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Fulvenes, ylidenecyclopentadiene derivatives, bearing heteroatom substituents on the carbon atom alpha to C_6 are unreported. This thesis reports the results of several attempts to construct fulvenes substituted in this manner. These new molecules are needed for continuing investigations into the effects on chemical reactivity of fulvene-type conjugation.

Following generally applicable routes to fulvenes involving aldol-type condensation of cyclopentadienide salts and ketones, we have prepared fulvene derivatives of the type described above at the oxidation level of the alcohol, aldehyde, and ketone. After suitably blocking the hydroxyl group of pyruvic alcohol as the tetrahydropyranyl ether, treatment with cyclopentadienyl lithium gave the tetrahydropyranyl ether of 6-methyl-6-hydroxymethylfulvene (13) which upon acid hydrolysis was smoothly converted to the new compound, 6-methyl-6-hydroxymethylfulvene (11). This molecule fulfilled the criteria of a simple fulvene containing a heteroatom on carbon alpha to C_6.

The tetrahydropyranyl ether of 6-methyl-6-hydroxymethylfulvene was also prepared by treating pyruvyl-2-tetrahydropyranyl ether (12) and cyclopentadiene in the presence of cyclopentadienylcopper(I)-isocyanide.

Other fulvene derivatives prepared at the oxidation level of the aldehyde or ketone were the dimethylacetal of 6-methyl-6-fulvene carboxaldehyde (9) and the ethylene ketal of 6-methyl-6-benzoylfulvene (18).

These new compounds were prepared by treating cyclopentadienyl lithium with methylglyoxal dimethylacetal or 2-acetyl-2-phenyl-1,3-dioxolane (17). Many attempts to hydrolyze these compounds to the respective aldehyde or ketone was unsuccessful.

SYNTHESES OF NEW FULVENE DERIVATIVES

by

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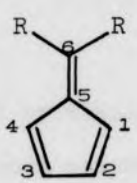
TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

INTRODUCTION

The supposition that various carbocyclic nonbenzenoid compounds might possess aromatic character resulted in the synthesis of many new types of conjugated compounds in the late 1800's and early 1900's. One specific class of compounds prepared as a consequence of these studies is that of the fulvenes. Fulvenes, of type structure 1, are isomeric



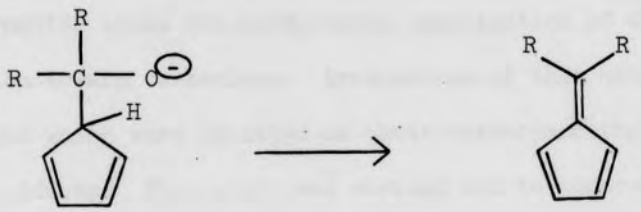
1

with benzene and derivatives of benzene. Fulvene was first prepared by Thiele (1) and has attracted interest since then because of its intermediate position with regard to reactivity between benzenoid isomers and olefins.

Since 1962 Chemical Abstracts has deemed fulvenes as derivatives of cyclopentadiene. This designation would name 1, with R = methyl, as 5-isopropylidenecyclopentadiene. The alternate nomenclature system denoting these compounds as fulvenes, with the numbering system shown in 1, is used by many authors at this time and will be used exclusively in this paper.

Although several synthetic procedures leading to fulvenes exist, normally considered the most generally applicable preparation is condensation of cyclopentadiene with aldehydes or ketones in the presence of a

base. Nucleophilic attack on the carbonyl compound by the cyclopentadienide anion (formed by the base) results in the intermediate 2. Following protonation of this alkoxide, dehydration of the resulting carbinol is then catalyzed by either acid or base to form a fulvene 3,

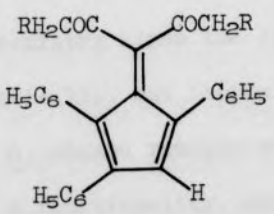


2 3

where substituents R are aryl or alkyl.

Recently fulvenes have been prepared with heteroatoms attached to C_6 by using immonium (2) or oxonium salts (3) in lieu of the carbonyl compound. These various fulvenes, their synthesis and reactions, are treated in detail by Day (4), Yates (5), and Bergmann (6).

To our knowledge there has been no simple fulvene prepared with a heteroatom on the carbon atom alpha to C_6. Eicher (7), however, has prepared 4a and 4b which does partially fit this criterion, but with phenyl substituents in three of the four positions on the ring.



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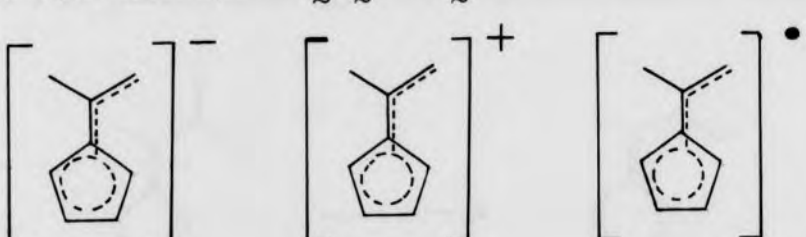
a: R=H

b: $R=CH_3$

Knight (8) has shown the conjugated fulvene system does isomerize through the anion. He has ionized dimethylfulvene with potassium tert-butoxide in bis(2-methoxyethyl) ether (diglyme) to form 97% of the dimethylfulvenide and only 3% of unionized dimethylfulvene. This large percentage of anion formation shows the unequivocal stablization of the conjugated fulvene system toward carbanions. Protonation of this anion formed three products which were isolated as their tetracyanoethylene (TCNE) Diels-Alder adducts. This study was carried out to observe the protonation product ratio. The total product ratio of the protonated species has not yet been rationalized.

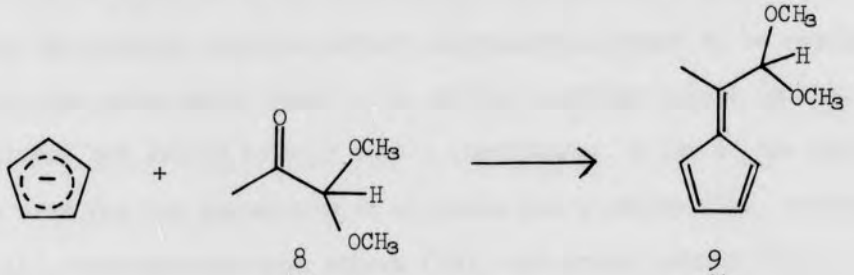
In view of this work, the next logical steps would be a study of the effects of fulvene-type conjugation on the reactivity of the carbonium ion and radical related to the anion described above. A combined study of these three systems 5, 6, and 7 could be extremely informative



5 6 7

with regards to fulvene chemistry since the class of fulvenes has been extensively studied theoretically, but little studied experimentally. The carbonium ion system, 6, seemed readily accessible by synthesizing a precursor which contained a functionality, such as a sulfonate or carboxylate ester attached to the carbon atom alpha to C_6. Solvolysis of this precusor could then form the mesomeric carbonium ion, 6.

The original purpose of this work was to construct a fulvene substituted at C_6 at the oxidation level of an aldehyde. Reduction of the aldehyde to an alcohol would then satisfy the above structural objectives. This was to be done by condensing cyclopentadienide with methylglyoxal dimethylacetal, 8, thereby forming the fulvene 9.



8 9

Acid catalysis of acetals yields aldehydes, even though the particular mechanism seems to depend on the specific molecule (9). Therefore, hydrolysis of 9 should yield 10, which could most likely be reduced by

10 11

sodium borohydride to the primary alcohol, 6-methyl-6-hydroxymethylfulvene, 11. Lithium aluminum hydride cannot be used for this reduction because it has been demonstrated that this reagent reduces the exocyclic double bond (10), (11). Sodium borohydride does not normally reduce double bonds, isolated or conjugated, albeit there are reported instances of reduction of a double bond when a carbonyl group is in conjugation with the double bond (12), (13).

In case there were any problems encountered that would cause any of these aforementioned reactions not to work, an alternative plan was considered. This was to construct a fulvene molecule substituted on the carbon atom alpha to C_6 at the oxidation level of an alcohol. Since the acidity of the alcohol group in a keto-alcohol must be considered in a condensation reaction with the cyclopentadienide anion, a protective group for the alcohol function before condensation seemed to be required. The protective group would have to be stable to strong alkali (during condensation) but labile to mild acidic conditions. A few of the systems commonly used for the protection of alcohols are acetates (14), nitrate esters (15), tetrohydropyranyl ethers (16), and trityl ethers (17). Consideration of these protective groups with respect to cost, ease of formation, stability to base, ease of hydrolysis, and yields demonstrated that tetrahydropyranyl ethers best met these requirements.

HISTORICAL REVIEW

It is not the intention to review the history of fulvenes here because excellent historical reviews are presented by Day (4) and Bergmann (6). Instead a literature search has been made concerning the use of 2H-dihydropyran as a protective group for alcohols.

Raymond Paul (18) first prepared 2H-dihydropyran in 1933 by passing tetrahydrofurfuryl alcohol over alumina at 370-80°. His interests at this point were in the hydrolysis products of 2H-dihydropyran rather than a protective group for synthesis. It was found that refluxing 2H-dihydropyran with 0.02 N aqueous hydrochloric acid yielded 1,5-epoxy-5-pentanol (19), but at room temperature in an aqueous solution this cyclic form was in equilibrium with the acyclic 5-hydroxyvaleraldehyde. In repeating this work using methanol as a solvent and gaseous hydrogen chloride, he obtained methyl-2-tetrahydropyranyl ether which was readily hydrolyzed at room temperature with acid. This was the first ether of this type prepared, but no further attempt was made to prepare any other tetrahydropyranyl ethers.

Paul's next contribution to this field was the preparation of various alkyl-2-tetrahydropyrans by hydrohalogenation at 0° of 2H-dihydropyran to form the halo-2-tetrahydropyran. This he reacted with a Grignard reagent to synthesize the alkyl-2-tetrahydropyran (20).

Essentially no work was done with 2H-dihydropyran until 1947 when Woods and Kramer (21) prepared a series of the tetrahydropyranyl ethers by extending Paul's work. In Table I are listed the ethers prepared and

TABLE I

Substituted-2-Tetrahydropyranyl Ethers (21)

Substituent	% Yield
Methyl	85
Ethyl	93
n-Propyl	91
Allyl (a)	70
n-Butyl	75
Phenyl	37
Benzyl	41
Furfuryl	34

(a) The relatively high yield of allyl-2-tetrahydropyranyl ether is noted here because the fulvene system using the tetrahydropyranyl protective group would also be an allylic system.

their yields. Further investigation into these various ethers by Parham (22) revealed several interesting facts to the synthetic chemist. These ideas are summarized below:

(1) They are stable to base.

(2) They are stable to organometallic reagents.

(3) They are unlike other ethers in that the hydrolysis conditions do not have to be vigorous.

(4) There is essentially no difference in conditions for aliphatic or aromatic ethers.

(5) Conditions for formation are mild.

(6) Yields are normally good.

Practical synthetic use of 2H-dihydropyran was finally realized and its use has made a tremendous impact on steroid synthesis. Hydroxyl functions can be protected while a series of reactions are carried out on the remainder of the molecule and then very easily the ether is hydrolyzed to restore the hydroxyl group. Elisberg (23) clearly demonstrated this by protecting the 3-hydroxyl group of 17β-acetoxyetiocholane-3α-ol with 2H-dihydropyran while saponifying the 17-acetoxy group with a base, chromic anhydride oxidation of the 17-hydroxyl groups to the 17-ketone and then reinstating the 3-hydroxyl group by hydrolysis of the tetrahydropyranyl ether. Ott (16) used 2H-dihydropyran to synthesize six new tetrahydropyranyl ethers with different steroids. He protected the 3-hydroxyl group with 2H-dihydropyran of a steroidal keto-alcohol while the 17-ketone was reduced to a hydroxyl group. The 17-hydroxyl was protected with an acid resistant ester followed by acid hydrolysis of the tetrahydropyranyl ether to reform the 3-hydroxyl and yield

5-androsten-3β,17β-diol 17-ester. Oppenauer oxidation of this product gave the testosterone acyl ester in a 74% yield. Previously, without the use of a tetrahydropyranyl ether, the yield had only been 25%.

Kipnis (24) discovered that thiols also react with 2H-dihydropyran to give tetrahydropyranyl thioethers. Later Parham (25) completed work on preferential pyranylation and found that the tetrahydropyranyl thioethers were in fact very difficult to cleave as opposed to Kipnis' conclusion of being easily hydrolyzed. More recently Robins et al. (26), have found that 6-substituted purines with 2H-dihydropyran by acid catalysis give 6-substituted-9-(tetrahydro-2-pyranyl) purines which provide a new synthetic route to the preparation of valuable models of specific purine deoxynucleosides which possess antitumor activity. These tetrahydropyran molecules have vastly improved the solubility of the purine derivatives in organic solvents and provided a blocking group that prevents undesirable side reactions due to the imidazole hydrogen, but is acid labile and easily regenerates the purine.

In view of the preceding experimental data on tetrahydropyranyl ethers, it is distinctly evident that this protective group could also be of importance in synthesis of fulvenes containing heteroatom substituents on the carbon atom alpha to C_6.

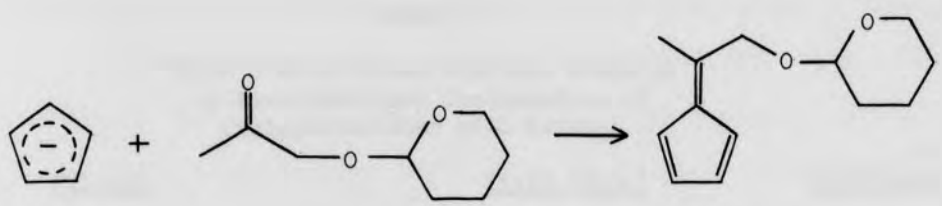
RESULTS

Two main routes to the desired fulvene derivatives were attempted. The first was condensation of cyclopentadienyl lithium with methylglyoxal dimethylacetal followed by subsequent hydrolysis to the fulvene carboxaldehyde. The second route was condensation of cyclopentadienyl lithium with pyruvyl-2-tetrahydropyranyl ether, followed by hydrolysis to the desired 6-methyl-6-hydroxymethylfulvene. Of these two routes, only the latter was successfully taken to completion.

A sample of pyruvyl-2-tetrahydropyranyl ether (12) was obtained (27) and a condensation type reaction was carried out with cyclopentadienyl lithium. There was enough spectral evidence for the formation of a fulvene, that it warranted synthesizing a quantity of 12 (to our knowledge this compound is not reported in the literature).

Conditions for the formation of 12 were monitored by gas chromatography (10% carbowax 20M on chromosorb W column). It was found that good conversions to 12 could be made by stirring a solution of 2.0 moles of 2H-dihydropyran, 1.3 moles of pyruvic alcohol, 0.8 ml of hydrochloric acid, and 800 ml of anhydrous ethyl ether for 20 hours at room temperature. Pyruvyl-2-tetrahydropyranyl ether was isolated by distillation in 74% yield. This yield is in line with what might be expected by noting the yield of allyl-2-tetrahydropyranyl ether in Table I.

Treatment of 12 with cyclopentadienyl lithium in benzene for 20 hours formed the tetrahydropyranyl ether of 6-methyl-6-hydroxymethylfulvene (13) as shown below. When the reaction mixture was distilled, decomposition



12 13

of 13 occurred. Compound 13 was isolated in 20% yield by dry column chromatography.

The product, 13, was also prepared in 18% yield by another synthetic procedure. Cyclopentadiene, 12, and cyclopentadienylcopper(I)-isocyanide were stirred for 24 hours in anhydrous ethyl ether to form 13. This method of preparing fulvenes by using cyclopentadienylcopper(I)-isocyanide as a catalyst was reported by Saegusa (28). None of his work was applied to fulvenes containing any atoms other than carbon and hydrogen. He reported 6,6-dimethylfulvene, 6-isopropylfulvene, and 6-methyl-6-phenylfulvene prepared in 95%, 43%, and 66% yield respectively.

The yields for 13 are low compared to those of Saegusa, but the yields he quoted were not for isolated fulvenes. Also, preparation of those particular fulvenes by other methods give relatively good yields. It is not uncommon for yields of fulvenes prepared by aldol-type condensations to be this low or even lower, especially in the case of 6-substituted fulvenes. In Table II are listed some representative 6-substituted fulvenes and their yields. As can be seen, some of the 6-alkyl and 6-aryl substituted fulvenes are formed in extremely low yields. There has been no good rationale put forth to clearly define the problem of poor yields for some of these fulvenes.

TABLE II

Some 6-Substituted Fulvenes Prepared by Base-Catalyzed Condensation of Cyclopentadienes with Ketones

Fulvene	Yield (%)(a)	Reference
6-p-Chlorophenyl-6-methyl	9	29
6-p-Anisyl-6-phenyl	21	29
6-p-Nitrophenyl-6-phenyl	32	30
6-p-Chlorophenyl-6-phenyl	17	31
6-Methyl-6-p-tolyl	27	29
6-Cyclohexyl-6-methyl	23	32
6-Ethyl-6-methyl	75	32
6-Methyl-6-vinyl	0.5	33
6,6-Diphenyl	56	34

(a) Based on ketone

Hydrolysis of 13 in methanol-water with a catalylic amount of hydrochloric acid gave 6-methyl-6-hydroxymethylfulvene (11). This compound, a yellow solid, was isolated by dry column chromatography in a 69% yield. Recrystallization of 11 from pentane gave yellow needles, mp 54.0-54.5°.

Condensation of methylglyoxal dimethylacetal with cyclopentadienyl lithium gave the dimethylacetal of 6-methyl-6-fulvene carboxaldehyde (9). This was isolated by distillation to give 9, an orange oil, in 51% yield. Hydrolysis of 9 was expected to give 10, 6-methyl-6-fulvene carboxaldehyde. After many attempts to hydrolyze 9 failed (Table IIa lists all of the hydrolysis conditions for 9 and the results), it was decided that either 10 did not form or it was unstable under the conditions in which it was formed. To determine if the molecule was formed, two different methods were used. First, an attempt was made to trap 10 as the bisulfite addition product. This was done by reacting compound 9 with 50% aqueous citric acid for 20 minutes, neutralization of the acid, and the addition of sodium bisulfite in 40% aqueous ethanol. No identifiable compound was isolated from this reaction. The other method employed was an hydrolysis attempt of 9 in the presence of a reducing agent. The reducing agent, sodium cyanoborohydride which is stable to acidic media, would reduce any of compound 10 formed to compound 11. This would not only prove the existence of 10 but also yield the desired fulvene. This reaction was carried out with equimolar amounts of 9 and glacial acetic acid and a two fold excess of sodium cyanoborohydride in tetrahydrofuran. This solution was stirred for three hours at 0° at which time a small amount of solid was observed in the reaction flask. The only compound recovered from this reaction was compound 9. Failure

TABLE IIa

Conditions for Hydrolysis of the Dimethylacetal of 6-Methyl-6-Fulvene Carboxaldehyde (9)

Aqueous Acid	Result
50% Citric	9 + unidentifiable product
10% Hydrochloric	unidentifiable product
10% Nitric	unidentifiable product
5% Perchloric (a)	black charred solid
10% Sulfuric	dark brown liquid
p-Toluenesulfonic (b)	some 9 recovered

(a) Carried out in ice bath at 0°

(b) In tetrahydrofuran

of these two reactions to prove the existence of 10 and obtain 11 caused this particular synthetic route to be abandoned.

Angyal and James (35) have shown that chromium trioxide in acetic acid oxidizes acetals of aldehydes to esters. Their work was done with glycosides, cyclic acetals, but this seemed to be a possible route to 11. Oxidation of the dimethylacetal of 6-methyl-6-fulvene carboxaldehyde (9) by this method could be expected to furnish the methyl ester of 9. Normally, reduction of esters to alcohols is carried out with a reducing agent such as lithium aluminum hydride which has already been shown to reduce the exocyclic double bonds of fulvenes. Sodium borohydride usually does not reduce esters but there are some exceptions known (36). The reagents that would be expected to reduce the methyl ester of 9 to 6-methyl-6-hydroxymethylfulvene are sodium borohydride in the presence of lithium chloride in diglyme (37). Brown has shown these reagents to be general for the reduction of esters to alcohols.

Several attempts to oxidize 9 to its methyl ester with chromium trioxide in acetic acid in a procedure similar to Angyal's resulted in complete decomposition of 9. When the amount of chromium trioxide was decreased, some 9 was recovered but no other organic product was isolated. Therefore, this route to 11 was also abandoned.

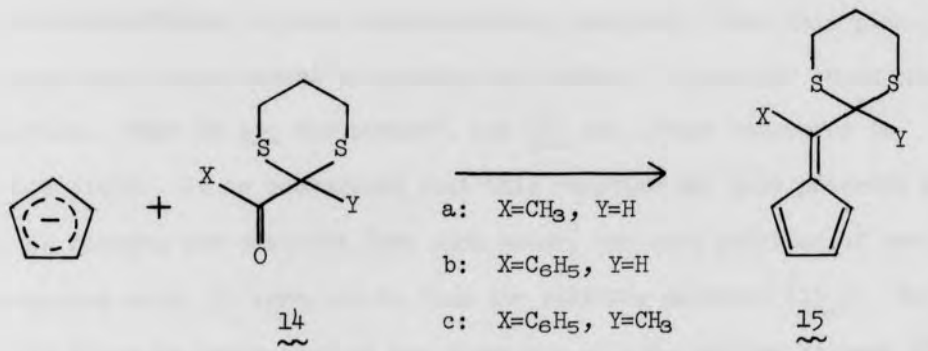
It might be expected that direct condensation of cyclopentadienyl lithium with a keto-carboxylic acid or a keto-alcohol would not occur due to the acidity of both of the carbonyl compounds. This was found to be the case in both reactions. Condensation type reactions were carried out with one equivalent of pyruvic acid and one equivalent of pyruvic alcohol respectively with two equivalents of cyclopentadienyl lithium. In each

case the product obtained was not a fulvene.

Pyruvic alcohol was also reacted with cyclopentadienylcopper(I)-isocyanide and cyclopentadiene in an attempt to obtain 11 directly. This reaction did not form any fulvene and only a small amount of pyruvic alcohol was recovered. Saegusa's mechanism (28) for the formation of fulvenes using the isocyanide complex as a catalyst could be used to explain why 11 did not form. Again, it would be due to the acidity of pyruvic alcohol.

In an effort to avoid the acidity problem in condensation, a salt of pyruvic acid was used, silver pyruvate. The fulvene expected from this reaction, the silver salt of 6-methyl-6-carboxylic acid fulvene could then be acidified and form 6-methyl-6-carboxylic acid fulvene. Unfortunately, silver pyruvate was not very soluble in organic solvents. Refluxing silver pyruvate with cyclopentadienyl lithium in tetrahydrofuran for 36 hours yielded only silver pyruvate.

Corey and Erickson's (38) efficient hydrolysis of 1,3-dithiane derivatives to carbonyl compounds suggested another possible route to 11. They have prepared several keto dithianes which upon oxidative hydrolysis gave either diones or keto-aldehydes. Specifically they have prepared 2-benzoyl-1,3-dithiane from 1,3-dithianyl lithium and benzonitrile. By using acetonitrile in place of benzonitrile with 1,3-dithianyl lithium, it was thought that it would be possible to get 2-acetyl-1,3-dithiane (14a). Condensing 14a with cyclopentadienyl lithium should give 15a. Then



14 15

oxidative hydrolysis of 15a with mercuric chloride would either give 10 or give more proof that it could not be formed. If 10 were formed, then the reduction with sodium borohydride to give 11 could be attempted. It was discovered that 14a could not be formed with acetonitrile due to the acidic protons alpha to the nitrile (39).

Replacing 14a with 2-benzoyl-1,3-dithiane (14b), which had been prepared by Corey (38), and condensing this with cyclopentadienyl lithium may give 15b. Oxidative hydrolysis of 15b followed by reduction of the aldehyde to an alcohol would give 6-phenyl-6-hydroxymethylfulvene instead of 6-methyl-6-hydroxymethylfulvene. But the original requirements of a simple fulvene substituted alpha to C-6 would still be fulfilled. Condensation to give 15b was not effected, however and some 14b was recovered.

It was thought that the methinyl proton on 14b was protonating cyclopentadienyl lithium, thus preventing condensation. To see if this was correct, 2-methyl-2-benzoyl-1,3-dithiane (14c) was prepared by Corey's procedure (38). With this compound, the methinyl proton was replaced with a methyl group to prevent protonation of cyclopentadienyl lithium. When a solution of 14c was added to cyclopentadienyl lithium

in tetrahydrofuran, a pink colored mixture resulted. When this pink mixture was either warmed or aqueous acid added, it resulted in an orange solution. None of 15c was present, but 14c was always recovered in 50-60% yield. It is postulated that this reaction may have preceded as far as forming the alkoxide (the pink color) but upon addition of heat or aqueous acid, it reversed to form the starting material (15c). The yellow color is indicative of the formation of 1,3-dithiane ketones (38).

Possibly with different or stronger reaction conditions, 15c could be formed. At this time, this has not proven to be true. Other conditions used to produce 15c which have failed are listed below:

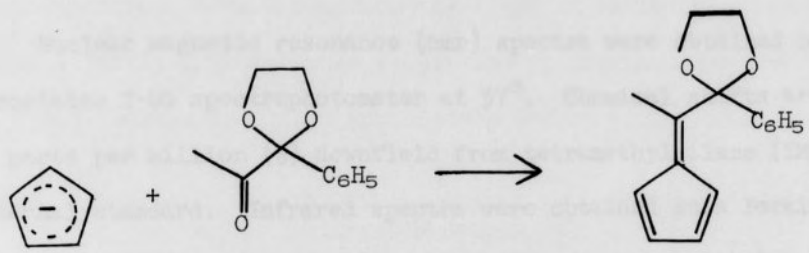
(1) 14c + cyclopentadienylmagnesium bromide $\xrightarrow{\text{ether}}$ N. R.

(2) 14c + cyclopentadiene + potassium tert-butoxide $\xrightarrow{\text{DMSO}}$ N. R.

(3) 14c + cyclopentadienylcopper(I)-isocyanide $\longrightarrow$ N. R.

In each case 2-methyl-2-benzoyl-1,3-dithiane was recovered in at least 40% yield.

From this dithiane precursor, another fulvene has been prepared, however. Corey reported that 14c was relatively resistant to oxidative hydrolysis (38), so he prepared 2-(2-methyl-1,3-dithianyl-2)-2-phenyl-1,3-dioxolane (16) by refluxing a mixture of 14c, benzene, ethylene glycol and p-toluenesulfonic acid for 72 hours. Oxidative hydrolysis of 16 with N-bromosuccinimide in aqueous acetonitrile gave 2-acetyl-2-phenyl-1,3-dioxolane (17). These procedures were repeated to obtain 17 which was condensed with cyclopentadienyl lithium to give the ethylene ketal of 6-methyl-6-benzoylfulvene (18).



17 18

EXPERIMENTAL

Nuclear magnetic resonance (nmr) spectra were obtained on a Varian Associates T-60 spectrophotometer at 37°. Chemical shifts are expressed in parts per million (δ) downfield from tetramethylsilane (TMS) as an internal standard. Infrared spectra were obtained on a Perkin Elmer 457 Grating Infrared double beam recording spectrophotometer. Visible and ultraviolet absorption spectra were recorded on a Beckman DK-2A Ratio Recording Spectrophotometer. Gas chromatography was carried out on either a Varian Aerograph Model 700 or an Aerograph Model 600-D. Mass spectra were obtained on a CEC 21-104 using 190/100 electron volts per stage (anode current). All of the spectral data is compiled in the Analysis of Spectra section on page 31.

All thin layer chromatography (tlc) was carried out on Eastman Chromagram Sheets with flourescent indicator (alumina-sheet 6063 and silica gel - sheet 6060). The tlc plates were activated by placing them in an oven at 110° for one hour prior to use. Column chromatography was performed with either Fisher No. A-540 Alumina (80-200 mesh) or Grace Silica Gel (100-200 mesh Davison Chemical).

All solvents, ACS reagent grade, were distilled from Na/K alloy under nitrogen and stored over type 4A molecular sieves (Davison Chemical) in a nitrogen atmosphere. Reactions were carried out under nitrogen using these purified solvents. Melting points were taken on a Thomas-Hoover Capillary Melting Point Apparatus. All melting points and boiling points are uncorrected.

Cyclopentadiene

Cyclopentadiene was prepared by dropping dicyclopentadiene from an addition funnel into a round-bottom flask of refluxing tetralin and flash distilling the monomer (40). The cyclopentadiene was stored at -10° and freshly distilled immediately before every reaction.

Synthesis of the Dimethylacetal of 6-Methyl-6-Fulvene Carboxaldehyde (9)

Cyclopentadienyl lithium was obtained from the reaction of cyclopentadiene and an organolithium compound in a method similar to that used by Doering (41).

A 250 ml three-neck round-bottom flask equipped with a magnetic stirrer, pressure equalizing addition funnel, reflux condensor, and a rubber septum was flame dried under vacuum, and the atmosphere replaced by dry nitrogen. In a typical run, cyclopentadiene (0.12 mole) was dissolved in 70 ml of benzene and n-BuLi (0.12 mole) in hexane was added with stirring under nitrogen to the solution. Evidence of the formation of cyclopentadienyl salt was seen by the evolution of gas (butane) and the presence of a white slurry. The mixture was stirred until the temperature was approximately 25° and a solution of methylglyoxal dimethylactetal (8) (0.10 mole) and 40 ml of benzene was added dropwise (30).

The mixture turned dark orange, became homogeneous and considerably less viscous with the continued addition of the acetal. The solution was then refluxed for fifteen minutes and stirred at room temperature an additional hour. Aqueous HCl (0.5M) was added until the color of the solution changed to a bright orange and that color remained. The pH was

checked at this point with Alkacid Test Paper and the mixture was strongly acidic. After the normal work-up procedure, 16.8 g of a dark orange oil was obtained.

Short path distillation gave 8.5 g of a viscous orange liquid, bp 63-66° at 0.9 mm of Hg. A representative yield of 9 was 51%, based on 8.

Synthesis of Pyruvyl-2-Tetrahydropyranyl Ether (12)

A 2 l. three-neck round-bottom flask equipped with a magnetic stirrer was flame dried under vacuum, and the atmosphere replaced by dry nitrogen. A solution of 2H-dihydropyran (2.0 mole, distilled from sodium hydroxide pellets), pyruvic alcohol (1.3 mole), concentrated HCl (0.8 ml), and 800 ml of anhydrous ethyl ether was stirred in the round-bottom flask at 25° under nitrogen. There was no visible change in the colorless solution.

Analysis of samples from the reaction solution was completed by gas chromatography (five foot 10% carbowax 20M on 60/80 mesh chromosorb W column). After 24 hours, the absence of pyruvic alcohol showed the reaction to be completed. Precedence for the protection of a hydroxyl function by converting it to a tetrahydropyranyl ether in ethyl ether is seen in Ott's work with steroids (16).

The reaction mixture was neutralized with aqueous bicarbonate, washed with saturated aqueous sodium chloride, dried over anhydrous sodium sulfate, and the solvent evaporated. The colorless liquid was vacuum distilled to give 152.3 g of a clear colorless oil, bp 65-67° at 0.2 mm of Hg. Examination of the nmr and ir spectra showed this to be pyruvyl-2-tetrahydropyranyl ether, obtained in 74% yield.

Synthesis of the Tetrahydropyranyl Ether of 6-Methyl-6-Hydroxymethylfulvene (13)

A 3 l. three-neck round-bottom flask equipped with a mechanical stirrer, pressure equalizing addition funnel, reflux condensor, and a rubber septum was flame dried under vacuum, and the atmosphere replaced by dry nitrogen. To the flask containing cyclopentadiene (0.5 mole) and 1.2 liters of benzene was added n-BuLi (0.5 mole) in hexane to form the cyclopentadienyl lithium. After cooling this white slurry to room temperature, pyruvyl-2-tetrahydropyranyl ether (0.4 mole), dissolved in 200 ml of benzene, was added to the cyclopentadienide mixture at the rate of 2-3 drops per second. Evidence of the reaction was noted by the appearance of an orange color and an increase in the homogeneity of the mixture.

The reaction was stirred for 20 hours at room temperature and then refluxed for 1.5 hours. To the still warm solution was added 0.5 M aqueous HCl until the bright orange color persisted and the mixture was strongly acidic. After the normal work-up and evaporation of solvent, 85 g of an orange oil was obtained. Every attempt to distill this oil resulted in the formation of dark brown oil which upon cooling became a brittle solid.

General Procedure for Work-up of a Condensation or Acetal Hydrolysis Reaction

The reaction mixture was extracted into a 1:1 methylene chloride-ethyl ether solution and washed with water until the aqueous phase was neutral to Alkacid Test Paper. The organic solution was then washed with saturated aqueous sodium chloride, dried over anhydrous sodium sulfate

and the solvents evaporated on a Büchi Rotavapor-R at aspirator pressure.

Synthesis of the Tetrahydropyranyl Ether of 6-Methyl-6-Hydroxymethylfulvene (13) Using Cyclopentadienylcopper(I)-Isocyanide Complex as a Catalyst

The tert-butyl isocyanide used in the formation of the complex was prepared by Ugi's procedure (42). The cyclopentadienylcopper(I)-isocyanide complex was prepared without any complications and the spectral parameters agreed with those of Saegusa (28).

A 75 ml three-neck round-bottom flask equipped with a magnetic stirrer was flame dried under vacuum, and the atmosphere replaced by dry nitrogen. A mixture of cyclopentadiene (30 mmol), cyclopentadienylcopper (I)-isocyanide (0.5 mmol), and tert-butyl isocyanide (0.5 mmol) was prepared and a brown-green color was observed. Rapid addition of pyruvyl-2-tetrahydropyranyl ether produced an orange-colored solution. Approximately ten minutes after the addition, the temperature had increased slightly and the solution had become very viscous. To keep the solution stirring evenly, 15 ml of ethyl ether was added to the reaction flask and stirring was continued for 24 hours under nitrogen.

The mixture was slightly alkaline at this point. This solution was washed with water until the aqueous phase was neutral. Then the organic solution was washed with saturated aqueous sodium chloride, dried over anhydrous sodium sulfate, and the solvent evaporated to yield 8.9 g of a viscous yellow-brown oil.

Thin layer chromatography of this crude product on silica gel (7:3 carbon tetrachloride-ethyl acetate) showed only one component that possessed

the same R_f value (0.71) as 13, previously prepared. This was isolated by dry column chromatography in approximately 18% yield.

Conditions for Chromatographic Purification of the Tetrahydropyranyl Ether of 6-Methyl-6-Hydroxymethylfulvene (13)

As was stated previously, 13 could not be purified by distillation. To isolate sizable quantities, column chromatographic methods were employed.

I. Wet Column Chromatography

A two inch diameter column was packed with 500 g of silica gel using hexane-benzene (4:1) as solvent. The crude product (50 g) containing 13 was dissolved in a small amount of this mixed solvent, placed on the column and eluted.

The first fraction, a distinct yellow band, came off the column rapidly. After this fraction was removed, the amount of benzene was increased in each portion of solvent added until the eluent was 100% benzene. The second fraction was dark yellow and yielded 16.2 g of an orange viscous oil after evaporation of solvent. NMR assay in carbon tetrachloride showed this to be primarily the tetrahydropyranyl ether of 6-methyl-6-hydroxymethylfulvene. Other fractions from the column were not identified. A total time of four hours was necessary to isolate compound 13 by this method.

II. Dry Column Chromatography (43), (44)

Conditions for the separation and purification of 13 were established by tlc because there is a direct transferability between tlc conditions and dry column chromatography (44). Optimum separation ($\Delta R_f = 0.51$) was

obtained on alumina with hexane as solvent.

The column chromatographic alumina was deactivated to grade III (44) by adding 6% water and equilibrating this mixture by rotation in a round-bottom flask on a closed rotary evaporator for three hours. At this point, the column alumina was the same activity as the tlc plates.

A 0.75 inch diameter column was packed with 100 g of the alumina without solvent. This was done by opening the stopcock to prevent air pockets and packing the alumina with the aid of a vibrator. The crude product (7.0 g) containing 13 was dissolved in 30 ml of ethyl ether and poured onto 60 g more of the alumina in a round-bottom flask. The solvent was removed on a rotary evaporator, leaving the crude product adsorbed on the alumina. This alumina was placed on the column, packed as before on top of the original portion of alumina. This gave a column that was "dry" and ready for elution.

The column was developed with hexane until the first band (13) had distinctly separated. The total time for this to occur was eight minutes. At this point, R_f = .51, the elution was stopped. The portion of alumina that contained 13 was mechanically poured into a beaker, extracted with methylene chloride, dried over anhydrous sodium sulfate, and the solvent evaporated. This furnished 1.4 g of an orange oil which within the limits detectable by nmr was pure tetrahydropyranyl ether of 6-methyl-6-hydroxymethylfulvene.

Preparation of 6-Methyl-6-Hydroxymethylfulvene (11)

A 500 ml three-neck round-bottom flask equipped with a magnetic stirrer was evacuated and the atmosphere was replaced by nitrogen.

Conditions for hydrolysis of the tetrahydropyranyl ether of 6-methyl-6-hydroxymethylfulvene were optimized using gas chromatography (10% SE-30 on 60/80 mesh chromosorb W, five foot column) to monitor hydrolysis. The varied hydrolysis conditions appear in Table III.

In one of the optimized reactions, 5.4 g of 13 was placed in the round-bottom flask with 142 ml of methanol, 36 ml of water, 0.7 ml of concentrated HCl, and 0.5 g of diphenyl ether (as an internal standard for gas chromatographic analysis) to form a cloudy yellow mixture. As time elapsed, the homogeneity of the mixture increased resulting in an orange solution.

At various time intervals a 2 ml sample was removed from the reaction flask, extracted into 1 ml of methylene chloride and washed with 5 ml of water. A portion of this sample was injected into the gas chromatograph. The decrease in 13 and formation of 11 was monitored by comparison with the authentic standard. After three hours the reaction was stopped and normal work-up of the mixture followed. Evaporation of the solvent produced 4.8 g of a dark orange oil.

Purification of the hydrolysis product was carried out by dry column chromatography. Very good separation (ΔR_f = 0.51) was obtained with alumina tlc plates and chloroform as eluent.

The 4.8 g of hydrolysis product was adsorbed on 40 g of deactivated alumina (as previously described) and this was added to 120 g of alumina already on a 0.75 inch column. The column was developed in twelve minutes and the second fraction was collected. Evaporation of the solvent gave 2.2 g of a yellow liquid, which upon standing solidified. The solid, compound 11, was recrystallized from pentane to yield yellow needles, mp 54.0-54.5°.

TABLE III

Hydrolysis Conditions of the Tetrahydropyranyl Ether of 6-Methyl-6-Hydroxymethylfulvene (13)

Reaction Number	Moles 13 x10^{-3}	Moles HCl x10^{-3}	Molar Ratio of 13:HCl:CH_3OH:H_2O	Results
1	3.6	1.2	3:1:412:233	(a) Approximately 80% conversion in 4 hours.
2	18	4	4.5:1:462:695	(a) Less than 50% conversion in 5 hours.
3	10.8	4	2.7:1:432:195	(a) Approximately 75% conversion in 5 hours.
4	36	4	9:1:1430:640	(a) Approximately 50% conversion in 8 hours.
5	3.6	4.8	1:1.3:108:78	(a) Loss of 13 and product by 2 hours. No more than 25% conversion.
6	3.6	9.6	1:2.7:108:78	(b) Conversion was fast but loss of 13 and product was fast also.
7	1.8	2.4	1:1.3:1:0	(b) No product formed and 13 was lost very fast.
8	3.6	1.2	3:1:412:233	(b) 75% conversion by 4 hours but loss of 13.
9	3.6	2.4	1.5:1:206:117	(b) 65% conversion in 4 hours but loss of 13.
10	3.6	2.4	1.5:1:154:229	(b) Slow conversion and rapid loss of 13.
11	3.6	1.2	3:1:371:370	(b) Good conversion but rapid loss of 13.
12	1.8	.6	3:1:180:270 (c)	(b) Immediate conversion and loss of 13.
13	26	8.5	3:1:412:233	(b) Best conditions, essentially complete conversion and small loss of 13.

(a) Monitored using tlc and estimated % conversion.
(b) Monitored using gas chromatography and determined peak areas by planimeter.
(c) CH_3CN in place of CH_3OH

The spectral parameters for compound 11, presented in the Analysis of Spectra section, leaves little doubt that compound 11 is 6-methyl-6-hydroxymethylfulvene. Elemental analysis by Galbraith Laboratories yielded 76.05% C and 7.90% H which did not compare favorably with the calculated values of 78.64% C and 8.27% H for $C_8H_{10}O$. However, the H:C ratio for the analysis is .104 and the ratio of the calculated values is .105 which were consistent. The agreement of the H:C ratios but inconsistency of the analysis with the calculated values is rationalized as being due to the volatility of 11. If some of the analytical sample were lost (due to volatility) before it was combusted, the analysis would be incorrect but the element ratio would remain constant. In view of the convincing spectral data for compound 11, this indeed seems to be true.

Synthesis of the Ethylene Ketal of 6-Methyl-6-Benzoylfulvene (18)

A 500 ml three-neck round-bottom flask equipped with a magnetic stirrer, pressure equalizing funnel, reflux condensor, and a rubber septum was flame dried under vacuum and the atmosphere replaced by dry nitrogen. Cyclopentadienyl lithium (36 mmol) was allowed to react with 27 mmol of 2-acetyl-2-phenyl-1,3-dioxolane (38) in 200 ml of tetrahydrofuran (THF). With this addition, enough heat was evolved from the reaction to reflux the THF. The resulting dark orange solution was stirred at room temperature for one hour. A total of 60 ml of 0.5 M aqueous HCl had to be added to obtain an acidic pH and catalyze dehydration of the carbinol. After normal work-up, 5.9 g of a dark orange oil was obtained.

Purification was accomplished by dry column chromatography on silica gel (deactivated with 15% water). A total of 235 g of silica gel was used on the column and eluted with benzene. The second fraction (R_f = 0.17) was 0.8 g of 18, a bright yellow paste.

Diels-Alder Adducts of Tetracyanoethylene and Fulvene Derivatives

Diels-Alder adducts of tetracyanoethylene with compounds 11 and 18 were prepared to give 5,5,6,6-tetracyano-7-(1-hydroxyisopropylidenyl) bicyclo[2.2.1]hept-2-ene (19) and the ethylene ketal of 5,5,6,6-tetracyano-7-(1-phenylisopropyliden-1-onyl) bicyclo[2.2.1]hept-2-ene (20), respectively. This was accomplished by adding approximately an equimolar amount of TCNE dissolved in acetone-d_6 to a solution of the compound (11 or 18) in an nmr tube. A transient dark color was observed but the solution did not clear completely. The nmr spectra were obtained without isolating these compounds.

ANALYSIS OF SPECTRA

Four new fulvenes have been prepared in this study. The spectral parameters of these new fulvenes and other compounds prepared are listed on pages 33 to 51.

The infrared spectra of the compounds prepared were obtained in carbon tetrachloride solution unless otherwise specified. The figures in parentheses beside the wave number represent an intensity factor based on ten. Those absorption maxima which are characteristic of fulvenes are underlined. The assignments of these characteristic absorptions are based on the vapor phase infrared spectrum of fulvene obtained by Brown (45). This work by Brown is invaluable to the chemist interested in fulvenes. To obtain the vapor phase spectrum of fulvene, a very unstable molecule, is in itself a tremendous task. After completing this, working from the symmetry aspects of the C_{2v} point group, the infrared absorptions were assigned to the thirty various modes of vibration of fulvene.

The mass spectral peaks are tabulated with relative intensity factors based on one thousand. The fragmenting patterns are shown in Figure 1.

The 60 MHz nmr spectra of all the compounds prepared are shown (Figures 2-9) and also, the absorptions are tabulated and assigned. The visible and ultraviolet spectrum of 6-methyl-6-hydroxymethylfulvene is listed, also.

TABLE IV

Infrared Spectrum of Fulvene by R. D. Brown (45)

3140	(5)	(a)	1642		(d)	986	(8)	(j)
3134	(6)	(a)	1520	(4)	(e)	926	(10)	(k)
3116	(8)	(a)	1486	(8)	(f)	907	(9)	
3100	(9)	(a)	1440	(8)	(g)	895	(7)	
3089	(8)	(a)	1324	(9)	(g)	769	(10)	(k)
3082	(9)	(a)	1340-1370		(h)	762,765		(l)
3008	(5)	(b)	1077	(5)		614	(8)	(m)
1670	(6)	(c)	900-1000		(i)			

(a) 3140-3082 cm^{-1}, two ring C-H symmetric stretches overlapping with three antisymmetric C-H stretches.

(b) Methylene C-H stretch

(c) Exocyclic C=C stretch

(d) Exocyclic C=C stretch in 6,6-dimethylfulvene by Wood (46)

(e) Ring mode, essentially C=C stretch

(f) Exocyclic C-H bend

(g) Ring in phase bend

(h) Ring bend in 6,6-dimethylfulvene by Wood (46)

(i) Ring modes

(j) Ring deformation

(k) Ring C-H out of plane bend

(l) Ring C-H out of plane bend in 6,6-dimethyfulvene by Wood (46)

(m) Exocyclic methylene wag

Infrared Spectral Data

TABLE V

Dimethylacetal of 6-Methyl-6-Fulvene Carboxaldehyde (9)

3105	(1)	shoulder	1477	(7)		1100	(10)	
3075	(3)		1441	(8)		1090	(9)	shoulder
3028	(2)	shoulder	1375	(7)		1070	(10)	
2993	(7)		1360	(9)		990	(8)	
2928	(8)		1339	(5)	shoulder	954	(9)	
2810	(7)		1260	(3)		914	(3)	
1662	(3)		1211	(8)		698	(7)	
1644	(5)		1187	(8)		631	(7)	
1610	(1)		1155	(8)				

TABLE VI

Pyruvyl-2-Tetrahydropyranyl Ether (12)

2948	(8)		1384	(3)		1131	(10)	
2930	(6)	shoulder	1353	(6)		1075	(9)	
2872	(4)	shoulder	1319	(2)		1047	(10)	
2854	(4)	shoulder	1280	(3)		1020	(5)	shoulder
1724	(10)		1260	(3)		960	(5)	
1465	(1)	shoulder	1208	(2)	shoulder	905	(5)	
1450	(2)	shoulder	1200	(6)		822	(4)	
1440	(4)		1182	(4)				

TABLE VII

Tetrahydropyranyl Ether of
6-Methyl-6-Hydroxymethylfulvene (13)

3108	(1)		1452	(4)		1184	(6)	
3086	(2)		1440	(5)		1136	(8)	shoulder
2950	(9)		1384	(3)	shoulder	1120	(9)	
2946	(8)	shoulder	1368	(7)		1021	(10)	
2888	(6)	shoulder	1350	(4)	shoulder	972	(6)	
2856	(5)	shoulder	1321	(4)		905	(7)	
1664	(3)	shoulder	1260	(3)		827	(3)	
1642	(5)		1208	(7)	shoulder	618	(4)	
1473	(4)		1201	(8)				

TABLE VIII

6-Methyl-6-Hydroxymethylfulvene (11)

3623	(3)		1616	(2)		1014	(6)	(a)
3413	(3)		1481	(6)		998	(4)	
3118	(2)		1442	(4)		919	(4)	
3083	(2)		1381	(5)		860	(4)	
3008	(1)		1373	(10)		773	(10)	
2958	(2)		1261	(1)		661	(2)	
2923	(2)		1194	(1)		619	(5)	
2883	(2)		1151	(2)				
1811	(1)		1123	(1)				
1648	(7)		1094	(3)				

(a) In CS_2

TABLE IX

Ethylene Ketal of 6-Methyl-6-Benzoylfulvene (18)

3068	(2)		1448	(4)		1078	(10)	
3035	(1)		1376	(3)		1032	(6)	
2988	(3)	shoulder	1366	(4)		1012	(5)	
2956	(4)		1260	(4)		980	(4)	
2928	(4)		1198	(3)		912	(2)	
2885	(5)		1175	(4)		697	(5)	
1628	(3)		1139	(4)		625	(3)	
1479	(3)		1100	(6)	shoulder			

Mass Spectral Data

TABLE X

Dimethylacetal of 6-Methyl-6-Fulvene Carboxaldehyde (9)

m/e	RI	m/e	RI		m/e	RI	
167	15	93	50		62	72	
166	68	92	190		53	48	
152	22	91	1000	(a)	52	56	
151	175	90	70		51	170	
136	60	89	110		50	80	
135	140	79	134	(a)	47	100	
123	140	78	58		43	120	
121	52	77	150	(a)	41	73	
120	50	75	116		40	45	
119	50	66	50		39	370	(a)
108	36	65	380	(a)	38	50	
105	63	64	60				
103	55	63	210				

(a) Tropylium mass spectral fragmenting pattern

TABLE XI

Tetrahydropyranyl Ether of
6-Methyl-6-Hydroxymethylfulvene (13)

m/e	RI	m/e	RI		m/e	RI	
206	1	121	26		63	65	
202	2	115	44		57	112	
188	2	106	88		56	285	
170	7	105	96		55	276	
157	13	103	91		53	78	
155	13	93	80		51	75	
150	13	91	342	(a)	43	127	
142	16	89	85		41	1000	
141	19	79	235	(a)	39	327	(a)
136	24	78	134		31	525	
129	29	77	338	(a)	29	800	
128	30	66	170		28	80	
123	7	65	193	(a)	27	520	
122	47						

(a) Tropylium mass spectral fragmenting pattern

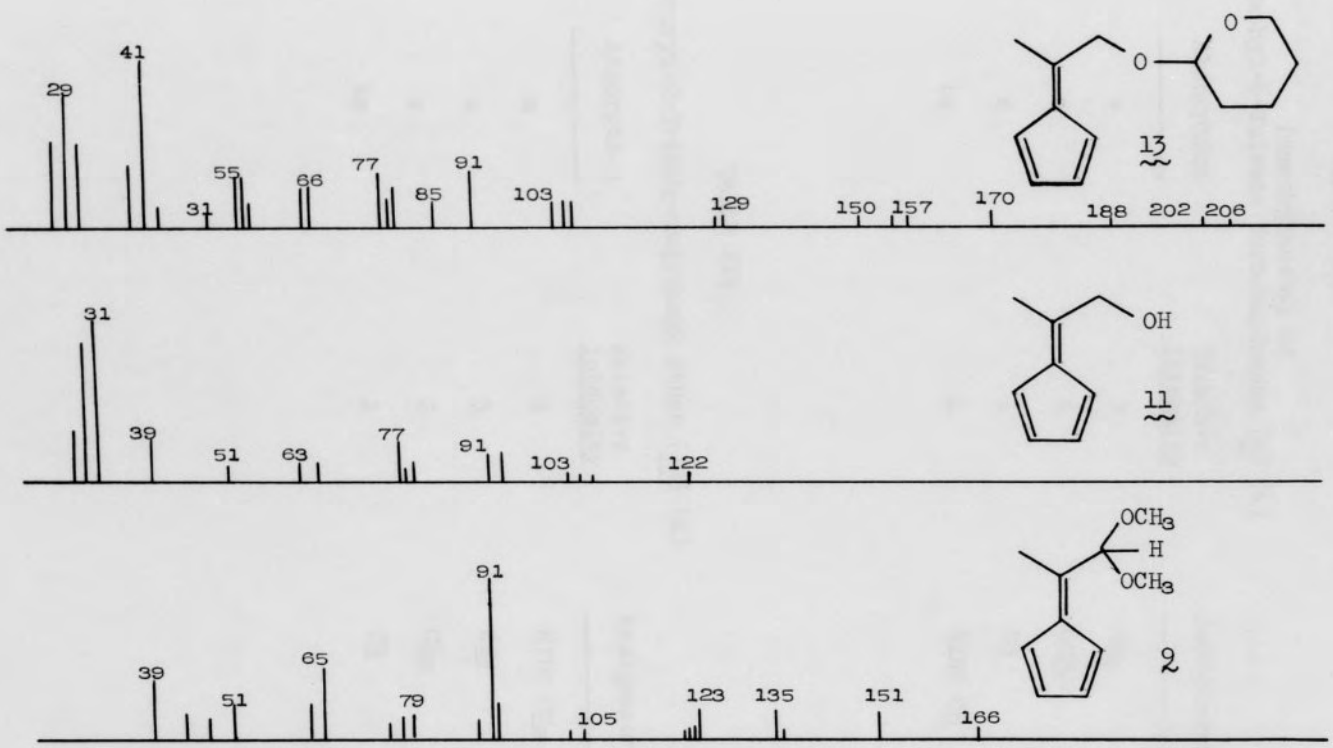
TABLE XII

6-Methyl-6-Hydroxymethylfulvene (11)

m/e	RI	m/e	RI		m/e	RI	
123	3	89	71		52	40	
122	16	79	124	(a)	51	81	
107	10	78	88		43	42	
105	6	77	193	(a)	39	227	(a)
103	13	65	121	(a)	31	1000	
93	158	63	129		29	910	
91	155	53	37		27	319	

(a) Tropylium mass spectral fragmenting pattern

Figure 1 Mass Spectral Fragmenting Pattern of Three Fulvene Derivatives



NMR Spectral Data

TABLE XIII

Dimethylacetal of
6-Methyl-6-Fulvene Carboxaldehyde (9) (a)

Chemical Shift (δ)	Absorption	Relative Intensity	Assignment
2.07	s	3	$C\underline{H}_3$
3.25	s	6	$OC\underline{H}_3$
5.08	s	1	$C\underline{H}$
6.43	bs	4	RING $C\underline{H}$

TABLE XIV

Pyruvyl-2-Tetrahydropyranyl Ether (12) (a)

Chemical Shift (δ)	Absorption	Relative Intensity	Assignment
1.31-1.90	m	8	RING $C\underline{H}_2$
2.08	s	3	$C\underline{H}_3$
4.02	s	2	$C\underline{H}_2$
4.63	bs	1	$C\underline{H}$

(a) In CCl_4

TABLE XV

Tetrahydropyranyl Ether of
6-Methyl-6-Hydroxymethylfulvene (13) (a)

Chemical Shift (δ)	Absorption	Relative Intensity	Assignment
1.20-1.93	m	8	RING CH_2
2.20	s	3	CH_3
4.37	s	2	CH_2
4.55	bs	1	CH
6.40	bs	4	RING CH

TABLE XVI

6-Methyl-6-Hydroxymethylfulvene (11) (b)

Chemical Shift (δ)	Absorption	Relative Intensity	Assignment
2.23	s	3	CH_3
3.72	bs	1	OH
4.45	s	2	CH_2
6.27-6.63	m	4	RING CH

(a) In CCl_4

(b) In Acetone-d_6

TABLE XVII

5,5,6,6-Tetracyano-7-(1-Hydroxyisopropylidenyl) Bicyclo[2.2.1]Hept-2-ene (19) (a)

Chemical Shift (δ)	Absorption	Relative Intensity	Assignment
1.93	s	3	CH_3
3.61	bs	1	OH
4.20	d	2	CH_2
4.82	m	1	BRIDGEHEAD CH
5.10	m	1	BRIDGEHEAD CH
6.83	t	2	OLEFINIC CH

TABLE XVIII

Ethylene Ketal of 6-Methyl-6-Benzoylfulvene (18) (b)

Chemical Shift (δ)	Absorption	Relative Intensity	Assignment
2.08	s	3	CH_3
3.90	s	4	RING CH_2
6.40	m	3	RING CH
7.04-7.42	m	6	PHENYL CH and ONE RING CH

(a) In Acetone-d_6

(b) In Polysol-d

TABLE XIX

Ethylene Ketal of 5,5,6,6-Tetracyano-7-(1-Phenylisopropyliden-1-onyl) Bicyclo[2.2.1] Hept-2-ene (20) (a)

Chemical Shift (δ)	Absorption	Relative Intensity	Assignment
1.57	s	3	CH_3
3.80	m	4	RING CH_2
4.80	m	1	BRIDGEHEAD CH
5.27	m	1	BRIDGEHEAD CH
6.77	m	2	OLEFINIC CH
7.07-7.42	m or bs	5	PHENYL CH

(a) In Polysol-d

Visible and UV Spectral Data

TABLE XX

6-Methyl-6-Hydroxymethylfulvene (11) (a)

nm	log ε
360	2.52
267	4.26
261	4.25
214	3.65

(a) In pentane

Figure 2 60 MHz NMR Spectrum of the Dimethylacetal of 6-Methyl-6-Fulvene Carboxaldehyde in Carbon Tetrachloride

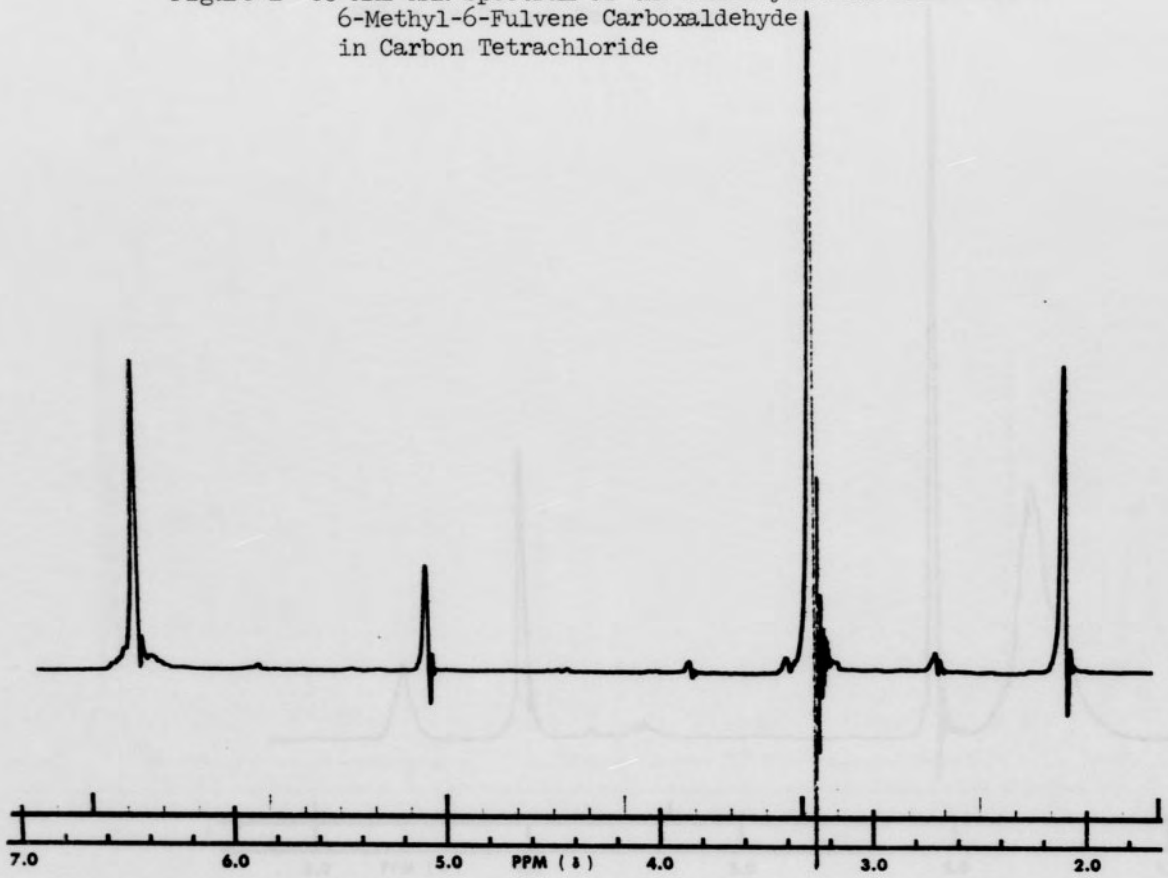


Figure 3 60 MHz NMR Spectrum of Pyruvyl-2-Tetrahydropyranyl Ether in Carbon Tetrachloride

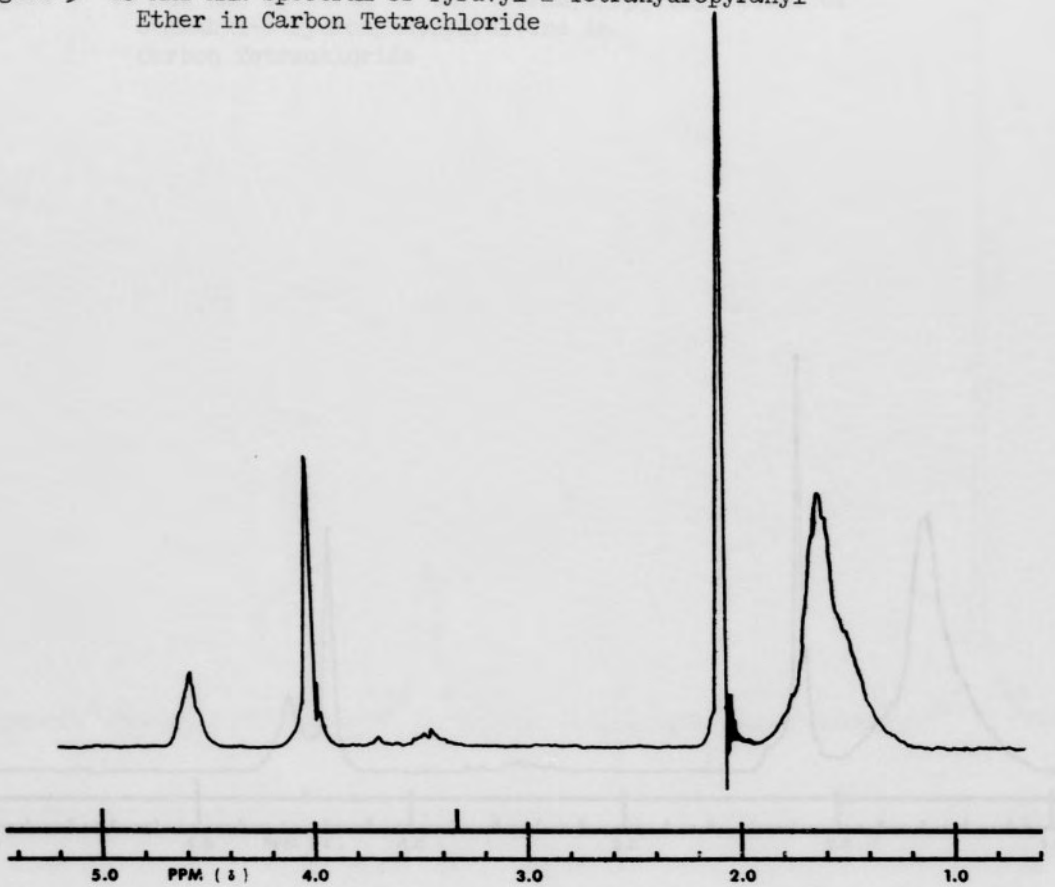


Figure 4 60 MHz NMR Spectrum of the Tetrahydropyranyl Ether of 6-Methyl-6-Hydroxymethylfulvene in Carbon Tetrachloride

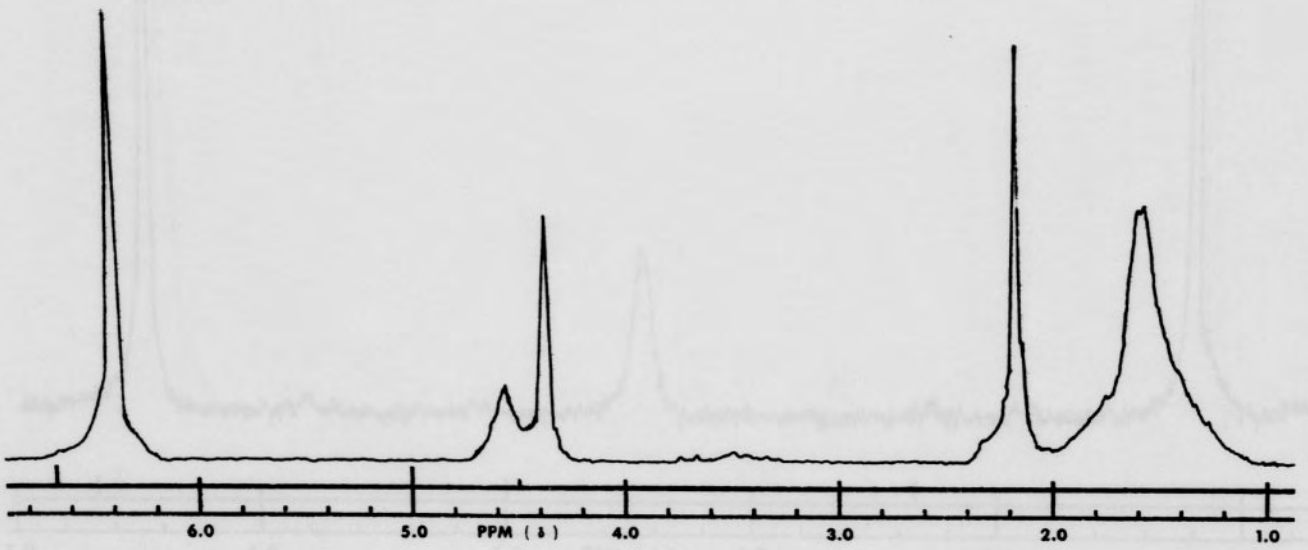


Figure 5 60 MHz NMR Spectrum of 6-Methyl-6-Hydroxymethylfulvene in Carbon Tetrachloride

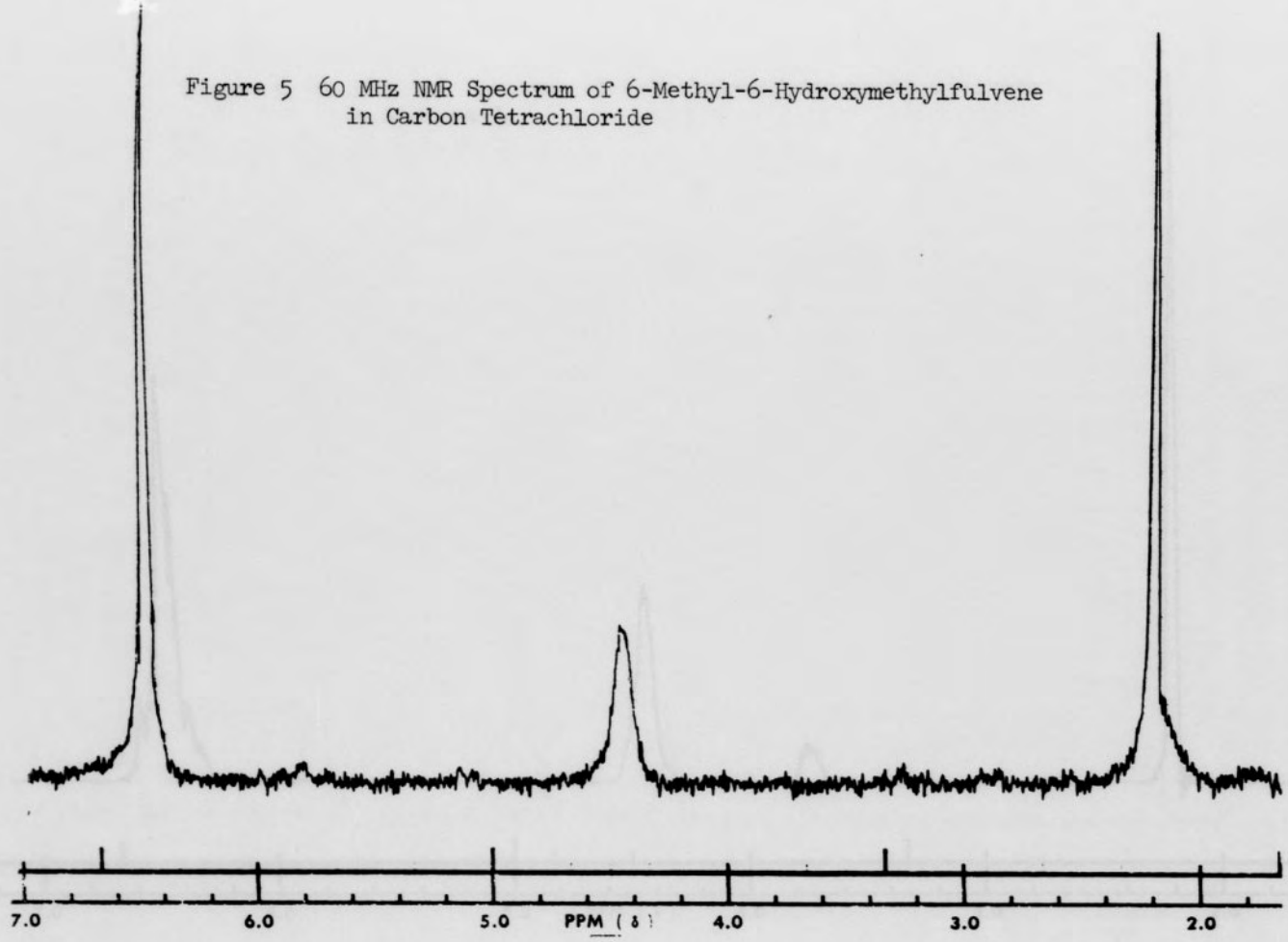


Figure 6 60 MHz NMR Spectrum of 6-Methyl-6-Hydroxymethylfulvene in Acetone-d_6

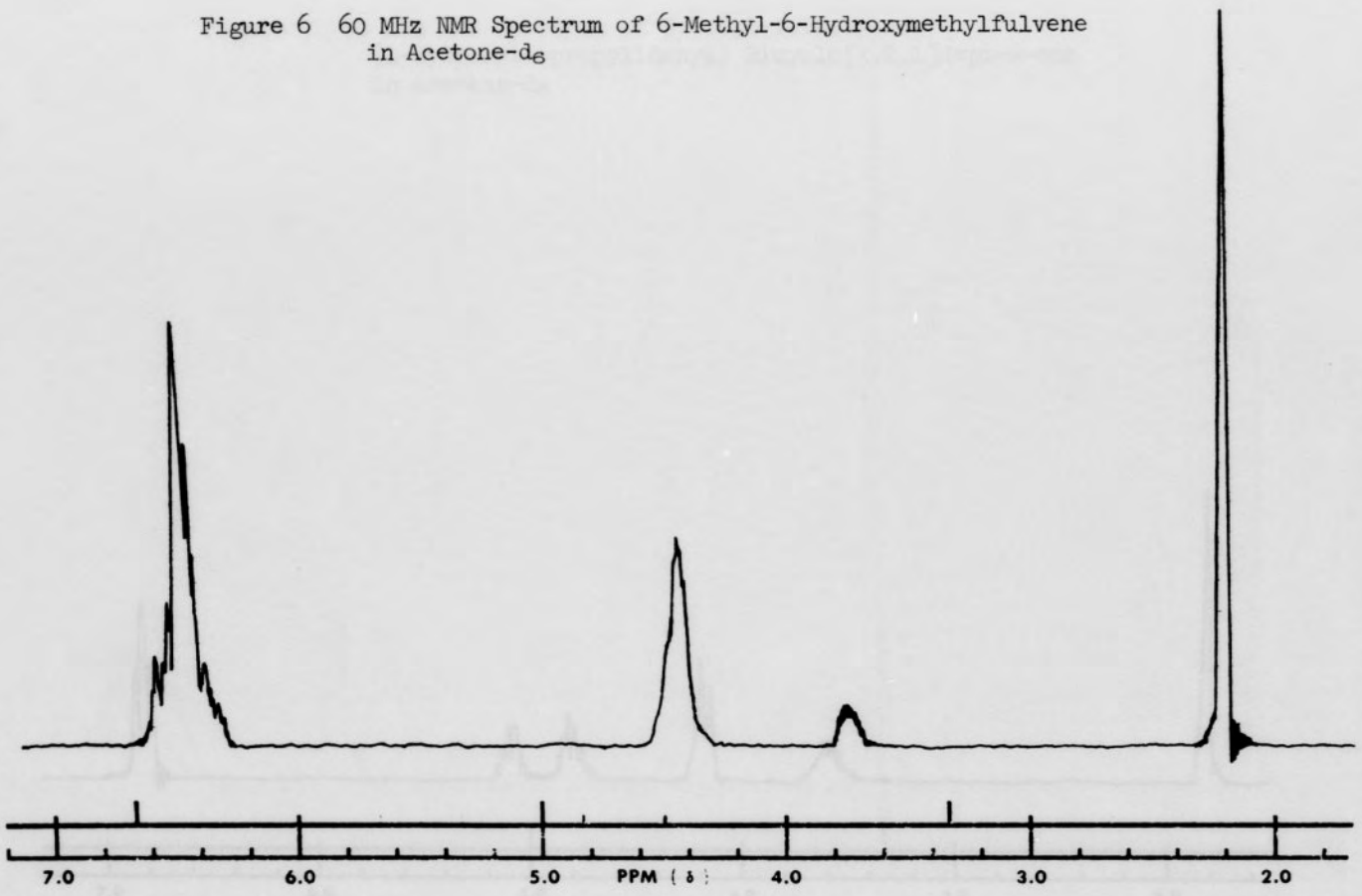


Figure 7 60 MHz NMR Spectrum of 5,5,6,6-Tetracyano-7-(1-Hydroxyisopropylidenyl) Bicyclo[2.2.1]Hept-2-ene in Acetone-d_6

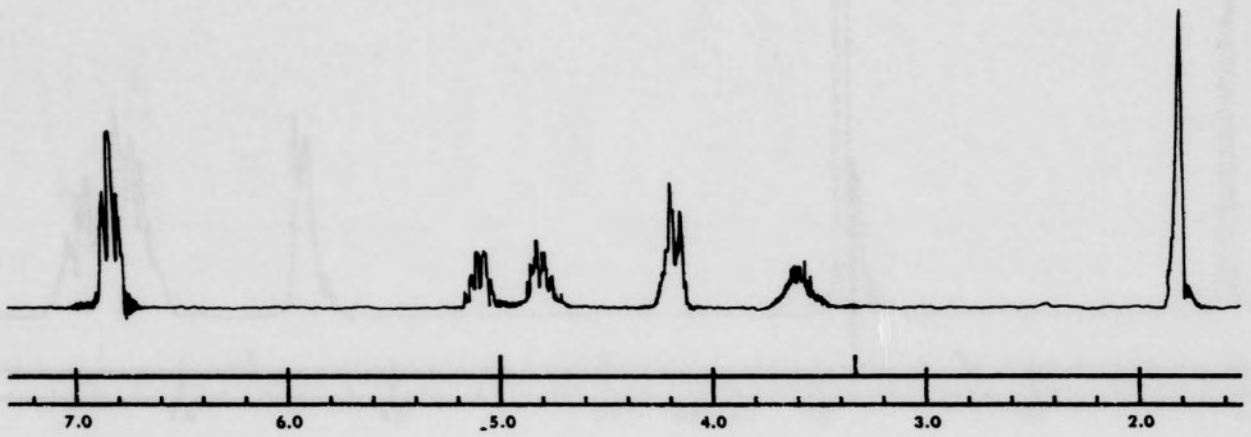


Figure 8 60 MHz NMR Spectrum of the Ethylene Ketal of 6-Methyl-6-Benzoylfulvene in Polysol-d

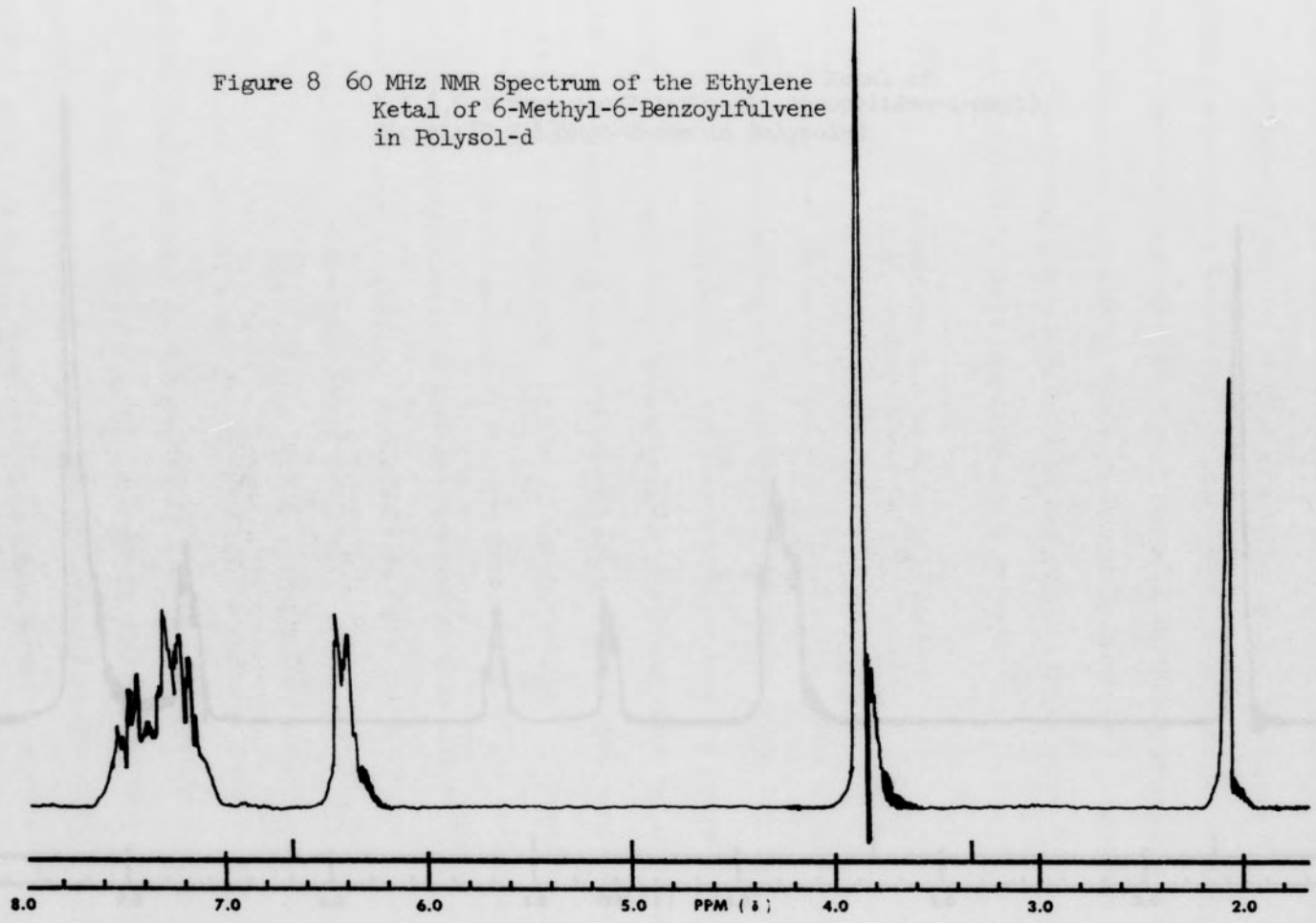
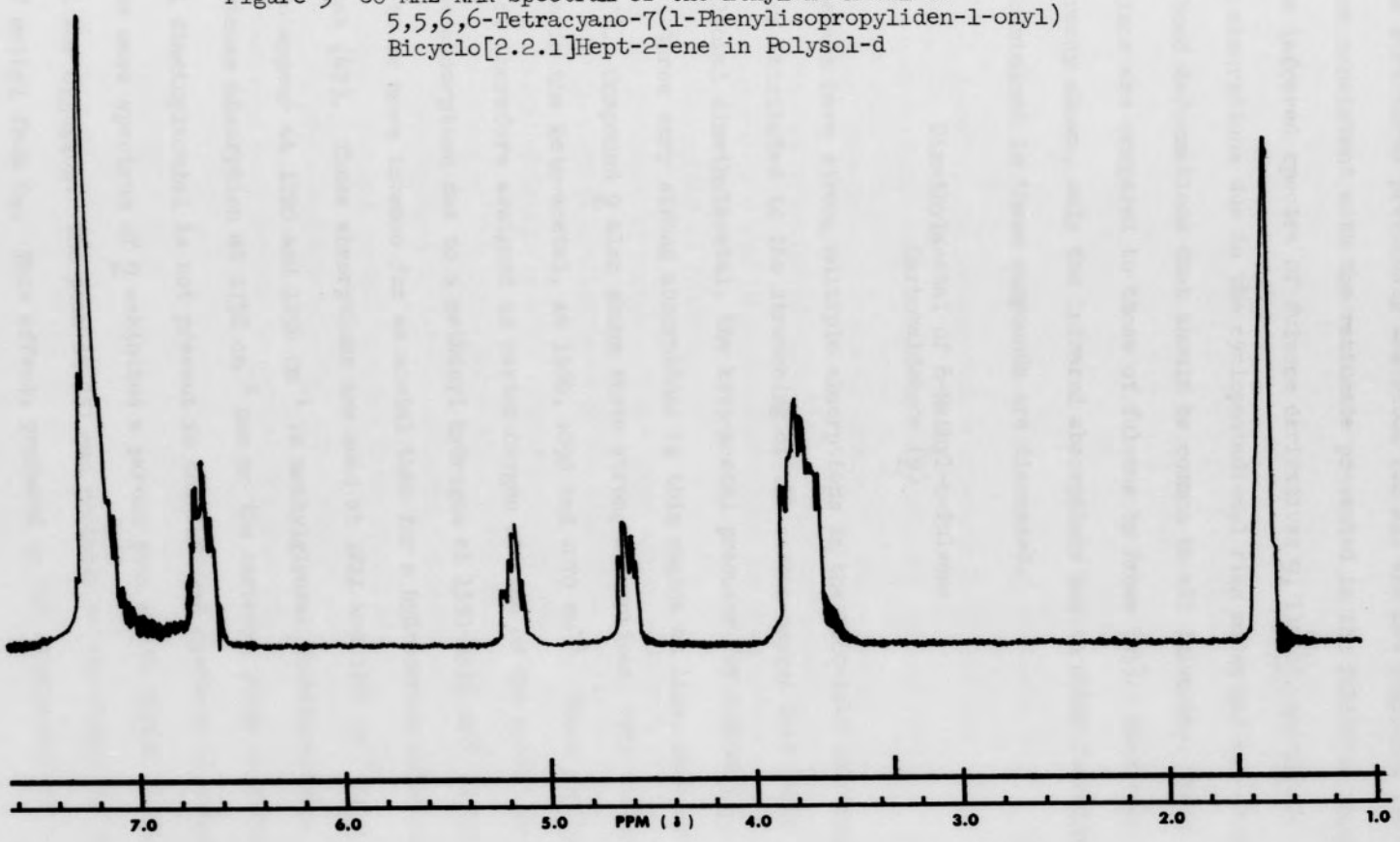


Figure 9 60 MHz NMR Spectrum of the Ethylene Ketal of 5,5,6,6-Tetracyano-7(1-Phenylisopropyliden-1-onyl) Bicyclo[2.2.1]Hept-2-ene in Polysol-d



The structures previously described for all the new compounds prepared are consistent with the rationale presented in the following pages.

The infrared spectra of fulvene derivatives 9, 11, 13, and 18 all contain absorptions due to the cyclopentadienyl ring modes and exocyclic double bond deformations that should be common to all fulvenes. These absorptions are compared to those of fulvene by Brown (45). With this data already shown, only the infrared absorptions due to other functional groups contained in these compounds are discussed.

Dimethylacetal of 6-Methyl-6-Fulvene Carboxaldehyde (9)

Acetals have strong multiple absorptions in the 1160-1040 cm^{-1} region which are attributed to the stretching of the carbon-oxygen bond (47). Methylglyoxal dimethylacetal, the keto-acetal precusor for compound 9, exhibits three very strong absorptions in this region at 1119, 1088 and 1077 cm^{-1}. Compound 9 also shows three strong absorptions, very similar to those in the keto-acetal, at 1100, 1090 and 1070 cm^{-1}. These absorptions are therefore assigned as carbon-oxygen stretch of the acetal in 9.

The absorption due to a methinyl hydrogen at 1350-1315 cm^{-1} is expected to be more intense for an acetal than for a hydrocarbon which is very weak (47). These absorptions are seen at 1211 and 1187 cm^{-1} in 9 and also appear at 1220 and 1194 cm^{-1} in methylglyoxal dimethylacetal. A very intense absorption at 1732 cm^{-1} due to the carbonyl group in methylglyoxal dimethylacetal is not present in the infrared spectrum of compound 9.

The mass spectrum of 9 exhibited a parent peak at 166 which is consistent for $C_{10}H_{14}O_2$. The peak at 151 can probably be attributed to the loss of methyl from C_6. This effect, produced by the elimination of a

fragment fifteen mass units from the corresponding parent ion, has been shown to be present in the mass spectra of four 6,6-dialkylfulvenes by Kitahara (48). Three of these fulvenes contained at least one methyl substituted at C_6, but the fourth compound was 6,6-diethylfulvene. This effect was even seen in the mass spectrum of pentamethylenefulvene, which has no methyl group attached to C_6. Kitahara explains this fragmentation process as the β-fission of the aliphatic moiety with a simultaneous expulsion of a methyl group. Also, present are peaks at 91, 79, 77, 65, and 39 which are interpreted by Kitahara to be the ions of tropylium, benzonium, phenyl, cyclopentadienyl, and cyclopropenyl, respectively. This fragmenting pattern is apparently characteristic of all isomers of the hydrocarbons of C_7H_8 (48). This same pattern is seen in the mass spectrum of 9 and it is concluded that the peaks are due to the same ions as described by Kithara.

The nmr spectrum of compound 9 gave four absorptions with relative areas of 3:6:1:4 which are assigned to the absorptions of protons of methyl, methoxy, methinyl and the cyclopentadienyl ring. The absorptions and relative areas of the first three absorptions of compound 9 are consistent with the absorptions of methyl, methoxy, and methinyl protons of methylglyoxal dimethyl acetal in which these groups absorb at δ2.07, δ3.40, and δ4.27, respectively. The broad singlet near δ6.4 for the cyclopentadienyl ring protons is general for fulvenes (33), (49).

Pyruvyl-2-Tetrahydropyranyl Ether (12)

The infrared absorption region for aliphatic ethers is near 1125 cm^{-1} due to carbon-oxygen asymmetric stretch (47). Cyclic ethers in a saturated ring also exhibit an absorption in the same region which is unusually strong, and a symmetric stretch near 825 cm^{-1} (47). For this reason the observed absorptions at 1131 and 822 cm^{-1} are assigned to these stretching vibrations. This is clearly illustrated with the spectrum of 2-(2-chloroethoxy)-tetrahydropyran (50) which shows strong absorptions at 1124 and 812 cm^{-1}. A moderate absorption is seen at 1200 cm^{-1} due to the asymmetric motion of the carbon atom bound to two oxygen atoms, as previously explained.

The methylene group adjacent to oxygen in ethers gives rise to absorptions in the regions 2955-2922 cm^{-1} due to an asymmetric stretch, 2878-2835 cm^{-1} due to a symmetric stretch, and 1475-1445 cm^{-1} due to a deformation (47). Absorptions are seen in all three of these regions in compound 12. The carbonyl group in the ketone shows a very strong absorption at 1724 cm^{-1}.

The nmr spectrum of 12 shows absorptions due to the methylene protons of the tetrahydropyran ring at δ1.31-1.90 just as 2H-dihydropyran does. The methylene protons adjacent to the carbonyl group in 12, appearing at δ4.02, are in the same immediate area as they are in pyruvic alcohol. The methinyl proton, a broad singlent at δ4.63, could be compared to the methinyl proton of 3-methyl-4-oxacyclopentanone (51). This absorption occurs at δ4.35

Tetrahydropyranyl Ether of 6-Methyl-6-Hydroxymethylfulvene (13)

The infrared spectrum of 13 exhibits all of the absorptions of fulvene and the same or similar absorptions due to carbon-oxygen stretches as was seen in compound 12. The only major difference in the spectra of this compound and compound 12 was the disappearance of the absorption at 1724 cm^{-1} due to the carbonyl group of the ketone.

The parent peak in the mass spectrum of compound 13, 206, is consistent for $C_{13}H_{18}O_2$. This spectrum, however, does not show the presence of an ion fifteen mass units less than the parent ion. This might be explained by the extremely small amount of the parent ion produced (intensity of 1 on scale of 1000). The most intense peak is seen at m/e of 41 which may be due to the $C_3H_5^+$ ion, but no explanation can be made yet for its formation or intensity.

6-Methyl-6-Hydroxymethylfulvene (11)

The 3650-3590 cm^{-1} range in the infrared spectrum is considered to be due to the stretching frequency of free OH in alcohols (47). Kuhn (52) has carried out the measurement of the free OH frequencies on thirty-five alcohols and phenols and found that this absorption occurred between 3644 and 3605 cm^{-1} in all but one compound. The observed absorption at 3623 cm^{-1} is therefore assigned to the free OH stretching frequency in compound 11.

The absorption at 3413 cm^{-1} in the infrared region is most likely due to polymeric intermolecular hydrogen bonding of the OH group. This conclusion is based on the fact that this type of polymeric association

is normally seen in the 3400-3200 cm^{-1} region as a broad absorption whose intensity diminishes upon dilution due to the decrease in these associations that occur on dilution (53).

The carbon-oxygen stretching frequency for primary alcohols is normally seen in the 1075-1000 cm^{-1} region (47). $\alpha\beta$-Unsaturation in secondary alcohols considerably lowers this frequency, and a similar shift to lower frequencies appears to occur with corresponding primary alcohols (53). This is consistent with the 1030 cm^{-1} stretching frequency seen in allyl alcohol (53). Measurement of three other allylic primary alcohols show this frequency is better expected near 1020 cm^{-1} (54) which very closely agrees with the absorption seen in 11 at 1014 cm^{-1}.

The parent peak in the mass spectrum of 11, 122, is consistent for the molecular formula of $C_8H_{10}O$. Again, the tropylium fragmenting pattern and a peak fifteen mass units less than the parent ion are present in the spectrum. The most intense peak is observed at 31. This is rationalized as being due to the CH_2OH^+ ion. Primary alcohols normally exhibit a very intense peak due to this stable ion, and a very weak parent ion (52) that is also seen in the mass spectrum of 11.

The nmr spectrum of compound 11 is consistent with the structure of 6-methyl-6-hydroxymethyfulvene. The chemical shift of the hydroxyl proton in 11 was shown to be concentration and solvent dependent. The upfield shift was observed in carbon tetrachloride and chloroform-d, but the hydroxyl proton more often came to resonance at the same point as the methylene protons, as seen on page

Further proof of the structure of compound 11 by derivatizing 11 as the Diels-Alder adduct of TCNE is seen by the nmr spectrum of 19. The

nmr spectrum of adduct 19 (on page 49) consisted of a triplet at δ6.83, a multiplet at δ5.10, a multiplet at δ4.82, a doublet at δ4.20, a broad singlet at δ3.61, and a singlet at δ1.93 which integrated in a ratio of 2:1:1:2:1:3. The absorptions were assigned to the olefinic, two non-equivalent bridgehead, methylene, alcoholic, and methyl protons, respectively. The assignments were made comparisons with the nmr spectra of 7-isopropylidene-5,5,6,6-tetracyanonorbornene and other fulvene isomers trapped as the Diels-Alder adducts of TCNE reported by Knight (8).

Brown (45) has reported the ultraviolet-visible absorption spectrum of fulvene with an absorption of 300-400 nm which has a maximum at 360 nm (ε_{max} = 200). A second transition is strong, ε_{max} = 14000 and extends from 267 to 205 nm with a maximum at 235 nm. A third transition, maximum at 201.7 nm, is reported to be of comparable intensity to the 235 nm system but no extinction coefficient is given. 6,6-Dialkylfulvenes are reported to show absorptions generally near 360 and 270 nm (5). Specifically, 6,6-dimethylfulvene is reported to show absorptions at 357 nm (ε_{max} = 380), 271 nm (ε_{max} = 17400), and 266 nm (ε_{max} = 17400).

The visible-ultraviolet spectrum of compound 11 with absorption maxima at 360 nm (ε_{max} = 330), 267 nm (ε_{max} = 18,400), 261 nm (ε_{max} = 18000) and 214 nm (ε_{max} = 4500) now presents an even more convincing arguement for the assigned structure.

Ethylene Ketal of 6-Methyl-6-Benzoylfulvene (18)

The infrared spectrum of compound 18 contains absorptions at 1100 and 1032 cm^{-1} which are assigned to the carbon-oxygen stretch of the cyclic ketal. This assignment is made because Corey (38) has assigned the

absorption at 1105 and 1033 cm^{-1} to be due to the same carbon-oxygen stretch in 2-acetyl-2-phenyl-1,3-dioxolane. Also, his assignment of the phenyl group at 698 cm^{-1} in 17 is seen at 697 cm^{-1} in compound 18.

The nmr spectrum of 18, showing absorptions at δ2.08 and δ3.90, is consistent with the nmr spectrum of 2-acetyl-2-phenyl-1,3-dioxolane for the methyl and ethylene ketal protons. The overall integrated area for 18 agrees for sixteen protons, but the ratio of the area is 6:3 for the phenyl and cyclopentadienyl protons. One of the cyclopentadienyl protons is apparently deshielded enough to come to resonance in the same region as the phenyl protons. This could be rationalized by an anisotropic effect due to the ketal oxygens or aromatic ring with the proton on C_1.

The structure for compound 18 is further substantiated by the nmr of compound 20, the TCNE Diels-Alder adduct of 18. The ratio of the areas are 5:2:1:1:4:3 and are assigned to the protons of phenyl, olefinic, both bridgehead positions, ethylene ketal, and methyl. The assignments are made in conjunction with Knight's (8) assignment of the nmr spectra of the TCNE adducts of fulvene isomers.

CONCLUSIONS

In this study a new class of fulvene derivatives has been synthesized for future investigations of the chemical reactivity of carbonium ions on fulvene-type conjugation. These new fulvenes, substituted at the oxidation level of the aldehyde, alcohol, and ketone, are the dimethylacetal of 6-methyl-6-fulvene carboxaldehyde (9), 6-methyl-6-hydroxymethylfulvene (11), and the ethylene ketal of 6-methyl-6-benzoylfulvene (18). Solvolysis of 6-methyl-6-hydroxymethylfulvene should produce the desired carbonium ion.

It has been shown that fulvene derivatives can be prepared by blocking the hydroxyl group of a keto-alcohol as a tetrahydropyranyl ether during aldol-type condensation and then regenerating the hydroxyl function. In this manner the tetrahydropyranyl ether of 6-methyl-6-hydroxymethylfulvene (13) was prepared, which upon hydrolysis gave 6-methyl-6-hydroxymethylfulvene.

It was decided that either 6-methyl-6-fulvene carboxaldehyde (10) did not form or that it was unstable under the conditions in which it was formed. The route to fulvenes containing a carbonyl group on carbon alpha to C_6 by using keto dithianes in aldol-type condensations was not successful because the reaction did not go to completion to form a fulvene dithiane.

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