To the Graduate Council:

I am submitting herewith a thesis written by Craig M. Bohlken entitled "NMR Studies of 1-phenyl-4,4,5-trimethyl-5-hydroxy-6-oxa-7,7-diphenyl-1-hydrindene-2-one and Derivatives." I have examined the final copy of this thesis for form and content and recommend that it be accepted in partial fulfillment of the requirements for the degree of Master of Science, with a major in Chemistry.

Donald C. Kleinfelter

Donald C. Kleinfelter, Major Professor

We have read this thesis
and recommend its acceptance:

Richard Fuson

George Kabalka

Accepted for the Council:

Associate Vice Chancellor and
Dean of The Graduate School

NMR STUDIES OF 1-PHENYL-4,4,5-TRIMETHYL-5-HYDROXY-6-OXA-7,7-DIPHENYL-1-HYDRINDENE-2-ONE AND DERIVATIVES

A Thesis

Presented for the

Master of Science

Degree

The University of Tennessee, Knoxville

Craig M. Bohlken

August 1997

DEDICATION

This thesis is dedicated to my parents. In special recognition of their love, support, and strength, I dedicate this thesis to my father, Jack, and to my mother, Lily.

ACKNOWLEDGMENTS

To Dr. Donald C. Kleinfelter, my research advisor and mentor, I wish to express my deepest gratitude and appreciation for his support, guidance, and advice on both professional and personal matters. I am also grateful to Neil Whittemore for his assistance on the 400 MHz NMR and to Cannon Turner for his assistance in the laboratory.

I wish to express my love and sincere gratitude to my family members, especially my parents whose support and encouragement were of immeasurable value. Finally and most importantly, I wish to thank my Lord and Savior, Jesus Christ, without whom my life would have no meaning.

ABSTRACT

Spectroscopic properties of 1-phenyl-4,4,5-trimethyl-5-hydroxy-6-oxa-7,7-diphenyl-1-hydrindene-2-one and some of its derivatives were studied using high resolution nuclear magnetic spectroscopy. The aryl groups present were the phenyl, *o*-anisyl, *o*-tolyl, and *o*-ethylphenyl.

The *o*-anisyl analog demonstrated restricted rotation on the NMR time scale through the appearance of two absorption positions for the *o*-substituent protons. The acid-catalyzed dehydration product of the *o*-anisyl compound also showed restricted rotation. However, the lithium aluminum hydride reduction product of the *o*-anisyl analog did not have restricted rotation since the six-membered ring was cleaved during the reduction process.

The *o*-tolyl analog showed an epimeric mixture. The acid-catalyzed dehydration product of this mixture, however, was not a mixture since the OH on the six-membered ring is absent. In addition, the *o*-tolyl analog mixture was found theoretically to give four sodium borohydride reduction products. It also gave two lithium aluminum hydride reduction products since the six-membered ring was not retained.

The analysis of the *o*-ethylphenyl analog showed one methyl absorption for the methyl portion of the ethyl group on the aryl ring. This indicated no restricted rotation had occurred for the system. In addition, NMR examination on the cyclic ketal of the phenyl oxidation product revealed that the methylene protons of the -OEt group were diastereotopic. The NMR spectrum of the two *o*-anisyl diols, the *o*-tolyl analog and derivatives, as well as the *o*-ethylphenyl analog have been found to be different than previously reported.

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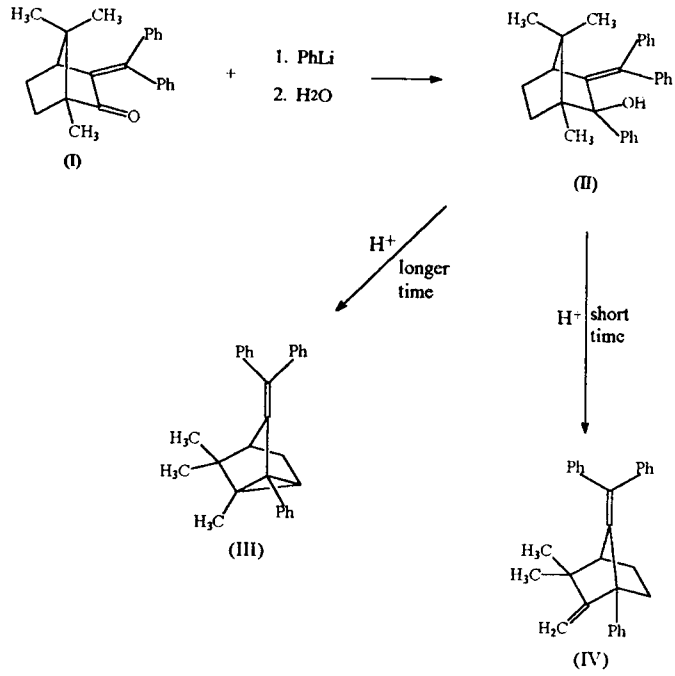
Chapter I

Introduction

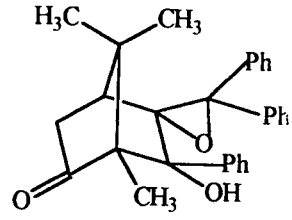
A. Historical

In the early 1940's Rupe and Hagenbach[1] allowed phenyllithium to react with diphenylmethylenecamphor (I). The alcohol (II) obtained reacted with trichloroacetic acid to give a mixture of isomeric hydrocarbons. Elemental analysis proved that the hydrocarbons had an empirical formula of $C_{29}H_{28}$. They also found that heating of the higher melting isomer with acetic acid in the presence of a strong acid converted it into the lower melting isomer. They believed that the higher melting compound was the tricyclene compound (III) and the lower melting compound was the camphene compound (IV). This seemed reasonable since, twenty five years earlier, Meerwein and Van Emster[2] demonstrated that tricyclene could be changed into camphene with acid.



The oxidation of what was assumed to be the camphene product with chromium trioxide in acetic acid produced a compound with an empirical formula of $C_{29}H_{28}O_3$. Rupe and Hagenbach assumed by chemical reactivity that this product was neither a ketone nor an acid. A hydroxyl group was indicated by a positive Zerewitinoff reaction, although no alcohol derivative could be obtained. The oxidation product was oxidized further with $KMnO_4$ and presumably gave an acid with the formula $C_{16}H_{16}O_3$, but esterification of this compound was unsuccessful.

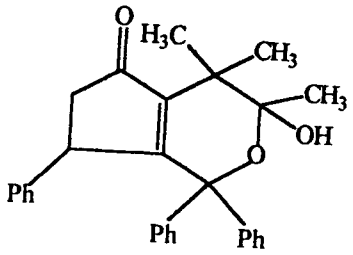
In 1964, Aaron[3] repeated the work of Rupe and Hagenbach utilizing NMR spectroscopy. He found the previously assigned structures of the two $C_{29}H_{28}$ isomers to be reversed. He showed that the lower melting isomer was the tricyclene compound, III, and the higher melting isomer was the camphene compound, IV. He also carried out a chromic acid oxidation of the tricyclene compound and assigned the structure (V) to the $C_{29}H_{28}O_3$ oxidation product based on its chemical reactivity, and from spectroscopic and analytical data.



(V)

In 1966, Kleinfelter and Wilde[4] disproved the above structure, V, through the use of NMR and IR spectroscopy, and assigned a new possible structure (VI), which is a cyclic hemiketal. In 1967, Bennett[5] investigated the chromic acid oxidation of the *o*-anisyl analog

of III. The NMR analysis of his oxidation product supported structure VI for the phenyl oxidation product. The NMR spectrum of the *o*-anisyl oxidation product (VII) showed two *o*-methoxy methyl signals in a ratio close to 1:1 and the other CH_3 signals in a ratio of: 0.5:0.5:1:1[6].



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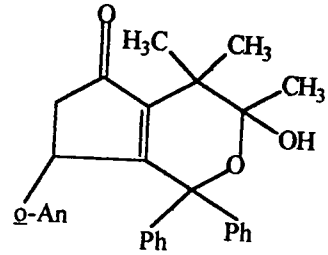
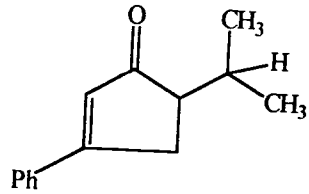


(VII)

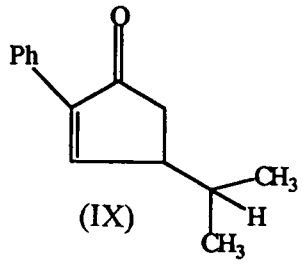
Later, Kleinfelter[7] allowed the phenyl oxidation product, thought to be VI, to reflux with alcoholic potassium hydroxide and obtained benzophenone and what was presumed to be 3-phenyl-5-isopropyl-2-cyclopentenone (VIII).



(VIII)

In 1968, Wei[8] continued the study of the products which were produced by the treatment of the phenyl oxidation product with alcoholic potassium hydroxide. In addition to obtaining the benzophenone, she also obtained the acetate ion, characterized as the p-nitrobenzyl ester derivative. Her investigation also led to the reassignment of the structure of

the cyclopentenone as being (IX), 2-phenyl-4-isopropyl-2-cyclopentenone. Hence, a different cyclic hemiketal structure, (X), was necessitated for the oxidation product of the tricyclene. The proposed mechanism for the formation of this cyclic hemiketal is shown in Scheme 1. The formation of the epoxide, (XI), as an intermediate is supported by the fact that it also gives (X) upon oxidation with chromic acid. Later, Aaron performed chemical reactions in support of X which included $NaBH_4$ reduction to the diol (XII) and $LiAlH_4$ reduction to the triol (XIII).



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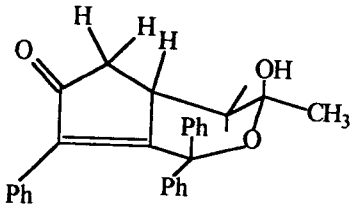
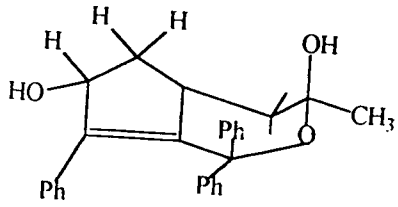


(X)



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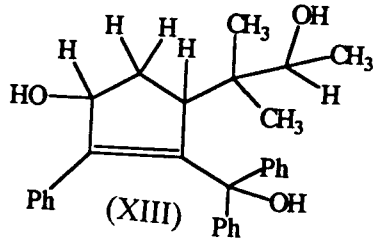
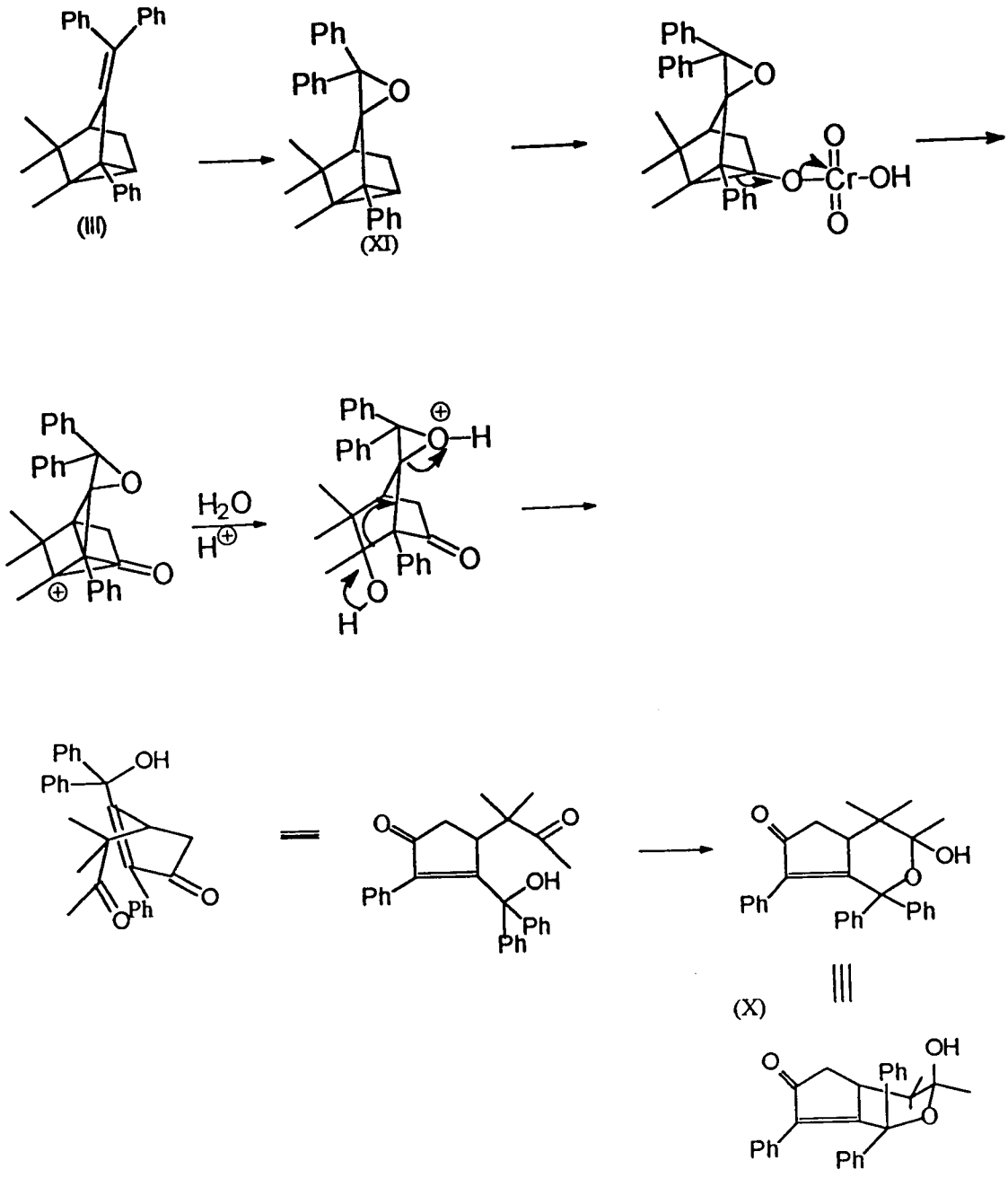


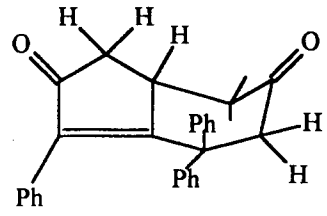
(XIII)

In 1971, Weichert[9] accomplished spectral studies (IR, 60 MHz NMR, 100 MHz NMR) on the cyclic hemiketal, X. He also carried out spectroscopic investigations on the products XII and XIII formed by reduction with $NaBH_4$ and $LiAlH_4$, respectively, as well as (XIV), the dehydration product formed from the reaction of X with acetic and sulfuric acids, and (XV), the product obtained from $LiAlH_4$ reduction of XIV. In addition, he carried out spectroscopic studies of the *o*-anisyl oxidation product (XVI), which had already been made

SCHEME 1:


Ph
Ph
Ph
(III)
Ph
Ph
O
Ph
(XI)
Ph
Ph
O
O
O
Cr-OH
O
Ph
Ph
Ph
O
H2O
H⊕
Ph
Ph
O
H
Ph
O
O
H
Ph
OH
Ph
O
O
Ph
O
Ph
OH
Ph
Ph
O
OH
O
Ph
Ph
Ph
(X)
OH
O
Ph
O
Ph
Ph

by Bennett, and newly synthesized compounds (XVII), (XVIII), and (XIX), the *o*-anisyl analogs of XII, XIII, and XIV, respectively. He also prepared the *o*-tolyl and *o*-ethylphenyl oxidation products, having structures (XX and XXI, respectively), to see if he could obtain additional products that showed restricted rotation in their NMR spectra.



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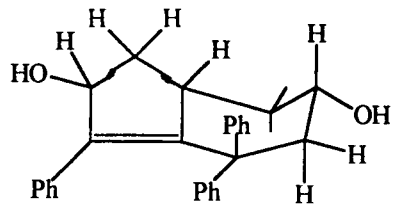

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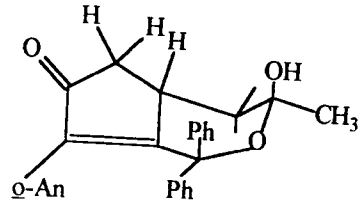

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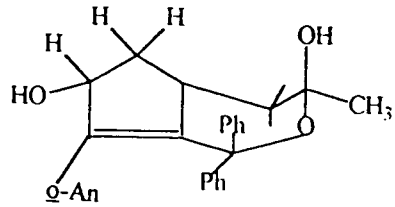

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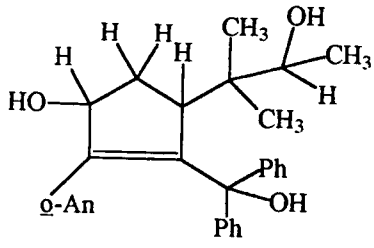

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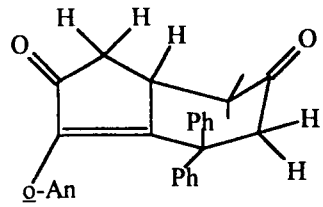

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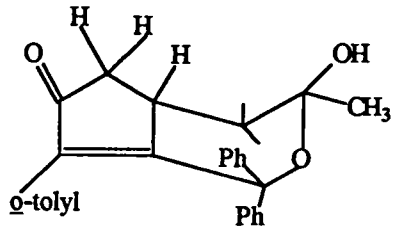
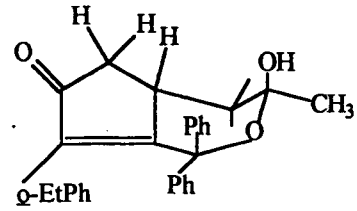


(XX)



(XXI)

B. Introduction to the Problem

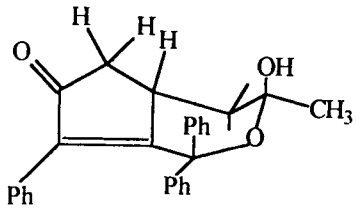
A preliminary report in Tetrahedron Letters is the foundation for the work to be described in this thesis. The purpose of this work is to report any new investigations on the phenyl, *o*-anisyl, *o*-tolyl, and *o*-ethylphenyl oxidation products, and other compounds. Since prior work was done on just the HA-100 and A-60 NMR instruments, a higher resolution NMR study seemed warranted in order to publish the work. This investigation was accomplished utilizing 250 MHz and 400 MHz NMR instruments.

Chapter II

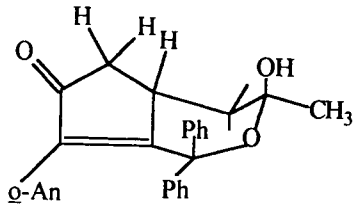
Discussion of Results

A. Oxidation Products and Related Compounds Studied

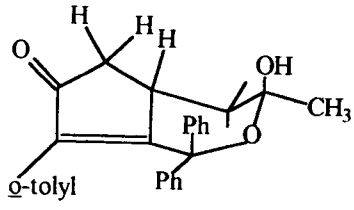
The oxidation products and other compounds, such as their dehydration products, desired for the investigation were either prepared or obtained from previous work. To simplify the reading of this discussion, all of the compounds are listed below and labeled with roman numerals. The compounds will be referred to in the text by shortened names and their appropriate numbers.



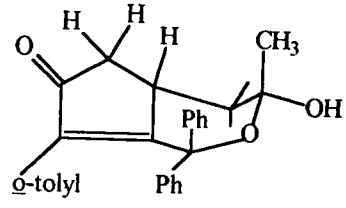
Phenyl oxidation product
(I)



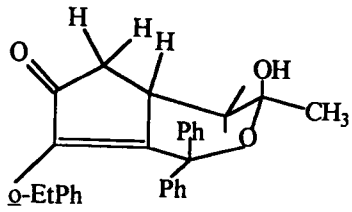
o-anisyl oxidation product
(II)



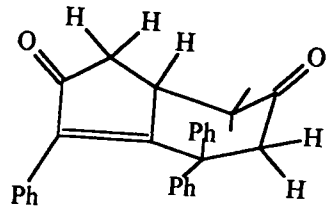
o-tolyl oxidation product
(IIIa)



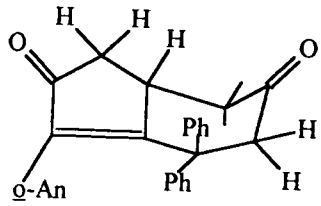
o-tolyl oxidation product
(IIIb)



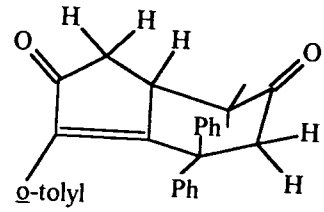
o-ethylphenyl oxidation product
(IV)



phenyl dehydration product
(V)

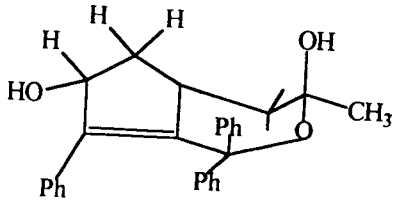


o-anisyl dehydration product
(VI)

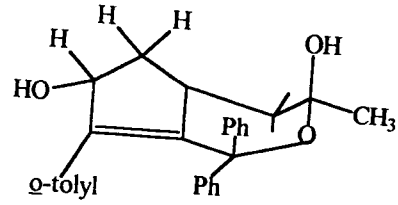


o-tolyl dehydration product
(VII)

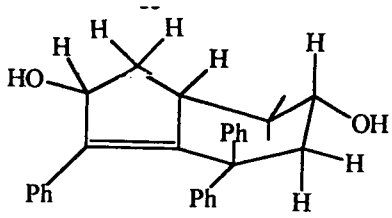
Unidentified product
(IX)



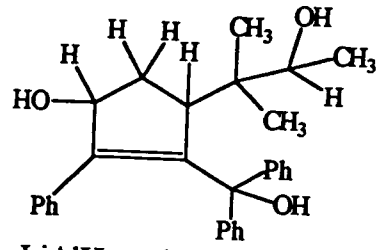
$NaBH_4$ reduction of the
phenyl oxidation product
(VIII)



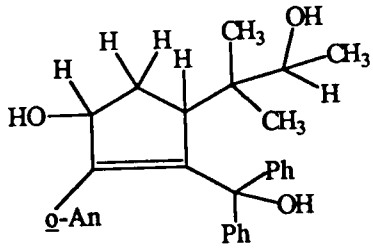
$NaBH_4$ reduction of the
o-tolyl oxidation product
(X)
(major product)



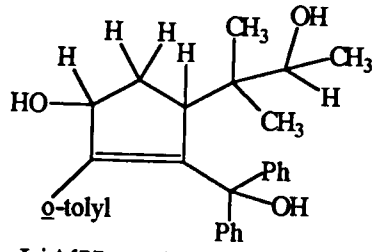
$LiAlH_4$ reduction of the acid catalyzed dehydration product
(XI)



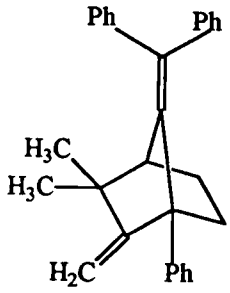
$LiAlH_4$ reduction of the phenyl oxidation product
(XII)



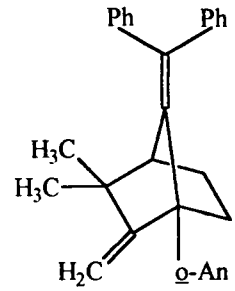
$LiAlH_4$ reduction of the o-anisyl oxidation product
(XIII)



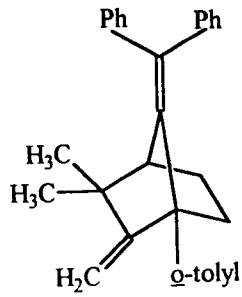
$LiAlH_4$ reduction of the o-tolyl oxidation product
(XIV)
(major product)



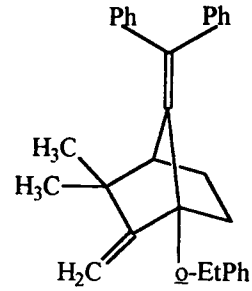
phenyl camphene compound
(XVa)



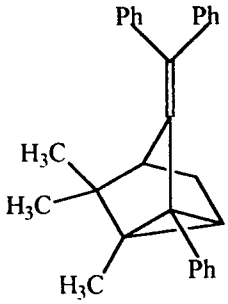
o-anisyl camphene compound
(XVb)



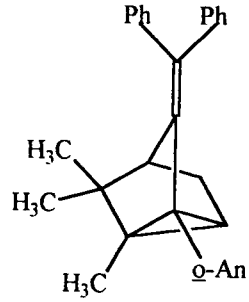
o-tolyl camphene compound
(XVc)



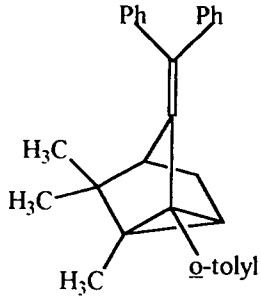
o-ethylphenyl camphene compound
(XVd)



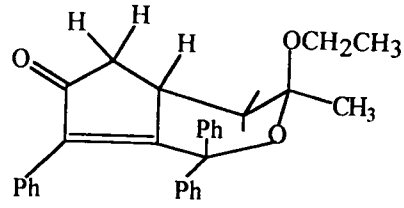
phenyl tricyclene compound
(XVIa)



o-anisyl tricyclene compound
(XVIb)



o-tolyl tricyclene compound
(XVIc)



Cyclic ketal of the
phenyl oxidation product
(XIX)

B. Preparation and NMR Examination of the Oxidation Products and their Derivatives

1. Preparation of Compounds

a. Preparation of the 1-aryl-4,4,5-trimethyl-5-hydroxy-6-oxa-7,7-diphenyl-1-hydrindene-2-ones (oxidation products). The procedure of Aaron[3] in preparing the four oxidation products (phenyl, *o*-anisyl, *o*-tolyl and *o*-ethylphenyl) was followed with minor modifications. The NMR data obtained from the oxidation products will be presented later in this section.

b. Sodium borohydride ($NaBH_4$) reduction of the oxidation products. The procedure of Aaron[3] was used to prepare the $NaBH_4$ reduction products of the phenyl, *o*-anisyl and *o*-tolyl, compounds. The $NaBH_4$ reduction product of the *o*-ethylphenyl compound was not prepared. The NMR data of the three diols studied will appear later in this section.

c. Acid catalyzed dehydration of the oxidation products. The *o*-anisyl, and *o*-tolyl acid catalyzed dehydration products were prepared by a procedure similar to the one Aaron[3] used for the acid catalyzed dehydration of the phenyl oxidation product. The *o*-ethylphenyl acid catalyzed dehydration product was not prepared. The NMR results of the three acid catalyzed dehydration products will be discussed later in this section.

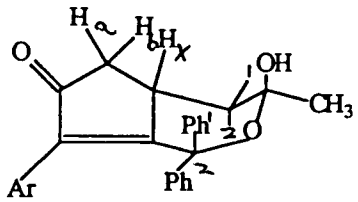
d. Lithium aluminum hydride ($LiAlH_4$) reduction of the oxidation products. For the preparation of the $LiAlH_4$ reduction products of the *o*-tolyl and *o*-anisyl oxidation products a procedure analogous to that used for the preparation of the $LiAlH_4$ reduction product of the phenyl oxidation product was used. The $LiAlH_4$ reduction product of the *o*-ethylphenyl oxidation product was not prepared. NMR data obtained for the three triols will be presented later in this section.

2. NMR discussion

a. Oxidation products and dehydration products. Tables I and II list the chemical shifts for the protons of the oxidation and dehydration products, respectively. A configurational representation of both of these types of compounds is also shown in the tables.

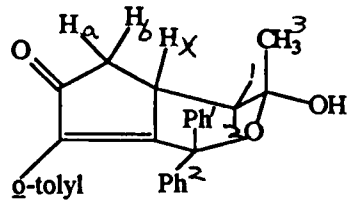
In both the oxidation and dehydration products the chemical shift positions for the protons of the aryl groups (Ar) and the equatorial phenyl group (Ph^2) appear together at a higher field position than those for the axial phenyl (Ph^1) protons. This is expected if one assumes that the preferred orientation of the Ar and Ph^2 is a parallel face-to-face alignment. The parallel planes would then mutually shield each other's hydrogens by the ring current effect.[10] By adopting this alignment there should be a minimal interaction between these two rings. This alignment of the aryl group requires it to be perpendicular to the plane of the five-membered ring.

The bridgehead hydrogen, H_x, appears unusually downfield in the oxidation products (3.67-3.84 ppm). This downfield shift is assumed to be due to the



(I-IV)

TABLE I
CHEMICAL SHIFTS OF THE OXIDATION PRODUCTS

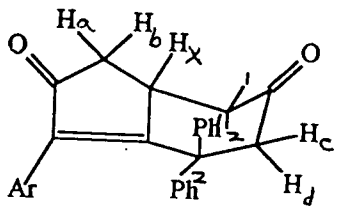


(IIIb)

Chemical Shifts, δ

Compound	Ph^1	Ph^2, Ar	H_x	H_a	H_b	OH	CH_3^1	CH_3^2	CH_3^3	substituent on 2-Aryl
Ar=phenyl or Ph. Oxid. Product (I)	7.30-7.45	6.45-6.85	3.78	2.58	2.38	1.48	1.07	1.18	1.50	----------
Ar=o-anisyl or o-An. Oxid. Product (II)	7.23-7.53	6.39-6.95	3.78 3.67	2.57 2.53	2.54 2.40	1.54 1.73	1.05	1.17[a] 1.13[b]	1.53	3.54[a], 3.38[b] (OCH_3)
Ar=o-tolyl or o-tolyl Oxid. Product. (III)	7.21-7.54	6.61-6.90	3.75[c] 3.84[d]	2.63 2.69	2.44 2.38	1.48 2.08	1.09	1.19	1.54	1.69 (CH_3)
Ar=o-ethyl-phenyl or o-ehtylphenyl Oxid. Pdt. (IV)	7.25-7.54	6.60-6.97	3.82	2.62	2.40	1.56	1.08	1.18	1.54	2.00, 1.90 (CH_2) 0.94 (CH_3)

[a] 53%, [b] 47%, [c] 85%, [d] 15%



(V-VII)

TABLE II
CHEMICAL SHIFTS OF THE DEHYDRATION PRODUCTS

Compound	Chemical Shifts, δ									
	Ph^1	Ph^2, Ar	H_x	H_a	H_b	H_c	H_d	$CH_3{}^1$	$CH_3{}^2$	substituent on 2-aryl
Ar=phenyl or Ph. Dehyd. Product (V)	7.25-7.50	6.50-7.00	3.18	2.58	2.49	3.53	3.32	1.14	1.22	---
Ar=o-anisyl or o-An. Dehyd. Product (VI)	7.25-7.62	6.20-7.00	3.17 3.22	2.56 2.62	2.51 2.43	3.57	3.35	1.09	1.27[a] 1.21[b]	3.62[a] 3.33[b] (OCH_3)
Ar=o-tolyl Dehyd. Product (VII)	7.25-7.50	6.50-6.95	3.58	2.63	2.57	3.54	3.32	1.12	1.24	1.93 (CH_3)

[a] 66%, [b] 34%

electrostatic deshielding effect of the axial OH group and maybe some deshielding by the axial phenyl group (ring current effect). Deshielding by electronegative groups (such as an OH group) has been discussed by Jackman and Sternhell.[11] Comparison of the H_x signals in the oxidation products with those of the dehydration products reveals the deshielding effect of the OH group. In the latter spectra H_x appears between 3.17-3.58 ppm or 0.38 ppm upfield, on the average, from the H_x of the oxidation products.

The methylene protons on the five-membered ring have been assigned the letters A and B. The proton cis to H_x is assigned the letter A and is downfield from the proton trans to H_x which is assigned the letter B. These assignments of the chemical shifts involved in this ABX system will be presented later.

The phenyl oxidation product (I) shows the presence of three non-equivalent methyls at 1.07, 1.18 and 1.50 ppm (Table I). The assignments were made as follows: The equatorial methyl (CH_3^3) is attached to the same carbon as the OH and the oxygen linkage and therefore is assumed to be deshielded by the two electronegative oxygen atoms, causing it to appear the furthest downfield (1.50 ppm). This assignment is supported by the disappearance of the downfield methyl signal in the NMR spectrum of V (Appendix A). With respect to the other two methyls, one is equatorial (CH_3^1) and one is axial (CH_3^2).

The NMR spectrum of the *o*-anisyl oxidation product (II) allows a distinction to be made between CH_3^1 and CH_3^2. In II there are two methoxy methyl signals (3.38 and 3.54 ppm), four other methyl signals (1.05, 1.13, 1.17 and 1.53 ppm) and two OH signals (1.54 and 1.73 ppm). The methoxy has two possible orientations depending on the rotation of the aryl ring. It can be "up" (above the five-membered ring and syn to the axial

phenyl) where it is shielded by the axial phenyl group or it can be "down" (below the plane and orientated away from the axial phenyl) where it is relatively unaffected by the axial phenyl. In the down position the methoxy is sufficiently close to the axial methyl group (CH_3^2) to cause it to be in a different environment than when the methoxy is up. There is no apparent affect on the methoxy by the equatorial phenyl, since models indicate the aryl ring can not rotate clockwise to bring the methoxy past the equatorial phenyl group. In other words, the aryl ring probably flip flops by 180° to go from $-OCH_3$ up to $-OCH_3$ down. Comparison of the chemical shifts of the methyls of the *o*-anisyl oxidation product with those of the other three oxidation products (Table I) indicate that the methyls which absorb at a chemical shift between that of the other two methyls (1.13 and 1.17 ppm) are affected by the methoxy's orientation and therefore are the axial methyls labeled CH_3^2. This leaves the remaining equatorial methyl as the one absorbing at the highest field position (1.05 ppm). Furthermore, the relative intensities of the two methoxy methyl signals and the two signals for the axial methyls (CH_3^2) of the *o*-anisyl oxidation product indicate an approximate 47:53 mixture of the orientations is present at any given time.

Analysis of the NMR spectrum of the oxidation product obtained from the *o*-tolyl tricyclene showed that the product was a mixture of epimers (IIIa and IIIb). Examination of the major product, IIIa, in Table I shows the chemical shifts of the OH and H_x protons to be similar to those of the phenyl oxidation product, I. However, when the CH_3^3 is in a 1,3-diaxial relationship with H_x, different chemical shifts for the OH and H_x protons were obtained. A possible explanation for obtaining this mixture of epimers might be due to the influence of the *o*-CH_3 group on the mode of addition of the OH to the C=O in

closing the methyl ketone to give the cyclic hemiketal.

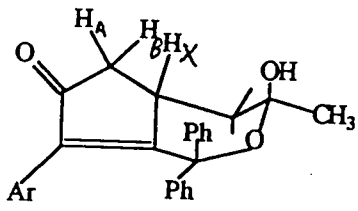
The analysis of the *o*-ethylphenyl oxidation product, (IV), was carried out to see if the system showed restricted rotation. The data in Table I indicate there is no restricted rotation, since only one methyl absorption appears for the methyl portion of the ethyl group on the aryl ring of IV. The CH_2 portion of the *o*-ethyl group in IV appears as a doublet of quartets, which indicate that the two hydrogens of the CH_2 group are experiencing two different environments and are magnetically nonequivalent; in essence they are diastereotopic. Since the CH_3 portion of the ethyl group is unaffected, then the CH_3 must be sufficiently orientated away from the shielding influence of the axial phenyl group. Otherwise the CH_3 would be shielded when the ethyl group is orientated up.

Table III lists the coupling constants for the oxidation and dehydration products. The assignment of the protons on the five-membered ring as H_a, H_b, and H_x has already been mentioned with regard to their chemical shifts. The alphabetical notation of these protons as A, B, and X was made following the designation rules of Pople, Schneider, and Bernstein.[12] Successive letters such as A and B (or C and D in the six-membered system) refer to nonequivalent protons which are separated from A or B (C or D) by a small chemical shift difference (ν_{AB}) compared to the coupling constants (J), and letters such as X or Y refer to protons which are separated from A or B by a large chemical shift difference compared to the coupling constants between X or Y and A or B. Usually successive letters are used for two protons (e.g. H_1 and H_2) when $\nu\ H_1H_2\ /\ J\ H_1H_2$ is less than ten (i.e. ν_{AB}/J_{AB}).

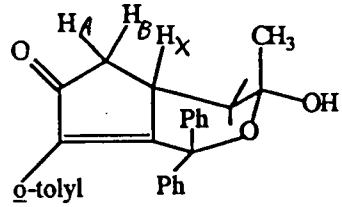
The values for J_{AB}, J_{AX}, and J_{BX} for all four oxidation products (including both ABX systems of the *o*-anisyl and *o*-tolyl oxidation products) are approximately the same

TABLE III

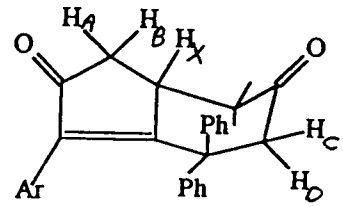
COUPLING CONSTANT OF THE OXIDATION PRODUCTS AND DEHYDRATION PRODUCTS



(I-IV)



(IIIb)



(V-VII)

Coupling Constants, Hz

Compound	J_{AB}	J_{AX}	J_{BX}	J_{CD}
Phenyl oxidation product (I)	19.40	6.50	2.40	-----
o-anisyl oxidation product (II)	19.30 19.30	6.60 6.50	2.50 2.70	-----
o-tolyl oxidation (IIIa) product (IIIb)	19.10 19.10	6.60 6.40	2.50 2.60	-----
o-ethylphenyl oxidation product (IV)	19.50	6.80	2.60	-----
Phenyl dehydration product (V)	19.10	7.20	2.00	14.80
o-anisyl dehydration product (VI)	19.00 19.10	7.10 7.30	1.90 1.70	14.85
o-tolyl dehydration product (VII)	19.00	7.20	2.10	14.80

(Table III). Two ABX systems appeared for the *o*-anisyl oxidation product for the same three protons, (H_a, H_b, and H_x), since these protons experience different magnetic environments depending on the orientation of the methoxy group. Two ABX systems also appeared for the *o*-tolyl oxidation product for the same three protons, (H_a, H_b, and H_x), since the NMR spectrum showed an epimeric mixture to be present.

The dehydration products have an AB system of four lines for the CH_2 group in the six-membered ring, and the chemical shifts of H_c and H_d for this system are listed in Table II. The chemical shift of H_x in the phenyl dehydration product (V) is approximately 0.60 ppm upfield from the H_x of I. Table II also reveals a similar change in chemical shifts of H_x in II versus VI and III (a and b) versus VII. This difference reveals the deshielding effect of the OH group. In the *o*-anisyl dehydration product (VI) the methoxy signals are at 3.33 and 3.62 ppm. Their intensities are in the ratio of 34% to 66%. The axial methyl ($CH_3{}^2$) signals appear at 1.21 and 1.27 ppm and their intensities are in the same ratio as the methoxy signals. Since the 3.33 ppm signal corresponds to the lower intensity ratio, it supports the idea that there is an electrostatic effect between the methoxy protons and the benzene ring. This indicates that the closer the methoxy is to the axial phenyl the more favored is the interaction between the axial phenyl pi electrons and the hydrogens of the methoxy. Hence, if the axial phenyl and the aryl ring move closer together, they should shield the methoxy group to a greater extent. This electrostatic effect is absent in the *o*-tolyl and *o*-ethylphenyl cases, which may be the reason for one CH_3 and one CH_3CH_2 signal, respectively. In addition, the upfield methoxy signal at 3.33 ppm, which is shielded by the axial phenyl group, is for the atropisomer with the methoxy group in the top position. The axial methyl proton with the

smaller intensity at 1.21 ppm indicates it is shielded slightly relative to the orientation when the methoxy is in the up position. Hence, the methoxy moiety in the down position deshields the axial methyl group. This is in agreement with a shielding effect of the same type by the methoxy group of the oxidation product, II. In addition, the chemical shifts of the axial CH_3^2 protons of V and VII are similar to VI, when the methoxy is in the up position. Furthermore the chemical shift for the methoxy in the up position of II and VI reveal the protons in II are further downfield than in VI.

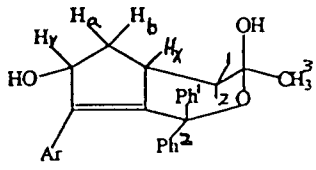
As mentioned earlier, IIIa and IIIb were found to be a mixture of epimers. However, as expected, the *o*-tolyl dehydration product (VII) can not be a mixture of epimers. The 1,3-diaxial relationship of H_x and the OH and CH_3 groups in IIIa and IIIb, respectively, is absent in VII. Thus, there is only one ABX system in VII.

The coupling constants of the phenyl dehydration product, (V), the atropisomers of the *o*-anisyl dehydration product, (VI), and the *o*-tolyl dehydration product, (VII), are all very similar. J_{AX} is slightly larger and J_{BX}slightly smaller in these compounds compared to the oxidation products.

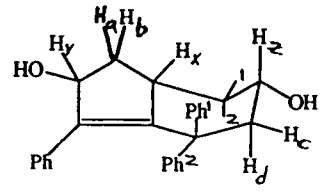
b. Diols and Triols. Table IV lists the chemical shifts for the two diols (VIII and X) obtained by the $NaBH_4$ reduction of the phenyl and *o*-tolyl oxidation products, respectively. Also included is, XI, the $LiAlH_4$ reduction product of the acid catalyzed dehydration product and the three triols (XII, XIII, and XIV) obtained by $LiAlH_4$ reduction of the phenyl, *o*-anisyl, and *o*-tolyl oxidation products. Table V lists the coupling constants for the diols and triols. The reduction of the carbonyl group in the five-membered ring alters the original ABX system present in the oxidation products to an AMXY system in XI and the

TABLE IV

CHEMICAL SHIFTS OF THE DIOLS AND TRIOLS



(VIII, X)

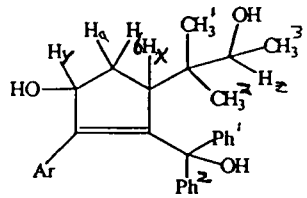


(XI)

Chemical Shifts, δ

Cmpd	Ph¹	Ph², Ar	H_y	H_x	H_a	H_b	OH	CH_3^1	CH_3^2	CH_3^3	H_z	H_c	H_d
VIII	7.20-7.45	6.40-6.90	4.80	3.41	2.49	1.60	1.29, 1.72	0.98	1.22	1.43	—	—	—
X	7.22 7.45	6.60-6.91	4.95	3.41	2.48	1.62	1.74, 4.81	0.98	1.22	1.50, 1.58	—	—	—
XI	7.22-7.60	6.55-6.88	4.83	3.09	2.50	1.68	1.05	1.00	1.15	—	3.62	2.88	2.95
XII	6.85-7.55	6.68-7.55	4.66	3.49	2.42	2.24	1.60, 3.09	0.93	0.68	0.98	4.13	—	—
XIII	6.55-7.55	6.55-7.55	4.39	3.42	2.32	2.27	1.60, 3.16, 5.09	0.90	0.62	1.02	4.31	—	—
XIV	6.45-7.55	6.45-7.55	4.59	3.42	2.39	2.23	1.60, 3.10, 5.00	0.96	0.68	1.02	4.21	—	—

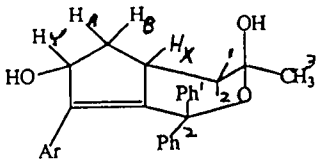
substituent on aryl (Ar) group: X-1.68 ppm (CH3); XIII-3.84 ppm (OCH3); XIV- 1.69 ppm (CH3)



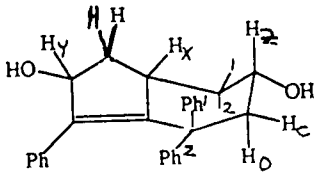
(XII, XIII, XIV)

TABLE V

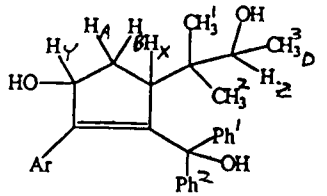
COUPLING CONSTANTS OF THE DIOLS AND TRIOLS



(VIII, X)



(XI)



(XII, XIII, XIV)

Compound	Coupling Constants, Hz								
	J_{AB}	J_{AX}	J_{BX}	J_{AY}	J_{BY}	J_{XY}	J_{CZ}	J_{DZ}	J_{CD}
VIII	13.80	8.70	6.80	8.30	5.40	1.20	-----	-----	-----
X	13.60 13.40	8.75 8.90	6.70 6.60	8.40 8.60	5.20 5.00	1.25 1.30	-----	-----	-----
XI	13.70	8.50	6.50	8.50	5.50	1.20	2.50	3.15	15.50
XII	14.50	7.00	4.10	8.30	0.60	1.10	-----	7.00	-----
XIII	14.60 14.50	7.10 7.20	4.20 4.30	8.20	0.80	1.00	-----	7.00	-----
XIV	14.60 14.40	7.10 7.30	4.20 4.00	8.20 8.10	0.90 1.00	1.00 1.10	-----	7.00	-----

two diols, VIII and X, and an ABXY system in the three triols, XII, XIII, and XIV. For discussion purposes the H_b notation will still be employed, instead of H_m, so as to avoid confusion and make the discussion of these systems more simplified. In addition, a CDZ notation will be used for the hydrogens on the six-membered system of XI in place of the ABX system.

The *o*-tolyl oxidation product mixture theoretically gives four $NaBH_4$ reduction products: (1) the OH is in a 1,3-diaxial relationship with H_x, (2) the CH_3 is in a 1,3-diaxial relationship with H_x, (3) the OH on the five-membered ring is in the axial position with respect to H_x, and (4) the OH on the five-membered ring is in the equatorial position with respect to H_x. It also gives two $LiAlH_4$ reduction products. One would expect only two since the six-membered ring is not retained. The H_a and H_y protons of the *o*-tolyl diol, X, are at approximately the same chemical shifts as the corresponding protons of VIII and XI in Table IV. The H_x protons of the two $NaBH_4$ diols, VIII and X, are deshielded compared to the dehydration products, but are not as deshielded as in the oxidation products. However, the H_x protons of the $LiAlH_4$ diol, XI, appear further upfield (more shielded) than the H_x of VIII, X, and the dehydration products. The H_x protons in the triols, XII, XIII, and XIV, are deshielded with respect to the dehydration products, but again not as much as the H_x of the oxidation products. Presumably it is the axial OH group on the six-membered ring of VIII, X, and the oxidation products as well as the OH^1 on the triols that are responsible for the variance in the chemical shift of H_x. Jackman and Sternhell[11] cite references which contain examples of both shielding and deshielding of adjacent protons by hydroxy groups. The degree of this shielding or deshielding is dependent on the orientation of the C-O-H bond and

the nonbonded electrons on the O atom. The chemical shift positions of H_x in VIII, X, XII, XIII, and XIV compared with the dehydration products, where the OH is absent, seem to be in agreement with the ability of an OH group to have both a shielding and deshielding ability. Shielding and deshielding of this type has been reported by Emsley, Feeney, and Sutcliffe.[13] The shielding of H_a and H_b is not as large in the triols, XII, XIII, and XIV, compared with the oxidation and dehydration products since the aryl groups in these compounds are not being forced by a phenyl group to be perpendicular to the plane of the 5-membered ring. In addition, since the oxidation and dehydration products contain a carbonyl group on the 5-membered ring, it may also contribute to the change in chemical shifts of H_a and H_b.

The spectra of IX and those of the $NaBH_4$ and $LiAlH_4$ reductions of the *o*-anisyl dehydration product show elimination of the methoxy methyl group. These compounds were not analyzed in detail since the structures were not identified. Hence, little additional spectral information could be obtained. A possible reason for the elimination of the methoxy methyl group might be due to steric interactions between it and one of the phenyl groups. However, the spectrum of the $LiAlH_4$ reduction of the *o*-anisyl oxidation product, XIII, shows one methoxy signal appearing at 3.84 ppm. This indicates that the further the methoxy is from the phenyl groups the less is the interaction between the phenyl pi electrons and the hydrogens of the methoxy. Hence, the steric effect between the methoxy group and the phenyl groups has been minimized. Since, the hemiketal ring is no longer fused, the two phenyl groups can move away from the aryl group to allow this ring to rotate more freely. The chemical shift of the methoxy group in XIII, 3.84 ppm, is considerably downfield (appearing 0.46-0.51 ppm downfield) from the methoxy protons, in the up position, in II and VI.

Furthermore, the aryl protons appear further downfield in the phenyl triol, XII, the *o*-anisyl triol, XIII, and the *o*-tolyl triol, XIV in comparison with the three diols and the oxidation and dehydration products. This indicates that these rings are no longer shielding each other's protons as much as they were in the oxidation and dehydration products. In addition, one of the methyl groups in XII, XIII, and XIV appears at 0.68, 0.62, and 0.68 ppm, respectively. These chemical shifts are considerably further upfield from the methyl signals of all the other compounds in this section. This suggests that one of the two phenyl systems is aligned toward one of these methyl groups, an alignment not allowed when the hemiketal ring is present.

C. Preparation and Spectral Properties of the 2-aryl-3-diphenylmethylenecamphenes and tricyclenes

1. Preparation of the 2-aryl-3-diphenylmethylenecamphenes and tricyclenes.

The phenyl, *o*-anisyl, and *o*-tolyl camphene and tricyclene products were prepared by the procedure of Kleinfelter[14] with minor modifications. It was deemed unnecessary to analyze the *o*-ethylphenyl camphene and tricyclene mixture since the spectrum was too complicated to obtain any significant spectral information.

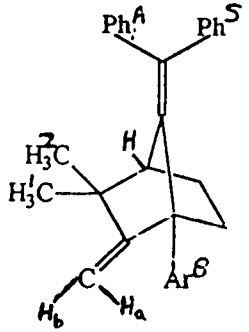
2. Spectral Properties of the 2-aryl-3-diphenylmethylenecamphenes and tricyclenes.

With Aaron's[3] spectroscopic proof for the reassignment of the camphene (IV) and tricyclene (III) products, (ch. I, pg. 1), Kleinfelter[14] was able to analyze the NMR

spectra of III, IV, and related camphene and tricyclene-type compounds and allocate the chemical shifts and the preferred orientations of the phenyl rings in III and IV. He concluded that the absorptions at 6.83 and 6.69 ppm were for the 1-phenyl and 7-syn-phenyl hydrogens of IV and the absorptions at 6.78 and 6.70 ppm were for the 1-phenyl and 7-syn-phenyl hydrogens of III. In both III and IV there is mutual shielding of the 1-phenyl and 7-syn-phenyl protons in a preferred face-to-face alignment of the rings. Apparently, as evidenced by a single, narrow, sharp NMR line for each of these rings, this face-to-face alignment and a smaller pi-orbital interaction exist in the tricyclene (III). However, the camphene (IV), in order to partially relieve the pi-orbital interactions present, shows some distortion of these rings, thereby causing a broader NMR signal for the hydrogens of each of these phenyls with some of the hydrogens of one ring experiencing a different degree of diamagnetic shielding from the other benzene ring.

Table VI lists some of the nmr spectral data for the phenyl (XVa), *o*-anisyl (XVb), *o*-tolyl (XVc), and *o*-ethylphenyl (XVd) camphene compounds. A comparison of the vinyllic hydrogen signals for XVa versus XVb, XVc, and XVd shows that something has affected the vinyllic proton labeled a in XVb, XVc, and XVd causing it to be shifted upfield by approximately 0.08, 0.11, and 0.15 ppm, respectively. This is presumably due to the *o*-methoxy, *o*-methyl, and *o*-ethylphenyl groups activating the benzene ring, thus increasing the shielding effect more than a phenyl group.

Table VII lists some of the nmr spectral data for the phenyl, *o*-anisyl and *o*-tolyl tricyclenes, XVIa, XVIb, and XVIc, respectively. The chemical shifts of the two phenyl groups on the carbon-carbon double bond, the 1-phenyl hydrogen, the three methyl groups,



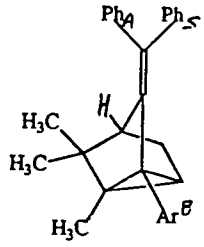
(XV)

TABLE VI
CHEMICAL SHIFTS OF THE 2-ARYL-3-DIPHENYLMETHYLENECAMPHENES

Compound	Chemical Shifts, δ							
	Phenyl^{A}	Phenyl^{B}	Phenyl^{S}	$CH_3{}^1$	$CH_3{}^2$	$=CH_2$	4-H	substituent on 2-aryl
Ar=Ph. camphene (XVa)	7.24	6.77	6.68	1.19	1.43	4.64^{a}, 4.00^{b}	2.43	------
Ar=o-anisyl camphene (XVb)	7.18	------	6.71	1.26	1.41	4.56^{a}, 4.06^{b}	2.45	3.39 (OCH_3)
Ar=o-tolyl camphene (XVc)	7.22	------	6.72	1.21	1.41	4.53^{a}, 4.07^{b}	2.44	2.01 (CH_3)

^{A} 7-anti-phenyl, ^{B} 1-bridgehead phenyl, ^{S} 7-syn-phenyl

* The NMR spectra of the o-ethylphenyl camphene/tricyclene mixture showed the protons of the $=CH_2$ group to be at 4.49^{a} and 4.09^{b}.



(XVI)

TABLE VII
CHEMICAL SHIFTS OF THE 2-ARYL-3-DIPHENYLMETHYLENETRICYCLENES

	Chemical Shifts, δ					
Compound	Phenyl[A]	Phenyl[B]	Phenyl[S]	CH_3's	4-H	substituent on 2-aryl
Ar=Ph. Tricyclene (XVIa)	7.24	6.77	6.68	0.79, 0.89, 1.32	2.19	------
Ar=o-anisyl tricyclene (XVIb)	7.18	------	6.71	0.78, 0.92, 1.37	2.23	3.39 (OCH_3)
Ar=o-tolyl tricyclene (XVIc)	7.22	------	6.72	0.83, 0.96, 1.38	2.28	1.98 (CH_3)

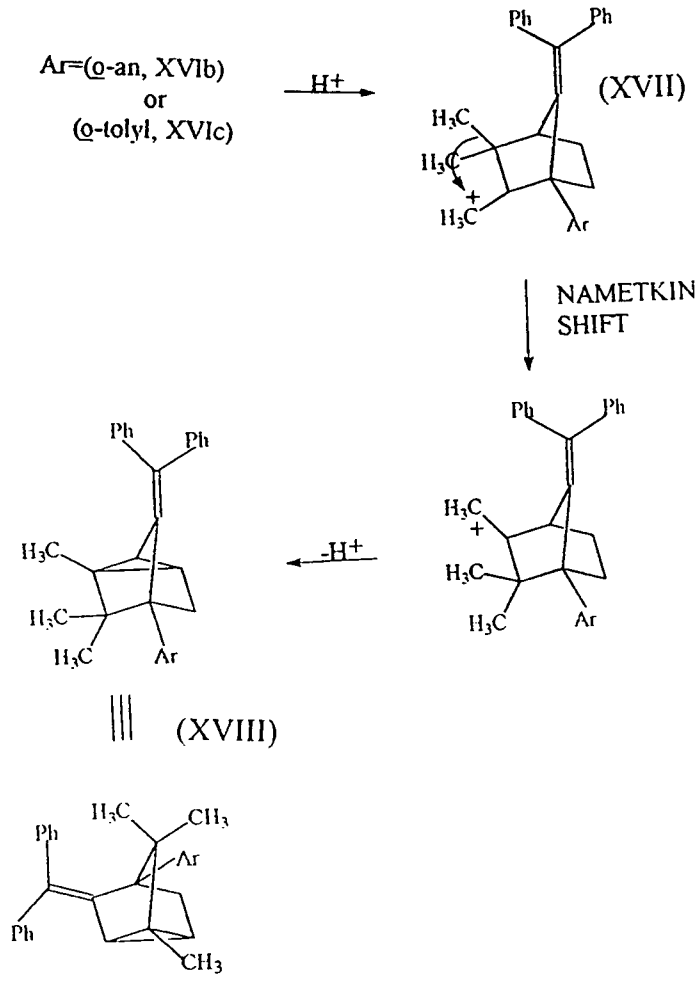
[A] 7-anti-phenyl, [B] 1-bridgehead phenyl, [S] 7-syn-phenyl

and the bridgehead hydrogen on XVIa are approximately the same as previously reported.[13] Table VII shows similar chemical shifts of the two phenyl groups on the carbon-carbon double bond and the three methyl groups for XVIa, XVIb and XVIc. However, the methoxy and methyl groups on XVIb and XVIc, respectively, appear to deshield the bridgehead proton causing it to appear further downfield than in XVIa. In addition the bridgehead hydrogen in the camphene compounds appears further downfield than in the tricyclene compounds. Presumably the C=C bond deshields the bridgehead hydrogen. The phenyl groups at 6.71 and 6.72 ppm are the 7-syn-phenyls which are presumably aligned face-to-face with the *o*-anisyl and *o*-tolyl groups, respectively. Absorptions indicative of another isomer being present appear in the spectra of XVIb and XVIc. In the *o*-anisyl compound, (XVIb), single, narrow absorption lines at 0.79, 0.94, 1.41, and 3.61 presumably represent the three methyl groups and the *o*-anisyl methoxy group in this other isomer. In addition, in the *o*-tolyl (XVIc) compound single, narrow absorption lines at 0.93, 1.11, 1.18, and 2.01 ppm presumably represent the three methyl groups and the *o*-tolyl methyl group in this other isomer.

Considering the chemical shifts of the other isomer, earlier work by Nametkin[14], and related work described by Berson,[21] most probably a Nametkin-type (vicinal methyl group shift) rearrangement of the original cation (XVII) takes place to give another tricyclene-type isomer (XVIII) as shown in Scheme 2.

Structure XVIII represents the only other tricyclene structure possible in this system. An exact replica of XVIII results if a Wagner-Meerwein shift occurs after the Nametkin shift but before loss of the proton. The possible effect of longer reaction times on the ratio of XVIc to XVIII was observed by Weichert[9]. He found that XVIII was obtained

SCHEME 2:



in a higher ratio with extended reaction times. This change in preference shows that while XVIc is thermodynamically preferred to the corresponding camphene-type compound, tricyclene XVIII is presumably preferred thermodynamically over XVIc.

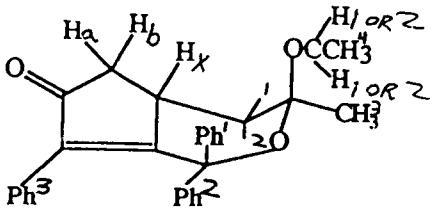
As mentioned earlier, II, (Ch.1, pg.1), in acid media proceeds to the camphene compound,IV, (Ch.I, pg.1) and the tricyclene compound,III, (Ch.I, pg.1). The relative percentages of these two hydrocarbons depend on the acid strength and reaction

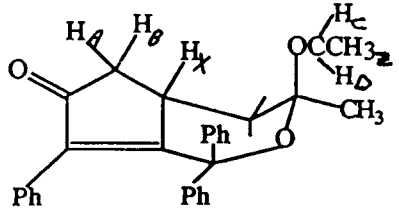
time. Brief heating with trichloracetic-acetic acid mixtures gives largely the camphene compound while the tricyclene compound predominates from heating the camphene compound with trichloroacetic acid for several hours or refluxing with acetic acid alone for twenty-four hours or more. These procedures are superior to the method reported earlier involving heating with $KHSO_4$.

D. NMR Examination of the Cyclic Ketal

Isolation of the cyclic ketal (XIX) has been achieved. Table VIII lists the chemical shifts for the protons of this compound. The same ABX notation used for the oxidation products was employed for XIX. Comparison of the spectrum of the phenyl oxidation product (I) with the spectrum of XIX reveals similar chemical shifts for the protons, H_a and H_b. The H_a and the H_b proton appear at 2.61 and 2.40 ppm compared to 2.58 and 2.38 ppm for I. The H_x proton of XIX, however, has a significantly different chemical shift than I. The bridgehead hydrogen, H_x, of XIX appears at 4.01 ppm but at 3.78 ppm for I. This downfield shift of Hx in XIX compared to I is presumably due to the electrostatic deshielding effect of the axial ethoxy group. Silverstein, Bassler and Morrill[17] present cyclohexane ring structures that reveal an electrostatic deshielding effect of an alkoxy substituent on a hydrogen in a 1,3-diaxial relationship. The chemical shift of the CH_3 (on the -OEt) is 0.20 ppm. When this chemical shift of the CH_3 (on the -OEt) is compared with that for the CH_3's in diethylether (1.15 ppm), a difference of 0.95 ppm is seen. The CH_3 on the (-OEt) in the ketal is affected by the axial phenyl (ring current effect).[6] Since the methylene protons of the -OEt group are

TABLE VIII
CHEMICAL SHIFTS AND COUPLING CONSTANTS OF THE CYCLIC KETAL
OF THE PHENYL OXIDATION PRODUCT





Chemical Shifts, δ

Ph^1	Ph^2, Ph^3	H_x	H_a	H_b	$CH_3{}^1$	$CH_3{}^2$	$CH_3{}^3$	CH^1-CH^2	$CH_3{}^4$
7.30-7.43	6.30-6.95	4.01	2.61	2.40	1.09	1.18	1.48	2.95-3.35	0.20

Coupling Constants, Hz

J_{AB}	J_{AX}	J_{BX}	J_{CD}	J_{CZ}	J_{DZ}
19.50	6.50	2.40	8.00	6.50	6.50

diastereotopic, decoupling by irradiation at the CH_3 portion revealed geminal coupling of 8.0 Hz. In addition, the coupling constants J_{AB}, J_{AX}, and J_{BX} are reported in Table VIII.

E. NMR Examination of the Epoxide Intermediate

The conversion of IV (Ch. 1, pg. 1) to the phenyl oxidation product, I, presumably involves the epoxide, XI (Ch. 1, pg. 5), since XI also gives I when it reacts with chromium trioxide in acetic acid. Epoxide formations in the reactions of hindered olefins with chromic acid are known.[18] The NMR spectrum of the epoxide revealed fifteen aromatic hydrogens as multiplets between 6.70-7.60 ppm. Two methylene hydrogens appeared at 2.14 and 1.82 ppm. In addition, the 4-bridgehead hydrogen absorbed at 2.16 ppm, the tricyclene ring hydrogen at 1.22 ppm, and the nine methyl hydrogens at 1.38, 1.05, and 0.85 ppm.

Chapter III

Experimental

All NMR spectra obtained in this work were run on the Bruker AC 250 MHz spectrometer. In addition, some spectra were run on the Bruker AMX 400 MHz spectrometer. Both instruments were calibrated with trimethylsilane (TMS, δ=0 ppm) and chloroform-d (δ= 7.24 ppm) which were used to determine chemical shifts. Chemical shifts were reported in ppm, δ, downfield from TMS. To aid in the interpretation of some of the spectra, the samples were shaken with deuterium oxide, D_2O, to remove the OH absorption. MestRe-C, Magnetic Resonance Companion, a NMR data processing program, version 1.1.1, for Windows 95 was used to determine the coupling constants of all the compounds. This program was presumably accurate to ±0.02 Hz.

Three new compounds have been prepared since Weichert's work. They are the cyclic ketal (XIX), obtained by John Chaney in the summer of 1991, and the *o*-tolyl triol (XIV) and the *o*-tolyl acid-catalyzed dehydration product (VII) prepared by D.C. Kleinfelter. Experimental procedures for the latter two compounds were similar to those reported originally by Weichert.[9] Since these compounds were not prepared by the author of this thesis, physical properties, yields, etc. are not reported.

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LIST OF REFERENCES

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APPENDIX

Supplementary NMR Spectra

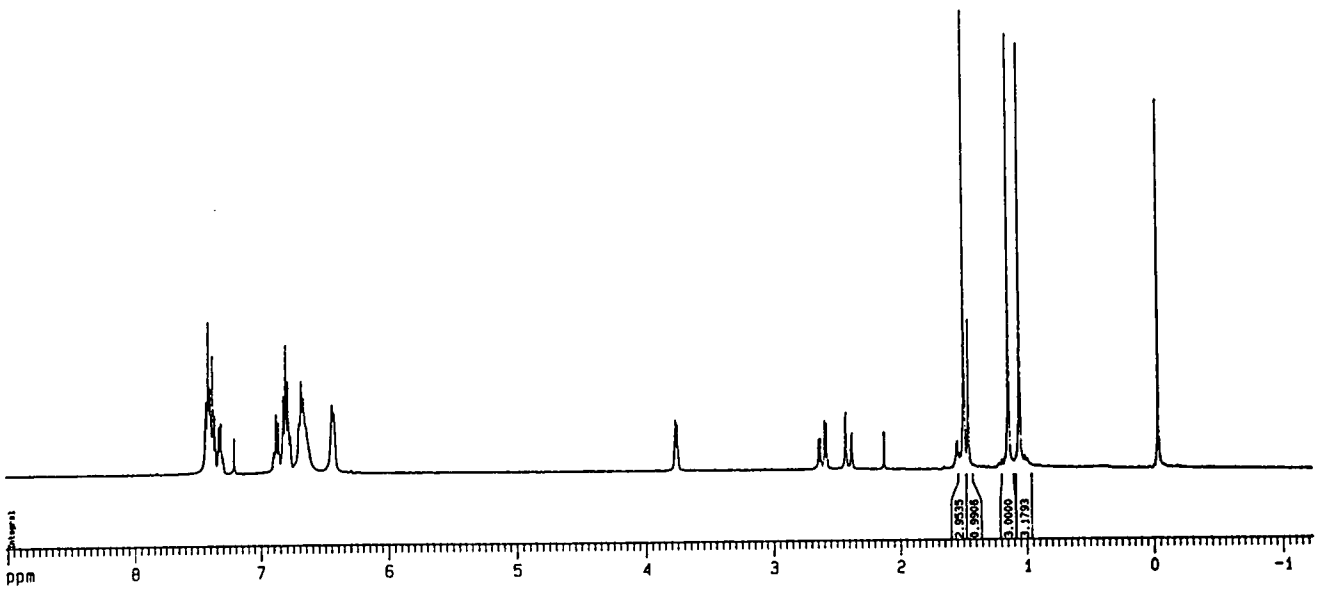

Figure 1: Phenyl oxidation product, (I)

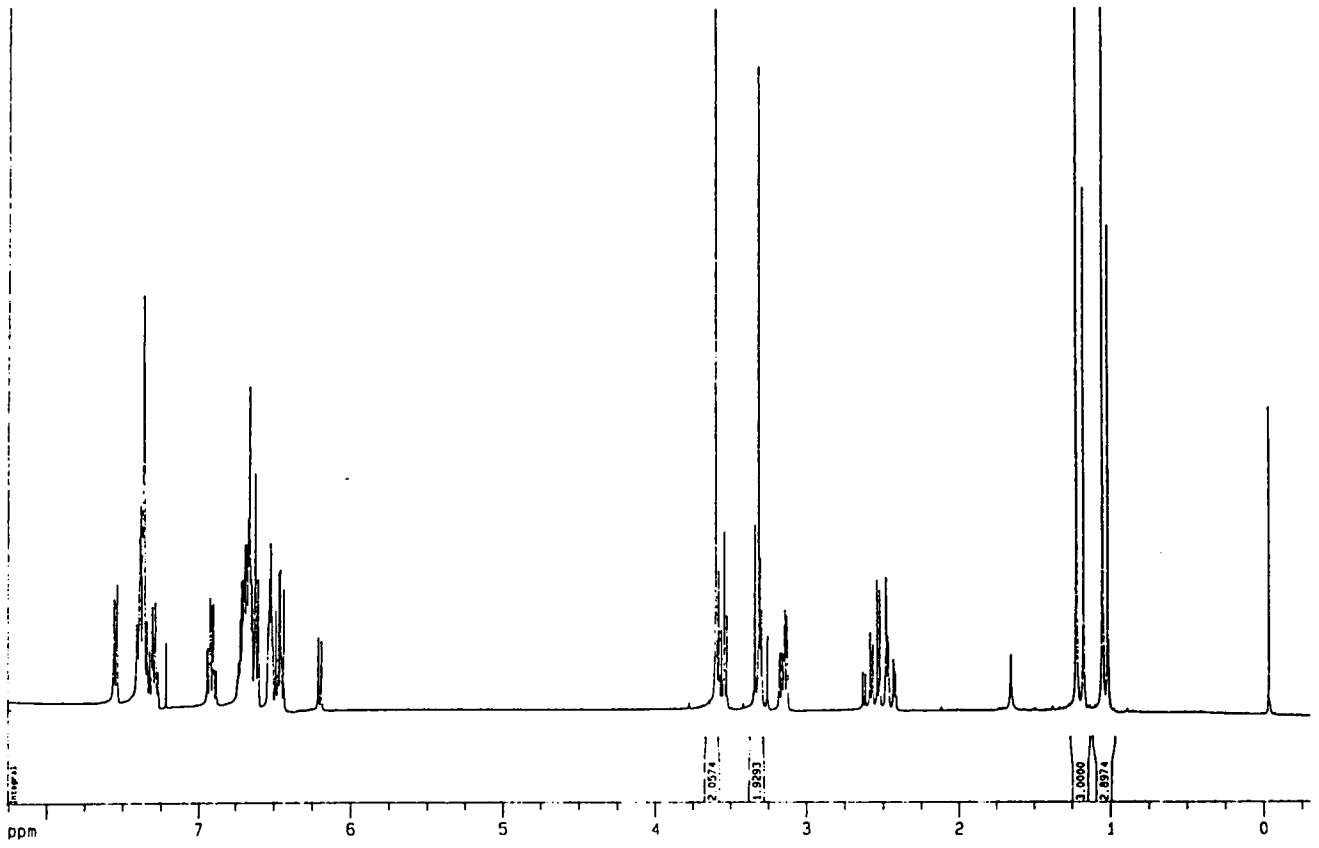

Figure 2: o-anisyl oxidation product, (II)

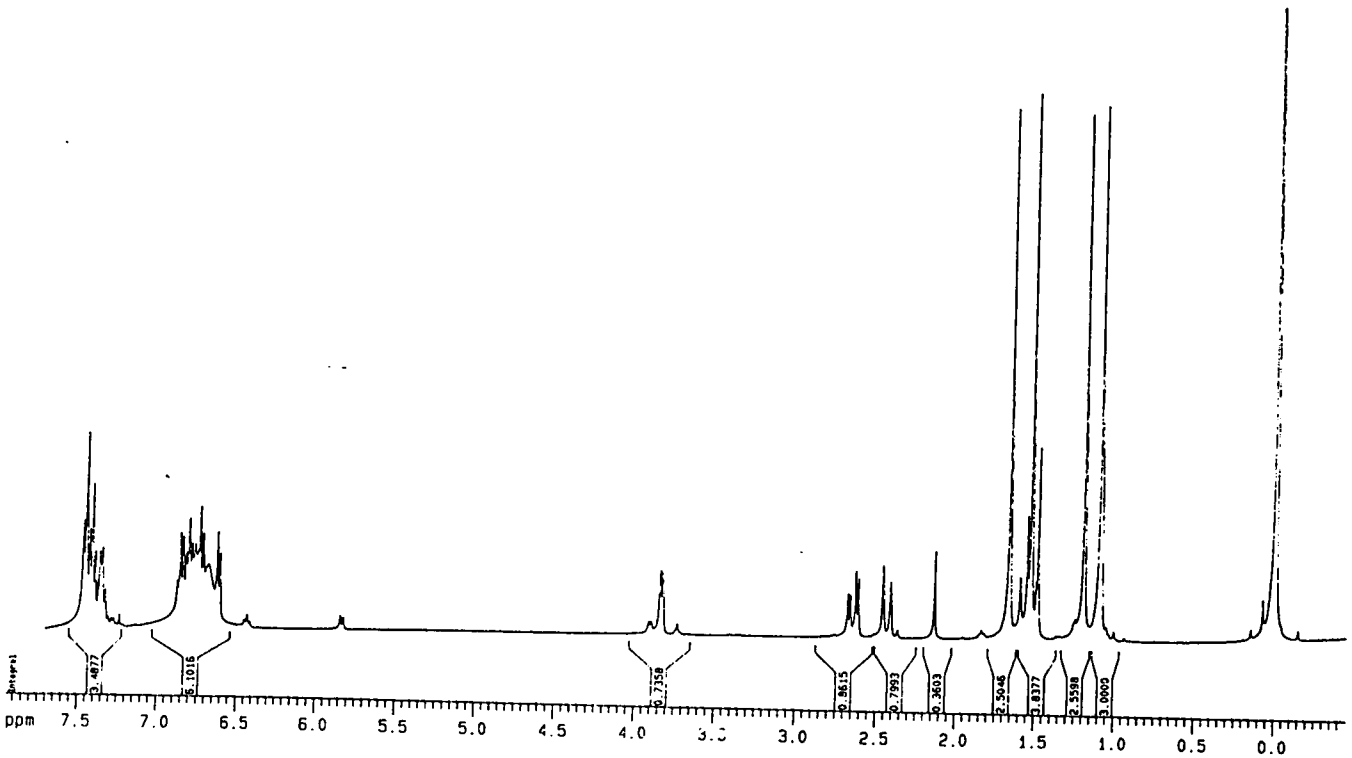

Figure 3: o-tolyl oxidation product, (III)

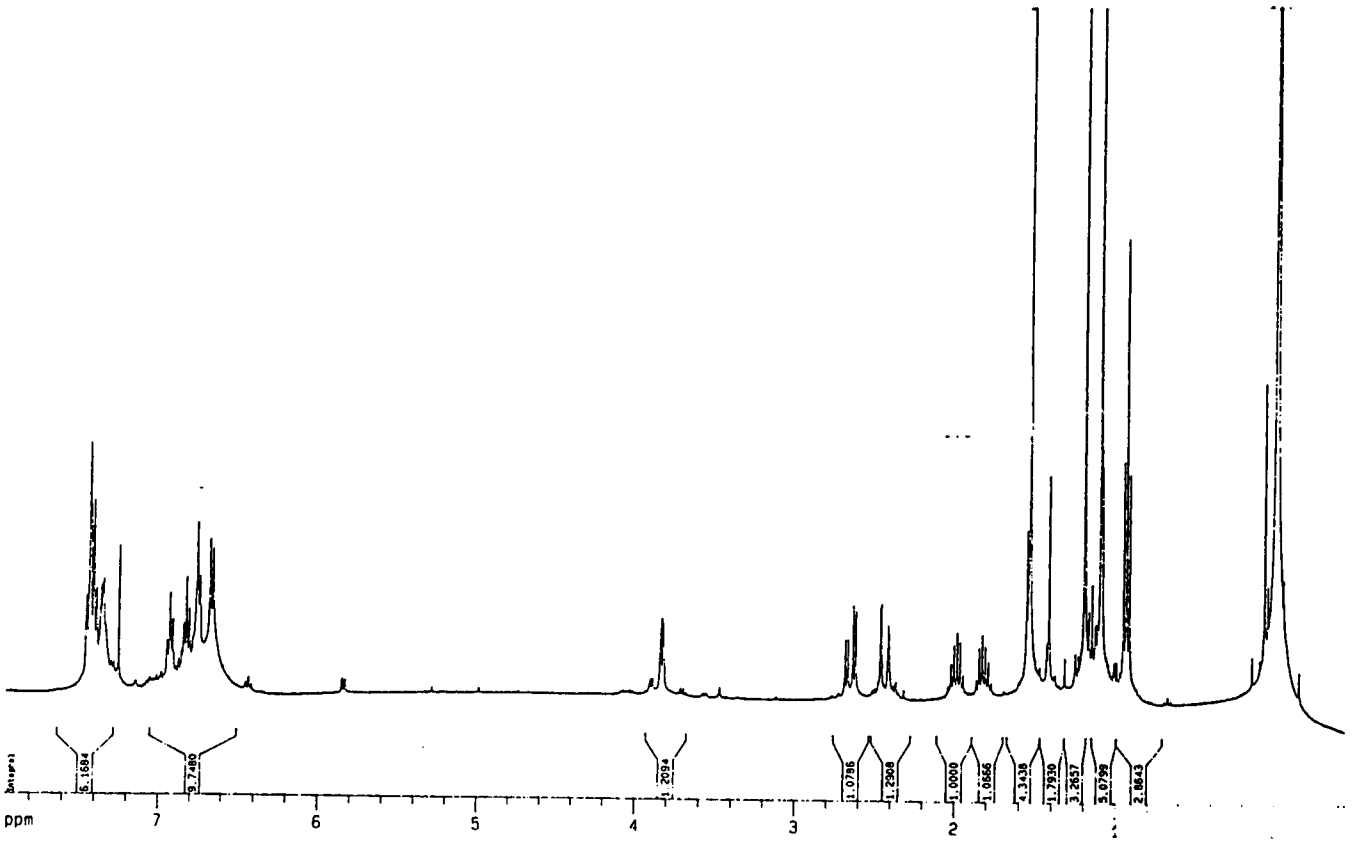

Figure 4: o-ethylphenyl oxidation product, (IV)

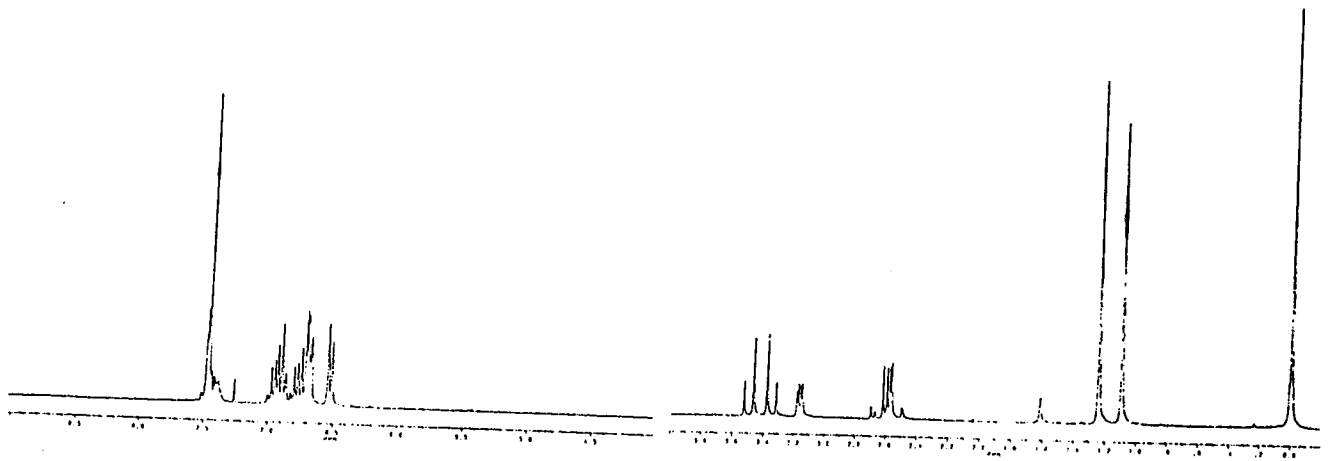

Figure 5: phenyl dehydration product, (V)

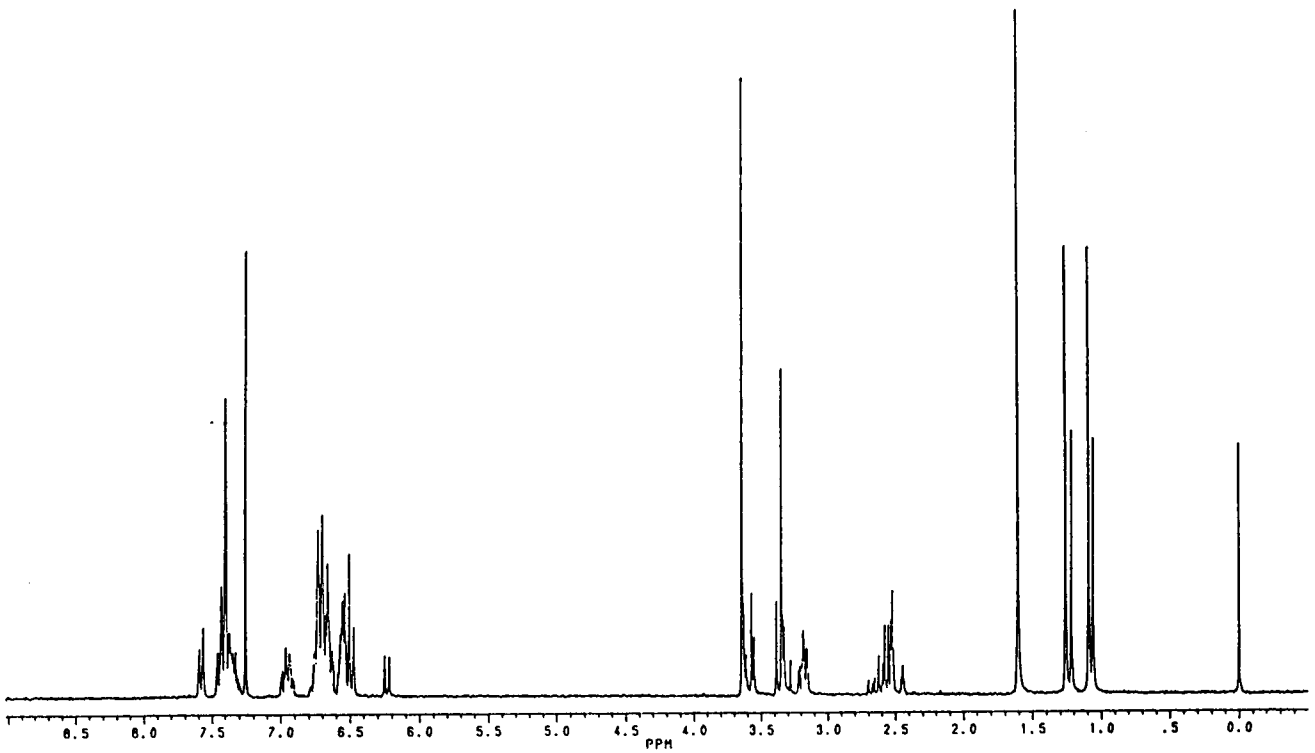

Figure 6: o-anisyl dehydration product, (VI)

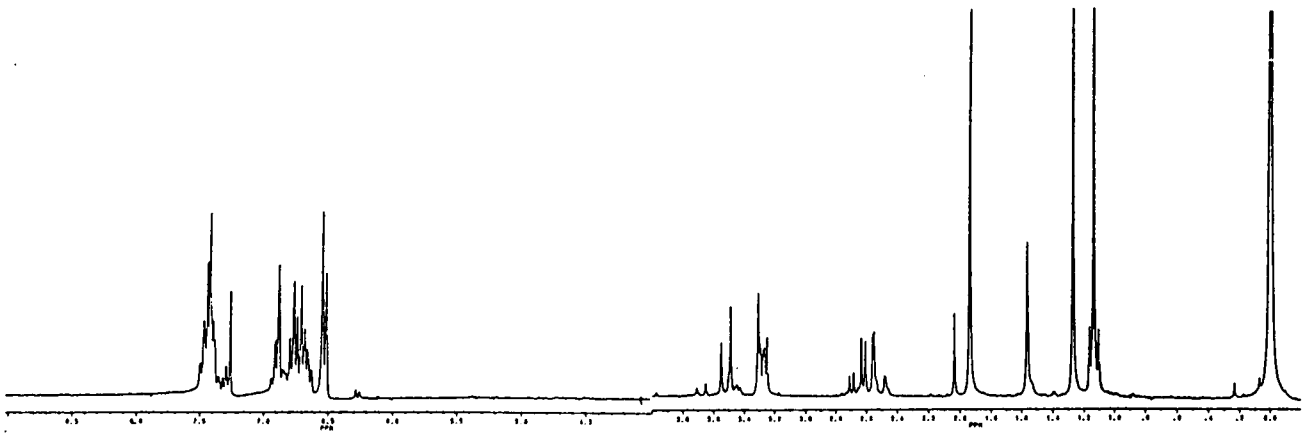

Figure 7: o-tolyl dehydration product, (VII)

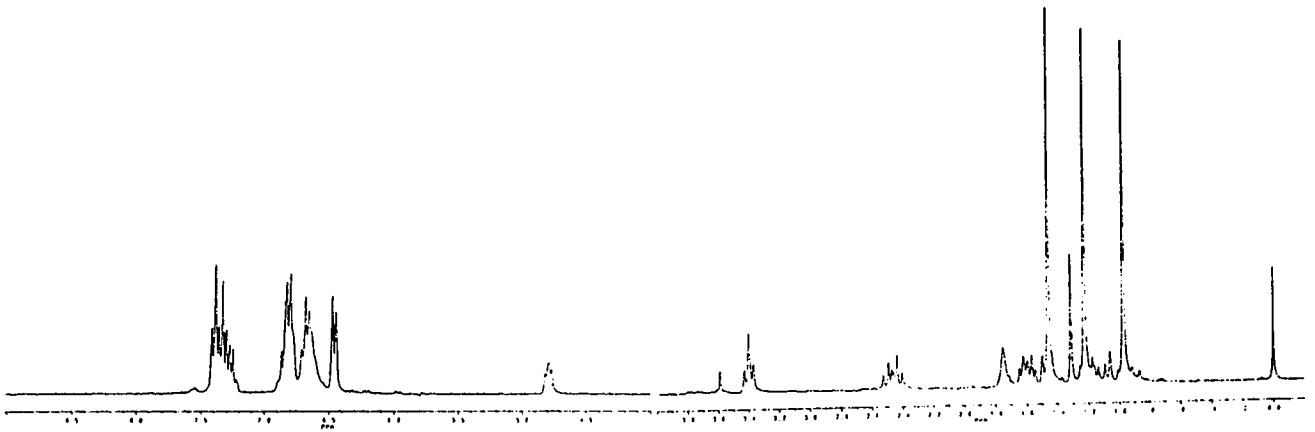

Figure 8: phenyl diol (VIII)

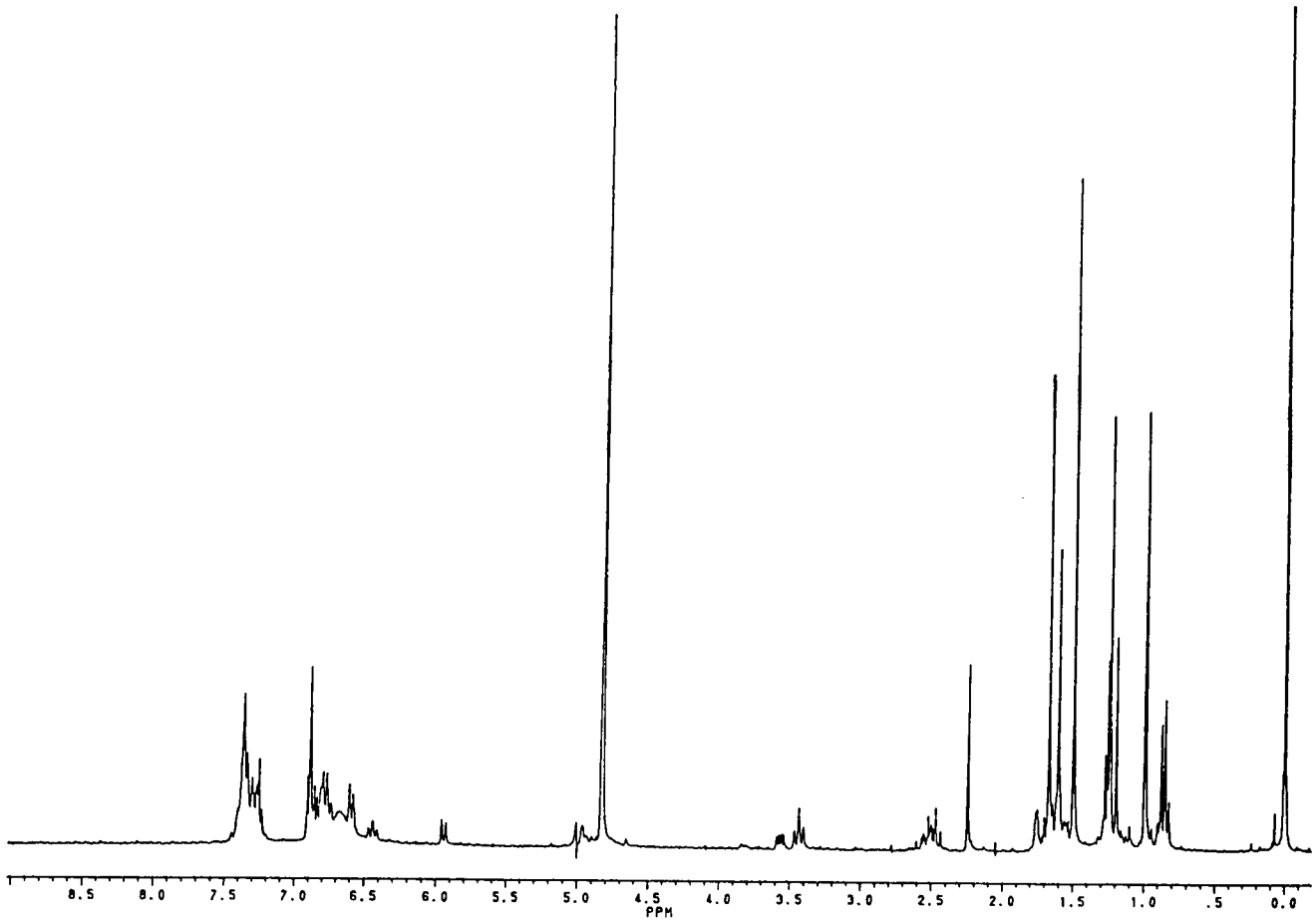

Figure 9: o-tolyl diol (X)

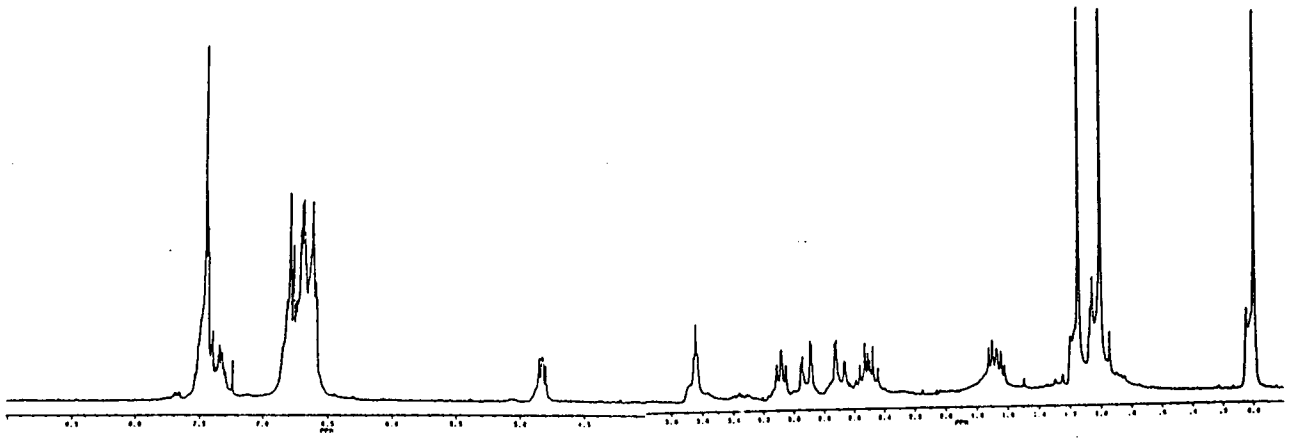

Figure 10: LiAl4 reduction of the acid catalyzed dehydration product, (XI)

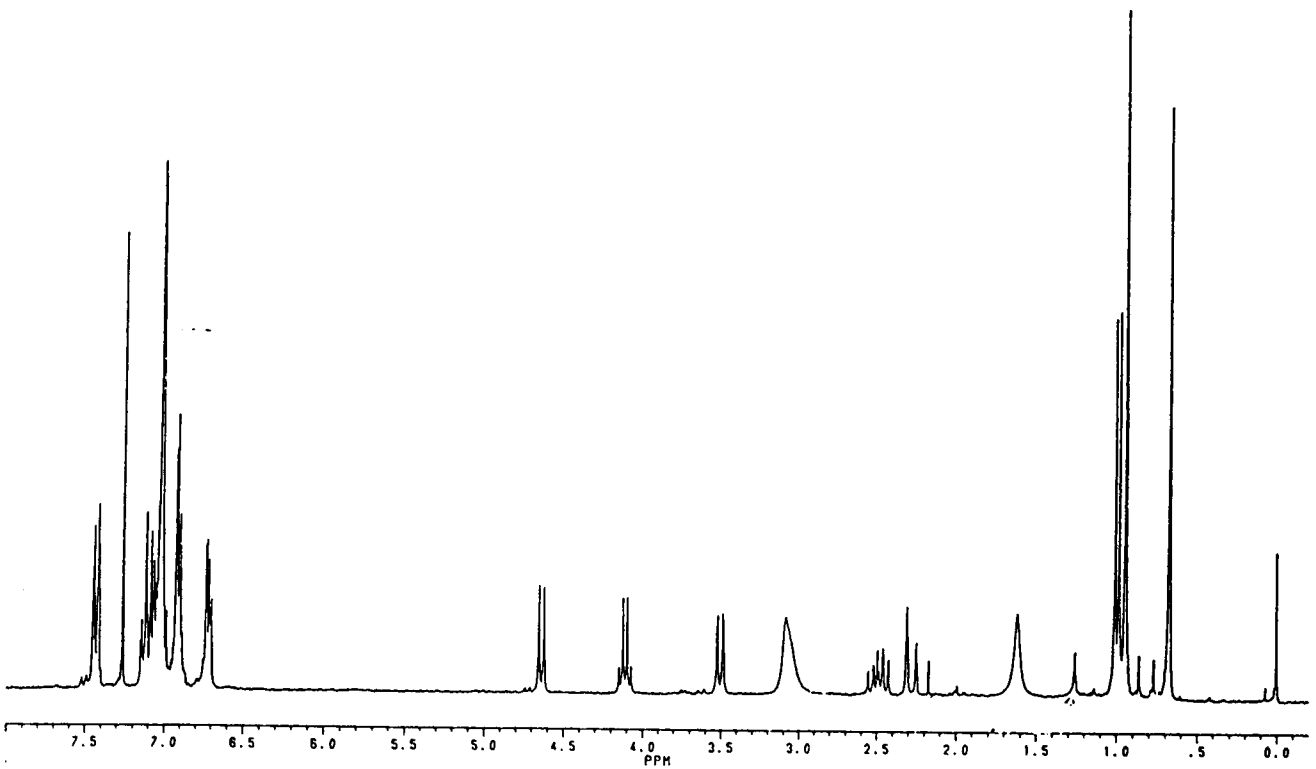

Figure 11: phenyl triol, (XII)

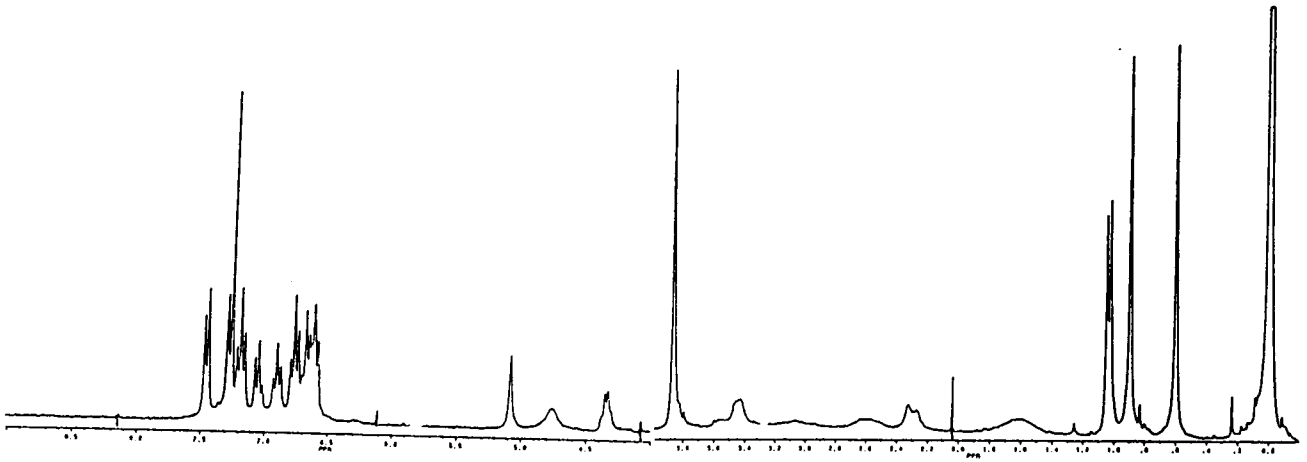

Figure 12: o-anisyl triol, (XIII)

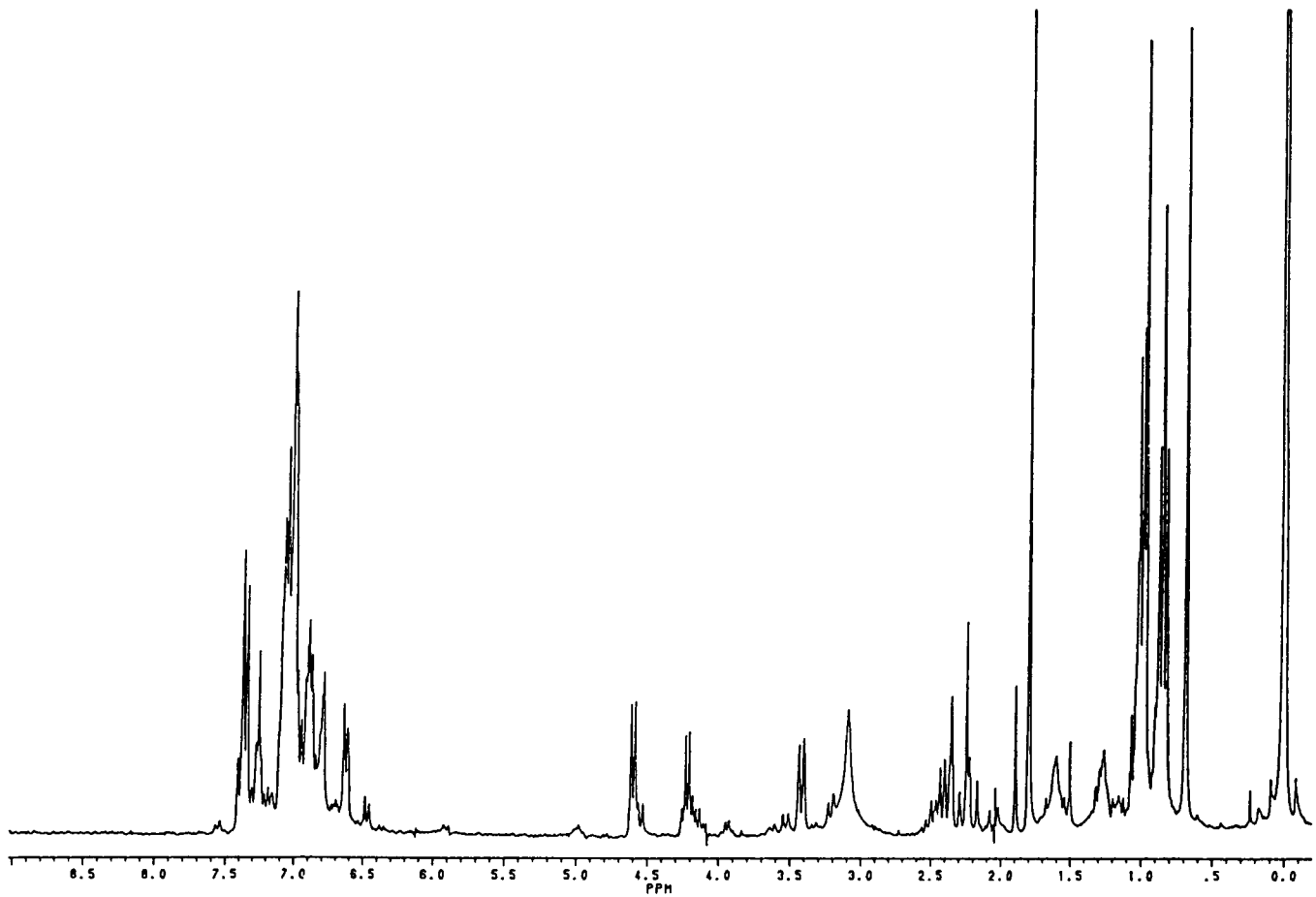

Figure 13: o-tolyl triol, (XIV)

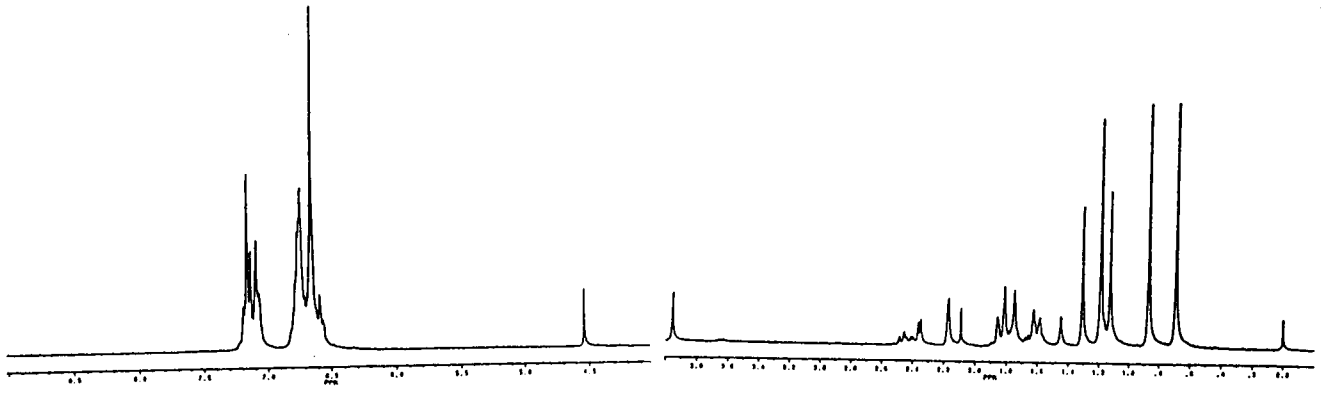

Figure 14: phenyl tricyclene mixture

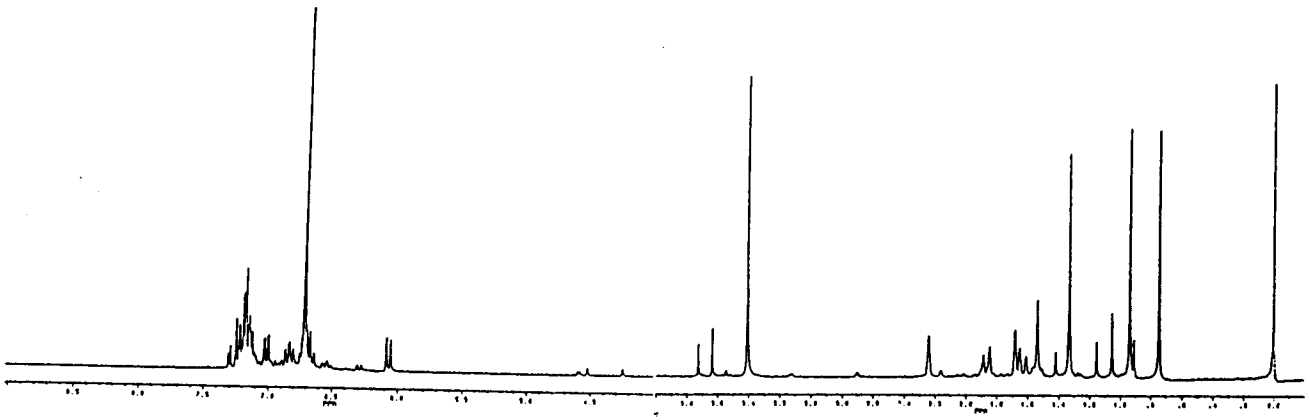

Figure 15: o-anisyl tricyclene mixture

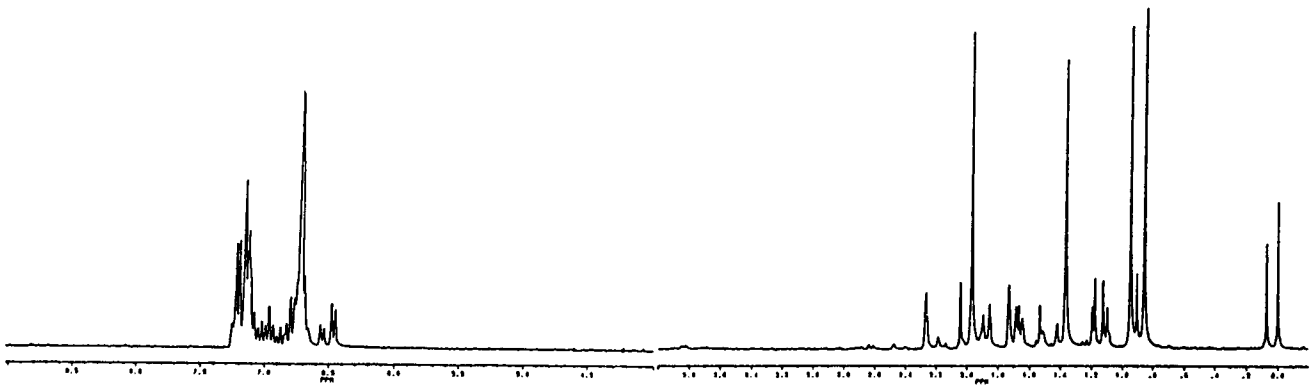

Figure 16: o-tolyl tricyclene mixture

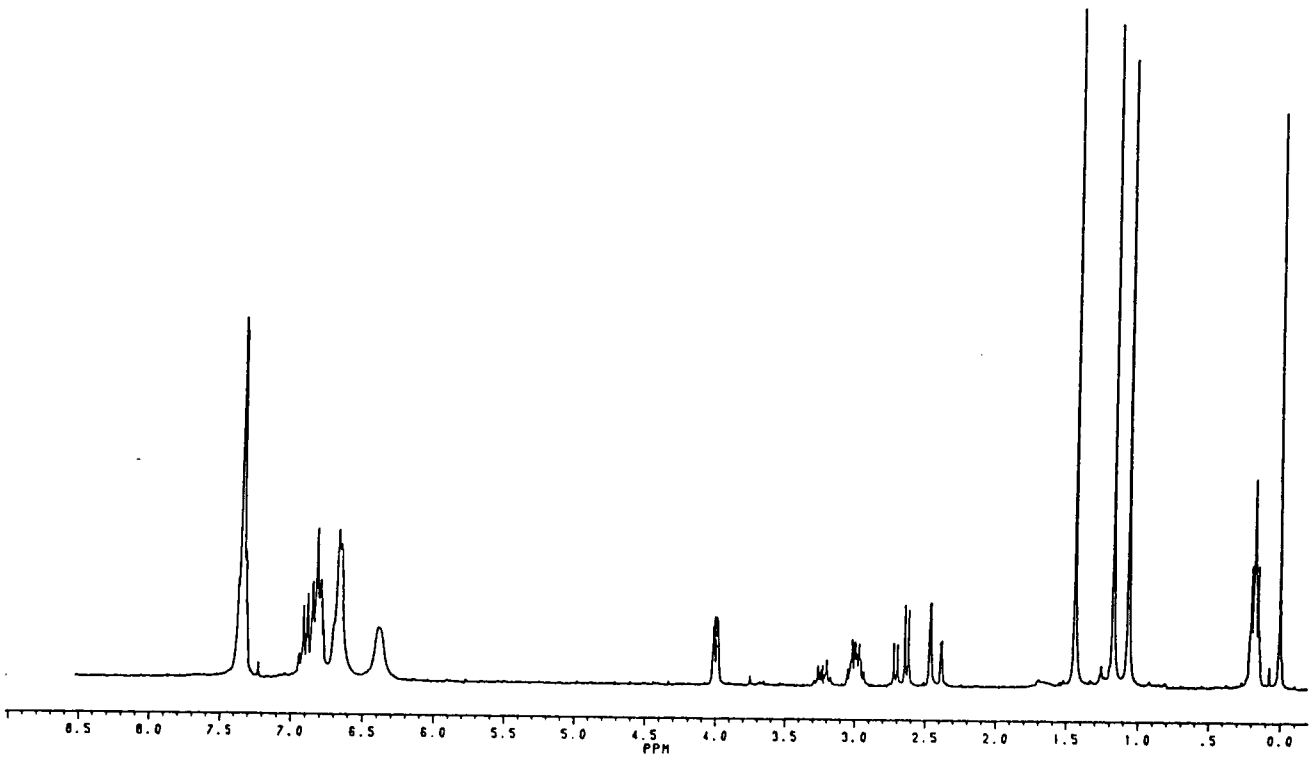

Figure 17: Cyclic ketal of the phenyl oxidation product, (XIX)

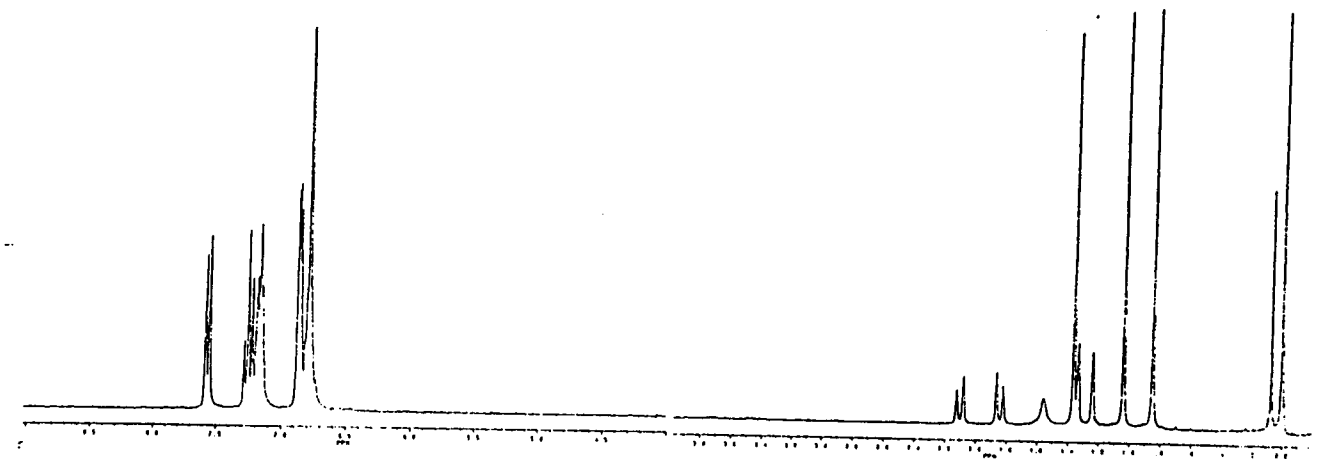

Figure 18: Epoxide Intermediate

VITA

Craig M. Bohlken was born on December 3, 1971, in Hamburg, Iowa, the son of Jack A. and Lily L. Bohlken. He received his high school education at Union City High in Union City, Tennessee, where he graduated with honors in 1990.

He began his undergraduate studies at The University of Mississippi in the fall of 1990 and graduated with a Bachelor of Arts in Chemistry with high distinction in August of 1994.

In August 1994, he began his graduate studies at the University of Tennessee, Knoxville where he held a teaching/research assistantship. He majored in Analytical/Organic Chemistry and did research under the guidance of Professor D.C. Kleinfelter.