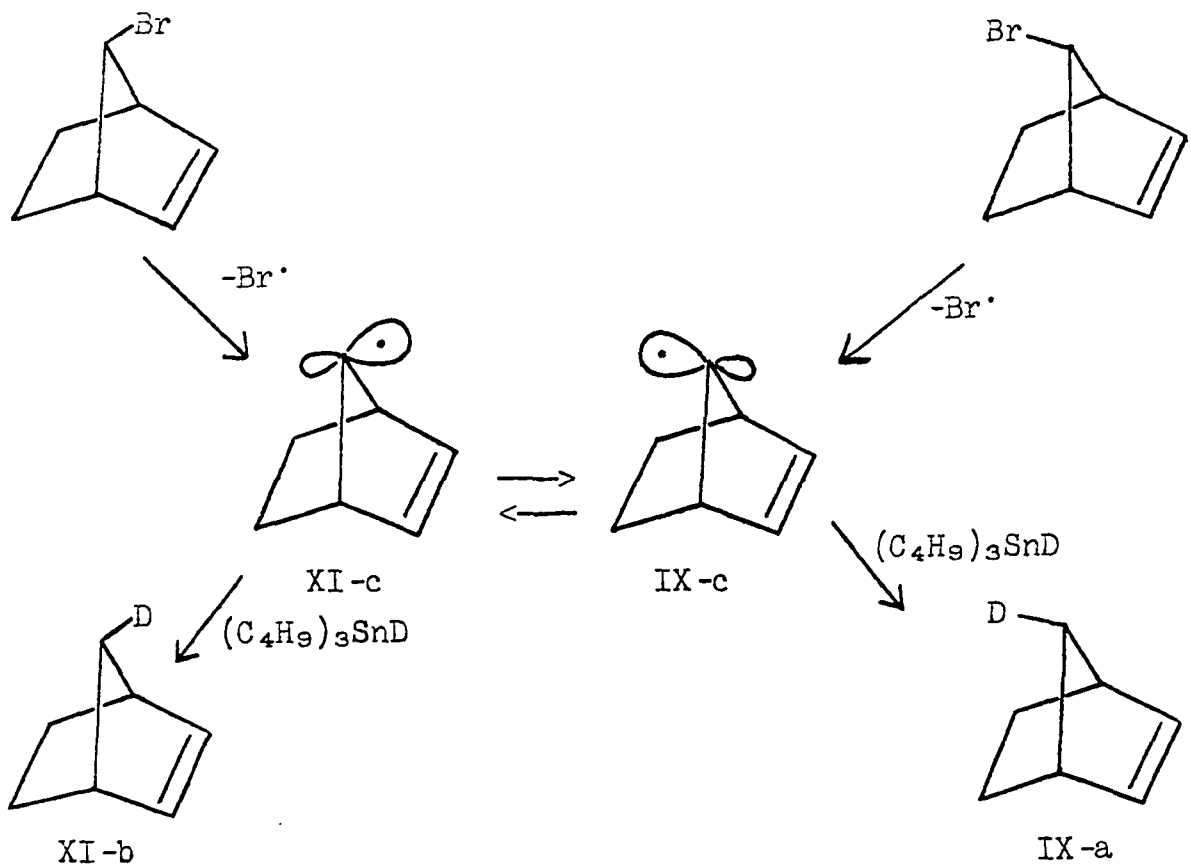
The stereochemical outcome of a number of radical reactions has been explained in terms of a pyramidal or planar configuration at the radical center (125 - 127). Warkentin and Sanford (51) recently reported that the tri-n-butyltin deuteride reduction of either syn or anti-7-bromobicyclo[2.2.1]-heptene lead to only one product, anti-7-deuterobicyclo[2.2.1]-heptene, and invoked a bridged radical (LXXVII) to describe the intermediate 7-bicyclo[2.2.1]heptenyl radical. However, the fact that an identical mixture of syn and anti-7-deuterobicyclo-[2.2.1]heptene (16% syn, 84% anti)* is actually obtained by the reduction of either syn- or anti-7-bromobicyclo[2.2.1]heptene (see Figure 10) clearly indicates that the reported results with this system are misleading. It is proposed that a better description for the 7-bicyclo[2.2.1]heptenyl radical is in terms of angular constriction of inversion which leads to two distance syn and anti (geometry retaining) nonplanar radicals (structures XI-c and IX-c). The observed C_1-C_7-C_4 angle of

---

*Analysis was preformed by comparison of the height of the wing peaks of XI (1/32 of total intensity) with the fourth peaks of IX (1/96 of total intensity). This, of course, assumes that the line widths of IX and XI are the same although it is realized that a slight error does arise due to line broadening (intensity decrease) from unresolved deuterium hfs in XI.

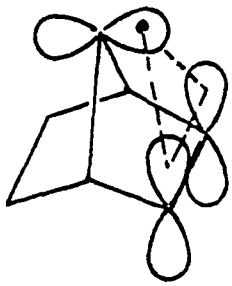
97 ± 1.3° (128,129) for the bicyclo[2.2.1]nucleus falls well below the 120° ideally required for a planar radical at C-7.

Scheme IX

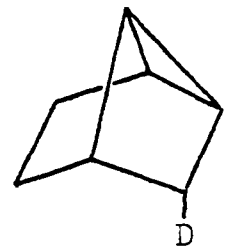


In the absence of π-overlap, a planar radical at C-7 would be expected to yield a nearly 1:1 syn/anti mixture of deuterated olefin since, in view of either steric or electronic considerations, neither the syn or anti side is favored for attack by tri-n-butyltin deuteride; at least they would not differ enough to favor anti over syn attack in the ratio of 4.9/1. If the bridged radical LXXVII were involved,one would expect a high percent of anti deuterated olefin, no syn, and some 5-deutero-

tricyclo[4.1.0.$0^{4,7}$]heptane (X). It would seem that the data best fits the reactions outlined in Scheme IX.



LXXVII



X

In this interpretation, IX-c and XI-c establish an equilibrium mixture with IX-c reacting to yield only anti-deuterated olefin and XI-c only syn-deuterated olefin. The fact that an identical mixture of products is obtained from either bromide indicates that the equilibrium is rapidly established and that the interconversion of IX-c and XI-c is much faster than deuteride abstraction from the tri-n-butyltin deuteride. The anti/syn ratio of 4.9 should then reflect the relative rates of reaction for IX-c and XI-c with tri-n-butyltin deuteride.

Further evidence not supporting the bridged or planar structures for IX-c and XI-c is the observation (130) and verification in this work that a nearly 1:1 mixture of syn-7 and anti-7-methylbicyclo[2.2.1]heptene was obtained in the tri-n-butyltin hydride reduction of syn-7-bromo-anti-7-methyl bicyclo[2.2.1]heptene (see Figure 5). It appears that the 7-methylbicyclo[2.2.1]heptenyl radical is more nearly planar at

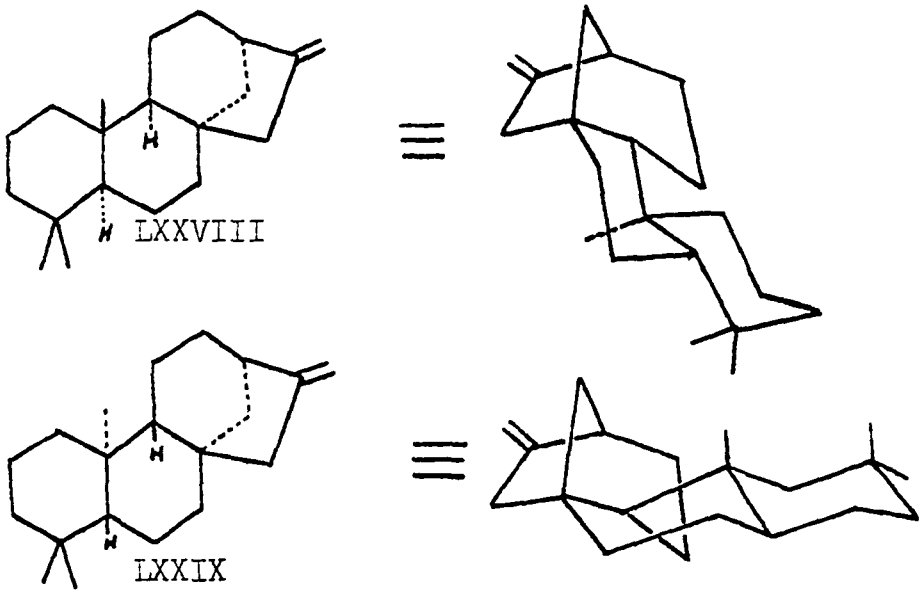
Figure 39. 60 MHz proton magnetic resonance spectrum of the vinyl protons of the mixture of syn- and anti-7-methylbicyclo[2.2.1]heptene (55.6% anti, 44.4% syn) obtained by reduction of syn-7-bromo-anti-7-methylbicyclo[2.2.1]heptene with tri-n-butyltin hydride.

C-7 than the 7-bicyclo[2.2.1]heptenyl radical. This result perhaps should have been anticipated since the intermediate C-7 radical can achieve planarity through hyperconjugative interactions with the methyl group.

Bicyclo[3.2.1]octan-6,7-semidiones Derived from Natural Products

The success achieved in the application of esr to the determination of the stereochemistry of A-B (131) and C-D (132) ring junctions of steroids prompted a similar study of naturally occurring bicyclic semidiones. It was anticipated that the stereochemistry at "W-plan" positions could be determined by comparison of the hfsc from these positions with those of the parent semidione. A search of the literature revealed that the bicyclo[3.2.1]octane nucleus was incorporated into at least three series of naturally occurring fused-ring compounds. Since many of these compounds contained a ketone or α-acetoxy ketone functional group on the C-6,7 bridge of the [3.2.1] system, this system was chosen for the study.

The two isomeric hydrocarbons, phyllocladene (LXXVIII) and kaurene (LXXIX), define the ring structure for two of these series and differ from each other only in the stereochemistry at C_2 in the [3.2.1] moiety.

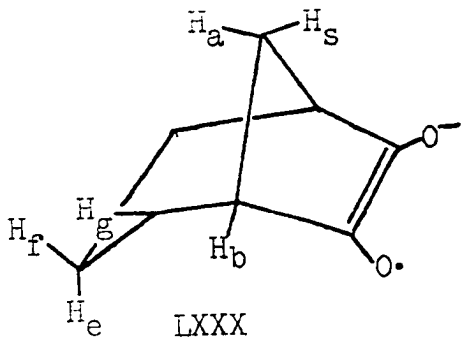


The results for the parent bicyclo[3.2.1]octan-6,7-semidione (LXXX)* and semidiones LXXXI - LXXXIII are listed in Chart X. The esr spectra (Figures 40-42) are so complex that only one or two hfsc can be extracted from them. By comparison to LXXX, these hfsc can be assigned to the anti-8 and bridgehead positions. Due to a relatively poor "W-plan" arrangement at C_2, interactions from this position are only around 0.51 G (e.g., semidione LXXX) and hence cannot be discerned in the complex spectra of semidiones LXXXI - LXXXIII . For this reason, an elucidation of the stereochemistry at C_2 in these semidiones is not feasible.

---

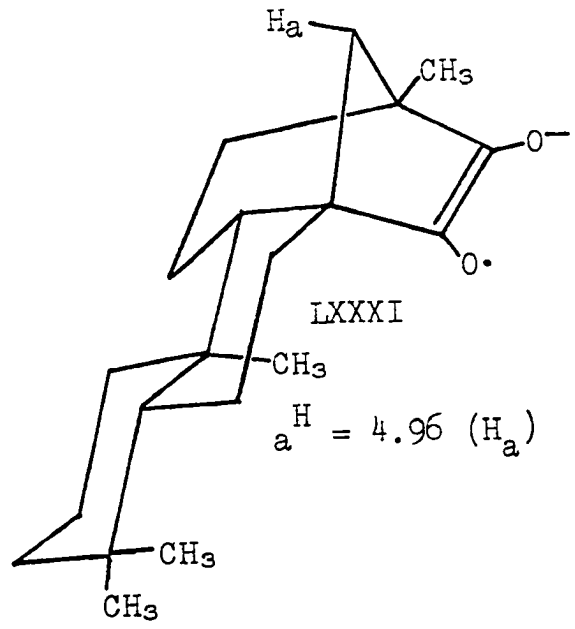
*This semidione was prepared by Dr. K.-Y. Chang and Mr. R.G. Keske at the Iowa State University of Science and Technology, Ames, Iowa.

Chart X



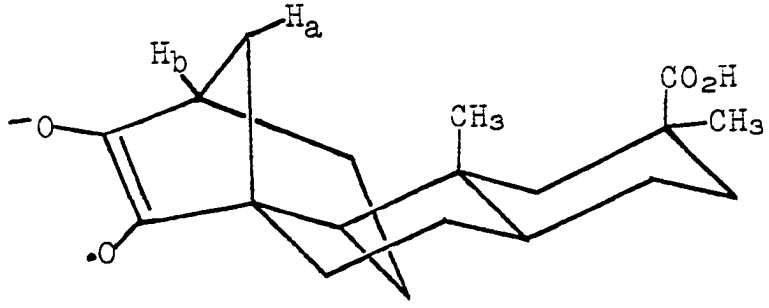
LXXX

a^H = 5.58 (H_b)
4.0 (H_a)
1.09 (H_e)
0.51 (H_g,H_s)
0.2 (H_f)



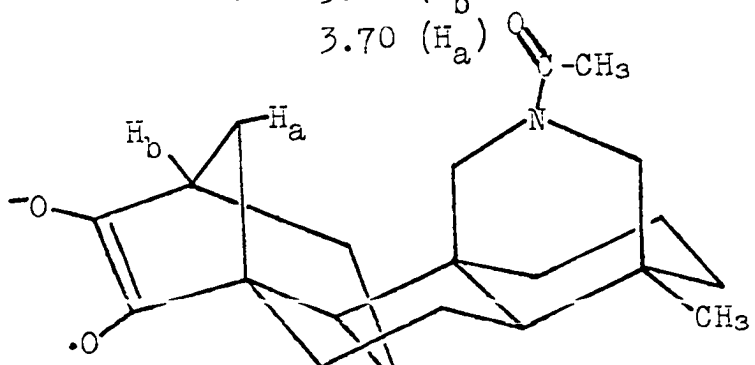
LXXXI

a^H = 4.96 (H_a)



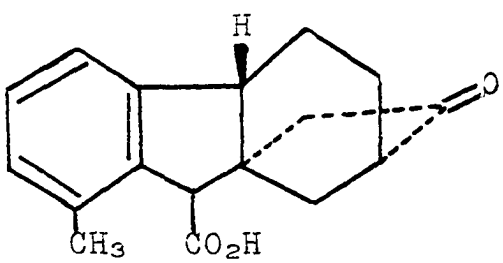
LXXXII

a^H = 5.46 (H_b)
3.70 (H_a)



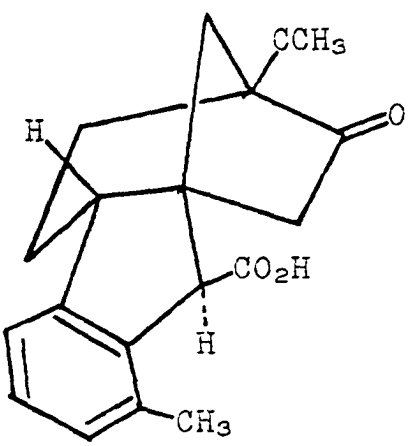
LXXXIII a^H=5.14 (H_b), 3.83 (H_a)

The third series of compounds is represented by gibberic acid (LXXXIV) which failed to generate a detectable concentration of radicals when oxidized with air in DMSO and potassium t-butoxide. It also failed to oxidize to the α-diketone with selenium dioxide. The monoketones of LXXXI and LXXXII were also resistant to oxidation in DMSO and potassium t-butoxide.



LXXXIV

≡



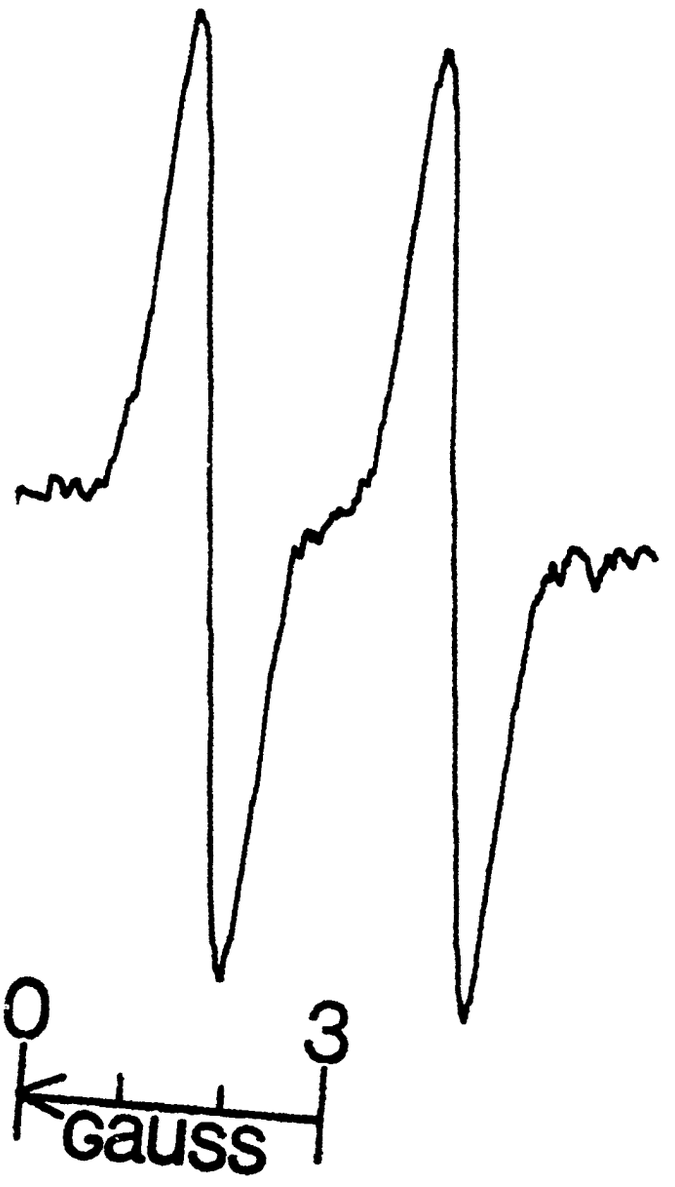


Figure 40. First-derivative esr spectrum of semidione LXXXI prepared by reduction of the α-diketone with the enolate anion of propiophenone in DMSO.

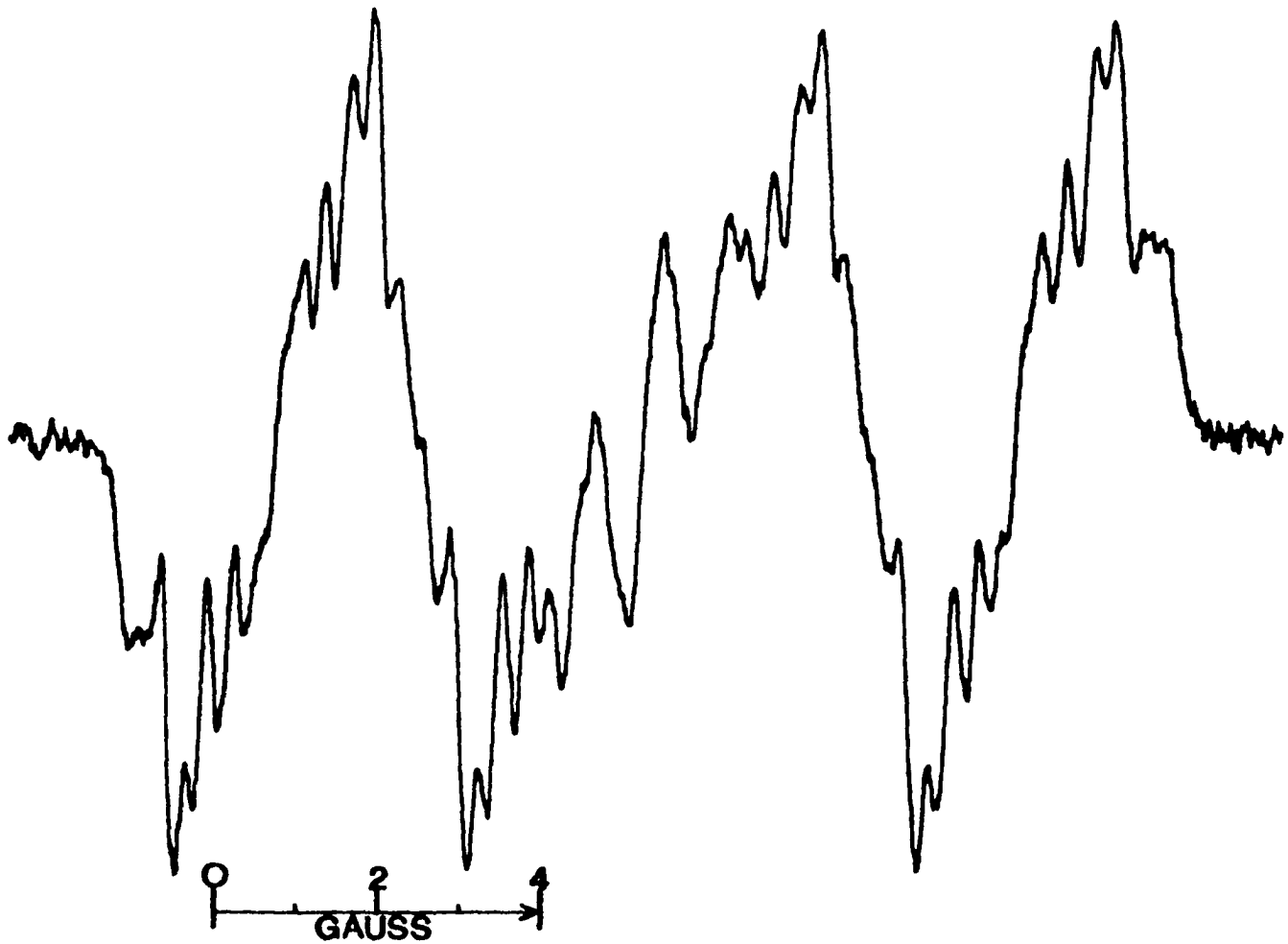


Figure 41. First-derivative esr spectrum of semidione LXXXII prepared from the α-acetoxy ketone in DMSO and potassium t-butoxide.

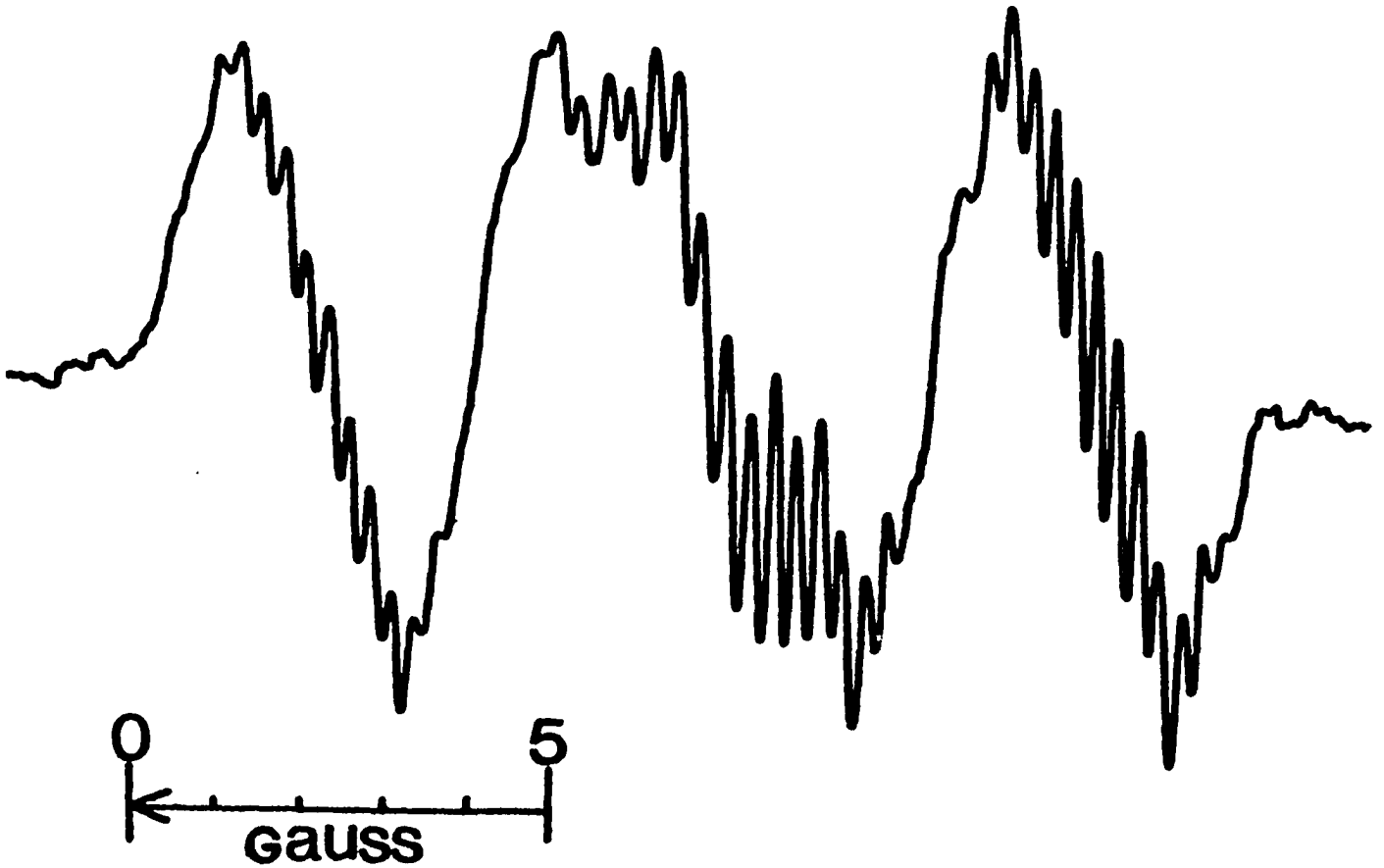


Figure 42. First-derivative esr spectrum of semidione LXXXIII prepared from the α-acetoxy ketone in DMSO and potassium t-butoxide.

BIBLIOGRAPHY

1. M. S. Blois, Jr., H. W. Brown and J. E. Maling, Neuvieme Colloque Ampere (Geneva: Librairie Payot, 1960) pp 243-255.

2. B. Venkataraman, B. G. Segal, and G. K. Fraenkel, J. Chem. Phys., 30, 1006 (1959).

3. M. Adams, M. S. Blois, Jr., and R. H. Sands, J. Chem. Phys. 28, 774 (1958).

4. R. W. Brandon and E. A. C. Lucken, J. Chem. Soc., 4273 (1961).

5. M. Bersohn and J. C. Baird, Ed., "An Introduction to Electron Paramagnetic Resonance," W. A. Benjamin, Inc., New York, N.Y., 1966, pp 70.

6. L. H. Piette, M. Okamura, G. P. Rabold, R. T. Ogata, R. E. Moore, and P. J. Scheuer, J. Phys. Chem., 71, 29 (1967).

7. G. A. Russell, E. T. Strom, E. R. Talaty, K.-Y. Chang, R. D. Stephens, and M. C. Young, Rec. Chem. Prog., 27, 3 (1966).

8. G. A. Russell in "Radical Ions", E. T. Kaiser and L. Kevan, Ed., Interscience Publishers, Inc., New York, N.Y., 1968, pp 87.

9. L. Michaelis and E. S. Fetcher, Jr., J. Amer. Chem. Soc., 59, 1246 (1937).

10. L. Michaelis, Chem. Revs., 16, 243 (1935).

11. D. H. Geske and A. L. Balch, J. Phys. Chem., 68, 3423 (1964).

12. G. A. Russell and P. R. Whittle, J. Amer. Chem. Soc., 89, 6781 (1967).

13. H. D. Scharf, W. Droste, and R. Liebig, Angew. Chem., 7, 215 (1968).

14. A. Weissberger, Ber., 65, 1815 (1932).

15. A. Weissberger, H. Mainz, and E. Strasser, Ber., 62, 1942 (1929).

16. G. A. Russell and G. R. Underwood, J. Phys. Chem., 72, 1074 (1968).

17. G. A. Russell, E. T. Strom, E. R. Talaty, and S. A. Weiner, J. Amer. Chem. Soc., 88, 1998 (1966).

18. G. A. Russell and R. S. Stephens, J. Phys. Chem., 70, 1320 (1966).

19. H. M. McConnell, J. Chem. Phys., 24, 764 (1956).

20. H. C. Heller and H. M. McConnell, J. Chem. Phys., 32, 1535 (1960).

21. G. A. Russell and K.-Y. Chang, J. Amer. Chem. Soc., 87, 4381 (1965).

22. G. A. Russell, K.-Y. Chang, and C. W. Jefford, J. Amer. Chem. Soc., 87, 4383 (1965).

23. Kuo-Yuan Chang, Ph.D. thesis, Iowa State University of Science and Technology, Ames, Iowa, 1965.

24. J. J. McDonnell, Ph.D. thesis, Iowa State University of Science and Technology, Ames, Iowa, 1968.

25. P. R. Whittle, Ph.D. thesis, Iowa State University of Science and Technology, Ames, Iowa, 1969.

26. G. A. Russell, G. W. Holland, and K.-Y. Chang, J. Amer. Chem. Soc., 89, 6629 (1967).

27. D. Kosman and L. M. Stock, J. Amer. Chem. Soc., 88, 843 (1966).

28. D. Kosman and L. M. Stock, Tetrahedron Letters, 1511 (1967).

29. D. Kosman and L. M. Stock, Chem. Commun., 551 (1968).

30. D. Kosman and L. M. Stock, J. Amer. Chem. Soc., 91, 2011 (1969).

31. S. F. Nelsen and B. M. Trost, Tetrahedron Letters, 5737, (1966).

32. A. Rassat, C. W. Jefford, J. M. Lehn, and B. Waegall, Tetrahedron Letters, 233 (1964).

33. J. Meinwald and A. Lewis, J. Amer. Chem. Soc., 83, 2769 (1961).

34. C. W. Jefford, B. Waegell, and K. Ramey, J. Amer. Chem. Soc., 87, 2191 (1965).

35. M. Barfield, J. Chem. Phys., 41, 3825 (1964).

36. T. Cohen and T. Tsuji, J. Org. Chem., 26, 1681 (1961).

37. T. Tsuji, Tetrahedron Letters, 2413 (1966).

38. G. A. Russell, R. D. Stephens, and E. R. Talaty, Tetrahedron Letters, 1139 (1965).

39. G. R. Underwood and R. S. Givens, J. Amer. Chem. Soc., 90, 3713 (1968).

40. H. C. Brown and K. J. Murray, J. Org. Chem., 26, 631 (1961).

41. G. T. Youngblood, C. D. Trivette, Jr., and P. Wilder, Jr., J. Org. Chem., 23, 684 (1958).

42. J. Meinwald, Y. C. Meinwald, and T. N. Baker, III, J. Amer. Chem. Soc., 86, 4074 (1964).

43. S. Beckmann and R. Mezger, Ber., 89, 2738 (1956).

44. D. R. Arnold, D. J. Trecker, and E. B. Whipple, J. Amer. Chem. Soc., 87, 2596 (1965).

45. W. C. Baird, Jr., B. Franzus, and J. H. Surridge, J. Amer. Chem. Soc., 89, 410 (1967).

46. B. Franzus, W. C. Baird, Jr., N. F. Chamberlain, T. Hines, and E. I. Snyder, J. Amer. Chem. Soc., 90, 3721 (1968).

47. H. C. Brown and H. M. Bell, J. Amer. Chem. Soc., 85, 2324 (1963).

48. S. Winstein, A. H. Lewin, and K. C. Pande, J. Amer. Chem. Soc., 85, 2324 (1963).

49. A. P. Marchand and J. E. Rose, J. Amer. Chem. Soc., 90, 3724 (1968).

50. H. G. Kuivila, Accounts of Chem. Research, 1, 299 (1968).

51. J. Warkentin and E. Sanford, J. Amer. Chem. Soc., 90, 1667 (1968).

52. S. J. Cristol and A. L. Noreen, J. Amer. Chem. Soc., 91, 3969 (1969).

53. W. L. Meyer and A. P. Lobo, J. Amer. Chem. Soc., 88, 3181 (1966).

54. D. Craig, J. Amer. Chem. Soc., 73, 4889 (1951).

55. S. Masamune, H. Cuts, and M. G. Hogben, Tetrahedron Letters, 1017 (1966).

56. W. G. Dauben and D. L. Whalen, Tetrahedron Letters, 3743 (1966).

57. D. D. Chapman, H. S. Wilgus, III, and J. W. Gates, Jr., Tetrahedron Letters, 6175 (1966).

58. K. Alder and W. Roth, Ber., 88, 407 (1955).

59. R. O. C. Norman and R. J. Pritchett, Chem. and Ind., 50, 2040 (1965).

60. E. Fermi, Z. Physik, 60, 320 (1930).

61. A. Carrington and A. D. McLachlan, "Introduction to Magnetic Resonance", Harper and Row, New York, N.Y., 1967, pp 81-85.

62. P. B. Ayscough, "Electron Spin Resonance in Chemistry", Methuen and Co., London, England, 1967, pp 71-78.

63. R. Dehl and G. K. Fraenkel, J. Chem. Phys., 39, 1793 (1963).

64. J. P. Colpa and E. deBoer, Mol. Phys., 7, 333 (1963).

65. A. Horsfield, J. R. Morton, and D. H. Whiffen, Mol. Phys., 5, 115 (1962).

66. S. Ogawa and R. Fessenden, J. Chem. Phys., 41, 994 (1964).

67. E. W. Stone and A. H. Maki, J. Chem. Phys., 37, 1326 (1962).

68. S. F. Nelsen and E. D. Seppanen, J. Amer. Chem. Soc., 89, 5740 (1967).

69. T. M. McKinney, J. Amer. Chem. Soc., 90, 3879 (1968).

70. G. A. Russell, G. W. Holland, K.-Y. Chang, and L. H. Zalkow, Tetrahedron Letters, 1955 (1967).

71. A. Nickon and J. L. Lambert, J. Amer. Chem. Soc., 84, 4604 (1962).

72. R. W. Fessenden and R. A. Schuler, J. Chem. Phys., 39, 2147 (1963).

73. R. W. Fessenden, J. Phys. Chem., 71, 74 (1967).

74. M. Bersohn and J. C. Baird, "An Introduction to Electron Paramagnetic Resonance", W. A. Benjamin, New York, N.Y., 1966, p 70.

75. G. A. Russell, E. G. Janzen, and E. T. Strom, J. Amer. Chem. Soc., 86, 1807 (1964).

76. H. M. Walborsky and D. F. Loncrini, J. Amer. Chem. Soc., 76, 5396 (1954).

77. N. J. Toivonen and J. Kaila, Suomen Kemistilehti, 28B, 91 (1955);Chem. Abstr., 49, 7529 (1955).

78. K. Alder, H. K. Schäfer, H. Esser, H. Krieger, and R. Reubke, Ann., 593, 23 (1955).

79. O. Diels and K. Alder, Ann., 460, 98 (1928).

80. M. S. Morgan, R. S. Tipson, A. Lowy, and W. E. Baldwin, J. Amer. Chem. Soc., 66, 404 (1944).

81. W. J. Bailey and W. B. Lawson, J. Amer. Chem. Soc., 77, 1606 (1955).

82. S. F. Birch, N. J. Hunter, and D. T. McAllen, J. Org. Chem., 21, 970 (1956).

83. K. Alder and W. Roth, Ber., 87, 161 (1954).

84. H. C. Brown and B. L. S. Rao, J. Amer. Chem. Soc., 81, 6428 (1959).

85. P. Wilder and L. A. Feliu-Otero, J. Org. Chem., 30, 2560 (1965).

86. P. S. Bailey, J. Org. Chem., 22, 1548 (1957).

87. H. Gault and L. Daltroff, Chimie and industrie, 45, 122 (1941).

88. L. Daltroff, Ann. chim., 14, 207 (1940).

89. L. Kaplan, H. Kwart, and R. von R. Schleyer, J. Amer. Chem. Soc., 82, 2341 (1960).

90. S. J. Cristol, W. K. Seifert, and S. B. Soloway, J. Amer. Chem. Soc., 82, 2351 (1960).

91. H. C. Brown and R. L. Sharp, J. Amer. Chem. Soc., 90, 2915 (1968).

92. K. Alder, G. Stein, and H. Finzenhagen, Ann., 485, 223 (1931).

93. H. Kwart and L. Kaplan, J. Amer. Chem. Soc., 76, 4072 (1954).

94. H. G. Kuivila and O. F. Beumel, Jr., J. Amer. Chem. Soc., 83, 1246 (1961).

95. P.Story, J. Org. Chem., 26, 287 (1961).

96. H. C. Brown and H. M. Bell, J. Org. Chem., 27, 1928 (1962).

97. G. Komppa and S. Beckmann, Ann., 523, 68 (1936).

98. H. C. Brown and C. P. Garg, J. Amer. Chem. Soc., 83, 2951 (1961).

99. R. R. Sauers and R. M. Hawthorne, Jr., J. Org. Chem., 29, 1685 (1964).

100. H.-D. Scharf, W. Droste, and R. Liebig, Angew. Chem., 7, 215 (1968).

101. W. R. Vaughen and M. Yoshimme, J. Org. Chem., 22, 7 (1957).

102. J. Meinwald and G. A. Wiley, J. Amer. Chem. Soc., 80, 3667 (1958).

103. G. Wittig and E. Knauss, Ber., 91, 895 (1958).

104. P. D. Bartlett and W. P. Giddings, J. Amer. Chem. Soc., 82, 1240 (1960).

105. J. S. Newcomer and E. T. McBee, J. Amer. Chem. Soc., 71, 946 (1949).

106. P. G. Gassman and P. G. Pape, J. Org. Chem., 29, 160 (1964).

107. P. G. Gassman and J. L. Marshall, J. Amer. Chem. Soc., 88, 2822 (1966).

108. O. Diels and K. Alder, Ber., 62, 2337 (1929).

109. R. B. Thompson, U. S. Patent 2,903,368 (1959); Chem. Abstr., 54, 3937 (1960).

110. B. Franzus, J. Org. Chem., 28, 2954 (1963).

111. K. Kitahonoki and Y. Takana, Tetrahedron Letters, 1597 (1963).

112. K. Takeda, S. Nagakura, and K. Kitahonoki, Pharmac. Bull. Japan, 1, 135 (1953).

113. K. Takeda and K. Kitahonoki, J. Pharm. Soc., Japan, 73, 280 (1953).

114. O. Diels and K. Alder, Ann., 486, 191 (1931).

115. S. J. Cristol and R. K. Bly, J. Amer. Chem. Soc., 81, 6155 (1960).

116. S. Wawzonek and J. V. Hallum, J. Org. Chem., 18, 288 (1953).

117. W. R. Vaughn and M. Yoshimine, J. Org. Chem., 22, 528 (1957).

118. K. Alder and G. Jacobs, Chem. Ber., 86, 1528 (1953).

119. E. P. Kohler, M. Tishler, H. Potter, and H. T. Thompson, J. Amer. Chem. Soc., 61, 1057 (1939).

120. M. S. Kharasch and P. O. Tawney, J. Amer. Chem. Soc., 63, 2308 (1941).

121. K. Ziegler, G. Schenck, E. W. Krockow, A. Siebert, A. Wenz, and H. Weber, Ann., 551, 1 (1942).

122. O. Diels and K. Alder, Ann., 490, 236 (1931).

123. E. Mosettig, U. Beglinger, F. Dolder, H. Lichti, P. Quitt, and J. A. Walters, J. Amer. Chem. Soc., 85, 2305 (1963).

124. F. Dolder, H. Lichti, E. Mosettig, and P. Quitt, J. Amer. Chem. Soc., 82, 246 (1960).

125. P. D. Bartlett, R. E. Pincock, J. H. Rolston, W. G. Schindel, and L. A. Singer, J. Amer. Chem. Soc., 87, 2590 (1965).

126. F. D. Greene and N. N. Lowry, J. Org. Chem., 32, 875 (1967).

127. F. D. Greene and N. N. Lowry, J. Org. Chem., 32, 882 (1967).

128. A. C. McDonald and J. Trotter, Acta Crystallogr., 18, 243 (1965).

129. A. C. McDonald and J. Trotter, Acta Crystallogr., 19, 456 (1965).

130. J. B. Dence, Ph.D. thesis, California Institute of Technology, Pasadena, California, 1968.

131. E. R. Talaty and G. A. Russell, J. Org. Chem., 31, 3455 (1966).

132. G. A. Russell, E. R. Talaty, and R. H. Horrocks, J. Org. Chem., 32, 353 (1967).

ACKNOWLEDGMENTS

I would like to express my gratitude to Professor Glen A. Russell for his conception of the problem, his many notes of suggestions, and his patience during periods of disappointingly slow progress. His efforts toward my acquisition of a National Institutes of Health postdoctoral fellowship under Professor H. C. Brown are most sincerely appreciated.

Heartfelt appreciation is extended to my parents, brother, and sisters for their patience and understanding in allowing me to break family ties long enough to establish myself and pursue my own goals.

The courage to continue came from many sources. Special acknowledgment is given to Betty for her love, understanding, and unyielding faith in me as a fellow chemist and friend. Our frequent discussions, good, bad, and in-between times all combined to make possible the often much needed reevaluation of personal goals and attitudes; all of this at a time when she herself was trying to find her own way. She alone was always reason enough to continue.

Many people, places, and things made life both in and out of the lab something special: Gary and Al who introduced me to golf, Dave's, and who always went out of their way to help me during my first year; Dr. Kuo-Yuan Chang who introduced me to bicyclic chemistry; the members of the Chemistry Department, especially the Russell Group, who were both scientifically and

socially enlightening; Drs. Chapman, Kinstle, Gerstein, and Graves who composed my graduate committee; the men of the "Polish Embassy" who by being themselves, made life in a basement more gratifying; the DSGA who made the long, hot summers too short; the Daytons, who made me feel at home and especially Louise, who typed the final copy of this thesis; Judy and Leo, whose friendship always made life a little easier; Mich, Judy, and Sue, whose "good neighbor" policy made our final year at ISU most memorable; the Claussens of Bettendorf for their continued interest and encouragement and especially for providing many opportunities to view Iowa on a down-to-earth level; Professor N. C. Deno and his research group at Penn State who pointed me in the direction of graduate school and Iowa State; all of those who turned me in for the "03" Bomb; and Dr. Ed Panek for his short course in writing research proposals.

I also wish to thank the National Science Foundation for a fellowship and the Chemistry Department of the Iowa State University for a teaching assistantship both of which provided the financial support during the course of this work.

VITA

George William Holland, Jr. was born September 21, 1943 in Altoona, Pennsylvania. He is the son of George William and Alice Jean Reese Holland and has an older sister, Betty Jane, and a younger brother and sister, John Charles and Judith Ann, who are twins.

Graduation from the Altoona Senior High School in June, 1961 was preceded by attendance at McKinley Elementary School and Theodore Roosevelt Junior High School in Altoona. In September of that year he enrolled as a chemistry major at the Altoona Campus of the Pennsylvania State University from which he was graduated in June, 1963. In September, 1963, he entered the University Park Campus of Penn State and graduated in March, 1965 with a Bachelor of Science in Chemistry. July of that same year saw him enter the graduate school of the Iowa State University of Science and Technology in Ames, Iowa.

In September, 1965, he was awarded a National Science Foundation Traineeship at Iowa State. He won a National Institutes of Health Postdoctoral Fellowship in 1969 and accepted a postdoctoral position under Professor H. C. Brown at Purdue University in West Lafayette, Indiana. He is a member of the American Chemical Society, Sigma Xi, Phi Kappa Phi, and Phi Lambda Upsilon.