SYNTHESIS AND REACTIONS OF BENZOCYCLOBUTENE DERIVATIVES

Thesis for the Degree of Ph. D.
MICHIGAN STATE UNIVERSITY

James A. Hartlage

1965


MICHIGAN STATE UNIVERSITY
DEPARTMENT OF CHEMISTRY
EAST LANSING, MICHIGAN


LIBRARY
Michigan State
University

ABSTRACT

SYNTHESIS AND REACTIONS OF
BENZOCYCLOBUTENE DERIVATIVES

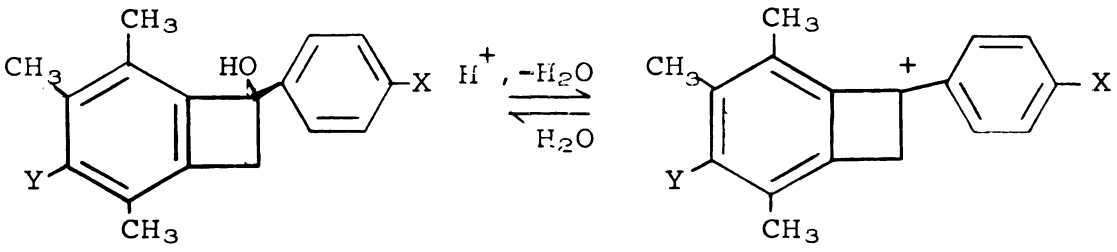
by James A. Hartlage

The purpose of this investigation was to synthesize and study the chemistry of benzocyclobutene derivatives having highly substituted aromatic rings. The entrance into the series of desired compounds was gained by way of the novel thermal ring closure of trichloromethylpentamethylbenzene and other substituted trichloromethylbenzenes (1,2) to produce 1,1-dichlorobenzocyclobutene derivatives. The preparative utility of this reaction was extended, and these dichlorides were used as starting materials in the synthesis of several new compounds having the benzocyclobutene ring system.

Several bicyclo[4.2.0]octa-1,3,5-triene-7-ol(benzocyclobutenol) derivatives having aromatic substituents in the seven position were found to produce stable carbonium ions in concentrated sulfuric acid solution. The structures of these ions were investigated by ultraviolet, visible and proton magnetic resonance spectroscopy. The stability of these ions with respect to rearrangement was established by

hydrolysis of the carbonium ions and reisolation of the compounds from which they were derived.

The pK's for the ionization process were measured spectroscopically and were found to correlate best for the following equilibrium type.



No evidence was found to indicate that these ions, which can be considered as protonated benzocyclobutadienes, undergo elimination in concentrated sulfuric acid.

A Hammett plot of σ^+ versus pH was made for five compounds having different X and Y substituents. A better linear correlation was obtained when Y substituents were assigned σ^+ values which were the sum of $\sigma_p^+ + \frac{1}{3}\sigma_m^+$. The enhanced σ^+ assignment for substituents in the benzocyclobutene ring can be explained best by postulating a 1-3 π interaction across the fused four membered ring equal to about 1/3 of a normal carbon-carbon bond.

N.m.r. studies of certain of the benzocyclobutenes prepared substantiate previous conclusions (3-5) that the four-membered ring is not planar.

REFERENCES

1) H. Hart and R. W. Fish, J. Am. Chem. Soc., 82, 749 (1960).

2) R. Rafos, Ph. D. Thesis, Michigan State University, 1961.

3) A. T. Blomquist and C. G. Bottomley, Ann., 653, 67 (1962).

4) H. Nozaki, R. Noyori and N. Kozaki, Tetrahedron, 20, 641 (1964).

5) G. Fraenkel, Y. Asahi, M. J. Mitchell and M. P. Cava, Tetrahedron, 20, 641 (1964).

SYNTHESIS AND REACTIONS OF BENZOCYCLOBUTENE DERIVATIVES

By

James A. Hartlage

A THESIS

Submitted to
Michigan State University
in partial fulfillment of the requirements
for the degree of

DOCTOR OF PHILOSOPHY

Department of Chemistry

1965

ACKNOWLEDGMENT

The author wishes to express his sincere appreciation to Professor Harold Hart for his guidance, and understanding during the course of this investigation.

Appreciation is also extended to the National Science Foundation for providing financial assistance from June, 1962 through June, 1965.

****

TABLE OF CONTENTS

TABLE OF CONTENTS - Continued

TABLE OF CONTENTS - Continued

LIST OF TABLES

LIST OF FIGURES

LIST OF FIGURES - Continued

FIGURE Page

LIST OF FIGURES - Continued

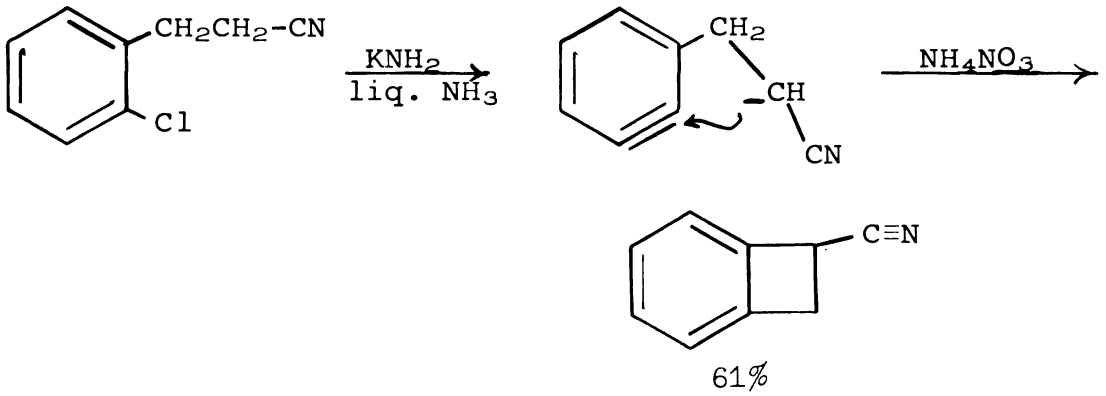
INTRODUCTION

The first successful preparation of a benzocyclobutene derivative was reported by Hans Finkelstein (1) in 1910. In that investigation it was found that by reacting sodium iodide in refluxing ethanol with $\alpha,\alpha,\alpha',\alpha'$-tetrabromo-o-xylene, 1,2-dibromobenzocyclobutene could be prepared in good yield. However, it wasn't until 1956 that this work was confirmed and extended by Cava and Napier (2). Since then several additional reactions have been discovered which permit convenient preparation of benzocyclobutenes. The earlier synthetic methods have been reviewed by Baker and McOmie (3) and by Fish (4).

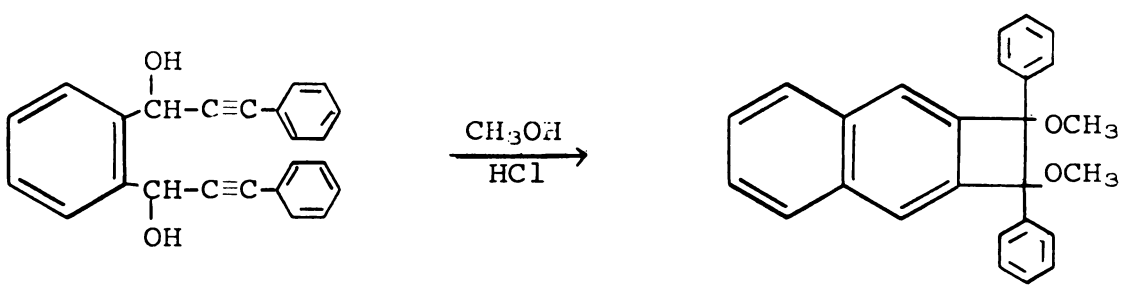
Interest in benzocyclobutene chemistry stems largely from curiosity about the reactivity of the highly strained four membered ring and the possibility that a derivative of the highly sought cyclobutadiene might be obtained in benzocyclobutadiene. The latter challenge was taken up with great enthusiasm after the appearance of a report by Streitweiser, Roberts and Regan (5) in which it was predicted, by HMO calculations, that benzocyclobutadiene should exist as a stable compound.

Several new approaches to the preparation of benzocyclobutenes which have shown considerable utility have been reported since 1960. Bunnett and Scorcz (6) have reported a method of preparing monosubstituted benzocyclobutenes which gives good yields and requires fewer steps

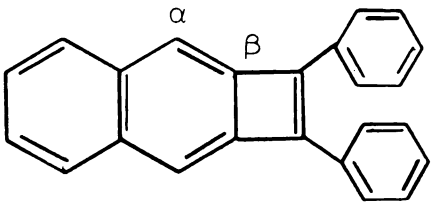
than the conventional preparative methods discussed in the reviews mentioned above. This method is illustrated by the following equation.



Cava, Hwang and Van Meter (7) have investigated the preparation of several naphthocyclobutenes using different approaches. The method of choice was reported to be the addition of phenylacetylene Grignard Reagent to o-phthalaldehyde, followed by the ring closing reaction illustrated below.

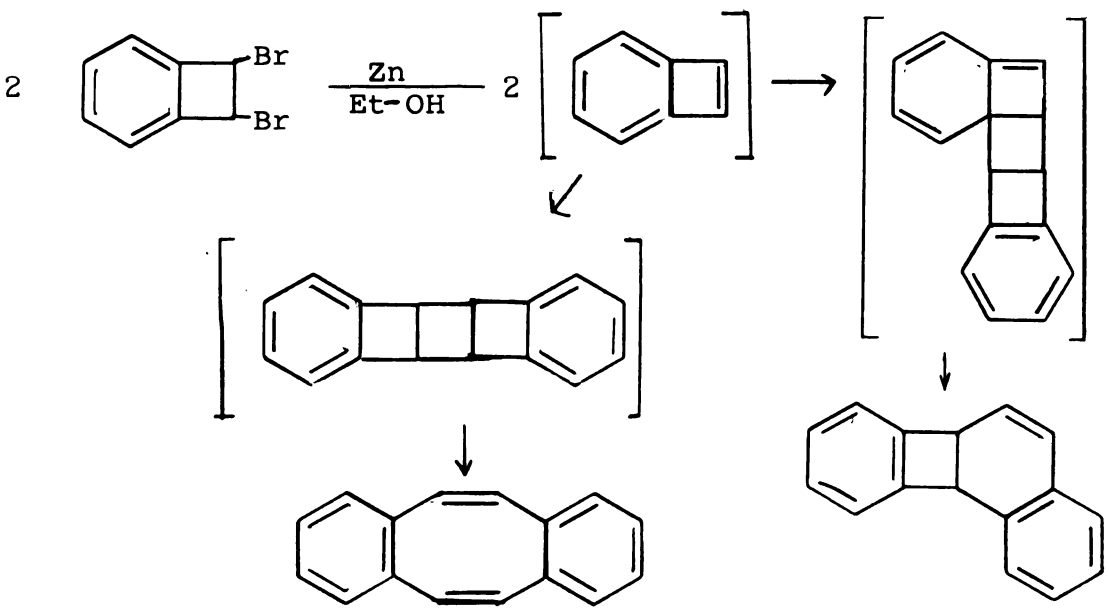


1,2-Dimethoxy-1,2-diphenylnaphtho[b]cyclobutene was used then to prepare 1,2-dichloro-1,2-diphenylnaphtho[b]-cyclobutene, which in turn was dehalogenated to produce the first stable cyclobutadiene derivative. This bright red crystalline compound has an n.m.r. spectrum which



consists of fourteen protons in the aromatic region and a two proton singlet at 3.5 τ which was assigned to the protons attached to the α-carbon atoms. This frequency is near that of the aliphatic protons of cis-stilbene, suggesting that the α-β bonds have enhanced double bond character.

Previous attempts to prepare stable cyclobutadiene derivatives have resulted in the formation of dimers or polymers which were apparently formed by way of cyclobutadiene intermediates. A good example of the types of reactions that occur are illustrated below for the debromination of 1,2-dibromobenzocyclobutene.



(8)

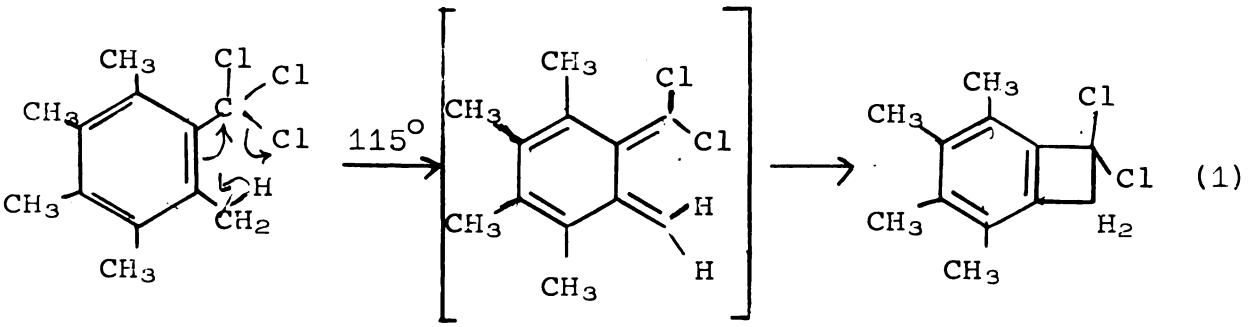
The purpose of the present investigation was to utilize the discovery of Fish (9), that trichloromethylpentamethylbenzene could be converted to 1,1-dichlorotetramethylbenzocyclobutene, in preparing new, highly substituted, benzocyclobutenes. It was of interest to explore the preparative methods which might be useful in carrying out reactions within the series, while avoiding conditions which might lead to destruction of the highly strained four-membered ring.

RESULTS AND DISCUSSION

Ring Closure of Benzotrichlorides

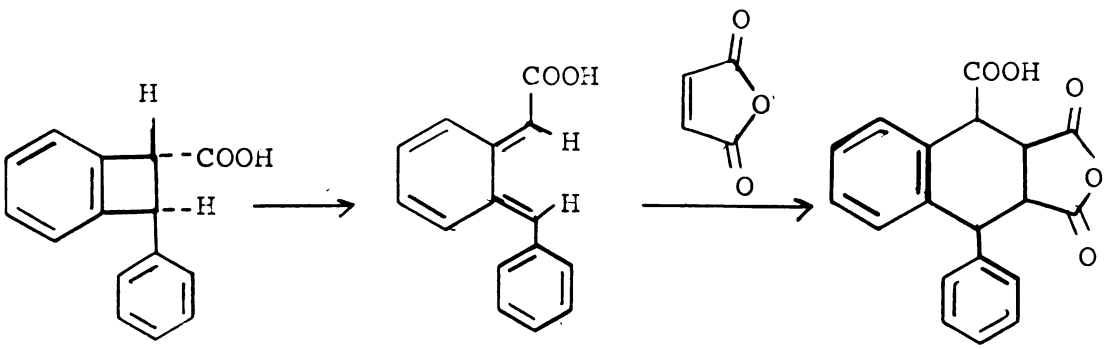
The ring closure reaction used in this work as an entry into the benzocyclobutene ring system was originally discovered by Fish (9) who found that trichloromethyl-pentamethylbenzene liberated hydrogen chloride when heated slightly above its melting point and produced 1,1,-dichloro-tetramethylbenzocyclobutene. Fish (4) also reported that trichloromethylmesitylene underwent a similar reaction when distilled at 126° under reduced pressure. However, he was unable to repeat this reaction. Rafos (10) found that 4-chloro-2,3,5,6-tetramethylbenzotrichloride underwent an analogous ring closure reaction when heated to 170° under a nitrogen atmosphere.

This reaction is thought to proceed through a cis-diene intermediate as indicated in the following equation.



I II III (1)

The intermediate II is proposed by way of analogy with the observations (11,12) that some benzocyclobutene derivatives react with dienophiles at low temperatures by way of similar cis-diene structures to produce Diels-Alder addition products. Thus, Blomquist and Bottomly (13) reported the following reaction to take place at 25°.



IV V VI

However, attempts by Fish (4) to trap the proposed intermediates in the thermal ring closure of trichloromethylbenzocyclobutene, with maleic anhydride resulted in a reduced yield of dichlorotetramethylbenzocyclobutene, but no Diels-Alder adduct could be isolated.

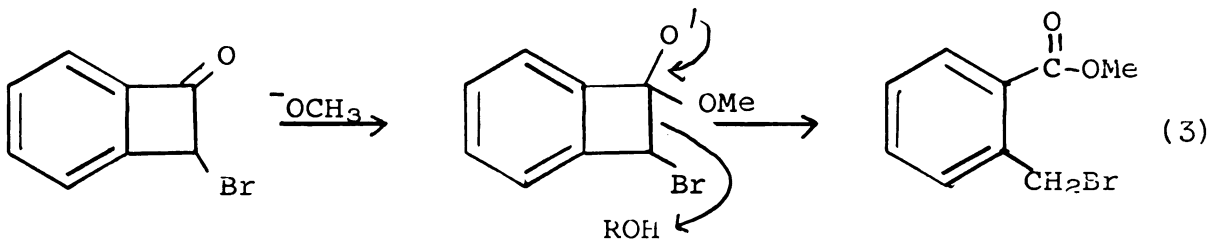
The ring closures of trichloromethylpentamethylbenzene and 4-chloro-2,3,5,6-tetramethylbenzotrichloride were found to proceed smoothly to the desired products when these substances were heated to 115° and 170°, respectively, under a stream of dry nitrogen in 8" test tubes. Less polymeric side products were obtained by carrying out the

reactions with small quantities of material in this manner. Using this method, it was found that trichloromethylmesitylene could be made to undergo the desired ring closure reaction repeatedly and in good yield at 170°.

Reduction of 2,3,4,5-Tetramethylbicyclo-[4.2.0.]octa-1,3,5-triene-7-one(tetramethylbenzocyclobutenone)

As a starting point in the attempt to prepare tetramethylbenzocyclobutadiene by the reaction series discussed on page 16 it was necessary to reduce tetramethylbenzocyclobutenone to tetramethylbenzocyclobutenol. When tetramethylbenzocyclobutenone was reduced with sodium borohydride in diglyme at 90° C. the only reduction product was pentamethylbenzyl alcohol. Reduction of the ketone with lithium aluminum hydride in tetrahydrofuran at reflux produced a mixture of pentamethylbenzyl alcohol and hexamethylbenzene after hydrolysis of the aluminate intermediate. These results are not surprising when the facility with which benzocyclobutene and benzocyclobutenol undergo ring opening under basic conditions is considered. Cava and Muth (14) have reported that these compounds can be ring opened in 0.25 N base after only one hour at 25°, and Fish (4) has found that tetramethylbenzocyclobutenone can be converted to pentamethylbenzoic acid in 0.1 N sodium hydroxide. In this investigation it was found (page 50) that tetramethylbenzocyclobutenol can be converted to pentamethylbenzaldehyde

with mild base treatment. This great ease of ring opening has recently been demonstrated by Cava, Mangold, and Muth (8) in the following reaction.

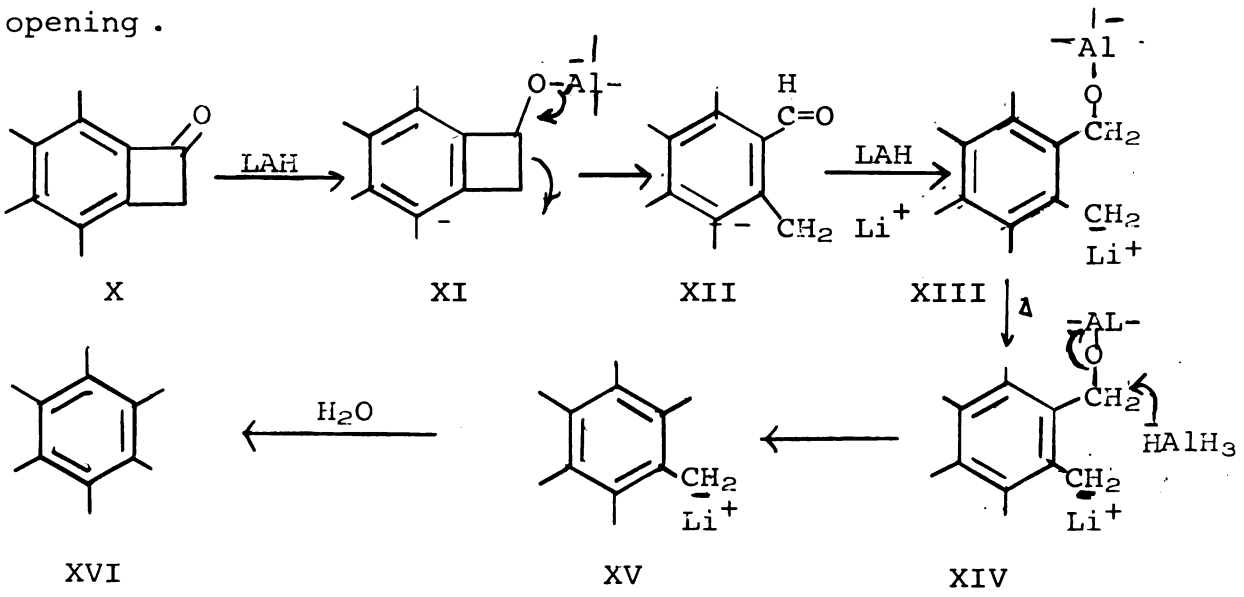


(3)

VII VIII IX

Attack of methoxide at the carbonyl carbon was concluded to be faster than displacement of the highly reactive benzylic bromine.

The formation of hexamethylbenzene in the lithium aluminum hydride reduction is not well understood, but its production in the reaction can be rationalized by a nucleophilic substitution of an aluminate species (16) after ring opening.



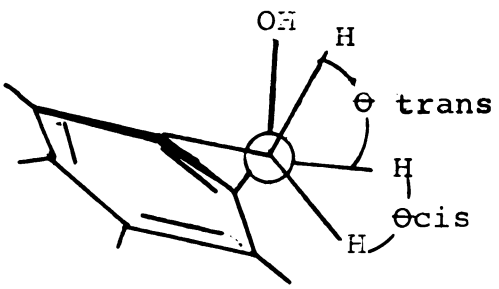
X XI XII XIII XIV XV XVI

A mechanism like the one above gains some support from the observation that pentamethylbenzaldehyde is reduced under the same conditions to pentamethylbenzyl alcohol and hexamethylbenzene. However, displacement of the aluminate species as a result of an intra-molecular electron reorganization, producing a cis-diene intermediate, which could then be reduced to XV, is not ruled out.

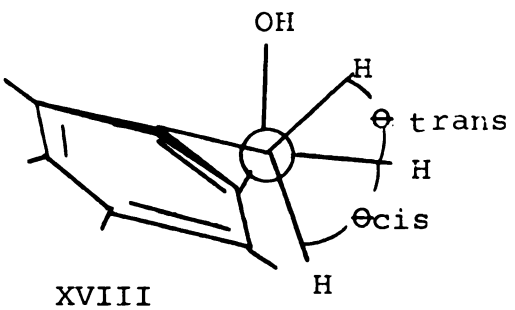
Tetramethylbenzocyclobutenol was eventually prepared in good yield by reducing tetramethylbenzocyclobutenone with aluminum hydride at room temperature. The alcohol thus obtained was oxidized with chromic acid back to the starting ketone in order to prove that no alteration in skeletal structure had taken place during the reduction step. The proton magnetic resonance spectrum of tetramethylbenzocyclobutenol (see Figure 6) exhibits an ABX pattern for the three hydrogens on the fused four-membered ring (17). The hydrogen on the α-carbon atom appeared as a doublet centered at $\tau = 4.20$ and the AB portion of the ABX pattern centered at $\tau = 6.94$ was assigned to the methylene hydrogens and consisted of six lines. The lower field portion of the AB pattern was coupled with the X proton ($J_{AX} = 4$ cps.), but the high field portion of the multiplet consisted of only two lines ($J_{BX} \cong 0$ cps.). These assignments were supported by the observation that 1 deutero-tetramethyl benzocyclobutenol, which was prepared by reduction of tetramethylbenzocyclobutenone with aluminum deuteride, showed no absorption at

τ = 4.20, and the methylene hydrogens appeared as an AB quartet centered at τ = 6.94 (see Figure 7).

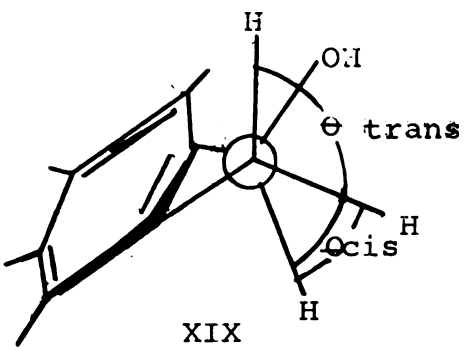
This n.m.r. spectrum is of interest in that some conclusions can be made concerning the conformation of the four-membered ring, from a qualitative consideration of the angles that the coupling constants imply (18). The figures below represent four of the possible conformations that the ring might assume.



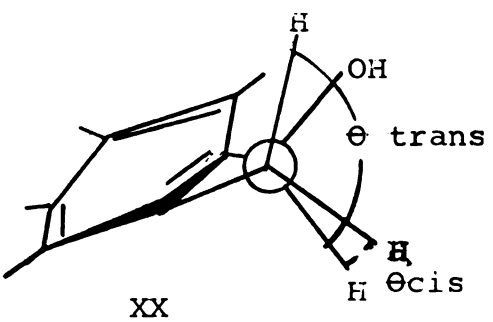
XVII



XVIII



XIX



XX

In structures XVII and XVIII the hydroxyl assumes an axial position with respect to the plane of the rings, and in XIX and XX an equatorial positioning of the hydroxyl is implied. The nomenclature, "equatorial" and "axial," is

derived from analogy with the conformational assignments for cyclohexane rings. In structure XVII, the larger coupling constant (J = 4 cps.) is assigned to the cis-hydrogens and corresponds to an angle of 45°. If the H-C-H angle is taken as 112° (12) then the trans dihedral angle, θ-trans, is equal to 112° minus 45° or approximately 67°. From the Karplus Equation an angle of 67° corresponds to a coupling constant of approximately one. In structure XVIII the θ-trans angle is taken as 45°, and a θ-cis of 67° is calculated. From coupling constant data then, both XVII and XVIII are possible conformations of tetramethylbenzo-cyclobutenol, although XVII implies less twisting of the ring.

If the same method of analysis is applied to the two equatorial conformations shown above, it is reasonable to assign θ-cis equal to approximately 45° as in XIX or θ-trans equal to approximately 130° (XX) from the larger coupling constant. However, if θ-cis is about 45° then θ-trans is 45° plus 112° or 157°, and the coupling constant calculated from the Karplus Equation is large ($J \cong 8$ cps.). If θ-trans is approximately 130°, then θ-cis would be 130° minus 112°, or 18°, and the coupling constant for the cis hydrogens would be about 7 cps. From these considerations then, it is most reasonable that a conformation in which the hydroxyl group prefers an axial position is assumed by the strained four-membered ring.

Several reports of the coupling constants for benzo-cyclobutene derivatives have been made (6,13,14), and in

each case it was observed that the size of the cis coupling constant was larger than the trans one. This observation lends support to the assignment of XVII as the conformation which is closest to reality. In addition a θ-cis dihedral angle of 67^{o}, calculated for XVIII, would seem to imply a prohibitively distorted molecule.

The conclusions drawn here concerning the conformation of tetramethylbenzocyclobutenol can also be applied to 1-bromotetramethylbenzocyclobutene since the coupling constants used in the above argument are the same as those measured for the analogous hydrogens in the bromo-derivative. The values obtained for the dihedral angles in the above calculation are similar to those reported by Fraenkel, Muth and Cava (21). The following table lists the data reported for benzocyclobutenes with the results reported here.

Table I. Dihedral Angles Between Bonds in Benzocyclobutenes

Compound	θ-cis	θ-trans[a]
1-Bromobenzocyclobutene	30^{o}	150^{o}
Benzocyclobutene	40^{o}	120^{o}
Benzocyclobutene-1-carboxamide	44^{o}	119^{o}
1-Methyl-2-phenylbenzocyclobutene	30^{o}	125^{o}
1-Bromotetramethylbenzocyclobutene	45^{o}	157^{o}
Tetramethylbenzocyclobutenol	45^{o}	157^{o}

[a]The θ-trans reported here is different than discussed in the text of this thesis. The angles are taken as the bond angle between "axial" substituents in the compounds listed.

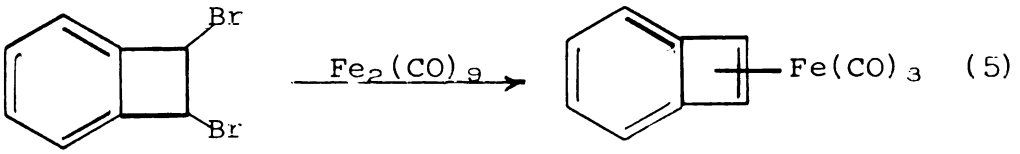
Inspection of models indicates that the calculated angles in the above table are probably too large, and X-ray studies of Hardgrove (22), which indicate that the four and six-membered rings of cis-1,2-dichlorobenzocyclobutene are nearly coplanar in the crystalline state, support this contention. The error in the calculation arises from the fundamental assumptions of the Karplus Equation, which was derived from a simple model consisting of two carbon and two hydrogen atoms. Karplus (23) has cautioned against the use of this equation for quantitative measurements due to inherent errors which arise from the basic assumptions of the model and in light of the observation (24) that the value of the coupling constant is significantly influenced by the electronegativity of neighboring substituents. An electronegative element is believed to effect the coupling constant not by withdrawing electron density from the carbon-carbon bond, but rather by changing the hybridization of the carbon to which it is bonded. The value of the coupling constant is also influenced by bond length and the H-C-C bond angle.

Attempts to Prepare 1-Aminotetramethylbenzocyclobutene

It was of interest to obtain 1-aminotetramethylbenzocyclobutene which might possibly be used as a precurser of tetramethylbenzocyclobutadiene by way of a Hoffman elimination reaction. It was hoped that the ring methyl

groups would serve as effective blocking groups to reactions of the highly strained and reactive double bond of the cyclobutadiene portion of the ring system.

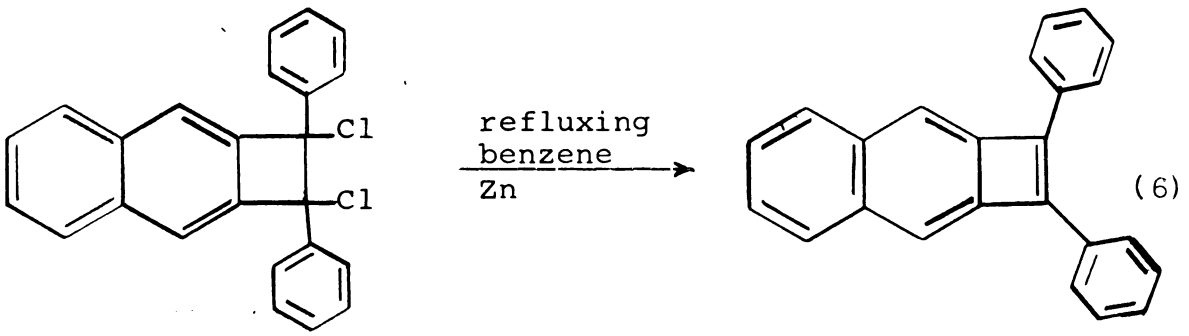
Since Roberts, Streitwieser, and Regan (5) predicted from molecular orbital calculations that benzocyclobutadiene should be a stable compound, several attempts to prepare benzocyclobutadiene derivatives have been made (25-31). In each case dimers of benzocyclobutadiene or compounds derived from these dimers were obtained. However, more recently Emerson, Watts and Pettit (32) have succeeded in isolating a stable iron carbonyl complex of benzocyclobutadiene by the following reaction,



(5)

XXI XXII

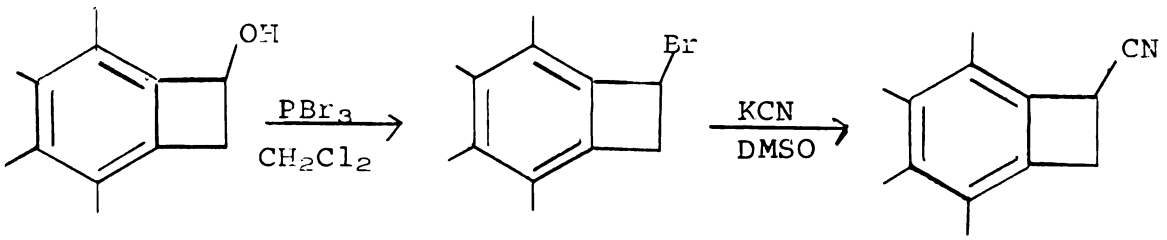
and Cava, Hwang and Van Meter (33) have prepared a diphenyl naphthalene derivative of cyclobutadiene as a stable crystalline compound.



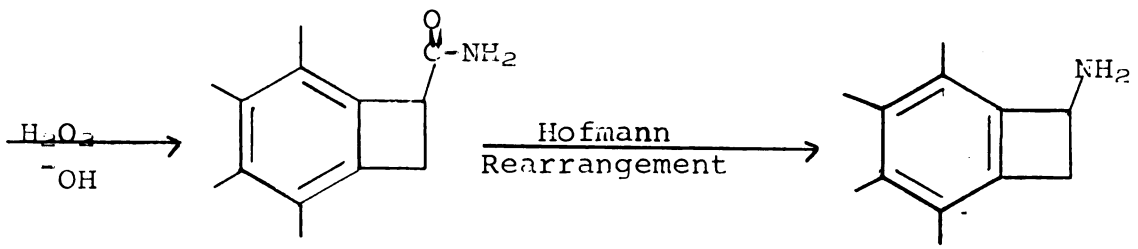
(6)

XXIII XXIV

Two different methods were attempted for preparing 1-aminotetramethylbenzocyclobutene. The first is illustrated by the following reaction scheme



XXV A XXVI B XXVII



C XVIII XXIX

Steps B and C in the sequence were accomplished by using adaptations of the procedures of Cava, Litle and Napier (34) for the analogous reactions with benzocyclobutene derivatives. However, step A was unreliable, giving yields from 31 to 70%. This method was abandoned at XVIII in view of the poor overall yields which were obtained for the reaction series.

In a second attempted method to prepare 1-aminotetramethylbenzocyclobutene a reduction of tetramethylbenzocyclobutenone oxime was undertaken. Aluminum hydride reduction gave a mixture of products, one of which was

identified as 4,5,6,7-tetramethyl-2,3-dihydroindole, and the other is suspected to be a dimer of 1-nitrosotetramethylbenzocyclobutene, although a positive identification was not obtained. The former product most likely arises by way of an aluminum chloride catalyzed Beckmann rearrangement of the oxime. Some aluminum chloride was apparently present as an impurity remaining from the aluminum hydride preparation. The product from attempts to prepare the amine from lithium aluminum hydride reduction of tetramethylbenzocyclobutenone oxime was also not identified, but it is suspected to be similar to the unidentified aluminum hydride product. At this point it was decided to abandon the attempts to prepare 1-aminotetramethylbenzocyclobutene in favor of more fruitful investigations.

Preparation of Tetramethylbenzocyclobutene

The preparation of tetramethylbenzocyclobutene had been attempted by Fish (4), through the reduction of tetramethylbenzocyclobutenone by catalytic hydrogenation and with sodium borohydride, without success. The desired product was prepared in this investigation by way of a Wolff-Kishner reduction of tetramethylbenzocyclobutenone, and its structure was proven by mass spectrometry and by nuclear magnetic resonance, infrared, and ultraviolet spectroscopy. The infrared spectrum (Figure 35) was only slightly different from that of hexamethylbenzene.

The mass spectrum and n.m.r. are shown (Figures 36 and 37) and interpreted in the Experimental Section.

The ultraviolet spectrum of tetramethylbenzocyclobutene is shown in Figure 1 with that of hexamethylbenzene. The B-band region, between 230 mμ and 270 mμ is of special interest, since changes in this portion of the spectrum are assigned to changes in the symmetry properties of the pi-electron system (35). Substitution in the aromatic nucleus causes these bands to shift and vary in intensity due to conjugation and steric effects. Comparisons of ultraviolet spectra of naphtho[b]cyclobutenes (36), and benzocyclobutene (30,37) with the corresponding 2,3-dimethylnaphthalene or ortho-xylene show the same general phenomenon of shift to slightly higher wavelength and an increase in intensity.

Chemical Stability of Carbonium Ions Formed from Benzocyclobutene Derivatives

Several benzocyclobutenols containing alkyl or aryl substituents in the 1-position were prepared by reaction of various Grignard Reagents with tetramethylbenzocyclobutenone, 4-chlorotetramethylbenzocyclobutenone, or dimethylbenzocyclobutenone. The chemical stability of these derivatives in sulfuric acid was investigated by observation of changes in the visible spectrum with time and by hydrolysis of the sulfuric acid solutions of the ions. Several of the derivatives which were investigated are represented in structure XXX a-e.

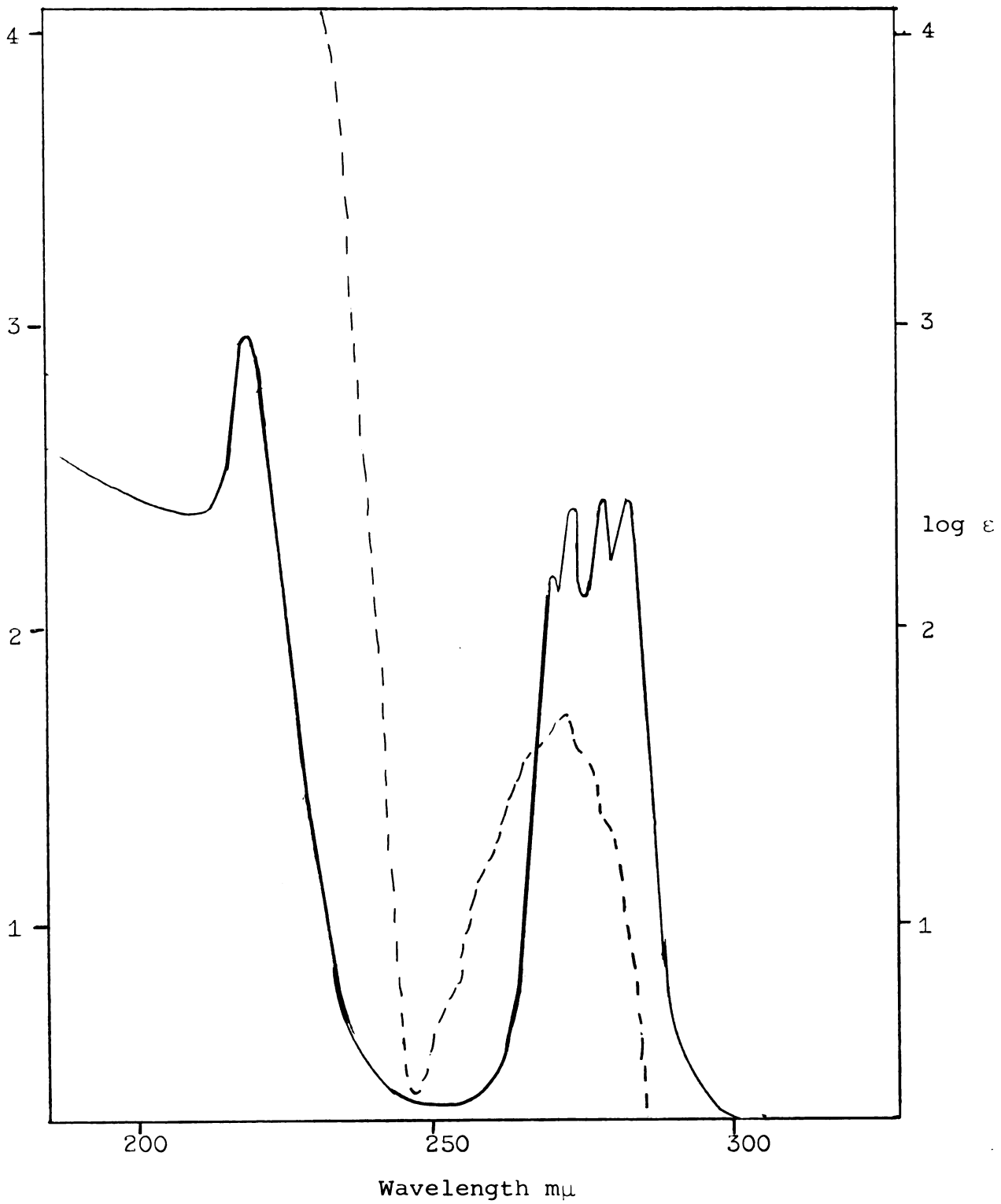
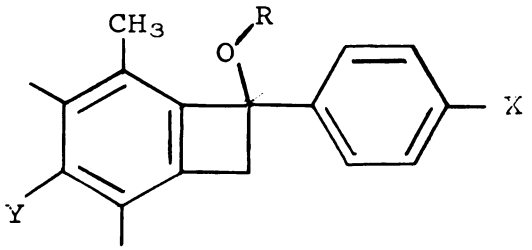


Figure 1. Comparison of the ultraviolet spectra of tetramethylbenzocyclobutene (——) and hexamethylbenzene (---).



XXX

a. X = H	Y = CH_3	R = H
b. X = OCH_3	Y = CH_3	R = CH_3
c. X = Cl	Y = CH_3	R = CH_3
d. X = CH_3	Y = Cl	R = CH_3
e. X = H	Y = Cl	R = H

In each case the compound dissolved in 96% sulfuric acid producing a highly colored solution which showed no changes in the visible spectrum after several hours. When sulfuric acid solutions of the ions were poured into cold methanol or water, high yields of the compounds from which the ions were formed could be recovered. This procedure demonstrated that the carbonium ions were stable with respect to skeletal rearrangement in concentrated sulfuric acid at room temperature.

The n.m.r. spectra of the ions were measured in concentrated sulfuric acid solutions using tetramethylammonium fluoroborate as an internal standard. The chemical shifts of the protons in these ions are reported in Table II. In each case the spectrum was quite different from that of the unionized compound. The entire spectrum was shifted to

Table II. Proton Magnetic Resonance Spectra of Benzocyclobutene Derivatives in 96% Sulfuric Acid

Compound	Positions (τ units)	Assignments[a] (benzocyclobutene numbering system)	Number of protons
1-Methoxy-1-(p-chlorophenyl)-3,4,5,6-tetramethylbenzocyclobutene	2.00[b]	aryl protons	4
	5.68	(2)	2
	7.30, 7.45	(4-6)	3, 3
	7.65, 7.73	(3-5)	3, 3
1-Phenyl-3,4,5,6-tetramethylbenzocyclobutenol	2.06	aryl protons	5
	5.67	(2)	2
	7.18, 7.47	(4-6)	3, 3
	7.63, 7.72	(3-5)	3, 3
1-Methoxy-1-(p-methoxyphenyl)-3,4,5,6-tetramethylbenzocyclobutene	2.23[b]	aryl ring	4
	5.88	(2)	2
	7.47, 7.65	(4-6)	3, 3
	7.75, 7.81	(3-5)	3, 3
	5.93	aryl methoxy	3
1-Methoxy-1-(p-tolylphenyl)-4-chloro-3,5,6-trimethyl-benzocyclobutene[c]	1.78	aryl protons	4
	5.62	(2)	2
	7.27		3
	7.30		3
	7.50		3
	7.63		3
1-Phenyl-4-chloro-3,5,6-trimethylbenzocyclobutenol[c]	1.89[b]	aryl protons	5
	5.57	(2)	2
	7.32		3
	7.38		3
	7.61		3
1-(p-chlorophenyl)-4,6-dimethylbenzocyclobutenol	1.96[b]	aryl protons	4
	2.58, 2.66	(3-5)	1, 1
	5.75	(2)	2
	7.23, 7.35	(4-6)	3, 3

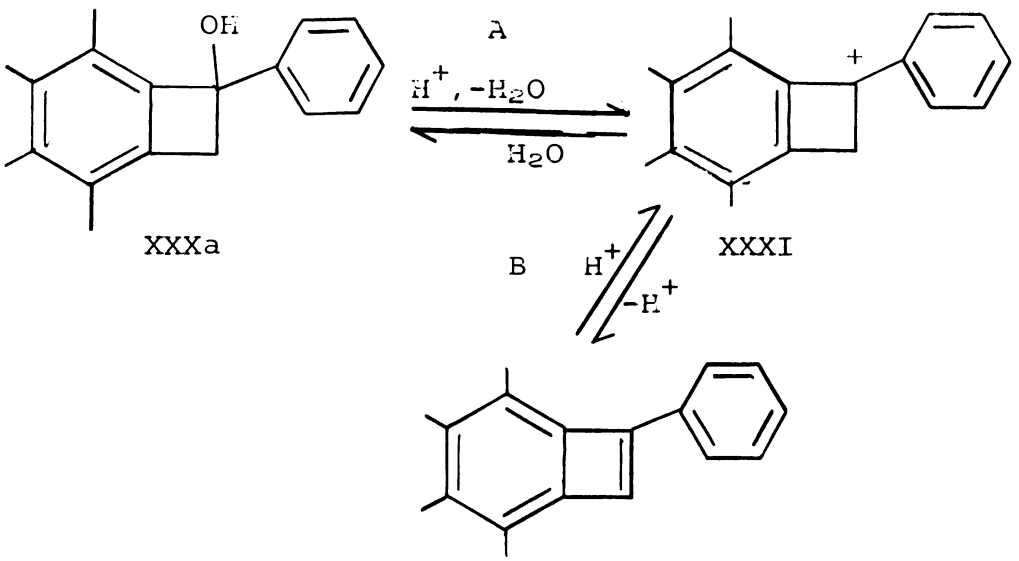
[a] Assignments of protons in the (4-6) and (3-5) positions were made from comparisons of methyl positions with 1-(p-chlorophenyl)-4,6-dimethylbenzocyclobutenol.

[b] Center of a quartet.

[c] Due to the uncertain shielding effects of neighboring chloro groups, no methyl assignments were possible.

lower field as expected, and each methyl group appeared as a well separated single peak. No positive assignment of these resonance frequencies could be made for all of the methyl groups, but from comparisons of the spectra of the 3,4,5,6-tetramethyl substituted ions with that of the 4,6-dimethyl substituted ion it was concluded that the two methyl peaks that appear at lower field in the former cases could be assigned to the methyl groups in the four and six positions. However, the appearance of the methyl resonances in all of the ions is sufficiently ambiguous to make even these assignments somewhat arbitrary.

Of particular interest is the fact that in each case the peak assigned to the methylene protons is a singlet, which is shifted by approximately 60 cps. downfield, and has a relative intensity of two. This intensity is of significance in a consideration of the equilibria shown below.



(7)

In 96% sulfuric acid the equilibrium A lies far to the right, but since the integrated spectrum shows a relative area of two for the methylene protons it can be concluded that XXXI is the major organic component of the solution. If one considers the carbonium ion XXXI as a protonated form of the benzocyclobutadiene XXXII, this benzocyclobutadiene derivative must then be completely protonated in 96% sulfuric acid. In order to test for the presence of small concentrations of XXXII in sulfuric acid, the n.m.r. spectrum of XXIa was measured in 70% sulfuric acid-d_2 - 30% deuterium oxide. There was no decrease in relative intensity of the peak at $\tau = 5.67$ which was assigned to the methylene protons. The conclusion from this experiment was that the concentration of XXXII in moderately strong sulfuric acid solution is negligible. The structure of the species present in the above equilibrium was investigated further by spectrophotometric determination of the pK's of the ions listed in Table II.

The visible spectra of the compounds were first measured in concentrated sulfuric acid. Each compound produced a bright red color when dissolved in acid, and the visible spectra of these solutions were very similar to those reported by Deno, Jaruzelski and Schriesheim (38) for similarly substituted triphenylcarbinols as may be seen from Table III.

Table III. Visible Spectra of Some Triphenyl—carbinols and 1-Arylbenzocyclobutenol Derivatives in H_2SO_4

Compound	Wavelength (mμ)	Molar Absorbancy Index (ε)
4-Methoxytriphenylmethanol	476	56,000
1-Methoxy-1-(p-methoxyphenyl)-3,4,5,6-tetramethylbenzocyclobutene	471	76,400
4,4',4"-trichlorotriphenylmethanol	465	93,000
1-Methoxy-1-(p-chlorophenyl)-3,4,5,6-tetramethylbenzocyclobutene	453	48,200
1-Methoxy-1-(p-tolylphenyl)-4-chloro-3,5,6-trimethylbenzocyclobutene	458	67,400
1-Phenyl-4-chloro-3,5,6-trimethylbenzocyclobutenol	444	54,200
Triphenylmethanol	431	37,300
1-Phenyl-3,4,5,6-tetramethylbenzocyclobutenol	435	25,900

The shifts in equilibrium with acidity were described well by equation 8 (39).

$$H_R = pK_{R^+} + \log(C_{ROH}/C_{R^+}) \qquad (8)$$

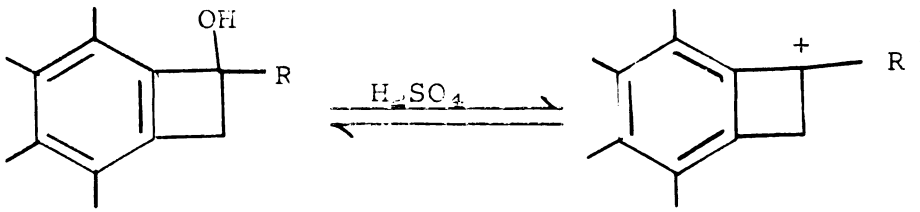
This was determined from the fact that constant pK values were calculated from the equation over the ionization range of the compounds (see Experimental).

This correlation with equation 8 is significant since it was determined by Deno, Groves, and Saines (40) that the protonation of diarylolefins widely deviates from this equation, as δ is used to describe the ionization of arylmethanols which are structurally prevented from dehydrating to olefins. It was concluded from this that, in general, compounds which are structurally able to eliminate to olefins do so, and the equilibrium shifts in various concentrations of sulfuric acid as described by equation 9.

$$H_R - \log a_{H_2O} = pK'_{R^+} + \log (C_{ol}/C_{R^+}) \qquad (9)$$

The correlation of ionization of XXX a-e with equation 8 indicates that even at the pK, equilibrium B in equation 7 is not operative, and XXXI is still the species in equilibrium with XXXa. However, it is possible that some XXXII is formed in sulfuric acid solutions in which XXXa is approximately half ionized, since the extinction coefficient does decrease slowly with time at such acid concentrations. It would not be surprising to find that the very reactive benzocyclobutadiene is formed, but quickly polymerized or dimerized under the conditions of the equilibrium.

The 1-alkyl, 1-benzyl and 1-cyclopropyl substituted benzocyclobutene derivatives which were prepared and investigated are represented with tetramethylbenzocyclobutenol by structures $XXXIII_{a-d}$.



XXXIII XXXIV (10)

a. R = CH_3
b. R = benzyl
c. R = cyclopropyl
d. R = H

When compounds XXXIII a-d were dissolved in concentrated sulfuric acid, bright red species were formed, but the spectra of these ions in solution varied with time, and hydrolysis of the solutions failed to produce recoverable starting material. These results indicate that elimination occurred to form olefinic materials which were able to react rapidly to form other products. The ionization of the compounds in various concentrations of sulfuric acid was studied as described for XXX a-e. For XXXIIIa and XXXIIIb the shift in equilibrium was found to be described best by equation 8. The absorbances used to calculate the ionization ratios were obtained by plotting absorbance versus time after mixing stock solutions of the appropriate compound with sulfuric acid, and extrapolating the data to time equal to zero. Correlation of the data with equation 8 is evidence that the above written equilibrium, 10, exists for a short length of time, but elimination soon occurs to produce new absorbing species.

Compounds XXXIIIc and XXXIIId produce colored ions which are very unstable in sulfuric acid. This is evidenced by the observation that the spectra change very rapidly after mixing stock solutions of the compounds with acid, and the equilibria of the ions, observed after three minutes, shifts with changes in acid strength according to equation 9. With these compounds it is evident that the ionic species is in equilibrium with olefin after a very short time. However, there is no evidence concerning the structure of the ions in solution.

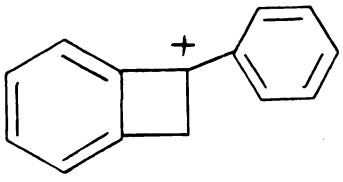
Thermodynamic Stability of the Ions

From the changes in n.m.r. spectra of the benzocyclobutene derivatives observed in sulfuric acid as compared with the same spectra in nonionizing solvent, an interesting observation can be made which has bearing on the question of charge distribution in the ions. The spectra of the compounds in carbon tetrachloride characteristically display three methyl groups with very similar chemical shifts, i.e., τ = 7.88, 7.92, 7.92, and one three-proton singlet at slightly higher field, i.e., τ = 8.00 (see Experimental), which is assigned to the protons on the methyl group in the six position and is apparently shielded by the aromatic ring in close proximity at the one position. When this methyl group pattern is compared with the characteristic pattern of the same methyl groups bonded to the ionized species it is readily

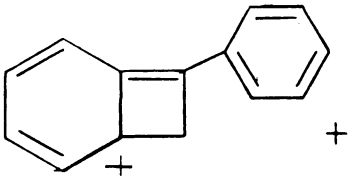
observed that peaks have been shifted to lower field by different amounts and appear as four clearly resolved three-proton singlets. Shifts in proton frequency in going from an uncharged molecule to an ion have been reported by Fraenkel and co-workers (41) to be equal to ten parts per million per charge, and this shift is attributed mainly to the difference in charge density on the carbon atom to which the hydrogen is bonded. Maclean and Mackor (42) have extended the study to aromatic systems containing several methyl substituents and have found that a relation exists between the chemical shifts of aromatic and methyl group hydrogens, and the amount of positive charge on adjacent carbon atoms in carbonium ion complexes. A shift of 4.75 cps. per charge on a carbon adjacent to a methyl group was reported for the hydrogens on the methyl group. The proton shift for hydrogen next to carbon was reported to be 13.4 cps. per unit charge. These values are in good agreement with those reported in Fraenkel's investigation.

From the above results and the observation that all of the methyl groups of the tetramethylbenzocyclobutene carbonium ions are shifted to lower field by different amounts, it was concluded that the chemical shift differences of the methyl groups is due to charge distribution differences. It is expected that the methyl groups in positions four and six should appear at significantly different resonance frequencies since they are <u>para</u> and <u>ortho</u> to the benzylic

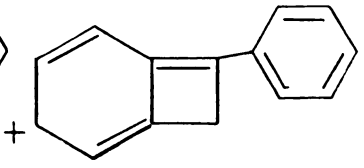
carbon at which ionization occurs, but the methyls in positions three and five are <u>meta</u> to the developing charge and are expected to appear at very nearly the same frequency, as they do in the uncharged molecule. The cause of the charge difference at positions three and five might then be due to resonance structures like XXXVe, XXXVf and XXXVg, having a significant role in the charge distribution of the ions.



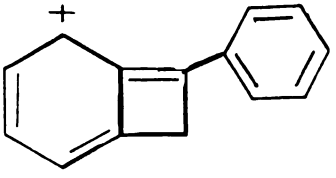
XXXVa



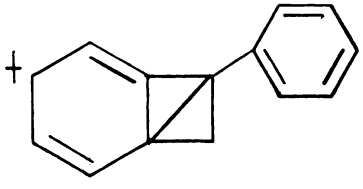
XXXVb



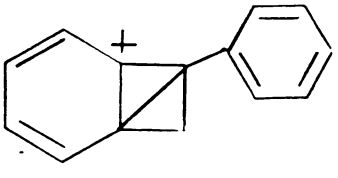
XXXVc



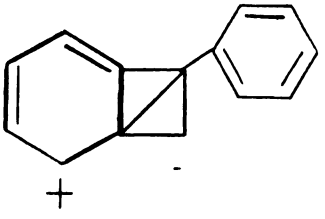
XXXVd



XXXVe

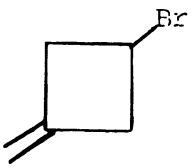


XXXVf

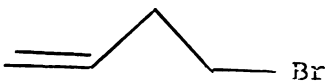


XXXVg

Analogous cross ring interactions have been calculated by Kiefer and Roberts (43) for cyclobutene carbonium ions as 0.2β to 0.5β, where β is the normal carbon-carbon 1,2 resonance integral. However, it was concluded, from the fact that **XXXVI** solvolyzes 160 times slower than **XXXVII**, that effective 1,3 interaction arises from arrangements of orbitals that will have σ rather than π overlap. Subsequent

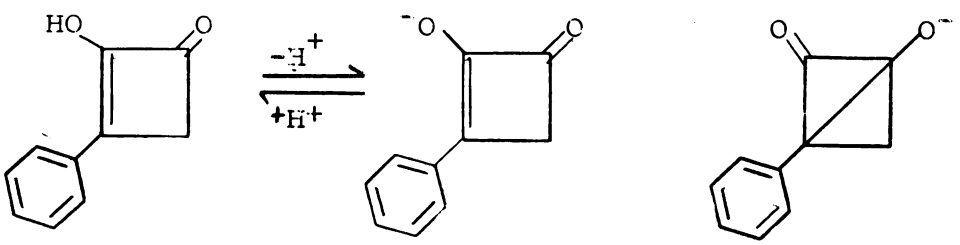


XXXVI



XXXVII

investigations by Roberts and his co-workers (44,45) support the conclusion that no significant overlap was existent for structures analogous to the carbonium ion formed in the solvolysis of **XXXVI**, but reason was found to postulate 1,3 interaction in the ionization of 2-hydroxy-3-phenyl-2-cyclobutenone **XXXVIII** (46).



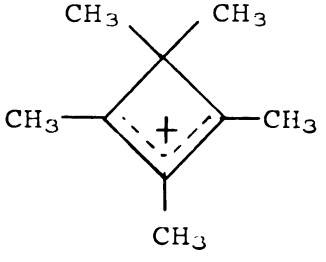
(11)

XXXVIII **XXXVIIIa** **XXXVIIIb**

The fact that the pK_a of **XXXVIII** was three to four units lower than 2-hydroxy-2-cyclopentenone and

2-hydroxy-2-cyclohexenone was explained by the postulation of a structure like **XXXVIIIb** as an important stabilizing influence on the anion. Analogous structures are not expected to be important in the ionization of 2-hydroxy-2-cyclohexanone, or 2-hydroxy-2-cyclopentenone, since the importance of 1-3 interactions is expected to decrease as the 1,3 distance increases.

More recently, Katz and Gold (47) have prepared several methyl-substituted cyclobutene carbonium ions in an effort to determine the extent of 1-3 interactions in **XXXIX** and structures like it. From the changes in methyl shift in going from an uncharged molecule to **XXXIX** it was estimated that the 1,3 interaction was approximately 0.5 β.



XXXIX

However, a comparison of the ultraviolet absorption maxima with the HMO excitation energies was considered to be a more sensitive probe of the 1,3 interaction. The wavelength maximum for the pentamethylcyclobutenylcarbonium ion was found to be 245 mμ. From the previously observed wavelength maxima

of normal allylic carbonium ions (approximately 300 mμ) and the cyclopropenyl carbonium ion (185 mμ) which correspond to calculated excitation energies of 1.4β and 3β, respectively, it was calculated that a λ_{max} of 245 mμ would require a transition energy of 1.93β. But in order to calculate a cyclobutenyl cation with a transition energy of 1.93β, a 1,3 resonance integral of 0.33β was required.

By analogy with these observations, it seems likely that some 1,3 interaction could be effective in stabilizing the carbonium ions which are generated from ionization at the one or two position in benzocyclobutene derivatives.

In an effort to demonstrate this additional stabilizing influence in the benzocyclobutene carbonium ion derivatives, plots of pK versus σ^+ (48) were made for the ionization of compounds XXXa-e. In Figure 2 a graph is shown which was obtained by plotting a summation of the σ^+-values for substituents X and Y in structure XXX (Figure 2) versus the pK's obtained from Table V. The best straight line calculated by the least squares method, which could be drawn through the points had a $\rho = -4.58$, and the variation of the points from the line was 0.123. However, a much better correlation of the data by a Hammett plot could be obtained if the σ^+ values for the Y substituents in the benzocyclobutene ring were assigned an additional 0.33 sigma meta effect, due to added stabilization or destabilization of the carbonium ions through the substituent effects on

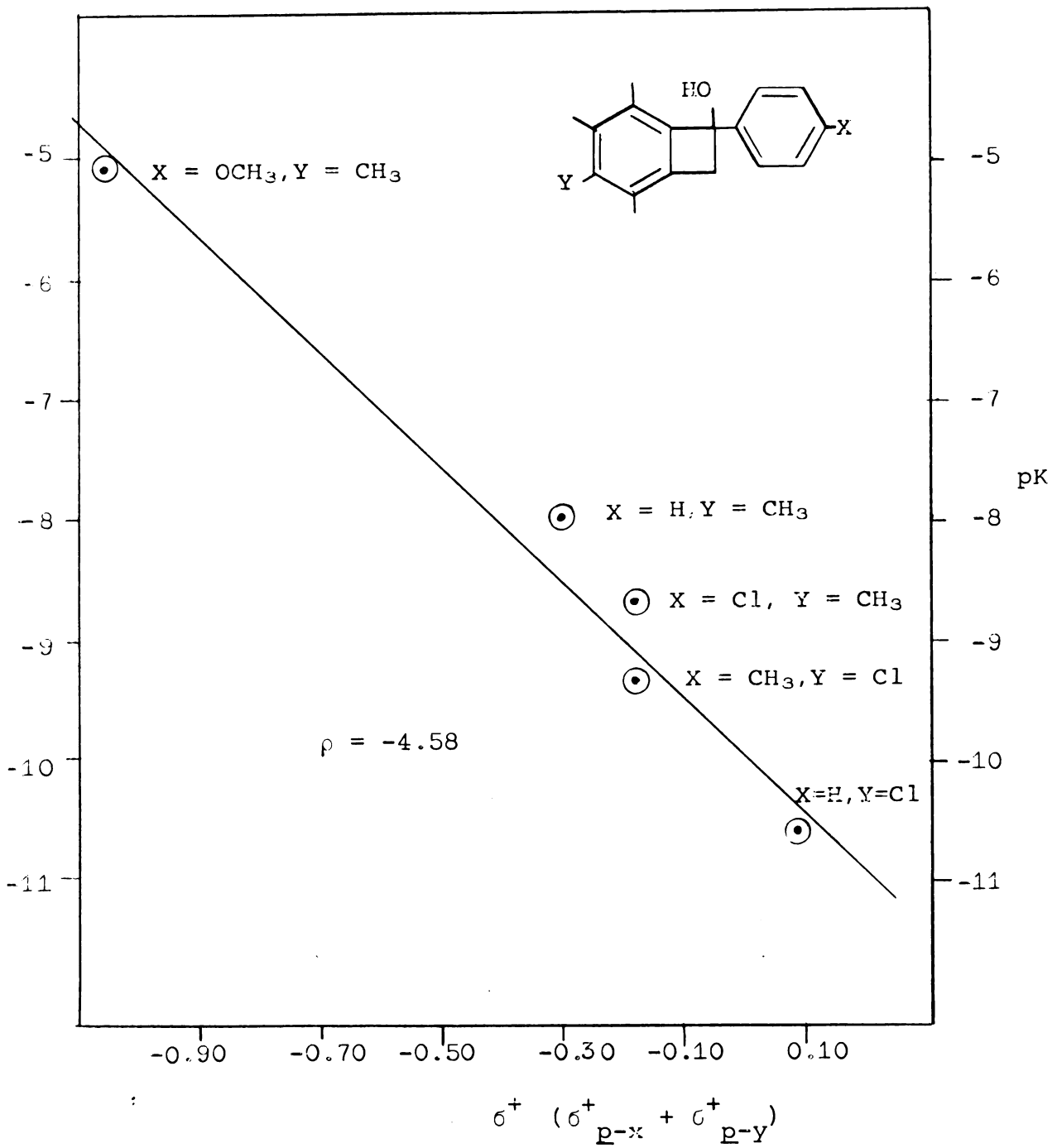


Figure 2. Plot of pK versus σ^+ of benzocyclobutenols without correction for 1,3 interaction.

the additional resonance contributors XXXVe-g. The following equation illustrates the way in which the σ^+ values were calculated in order to obtain the plot shown in Figure 3.

$$\sigma^+ = \text{para-}\sigma^+_X + \text{para-}\sigma^+_Y + \tfrac{1}{3}\ \text{meta-}\sigma^+_Y \qquad (12)$$

The meta constant was chosen as the proper correction parameter to use in the calculation since the added substituent effect operates through structures XXXe-g., in which the substituent is not in direct conjugation with positive charge. The graph thus obtained by plotting pK versus the adjusted sigma plus constants has a $\rho = -4.15$. The variance of the points from this straight line is 0.0139. Thus it is concluded that in the case of the benzocyclobutene carbonium ions investigated here, there is a 1,3 interaction across the fused four-membered ring which is equal to approximately 0.33β, in close agreement with the value found by Katz (47) for cyclobutene carbonium ions. Several additional calculations were made using different values for the magnitude of 1,3 interaction. Using a value of 0.25β, it was found that the straight line correlation was not as good as that obtained when 0.33 was used. However, increasing the value of the 1,3 interaction term to 0.40β improved the fit somewhat (variance equals 0.00980, but a further increase of the parameter to 0.50β causes the variance to increase to 0.0105. These calculations then indicate that

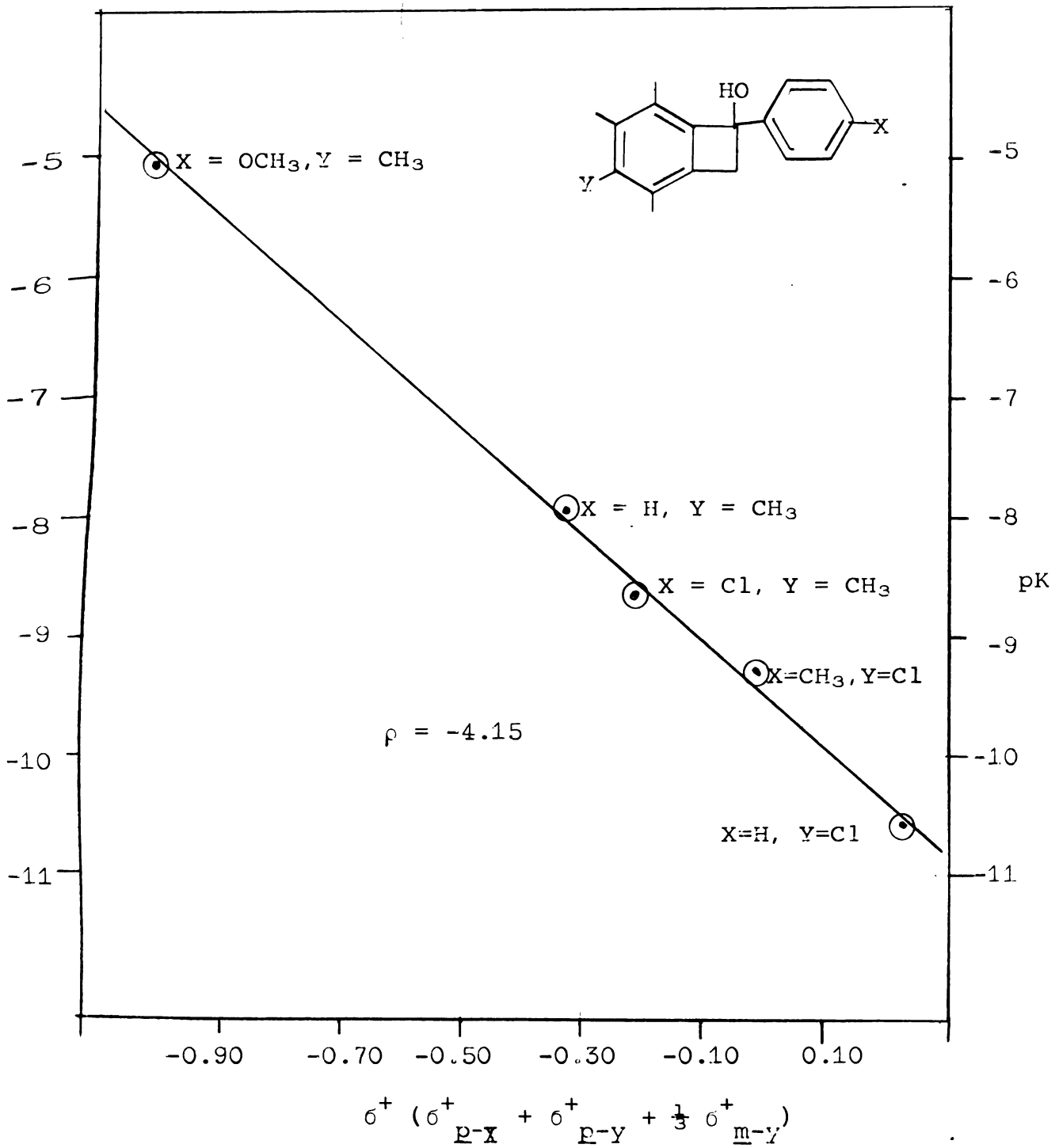
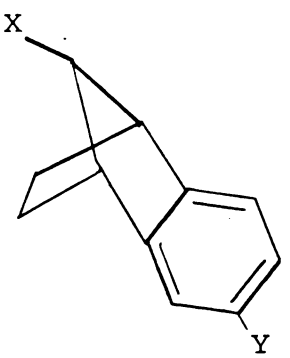


Figure 3. Plot of pK versus σ^+ of benzocyclobutenols with correction for 1,3 interaction.

the 1,3 interaction term may be slightly greater than one-third. Tanida, Teruji and Tshitobi (49) have reported for the solvolysis of substituted benzonorbornenes, (XL), that it is necessary to postulate enhanced substituent effects in order to obtain good straight line correlation of a Hammett plot. Here too, there are two mechanisms by which charge can be transferred to the aromatic ring.



XL

As a comparison of ρ values, a plot of pK versus σ^+ was made for the mono and disubstituted triphenylmethanols available from the investigations of Deno and Jaruzelski and Schriesheim (38). In this case a good straight line was obtained by plotting pK versus the sum of the σ^+ constants involved. The ρ for the graph was -3.50, which is similar to the value reported here for benzocyclobutene carbonium ions. The variance of the points from the straight line is 0.0509 (see Figure 4).

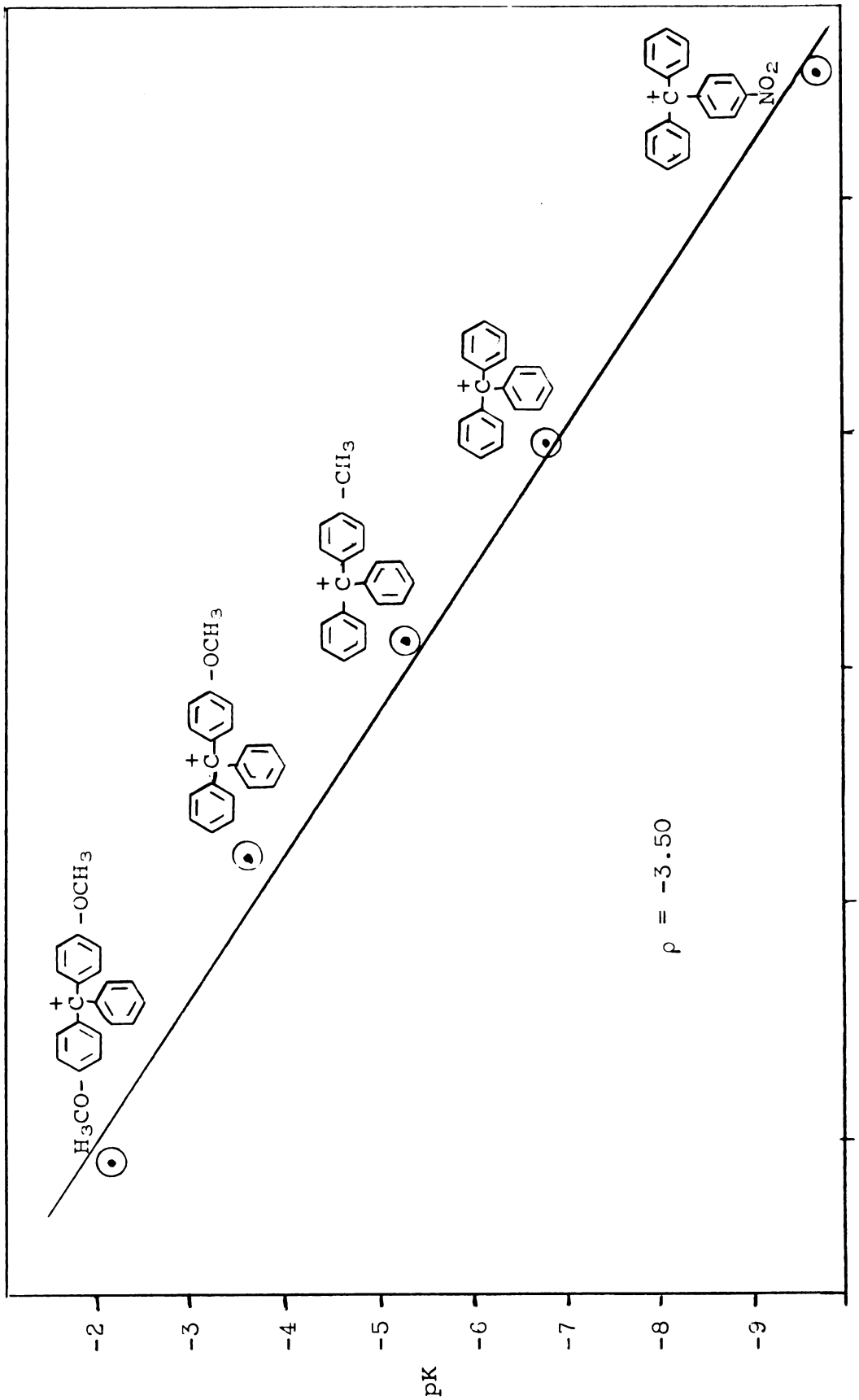


Figure 4. Plot of pK versus σ^+ for monosubstituted and disubstituted triphenylcarbinols.

The pK of 1-(p-chlorophenyl)-4,6-dimethylbenzocyclobutenol was measured in sulfuric acid, and found to be -9.44. This value is very close to the expected value, but the data were not used in the plots found in Figures 2 and 3 since there are several different stability factors which could be expected to influence the ionization constant of the compound. Two of these factors which are worthy of mention are solvation and buttressing effects. It has been shown (50) that steric inhibition to solvation can be an important destabilizing factor with triphenylcarbonium ion derivatives.

The methyl group in the six position on the benzocyclobutene ring certainly has some effect on the steric requirements of the neutral and ionized states, but the direction and extent of this steric influence is not certain. It is expected that the steric factor is constant throughout the series of compounds used in the sigma plus plots. However, buttressing of the methyl group in the six position by the other substituents on the ring should be decreased with 1-(p-chlorophenyl)-4,6-dimethylbenzocyclobutenol leading to a diminished steric influence of the methyl group in close proximity to the ionization site.

Attempted Acid and Base Catalyzed Deuterium Exchange in Tetramethylbenzocyclobutenone

Several attampts were made to exchange the alpha hydrogen atoms of tetramethylbenzocyclobutenone by treating the

ketone with sulfuric acid-d_2 and sodium ethoxide-deuterium oxide in dry ethanol. In either case it was found by n.m.r. analysis that no deuterium was incorporated into the molecule, and thus enolization of the molecule is energetically very unfavorable. In previous attempts to effect the enolization (4), one base catalyzed attempt to effect exchange was reported as successful, but the experiment could not be repeated. In this investigation that experiment was once more attempted, with the same negative results. It was found that ring opening to yield pentamethylbenzoic acid was accomplished before any deuterium exchange could be detected.

In the extreme case of acid catalysis it was demonstrated that tetramethylbenzocyclobutenone could be protonated to produce a colored species (λ_{max} = 380 mμ) having a completely different n.m.r. spectrum. Even under these conditions the peak at τ = 4.20 (assigned to the methylene protons) was not diminished in intensity, and unexchanged tetramethylbenzocyclobutenone could be isolated from the solution after hydrolysis.

EXPERIMENTAL

A. Synthesis:

Trichloromethylpentamethylbenzene

Trichloromethylpentamethylbenzene was prepared as described by Fish (4). Reported below is a more detailed procedure which includes some suggestions for improving the reproducibility of the method.

In an air-dried one-liter three-necked round-bottomed flask equipped with an addition funnel, Tru-bore stirrer, and a thermometer suspended through a drying tube was placed 100 g. (0.751 mole) of anhydrous powdered aluminum chloride and 125 ml. of carbon tetrachloride. To this stirred suspension was added slowly (ca 2 hours) a solution containing 50.0 g. (0.367 mole) of pentamethylbenzene in 100 ml. of carbon tetrachloride. During this addition, the temperature of the reaction was raised to and maintained at 37-42°. Hydrogen chloride started to evolve soon after heating and the addition of pentamethylbenzene was initiated. The reaction mixture quickly turned dark purple. After maintaining the reaction mixture at 37-42° with stirring for four hours, the purple complex was poured slowly into a three-liter beaker containing

---

*All analysis were done by Spang Microanalytical Laboratory, Ann Arbor, Michigan. Melting points are uncorrected.

50 ml. of concentrated hydrochloric acid, 100 ml. of carbon tetrachloride and about 200 g. of ice. The addition was interrupted from time to time while the slurry was stirred, until most of the purple complex was decomposed. More ice was added as needed to keep the hydrolysis mixture cool, and the addition of complex was continued until the entire reaction mixture was hydrolyzed. The orange organic layer was separated, washed with 50 ml. of 5% sodium bicarbonate solution, two 50-ml. portions of warm (40°) water, and dried over anhydrous magnesium sulfate. The solvent was evaporated on a rotary evaporator keeping the temperature below 60°. A light tan solid remained which was recrystallized three times from pentane to give 53.7 g. (77.5%) of white platelets m.p. 93-94.5°. The infrared spectrum of this material was identical to that reported (4).

Tetramethylbenzocyclobutenone (2,3,4,5-tetramethylbicyclo[4.2.0]octa-1,3,5-triene-7-one)

Into each of three 8" test tubes was placed 3.00 g. (0.0119 mole) of trichloromethylpentamethylbenzene. The reaction tubes were heated in an oil bath at 115-120° under a stream of nitrogen for three hours. Hydrogen chloride was evolved during the course of the reaction, but evolution stopped after three hours. The brown oil which remained solidified upon cooling. The combined solid from the three tubes was transferred to a 150 ml. round-bottomed flask and refluxed four hours in 75 ml. of 10% aqueous acetone.

The acetone was evaporated over a steam bath to give a tan solid which was recrystallized twice from 95% ethanol, giving 4.84 g. (71.0%) of white needles, m.p. 153-154°. The infrared spectrum was identical to one obtained from a sample of tetramethylbenzocyclobutenone prepared by Fish (4).

Tetramethylbenzocyclobutenol (1,2,3,4,5-Tetramethylbicyclo [4.2.0] octa-1,3,5-triene-7-ol)

1. Lithium aluminum hydride reduction of the ketone at reflux.

In a 500-ml. three-neck round-bottomed flask equipped with an addition funnel, reflux condenser, and Tru-bore stirrer was placed 2.00 g. (0.0527) mole of lithium aluminum hydride and 100 ml. of tetrahydrofuran, which was freshly distilled from lithium aluminum hydride. To this stirred refluxing solution was added 1.80 g. (0.0120 mole) of tetramethylbenzocyclobutenone dissolved in 50 ml. of freshly dried tetrahydrofuran, over a one-hour period. The solution was stirred at reflux for four hours after addition was complete. The mixture was cooled and excess lithium aluminum hydride was hydrolyzed by dropping water slowly into the reaction mixture. The reaction mixture was poured into 100 ml. of water and 10 ml. of concentrated hydrochloric acid, extracted with two 50-ml. portions of ether, and the combined organic portions were evaporated in an air stream, yielding 1.62 g. of a white powder, m.p. 153-157°. Its infrared spectrum showed no carbonyl absorption. The mixture was chromatographed on 25g. of 24 F Alcoa alumina using petroleum ether

as eluant. The first and minor product (~10%) through the column was hexamethylbenzene, m.p. 160-161°. The second material obtained from the column was the major product (~90%), white needles, m.p. 158-159° and its infrared spectrum in carbon tetrachloride was similar to that reported by Fish (4) for tetramethylbenzocyclobutenol in that solvent, but it was also similar to the spectrum he reported for pentamethylbenzyl alcohol in carbon disulfide. A sample of pentamethylbenzyl alcohol prepared by Fish gave a spectrum in carbon tetrachloride identical to the product obtained from this reduction.

Anal.: Calcd. for $C_{12}H_{18}O$: C, 80.85; H, 10.18.
Found: C, 80.91; H, 10.22. (Calcd. for $C_{12}H_{16}O$: C, 81.77; H, 9.15).

2. Reduction of Tetramethylbenzocyclobutenone with Sodium Borohydride.

To a 500-ml. three-necked round-bottomed flask equipped with a reflux condenser, addition funnel, and Tru-bore stirrer was added 2.50 g. (0.060 mole) of sodium borohydride and 50 ml. of diglyme. To this stirred reaction mixture was added 1.90 g. (0.0120 mole) of tetramethylbenzocyclobutenone in 50 ml. of diglyme. The addition was completed in 1.5 hours, after which the temperature was raised to 90° and maintained there for eight hours. The mixture was then poured over 100 g. of ice and 25 ml. of concentrated hydrochloric acid. The white precipitate which formed was

extracted with three 25-ml. portions of ether. The combined ether layers were washed with two 25-ml. portions of water, dried over anhydrous calcium chloride, and evaporated to give a crude product which showed carbonyl and hydroxyl absorption in the infrared. The product was chromatographed on an alumina column using 30-60° petroleum ether as solvent. Two materials were separated and identified by melting point and infrared spectrum. They were unreacted starting material, m.p. 155-156° (18%) and pentamethylbenzyl alcohol, m.p. 158-159° (50%).

3. Reduction of Tetramethylbenzocyclobutenone with Lithium Aluminum Hydride at Room Temperature.

In a 500-ml. three-necked flask was placed 2.00 g. (0.050 mole) of lithium aluminum hydride with 100 ml. of freshly dried tetrahydrofuran. The solution was stirred at room temperature while 2.00 g. (0.012 mole) of tetramethylbenzocyclobutenone in 100 ml. of tetrahydrofuran was added from a dropping funnel over a one-half hour period. The suspension which quickly formed was stirred for four hours, then hydrolyzed by the slow addition of water until there was no further vigorous reaction. The remaining mixture was poured into an equal quantity of water and extracted twice with 50-ml. of ether. The combined ether layers were washed with water, separated and dried over anhydrous potassium carbonate. The solvent was evaporated using a

Rinco rotary evaporator leaving 1.96 g. of white solid, m.p. 134-136.° The infrared spectrum showed absorption at 2.83μ and a small carbonyl peak at 5.95μ. Chromatography of the mixture on Alcoa 20F alumina using 30-60° petroleum ether as eluant separated traces of a carbonyl containing compound from a mixture of alcohols, m.p. 138-140°. This mixture could not be separated by chromatography, recrystallization from 60-90° petroleum ether or sublimation. The n.m.r. of the white material was like that of tetramethylbenzocyclobutenol except for absorbances at τ = 4.60, 2.34 and 2.22 which were assigned to pentamethylbenzyl alcohol impurity.

4. Preparation of Tetramethylbenzocyclobutenol by Reduction of Tetramethylbenzocyclobutenone with Aluminum Hydride.

Aluminum hydride was prepared by reaction of lithium aluminum hydride with aluminum chloride (51). Into a 100-ml. round-bottomed flask was placed 1.05 g. (0.0273 mole) of lithium aluminum hydride and 50 ml. of anhydrous ethyl ether. The solution was stirred with a magnetic stirrer while 1.19 g. (0.00901 mole) of aluminum chloride was added slowly with care. There was evidence for an immediate reaction, because the reaction vessel became warm and lithium chloride precipitated. The reaction mixture was stirred for one-half hour, then filtered under a dry nitrogen stream into a dry 300-ml. round-bottomed,

three-necked flask equipped with an addition funnel, and drying tube. A clear solution of aluminum hydride was obtained which was diluted with 50 ml. of dry ether. The ether solution was stirred with a magnetic stirrer while 6.00 g. (0.0366 mole) of tetramethylbenzocyclobutenone in 50 ml. of ether was added slowly over a three-fourths hour period. After the addition was complete the reaction mixture was stirred for four hours. Small chips of ice were added to hydrolyze any excess aluminum hydride before the reaction mixture was poured into 100 ml. of water containing 10 ml. of concentrated hydrochloric acid. The ether layer was separated, washed with 50 ml. of water and dried over anhydrous calcium chloride. The ether was evaporated, leaving 6.24 g. (96.5%) of white solid which was recrystallized once from 60-90° petroleum ether to produce 6.00 g. (92.1%) of fine white needles, m.p. 137-138°. The infrared and n.m.r. spectra are presented in Figures 5 and 6.

Anal.: Calcd. for $C_{12}H_{14}O$: C, 81.77; H, 9.15.

Found: C, 81.66; H, 9.08.

Tetramethylbenzocyclobutenone from Tetramethylbenzocyclobutenol

Into a 25-ml. round-bottomed flask was placed 0.50 g. (0.0027 mole) of tetramethylbenzocyclobutenol with 10 ml. of ethyl ether. This solution was stirred with a magnetic stirrer while a solution containing 5 ml. of water, 0.5 ml. of 96% sulfuric acid and 0.30 g. (0.0010 mole) of

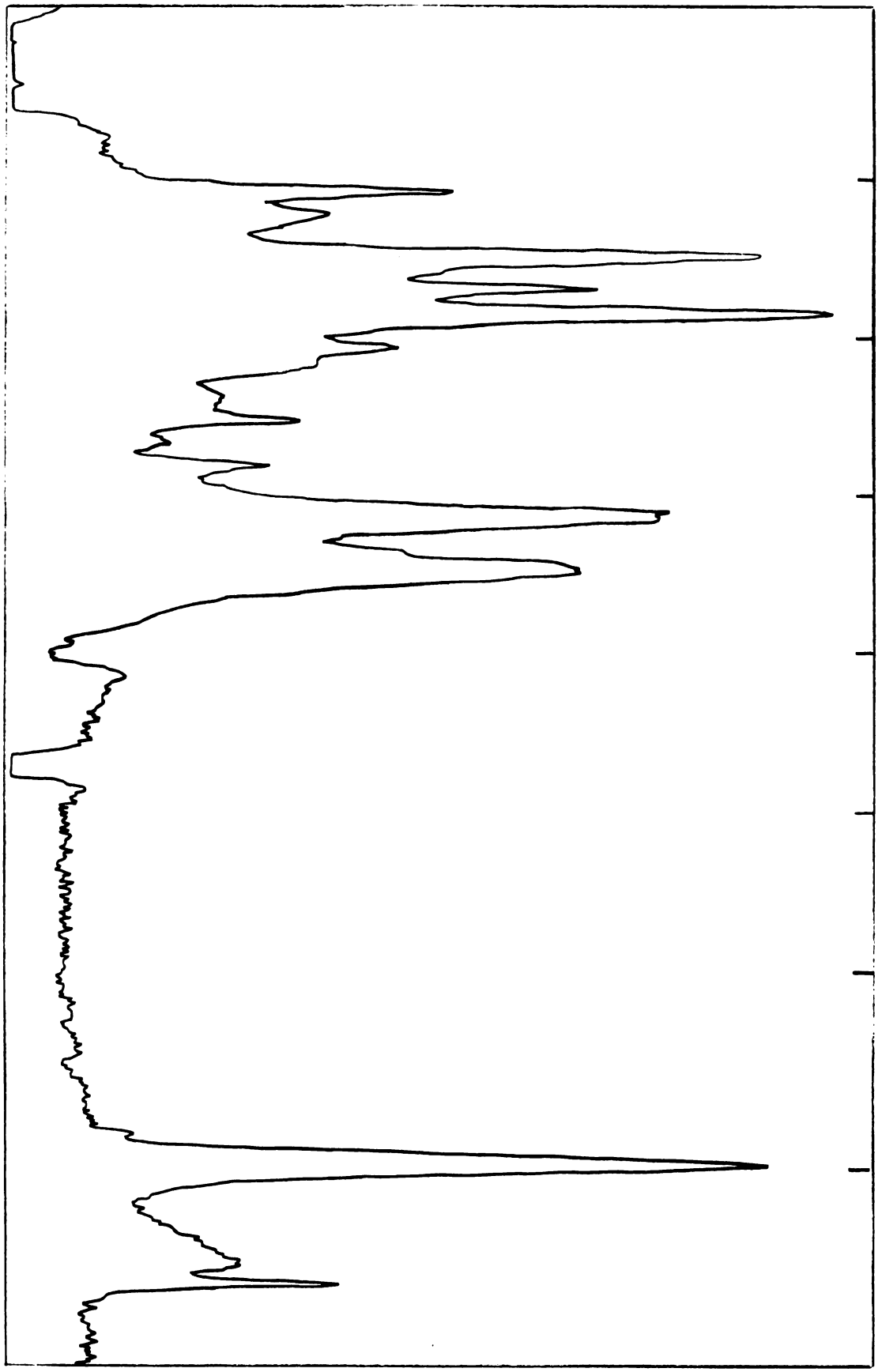


Figure 5. Infrared spectrum of tetramethylbenzocyclobutenol (CCl_4 solution)

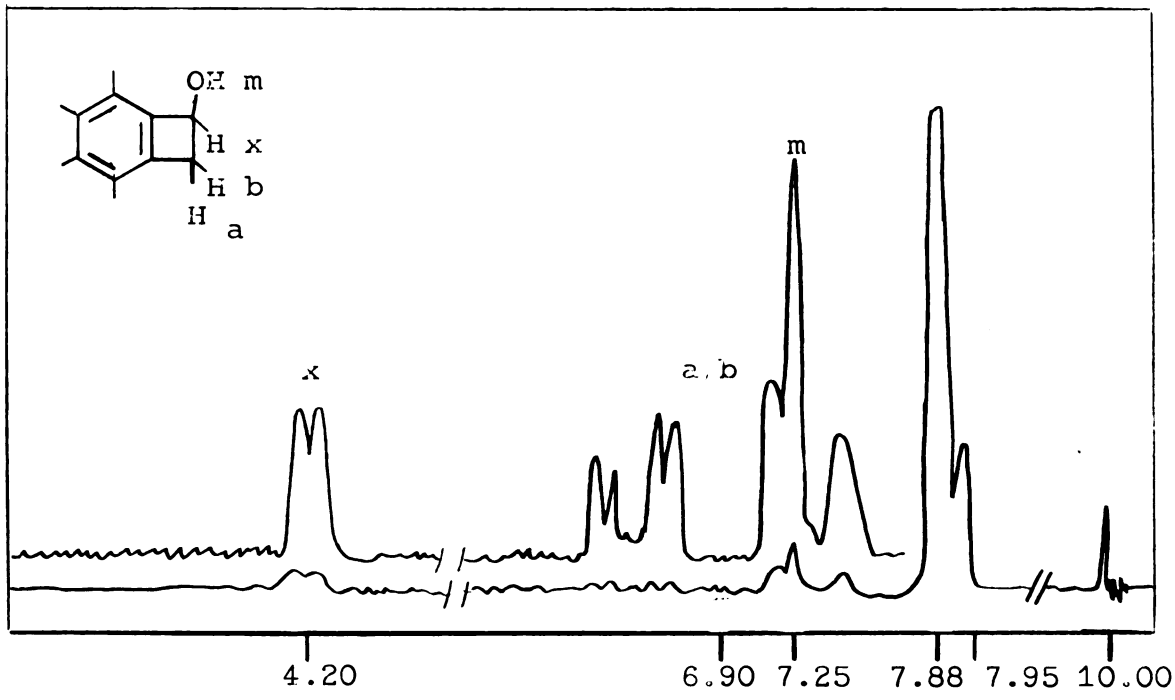


Figure 6. Proton magnetic resonance spectrum of tetramethylbenzocyclobutenol. ($CDCl_3$ solution)

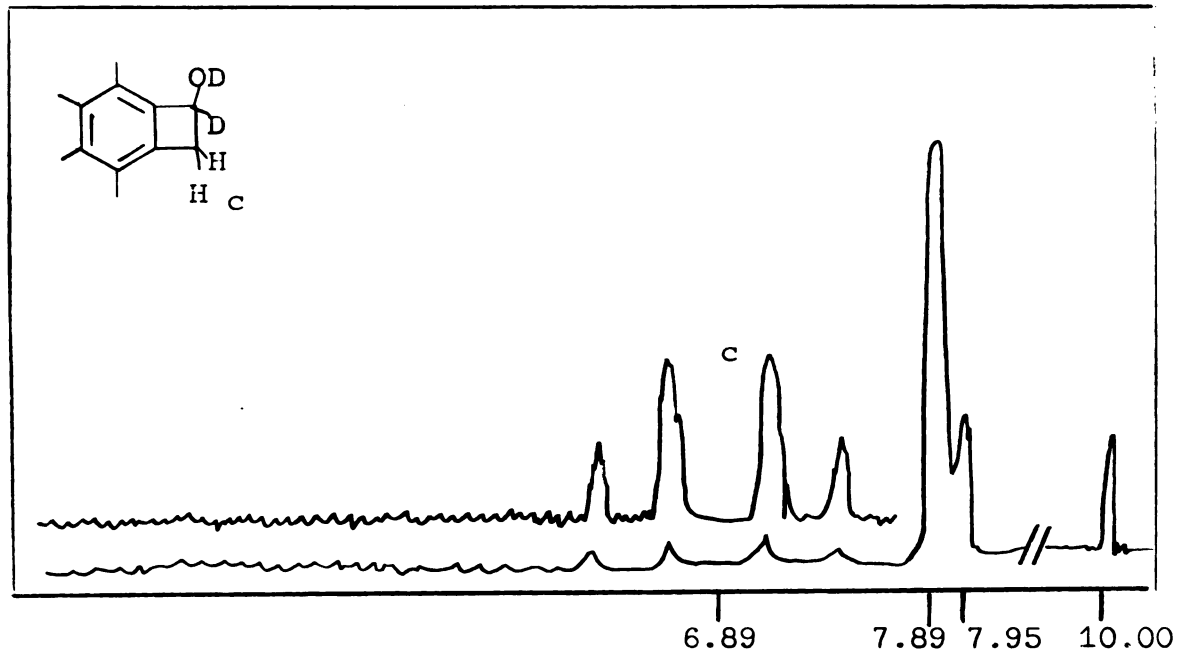


Figure 7. Proton magnetic resonance spectrum of 1-deuterotetramethylbenzocyclobutenol. ($CDCl_3$ solution)

sodium dichromate was added over a fifteen minute period. The aqueous layer turned green in a short time. After an hour and one-half the ether layer was separated, washed with 15 ml. of 5% sodium bicarbonate solution, two 15-ml. portions of water and the ether was evaporated to give white product, m.p. 130-132°. This product was shown to be mostly unoxidized tetramethylbenzocyclobutenol with some tetramethylbenzocyclobutenone by its infrared spectrum. The recovered starting material was treated again as described above with the reaction period extended to five hours. White needles were obtained from ethanol, m.p. 153-154°. The infrared spectrum was identical to that of tetramethylbenzocyclobutenone.

1-Deuterotetramethylbenzocyclobutenol

Into a 50-ml. round-bottomed flask was placed 0.18 g. (0.0043 mole) of lithium aluminum deuteride. To this was added 0.20 g. (0.0015 mole) of anhydrous powdered aluminum chloride and 25 ml. of anhydrous ether. The aluminum deuteride solution was filtered under nitrogen into a 150-ml. round-bottomed flask. To this solution, which was stirred magnetically, was added 1.00 g. (0.0061 mole) of tetramethylbenzocyclobutenone in 10 ml. of anhydrous ether. After two hours of stirring, the mixture was poured into 50 ml. of 2 N hydrochloric acid and the organic layer was separated, dried over calcium chloride and the ether evaporated. The white solid which remained was recrystallized from 60-90°

petroleum ether to produce fine white needles, m.p. 127-129°. One more recrystallization from petroleum ether gave 0.93 g. (87%) of white needles, m.p. 137-138°. The infrared spectrum was like that of tetramethylbenzocyclobutenol except for a weak band at 4.63μ which is assigned to C-D stretch. The n.m.r. spectrum is presented in Figure 7.

Stability of Tetramethylbenzocyclobutenol Toward Base

Into a small stoppered test tube was placed 0.05 g. (0.2 mmoles) of tetramethylbenzocyclobutenol with 2 ml. of 0.25 N sodium hydroxide. The tube was shaken for two hours at room temperature; then the contents were filtered and washed with distilled water. The infrared spectrum of the product was identical to that of starting material. The same material was heated on a steam bath in 2 ml. of 0.25 normal base for three hours. After filtering and washing the product, an infrared spectrum showed that the material was largely pentamethylbenzaldehyde with some minor absorbances attributable to tetramethylbenzocyclobutenol. After two additional hours of 0.25 normal base treatment at 100°, and reisolation, the conversion was complete as evidenced by the exact match of the spectrum with that of the spectrum obtained from an authentic sample of pentamethylbenzaldehyde. The small amount of compound was recrystallized from ethanol-water to give platelets, m.p. 137-138°. An authentic sample of pentamethylbenzaldehyde had a melting point 139-140°.

Reduction of Pentamethylbenzaldehyde

Into a 100-ml. round-bottomed flask equipped with a dropping funnel, reflux condenser, and Tru-bore stirrer was placed 1.50 g. (0.0395 mole) of lithium aluminum hydride and 25 ml. of freshly dried tetrahydrofuran. The mixture was heated to reflux and 1.50 g. (0.00715 mole) of pentamethylbenzaldehyde in 25 ml. of tetrahydrofuran was added dropwise. After the addition was complete, the mixture was stirred and maintained at reflux temperature for eight hours. The reaction mixture was poured into 50 ml. of 2 N hydrochloric acid and extracted twice with 25-ml. portions of ether. The organic layer was washed with water, dried over anhydrous calcium chloride and evaporated on a Rinco rotary evaporator. The white product which remained could be separated into two products using an Alcoa 20F alumina column. The first product was eluted from the column with 30-60° petroleum ether, and was identified by its melting point (159-160°) and infrared spectrum as hexamethylbenzene. The other product was eluted with 75% petroleum ether and 25% diethyl ether, and was identified by melting point (159-160°) and infrared spectrum as pentamethylbenzyl alcohol. The products were also identified by their retention times on a 20% silicon on chromosorb v.p.c. column at 180°, and the product yields were found to be 90% pentamethylbenzyl alcohol and 10% hexamethylbenzene.

1-Bromobenzocyclobutene (7-Bromo-2,3,4,5-tetramethylbicyclo[4.2.0]octa-1,3,5-triene)

In a 50-ml. round-bottomed flask was placed 5.40 g. (0.200 mole) of phosphorus tribromide. The flask was chilled in an ice bath and 7.00 g. (0.0397 mole) of tetramethylbenzocyclobutenol in 100 ml. of methylene chloride was added dropwise. After the addition was complete, stirring was continued for one hour. Small chips of ice were added to slowly hydrolyze excess phosphorus tribromide, and then the reaction solution was poured into 100 ml. of water. The methylene chloride layer was separated, washed with water and dried over anhydrous calcium chloride. The methylene chloride was evaporated, leaving a low melting solid which was recrystallized from methanol-water to give 5.60 g. (59.5%) white crystals, m.p. 44.5-46°. One more recrystallization gave small needles, m.p. 45-46°. Repetition of this reaction produced 1-bromotetramethylbenzocyclobutene in 71.1, 31.0 and 57.5 percent yields. The infrared spectrum is presented in Figure 8. The n.m.r. spectrum (Figure 10) showed a doublet centered at 4.78 τ (J = 4 c.p.s.) which integrated for one proton, an AB pattern centered at 6.58 τ ($\delta A - \delta B$ = 26.9 c.p.s.) with the A portion of the multiplet split into doublets (J = 4 c.p.s.) and two singlets at 7.88 and 7.94 τ which integrated for twelve protons (the ratio of the latter two peak areas was approximated visually as 3:1). These absorbances were assigned to

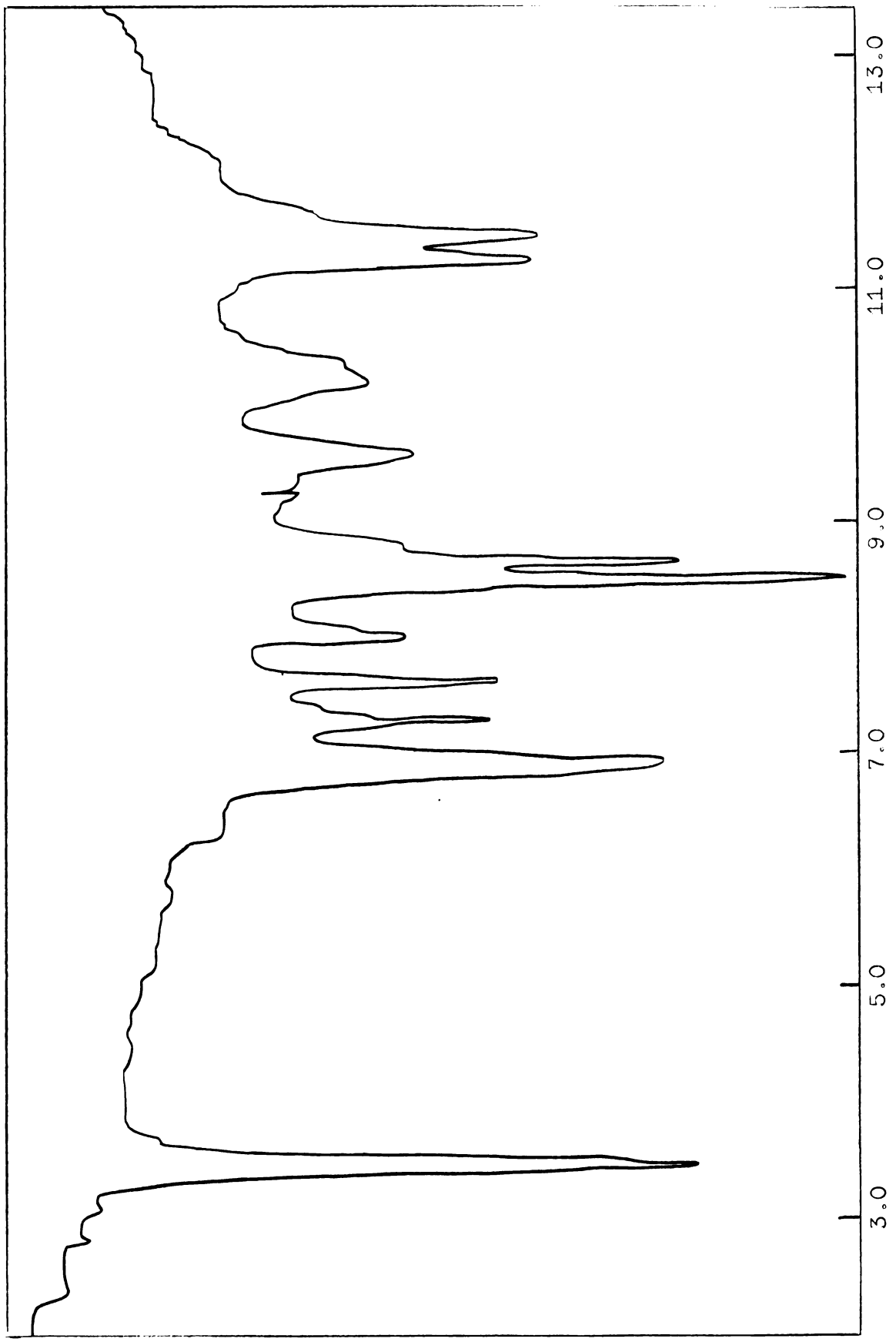


Figure 8. Infrared spectrum of 1-bromotetramethylbenzocyclobutene. (CCl_4 solution)

the hydrogen α to the bromine, the methylene protons, and the four methyl groups, respectively.

Anal.: Calcd. for $C_{12}H_{15}Br$: C, 60.26; H, 6.32.

Found: C, 60.34; H, 6.37.

1-Cyanotetramethylbenzocyclobutene(7-Cyano-2,3,4,5-tetramethylbicyclo[4.2.0]octa-1,3,5-triene]

1-Cyanotetramethylbenzocyclobutene was prepared according to an adaptation of the procedure reported by Cava, Litle and Napier (2). Into a 25-ml. round-bottomed flask was placed 0.80 g. (0.0030 mole) of 1-bromotetramethylbenzocyclobutene with 0.34 g. (0.0060 mole) of sodium cyanide and 9 ml. of dimethylsulfoxide. The solution was allowed to stand for one-half hour. The solution was cooled in an ice bath and 30 ml. of water was added, causing a white precipitate to form which was extracted with 30 ml. of diethyl ether. The ether was evaporated leaving a cream colored solid whose infrared spectrum showed absorption at 4.51μ. Recrystallization of this material once from petroleum ether produced 0.41 g. (83%) of white crystals, m.p. 62-65°. Two more recrystallizations from ethanol produced white needles m.p. 70-71°. The infrared spectrum is presented in Figure 9. The n.m.r. spectrum (Figure 11) showed unresolved multiplets at 6.15 and 6.70 τ, and two singlets at 7.87 and 7.97 τ, with relative areas 1:2:9:3. These resonance frequency absorbances were assigned to the α-hydrogen, methylene hydrogens, and the four methyl groups.

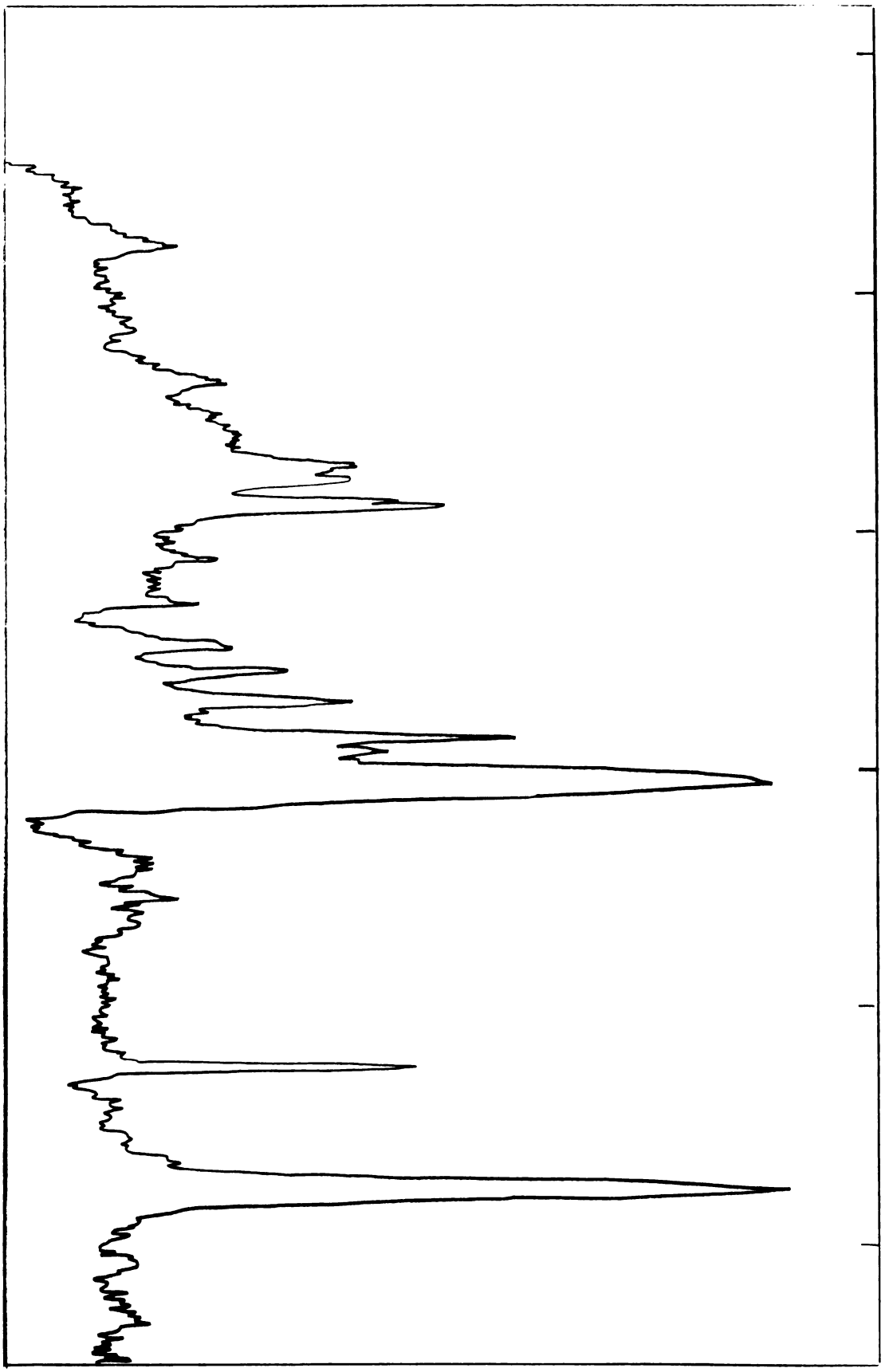


Figure 9. Infrared spectrum of 1-cyanotetramethylbenzocyclobutene. (CCl_4 solution)

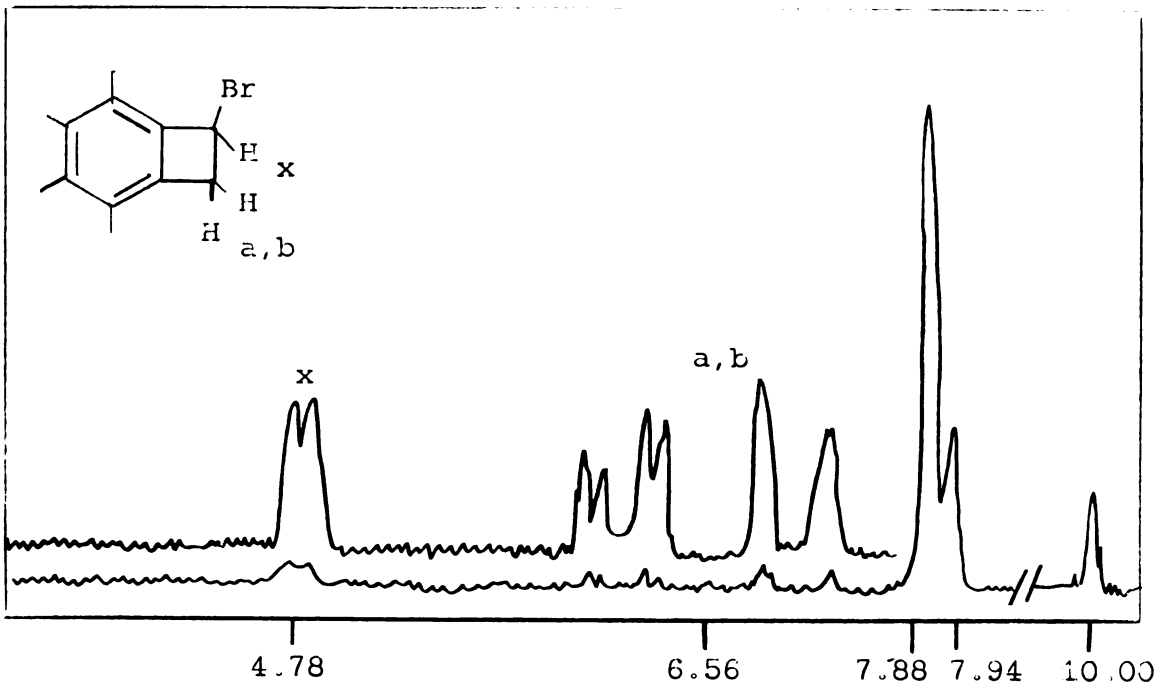


Figure 10. Proton magnetic resonance spectrum of 1-bromo-tetramethylbenzocyclobutene. (CCl_4 solution)

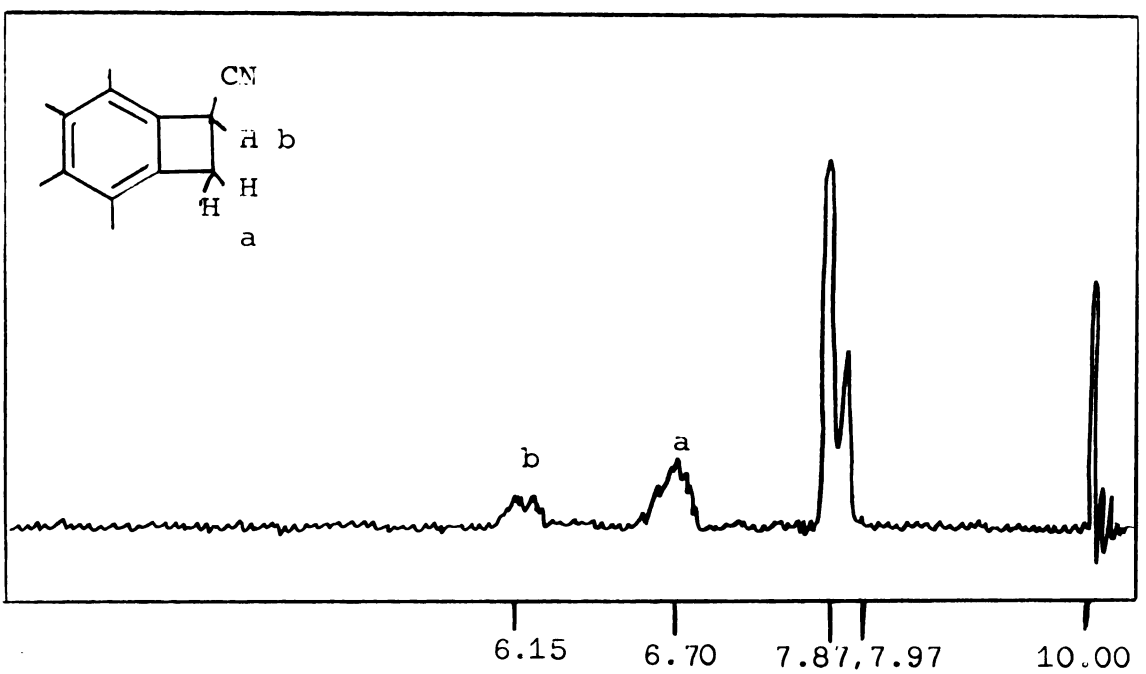


Figure 11. Proton magnetic resonance spectrum of 1-cyano-tetramethylbenzocyclobutene. (CCl_4 solution)

Anal.: Calcd. for $C_{13}H_{15}N$: C, 84.28; H, 8.16.

Found: C, 84.16; H, 8.00.

This reaction was repeated several times with different amounts of starting material. The yields were quite inconsistent, largely due to the difficulty in obtaining good recrystallizations of the compound. When 5.00, 0.80 and 3.85 grams of 1-bromotetramethylbenzocyclobutene were used as starting material in the reaction, the yields were 55.7, 76, and 10 percent, respectively.

1-Carbcxamidotetramethylbenzocyclobutene-(7-Carboxamido-2,3,4,5-tetramethylbicyclo-[4.2.0]octa-1,3,5-triene)

The reaction of 1-cyanotetramethylbenzocyclobutene with hydrogen peroxide and base to form the amide was carried out according to a procedure reported by Cava, Litle and Napier (52) for the hydrolysis of 1-cyanobenzocyclobutene.

Into a 6" test tube was placed 0.50 g. (0.0027 mole) of 1-cyanotetramethylbenzocyclobutene. To this was added one ml. of 30% (0.0085 mole) hydrogen peroxide and 2 ml. of 20% sodium hydroxide solution. The mixture was stirred for fifteen minutes and warmed on a steam bath to 60° until oxygen evolution ceased (15 min.). Ten ml. of ethanol was added to the reaction and warming was continued for an additional ten minutes. On cooling a white precipitate formed which was filtered, washed with water and dried to produce 0.30 g. (55%) of white solid, m.p. 237-240°.

The compound was recrystallized from methanol to give white needles m.p. 260-261°. The infrared spectrum taken from a mineral oil smear is illustrated in Figure 12.

Anal.: Calcd. for $C_{13}H_{16}ON$: C, 77.19; H, 7.97.

Found: C, 76.93; H, 7.91.

1-Phenyltetramethylbenzocyclobutenol (7-Phenyl-2,3,4,5-tetramethylbicyclo-[4.2.0]octa-1,3,5-triene-7-ol)

Into a three-necked 250-ml. round-bottomed flask, fitted with a Tru-bore stirrer, reflux condenser, gas inlet tube, and a dropping funnel was placed 1.21 g. (0.050 g.-atom) of magnesium turnings and 20 ml. of tetrahydrofuran which was freshly distilled over lithium aluminum hydride. A stream of dry nitrogen was passed over the stirred mixture and 0.50 g. (4.5 mmoles) of bromobenzene was added dropwise in 5 ml. of tetrahydrofuran. The reaction was heated to reflux and maintained for one hour, and then 2.00 g. (12.4 mmoles) of tetramethylbenzocyclobutenone in 10-ml. of tetrahydrofuran was added slowly. After the addition was complete (ca. 30 min.) the reaction mixture was maintained under reflux for four hours.

The reaction mixture was poured into an equal quantity of 5% aqueous hydrochloric acid and extracted with 30 ml. of ether. The organic layer was separated, washed twice with 15 ml. of water and dried over anhydrous calcium chloride. The solvent was removed on a Rinco rotary evaporator, leaving

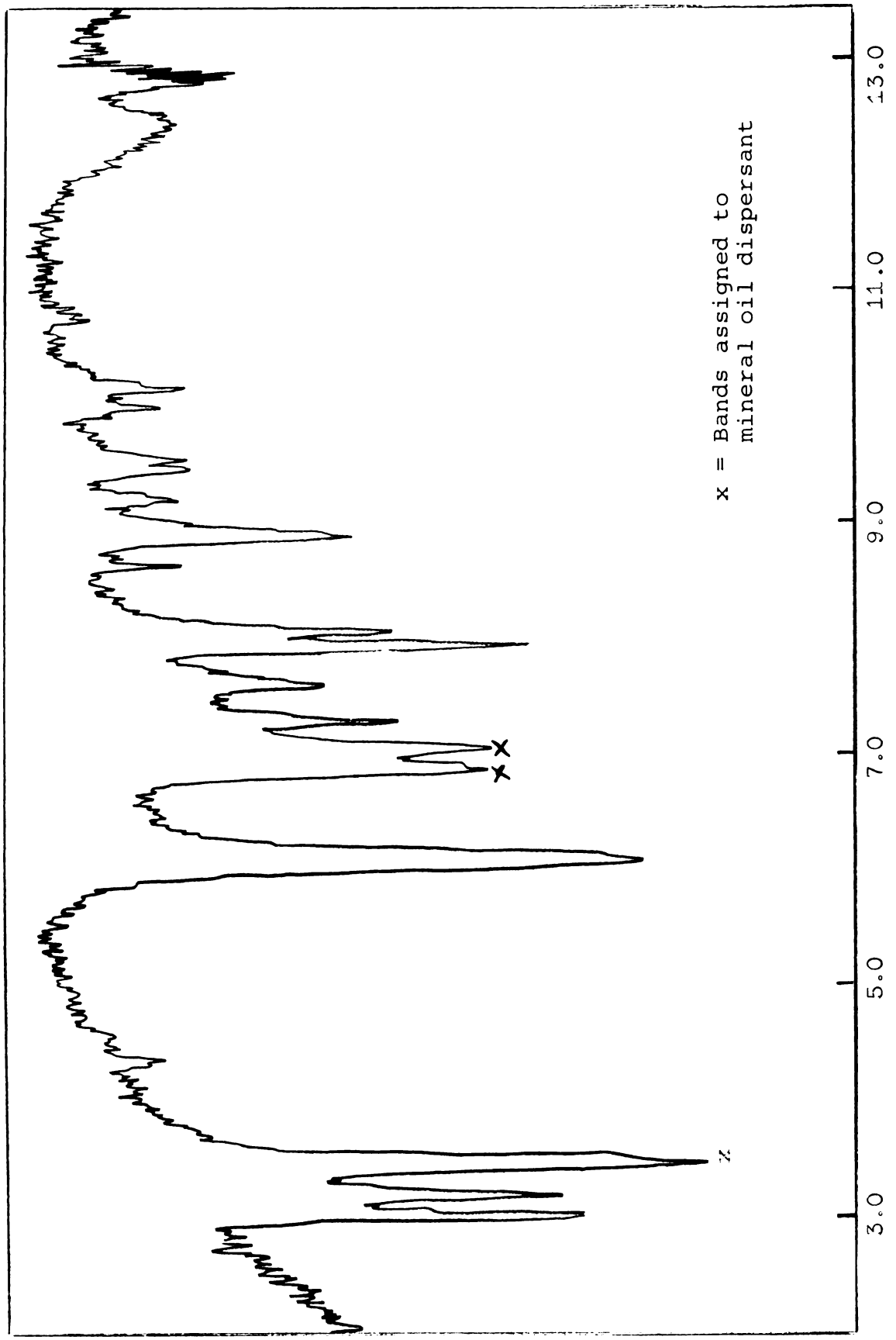


Figure 12. Infrared spectrum of 1-Carboxamidotetramethylbenzocyclobutene.

a viscous oil which was separated from impurities by column chromatography on Alcoa 20 F alumina using 30-60° petroleum ether as solvent.

The white solid obtained was recrystallized three times from 60-90° petroleum ether to give 1.03 g. (34.9%) white cubes, m.p. 89-90°. The n.m.r. and infrared spectra were consistent with the assigned structure and are illustrated in Figures 13 and 15.

Anal.: Calcd. for $C_{18}H_{20}O$: C, 85.67; H, 7.99.

Found: C, 85.34; H, 7.90.

1-Methoxy-1-(p-chlorophenyl)-tetramethyl-benzocyclobutene(7-Methoxy-7-(p-chloro-phenyl)-2,3,4,5-tetramethylbicyclo[4.2.0]-octa-1,3,5-triene)

Into a three-necked 250-ml. round-bottomed flask, fitted with a Tru-bore stirrer, reflux condenser, gas inlet tube and a dropping funnel was placed 0.96 g. (0.039 g.-atom) of magnesium turnings and 10 ml. of tetrahydrofuran which was freshly distilled from lithium aluminum hydride and 3.82 g. (0.020 mole) of p-chlorobromobenzene. The reaction mixture was stirred and heated to reflux for one hour. During this time the reaction mixture turned dark grey. At the end of the initial reflux period 2.00 g. (0.0115 mole) of tetra-methylbenzocyclobutenone in 15 ml. of tetrahydrofuran was added slowly (ca. 20 minutes). The reaction solution was refluxed and stirred for three hours, then poured into 50 ml. of cold water and 5 ml. of hydrochloric acid. The organic

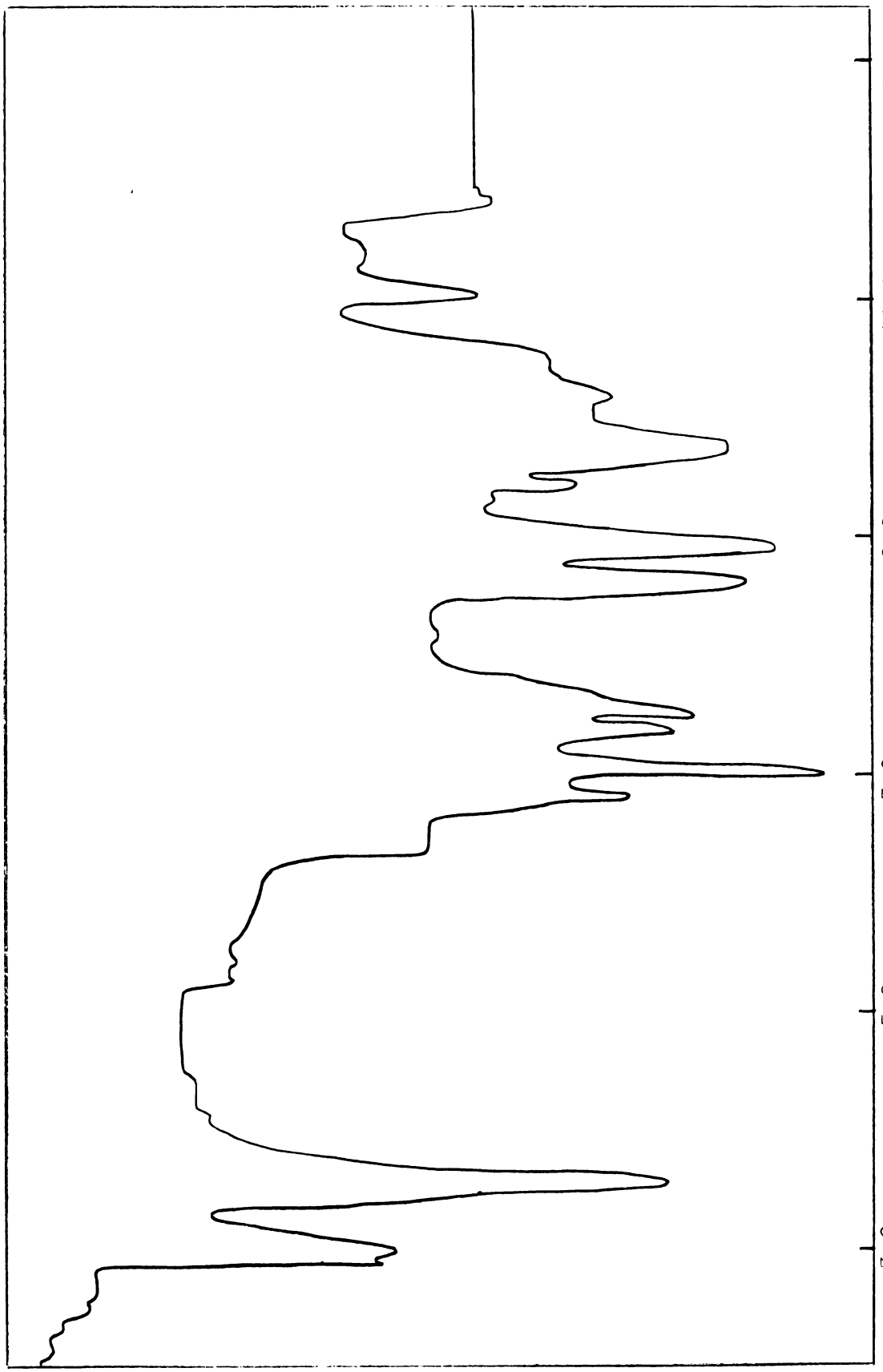


Figure 13. Infrared spectrum of 1-phenyltetramethylbenzocyclobutenol. (CCl_4 solution)

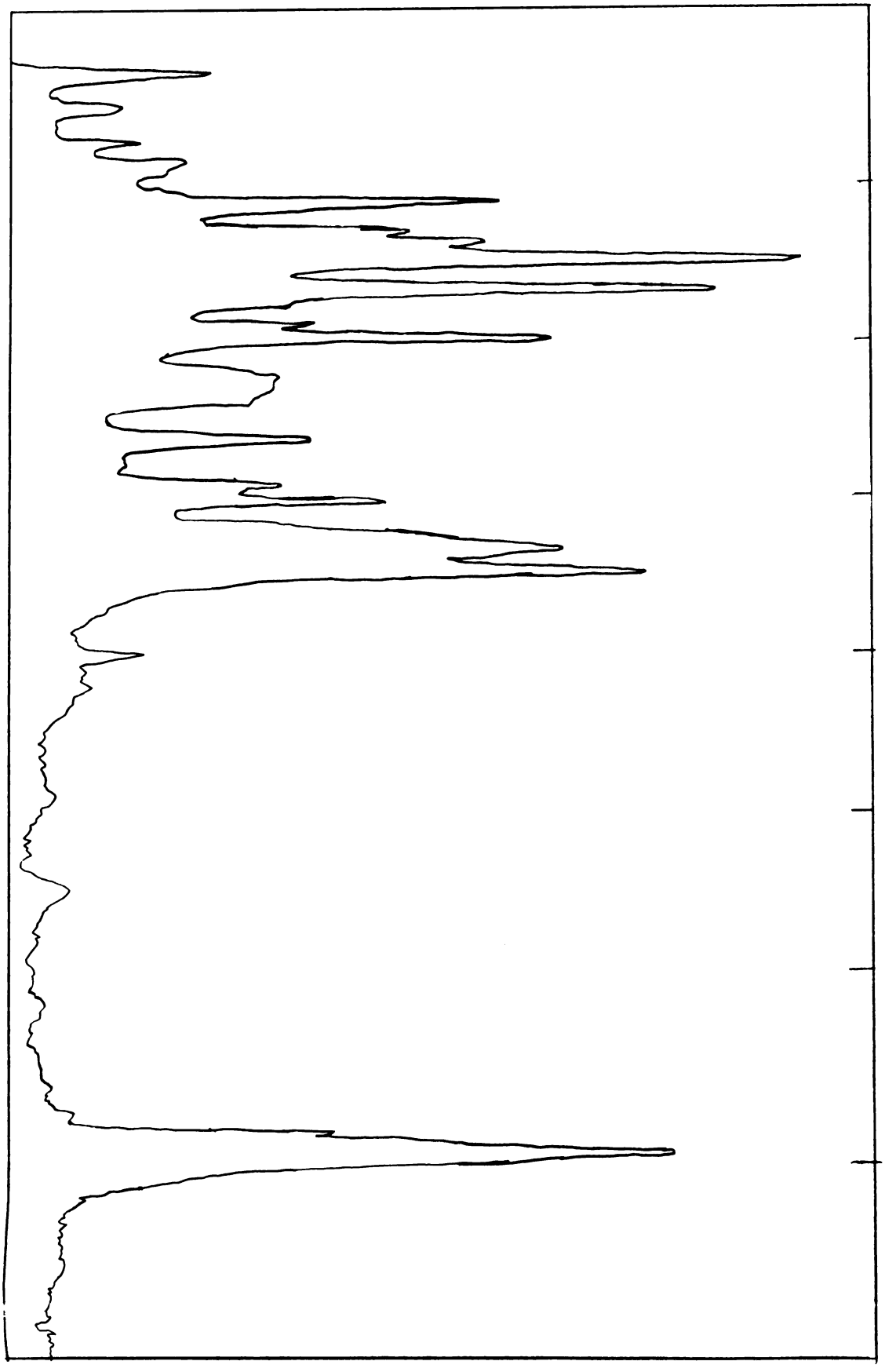


Figure 14. Infrared spectrum of 1-methoxy-1-(p-chlorophenyl)tetramethylbenzocyclobutene. (CCl_4 solution)

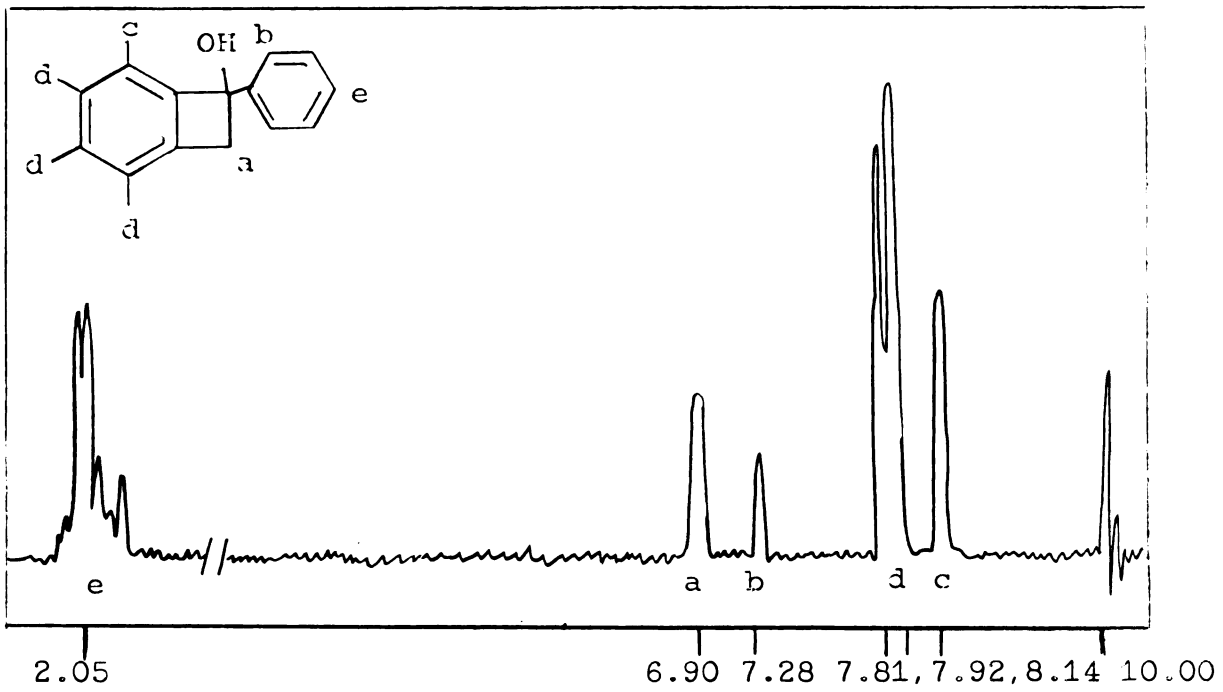


Figure 15. Proton magnetic resonance spectrum of 1-phenyl-tetramethylbenzocyclobutenol. (CCl_4 solution)

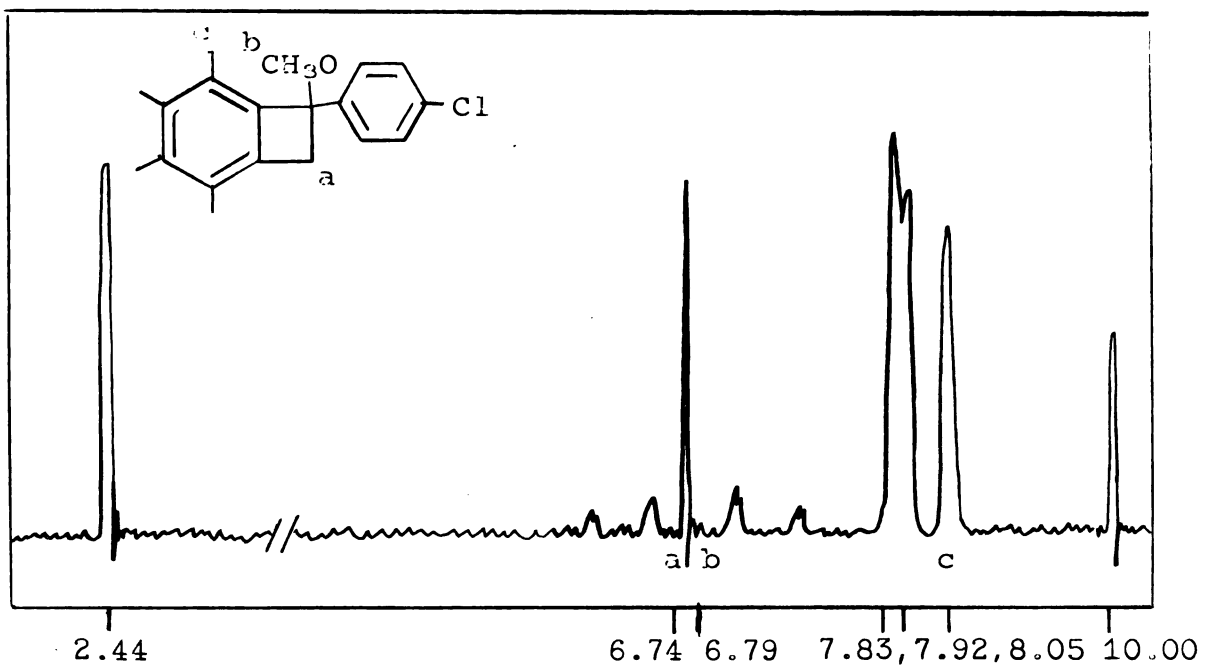


Figure 16. Proton magnetic resonance spectrum of 1-methoxy-1-(p-chlorophenyl)tetramethylbenzocyclobutene. (CCl_4 solution)

layer was extracted twice with 25-ml. of ether, and the ether layers were separated, combined and dried over anhydrous magnesium sulfate. The ether was evaporated on a rotary evaporator leaving a light oil which was chromatographed on an Alcoa 20 F alumina column using 30-60° petroleum ether as eluant. Attempts to crystallize this material from petroleum ether, pentane and methylene chloride were unsuccessful. Some crystalline material was eventually obtained from methanol. Two additional recrystallizations from methanol gave 0.63 g. (18%) of white crystals, m.p. 69-70°. The infrared and the p.m.r. spectra indicated that the product was a methyl ether (see Figures 14 and 16).

Anal.: Calcd. for $C_{19}H_{21}OCl$: C, 75.53; H, 7.03.
Found: C, 75.62; H, 7.04.

1-Chloro-1-(p-chlorophenyl)-tetramethyl-benzocyclobutene(7-Chloro-(p-chlorophenyl)-2,3,4,5-tetramethylbicyclo[4.2.0]octa-1,3,5-triene)

Approximately 0.2 g. of the oil which was obtained as the initial product in the above preparation was treated with 20 drops of acetyl chloride in a 3" test tube. The solution which formed immediately was dark red and quickly warmed the sides of the test tube. When the red solution was poured into 5-ml. of water a dark brown solid formed which was recrystallized twice from 30-60° petroleum ether to give white crystals, m.p. 112-113°. This product gives a white precipitate of silver chloride when treated with

alcoholic silver nitrate solution. The infrared and n.m.r. spectra were consistent with the assigned structure and are presented in Figures 17 and 19.

When 1-chloro-1-(p-chlorophenyl)tetramethylbenzocyclobutene was warmed in methanol on a steam bath for one hour and then cooled in an ice bath white needles formed, m.p. 73-74°. The infrared spectrum of these needles was identical with that of 1-methoxy-1-(p-chlorophenyl)tetramethylbenzocyclobutene.

Anal.: Calcd. for $C_{18}H_{18}Cl_2$: C, 70.83; H, 5.94.
Found: C, 71.27; H, 5.99.

1-Methoxy-1-(p-methoxyphenol)tetramethylbenzocyclobutene (7-Methoxy-7-(p-methoxyphenyl)-2,3,4,5-tetramethylbicyclo[4.2.0]octa-1,3,5-triene)

Into a 100-ml. round-bottomed three-necked flask equipped with a Tru-bore stirrer, dropping funnel and nitrogen inlet was placed 0.96 g. (0.039 g.-atom) of magnesium, 5.61 g. (0.0300 mole) of p-bromoanisole and ten ml. of tetrahydrofuran which was freshly distilled from lithium aluminum hydride. A stream of dry nitrogen was passed over the stirred mixture while it was heated to reflux and maintained at that temperature for three hours. A dark grey reagent solution appeared slowly. To the Grignard reagent was added 2.00 g. (0.0115 mole) of tetramethylbenzocyclobutenone in 15 ml. of dry tetrahydrofuran slowly over a one-half hour period. The reaction mixture was stirred at reflux temperature an additional three hours

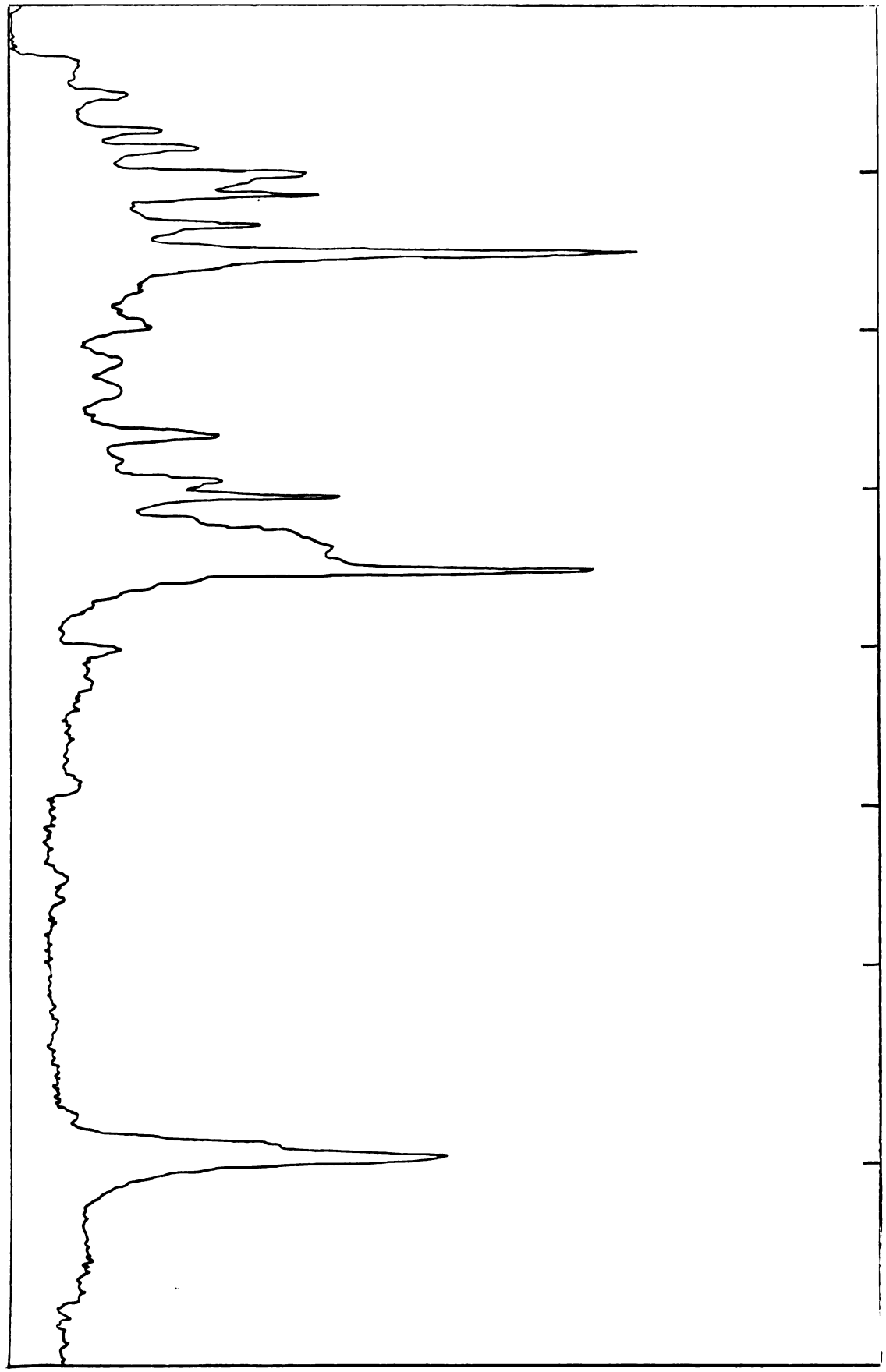


Figure 17. Infrared spectrum of 1-chloro-1-(p-chlorophenyl)tetramethylbenzocyclobutene. (CCl_4 solution)

under a nitrogen atmosphere, and then it was poured into 50 ml. of water and 10 ml. of concentrated hydrochloric acid. The resulting mixture was extracted three times with 50 ml. of ether. The ether layers were separated, combined, washed with water, dried over magnesium sulfate and the ether was evaporated with a rotary evaporator. The light colored oil which remained was chromatographed on an Alcoa 20 F alumina column using 30-60° petroleum ether as the solvent. The oily product came through the column with the solvent front. This oil was dissolved in methanol at room temperature and chilled in dry ice. A white solid material was obtained which was quickly filtered and washed with distilled water. The solid was recrystallized twice from ethanol to produce white crystals, m.p. 84-85° (10%). The infrared and p.m.r. spectra are presented in Figures 18 and 20.

Anal.: Calcd. for $C_{20}H_{24}O_2$: C, 81.04; H, 8.16.
Found: C, 79.70, 79.77; H, 8.06, 8.02;
Ash, 1.56, 1.48.
Corrected for 1.53% incombustible impurity:
C, 80.93, 81.00; H, 8.18, 8.10.

1,1-Dichloro-4,6-dimethylbenzocyclobutene (3,5-Dimethylbicyclo[4.2.0]octa-1,3,5-triene-7,7-dichloride)

Into each of three 8" test tubes was placed 5.68 g. (0.024 mole) of trichloromethyl-2,4,6-trimethylbenzene

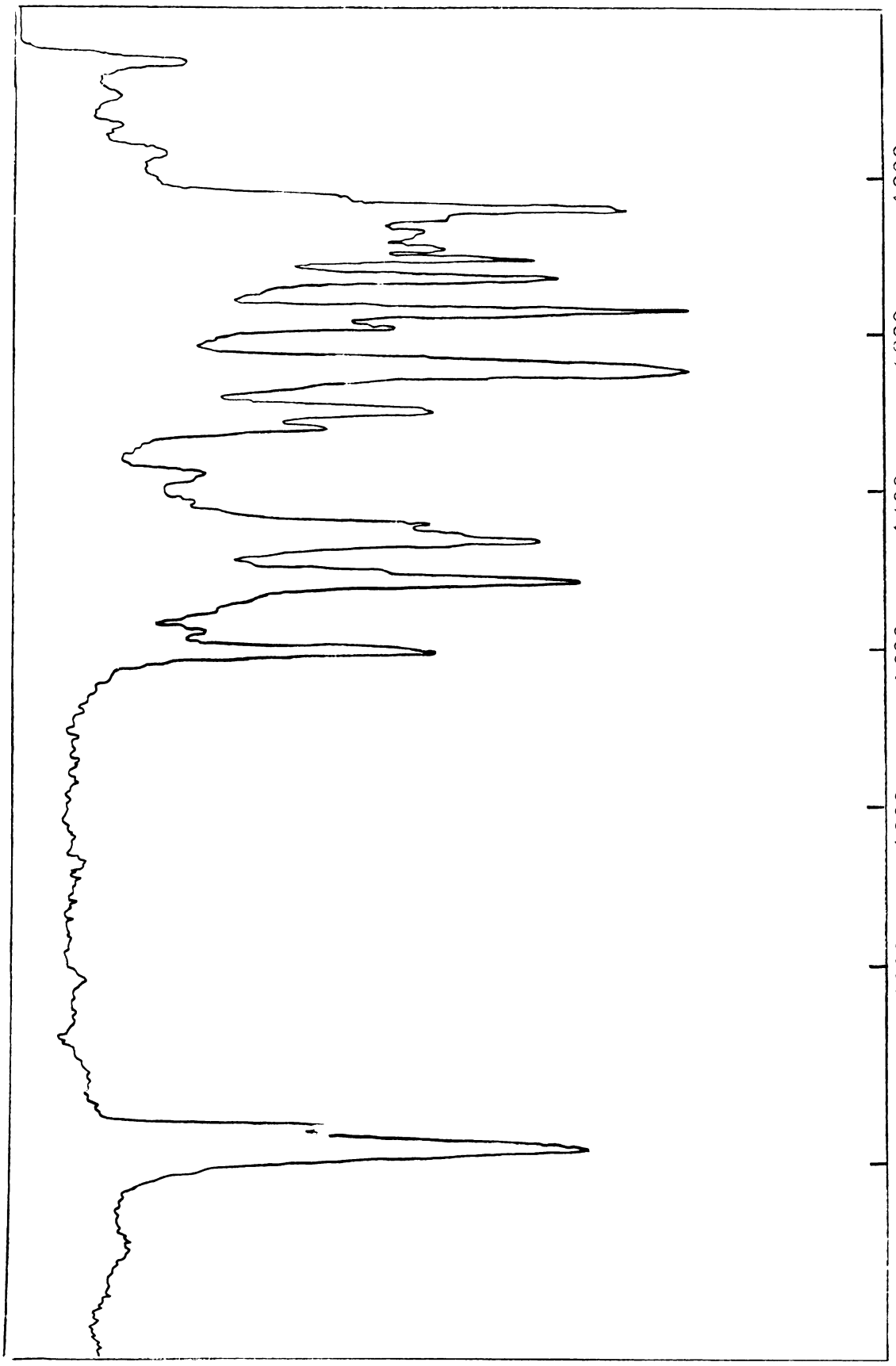


Figure 18. Infrared spectrum of 1-methoxy-1-(p-methoxyphenyl)tetramethylbenzocyclobutene. (CCl_4 solution)

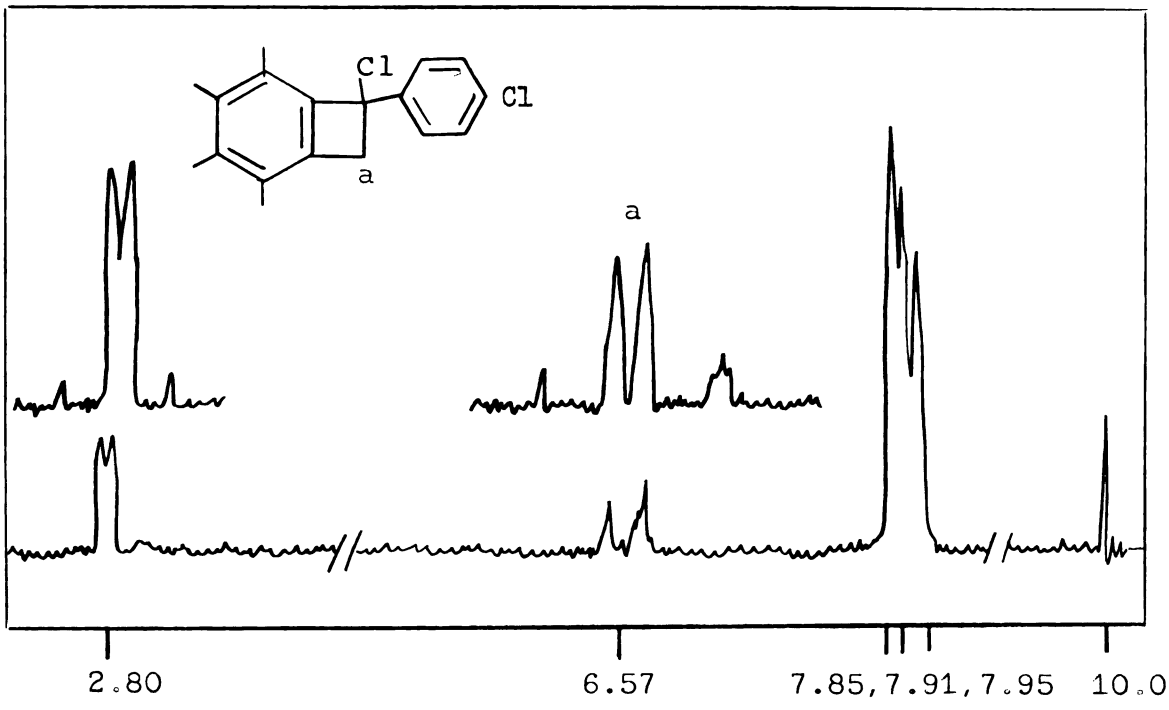


Figure 19. Proton magnetic resonance spectrum of 1-chloro-1-(p-chlorophenyl)tetramethylbenzocyclobutene. (CCl_4 solution)

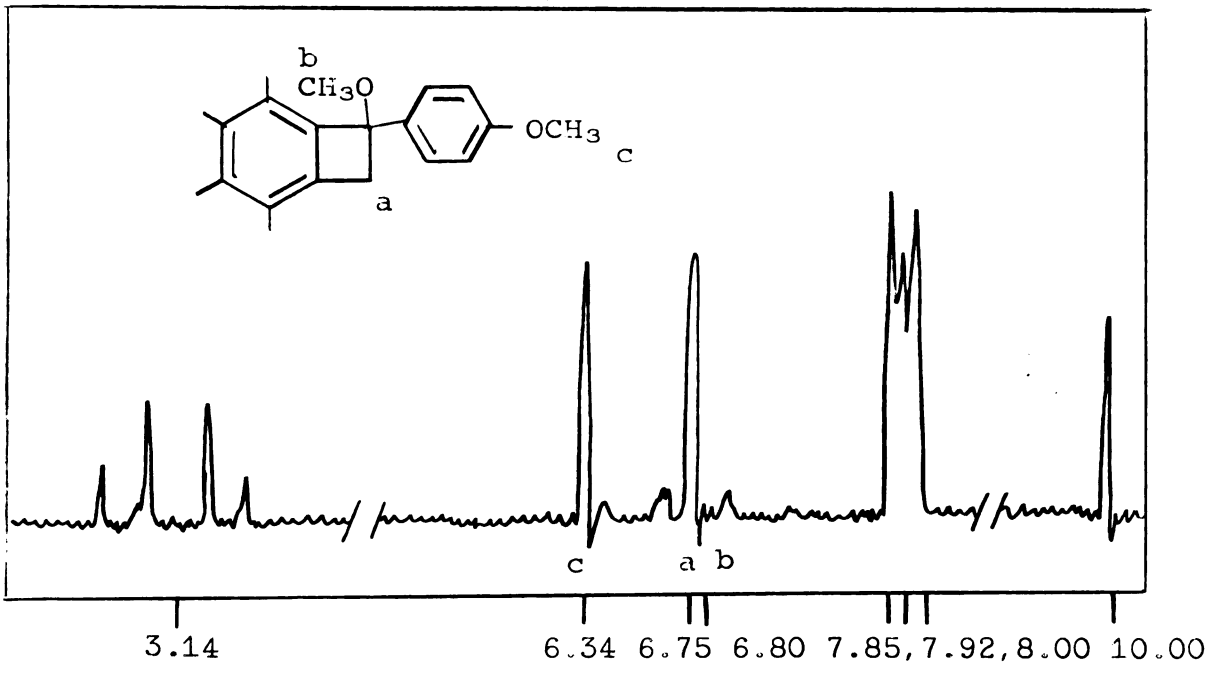


Figure 20. Proton magnetic resonance spectrum of 1-methoxy-1-(p-methoxyphenyl)tetramethylbenzocyclobutene. (CCl_4 solution)

which was prepared according to the procedure reported by Fish (4). The reaction tubes were heated in an oil bath under a stream of dry nitrogen. When the temperature of the bath reached 160° hydrogen chloride began to evolve. The temperature was increased to and maintained at 170° for three hours. Evolution of hydrogen chloride had ceased by the end of the three hour period. The reaction tubes were allowed to cool to room temperature leaving a light tan solid. The combined solid from the three tubes was recrystallized twice from pentane to yield 12.10 g. (84%) of white cubes, m.p. 55-56°. The infrared spectrum was identical to the one reported by Fish (4) for 1,1-dichloro-4,6-dimethylbenzocyclobutene.

4,6-Dimethylbenzocyclobutenone (3,5-Dimethylbicyclo[4.2.0]octa-1,3,5-triene-7-one)

Into a 100-ml. round-bottomed three-necked flask equipped with a dropping funnel, and a tube through which gas could escape was placed 55 ml. of concentrated sulfuric acid. This solution was stirred magnetically and cooled in an ice bath while 9.00 g. (0.045 mole) of 3,5-dimethylbicyclo[4.2.0]octa-1,3,5-triene-7,7-dichloride in 15 ml. of ethanol was added slowly over a one hour period. Hydrogen chloride evolved from the reaction solution immediately, and it quickly turned dark red. The reaction solution was poured over 300 g. of ice, and a white precipitate formed

immediately. This precipitate was taken up in 50 ml. of pentane, washed once with 25 ml. of 5% sodium bicarbonate and twice with 25 ml. of distilled water. The pentane was evaporated under a stream of dry air leaving a white solid which was recrystallized twice from ethanol-water to yield 5.71 g. (86.8%) of white needles, m.p. 45-46°. The infrared spectrum reported in Figure 21 is identical to an infrared spectrum of the ketone obtained by treating 1,1-dichloro-4,6-dimethylbenzocyclobutene with ethanolic silver nitrate. The p.m.r. spectrum is reported in Figure 23.

Anal.: Calcd. for $C_{10}H_{10}O$: C, 82.16; H, 6.89.

Found: C, 81.84; H, 7.07.

1-(p-Chlorophenyl)-4,6-dimethylbenzocyclobutenol (7-(p-Chlorophenyl)-4,6-dimethylbenzocyclobutene-7-ol)

Into a 100-ml. round-bottomed three-necked flask equipped with a nitrogen inlet, reflux condenser and dropping funnel was placed 0.61 g. (0.020 g.-atom) of magnesium turnings, 3.90 g. (0.0200 mole) of p-chlorobromobenzene and 20-ml. of anhydrous ether. After one hour of stirring magnetically 2.00 g. (0.0137 mole) of 4,6-dimethylbenzocyclobutenone in 10-ml. of dry ether was added slowly (ca. one half hour) to the grey Grignard reagent solution. After the red reaction mixture had been refluxed with stirring for two hours, it was poured into 50 ml. of water

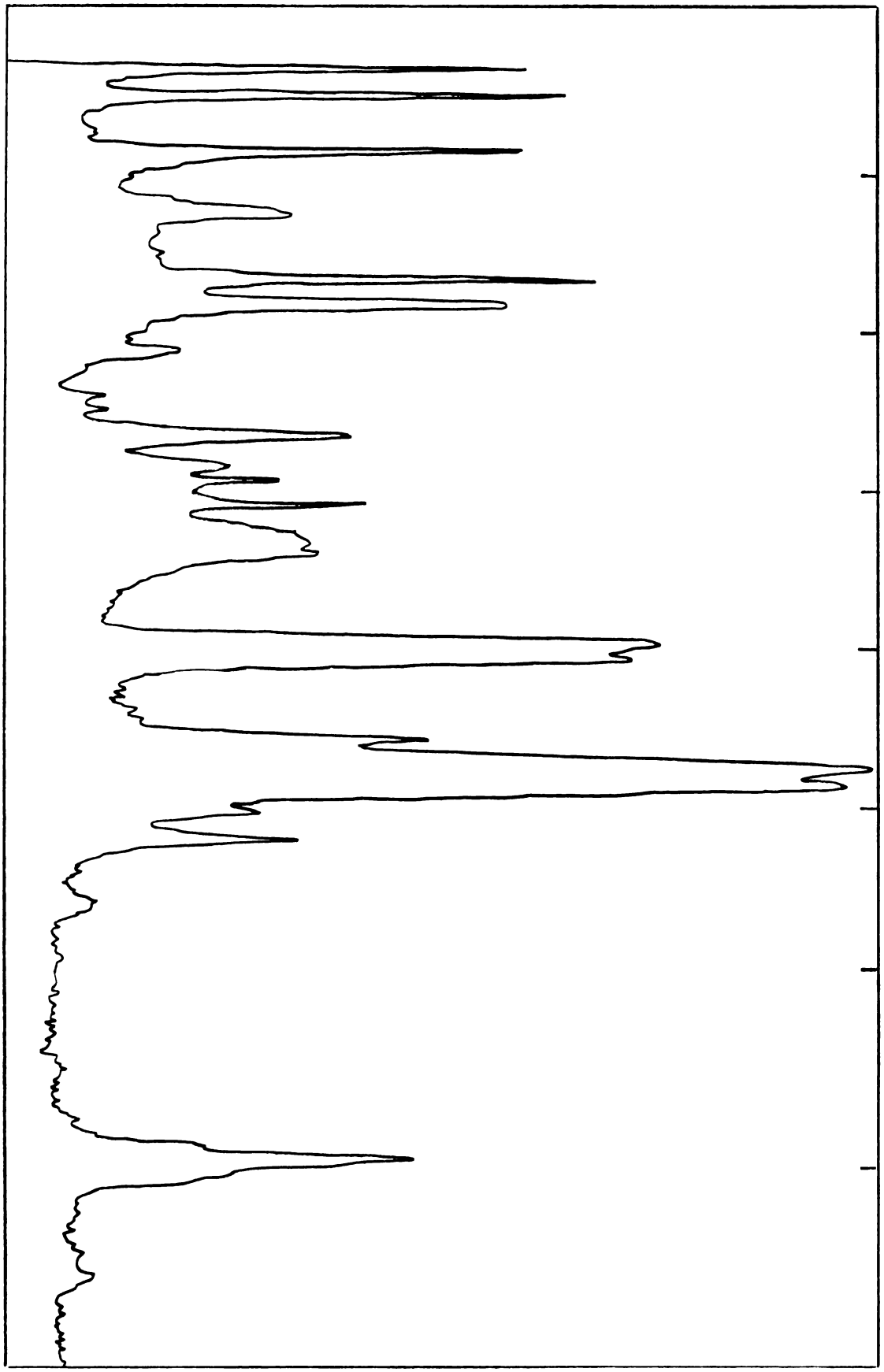


Figure 21. Infrared spectrum of 4,6-dimethylbenzocyclobutenone. (CCl_4 solution)

and 5 ml. of concentrated hydrochloric acid. The ether layer was separated, washed with 10 ml. of water and dried over calcium chloride. The ether was evaporated leaving a light oil which could not be crystallized in petroleum ether, methanol, methylene chloride or pentane. The oil passed through Woelm, neutral, activity 1 alumina and Alcoa 20 F alumina with the solvent front when pentane was used as eluant.

Infrared examination of the product showed that it was an alcohol, a portion of which could be converted into an ether by dissolving it in concentrated sulfuric acid and pouring the red solution which formed into methanol. A portion of this ether was distilled at 130-140^{o} at 0.5 mm. but the distillate showed conjugated carbonyl in the infrared spectrum.

Chromatography of the alcohol on a silica gel column using Fisher S157, 28-200 mesh silica gel and petroleum ether as solvent was employed. The product was held on the column as petroleum ether and 25% ether-75% petroleum ether was passed through. The product was eluted with a solvent mixture consisting of equal parts of petroleum ether and ethyl ether. Attempts to crystallize this oil failed. However, its infrared spectrum and p.m.r. spectrum were consistent with the proposed structure (see Figures 24 and 26). The n.m.r. spectrum of the compound in 96%

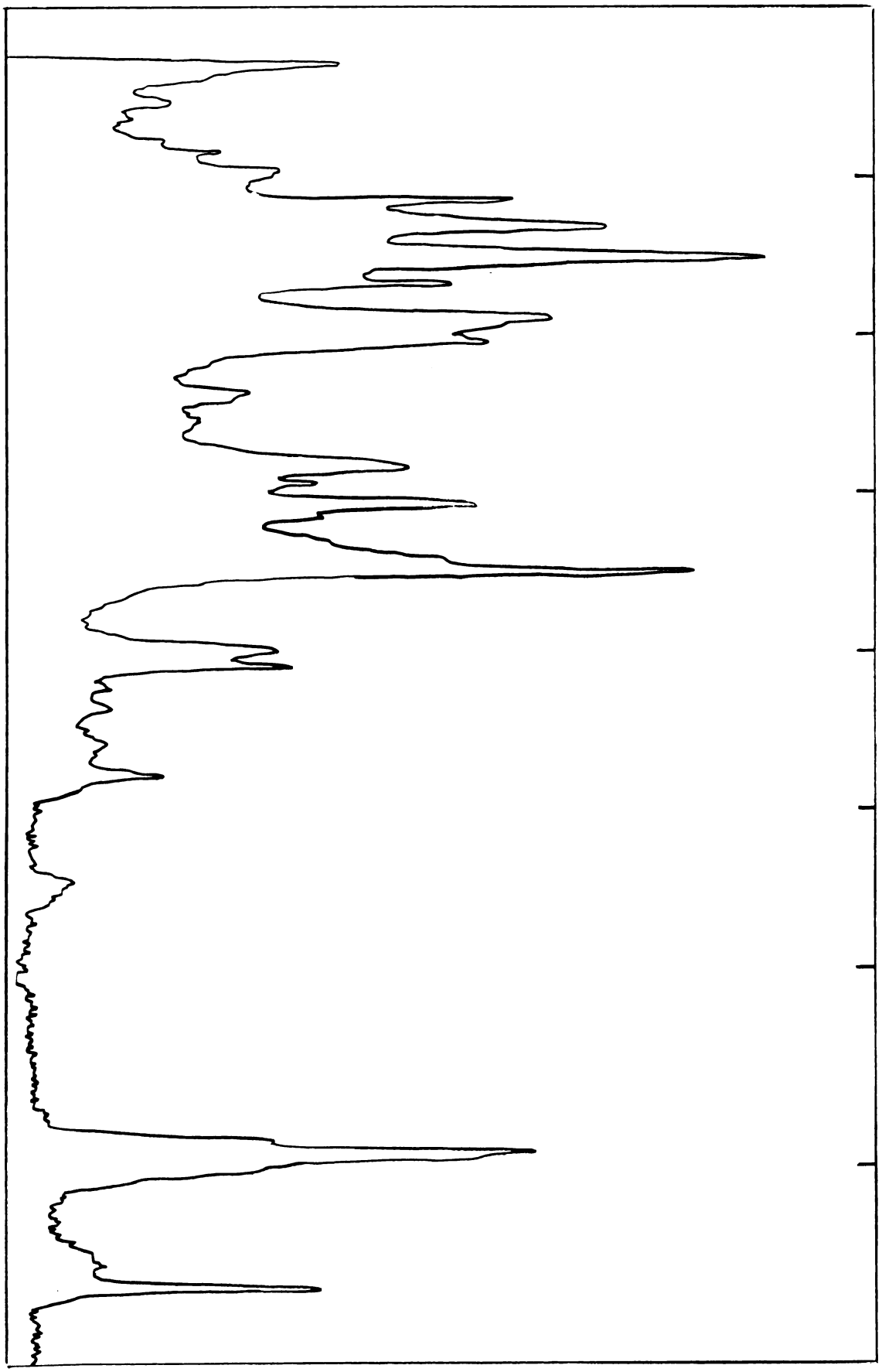


Figure 22. Infrared spectrum of 1-(p-chlorophenyl)-4,6-dimethylbenzocyclobutenol. (CCl_4 solution)

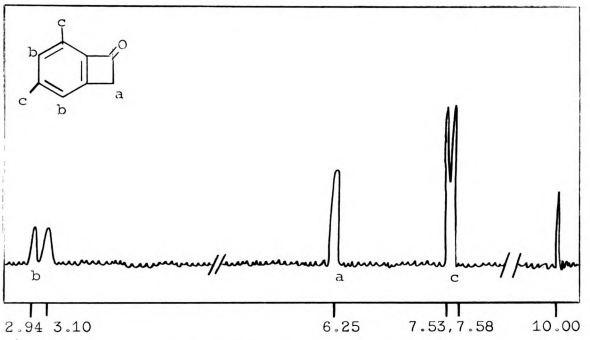


Figure 23. Proton magnetic resonance spectrum of 4,6-dimethylbenzocyclobutenone. (CCl_4 solution)

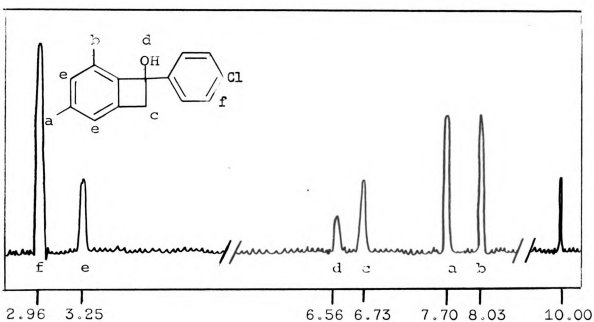


Figure 24. Proton magnetic resonance spectrum of 1-(p-chlorophenyl)-4,6-dimethylbenzocyclobutenol. (CCl_4 solution)

sulfuric acid is also consistent with the proposed structure of the product (see Table II).

Anal.: Calcd. for $C_{16}H_{15}OCl$: C, 74.27; H, 5.84.

Found: C, 74.16; H, 5.72.

4-Chloro-1-methoxy-1-(p-tolyl)-3,5,6-trimethylbenzocyclobutene (3-Chloro-7-methoxy-7-(p-tolyl)-2,4,5-trimethylbicyclo[4.2.0]-octa-1,3,5-triene)

4-Chloro-1-methoxy-1-(p-tolyl)-3,5,6-trimethylbenzocyclobutene was prepared by the Grignard reaction of p-tolyl magnesium bromide with 4-chloro-3,5,6-trimethylbenzocyclobutenone which was prepared according to the method described by Rafos (10).

Into a 100-ml. three-necked round-bottomed flask equipped with a nitrogen inlet tube, condenser, and dropping funnel was added 0.36 g. (0.015 g.-atom) of magnesium, 2.22 g. (0.013 mole) of p-bromotoluene and 30-ml. of tetrahydrofuran which was freshly distilled from lithium aluminum hydride. The reaction mixture was heated to reflux with a heating mantle and stirred magnetically for one hour. To the dark colored reagent which formed was added 2.00 g. (0.0103 mole) of 4-chloro-3,5,6-trimethylbenzocyclobutenone in 10 ml. of dry tetrahydrofuran over a twenty minute period.

After four hours of stirring at reflux temperature the reaction mixture was poured into 50 ml. of 10% hydrochloric acid and extracted twice with 25 ml. of ether.

The ether layers were separated, combined, and washed with 15 ml. of 5% sodium bicarbonate solution. The ether was evaporated under a stream of dry air leaving a light yellow oil. Attempts to purify this material by recrystallization from methanol, petroleum ether and methylene chloride failed. A purification on Woelm, neutral, activity 1 alumina and on Alcoa 24 F alumina using petroleum ether as solvent failed to produce crystalline product.

The oil was allowed to stand in methanol overnight, and the next day the infrared spectrum of this material indicated that an ether was present. Vapor phase chromatography indicated that the oil consisted of one major product (95%) and two minor impurities. The v.p.c. was done on a 5 ft. 30% silicone on chromosorb column at 220°. The compound could not be swept from the column at lower temperatures. An infrared spectrum of a collected sample of the major constituent of the mixture showed that a small amount of rearrangement was occurring on the column or in the detector. This was indicated by a small carbonyl peak at 1662 cm^{-1}. Two crude recrystallizations were carried out by chilling a methanol solution of the oil in a dry ice container. However, the crystals which formed melted at room temperature. When the oil was pumped free of solvent overnight, small crystals formed. These crystals, when used to seed a methanol solution of the product, induced crystallization. Two recrystallizations from methanol gave white cubes

m.p. 78-79°. The infrared and p.m.r. spectra are illustrated in Figures 25 and 27.

Anal.: Calcd. for $C_{19}H_{21}OCl$: C, 75.86; H, 7.03.

Found: C, 75.83; H, 6.94.

4-Chloro-1-phenyl-3,5,6-trimethylbenzocyclobutenol (3-Chloro-7-phenyl-2,4,5-trimethylbicyclo[4.2.0]octa-1,3,5-triene-7-ol)

4-Chloro-1-phenyl-3,5,6-trimethylbenzocyclobutenol was prepared and purified in a way analogous to the preparation of 1-phenyltetramethylbenzocyclobutenol. The white cubic crystals which were obtained in 74% yield from ligroin after two recrystallizations melted at 101-102°. The n.m.r. and infrared spectra were consistent with the assigned structure and are illustrated in Figures 26 and 28.

Anal.: Calcd. for $C_{17}H_{17}OCl$: C, 74.85; H, 6.28.

Found: C, 74.71; H, 6.32

1,3,4,5,6-Pentamethylbenzocyclobutenol (2,3,4,5,7-Pentamethylbicyclo[4.2.0]-octa-1,3,5-triene-7-ol)

Into a 100-ml. three-necked, round-bottomed flask equipped with a reflux condenser, Tru-bore stirrer and dropping funnel was placed 0.50 g. (0.002 g.-atom) of magnesium turnings in 15 ml. of anhydrous ether. To the stirred mixture was added 2.13 g. (0.015 mole) of methyl iodide in one portion. The reaction soon turned dark grey. After a one-half hour period of stirring, 1.00 g. (6.20 mmole)

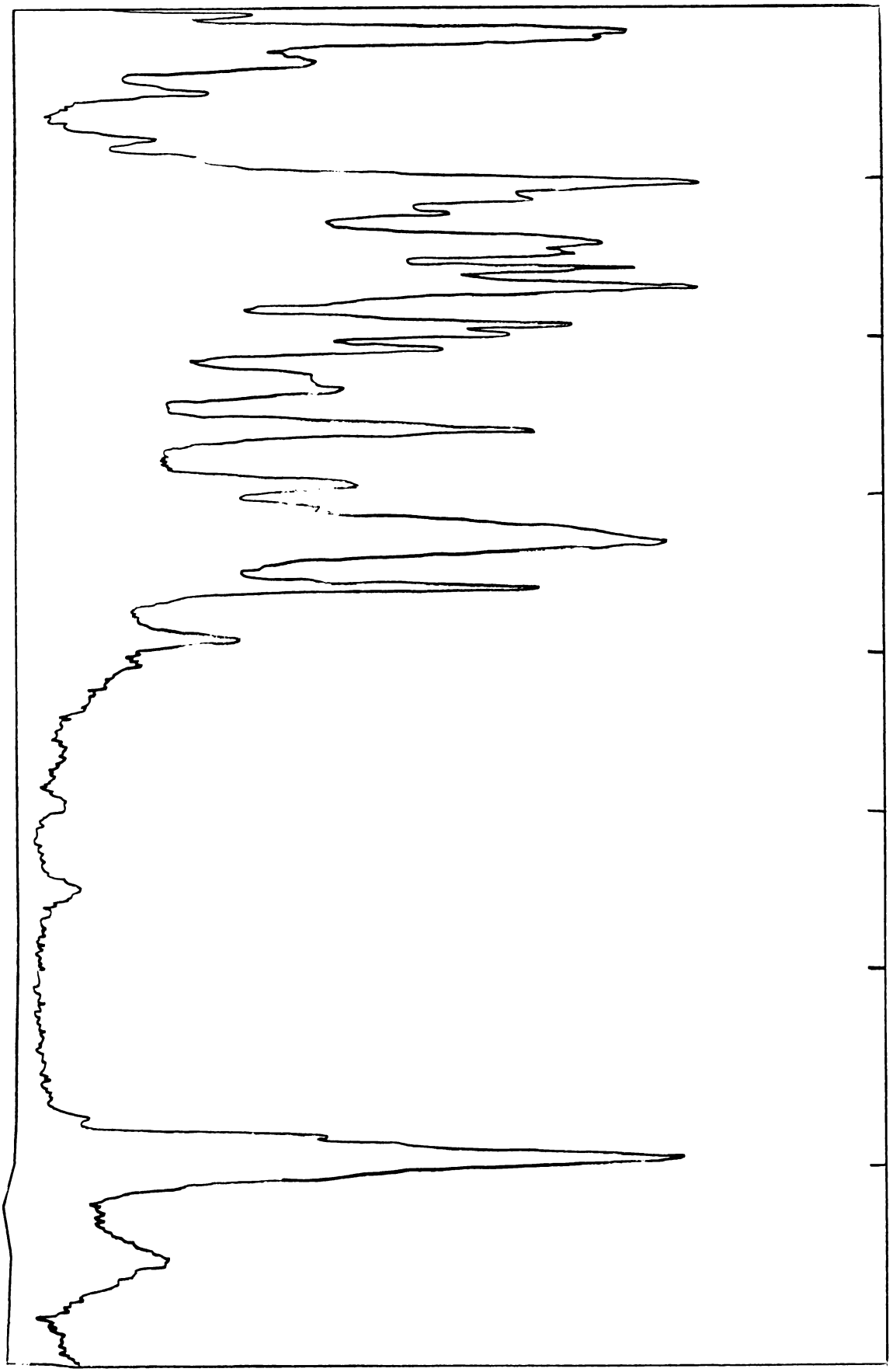


Figure 25. Infrared spectrum of 4-chloro-1-methoxy-1-(p-tolyl)-3 5,6-trimethyl-benzocyclobutene (CCl_4 solution)

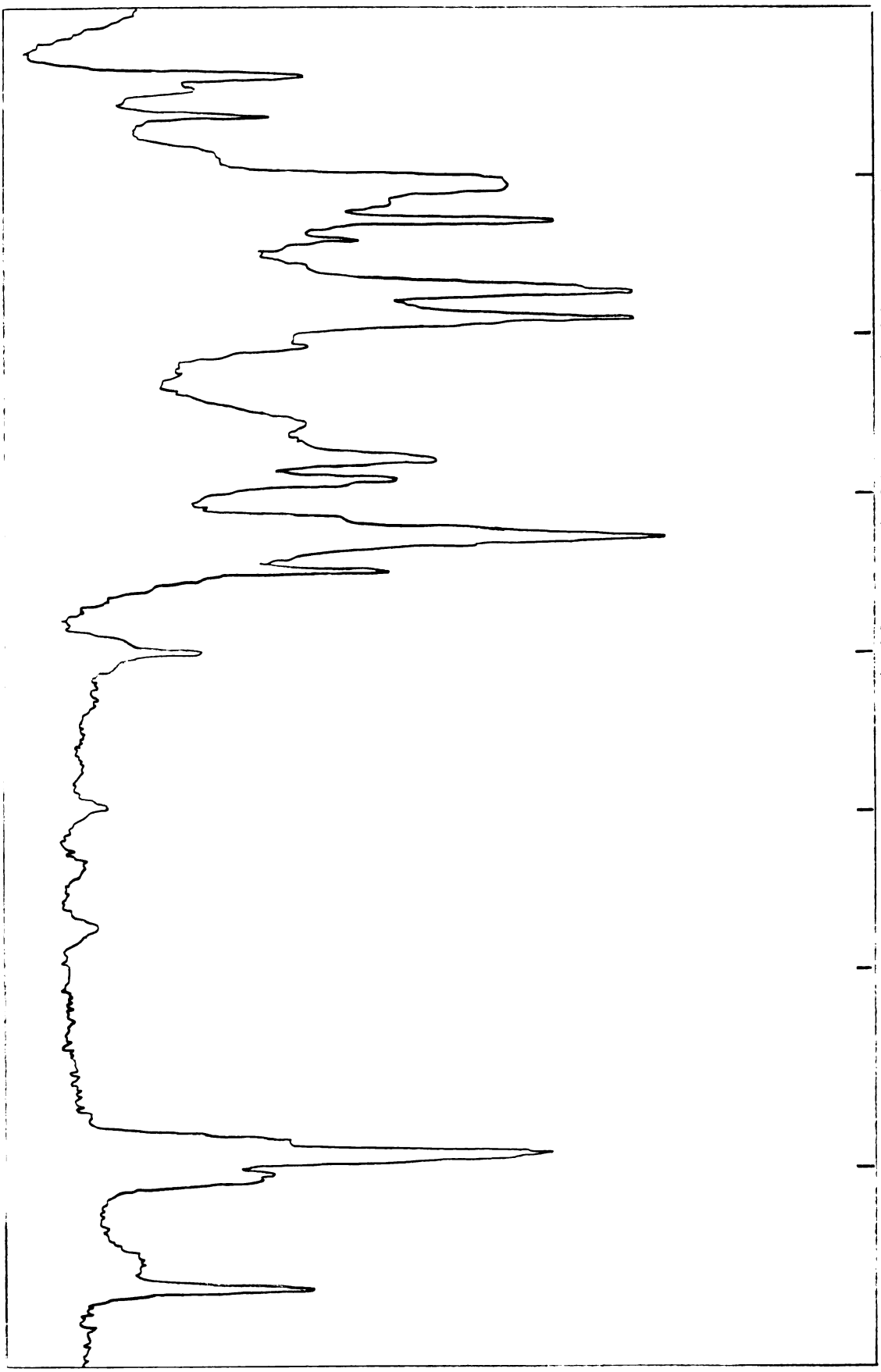


Figure 26. Infrared spectrum of 4-chloro-1-phenyl-3,5,6-trimethylbenzocyclobutenol. (CCl_4 solution)

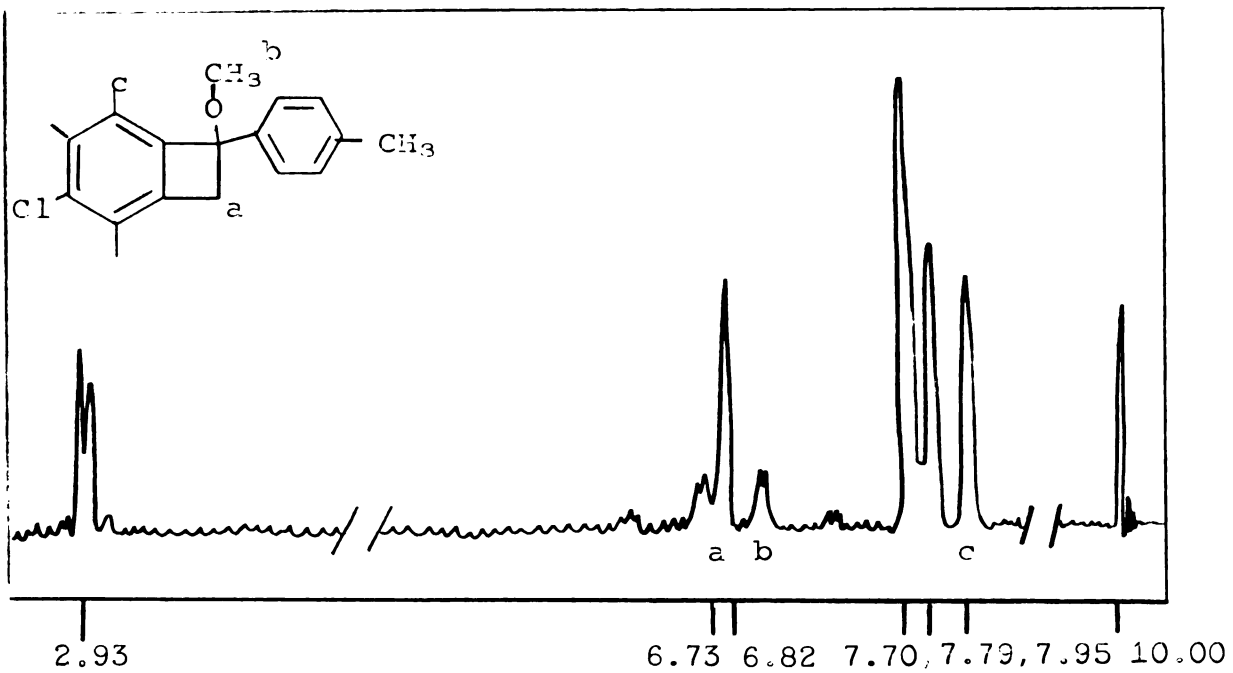


Figure 27. Proton magnetic resonance spectrum of 4-chloro-1-methoxy-1-(p-tolyl)-3,5,6-trimethylbenzocyclobutene. (CCl_4 solution)

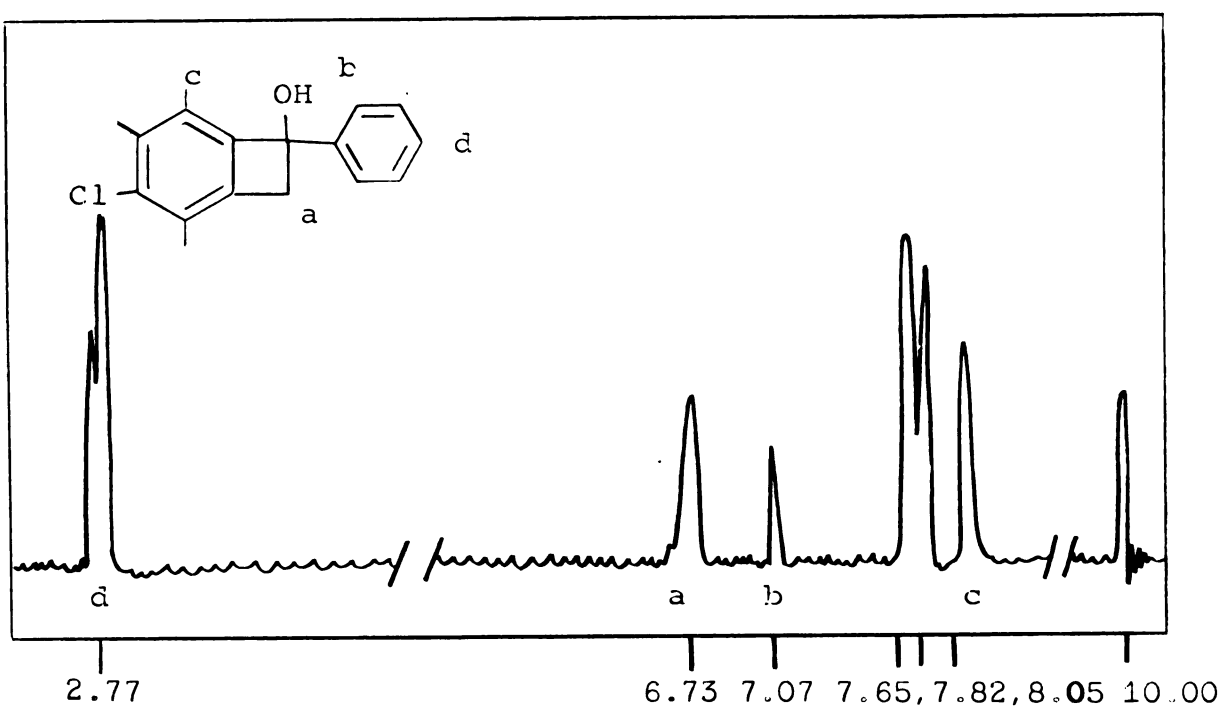


Figure 28. Proton magnetic resonance spectrum of 4-chloro-1-phenyl-3,5,6-trimethylbenzocyclobutenol. (CCl_4 solution)

of tetramethylbenzocyclobutenone in 20 ml. of anhydrous ether was added over a 15 minute period. The reaction mixture, which soon contained a white suspended material, was stirred for four hours at room temperature and then poured into 50 ml. of cold water with 5 ml. of hydrochloric acid. The ether layer was separated, dried over anhydrous calcium chloride and the ether was evaporated by passing a stream of dry air over the solution leaving a yellow impure solid which was recrystallized from 60-90° petroleum ether. One recrystallization produced 0.71 g. (63%) white cubes, and one additional recrystallization yielded 0.53 g. of product, m.p. 90-91°. The infrared and n.m.r. spectra are consistent with the proposed structure (see Figures 29 and 31).

Anal.: Calcd. for $C_{13}H_{18}O$: C, 82.05; H. 9.53.

Found: C, 82.04, 82.09; H, 9.58, 9.44.

1-Cyclopropyltetramethylbenzocyclobutenol (2,3,4,5-Tetramethyl-7-cyclopropylbicyclo-[4.2.0]octa-1,3,5-triene-7-ol)

The Grignard reaction was carried out as described above. Cyclopropyl bromide was prepared according to a procedure described by Cristol and Firth (53).

The initial product of the reaction was a brown oil which was separated by column chromatography on Alcoa 20 F alumina. Using 30-60° petroleum ether as eluant, 28% of tetramethylbenzocyclobutenone was isolated and identified by melting point and infrared. An alcohol was eluted from

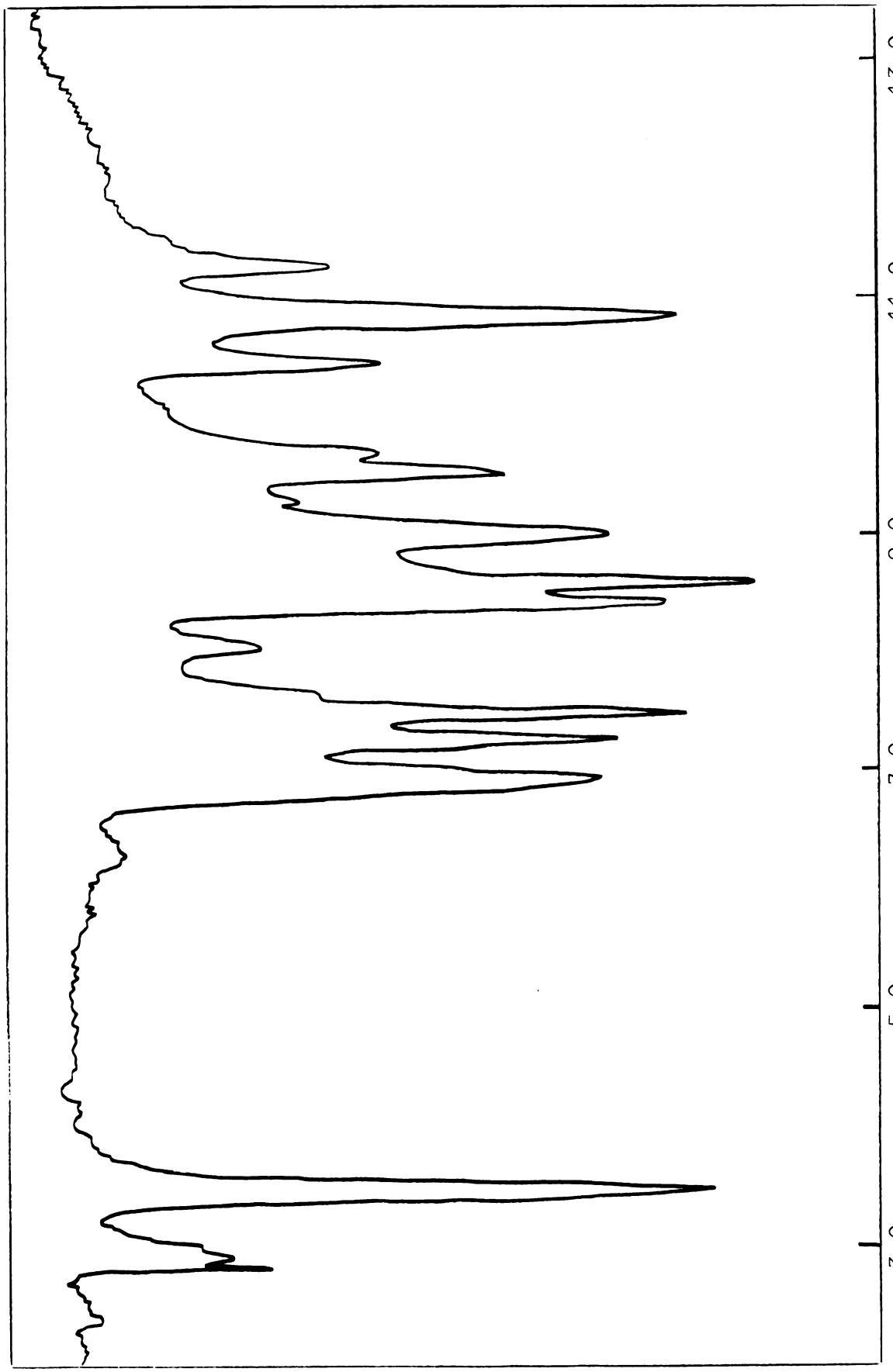


Figure 29. Infrared spectrum of 1,3,4,5,6-pentamethylbenzocyclobutenol. (CCl_4 solution)

the column using 80% petroleum ether and 20% ethyl ether. The material was a clear oil which was identified as an alcohol by infrared analysis. This oil was once again chromatographed carefully as described above. An oil was obtained which crystallized when dried for five hours under vacuum at room temperature. The white crystalline product 0.20 g. (7.1%) which was obtained melted at 66-67° and had an infrared and n.m.r. spectrum which was consistent with the proposed structure (see Figures 30 and 32).

Anal.: Calcd. for $C_{15}H_{20}O$: C, 83.28; H, 9.31.

Found: C, 83.14, 83.22; H, 9.19, 9.24.

1-Benzyltetramethylbenzocyclobutenol (2,3,4,5-tetramethyl-7-benzylbicyclo-[4.2.0]octa-1,3,5-triene-7-ol)

Into a 100-ml. three-necked, round-bottomed flask equipped with a dropping funnel, reflux condenser and Trubore stirrer was placed 1.21 g. (0.050 mole) of magnesium turnings, 0.76 g. (0.045 mole) of benzyl bromide, and 20 ml. of tetrahydrofuran which was freshly distilled from lithium aluminum hydride. After refluxing the Grignard reagent for one hour, 2.00 g. (0.0124 mole) of tetramethylbenzocyclobutenone in 20 ml. of tetrahydrofuran was added over a one-half hour period. The reaction mixture quickly turned milky-white. The reaction mixture was then refluxed for four hours and poured into 100 ml. of water and 10 ml. of hydrochloric acid. The mixture which resulted was extracted twice with 20 ml. of ether.

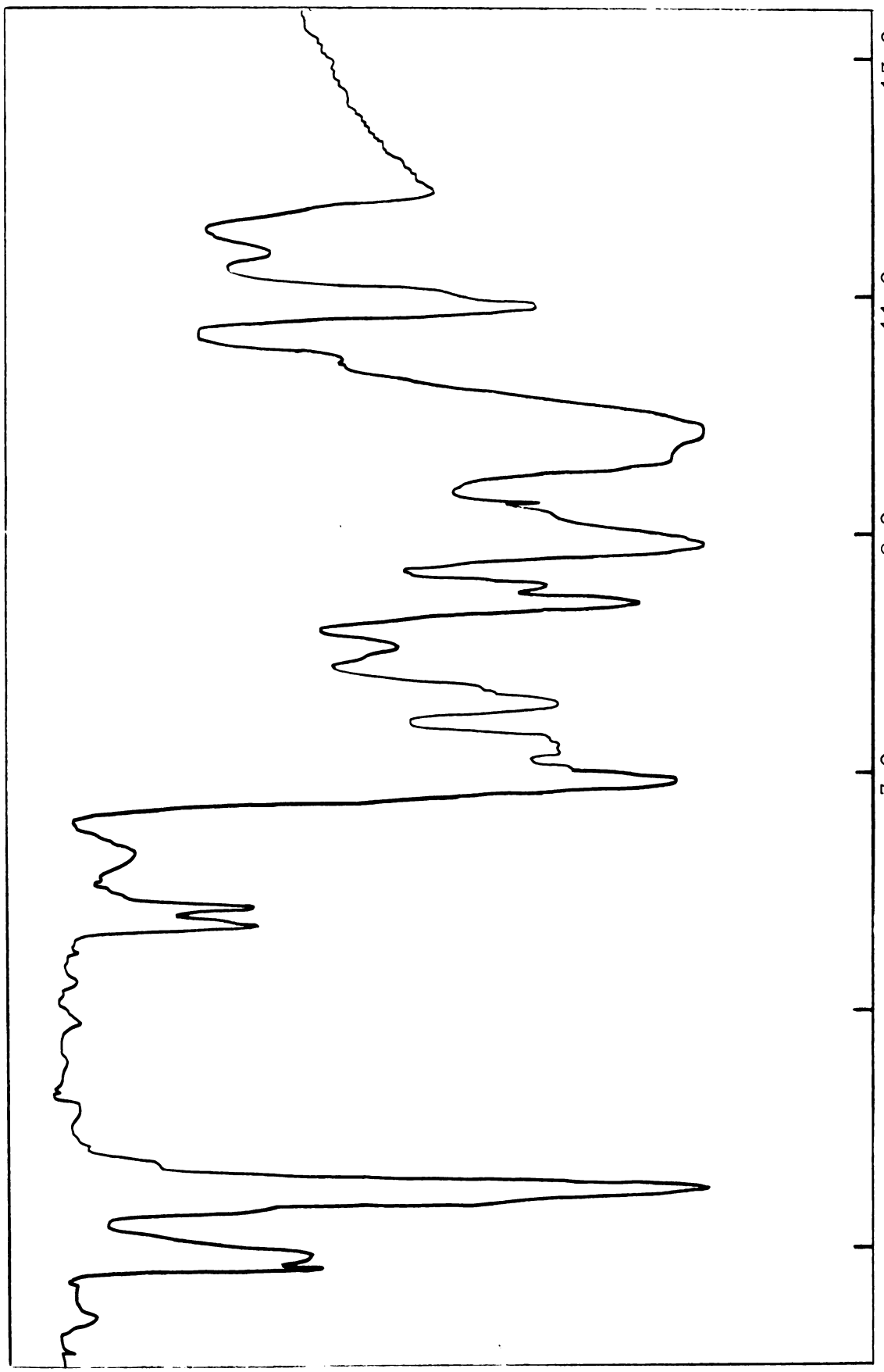


Figure 30. Infrared spectrum of 1-cyclopropyltetramethylbenzocyclobutenol. (CCl_4 solution)

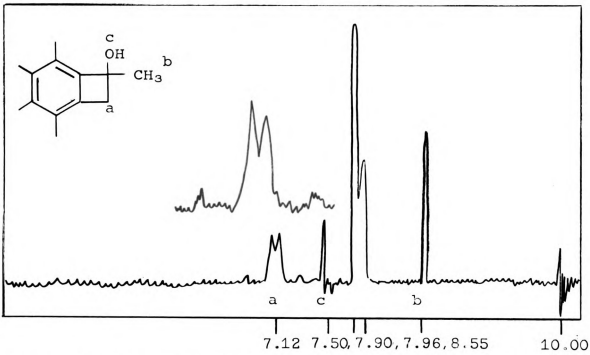


Figure 31. Proton magnetic resonance spectrum of 1,3,4,5,6-pentamethylbenzocyclobutenol. (CCl_4 solution)

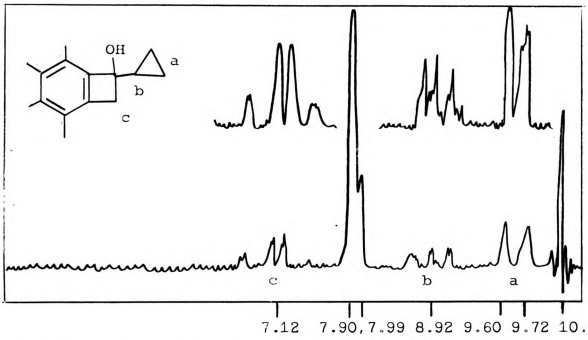


Figure 32. Proton magnetic resonance spectrum of 1-cyclopropyltetramethylbenzocyclobutenol. (CCl_4 solution)

The combined ether solutions were washed with 15 ml. of water and the ether was evaporated under a stream of dry air, leaving an oil which did not crystallize in petroleum ether. This oil was placed on an Alcoa 20 F alumina column and eluted with 30-60° petroleum ether. Unreacted tetramethylbenzocyclobutenone, 0.30 g. (15%), was first recovered from the column and identified by its melting point and infrared spectrum. An alcohol was eluted next from the column. Four recrystallizations of the solid from petroleum ether gave 0.43 g. (39% based on recovered tetramethylbenzocyclobutenone) of white needles, m.p. 83-83.5°. The infrared and n.m.r. spectra are reported in Figures 33 and 34.

Anal.: Calcd. for $C_{19}H_{22}O$: C, 85.69; H, 8.32.
Found: C, 85.68; H, 8.11.

Tetramethylbenzocyclobutene (2,3,4,5-tetramethylbicyclo[4.2.0]octa-1,3,5-triene)

Tetramethylbenzocyclobutenone was reduced to tetramethylbenzocyclobutene by use of the Huang-Minlon (54) modification of the Wolff-Kishner method.

In a 50 ml. round-bottomed flask was placed 2.00 g. (0.0113 mole) of tetramethylbenzocyclobutenone, 35 ml. of triethylene glycol and 30 ml. of 85% hydrazine hydrate. The reaction mixture was heated to reflux for one-half hour before 2.00 g. of potassium hydroxide in 10 ml. of water was added. The reflux was continued for another half hour.

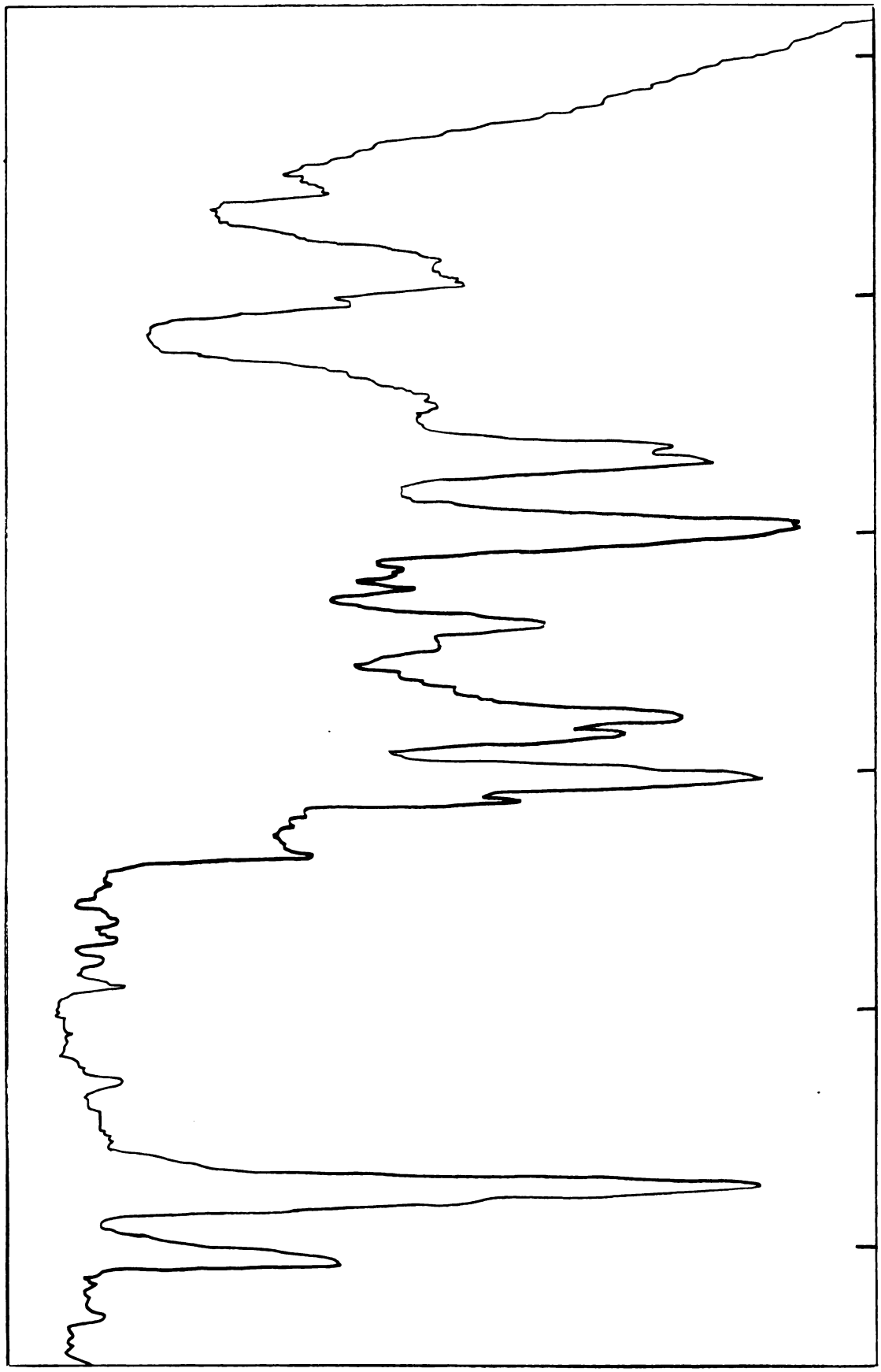


Figure 33. Infrared spectrum of 1-benzyltetramethylbenzocyclobutenol. (CCl_4 solution)

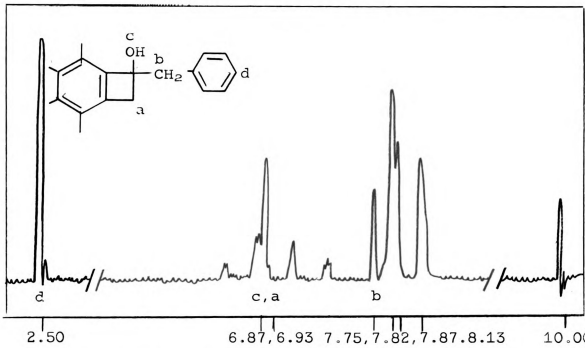


Figure 34. Proton magnetic resonance spectrum of 1-benzyl-tetramethylbenzocyclobutenol. (CCl_4 solution)

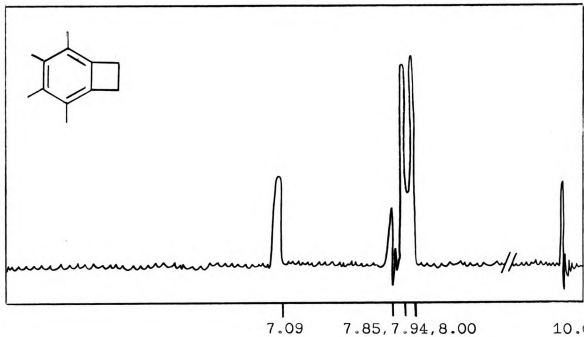


Figure 35. Proton magnetic resonance spectrum of tetramethyl-benzocyclobutene. (CCl_4 solution)

Water and excess hydrazine were distilled from the flask until the reaction temperature reached 180°. White material began to sublime and collect on the sides of the reaction vessel. The reaction temperature was maintained at 180° for three more hours. The subliming material was collected on a cold condenser and recrystallized from 30-60° petroleum ether to give 0.83 g. (46%) of white crystals m.p. 138-139°. The infrared spectrum was only slightly different from hexamethylbenzene and is reported in Figure 36. The material showed only one peak when submitted to v.p.c. analysis on a 5 ft., 20% silica on chromosorb column at 180°. This peak had a shorter retention time than hexamethylbenzene.

Anal.: Calcd. for $C_{12}H_{16}$: C, 89.95; H, 10.05.

Found: C, 89.76, 89.82; H, 9.97, 10.04.

The mass spectrum of the compound is reported in Figure 37 and is consistent with the assigned structure. The parent peak is at 160 m/e and the P+2 peak is 1.9% of the parent peak. This is a little higher than the calculated peak height which is 0.8%. The n.m.r. spectrum indicates that there is 3.5% of hexamethylbenzene impurity which could not be removed by fractional sublimation at 0.5 mm. and 40° or by recrystallization. The n.m.r. spectrum (see Figure 35) consisted of three singlets at τ = 7.09, 7.94 and 8.00 with relative areas 4:6:6. A small peak at 7.85 τ increased in area with addition of hexamethylbenzene.

Attempted preparation of 1-aminotetramethyl-benzocyclobutene (2,3,4,5-tetramethylbicyclo-[4.2.0]octa-1,3,5-triene-7-amine)

One hundred ml. of ether containing 0.0091 mole of aluminum hydride was prepared as described on page 42. To this solution in a 300-ml. round-bottomed, three-necked flask equipped with an addition funnel and a nitrogen inlet tube, was added 1.70 g. (0.0106 mole) of tetramethylbenzocyclobutenone oxime in 100 ml. of ethyl ether. The reaction mixture was stirred magnetically at room temperature under a stream of dry nitrogen for four hours, then poured into an equal quantity of water, extracted with 25 ml. of 5% hydrochloric acid, and washed with 25 ml. of water. The hydrochloric acid solution was neutralized to a pH of 8, as indicated with Hydrion pH paper, and treated with 5 ml. of acetic anhydride. Sodium acetate was added to the solution until it was neutral. A white precipitate formed which was filtered and recrystallized twice from pentane to give 0.10 g. of white needles, m.p. 120-121°. The infrared spectrum (see Figure 38) had strong absorption at 1650 $cm.^{-1}$, but no absorption in the frequency range characteristic of N-H stretch. The n.m.r. spectrum showed two triplets of equal intensity centered at τ = 6.00 and 7.15 (J = 7.0 cps.) which integrated for two protons each (see Figure 39). There were three singlets at τ = 7.89, 7.95 and 7.97 which integrated for 15 protons. This compound was identified as N-acetyl-4,5,6,7-tetramethyl-2,3-dihydroindole.

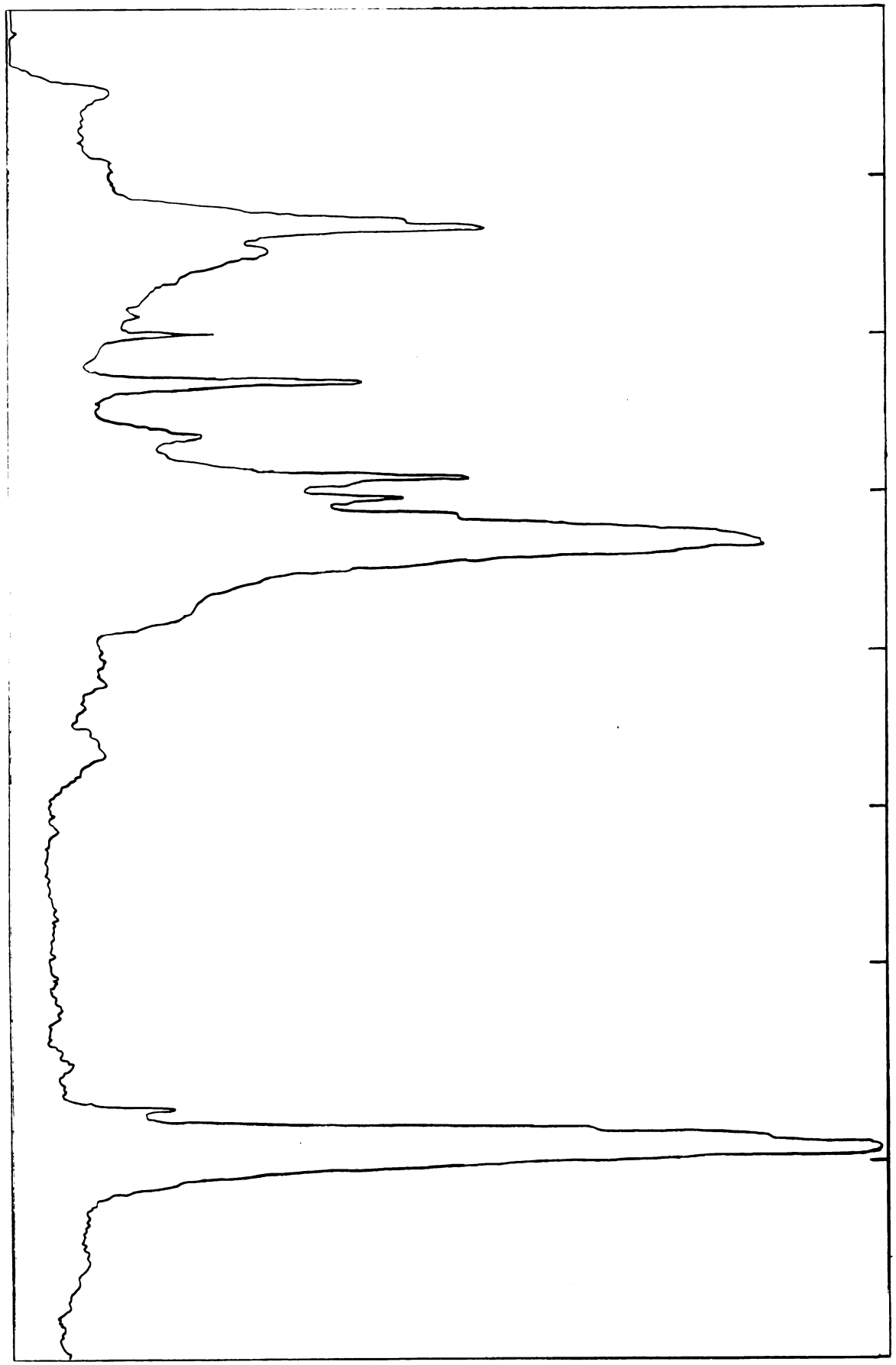


Figure 36. Infrared spectrum of tetramethylbenzocyclobutene. (CCl_4 solution)

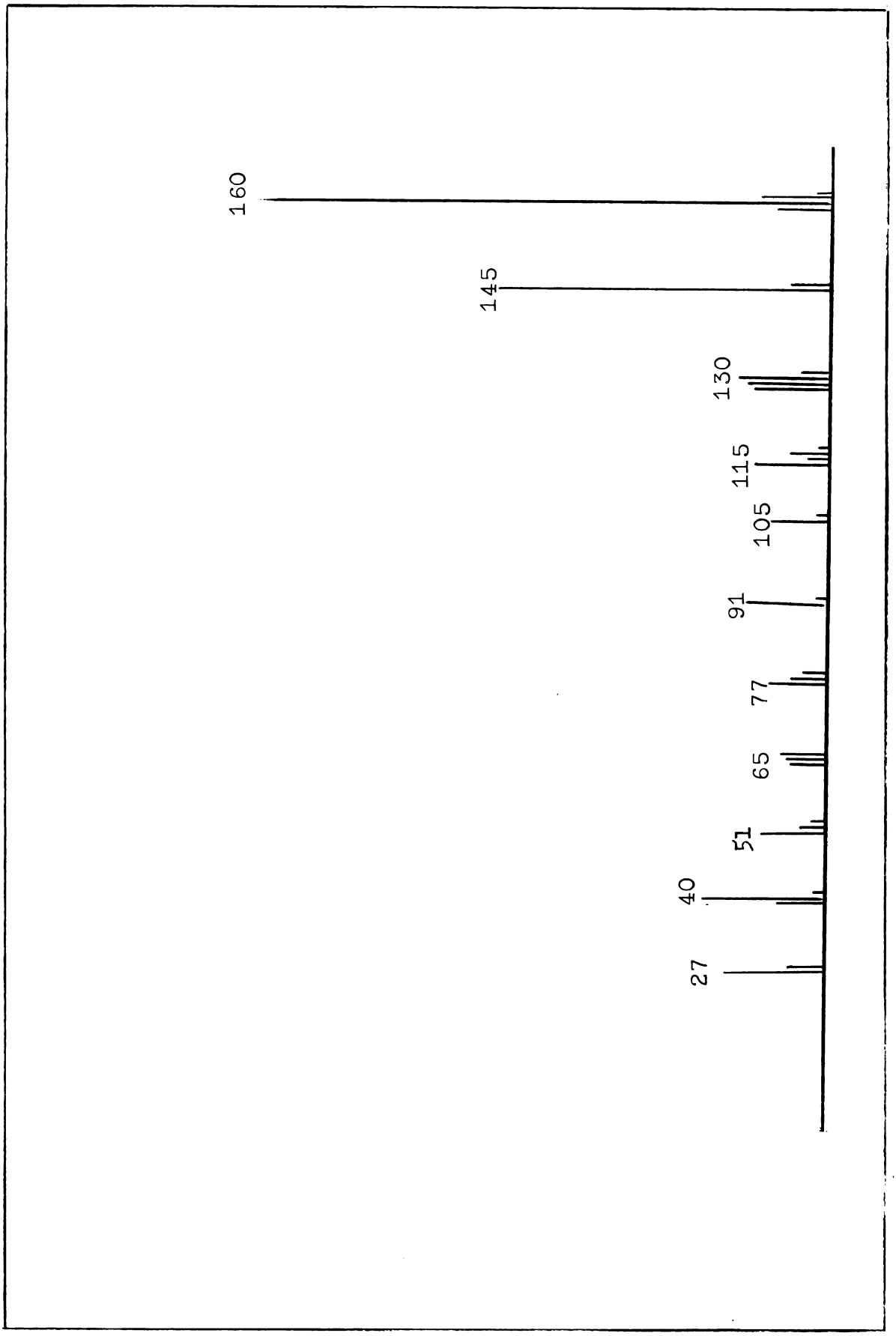


Figure 37. Mass spectrum of tetramethylbenzocyclobutene.

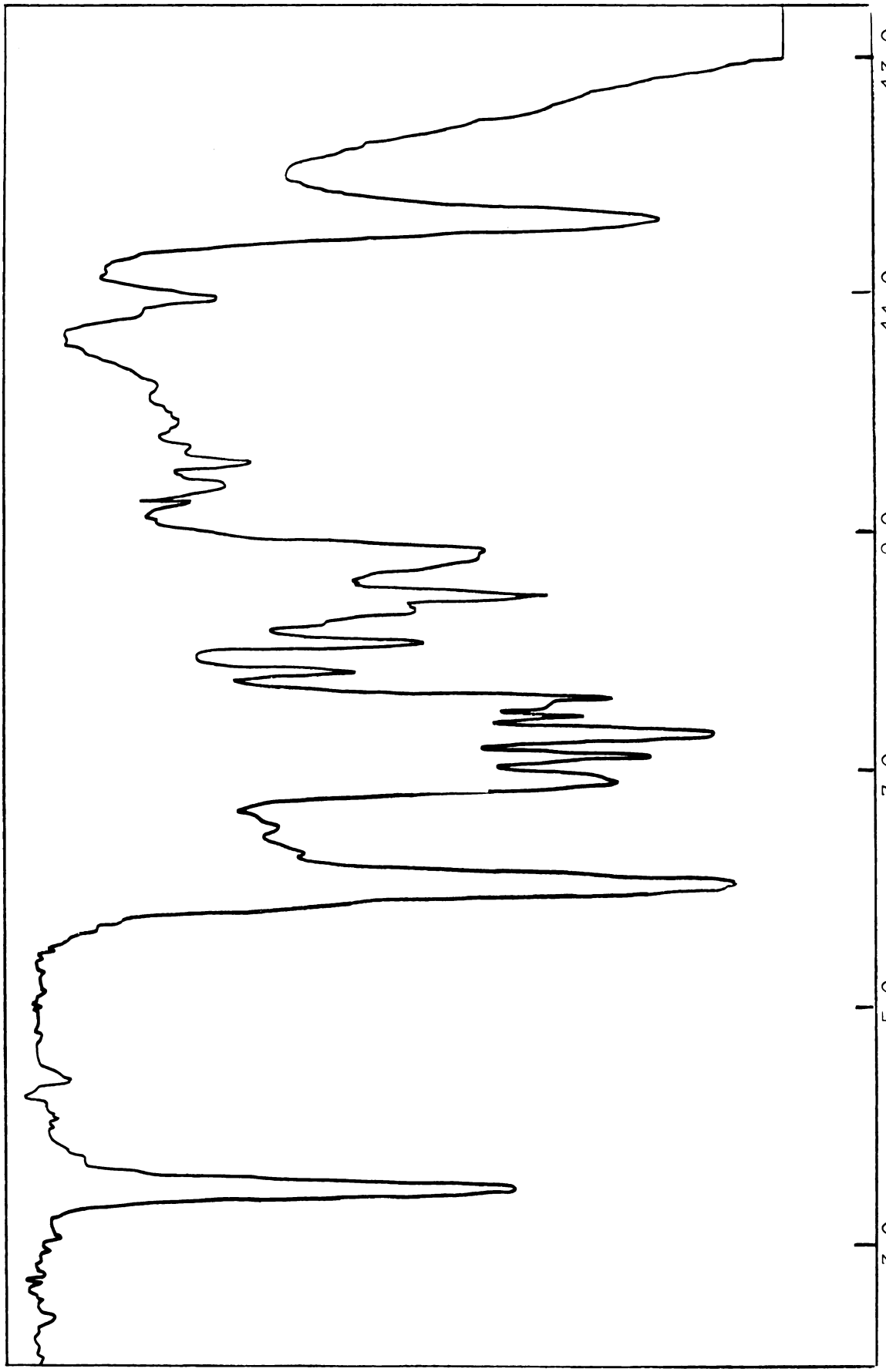


Figure 38. Infrared spectrum of N-acetyl-4,5,6,7-tetramethyl-2,3-dihydroindole. (CCl_4 solution)

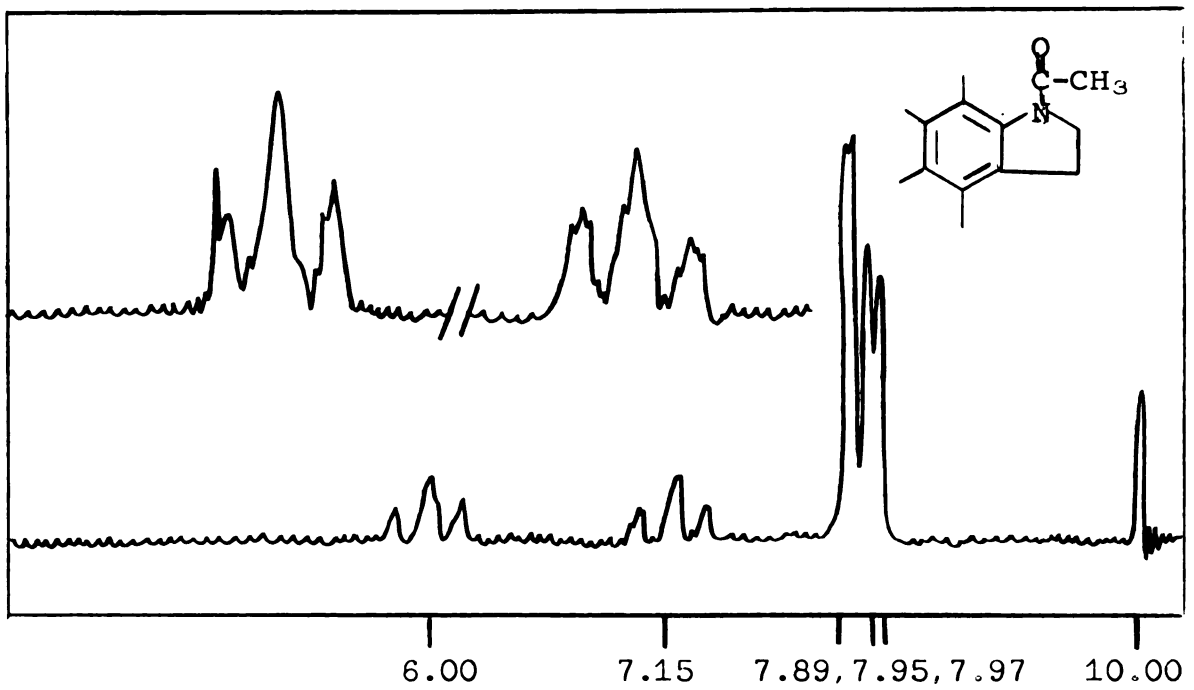


Figure 39. Proton magnetic resonance spectrum of N-acetyl-4,5,6,7-tetramethyl-2,3-dihydroindole. (CCl_4 solution)

Anal.: Calcd. for $C_{14}H_{19}NO$: C, 77.38; H, 8.81; N, 6.44.
Found: C, 77.15; H, 8.91; N, 6.40.

The ether-soluble product which was not extracted into the hydrochloric acid gave a heavy precipitate, which quickly turned black, when hydrogen chloride was bubbled through the ether solution. The product melted and decomposed at 182-184° and gave a melting point of 177-179° when mixed with starting material. The infrared spectrum is given in Figure 40. The n.m.r. spectrum in deutero-chloroform showed singlets at τ = 6.20, 6.37, and 7.44 with area ratios 2:1:2 and a multiplet at 7.78. This product has not been positively identified, but it is thought that the most plausible structure is that of a nitroso dimer.

Strong infrared absorption at 1280 $cm.^{-1}$ can be assigned to the trans nitroso dimer which has been reported as characteristic (55) for trans-NONO- and absorption at 2320 $cm.^{-1}$ can be assigned to a -N-O-,-N=O combination band (56).

It is well decumented (57) that nitroso dimers are easily converted to oximes when refluxed in isopropyl alcohol. Approximately 0.10 g. of the white solid product from the reduction was refluxed for four hours in 5 ml. of isopropyl alcohol and the solution was cooled in the refrigerator. A small amount of white crystals formed, m.p. 171-175°. (The melting point of tetramethylbenzocyclobutenone oxime is 179-180°.) The infrared spectrum of this material in a mineral oil mull was identical to tetramethylbenzocyclobutenone oxime.

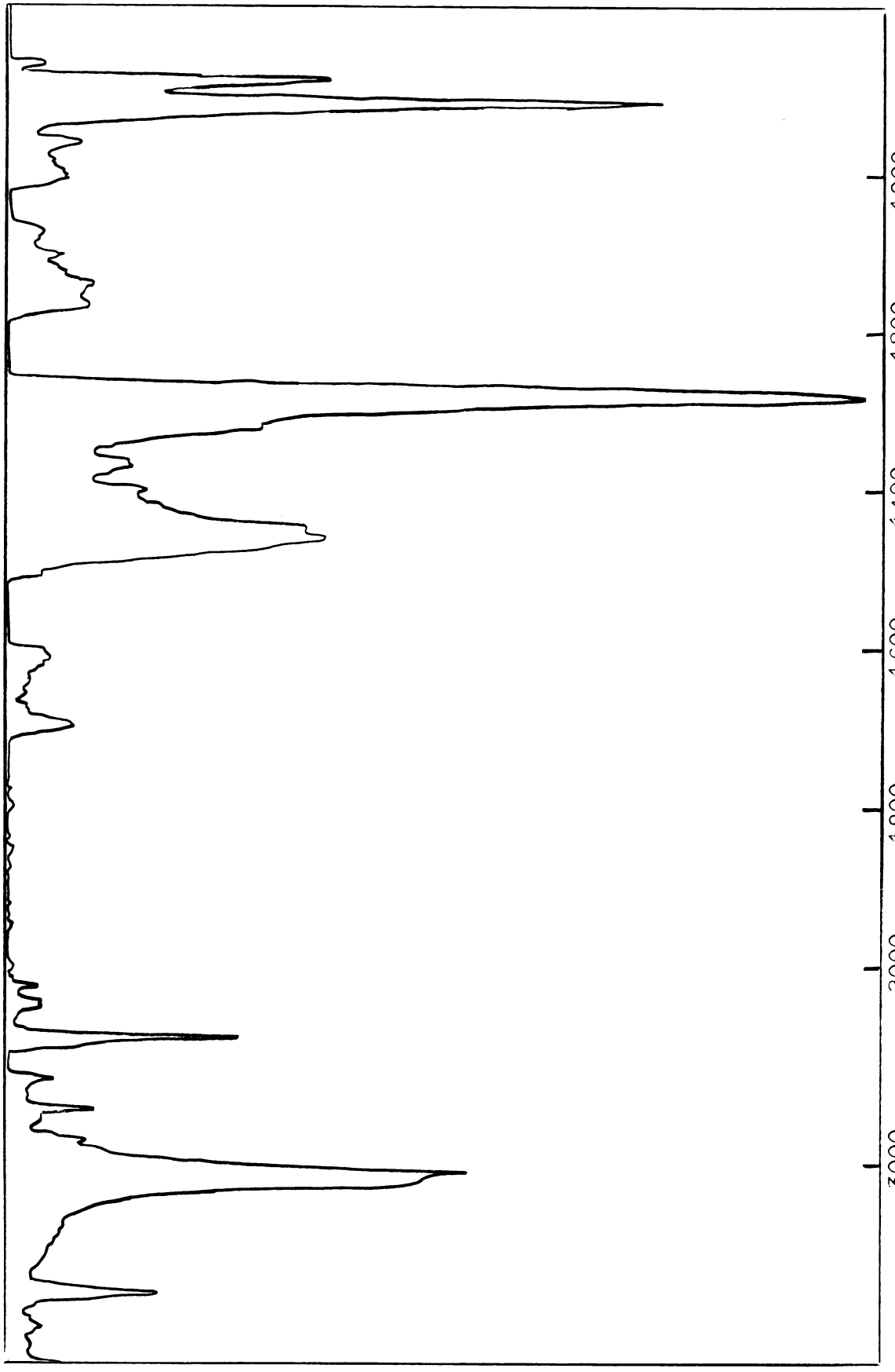


Figure 40. Infrared spectrum of the dimer of 1-nitrosotetramethylbenzocyclobutene. (CCl_4 solution)

Additional attempts to reduce tetramethylbenzocyclobutenone oxime with lithium aluminum hydride were made, but in each case products were formed which quickly decomposed to highly colored materials which decomposed further. No attempts were made to characterize these products.

B. Measurement of the Ultraviolet-Visible Spectra and pK's

The visible and ultraviolet spectra of compounds Xa-e and XXXIIIa-d were measured in sulfuric acid solution at 25° with a Beckman DB spectrophotometer equipped with a Sargent recorder.

The spectra of the ions which were produced by dissolving these compounds in 96% sulfuric acid are reported in Table IV. Stock solutions of the compounds in dry methanol were prepared so that 0.100 ml. aliquots in 10.0 ml. of sulfuric acid gave measurable spectra on the Beckman DB spectrophotometer.

The spectra of the ions derived from compounds having aromatic substituents in the seven position did not change as a function of time in 96% sulfuric acid, but a gradual decrease in extinction coefficient was observed in sulfuric acid solutions of such a concentration that the compound was approximately half ionized. The shortest lived ion in dilute sulfuric acid solution was the one derived from 1-methoxy-1-(p-chlorophenyl)tetramethylbenzocyclobutene. This ion had a half life of nine minutes in 59.43% sulfuric

Table IV. Visible and Ultraviolet Absorption Spectra of Some Benzocyclobutene Compounds in 96% H_2SO_4

Compound	Wavelength $\lambda_{max.}$ (mμ)	Molar Absorbancy Index (ε)
1-Phenyltetramethylbenzocyclobutene	435 310	25,900 6,110
1-Methoxy-1-(p-chlorophenyl)-tetramethylbenzocyclobutene	453 324	48,200 5,750
1-Methoxy-1-(p-methoxyphenyl)-tetramethylbenzocyclobutene	471 324	76,400 16,200
4-Chloro-1-methoxy-1-(p-tolyl)-3,5,6-trimethylbenzocyclobutene	458 323	67,400 4,500
4-Chloro-1-phenyl-3,5,6-trimethylbenzocyclobutenol	444 304	54,200 6,080
1-(p-Chlorophenyl)-4,6-dimethyl benzocyclobutenol	450 310	47,400 4,050
1,3,4,5,6-Pentamethylbenzocyclobutenol *	422 353	3,790 5,550
1-Cyclopropyltetramethylbenzocyclobutenol *	425 368	3,730 11,900
1-Benzyltetramethylbenzocyclobutenol *	452 348	8,210 4,000
Tetramethylbenzocyclobutenol *	520 344	6,860 5,490

* The spectra of these compounds altered with time. Reported here are the wavelengths and molar absorbancy extrapolated to the time of mixing the stock solution with sulfuric acid. See pages 103-4 for more detailed information.

Table V. pK Data for Benzocyclobutene Compounds Whose Ionization Follows H_r

% H_2SO_4	$C_r^+/C_{r\,OH}$	log $C_r^+/C_{r\,OH}$	H_r		pK_r
1-Phenyltetramethylbenzocyclobutenol measured at 435 mμ					
62.64	30.37	1.481	-9.35		-7.97
58.51	2.11	0.326	-8.22		-7.90
56.23	0.577	$\bar{1}$.761	-7.73		-7.97
55.12	0.346	$\bar{1}$.539	-7.58		-7.94
53.81	0.111	$\bar{1}$.045	-7.19		-8.24
				Average	-7.98
1-Methoxy-1-(p-chlorophenyl)tetramethylbenzocyclobutene measured at 453 mμ					
62.72	5.00	0.690	-9.38		-8.69
61.40	2.08	0.318	-9.00		-8.68
59.80	0.847	$\bar{1}$.92	-8.56		-8.64
58.68	0.380	$\bar{1}$.58	-8.22		-8.68
				Average	-8.67
1-Methoxy-1-(p-methoxyphenyl)tetramethylbenzocyclobutene measured at 471 mμ					
48.87	12.07	1.078	-6.17		-5.10
45.08	2.29	0.360	-5.43		-5.07
44.22	1.47	0.168	-5.26		-5.10
44.19	0.652	$\bar{1}$.178	-4.90		-5.10
				Average	-5.09
4-Chloro-1-methoxy-1-(p-tolyl)-3,5,6-trimethylbenzocyclobutene measured at 458 mμ					
64.77	4.65	0.668	-9.99		-9.32
61.95	1.27	0.104	-9.44		-9.34
60.75	0.598	$\bar{1}$.775	-9.09		-9.32
59.80	0.194	$\bar{1}$.289	-8.56		-9.27
				Average	-9.30

4-Chloro-1-phenyl-3,5,6-trimethylbenzocyclobutenol measured at 444 mμ

67.63	2.04	0.310	-10.91	-10.60
66.71	1.03	0.012	-10.59	-10.58
66.27	0.697	1.844	-10.45	-10.61
65.27	0.346	1.539	-10.14	-10.60
			Average	-10.59

1-(p-Chlorophenyl)-4,6-dimethylbenzocyclobutenol measured at 450 mμ

64.77	3.56	0.551	-9.99	-9.44
61.95	0.938	1.972	-9.44	-9.47
60.75	0.469	1.670	-9.09	-9.42
59.80	0.175	1.243	-8.56	-9.44
			Average	-9.44

1,3,4,5,6-Pentamethylbenzocyclobutenol measured at 422 mμ

86.3	3.91	0.592	-17.30	-16.7
85.1	2.07	0.316	-16.93	-16.6
84.2	1.15	0.061	-16.64	-16.7
82.6	0.326	1.326	-16.13	-16.6
			Average	-16.7

1-Benzyltetramethylbenzocyclobutenol measured at 488 mμ

87.8	3.59	0.530	-17.75	-17.2
85.9	1.04	0.018	-17.21	-17.2
85.0	0.390	1.59	-16.84	-17.2
84.2	0.290	1.47	-16.64	-17.2
			Average	-17.2

Table VI. pK Data for Benzocyclobutene Compounds Whose Ionization Follows H_r - log a^{H_2O}

% H_2SO_4	C_r^+/C_{rol}	log C_r^+/C_{rol}	H_r-log a^{H_2O}	pK	pK*
Tetramethylbenzocyclobutenol measured at 480 mμ					
93.1	3.66	0.56	-15.08	-14.5	-18.7
90.4	1.42	0.15	-14.83	-14.7	-18.4
87.8	0.384	1.58	-14.44	-14.8	-18.2
86.6	0.277	1.44	-14.24	-14.8	-18.0
84.2	0.104	1.02	-13.64	-14.6	-17.5
82.0	0.029	2.46	-13.39	-14.9	-17.5
			Average	-14.7	
1-Cyclopropyltetramethylbenzocyclobutenol measured at 432 mμ					
84.2	2.20	0.342	-13.32	-12.98	-16.30
82.0	1.08	0.033	-13.09	-13.06	-15.91
79.8	0.557	1.745	-12.86	-13.11	-15.47
77.9	0.384	1.584	-12.54	-12.96	-14.98
			Average	-13.02	

*These pK's were calculated using H_r rather than H_r-log a^{H_2O}. See the discussion on page 25.

acid. Good straight line plots of absorbance versus time were obtained in all cases, and extrapolated to zero time in order to obtain the absorbances from which ionization ratios were calculated.

The 7-benzyl substituted compound (XXXIIIb) was observed 2.3 minutes after mixing of the stock solution with concentrated sulfuric acid to have wavelength maxima at 348 mμ (ε = 4,000) and 452 mμ (ε = 8,210). After 44 minutes the high wavelength maxima had shifted to 485 mμ (ε = 6,980). Twelve hours later the spectrum was no different from the one measured after 44 minutes.

1,3,4,5,6-Pentamethylbenzocyclobutenol (XXXIIIa) showed no change in wavelength maxima with time, but the absorbance decreased by 20% during the first five minutes and then by another 20% in the next 35 minutes.

No wavelength maxima shift was observed for the 7-cyclopropyl compound (XXXIIIc) at six minutes up to one hour. The extinction coefficient of the maximum at 368 mμ decreased by 50% during the one hour period. When plots of absorbance versus time were made for the ion produced from (XXXIIIc) in various concentrations of sulfuric acid it was found that a much more completely ionized species is initially produced. This is evidenced by the very sharp decrease in absorbance during the first three minutes after mixing the stock solution with sulfuric acid. This absorbance change was too rapid for accurate pK measurement. Plots of absorbance versus time

were extrapolated to zero from the straight line plots of A versus T obtained after the first three minutes.

Tetramethylbenzocyclobutenol (XXXIIId) when dissolved in sulfuric acid produced an ion whose visible $\lambda_{max.}$ at 560 mμ (ε= 6,860) shifted to 483 mμ (ε= 12,300) after 48 minutes. Twelve hours later no further changes were observed.

C. Hydrolysis of the Ions Produced from Bicyclooctatriene compounds

1-Phenyltetramethylbenzocyclobutenol (XXXa)

Into a 3" test tube was placed 0.10 g. (0.40 mole) of XXXa and 0.5 ml. of concentrated sulfuric acid. The familiar deep red color of the ion was immediately produced. After ten minutes the sulfuric acid solution was poured over approximately 5 g. of ice. A white precipitate formed immediately which was filtered and dried, yielding 90% of white solid, m.p. 88-89°, which had an infrared spectrum identical with starting material.

1-Methoxy-1-(p-methoxyphenyl)tetramethyl-benzocyclobutene (XXXb)

Using a procedure analogous to that described above, 0.30 g. (11.0 mmole) of XXXb was dissolved in 1 ml. of sulfuric acid, and hydrolyzed by pouring over ice. However, on warming to room temperature the solid began to melt. It was quickly dissolved in methanol and was allowed to stand at room temperature for several days. White cubic

crystals formed which were filtered and dried to give 0.23 g. (76%) of product which had an infrared spectrum and melting point (83.5-84.5°) identical to starting material.

1-Methoxy-1-(p-chlorophenyl)tetramethyl-benzocyclobutene (XXXc)

Into 1-ml. of 70% sulfuric acid was placed 0.10 g. of XXXc. After ten minutes the sulfuric acid solution was poured into 30 ml. of cold methanol. A solid was precipitated by slowly adding distilled water. The product, when filtered and dried, was obtained in 80% yield, m.p. 69-70°. The infrared spectrum was identical with starting material.

4-Chloro-1-phenyl-3,5,6-trimethylbenzo-cyclobutenol (XXXe)

The procedure described for the hydrolysis of the ion derived from XXXa on the preceding page was followed in the recovery of XXXe from concentrated sulfuric acid. Into 0.6 ml. of concentrated sulfuric acid was dissolved 0.174 g. of XXXe. After ten minutes, followed by hydrolysis, 0.153 g. (87.9%) of starting material was obtained, m.p. 94-95°. The infra-red spectrum in carbon tetrachloride was identical with starting material (XXXe).

4-Chloro-1-methoxy-1-(p-tolyl)-3,5,6-trimethylbenzocyclobutene (XXXd)

The same procedure was employed here as the one described for the recovery of XXXc from sulfuric acid solution.

Into 0.6-ml. of sulfuric acid was dissolved 0.102 g. of XXXd. After ten minutes the sulfuric acid solution was poured into 15-ml. of cold methanol. The solid was precipitated by slowly adding distilled water. The product was washed thoroughly with distilled water and dried yielding 0.091 g. (89.0%) of recovered XXXd, m.p. 78-79°. The infrared spectrum was identical to starting material.

1-(p-Chlorophenyl)-4,6-dimethylbenzocyclobutenol (IXL)

Into a 3" test tube was placed 0.133 g. of IXL with 0.5-ml. of 96% sulfuric acid. After ten minutes the red solution was poured into 5 ml. of cold water and the oil which formed was extracted twice with 10 ml. of pentane. The pentane layer was separated, washed with 5 ml. of water, and dried over anhydrous magnesium sulfate. The pentane was evaporated in a stream of dry air leaving 0.102 g. (77%) of oil whose infrared spectrum was identical with starting material.

Tetramethylbenzocyclobutenol (XXXIIId), 1,3,4,5,6-Pentamethylbenzocyclobutenol (XXXIIIa), 1-Cyclopropyltetramethylbenzocyclobutenol (XXXIIIc), and 1-Benzyltetramethylbenzocyclobutenol (XXXIIIb)

Attempts to recover starting materials from the sulfuric acid solutions of compounds XXXIIIa-d met with failure in every case. Solutions of these compounds of approximately

10% concentration in concentrated sulfuric acid quickly turned black. In less concentrated solution the compounds were more stable, and were treated as described below. The ionization and hydrolysis was carried out using the rapid dispersal technique of Deno (58).

Into a 3" test tube was placed 2 ml. of 96% H_2SO_4 and 0.10 g. of tetramethylbenzocyclobutenol in 0.5 ml. of methanol. The red solution which formed was stirred for two minutes. It was then taken up in a syringe and ejected slowly into a 60 ml. beaker containing 10 ml. of water which was kept cold with an ice bath and stirred rapidly with a magnetic stirrer. The sulfuric acid solution was injected into the water near the sides of the beaker and close to the surface of the water. A white precipitate formed initially which quickly reacted further to form a red material that was immediately filtered off giving a red powder having a long decomposition range from 130-150°. The infrared spectrum in carbon tetrachloride showed bands at 5.88, 7.55, and broad absorption at 10μ. No further attempt to identify this material was carried out.

The same procedure as described for the hydrolysis of (XXXIIId) was carried out with XXXIIIa-c. In each case no starting material was recovered.

D. Attempted Base Catalyzed Deuterium Exchange of Tetramethylbenzocyclobutenone (X)

In an attempt to clarify the work of Fish (4) on the

base catalyzed deuterium exchange of tetramethylbenzocyclobutenone in deuterium oxide-ethanol, the following experiments were performed, and the products were studied by integrating the n.m.r. spectra and comparing the relative areas of the methylene protons absorption peaks before and after base treatment.

Experiment I. In a dry 50-ml. round-bottomed flask equipped with a reflux condenser fitted with a drying tube, was placed 0.29 g. of X, 5 ml. of ethanol which was dried by distilling from sodium and ethyl phthalate, and 3 ml. of deuterium oxide (99% D_2O). To this reaction mixture was added 0.10 g. of metallic sodium. After three hours of refluxing, the reaction was quenched by adding 30 ml. of ice cold distilled water. Only a trace of compound was extracted with pentane. The infrared spectrum of this material was identical with the spectrum of starting ketone. Neutralization of the aqueous layer produced a white precipitate which was filtered off and identified as pentamethylbenzoic acid.

Experiment II. The above experiment was repeated except that the reflux period was decreased to two hours, and the amount of sodium was decreased to 0.05 g. (0.00158 g.-atom). From this reaction mixture 0.12 g. (41%) of tetramethylbenzocyclobutenone was recovered. Infrared analysis of this ketone showed no C-D stretch. The n.m.r. spectrum was measured and integrated in carbon tetrachloride

solution. The integration showed no decrease in the area of the peak at τ = 6.32 which is assigned to the methylene protons of tetramethylbenzocyclobutenone. When the base-soluble portion of the reaction was neutralized, 0.14 g. (44%) of pentamethylbenzoic acid was isolated and identified by infrared spectrum and melting point.

E. Attempted Acid Catalyzed Deuterium Exchange of Tetramethylbenzocyclobutenone

Experiment I. In a 50-ml. round-bottomed flask equipped with a reflux condenser fitted with a drying tube was placed 0.29 g. of tetramethylbenzocyclobutenone with 3 ml. of deuterium oxide, 5 ml. of freshly dried ethanol, and 0.05 g. of p-toluenesulfonic acid. The reaction was chilled in ice and the organic product was extracted three times with 5 ml. of pentane. The pentane was evaporated leaving 0.24 g. of tetramethylbenzocyclobutenone whose infrared spectrum showed no C-D stretch. An integration on the n.m.r. spectrum showed no decrease in the area of the peak at τ = 6.32.

Experiment II. The n.m.r. spectrum of tetramethylbenzocyclobutenone was observed in 98% sulfuric acid-d_2. The spectrum displayed three single peaks at τ = 5.80, 7.67 and 7.84 with relative areas 2:6:6. No decrease in the relative area of the peak at τ = 5.80 had occurred after two hours. The solution in the n.m.r. tube was poured over ice, and the white precipitate which formed was identified as tetramethylbenzocyclobutenone by its infrared spectrum,

n.m.r. and melting point. The visible-ultraviolet spectrum of the protonated ketone in 100% sulfuric acid showed peaks at 380 mμ (ε = 2,050) and 320 mμ (ε = 18,100).

F. Spectra

The ultraviolet and visible spectra were obtained with the Beckman DK-2 recording spectrophotometer using 1 cm. glass stoppered cells. The sulfuric acid solutions were prepared as described on page 98.

The infrared spectra were scanned on a Perkin-Elmer Model 21 or a Unicam SP 200 Recording Infrared Spectrophotometer.

Proton magnetic spectra were measured with a Varian Associates Model A-60 analytical NMR Spectrophotometer.

G. Vapor Phase Chromatography

Vapor phase chromatography separations reported in this thesis were carried out on an Aerograph Model A-90-P Gas Chromatograph (Wilkens Instrument and Research, Inc., Walnut Creek, California).

SUMMARY

1. Several new benzocyclobutene derivatives were prepared, including tetramethylbenzocyclobutenol, 1-bromotetramethylbenzocyclobutene, tetramethylbenzocyclobutene, and several 1-arylbenzocyclobutenol derivatives.

2. From the coupling constants observed for the hydrogens on carbons one and two for tetramethylbenzocyclobutenol and 1-bromotetramethylbenzocyclobutene, it was shown that the bromo and hydroxy substituents on carbon one prefer an axial position with respect to the plane of the four-membered ring. From these calculations it was also demonstrated that the twist of the four-membered ring was similar to that of other benzocyclobutenes.

3. The 1-arylbenzocyclobutenol derivatives were found to produce carbonium ions in sulfuric acid. Hydrolysis of sulfuric acid solutions of the ions produced good yields of the compounds from which the ions were formed. In this way the stability of the ions with respect to rearrangement was definitely established.

4. The structure of the species involved in the equilibria of the 1-arylbenzocyclobutenols in sulfuric acid was investigated by n.m.r. and through acidity function calculations. It was concluded that elimination to form

benzocyclobutadiene derivatives was energetically unfavorable in the equilibria studied.

5. From Hammett plots of pK versus σ^+, and from observation of n.m.r. spectral data, good evidence for 1-3 interaction across the four-membered ring of benzocyclobutene carbonium ion derivatives was established.

6. Several attempts at acid and base catalyzed enolization of tetramethylbenzocyclobutenone were carried out in deuterated solvents. Failure to observe deuterium incorporation into the 2-position of tetramethylbenzocyclobutenone indicated again the extreme unfavorability of forming a double bond between the one and two carbon atoms.

LITERATURE CITED

1) H. Finkelstein, Ber., 43, 1530 (1910).

2) M. P. Cava and D. R. Napier, J. Am. Chem. Soc., 78, 500 (1956).

3) W. Baker and J. F. W. McOmie, "Non Benzenoid Aromatic Hydrocarbons" Interscience Publishers, N. Y., 1955, pp. 43-105.

4) R. W. Fish, Ph. D. Thesis, Michigan State University, 1960.

5) J. D. Roberts, A. Streitwieser, Jr. and C. M. Regan, J. Am. Chem. Soc., 74, 4579 (1952).

6) J. F. Bunnett and J. A. Scorcz, J. Org. Chem., 27, 3836 (1962).

7) M. P. Cava, B. Hwang and J. P. Van Meter, J. Am. Chem. Soc., 85, 4031 (1963).

8) M. P. Cava and R. Pohlke, J. Org. Chem., 28, 1013 (1963).

9) H. Hart and R. W. Fish, J. Am. Chem. Soc., 82, 749 (1960).

10) R. Rafos, Ph. D. Thesis, Michigan State University, 1961.

11) F. R. Jensen and W. E. Coleman, J. Am. Chem. Soc., 80, 6149 (1958).

12) K. Alderman and M. Fremery, Tetrahedron, 14, 190 (1961).

13) A. T. Blomquist and C. G. Bottomley, Ann., 653, 67 (1962).

14) M. P. Cava and K. Muth, J. Am. Chem. Soc., 82, 652 (1960).

15) M. P. Cava, D. Mangold, and K. Muth, J. Org. Chem., 89, 2947 (1964).

16) M. J. Jorgenson and A. W. Friend, J. Am. Chem. Soc., 87, 1815 (1965).

17) K. B. Wiberg, and B. J. Nist, "The Interpretation of N.M.R. Spectra," W. A. Benjamin, New York, 1962, pp. 21-24.

18) M. Karplus, J. Chem. Phys., 30, 11 (1959).

19) A. Bauder, F. Tank and Hs. H. Günthard, Helv. Chim. Acta., 46, 1456 (1963).

20) H. Nozaki, R. Noyori, and N. Kozaki, Tetrahedron, 20, 641 (1964).

21) G. Fraenkel, Y. Asahi, M. J. Mitchell, and M. P. Cava, Tetrahedron, 20, 641 (1964).

22) G. L. Hardgrove Jr., U. S. At. Energy Comm. UCRL, 8803, p. 70 (1959). C. A. 54:2875$_8$.

23) M. Karplus, J. Am. Chem. Soc., 85, 2870 (1963).

24) K. L. Williamson, J. Am. Chem. Soc., 85, 516 (1963).

25) M. P. Cava and D. R. Napier, J. Am. Chem. Soc., 79, 1701 (1957).

26) M. Avram, D. Dinu and C. D. Nenitzescu, Chem. and Ind. (London), 257 (1959).

27) M. P. Cava and M. J. Mitchell, J. Am. Chem. Soc., 81, 5409 (1959).

28) M. P. Cava and R. Pohlke, J. Org. Chem., 27, 1564 (1962).

29) M. P. Cava and R. Pohlke, J. Org. Chem., 28, 1012 (1963).

30) M. P. Cava and D. R. Napier, J. Am. Chem. Soc., 80, 2255 (1958).

31) A. T. Blomquist and C. R. Bottomley, J. Am. Chem. Soc., 87, 86 (1965).

32) G. F. Emerson, L. Watts and R. Pettit, J. Am. Chem. Soc., 87, 131 (1965).

33) M. P. Cava, B. Hwang and J. P. VanMeter, J. Am. Chem. Soc., 85, 4032 (1963).

34) M. P. Cava, R. L. Litle and D. R. Napier, J. Am. Chem. Soc., 80, 2257 (1958).

35) E. A. Braude and F. C. Nachod, "Determination of Organic Structures by Physical Methods," Academic Press, Inc., New York, N. Y., 1955, pp. 150-151.

36) M. P. Cava and R. L. Shirley, J. Am. Chem. Soc., 82, 655 (1960).

37) W. R. Moore, E. Marcus, S. E. Fenton and R. T. Arnold, Tetrahedron, 5, 179 (1959).

38) N. C. Deno, J. J. Jaruzelski, and A. Schriesheim, J. Am. Chem. Soc., 77, 3044 (1955).

39) E. M. Arnett, and R. D. Bushick, J. Am. Chem. Soc., 86, 1564 (1964).

40) N. C. Deno, P. T. Groves, and G. Saines, J. Am. Chem. Soc., 81, 5790 (1959).

41) G. Fraenkel and R. E. Carter, A. M. McLachlan and J. H. Richards, J. Am. Chem. Soc., 82, 5846 (1960).

42) C. Maclean and E. L. Mackor, Mol. Phys., 4, 241 (1961).

43) E. F. Kiefer and J. D. Roberts, J. Am. Chem. Soc., 84, 784 (1962).

44) F. F. Caserio, Jr. and J. D. Roberts, J. Am. Chem. Soc., 80, 5837 (1958).

45) F. F. Caserio, Jr., S. H. Parker, R. Piccolini and J. D. Roberts, J. Am. Chem. Soc., 80, 5507 (1958).

46) E. F. Silversmith and J. D. Roberts, J. Am. Chem. Soc., 80, 4083 (1958).

47) T. J. Katz and E. H. Gold, J. Am. Chem. Soc., 86, 1600 (1964).

48) Y. Okamoto and H. C. Brown, J. Org. Chem., 22, 485 (1957).

49) H. Tanida, T. Teruji and H. Tshitobi, J. Am. Chem. Soc., 86, 4904 (1964).

50) N. Deno, J. Jaruzelski and A. Schriesheim, J. Org. Chem., 19, 155 (1954).

51) M. J. Jorgenson, Tetrahedron Let. 13, 559 (1962).

52) M. P. Cava, R. L. Litle and D. R. Napier, J. Am. Chem. Soc., 2255 (1958).

53) S. J. Cristol and W. C. Firth, J. Org. Chem., 26, 280 (1961).

54) Huang-Minlon, J. Am. Chem. Soc., 68, 2487 (1946).

55) P. Kabasakalian and E. R. Townley, J. Am. Chem. Soc., 84, 2711 (1962).

56) L. J. Bellamy, "The Infra-red Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, 1958, p. 307.

57) D. H. R. Barton, J. M. Beaton, L. E. Geller and M. M. Pechet, J. Am. Chem. Soc., 82, 2640 (1960).

58) N. C. Deno, H. G. Richey, Jr., N. Friedman, J. D. Hodge, J. H. House and C. V. Pittman, Jr., J. Am. Chem. Soc., 85, 2991 (1961).