1963

Deuterium exchange studies of some cyclopentenone derivatives

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DEUTERIUM EXCHANGE STUDIES OF SOME CYCLOPENTENONE DERIVATIVES

by

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Signature was redacted for privacy.

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Signature was redacted for privacy.

Dean of Graduate College

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TABLE OF CONTENTS

INTRODUCTION

Synthetic methods for the preparation of highly substituted 5-benzylidenecyclopentenones have long been known. However, synthetic methods for the preparation of the less substituted derivatives were not available in the literature. These compounds are of interest not only as possible starting materials for the synthesis of other highly unsaturated five-membered ring compounds, but also because they are tautomeric with the 1-hydroxyfulvenes. Because of this relationship, it was desired to synthesize some of the simpler 5-benzylidenecyclopentenones and investigate their chemical properties.

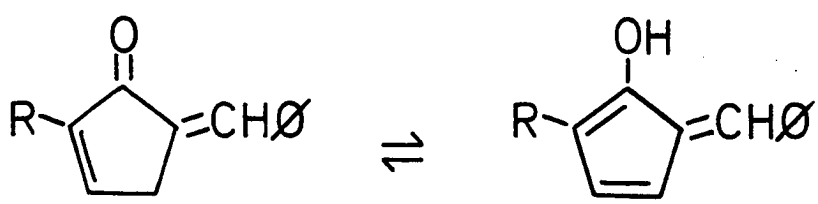


Figure 1. The potential keto-enol equilibrium of a 5-benzylidenecyclopentenone

In addition to these potential equilibria, deuterium exchange kinetics should allow the direct comparison of the acidities of these compounds with those of other cyclo-

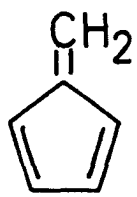
pentenone systems and so offer some indication of the relative stabilities of the intermediate ions of a variety of unsaturated five-membered ring compounds.

Many reactions of the 5-benzylidenecyclopentenones can be envisaged. There is the possibility of Michael addition at two positions, Claisen condensations at the 4-position, and O-alkylations or acylations at the carbonyl. These, and other possibilities, point up the fact that these derivatives of cyclopentenone are of potentially great value as starting materials for further syntheses.

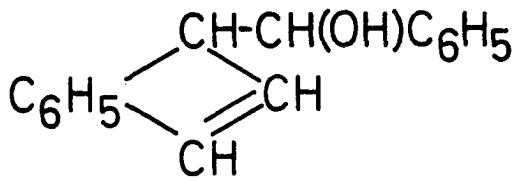
The objects of this work are twofold. First, it was necessary to devise suitable synthetic methods for some of the simpler 5-benzylidenecyclopentenones and, second, it was desired to determine their rates of deuterium exchange.

HISTORICAL

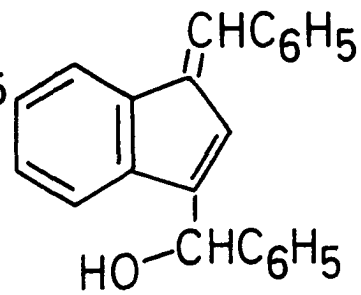
One of the earliest reported syntheses of a fulvene (I) was the reaction of indene with benzaldehyde as reported by Marckwald[1] in 1895. He incorrectly reported the structure (II) for the product of this reaction. This reaction was later reinvestigated by Thiele[2] and the structure assigned to the product was (III). Thiele then proceeded to prepare a series of fulvenes which resulted from the condensation of indene and benzaldehydes of varying degrees and types of substitution.[3]



I



II



III

Thiele, by his researches into the syntheses of the fulvenes, opened the field for the later workers. In 1900, he reported condensation products from the reaction of cyclo-

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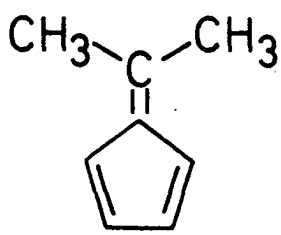
[1]Marckwald, W., Ber. 28, 1501 (1895).

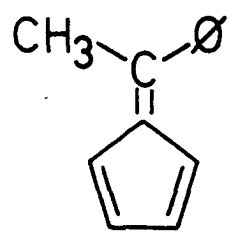
[2]Thiele, J., Ber. 33, 3395 (1900).

[3]Thiele, J., Ann. 347, 250 (1906).

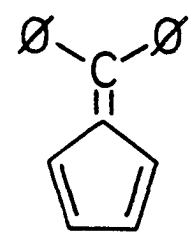
pentadiene with acetone, acetophenone, and benzophenone. He gave these materials the generic name Fulvene because of their yellow colors (the word for yellow in Latin is fulvus). Thus, the names of the three condensation products became, respectively, dimethylfulvene (IV), methylphenylfulvene (V), and diphenylfulvene (VI).[4]



IV



V



VI

Thiele later prepared several other fulvenes including several dialkyl and monoaryl derivatives. He also attempted the synthesis of the parent, unsubstituted fulvene, which he was unable to isolate. He observed, however, a yellow color due to fulvene and isolated polymerization products of fulvene.[5]

Thiele's method for the preparation of fulvenes was to condense cyclopentadiene with an aryl aldehyde or any ketone using base as a catalyst. There are other methods which later

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[4]Thiele, J., Ber. 33, 666 (1900).

[5]Thiele, J. and Balhorn, H., Ann. 348, 1 (1906).

became available for the synthesis of fulvenes. These included the work of Grignard and Courtout who used a Grignard reagent prepared by treating cyclopentadiene with another Grignard reagent and an appropriate ketone to make a fulvanol which could then be dehydrated to give the desired fulvene.[6,7,8,9] This method was not as satisfactory as Thiele's method because of lower yields. It has the advantage that the fulvenes thus produced are somewhat easier to purify.[10]

Another more specialized method involves the addition of a Grignard reagent to a highly arylated cyclopentadienone such as tetracyclone, 2,3,4,5-tetraphenylcyclopentadienone.[10,11,12]

Theic and Wiemann[13] reported the synthesis of fulvene in 1956 using Thiele's method. They were interested in obtaining several different types of physical measurement such as molecular refraction, UV and IR spectra, dipole moment and

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[6]Grignard, V. and Courtout, C., Compt. rend. 158, 1763 (1914).

[7]Courtout, C., Ann. Chim. 4, 58 (1915)

[8]Courtout, C., Ann. Chim. 4, 168 (1915).

[9]Courtout, C., Ann. Chim. 4, 188 (1915).

[10]Day, J. H., Chem. Revs. 53, 167 (1953).

[11]Lowenbeim, A. and Ulrich, G., Ber. 58B, 2662 (1923).

[12]Dilthey, W. and Huchtemann, P., J. prakt. Chem. 154, 238 (1940).

[13]Theic, J. and Wiemann, J., Bull. Soc. Chim. France 1956, 177.

magnetic susceptibility measurements on fulvene. However, Angus and Bryce-Smith[14] reported in 1960 that they were unable to duplicate Theic and Wiemann's syntheses. Theic and Weimann replied to this by reporting their procedure in detail and stating that they prepared fulvene in from 12 to 36% yields by Thiele's method.[15]

A recent and convenient method for the preparation of fulvenes has been reported by Freiesleben.[16] Dimethylfulvene was synthesized in quantitative yield and a high state of purity by treating an equimolar mixture of cyclopentadiene and acetone with a small amount of a primary amine such as an aqueous solution of methylamine. The fulvene separates from the aqueous layer in high yield and contains only the easily removed amine catalyst as an impurity.

Diazocyclopentadiene, which was first prepared by Doering and DePuy[17] in 1953, closely resembles fulvene in some respects. In the decade since it was first reported, there has been considerable interest evoked by this compound.

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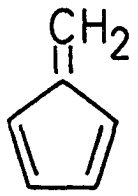
[14]Angus, H. J. F. and Bryce-Smith, D., J. Chem. Soc. 1960, 1409.

[15]Theic, J. and Wiemann, J., Bull. Soc. Chim. France 1960, 1066.

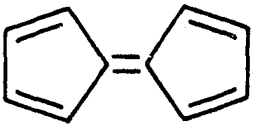
[16]Freiesleben, W., Angew. Chem. Intern. Ed. Engl. 2, 396 (1963).

[17]Doering, W. v. E. and DePuy, C. H., J. Am. Chem. Soc. 75, 5955 (1953).



I

VII



VIII

De More et al.[18] reported the synthesis of fulvalene (VIII) from diazocyclopentadiene and Paulson and Williams[19] reported the synthesis of 1,2,3,1',2',3'-hexaphenylfulvalene from 1,2,3-triphenyldiazocyclopentadiene. Paulson and Williams were also able to prepare 1,2,4,1',2',4'-hexaphenylfulvalene from the 1,2,4-isomer of triphenyldiazocyclopentadiene.[20]

A rather extensive investigation of the chemistry of diazocyclopentadiene was recently published by Cram and Partos.[21] They were able to run nitration reactions and

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[18]De More, W. B., Pritchard, H. O., and Davidson, N., J. Am. Chem. Soc. 81, 5874 (1959).

[19]Paulson, P. L. and Williams, B. J., J. Chem. Soc. 1961, 4153.

[20]Paulson, P. L. and Williams, B. J., J. Chem. Soc. 1961, 4158.

[21]Cram, D. J. and Partos, R. D., J. Am. Chem. Soc. 85, 1273 (1963).

several other types of electrophilic substitution reactions which indicate a rather high degree of aromatic character for diazocyclopentadiene (VII).

Recently, Weil and Cais[22] reported a simplified procedure for the preparation of diazocyclopentadiene using a variation of the procedure used by Doering and DePuy.

Many authors have carried out molecular orbital calculations on fulvene, a molecule of great interest because it is a non-alternant hydrocarbon and an isomer of benzene. Peters,[23] using the secular equations for benzene and fulvene, arrived at values of 2.00 and 1.47 beta for the resonance energies of benzene and fulvene respectively. Peters also used a variation of Dewar and Pettit's cyclic polyene method[24] which gave values of 1.59 and 0.99 beta for the resonance energies of benzene and fulvene.

Scherr[25] used a free electron network model for conjugated systems to arrive at values of 99.7 and 36.5 kilocalories per mole for the delocalization energies of the same compounds, while Wheland[26] calculated resonance energies for

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[22]Weil, T. and Cais, M., J. Org. Chem. 28, 2472 (1963).

[23]Peters, D., J. Chem. Soc. 1958, 1023.

[24]Dewar, M. J. S. and Pettit, R., J. Chem. Soc. 1954, 1617.

[25]Scherr, C. W., J. Chem. Phys. 21, 1413 (1953).

[26]Wheland, G. W., J. Am. Chem. Soc. 63, 2025 (1941).

benzene and fulvene of 1.07 and 0.64 β, where β has a value of approximately 17 kilocalories per mole. This gives a value of approximately 11 kcal. per mole for the resonance energy of fulvene.

It is of interest to note that Day and Oestreich,[27] the only persons to report an experimentally measured value for the resonance energy of fulvene (by heats of combustion), report a value of 11.9 kcal. per mole for the resonance energy of dimethylfulvene and 85.4 kcal. per mole for the resonance energy of diphenylfulvene. When they subtracted the resonance energy of two phenyl groups from this value they obtained 12.6 kcal. per mole for the resonance energy of the fulvene part of the molecule.

Unfortunately, neither calculations nor experimentally derived values for the resonance energy of diazocyclopentadiene are to be found in the literature.

Since the early 1900's there have been several 5-benzylidene derivatives of cyclopent-2-enone reported. Most of the earlier derivatives were prepared from highly substituted cyclopentenones. In 1901, Japp and Meldrum[28] prepared a series of 5-benzylidene-4-hydroxy-3,4-diphenylcyclopent-2-enones which varied only in the 2-substituent. The 2-substi-

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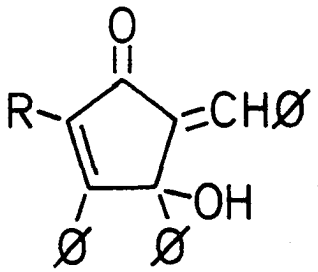
[27]Day, J. H. and Oestreich, C., J. Org. Chem. 22, 214 (1957).

[28]Japp, F. R. and Meldrum, A. N., J. Chem. Soc. 1901, 1024.



IX R= CH_3

X C_2H_5

XI C_3H_7

XII C_5H_{11}

tuent was either methyl, ethyl, propyl, or pentyl. In 1938, Koelsch and Geissman[29] reported another compound in the same series which had a phenyl group at the 2-position. A similar compound, 5-benzylidene-4-methoxy-3,4-diphenylcyclopent-2-enone, was prepared from 4-methoxy-3,4-diphenylcyclopent-2-enone by Allen and Spanagel[30] in 1932.

Borsche and Klein[31] synthesized, in 1939, 5-benzylidene-2,3-diphenylcyclopent-2-enone, and Borsche and Menz[32] reported the synthesis of 5-benzylidene-3-phenylcyclopent-2-enone in 1908. These two compounds are the least-substituted deriva-

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[29]Koelsch, C. F. and Geissman, T. A., J. Org. Chem. 3, 480 (1938).

[30]Allen, C. F. H. and Spanagel, E. W., J. Am. Chem. Soc. 54, 4338 (1938).

[31]Borsche, W. and Klein, A., Ber. 72B, 2082 (1939).

[32]Borsche, W. and Menz, W., Ber. 41, 190 (1908).

tives of 5-benzylidenecyclopent-2-enone which have appeared in the literature between 1900 and the 1940's.

All of the previous benzylidene compounds were prepared under basic conditions. In 1955, Wanzlick and Gollmer[33] synthesized 5-benzylidene-2-chlorocyclopent-2-enone from 2-chlorocyclopent-2-enone and benzaldehyde using hydrochloric acid as a catalyst and acetic acid as the solvent.

In every case, the benzylidene compounds were prepared as part of a structure proof to illustrate the fact that a compound had an active methylene group which could react with benzaldehyde. There was no mention made of a use for the benzylidene derivative itself.

In 1952, French[34] reported the synthesis of unsubstituted 5-benzylidenecyclopent-2-enone (XIII) in connection with her studies of the effect of cross-conjugation upon the spectra of alpha-beta unsaturated ketones. She gave the melting point of 5-benzylidenecyclopent-2-enone as 160°. The method she used was that of Allen and Spanagel[30] in which the cyclopentenone was treated with benzaldehyde and sodium ethoxide in refluxing ethanol for a few minutes. This is the only report of the synthesis of 5-benzylidenecyclopent-2-enone (XIII) in the literature.

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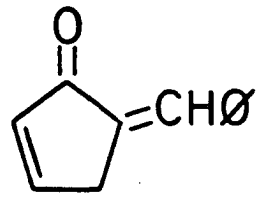
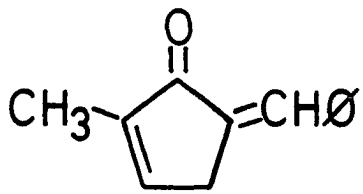
[33]Wanzlick, H. W. and Gollmer, G., Chem. Ber. 88, 281 (1955).

[34]French, H. S., J. Am. Chem. Soc. 74, 514 (1952).

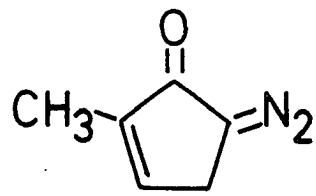


XIII

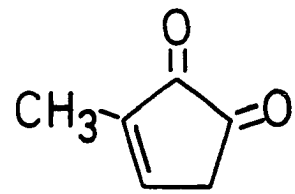
5-Benzylidene-2-methylcyclopent-2-enone (XIV) does not appear in the literature; however, both 5-diazo-2-methylcyclopent-2-enone (XV) and the corresponding dione (XVI) were prepared by Condon[35] in 1960.



XIV



XV



XVI

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[35]Condon, E. H. Chemistry of 1-methylcyclopentene-4,5-dione. Unpublished M.S. thesis. Ames, Iowa, Library, Iowa State University of Science and Technology. 1960.

There has been considerable interest in recent years in the synthesis of highly unsaturated five-membered ring compounds. Although some of these compounds are readily available in respectable yield from available starting materials, many others are either obtainable in low yield or not at all. For example, cyclopenten-3,5-dione was prepared in satisfactory manner by DePuy and Zaweski,[36,37] while, cyclopenten-3,4-dione can be prepared only in very low yields by present methods[38] and cyclopentadienone has never been isolated. In fact, the cyclic ethylene ketal of cyclopentadienone which one would expect to be somewhat less reactive than cyclopentadienone has also never been isolated. The nearest that anyone has ever come to this was the work of Vogel and Wyes[39] in which they succeeded in trapping the cyclic ethylene ketal of cyclopentadienone as its Diels-Alder adduct with maleic anhydride.

DePuy et al.[40] were also able to observe the formation

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[36]DePuy, C. H. and Zaweski, E. F., J. Am. Chem. Soc. 81, 4920 (1959).

[37]Rasmusson, G. H., House, H. O., Zaweski, E. F., and DePuy, C. H., Org. Syn. 42, 36 (1962).

[38]Wanzlick, H. W. and Sucrow, W., Chem. Ber. 91, 2727 (1958).

[39]Vogel, E. and Wyes, E. -G., Angew. Chem. Intern. Ed. Engl. 1, 404 (1962).

[40]DePuy, C. H., Ponder, B. W., and Fitzpatrick, J. D., Angew. Chem. Intern. Ed. Engl. 1, 404 (1962).

of the cyclic ethylene ketal of cyclopentadienone as a transient intermediate species as evidenced by the isolation of its dimer from the Hofmann elimination of the methiodide salt of 4-(N,N-dimethylamino)cyclopent-2-enone ethylene ketal. This dimer could not be cracked back to the monomeric species.

Only a few simple 5-substituted cyclopentenones have been prepared. Fitzpatrick[40,41] has synthesized 5-bromo and 5-(para-nitrobenzoyloxy)cyclopentenone. He prepared these compounds by a rather long procedure passing through the cyclic ethylene ketal of cyclopentenone. DePuy et al.[42] have also reported the synthesis of 5-ethoxycyclopent-2-enone after a rather long synthetic procedure. As mentioned, cyclopenten-3,4-dione, which, for purposes of comparison, could perhaps be better named 5-ketocyclopent-2-enone, has been made but only in very low yields.[38]

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[41]Fitzpatrick, J. D., Ethylene ketal of cyclopentadienone. Unpublished M.S. thesis. Ames, Iowa, Library, Iowa State University of Science and Technology. 1963.

[42]DePuy, C. H., Thurn, R. D., and Isaks, M., J. Org. Chem. 27, 744 (1962).

DISCUSSION

The 5-benzylidenecyclopentenones are of theoretical importance because they are tautomeric with the phenylfulvenes and they are of practical interest as potential precursors of other five-membered ring compounds. Since no procedures have appeared in the literature for the preparation of simple 5-benzylidenecyclopentenones, it was necessary to explore synthetic pathways to these compounds.

The preparation of 5-benzylidenecyclopentenone itself, as the simplest possible member of the series, was desirable. Both basic and acidic conditions were tried for the reaction between cyclopentenone and benzaldehyde, and, under neither set of conditions did it prove possible to isolate the desired product from the reaction mixture. The basic conditions used were essentially the same as those reported to be successful for the same synthesis by French.[34] Under these conditions the only isolable material from the reaction was cyclopentenone polymer.

The same reaction was attempted under acidic conditions. The only isolable product from this reaction was 2,5-dibenzylidenecyclopent-3-enone (XVII), which was previously reported by Wanzlick.[43] The 2,5-dibenzylidenecyclopent-3-enone prepared melted at 150-154° (reported by Wanzlick, 150°). The

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[43]Wanzlick, H., Chem. Ber. 86, 41 (1953).

melting point reported by Chapman and Pasto[44] for specially purified XVII was 156-157°. The melting point reported by French for 5-benzylidenecyclopent-2-enone was 160°. In view of the fact that the melting point determined for 5-benzylidene-2-methylcyclopent-2-enone in this work was 80.5-81.5° and the nearness of the melting points of dibenzylidene cyclopentenone and benzylidenecyclopentenone and also the experimental difficulty of synthesizing 5-benzylidenecyclopentenone encountered in this laboratory, there is some doubt cast upon the structure of French's 5-benzylidenecyclopent-2-enone. However, her work can not be discredited on the basis of the present work alone. An NMR spectrum of this compound would serve to either prove or disprove its structure.

In order to determine whether it is possible to perform base catalyzed condensations with cyclopentenone, condensations with several esters were attempted. Cyclopentenone with diethyl oxalate and base gave a 56% yield of ethyl 2-oxocyclopent-3-englyoxylate (XVIII). The use of other esters and a variety of bases for similar condensations resulted only in the formation of cyclopentenone polymer. These results indicate that base catalyzed condensations with cyclopentenone are possible only if the other reagent is sufficiently reac-

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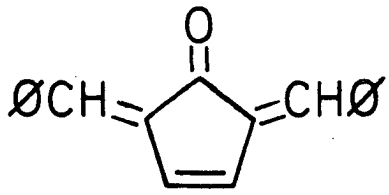
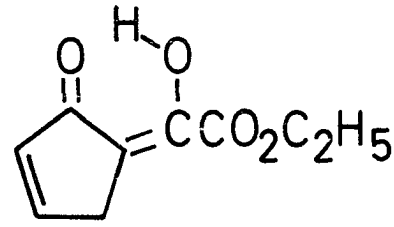
[44]Chapman, O. L. and Pasto, D. J., J. Org. Chem. 24, 120 (1959).



XVII



XVIII

tive to trap the cyclopentenone anion as it is formed. Benzaldehyde is apparently not capable of accomplishing this.

In view of the experimental difficulties encountered in the attempted synthesis of 5-benzylidenecyclopentenone from cyclopentenone and benzaldehyde, it was decided to try to introduce another double bond into 2-benzylidenecyclopentanone, and thereby accomplish the desired synthesis.

2-Benzylidenecyclopentanone was easily prepared in large quantities from cyclopentanone and benzaldehyde by the method of Emerson et al.[45] This material reacts readily with N-bromosuccinimide (NBS) in carbon tetrachloride solution, but the bromide (XIX or XX) formed by this reaction was not isolable as such. Attempts to concentrate the carbon tetrachloride solution resulted only in the formation of tar, even

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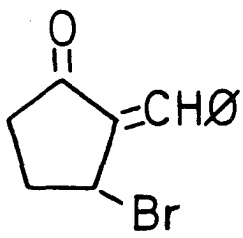
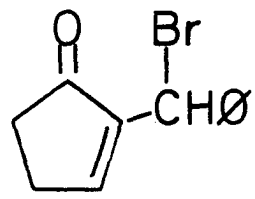
[45]Emerson, W. S., Birum, G. H., and Longley, R. I., Jr., J. Am. Chem. Soc. 75, 1312 (1953).

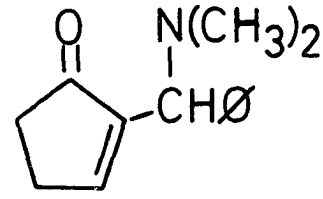
when the solvent was removed from the solution at low temperature and pressure. The bromo-compound could, however, be treated with anhydrous dimethylamine to give 2-(N,N-dimethyl-α-aminobenzyl)-cyclopent-2-enone (XXI). This amine is a



XIX



XX

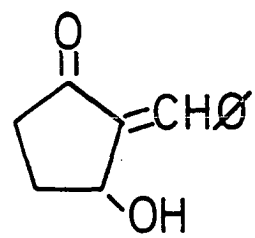


XXI

stable oil which can be distilled easily. From it was prepared its methiodide salt, 2-(N,N,N-trimethyl-α-ammonium-benzyl)-cyclopent-2-enone iodide, by reaction with methyl iodide in acetonitrile.

Attempts to run Hofmann type eliminations on the methiodide salt using a variety of strong bases resulted in the formation of tar along with a strong odor of trimethylamine. It was only when a weak base, sodium bicarbonate, was used in an attempt at elimination that an isolable product was formed. This product was not the expected diene, however, but contained a hydroxyl group. The NMR of this product suggested strongly that the compound is 2-benzylidenecyclopentan-3-ol-1-one. Hydrogenation of this compound results

in the uptake of 2 moles of hydrogen. The 2,4-dinitrophenylhydrazone (2,4-D) of the hydrogenated product melted at the same temperature as the 2,4-D of 2-benzylcyclopentanone. Mixed melting point showed no depression. On the basis of the NMR and hydrogenation data the alcohol was assigned structure XXII, 2-benzylidenecyclopentan-3-ol-1-one.



XXII

The formation of this alcohol rather than the desired 5-benzylidenecyclopent-3-enone or, preferably, the 2-ene isomer which could reasonably be expected by isomerization of the 3-ene isomer by the action of either acid or base, was, at first, quite surprising. On second thought, however, the product from this reaction can reasonably be explained. The exact mechanism for its formation is unknown, but it certainly involves attack by hydroxide ion (or possibly bicarbonate ion) at the 3-carbon and loss of trimethylamine to form the exocyclic double bond. Whether the mechanism is concerted or not is a matter of conjecture. Whatever the mechanism, this reaction shows the facility of shifting an endocyclic

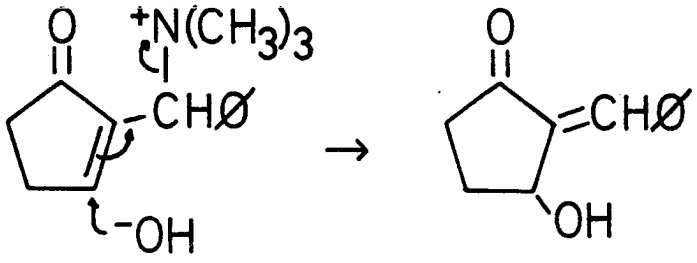
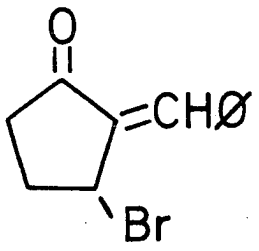


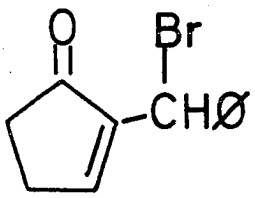
Figure 2. Possible mechanism for the formation of alcohol XXII

double bond in this system to an exocyclic position.

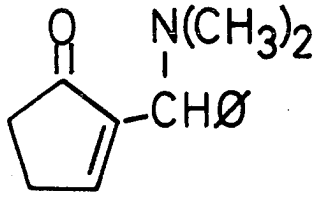
Since it did not prove possible to isolate the brominated derivative of 2-benzylidenecyclopentanone, its structure could not be determined. There are two possible structures for this compound, XIX and XX. If the bromo-compound posseses the structure XX, then the formation of the amine (XXI) was the result of either a simple SN2 or SN1 displacement. If, however, the bromo-compound posseses the structure XIX, which was the expected product from the NBS bromination, then the formation of the amine (XXI) was the result of a mechanism analogous to that for the formation of the alcohol (XXII) from the methiodide salt. If this is the case then this reaction shows the facility of shifting an exocyclic double bond to an endocyclic position. Thus, it would appear that



XIX



XX



XXI

there is relatively little energy difference between an exocyclic and an endocyclic double bond in this system.

Attempted direct dehydration of the alcohol (XXII) using acid catalysis by several methods led to either the formation of tar or the recovery of starting material. Attempts to convert the alcohol (XXII) to its acetate or tosylate by several methods resulted, again, in either tar formation or recovery of unchanged alcohol.

Models show that the phenyl group of the alcohol (XXII) can seriously hinder the approach of derivatizing agents. If the phenyl group prefers to be coplanar with the rest of the molecule in order to maximize pi overlap, then the proton ortho to the benzylic carbon lies practically on top of the hydroxyl group.

Although some interesting chemistry was uncovered in the preceding series of reactions, it was decided to abandon

this approach to 5-benzylidenecyclopentenone and concentrate instead on the synthesis of the 2-methyl derivative. Since 2-methylcyclopentenone is available from cyclopentanone *via* a several step synthesis, and, both 5-diazo-2-methylcyclopent-2-enone and the corresponding dione in this series are known compounds, 5-benzylidene-2-methylcyclopent-2-enone was an interesting candidate for deuterium exchange studies.

Cyclopentanone was chlorinated by the method of Wanzlick *et al.*[46] Hydrolysis of the chloro-ketone (XXIII) to the hydroxy-ketone followed by oxidation of the hydroxy-ketone by the action of ferric chloride gave 65 to 80% yield of cyclopentan-1,2-dione (XXIV) by the method of Inhoffen and Krämer.[47] The dione XXIV was then converted to 2-methylcyclopent-2-enone XXV by the method of Ansel and Ducker[48] by treating the dione with a large excess of methyl Grignard reagent. Several reactions occur sequentially during the reaction and the work up procedure giving 2-methylcyclopent-2-enone XXV in about 40 to 45% yield from the dione (XXIV).

The isobutyl[48] and benzyl enol ethers of cyclopentan-1,2-dione (XXVI and XXVII) were prepared directly from the

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[46]Wanzlick, H. W., Gollmer, G., and Milz, H., Chem. Ber. 88, 69 (1955).

[47]Inhoffen, H. H. and Krämer, H., Chem. Ber. 87, 488 (1954).

[48]Ansel, M. F. and Ducker, J. W., J. Chem. Soc. 1959, 329.

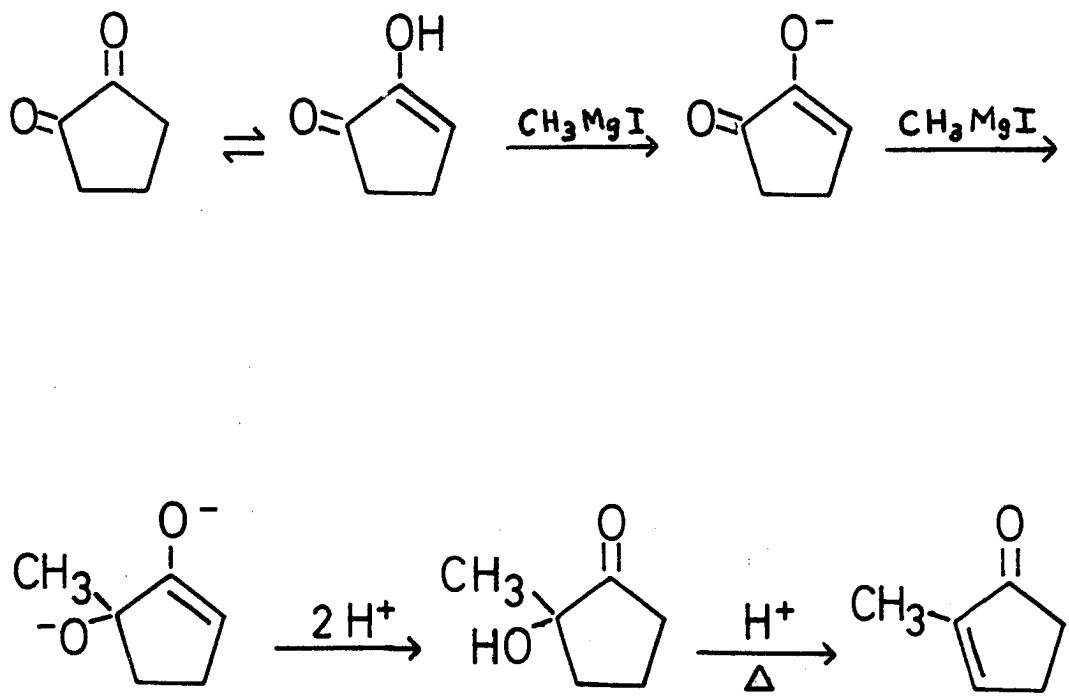


Figure 3. Formation of 2-methylcyclopentenone from cyclopentan-1,2-dione

dione (XXIV) by treating an equimolar solution of the dione and the corresponding alcohol in benzene with acid. The water formed by the reaction was removed azeotropically.

5-Benzylidene-2-methylcyclopent-2-enone (XIV), after several unsuccessful attempts using basic catalysis, was satisfactorily prepared by running the reaction between benzaldehyde and 2-methylcyclopentenone (XXV) under acidic conditions. The method used was essentially that used by

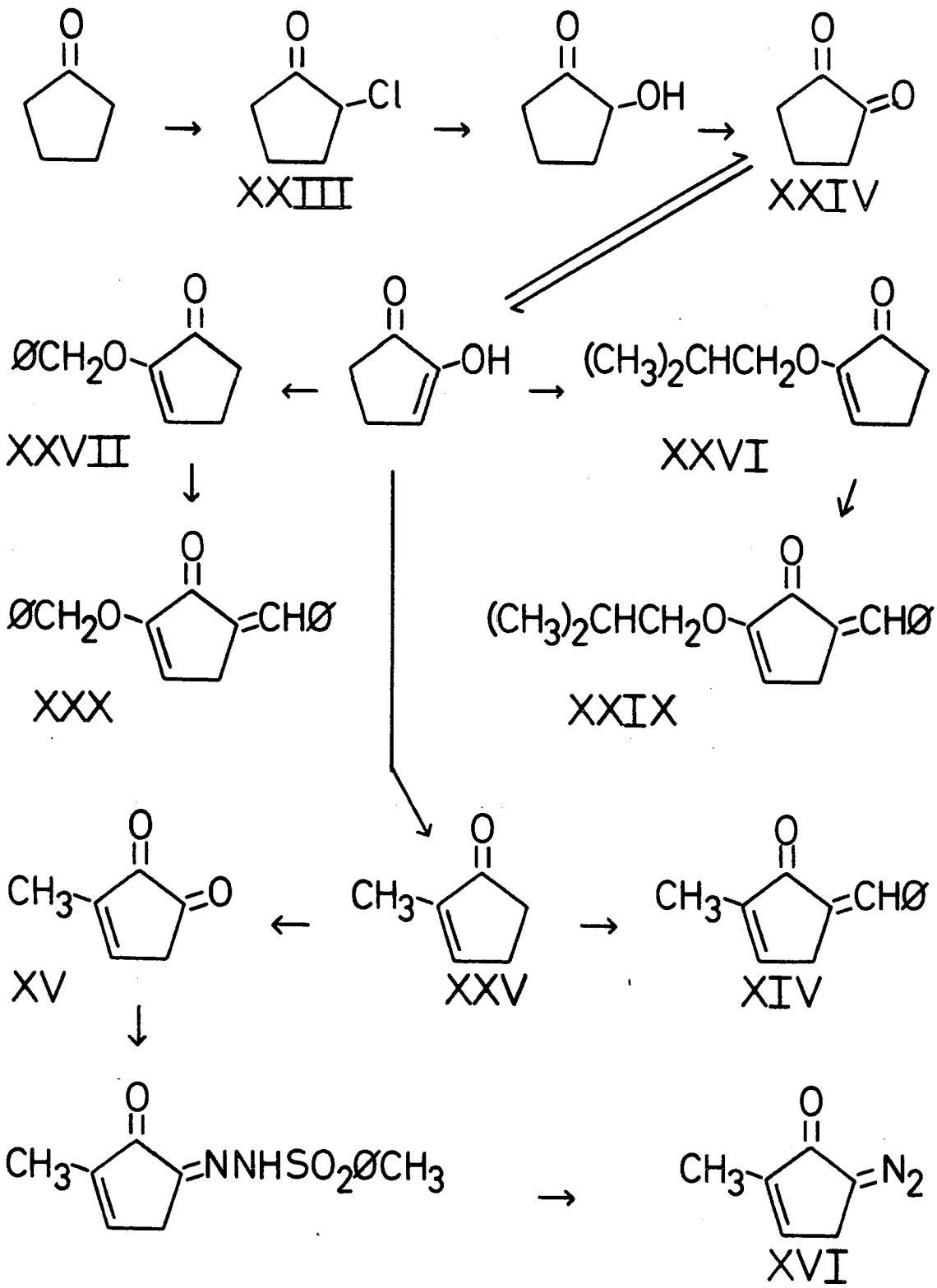
Wanzlick and Gollmer[33] for the preparation of 5-benzylidene-2-chlorocyclopent-2-enone.

The 5-benzylidene derivatives of the two enol ethers (XXIX and XXX) were prepared in satisfactory yield by treating an equimolar solution of benzaldehyde and the enol ether in 95% ethanol with a dilute aqueous solution of sodium hydroxide.

3-Methylcyclopent-3-en-1,2-dione (XVI) and 5-diazo-2-methylcyclopent-2-enone (XV) were prepared by the method of Condon.[35] 2-Methylcyclopentenone (XXV) was oxidized to the dione (XVI) by the action of selenium dioxide. The dione (XVI) was then treated with tosylhydrazide in methanol and the resulting monotosylhydrazone was treated with aqueous sodium hydroxide. The resulting diazo-ketone (XV) was removed from the reaction mixture as fast as it was formed by stirring the reaction mixture with methylene chloride.

The structural assignments of many of the compounds are based on the interpretation of their NMR spectra. Several of these structures were the ones predicted, and the NMR's serve only to confirm the expected. In the case of 2-benzylidene-cyclopentan-3-ol-1-one (XXII) and 2-(N,N-dimethyl-α-amino-benzyl)-cyclopent-2-enone (XXI), the product isolated from the reaction mixture was not the one expected. For this reason the spectra of these two compounds shall be discussed in some detail.

Figure 4. The general synthetic scheme for the preparation of some 2- and 2,5-substituted cyclopent-2-enones


XXIII
XXIV
XXVII
XXVI
XXX
XXIX
XV
XXV
XIV
XVI

The NMR spectrum of the alcohol (XXII) has a 4-proton multiplet, which is assigned to the 4 methylene protons, at 136 cycles per second downfield from tetramethylsilane. The splitting of this multiplet is quite complex. None of these protons is expected to be identical to another since the two methylene groups are not equivalent and each proton of each methylene group is either cis or trans to the hydroxyl group. The 1 proton peak at 241 cps. is assigned to the hydroxylic proton, since it disappears completely when the contents of the NMR tube are shaken with a drop of D_2O. The broad 1 proton singlet at 295 cps. is assigned to the proton on the carbon bearing the hydroxyl group. It is split by the four non-equivalent methylene protons and also possibly the benzylic proton by allylic coupling. The only large coupling constant possible for this proton is with the beta methylene. Coupling with the other protons serves only to smear the peak into a large number of very close lines which appear as a broad singlet.

The 4 and 2 proton multiplets at ·432 and 452 cps. are assigned to the aromatic protons. The multiplet at 452 cps. is assigned to the two protons of the phenyl group which are ortho to the benzylic carbon. It is expected that these two hydrogen atoms would be shifted downfield slightly due to their close proximity to the hydroxyl group. The upfield multiplet is assigned to the other three aromatic protons.

This multiplet is further complicated by the peak for the benzylic proton which occurs at this position.

Due to the extreme complexity of the individual peaks it is not possible to obtain coupling constants.

That the benzylic protons of these sytems do appear in the aromatic region of the spectrum is confirmed by examination of the spectrum of 2-paramethoxybenzylidenecyclopent-2-enone. In this compound, the aromatic protons are split into an A_2B_2 pattern which has collapsed into an approximate AB pattern of double intensity. The peak caused by the benzylic proton is seen as a 1 proton triplet in the center of the aromatic pattern.

The NMR spectrum of the amine (XXI) has a 6 proton singlet at 126 cps. which can only be caused by the two equivalent methyl groups. The 4 proton multiplet centered at 137 cps. is assigned to the 4 methylene protons. The downfield half of this pattern can tentatively be assigned to the methylene group beta to the carbonyl, since it appears to be more highly split by the proton on the vinylic carbon atom. This can not be stated definitely since the upfield portion of the pattern is partly obscured by the 126 cps. peak. The upfield portion of the multiplet is assigned to the remaining methylene group alpha to the carbonyl. The 1 proton singlet at 236 cps. is assigned to the benzylic proton. The 6 proton multiplet at 422 cps. is assigned to

the 5 aromatic protons and the vinylic proton. The aromatic protons are expected to show a complex pattern. The complexity of the multiplet is increased by the peak caused by the vinylic proton. This proton can be expected to show at least a triplet due to splitting by the methylene group beta to the carbonyl. It can also be further split by the other methylene group, although the coupling constant for this splitting should be smaller than that for the coupling with the adjacent methylene group.

Due to the extreme complexity of this spectrum it is impossible to obtain coupling constants for the various splittings.

Since considerable importance is to be attached to 5-benzylidene-2-methylcyclopent-2-enone (XIV), it is desirable to consider its NMR spectrum separately from those of lesser importance. The NMR spectrum of XIV shows a 3 proton multiplet at 111 cps. which is assigned to the methyl group. The 2 proton multiplet at 202 cps. is assigned to the methylene group and the 7 proton multiplet at 447 cps. is assigned to the 5 aromatic protons, the benzylic proton, and the 5-membered ring vinylic proton. Under high resolution, the methyl peak is a six line multiplet and the methylene peak is a perfectly symmetrical sextet.

Double resonance experiments were carried out on this compound. When the methyl group was irradiated, the peak for

the methylene group collapsed into a doublet of doublets, which is what one would expect for the methylene group when coupled with the two olefinic protons, J = 2.7 and 2.9 cps. When the olefinic protons were irradiated, the methylene peak collapsed to a perfect quartet showing the coupling of the methylene protons to the methyl group, J = 2.1 cps. When the methylene group was irradiated, the methyl peak collapsed to a doublet showing the coupling of the methyl group with the vinylic proton of the 5-membered ring, J = 1.8 cps.

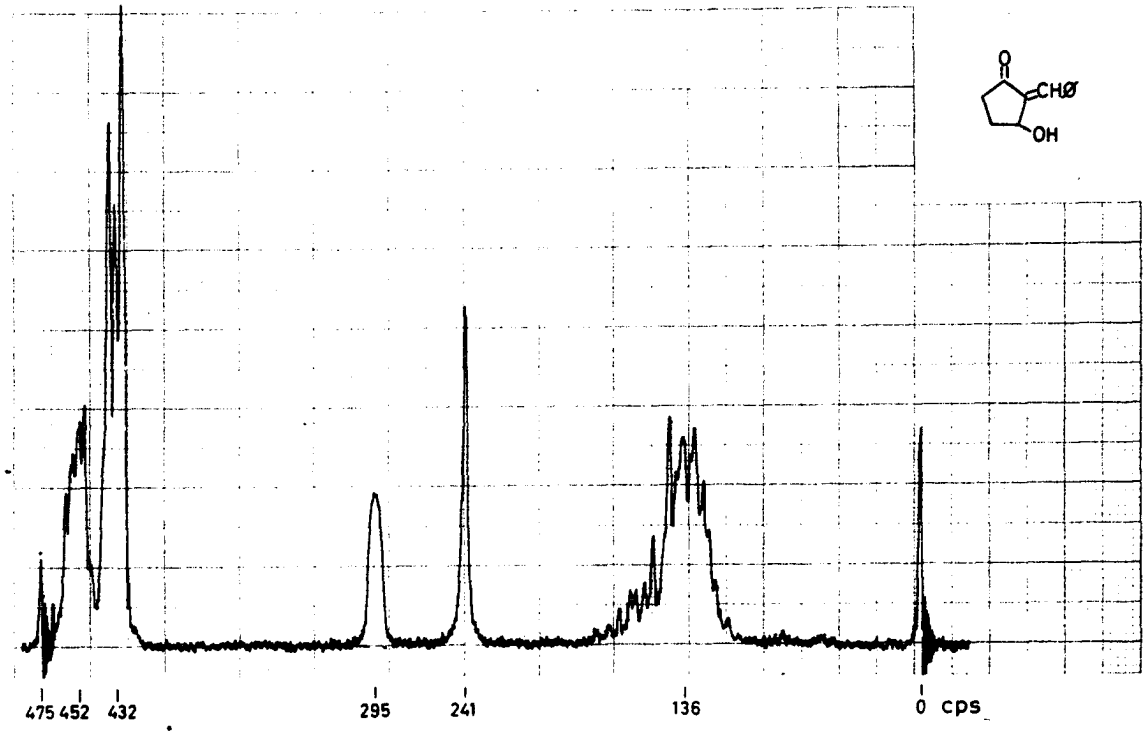
The coupling constants are approximate values obtained by interpolations from the double resonance spectra.

The possible synthetic utility of several of the compounds prepared during the course of this work is manifold. One of the most intriguing possibilities is entry into the benzpentalene (XXXI) system, via the 5-benzylidenecyclopent-2-enones, by forming a bond between the 4-carbon of the five-membered ring and the carbon atom of the aromatic ring which is <u>ortho</u> to the benzylic carbon. Models show that, sterically at least, this is feasible. Also, the 5-benzylidenecyclopentenones are in the correct oxidation state for this transformation.

Another interesting possibility lies in the possible entry into the cyclobutene series via 5-diazo-2-methylcyclopent-2-enone. A ring contraction reaction such as used by

Figure 5. NMR spectrum of 2-benzylidenecyclopentan-3-ol-1-one (XXII)

Figure 6. NMR spectrum of 2-(N,N-dimethyl-α-aminobenzyl)-cyclopent-2-enone (XXI)


CHØ
OH
475 452 432
295
241
136
0 cps

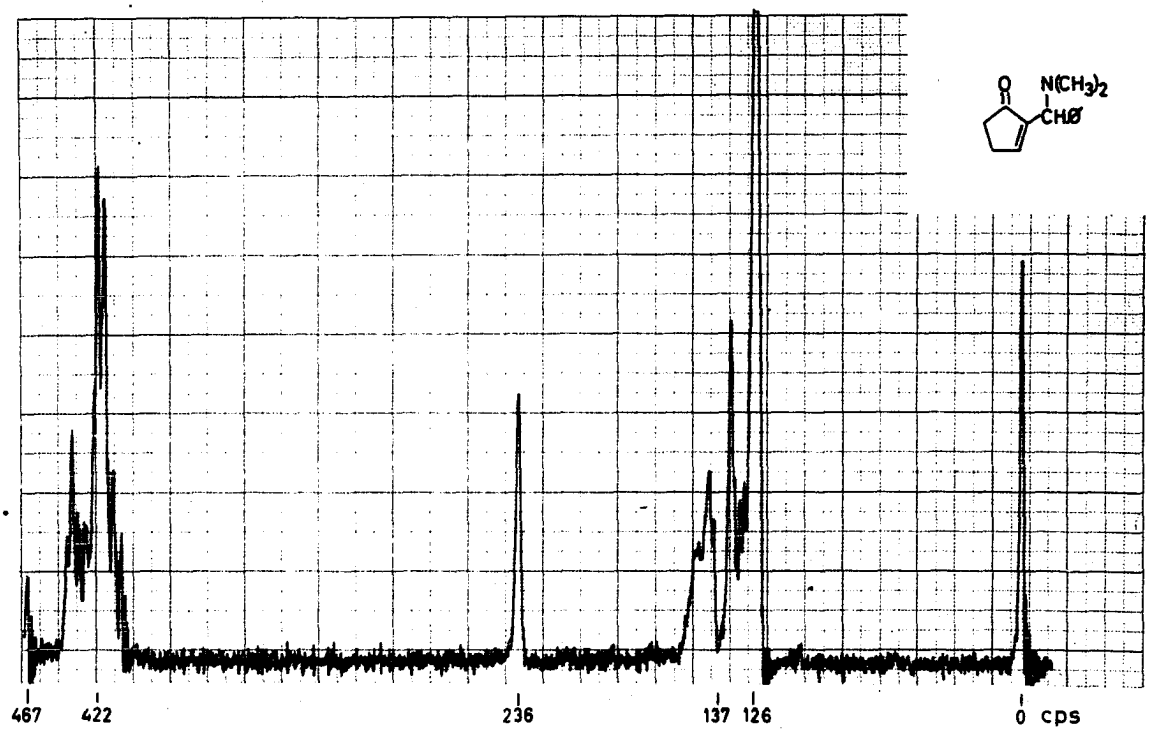
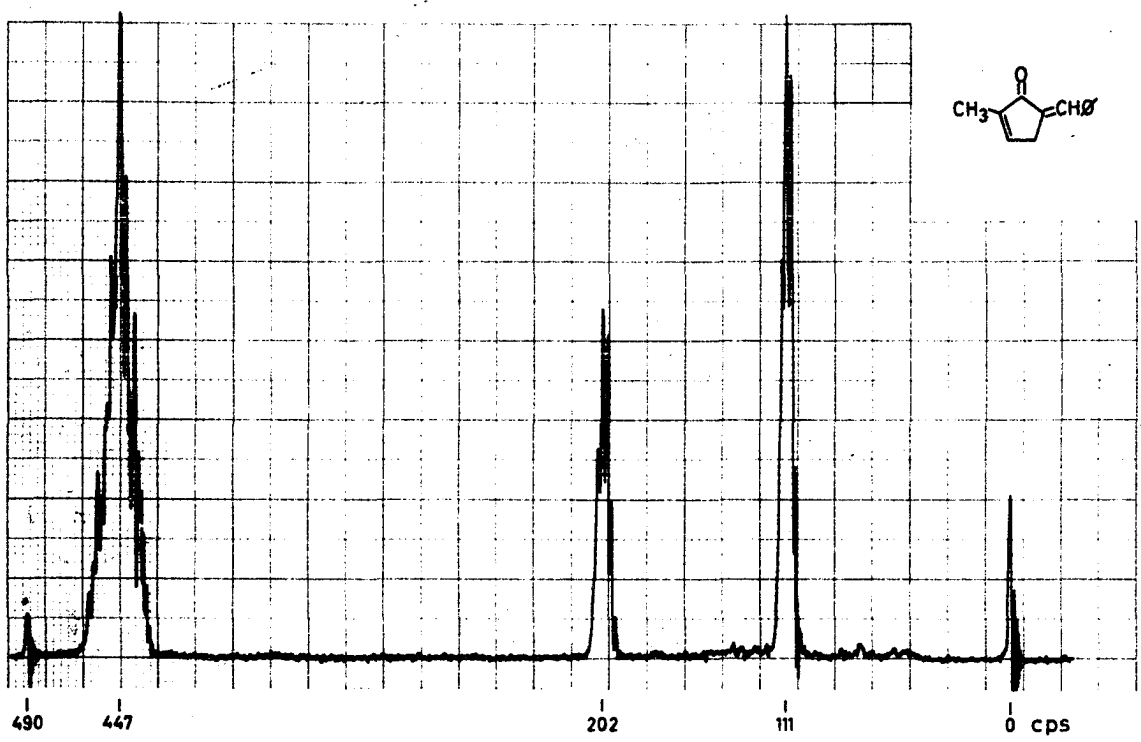

N(CH3)2
CHØ
467 422
236
137 126
0 cps

Figure 7. NMR spectrum of 5-benzylidene-2-methyl-cyclopent-2-enone (XIV)


CH3
CHØ
490
447
202
111
0 cps

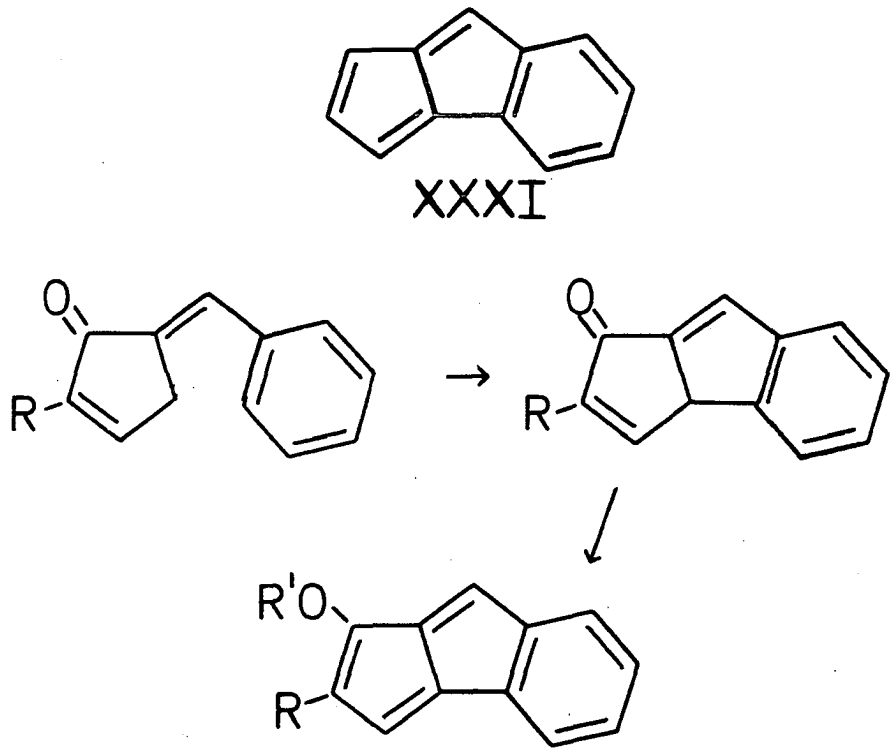


Figure 8. Possible entry into the benzpentalene system

Horner and Spietschka[49] could conceivably effect this transformation.

Entry into the tautomeric fulvene sytem from the 5-benzylidenecyclopent-2-enones could be effected by O-alkylation or acylation.

The fact that some of these compounds, in particular,

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[49]Horner, L. and Spietschka, E., Chem. Ber. 88, 934 (1955).

all of those containing the benzylidene, keto, or diazo groupings in the 5-position and a methyl group in the 2-position, are obtainable only after a rather long synthetic process can be overcome. Recently, there has become available commercially a cyclopentenone bearing a six carbon substituent in the 2-position.[50] If one is not expressly interested in having the methyl group in the 2-position, then one can use the commercially available material.

The method selected for measuring the rates of deuterium exchange was that of Dessy et al.[51] A 1 molar solution of the compound to be studied was made in a solvent which consisted of 5 molar D_2O and 1 molar triethylamine in N,N-dimethylformamide (DMF). The reaction was then followed by measuring spectrophotometrically the amount of HOD produced by the reaction.

The rates of deuterium exchange were measured for 5-benzylidene-2-methylcyclopent-2-enone (XIV), 5-benzylidene-2-isobutoxycyclopent-2-enone (XXIX), 5-diazo-2-methylcyclopent-2-enone (XVI), cyclopent-2-enone, and cyclopentanone. 5-Benzylidene-2-benzyloxycyclopent-2-enone (XXX) is not soluble enough in the exchange solvent for its rate of exchange to be measured by this method.

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[50] 2-Hexylcyclopent-2-enone, Aldrich Chemical Co.

[51] Dessy, R. E., Okuzumi, Y., and Chen, A., J. Am. Chem. Soc., 84, 2899 (1962).

3-Methylcyclopent-3-ene-1,2-dione (XV) is not stable to the exchange conditions, decomposing virtually instantaneously.

Table 1. Summary of results of kinetic measurements

Compound	$K_{40°}$ sec^{-1} [a]	Rel. rate	$K_{80°}$ sec^{-1} [a]	Rel. rate
5-Benzylidene-2-methylcyclopent-2-enone	1.01×10^{-5}	1	1.91×10^{-4}	62.1
5-Benzylidene-2-isobutoxycyclopent-2-enone	--	--	3.08×10^{-6}	1
5-Diazo-2-methylcyclopent-2-enone	4.33×10^{-4}	42.9	Large	Large
Cyclopent-2-enone alpha protons	7.60×10^{-5}	7.5	--	--
Cyclopentanone	6.9×10^{-5}	6.8	--	--

[a]Corrected for statistical effects.

The rate of exchange of cyclopentanone was measured in order to serve as a check of the kinetic method as used in these laboratories. The rate constant obtained, 6.91×10^{-5}, agrees quite satisfactorily with that obtained by the same method by Shechter et al.,[52] 6.80×10^{-5}.

There are two competing effects which would predict

[52]Shechter, H., Collis, M. J., Dessy, R., Okuzumi, Y., and Chen, A., J. Am. Chem. Soc. 84, 2905 (1962).

different results in comparing the rates of exchange for 5-benzylidene-2-methylcyclopent-2-enone (XIV) and 5-benzylidene-2-isobutoxycyclopent-2-enone (XXIX). The enol oxygen of XXIX can reduce the amount of positive character of the 3-carbon by resonance and thereby reduce the acidity of the 4-methylene group causing slower exchange. The enol oxygen of XXIX can also inductively stabilize any anion formed on the 2-carbon during the exchange process and thereby increase the rate of exchange. The fact that there is a rather large decrease in the rate of exchange of XXIX compared to XIV indicates that the resonance effect is the more important of the two.

NMR evidence indicates that in the ground state of 5-benzylidene-2-isobutoxycyclopent-2-enone (XXIX) there is considerable participation of the enol oxygen with the double bond, as shown by the fact that the 3-proton is found at considerably higher field than the corresponding proton of XIV (378 cps. vs. approximately 447 cps.). This can be accounted for by an increased amount of electrons available for greater shielding at the 3-carbon due to resonance of the enolic oxygen with the double bond.

These data also serve to confirm that the two resonance forms of the anions of the 5-benzylidenecyclopentenones are not extremely important to the overall resonance hybrid of these anions. Thus, it appears that most of the negative

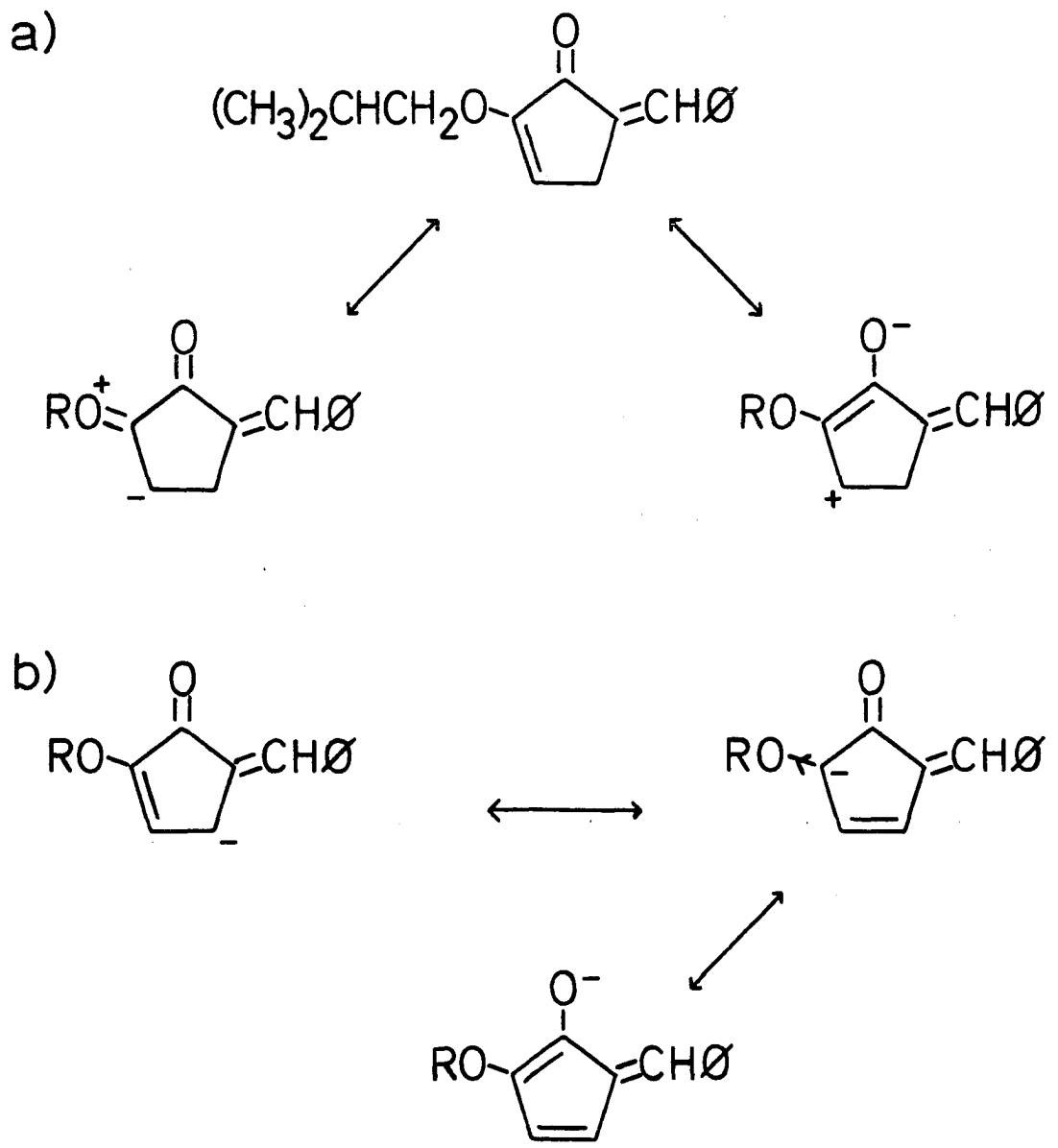
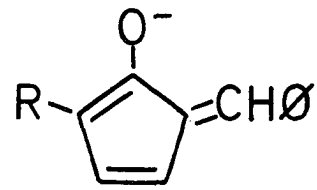


Figure 9. a) Resonance interaction of the enolic oxygen of 5-benzylidene-2-isobutoxycyclopent-2-enone (XXIX) in the ground state; b) inductive interaction of the enolic oxygen of XXIX in the anion of XXIX

charge of the anions resides on the carbonyl oxygen and that the resonance hybrid of these anions can best be represented by structure XXXII.



XXXII

Since Lyons[53] showed that the alpha protons of cyclopentenone exchange much faster than do the beta protons, the rate measured for the exchange of cyclopentenone is that for the exchange of the alpha protons. From Lyons' data it appears that the alpha protons of cyclopentenone exchange at least 100 times faster than do the beta protons. Thus, since cyclopentenone exchanges only 7.5 times as fast as does 5-benzylidene-2-methylcyclopent-2-enone (XIV) it would appear that XIV exchanges at least 13 or more times faster than the beta protons of cyclopentenone.

This increase in the acidity of the beta protons by addition of a benzylidene group is, perhaps, an example of

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[53]Lyons, C. E. Nuclear magnetic resonance study of cyclopentenone and some of its derivatives. Unpublished Ph.D. thesis. Ames, Iowa, Library, Iowa State University of Science and Technology. 1961.

a new type of increased stabilization of an anion by the participation of a fulvene, the increased stability being due, at least in part, to the aromatic character of fulvene.

The 5-benzylidenecyclopentenones are more highly strained than are the cyclopentenones, but their increased acidity can not be explained by release of extra strain since rehybridization of the 4-carbon from sp^3 to sp^2 would actually increase the strain of the system.

The kinetic data clearly show that a 5-diazo group has a greater acidifying effect than does a 5-benzylidene group on the protons of the 4-carbon of the cyclopentenones. This can be the result of several factors. First, the ground state energy of 5-diazo-2-methylcyclopent-2-enone (XVI) may be considerably higher than the ground state energy of 5-benzylidene-2-methylcyclopent-2-enone (XIV). Thus, if the transition state energies are closer energetically, the energy of activation for the ionization of XVI may be less than that for XIV. However, there is a possibility of resonance in the ground state for the diazo-ketone (XVI) which is much less important for the benzylidene-ketone (XIV). This added resonance form should lower the ground state energy of the diazo-ketone. The fact that the diazo-ketone can be stored fairly well at room temperature without excessive decomposition indicates that it is not extremely reactive, as are many other diazo compounds.

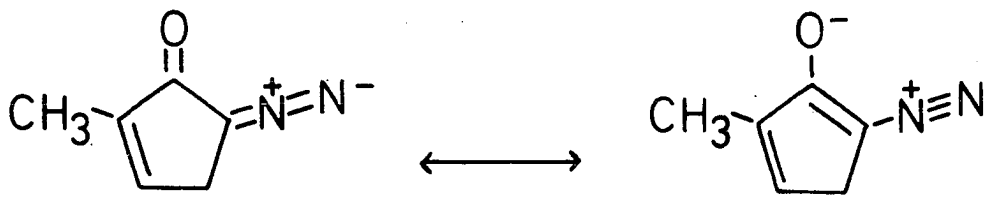

Figure 10. Ground state resonance of XVI

Second, the anion of the diazo-ketone (XVI) has a possible resonance form for which the corresponding resonance form of the anion of 5-benzylidene-2-methylcyclopent-2-enone (XIV) should be of high energy. This could cause the energy of the transition state to be lowered relative to the ground state so that the exchange would proceed faster for XVI. However, this resonance form of the anion of the diazo-ketone should also be of high energy since it involves a structure similar to the anion of diimide.

Third, the diazo group of the diazo-ketone (XVI) should inductively stabilize a negative charge better than the benzylidene group of the benzylidene-ketone (XIV). The diazo group is insulated from the nearest position of the negative charge by a carbon atom. Also, in the case of 5-benzylidene-

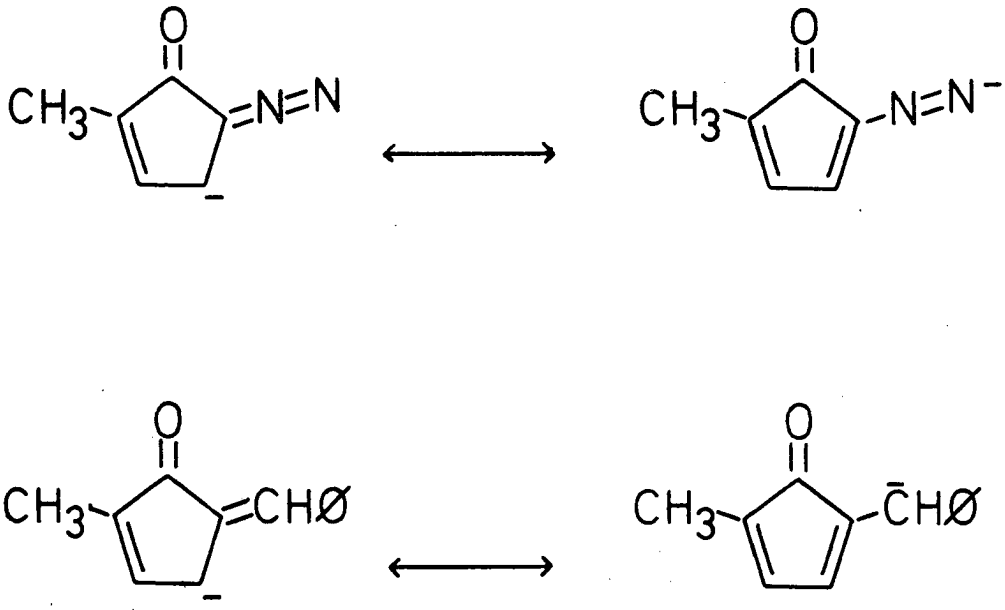

Figure 11. Some resonance forms of the anions of 5-diazo-2-methylcyclopent-2-enone (XVI) and 5-benzylidene-2-methylcyclopent-2-enone (XIV)

2-isobutoxycyclopent-2-enone (XXIX), where the oxygen atom which should inductively effect the anion, the oxygen atom is attached directly to an atom which can have a negative charge. Since the effect of the oxygen atom on the anion of XXIX is apparently quite small, one would expect the effect of the insulated diazo group also to be small.

Fourth, the expected principle resonance forms of the

Figure 12. Probable principle resonance forms of the anions of the diazo-ketone (XVI) and the benzylidene-ketone (XIV)

anions of the diazo-ketone (XVI) and the benzylidene-ketone (XIV) are different only in one respect. The anion of the diazo-ketone possesses a diazocyclopentadiene structure while the anion of the benzylidene-ketone possesses a fulvene structure. If, as predicted, all other effects are about equal, then the difference in acidity of the two compounds can be attributed to the difference in stabilization of the two ions by the respective aromatic character of diazocyclopentadiene and fulvene. Since the diazo-ketone undergoes exchange more rapidly than does the benzylidene-ketone, then, the resonance energy of diazocyclopentadiene is apparently greater than that of fulvene.

EXPERIMENTAL

Reagents

Azobis (isobutyronitrile) - This compound was obtained from Chemical Intermediates and Research Laboratories, Inc., Cuyahoga Falls, Ohio. It was recrystallized from anhydrous methanol to give a white crystalline product, m.p. 104°C.

Benzaldehyde - Matheson, Coleman, and Bell technical grade was used without further purification.

Benzyl alcohol (chlorine free) - This was used as received from Eastman Organic Chemicals.

N-Bromosuccinimide - Eastman practical grade was used as received.

Isobutyl alcohol - This was used as received from Mallinkrodt Chemical Works, St. Louis, Missouri.

Chlorine gas - A five pound cylinder was obtained from the Matheson Company, East Rutherford, New Jersey.

Cyclopentanone - This was used as received from Arapahoe Chemicals, Inc., Boulder, Colorado.

Dimethylamine (anhydrous) - Eastman white label grade was used without further purification.

Methyl iodide - This was used as obtained from Matheson, Coleman, and Bell.

para-Toluenesulfonhydrazide - This was used as received from Aldrich Chemical Co., Inc., Milwaukee, Wisconsin.

para-Toluenesulfonic acid - Matheson, Coleman, and Bell practical grade was used without further purification.

Instruments

Infrared spectra were recorded on a Perkin-Elmer Model 21 infrared spectrophotometer. Abbreviations used in reference to infrared spectra are: i, intense; m, moderate; and w, weak.

Near-infrared spectra were recorded on a Beckman DK-2A ratio recording spectrophotometer.

Nuclear magnetic resonance spectra were recorded on a Varian Model HR-60 high resolution nuclear magnetic resonance spectrometer at 60 megacycles. Unless otherwise specified, chemical shifts were measured with respect to tetramethylsilane as an internal standard by means of sidebands applied with the aid of a calibrated audio oscillator. Cycles per second are referred to as cps.

Analyses

All analyses were performed by either Spang Microanalytical Laboratory, Post Office Box 1111, Ann Arbor, Michigan, or by Midwest Microlab, Inc., 7838 Forest Lane, Indianapolis, Indiana.

All boiling points and melting points are uncorrected.

Syntheses

Cyclopent-2-enone[54]

Cyclopentenone was prepared from 250 g. (2.5 moles) of the mixed 3,4- and 3,5-cyclopentendiols by distillation from 1 g. of para-toluenesulfonic acid at aspirator vacuum. The fraction boiling up to 55° was collected and redistilled at atmospheric pressure to give 105 g. (51%) of cyclopent-2-enone, b.p. 149-152°. The material which was used for the kinetic measurements was redistilled and the constant boiling fraction which boiled at 151.5° was used.

Ethyl 2-oxocyclopent-3-englyoxylate (XVIII)

A solution of 2.3 g. (0.1 g.-atom) of sodium was dissolved in 50 ml. of dry ethanol. A solution of 16.1 g. (0.11 mole) of diethyloxalate in enough ethanol to make the total volume of the solution 100 ml. was added rapidly, and 8.2 g. (0.10 mole) of cyclopentenone in 25 ml. of ethanol was added at a moderate rate. The reaction mixture was allowed to stir for about 10 minutes. After this time, the reaction mixture was poured into ice-cold dilute sulfuric acid solution and extracted twice with methylene chloride. The methylene chloride solution was washed with sodium

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[54]DePuy, C. H. and Eilers, K. L., J. Org. Chem., 24, 1380 (1959).

bicarbonate solution, then water, and dried over magnesium sulfate. The solution was filtered and the methylene chloride was removed under reduced pressure. The crude solid residue was recrystallized from hexane to give 10.15 g. (56%) of ethyl 2-oxocyclopent-3-englyoxylate (XVIII) m.p. 66.5-67.5°.

Anal.: Calc. for $C_9H_{10}O_4$; C, 59.33%, H, 5.53%. Found: 58.88% C, 5.66% H.

Infrared: 5.76 μ (i), 6.03 μ (i), 8.07 μ (i), 8.40 μ (i), 8.87 μ (m), 9.79 μ (m).

NMR: The spectrum of XVIII consists of a 3 proton triplet and a 2 proton quartet at 83 and 259 cps respectively which are characteristic of an ethyl group, a 2 proton multiplet at 210 cps for the five-membered ring methylene group, two 1 proton multiplets at 382 and 454 cps which are characteristic of the alpha and beta protons of cyclopentenone, and a 1 proton singlet at 762 cps for the enolic proton.

Attempted Claisen condensations on cyclopent-2-enone

The reaction of cyclopentenone was attempted with ethyl carbonate, ethyl formate, and phenyl benzoate using several different bases including sodium ethoxide in ethanol, sodium hydride in ether, sodium ethoxide in refluxing benzene, and sodamide in liquid ammonia. Addition of cyclopentenone to the ester in base, simultaneous addition of cyclopentenone and the ester to the base, and addition of the ester to

cyclopentenone in base were tried. All attempts resulted in from 60-80% yields of cyclopentenone polymer and recovered ester.

Attempted reaction of cyclopentenone with benzaldehyde (base)

The reaction of cyclopentenone with benzaldehyde under the basic conditions which led to satisfactory yield of ethyl-2-oxocyclopent-3-englyoxylate (XVIII) was attempted. Only cyclopentenone polymer was isolable.

Attempted reaction of cyclopentenone with benzaldehyde (acid)

A mixture of 4.1 g. (0.05 mole) of cyclopentenone and 5.03 g. (0.05 mole) of benzaldehyde in ether was added to 500 ml. of ether which had been saturated with dry HCl gas. The mixture was allowed to stand with occasional shaking for 8 hours. The ether and HCl were removed under reduced pressure. A small amount of greenish-yellow solid which was identified as 2,5-dibenzylidenecyclopent-3-enone was left as a residue, m.p. 150-154°.

The NMR of this sample was identical to the NMR of an authentic sample which was kindly supplied by Dr. O. L. Chapman of these laboratories.

Preparations

2-Benzylidenecyclopentanone[45]

A mixture of 185 g. of benzaldehyde (1.75 moles), 440 g. of cyclopentanone (5.25 moles), 40 g. of sodium hydroxide (1 mole), and 10 liters of water were stirred in a 12 liter flask for 8 hours at room temperature. The aqueous suspension was then neutralized with 60 g. (1 mole) of acetic acid and extracted three times with benzene. The combined benzene layers were dried, the benzene was removed under reduced pressure, and the residue was distilled at water aspirator vacuum using an air condenser. In this manner there was obtained 210 g. (70%) of 2-benzylidenecyclopentanone, b.p. 175°/13 mm., m.p. 68.5° (after recrystallization from ether).

Infrared: 5.82 μ (i), 6.15 μ (i).

2-(N,N-Dimethyl-α-aminobenzyl)-cyclopent-2-enone (XXI)

2-Benzylidenecyclopentanone, 25.8 g. (0.15 mole), 26.7 g. (0.15 mole) of N-bromosuccinimide, and 500 ml. of carbon tetrachloride in a 1 liter flask fitted with a reflux condenser and a magnetic stirrer were irradiated with a General Electric sunlamp until the reaction "flashed". The "flashing" was evidenced by the rapid disappearance of the green color which had built up in the solution and the vigorous boiling of the solution as the reaction rapidly proceeded to completion.

After the reaction was over, the solution was cooled in an ice bath and, when cool, the succinimide formed by the reaction was removed by filtration. Anhydrous dimethylamine, 30 g. (0.66 mole), was added and the solution was allowed to stand at 0 to -10° overnight. The carbon tetrachloride solution was extracted three times with dilute hydrochloric acid, the aqueous layers were neutralized with sodium bicarbonate solution and extracted with ether until color was no longer observed in the fresh ether layers. The combined ether layers were dried over magnesium sulfate, filtered, and distilled under reduced pressure yielding 17.5 g. (70%) of 2-(N,N-dimethyl-α-aminobenzyl)-cyclopent-2-enone (XXI), b.p. 101°/ 0.01 mm.

Several attempts were made to isolate the intermediate bromo-compound. All these attempts failed since upon attempted concentration of the carbon tetrachloride solution the compound invariably decomposed.

Anal.: picrate salt, calc. for $C_{20}H_{20}N_4O_8$; C, 54.05%, H, 4.54%, N, 12.61%. Found: 53.16% C, 4.75% H, 11.73% N.

Infrared: 3.26 μ (w), 3.30 μ (w), 3.35 μ (m), 3.39 μ (m), 3.50 μ (m), 3.55 μ (m), 3.61 μ (m), 5.88 μ (i), 6.15 μ (i).

NMR: The spectrum of XXI consists of a 6 proton singlet at 126 cps for the dimethylamino group, a complex 4 proton multiplet centered at 137 cps for the two methylene groups,

a 1 proton singlet at 236 cps for the benzylic proton, and a 6 proton multiplet at 422 cps for the five aromatic protons and the beta vinylic proton of the cyclopentenone system.

In an attempt to obtain an NMR spectrum of the intermediate bromo-compound (XIX or XX) the NBS bromination was carried out at a concentration suitable for NMR spectra. The succinimide was removed by filtration and an NMR spectrum of the resulting carbon tetrachloride solution was taken. It appeared that either the bromo-compound was a mixture of isomers or very impure since the spectrum was extremely complicated. Therefore, the structure of this unstable compound could not be determined.

2-(N,N,N-Trimethyl-α-ammoniumbenzyl)-cyclopent-2-enone iodide

A solution of 17.50 g. (0.815 mole) of 2-(N,N-dimethyl-α-aminobenzyl)-cyclopent-2-enone in 20 ml. of anhydrous acetonitrile was treated with 12.00 g. (0.845 mole) of methyl iodide and allowed to stand at -10° overnight. The supernatant liquid was decanted from the off-white crystalline mass which had formed, and was added to 20 ml. of ether. A small amount of white particles formed. These particles were combined with the rest of the crystalline mass, and the whole batch was ground to a fine powder in a mortar and pestle. The powder was transferred to a Pyrex Buchner funnel and washed thoroughly with ether. After drying, the powder

was found to weigh 28.15 g. (97%). Attempts to purify the product further failed because the salt was found to be extremely insoluble in every solvent tried, except water in which it is very soluble. For this reason, a sample of analytical purity was unobtainable.

Infrared: 5.90 μ (i), 6.18 μ (i).

NMR: The spectrum of the methiodide salt in D_2O using benzene as an external standard consists of a 2 proton multiplet at +240 cps for the methylene group alpha to the carbonyl, a 2 proton multiplet at +219 cps for the methylene group beta to the carbonyl, a 9 proton singlet at +203 cps for the trimethylammonium group, a singlet at +108 cps for DOH, a 1 proton singlet at +67 cps for the benzylic proton, a 5 proton multiplet at -66 cps for the aromatic protons, and a 1 proton triplet at -132 cps for the vinylic proton.

Attempted preparations of 5-benzylidene-cyclopent-2 (or 3)-enone

Several attempts were made to carry out Hofmann eliminations upon 2-(N,N,N-trimethyl-α-ammoniumbenzyl)-cyclopent-2-enone iodide, using different bases. The bases used were silver oxide, potassium tert-butoxide in tert-butanol, aqueous sodium hydroxide, and potassium hydroxide in ethanol. All of these attempts failed to give any isolable product. Also tried, with the same results, were heating the methiodide salt with pyridine and quinoline.

2-Benzylidenecyclopentan-3-ol-1-one (XXII)

A solution of 1 g. (0.012 mole) of sodium bicarbonate in 10 ml. of water was added to a solution of 3.57 g. (0.01 mole) of the preceding methiodide salt in 30 ml. of water. After a few minutes, a yellow oil began to form and a strong odor of trimethylamine was detected. After about 20 min. the reaction mixture was extracted three times with chloroform, the combined chloroform layers were dried over magnesium sulfate, and filtered. The chloroform was evaporated, and the residue recrystallized from hexane. In this manner 1.09 g. (70%) of 2-benzylidenecyclopentan-3-ol-1-one (XXII), m.p. 80.5-81.5°, was obtained.

Anal.: Calc. for $C_{12}H_{12}O_2$: C, 76.57%, H, 6.43%. Found: 76.46% C, 6.59% H.

Infrared: 3.15 μ (i, broad), 5.85 μ (i), 6.17 μ (i), 8.51 μ (i).

NMR: The NMR of XXII consists of a 4 proton broad multiplet at 136 cps for the two methylene groups, a 1 proton singlet at 241 cps (which completely disappears when the sample is shaken with a small amount of D_2O) for the hydroxylic proton, a 1 proton broad singlet at 295 cps for the proton on the 3 carbon atom, a 4 proton multiplet at 432 cps and a 2 proton multiplet at 452 cps totalling 6 protons for the aromatic protons and the benzylic proton.

Structure proof: Samples of 2-benzylidenecyclopentanone and 2-benzylidenecyclopentan-3-ol-1-one were hydrogenated in 95% ethanol over Adam's catalyst, taking up 1 and 2 moles of hydrogen respectively. The hydrogenation mixtures were filtered to remove the catalyst and concentrated. 2,4-Dinitrophenylhydrazones were prepared from both samples, and both derivatives melted at 119-120°. Mixed melting point showed no depression. These data taken in conjunction with the spectral evidence conclusively prove the structure of 2-benzylidenecyclopentan-3-ol-1-one (XXII).

Attempted esterifications of 2-benzylidenecyclopent-3-ol-1-one

Esterification of 2-benzylidenecyclopent-3-ol-1-one was attempted with a variety of reagents. Among these were acetyl chloride in pyridine, acetic anhydride with sulfuric acid as catalyst, acetic anhydride in pyridine, ketene in ether with para-toluenesulfonic acid as catalyst, and para-toluenesulfonyl chloride in pyridine. All of these attempts met with failure, the basic conditions leading to recovered starting material and the acidic conditions producing black tar-like masses.

Attempted elimination of water from 2-benzylidenecyclopent-3-ol-1-one

A sample of 2-benzylidenecyclopent-3-ol-1-one was heated in vacuum in a short path distilling apparatus with a small

amount of para-toluenesulfonic acid. The alcohol turned black and the flask was filled with a brittle black residue of decomposition products.

A sample of the alcohol was also dissolved in refluxing benzene with a small amount of para-toluenesulfonic acid and any water that was formed overnight was removed azeotropically. The only isolable material was 50% recovery of starting material.

2-Chlorocyclopentanone (XXIII)[46]

A 3 liter 3 necked flask fitted with a stirrer, gas delivery tube, and an efficient condenser was set up in a hood. The gas delivery tube (which must extend to below the surface of the reaction mixture) was connected through a trap to a cylinder of chlorine. In the flask were placed 500 g. (5.94 moles) of cyclopentanone, 290 g. (2.90 moles) of calcium carbonate, 290 g. of a 40% solution of calcium chloride in water, 320 ml. of water, and approximately 200 mg. of azobis (isobutyronitrile). The chlorine was turned on and when the reaction mixture had assumed a strong green color, the chlorine was turned off and the reaction mixture was irradiated for a while with a General Electric sun lamp. When the reaction started, the green color disappeared and bubbles of carbon dioxide were seen rising from the surface of the aqueous layer. At this time the flask was immersed

in a previously prepared ice bath, the chlorine flow was restarted, and the stirrer was started. The chlorine was added at a rate that held the temperature in the flask to about 40-45°, which provided about the best compromise between speed and loss of chlorine from the system. When the reaction was over as evidenced by the disappearance of the solid calcium carbonate, the chlorine was shut off, the layers were separated, the aqueous layer was washed three times with chloroform, and the combined organic layers were dried over magnesium sulfate. After filtration, the organic layer was distilled through a 30 inch insulated, electrically heated column packed with 1/4 inch Pyrex helices. The distillation is best accomplished in two steps. The first distillation gave 350-415 g. (50-59%) of 2-chlorocyclopentanone (XXIII), b.p. 70-80°/13 mm. Redistillation gave 315-380 g. (45-54%), b.p. 74-75°/13 mm.

Infrared: 5.75 μ (i).

Cyclopentan-1,2-dione (XXIV)[47]

A 3 liter 3 necked flask fitted with stirrer, condenser, and an addition funnel was set up in a hood. Water (1.2 liters) was added to the flask and heated to the boiling point. At this time, 120 g. (1 mole) of 2-chlorocyclopentanone (XXIII) was added and the mixture was stirred until all the chloro-ketone went into solution (as the hydroxy-ketone).

The heat was removed and a solution of 500 g. (1.85 moles) of ferric chloride hexahydrate in 250 ml. of water was added rapidly. At first the brown color of the ferric chloride disappeared rapidly, but, toward the end of the addition, the color was retained. After the addition was completed, the mixture was allowed to stir for about 1/2 hour. After this time, the solution was cooled in an ice bath to below 30° and was placed in a continuous extraction apparatus and extracted overnight with ether. The ether layer was dried over magnesium sulfate and distilled under aspirator vacuum through a 6 inch Vigreaux column, using an air condenser. Obtainable in this manner were from 65 to 80 g. (65-80%) of cyclopentan-1,2-dione (XXIV), b.p. 81-86°/13 mm., m.p. (after recrystallization from hexane) 55-56°.

Infrared: 3.09 μ (broad, i), 5.95 μ (i), 6.10 μ (i), 9.10 μ (i).

2-Isobutoxycyclopent-2-enone (XXVI)[48]

Cyclopentan-1,2-dione (XXIV), 10 g. (0.10 mole), 7.4 g. (0.10 mole) of isobutyl alcohol, approximately 100 mg. of para-toluenesulfonic acid, and 250 ml. of benzene were heated at reflux in a flask fitted with a Dean-Stark water separator and a reflux condenser. When water was no longer formed by the reaction, the benzene solution was cooled, washed with water, sodium bicarbonate solution, and water again. After

drying the benzene solution over magnesium sulfate and filtering it, the benzene was removed under reduced pressure and the residue was distilled. From this reaction was obtained 9.7 g. (62%) of 2-isobutoxycyclopent-2-enone (XXVI), b.p. 119°/13 mm.

Infrared: 5.82 μ (i), 6.15 μ (i), 8.95 μ (broad, i).

2-Benzyloxycyclopent-2-enone (XXVII)

A procedure identical to that for the preparation of 2-isobutoxycyclopent-2-enone was used, substituting benzyl alcohol for the isobutyl alcohol. From 10 g. (0.10 mole) of cyclopentan-1,2-dione was obtained 14.0 g. (75%) of 2-benzyloxycyclopent-2-enone (XXVII), b.p. 140-144°/0.15 mm., m.p. (after recrystallization from ether) 96-97°.

Anal.: Calc. for $C_{12}H_{12}O_2$; C, 76.57%, H, 6.43%. Found: 76.50% C, 6.31% H.

Infrared: 5.83 μ (i), 6.14 μ (i), 8.97 μ (broad, i).

NMR: The spectrum of XXVII consists of a 4 proton broad singlet at 142 cps for the two methylene groups, a 2 proton singlet at 294 cps for the benzylic protons, a 1 proton triplet at 383 cps for the vinylic proton, and a 5 proton broad singlet at 440 cps for the aromatic protons.

2-Methylcyclopent-2-enone (XXV)[48]

A solution of methyl Grignard reagent was prepared from 285 g. (2.0 moles) of methyl iodide and 48.6 g. (2.0 g. atoms)

of magnesium in 2 liters of ether in a 5 liter 3 necked flask fitted with stirrer, condenser, and dropping funnel. Cyclopentan-1,2-dione (XXIV), 49 g. (0 50 mole) in 500 ml. of ether was added dropwise. After the addition was complete, the mixture was allowed to stir for about 1 hour. At the end of this time, 200 ml. of water was added very cautiously. The water was followed with enough dilute sulfuric acid to dissolve the magnesium salts and to make the solution definitely acidic. The ether during this time was allowed to distill from the flask through a condenser set for take-off. The aqueous mixture was then distilled from the flask, more water being added from time to time to maintain the water level in the flask roughly constant at about 1.5 liters. The steam distillate was placed in a continuous extraction apparatus and extracted with ether for about 8 hours. The ether extract was dried over magnesium sulfate, filtered, and the ether was removed by distillation. The residual oil was distilled at atmospheric pressure and the fraction boiling at 156-158° was collected yielding 39.4 g. (41%) of 2-methylcyclopent-2-enone (XXV).

Infrared: 5.88 μ(i), 6.11 μ(m).

5-Benzylidene-2-isobutoxycyclopent-2-enone (XXIX)

A solution of 1.00 g. (6.5 mmoles) of 2-isobutoxycyclopent-2-enone and 0.69 g. (6.5 mmoles) of benzaldehyde in 25 ml. of 95% ethanol was placed in a 50 ml. Erlenmeyer flask and

stirred magnetically. To this solution was added a solution of 0.3 g. (7.5 mmoles) of sodium hydroxide in 3 ml. of water. The mixture rapidly became wine-red in color and after a few minutes white particles of a solid were observed. After about 20 minutes, 2 N. hydrochloric acid was added until there was no more color change produced by the addition of acid, the mixture taking on a yellow-orange color. The mixture was then poured into 100 ml. of water, the flask rinsed with ether, and the aqueous mixture extracted three times with ether. The combined ethereal layers were washed with sodium bicarbonate solution and dried over magnesium sulfate. After filtration, the ether was partially evaporated and hexane was added to the remaining ether solution until the cloud point was reached. The product was allowed to crystallize at room temperature. A second crop was obtained by adding more hexane to the mother liquors and boiling the solution to remove most of the remaining ether. This solution was allowed to cool and the resulting crystals were combined with the first crop. A total of 1.25 g. (79%) of 5-benzylidene-2-isobutoxycyclopent-2-enone (XXIX), m.p. (after recrystallization from hexane) 96.5-97.5°, were obtained in this manner.

Anal.: Calc. for $C_{16}H_{18}O_2$; C, 79.31%, H, 7.49%. Found: 79.31% C, 7.57% H.

Infrared: 5.90 μ(i), 6.07 μ(i), 8.73 μ(i), 9.66 (i), 12.95 μ (i), 14.57 μ (i).

NMR: The spectrum of XXIX consists of a 6 proton doublet for the two methyl groups of the isobutoxy group, a 1 proton multiplet (seven lines are seen of a nine line multiplet) for the proton on the tertiary carbon of the isobutoxy group, a 2 proton doublet of doublets at 206 cps. for the five membered ring methylene group, a 2 proton doublet at 222 cps. for the methylene group of the isobutoxy group, a 1 proton triplet at 378 cps. for the five membered ring vinylic proton, and a 6 proton multiplet at 445 cps. for the aromatic protons and the benzylic proton.

5-Benzylidene-2-benzyloxycyclopent-2-enone (XXX)

A procedure identical to that for the preparation of 5-benzylidene-2-isobutoxycyclopent-2-enone (XXIX) was used, substituting the benzyl enol ether for the isobutoxy enol ether. From 1.00 g. (5.32 mmoles) of 2-benzyloxycyclopent-2-enone was prepared 1.32 g. (90%) of crude 5-benzylidene-2-benzyloxycyclopent-2-enone (XXX) which after recrystallization from chloroform melts at 181-182°.

Anal.: Calc. for $C_{19}H_{16}O_2$; C, 82.58%, H, 5.84%. Found: 82.62% C, 5.93% H.

Infrared: 5.91 μ(i), 6.10 μ(i), 6.15 μ (m), 8.76 μ (i), 9.65 μ(i), 9.69 μ(i), 12.93 μ(i), 13.60 μ (i), 14.50 μ (i).

NMR: The spectrum of XXX consists of a 2 proton doublet of doublets at 202 cps. for the five membered ring methylene

group, a 2 proton singlet at 302 cps. for the benzyloxy benzylic protons, a 1 proton triplet at 376 cps. for the five membered ring vinylic proton, and an 11 proton multiplet for the ten aromatic protons and the benzylidene group benzylic proton.

5-Benzylidene-2-methylcyclopent-2-enone (XIV)

A method similar to that used by Wanzlick and Gollmer[33] for the preparation of 5-benzylidene-2-chlorocyclopent-2-enone was used for this preparation. One g. (9.1 mmoles) of 2-methylcyclopent-2-enone and 2 ml. of benzaldehyde in 1 ml. of actic acid were treated with 10 drops of conc. hydrochloric acid and warmed to about 80° for 1 hour. At the end of this time, the reaction mixture was poured into 50 ml. of ether and dried over a mixture of magnesium sulfate and anhydrous potassium carbonate. After filtration, the ether was removed under vacuum and the residual oil was heated with hexane for a few minutes. The hexane was decanted from the remaining oil and allowed to cool. This process was repeated several times. The combined hexane leachings were then crystallized from hexane twice. Obtainable in this manner were 1.05 g. (63%) of crude 5-benzylidene-2-methylcyclopent-2-enone (XIV). The crude material was chromatographed on silica gel eluted from the column with 2% ether in benzene. The chromatographed product was recrystallized once from

hexane to produce a sample, which melted at 80.5-81.5°, for analysis and kinetic experiments.

Anal.: Calc. for $C_{13}H_{12}O_2$; C, 84.75%, H, 6.57%. Found: 84.75% C, 6.61% H.

Infrared: 5.94 μ (i), 6.09 μ(i), 6.18 μ(i), 12.16 (i), 13.14 μ (i), 14.55 μ (i).

NMR: The spectrum of XIV consists of a 3 proton multiplet at 111 cps. for the methyl group, a 2 proton multiplet at 202 cps. for the methylene group, and a 7 proton multiplet for the five aromatic protons and the two vinylic protons.

3-Methylcyclopent-3-en-1,2-dione (XV)[35]

2-Methylcyclopent-2-enone (XXV), 10 g. (104 mmoles) and 10 g. (91 mmoles) of selenium dioxide and 10 ml. of acetic acid were placed in a 50 ml pear-shaped flask and warmed gently with a microburner. After the reaction commenced, the heat was removed and the reaction proceeded spontaneously to completion. The acetic acid was removed under reduced pressure and the residue was distilled at 0.5 mm. or less pressure. The yellow solid dione collected on the walls of the condenser and receiver. After recrystallization from ether, 3.32 g. (29%) of 3-methylcyclopent-3-en-1,2-dione (XV), m.p. 83-84°, was found.

Infrared: 5.61 μ (i), 5.80 μ (i), 6.16 μ (m).

Monotosylhydrazone of 3-methylcyclopent-3-en-1,2-dione[35]

A solution of 1.90 g. (0.173 mole) of 3-methylcyclopent-3-en-1,2-dione in 20 ml. of hot methanol was added to a solution of 3.13 g. (0.173 mole) of para-toluenesulfonhydrazide in 10 ml. of hot methanol. The solution was allowed to stand at room temperature for about 3 hours and then placed in the refrigerator overnight. The brownish crystals were filtered from the dark crown solution and recrystallized from methanol. Obtained in this manner were 1.84 g. (33%) of the monotosylhydrazone, m.p. 161-163°.

5-Diazo-2-methylcyclopent-2-enone (XVI)[35]

A solution of 1.08 g. (30 mmoles) of the monotosylhydrazone of 3-methylcyclopent-3-en-1,2-dione in 30 ml. of 0.1 N. sodium hydroxide solution was prepared. Methylene chloride, 40 ml., was added to this solution and the mixture was stirred magnetically for 30 minutes. At the end of this time the layers were separated, the methylene chloride solution was washed with water and dried over magnesium sulfate. After filtration, the solvent was removed under reduced pressure and the yellow residue of crude diazo-ketone was sublimed at less than 1 mm. of pressure. There were obtained 190 mg. (52%) of pure 5-diazo-2-methylcyclopent-2-enone (XVI), m.p. 52-52.5°.

Infrared: 4.79 μ (i), 6.05 μ (i), 7.38 μ (i), 10 28 μ (m).

NMR: The spectrum of XVI consists of a 3 proton multiplet at 108 cps. for the methyl group, a 2 proton multiplet at 214 cps. for the methylene group, and a 1 proton multiplet at 403 cps. for the vinylic proton.

Kinetics

Equipment

The instrument with which the near-infrared spectral measurements were made is a Beckman DK-2A ratio recording spectrophotometer.

Constant temperature for the kinetic measurements was maintained by use of the accessory constant temperature cell holder for the Beckman DK-2A. The cell holder was found to be able to maintain the desired temperature to within 0.5°.

Near-infrared silica cells with 1 mm. light paths and fitted with glass stoppers were purchased from Pyrocell Mfg. Co.

Calibration of the Beckman DK-2A

Standard samples of known concentration of HOD were prepared by first preparing a stock solution of HOD at a very accurately known concentration of HOD and then diluting samples of this solution by weight. Approximate dilutions

were made by volume and then each solution was weighed to within 0.00002 g. using a very accurate microbalance.

The stock solutions used were sealed in small Erlenmeyer flasks under dry nitrogen. Transfers were made with a syringe and hypodermic needle, withdrawing samples through a rubber septum. After the standard solutions were prepared, their spectra versus a blank cell containing the HOD free stock solution were run in the 2.8 to 3.0 micron region of the near infrared.

The points thus obtained were plotted on a large graph, and the curve was used as a direct reference for the determination of the concentration of HOD for the various kinetic runs. The data from which the calibration curve was plotted are presented in Table 2.

Preparation of solutions

Stock solutions of triethylamine and D_2O were prepared which were 4 and 20 molar respectively. The solvent for these stock solutions was N,N-dimethylformamide. The dimethylformamide (DMF) was dried by allowing it to flow through a 16 inch column of molecular sieves (type 4A), and then distilling the dry DMF through a 30 inch, insulated, electrically heated column which was packed with 1/4 inch Pyrex helices. A constant boiling middle fraction was used as the solvent for all solutions used for kinetics, b.p. 150.8°. The

Table 2. Data for calibration curve of M HOD vs. A

Molarity HOD	Absorbance (A)
0.0000	0.000
0.0100	0.067
0.0202	0.108
0.0305	0.165
0.0411	0.217
0.0504	0.258
0.0603	0.337[a]
0.0709	0.339
0.0808	0.365
0.0926	0.410
0.1029	0.436
0.1225	0.494
0.1439	0.548
0.1631	0.580
0.1833	0.618
0.2065	0.651
0.2449	0.702
0.2687	0.728
0.3135	0.769
0.3407	0.800
0.3647	0.816
0.4071	0.846

[a]This point was rejected because it came nowhere near a smooth curve plotted through the other points.

stock DMF was stored in a dessicator in a standard taper flask with a Pyrex stopper.

The triethylamine was dried by distillation from P_2O_5. Again, only the middle portion of a constant boiling fraction was used, b.p. 88.3°. Spectral examination of both the DMF

and the triethylamine by both near-infrared and NMR gave no indication of any water being present. A solution of 1 microliter of water in 1 ml. of DMF was prepared. The NMR spectrum of this solution gave very strong indications of the presence of water. It was estimated that water present in amounts as low as 0.001% could be detected by NMR.

The D_2O which was used for the kinetic experiments was purchased from General Dynamics Corporation and was analyzed as greater than 99.7% D_2O.

The stock solutions of triethylamine and D_2O were prepared in 50 and 100 ml. volumetric flasks respectively, and stored in the same dessicator as the stock of dry DMF solvent. The D_2O solution appeared to remain as prepared indefinitely. However, the triethylamine solution slowly turned a yellowish-brown color and, therefore, was periodically prepared fresh.

Kinetic procedure

A sample of exactly 1 mmole of the compound to be exchanged was accurately weighed (to within 0.2 mg.) into a 1 ml. volumetric flask. A fresh sample of exchange solvent was prepared by pipetting 1.25 ml. each of the triethylamine and D_2O stock solutions into a 5 ml. volumetric flask and filling the flask to the mark with dry DMF. This solution was used as a reference solvent to fill the reference cell and also to fill the sample cell when balancing the instrument. After the

instrument was balanced and a good baseline was obtained, the sample cell was emptied and dried, and the kinetic solution was prepared.

Into the 1 ml. volumetric flask containing the previously weighed out sample were pipetted 0.25 ml. of both the triethylamine and D_2O stock solutions, in that order. The flask was filled to the mark with dry DMF. After shaking the sample well, a portion of the solution was transferred to the sample cell using a syringe and needle. This transfer was accomplished as quickly as possible to avoid uptake water from the atmosphere. The filled cell was stoppered and placed into the cell holder. After a few seconds, the clock was started and the first point taken. Later points were taken at appropriate intervals as the exchange proceeded.

The exchange of 5-benzylidene-2-isobutoxycylopent-2-enone, because of its slower rate, was carried out using a slightly different procedure. An exact 5 mmole sample was accurately weighed into a 5 ml. volumetric flask and 1.25 ml. each of the D_2O and triethylamine stock solutions were transferred into the flask and DMF was added to the mark. Since the compound was not soluble enough at room temperature so that 1 molar solution could be prepared, it was necessary to warm the solution to approximately 50° to effect solution. When the solution had been prepared, samples of approximately 0.3 ml. were transferred into small Pyrex vials, which had

been sealed at one end and constricted at the other end, and sealed. The tubes were placed in a basket and lowered into an oil bath regulated to 79.98 ± 0.02°. After several minutes during which time thermal equilibrium was reached, the first point was removed from the bath. Later tubes were removed at 1 hour intervals and placed in ice until all the tubes had been removed from the bath. At this time, the tubes were emptied directly into the cells and their absorbances were measured. For this purpose the tubes had to be warmed to redissolve the benzylidene compound and the cell holder was regulated to 50° to prevent the compound from crystallizing in the cell.

Calculation of rate constants

For all runs which were slow enough, it was assumed that it would take about 10 minutes for the cell and its contents to reach thermal equilibrium with the cell holder, when calculating the rate of the reaction. This could not be done for the most rapid exchange.

The absorbance of the solution at any time could be read directly from the spectra as recorded by the DK-2A. In calculating the rates, it was assumed that they would be pseudo-first order, at least over the first 50% of exchange of 1 proton. This is the same assumption made by Dessy *et al.*[51] That this assumption is valid appears reasonable when one

examines the rates that were calculated using this assumption.

The compounds followed the rate law $dx/dt = -kx$. This equation was rewritten as $k = \frac{2.303}{t} \log(A_0/A_0-x)$. From this equation, in which t = time in seconds, A_0 = concentration in moles per liter of reactant at time zero and x = concentration of HOD in moles per liter at time t, the rates of the reactions were calculated. The rate constants thus obtained were then divided by the number of protons available for exchange to correct for statistical effects.

Table 3 (page 72) presents the results which were obtained from the various runs in somewhat more detail than Table 1 in the Discussion section of this work.

Product analyses

Samples of the compounds after exchange were isolated by evaporating the solvent at low temperature and pressure. NMR spectra of the three solid compounds obtained in this manner showed that exchange occurred only at the position expected and that there was no significant decomposition of the compounds under the conditions of exchange.

Since cyclopent-2-enone and DMF boil at very nearly the same temperature, product analysis was not attempted for this exchange. However, Lyons'[53] data show that under his conditions (Na_2CO_3 in D_2O) the only exchange which occurs is at the alpha position. Also, the exchange solution was com-

pletely colorless at the end of the exchange. This is only weak negative evidence, but it indicates that no significant decomposition occurred.

No attempt was made to obtain a product analysis on the cyclopentanone exchange. The only possible positions from which a proton could be abstracted by the weak base used are the two alpha positions.

Table 3. Summary of results of kinetic measurements

Compound	$K_{40}sec^{-1}$[a]	Average $K_{40}sec^{-1}$	Relative rate
5-Benzylidene-2-methylcyclopent-2-enone	$1.02 \pm 0.05 \times 10^{-5}$ $1.00 \pm 0.03 \times 10^{-5}$	1.01×10^{-5}	1
5-Diazo-2-methylcyclopent-2-enone	$4.27 \pm 0.35 \times 10^{-4}$ $4.39 \pm 0.24 \times 10^{-4}$	4.33×10^{-4}	42.9
Cyclopent-2-enone alpha protons	$7.50 \pm 0.35 \times 10^{-5}$ $7.70 \pm 0.25 \times 10^{-5}$	7.60×10^{-5}	7.5
Cyclopentanone	$6.28 \pm 0.35 \times 10^{-5}$ $7.55 \pm 0.33 \times 10^{-5}$	6.91×10^{-5}	6.8
Compound	$K_{80}sec^{-1}$[a]	Average $K_{80}sec^{-1}$	Relative rate
5-Benzylidene-2-methylcyclopent-2-enone	$1.92 \pm 0.11 \times 10^{-4}$ $1.89 \pm 0.12 \times 10^{-4}$	1.91×10^{-4}	62.1
5-Benzylidene-2-isobutoxycyclopent-2-enone	$3.05 \pm 0.23 \times 10^{-6}$ $3.11 \pm 0.23 \times 10^{-6}$	3.08×10^{-6}	1

[a]The rate constants have been corrected for statistical effects.

Table 4. Exchange of 5-benzylidene-2-methylcyclopent-2-enone. Weight sample: 184.3 mg. Volume: 1.00 ml. Temperature: 40°. Run number 1.

Time sec.	A	X	K x 10^5	
0	0.444	0.1040		
1199	495	1226	1.76	
1498	511	1288	1.87	$K = 2.04 \pm 0.10 \times 10^{-5}$
1800	522	1334	1.85	
2099	532	1376	1.82	$K_{corr} = 1.02 \pm 0.05 \times 10^{-5}$
2399	541	1426	1.83	
2699	555	1480	1.87	
3001	567	1534	1.89	
3299	578	1600	1.96	
3599	589	1654	1.97	
3901	599	1722	2.02	
4201	610	1791	2.08	
4500	616	1828	2.04	
4800	624	1880	2.05	
5100	633	1942	2.08	
5400	641	1992	2.08	
5700	650	2056	2.11	
5999	659	2120	2.14	
6301	666	2171	2.14	
6609	676	2245	2.18	
6902	681	2284	2.16	
7199	688	2339	2.17	
7499	695	2396	2.18	
7799	699	2430	2.16	
8102	705	2480	2.16	
8400	710	2523	2.15	
8700	711	2532	2.09	
9001	718	2593	2.11	
9300	721	2621	2.09	
9601	728	2684	2.11	
9901	735	2751	2.14	

Table 5. Exchange of 5-benzylidene-2-methylcyclopent-2-enone. Temperature: 40°. Run number 2.

Time sec.	A	X	K x 10^5	
0	0.610	0.1790		
1201	640	1988	2.03	
1500	645	2022	1.96	$K = 2.01 \pm 0.05 \times 10^{-5}$
1800	657	2106	2.18	
2101	661	2132	2.02	$K_{corr} = 1.00 \pm 0.03 \times 10^{-5}$
2401	667	2179	2.03	
2701	672	2216	1.97	
3002	675	2239	1.88	
3300	685	2315	2.00	
3601	689	2348	1.92	
3901	695	2397	1.97	
4201	699	2430	1.93	
4501	707	2493	1.96	
4801	712	2543	2.00	
5101	717	2585	2.00	
5404	723	2639	2.02	
5701	727	2677	2.00	
6002	734	2740	2.04	
6302	745	2847	2.18	

5-Benzylidene-2-methylcyclopent-2-enone:

Run #1 K = 1.02
Run #2 = 1.00

Average 1.01 x 10^{-5}

Table 6. Exchange of 5-benzylidene-2-methylcyclopent-2-enone. Weight sample: 184.2 mg. Volume: 1.00 ml. Temperature: 80°. Run number 1.

Time sec.	A	X	K x 10^4	
0	0.529	0.1362		
61	569	1554	3.68	
180	630	1920	3.71	$K = 3.84 \pm 0.22 \times 10^{-4}$
239	651	2065	3.54	
299	678	2260	3.67	$K_{corr} = 1.92 \pm 0.11 \times 10^{-4}$
421	725	2658	3.85	
480	745	2846	3.92	
542	764	3042	3.98	
600	780	3215	4.01	
660	796	3400	4.06	
721	811	3585	4.12	
783	827	3792	4.21	
852	839	3962	4.20	

Table 7. Exchange of 5-benzylidene-2-methylcyclopent-2-enone. Temperature: 80°. Run number 2.

Time sec.	A	X	K x 10^4	
0	0.529	0.1362		
61	565	1532	3.26	
122	599	1722	3.48	$K = 3.78 \pm 0.24 \times 10^{-4}$
182	628	1906	3.57	
243	651	2065	3.49	$K_{corr} = 1.89 \pm 0.12 \times 10^{-4}$
303	678	2260	3.62	
363	699	2430	3.63	
423	721	2620	3.71	
485	744	2837	3.81	5-Benzylidene-2-methyl-
544	764	3042	3.97	cyclopent-2-enone:
605	779	3204	3.96	Run #1 K = 1.92
664	796	3400	4.05	Run #2 = 1.89
725	809	3560	4.05	
785	823	3740	4.10	Average 1.91×10^{-4}
845	836	3918	4.15	

Table 8. Exchange of 5-diazo-2-methylcyclopent-2-enone.
Weight sample: 122.2 mg. Volume: 1.00 ml.
Temperature: 40°. Run number 1.

Time sec.	A	X	K x 10^4	
0	0.500	0.1256		
61	583	1628	7.12	
122	651	2065	7.95	$K = 8.55 \pm 0.70 \times 10^{-4}$
181	707	2498	8.46	
244	758	2978	9.36	$K_{corr} = 4.27 \pm 0.35 \times 10^{-4}$
303	792	3354	9.06	
363	825	3765	9.30	

Table 9. Exchange of 5-diazo-2-methylcyclopent-2-enone.
Temperature: 40°. Run number 2.

Time sec.	A	X	K x 10^4	
0	0.688	0.2340		
42	719	2602	8.28	
82	744	2837	8.18	$K = 8.77 \pm 0.48 \times 10^{-4}$
122	768	3084	8.36	
156	789	3320	8.76	$K_{corr} = 4.39 \pm 0.24 \times 10^{-4}$
192	809	3560	9.02	
227	839	3820	9.45	
265	850	4125	10.00	

5-Diazo-2-methylcyclopent-2-enone:

Run #1 K = 4.27
Run #2 = 4.39

Average 4.33×10^{-4}

Table 10. Exchange of cyclopent-2-enone. Weight sample: 82.2 mg. Volume: 1.00 ml. Temperature: 40^{o}. Run number 1.

Time sec.	A	X	K x 10^4	
0	0.609	0.1782		
57	621	1858	1.59	
93	626	1894	1.23	$K = 1.50 \pm 0.07 \times 10^{-4}$
124	630	1920	1.36	
152	638	1984	1.64	$K_{corr} = 7.50 \pm 0.35 \times 10^{-5}$
184	643	2008	1.51	
213	647	2036	1.47	
243	651	2065	1.44	
276	657	2106	1.52	
307	664	2156	1.53	
336	669	2194	1.45	
366	671	2208	1.54	
395	679	2269	1.54	
423	683	2300	1.56	
456	689	2348	1.51	
485	693	2380	1.49	
514	694	2389	1.55	
571	706	2490	1.59	
602	711	2532		

Table 11. Exchange of cyclopent-2-enone. Temperature: 40°. Run number 2.

Time sec.	A	X	K x 10^4	
0	0.723	0.2640		
115	737	2770	1.55	
142	741	2808	1.62	$K = 1.54 \pm 0.05 \times 10^{-4}$
170	745	2846	1.67	
198	747	2866	1.57	$K_{corr} = 7.70 \pm 0.25 \times 10^{-5}$
226	749	2886	1.50	
254	751	2906	1.45	
281	755	2946	1.51	
132	759	2988	1.55	
339	764	3040	1.65	
367	766	3062	1.61	
394	767	3074	1.54	
421	771	3107	1.55	
449	771	3107	1.46	
476	774	3150	1.50	
504	778	3192	1.55	
530	781	3226	1.56	
558	784	3260	1.57	
585	788	3308	1.62	
612	791	3342	1.63	
642	793	3364	1.61	
670	793	3364	1.54	

Cyclopent-2-enone:

Run #1 K = 7.50
Run #2 = 7.70

Average 7.60 x 10^{-5}

Table 12. Exchange of cyclopentanone. Weight sample: 84.2 mg. Volume: 1.00 ml. Temperature: 40°. Run number 1.

Time sec.	A	X	K x 10^4	
0	0.537	0.1399		
120	584	1634	2.31	
180	601	1734	2.21	$K = 2.51 \pm 0.14 \times 10^{-4}$
241	621	1858	2.28	
302	641	1994	2.37	$K_{corr} = 6.28 \pm 0.35 \times 10^{-5}$
361	659	2120	2.42	
422	673	2223	2.38	
482	691	2364	2.47	
543	708	2506	2.54	
602	716	2576	2.44	
662	731	2712	2.50	
723	743	2801	2.46	
782	757	2967	2.57	
844	770	3160	2.71	
905	782	3239	2.66	
964	792	3354	2.67	
1024	800	3450	2.66	
1084	808	3548	2.65	
1146	819	3689	2.70	
1206	830	3833	2.76	

Table 13. Exchange of cyclopentanone. Temperature: 40°. Run number 2.

Time sec.	A	X	K x 10^4	
0	0.777	0.3181		
32	782	3239	2.67	
61	789	3319	3.35	$K = 3.02 \pm 0.13 \times 10^{-4}$
90	795	3389	3.43	
120	799	3437	3.19	$K_{corr} = 7.55 \pm 0.33 \times 10^{-5}$
152	804	3498	3.13	
181	807	3536	2.95	
209	812	3600	3.03	
240	816	3650	2.97	
271	819	3689	2.86	
299	822	3726	2.78	
327	831	3847	3.14	
353	832	3860	2.97	
383	837	3932	3.04	
410	840	3978	3.03	
435	842	4008	2.97	
461	847	4085	3.08	
488	849	4115	3.01	

Cyclopentanone:

Run #1 K = 6.28
Run #2 = 7.55

Average 6.91×10^{-5}

Table 14. Exchange of 5-benzylidene-2-isobutoxycyclopent-2-enone. Weight sample: 1.2114 g. Volume: 5.00 ml. Temperature: 80°. Run number 1.

Time sec. x 10^4	A	X	K x 10^6	
0	0.011	0.0016		
0.36	138	0250	6.60	
1.08	335	0699	6.58	$K = 6.10 \pm 0.46 \times 10^{-6}$
1.80	457	1086	6.29	
4.086	650	2055	5.59	$K_{corr} = 3.05 \pm 0.23 \times 10^{-6}$
5.08	700	2439	5.46	

Table 15. Exchange of 5-benzylidene-2-isobutoxycyclopent-2-enone. Temperature: 80°. Run number 2.

Time sec. x 10^4	A	X	K x 10^6	
0	0.140	0.0254		
0.36	254	0495	6.96	
0.72	337	0704	6.55	$K = 6.22 \pm 0.45 \times 10^{-6}$
1.08	409	0922	6.57	
1.44	463	1108	6.38	$K_{corr} = 3.11 \pm 0.23 \times 10^{-6}$
1.80	504	1262	6.06	
2.16	535	1389	5.74	
3.24	511	1794	5.30	

5-Benzylidene-2-isobutoxycyclopent-2-enone:

Run #1 K = 3.05
Run #2 = 3.11

Average 3.08 x 10^{-6}

SUMMARY

Several previously unreported compounds have been prepared in satisfactory yields. These include 5-benzylidene-2-methylcyclopent-2-enone (XIV), 5-benzylidene-2-isobutoxycyclopent-2-enone (XXIX), 5-benzylidene-2-benzyloxycyclopent-2-enone (XXX), 2-benzyloxycyclopent-2-enone (XXVII), 2-(N,N-dimethyl-α-aminobenzyl)-cyclopent-2-enone (XXI), 2-benzylidenecyclopent-3-ol-1-one (XXII), and ethyl 2-oxocyclopent-3-englyoxylate (XVIII).

Rates of deuterium exchange were measured for XIV, XXIX, 5-diazo-2-methylcyclopent-2-enone (XVI), and cyclopent-2-enone. Comparison of these rates supports the view that there is stabilization of an anion by participation of a fulvene moiety. These comparisons also suggest that the resonance energy of diazocyclopentadiene (VII) is greater than that of fulvene (I).

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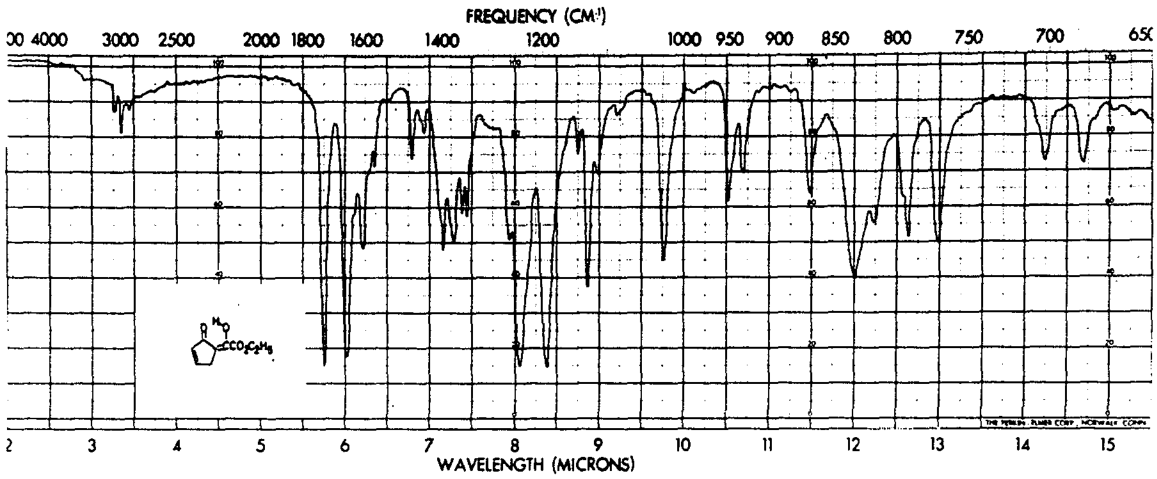
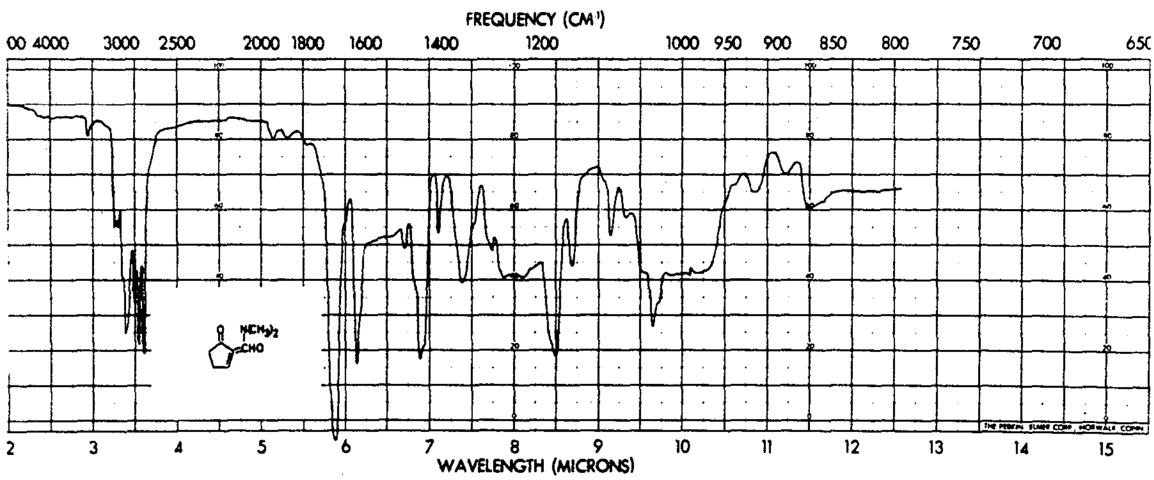
APPENDIX

Figure 13. Infrared spectrum of ethyl 2-oxocyclopent-3-englyoxylate (XVIII) (KBr)

Figure 14. Infrared spectrum of 2-(N,N-dimethyl-α-aminobenzyl)-cyclopent-2-enone (XXI) (CCl_4)

Figure 15. Infrared spectrum of 2-benzylidenecyclopent-3-ol-1-one (XXII) (KBr)


FREQUENCY (CM⁻¹)
4000 3000 2500 2000 1800 1600 1400 1200 1000 950 900 850 800 750 700 650
2 3 4 5 6 7 8 9 10 11 12 13 14 15
WAVELENGTH (MICRONS)


FREQUENCY (CM⁻¹)
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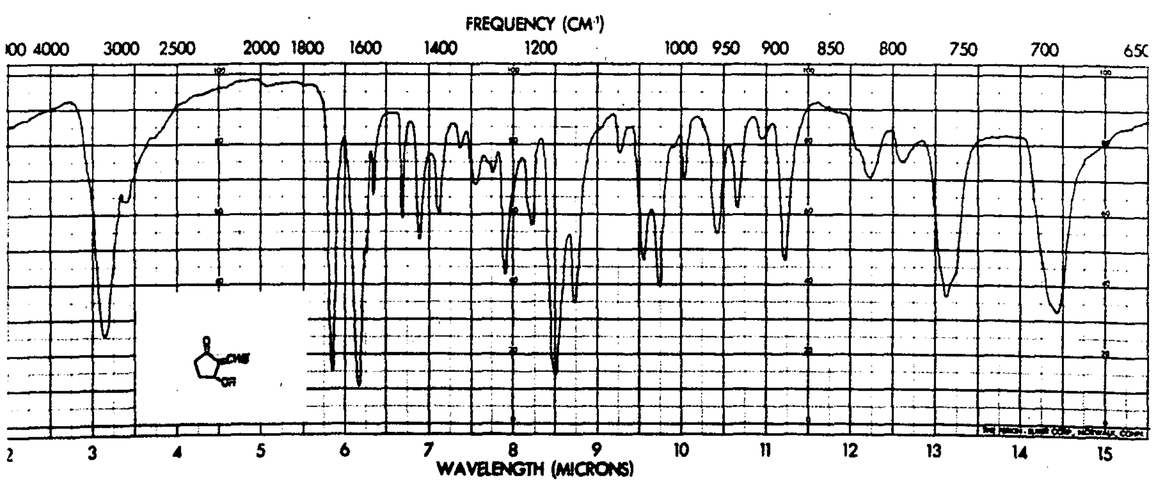
2 3 4 5 6 7 8 9 10 11 12 13 14 15
WAVELENGTH (MICRONS)


FREQUENCY (CM⁻¹)
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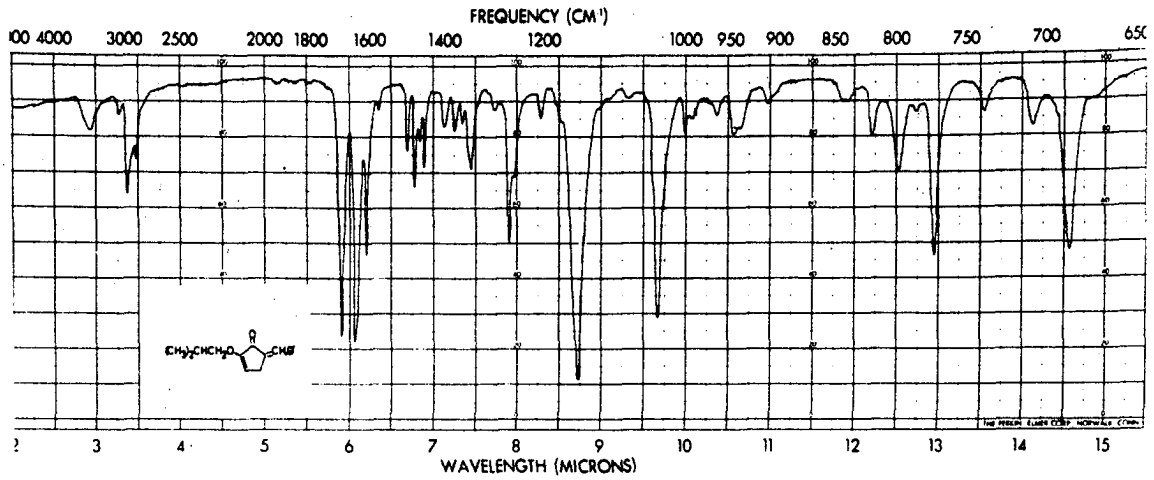
2 3 4 5 6 7 8 9 10 11 12 13 14 15
WAVELENGTH (MICRONS)

Figure 16. Infrared spectrum of 5-benzylidene-2-isobutoxy-cyclopent-2-enone (XXIX) (KBr)

Figure 17. Infrared spectrum of 2-benzyloxycyclopent-2-enone (XXVII) (KBr)

Figure 18. Infrared spectrum of 5-benzylidene-2-benzyloxy-cyclopent-2-enone (XXX) (KBr)


FREQUENCY (CM⁻¹)
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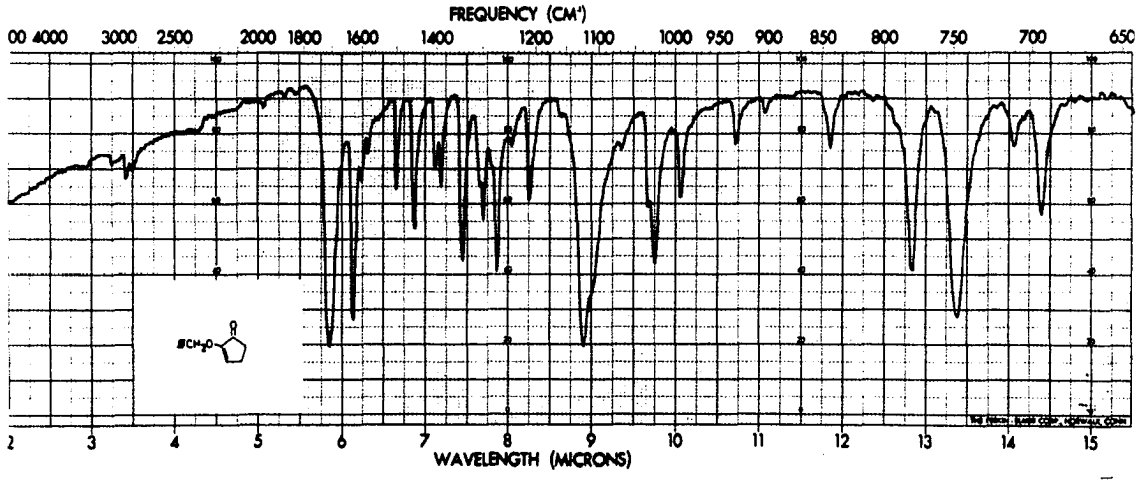
2 3 4 5 6 7 8 9 10 11 12 13 14 15
WAVELENGTH (MICRONS)


FREQUENCY (CM⁻¹)
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2 3 4 5 6 7 8 9 10 11 12 13 14 15
WAVELENGTH (MICRONS)

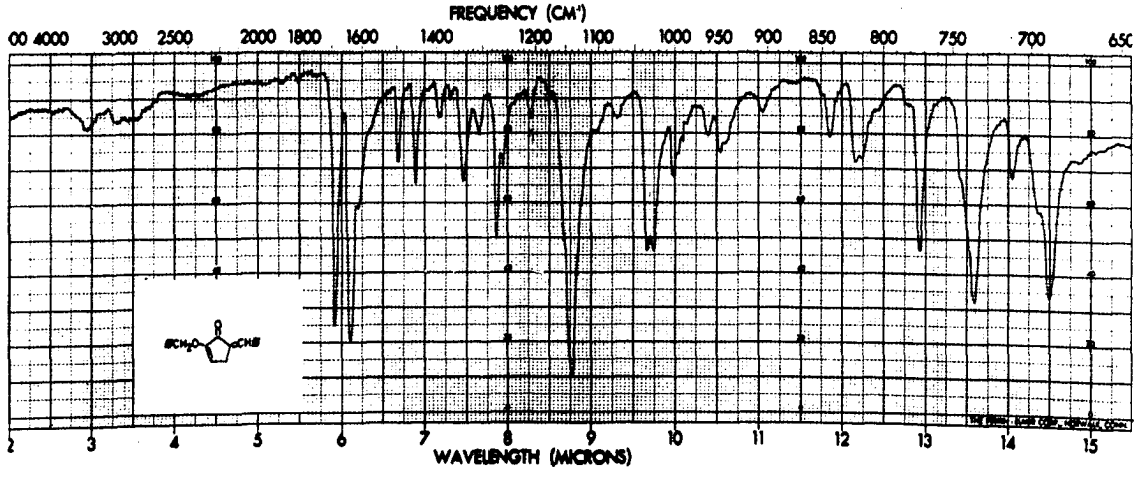

FREQUENCY (CM⁻¹)
00 4000 3000 2500 2000 1800 1600 1400 1200 1100 1000 950 900 850 800 750 700 650
2 3 4 5 6 7 8 9 10 11 12 13 14 15
WAVELENGTH (MICRONS)

Figure 19. Infrared spectrum of 5-benzylidene-2-methylcyclopent-2-enone (XIV) (KBr)

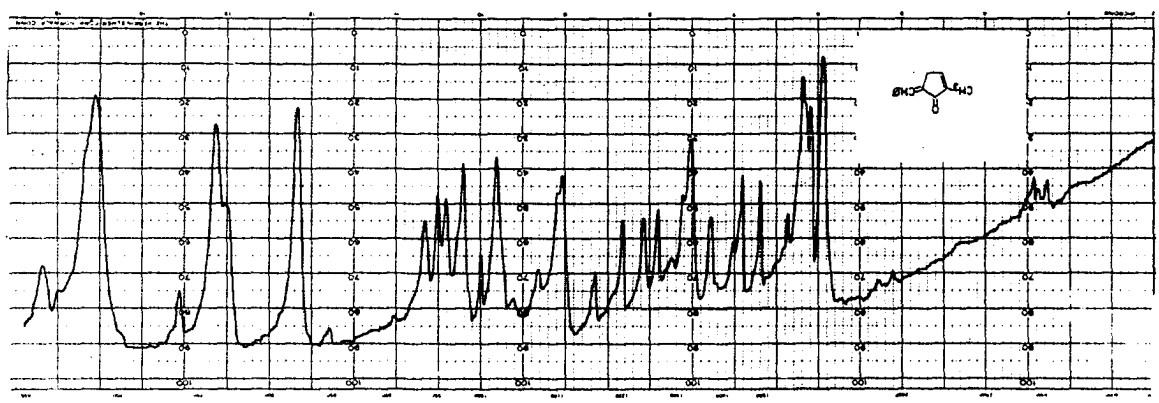
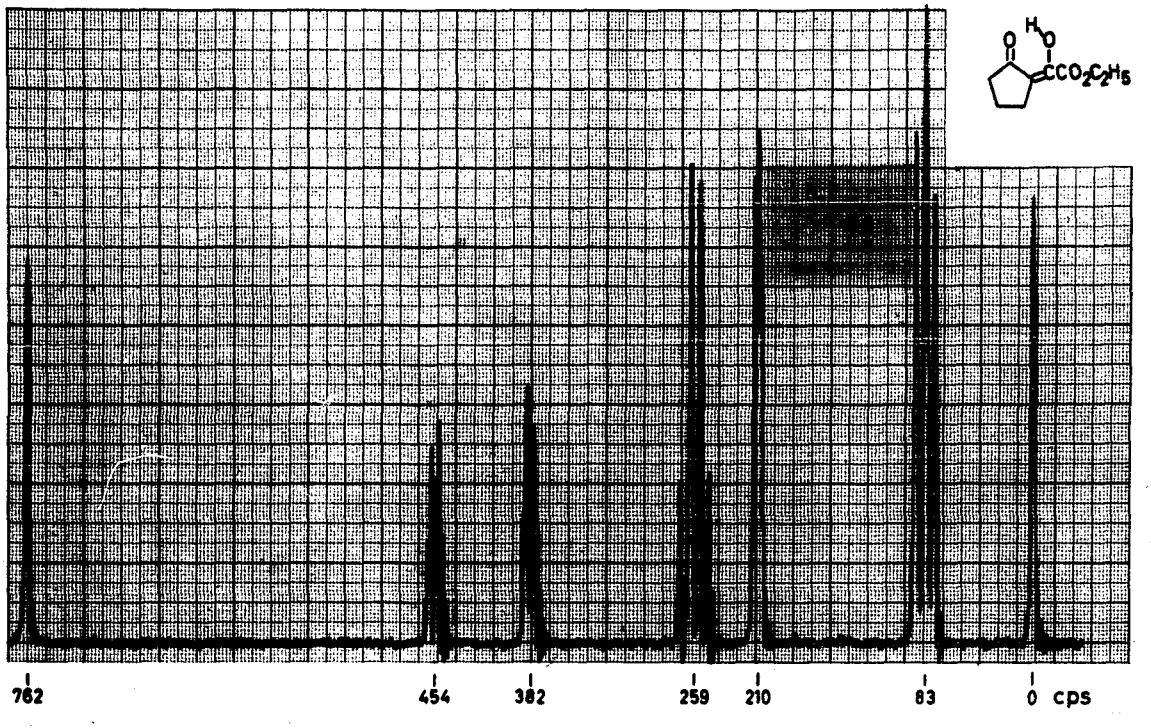


Figure 20. NMR spectrum of ethyl 2-oxocyclopent-3-englyoxylate (XVIII)

Figure 21. NMR spectrum of 2-benzyloxycyclopent-2-enone (XXVII)


782
454
382
259
210
83
0 cps

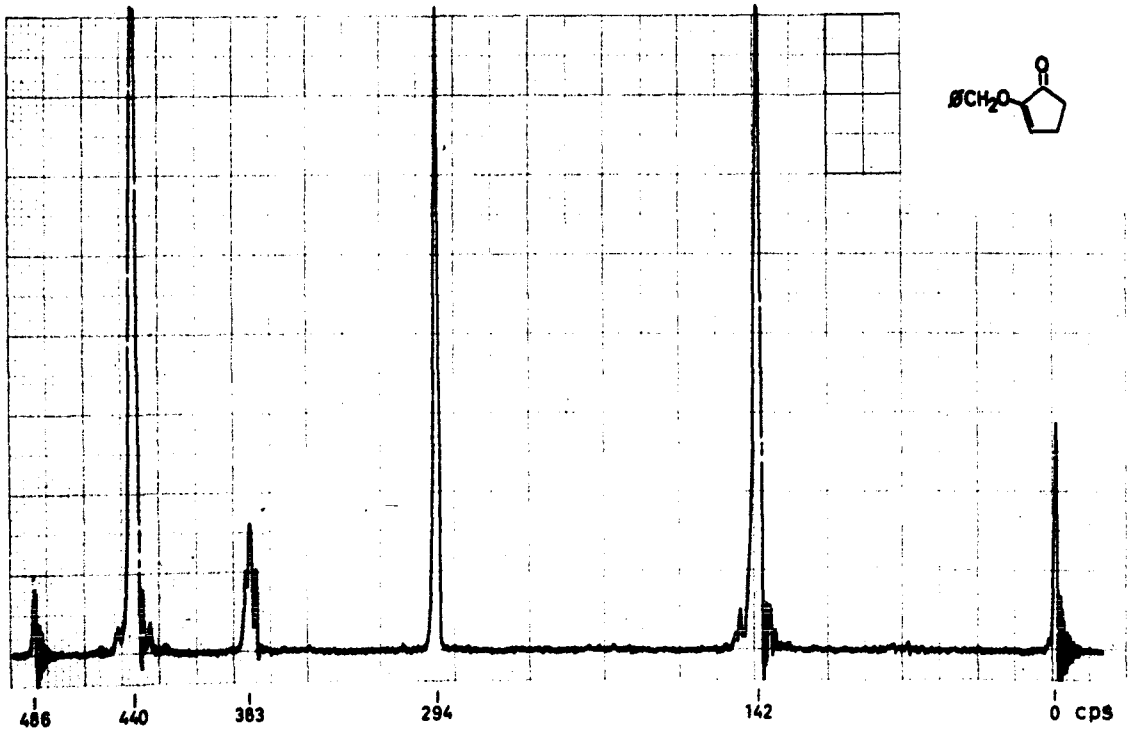
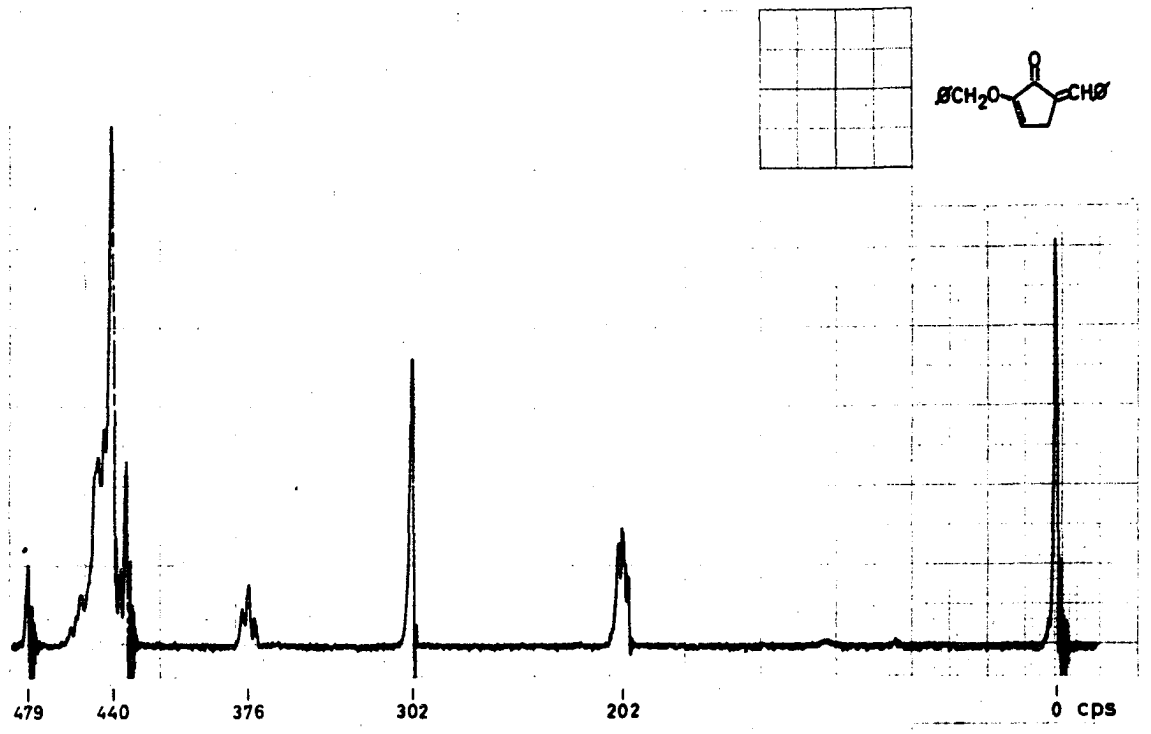

486
440
383
294
142
0 cps

Figure 22. NMR spectrum of 5-benzylidene-2-benzyloxy-cyclopent-2-enone (XXX)

Figure 23. NMR spectrum of 5-benzylidene-2-isobutoxy-cyclopent-2-enone (XXIX)


ØCH2O
CHØ
479
440
376
302
202
0 cps

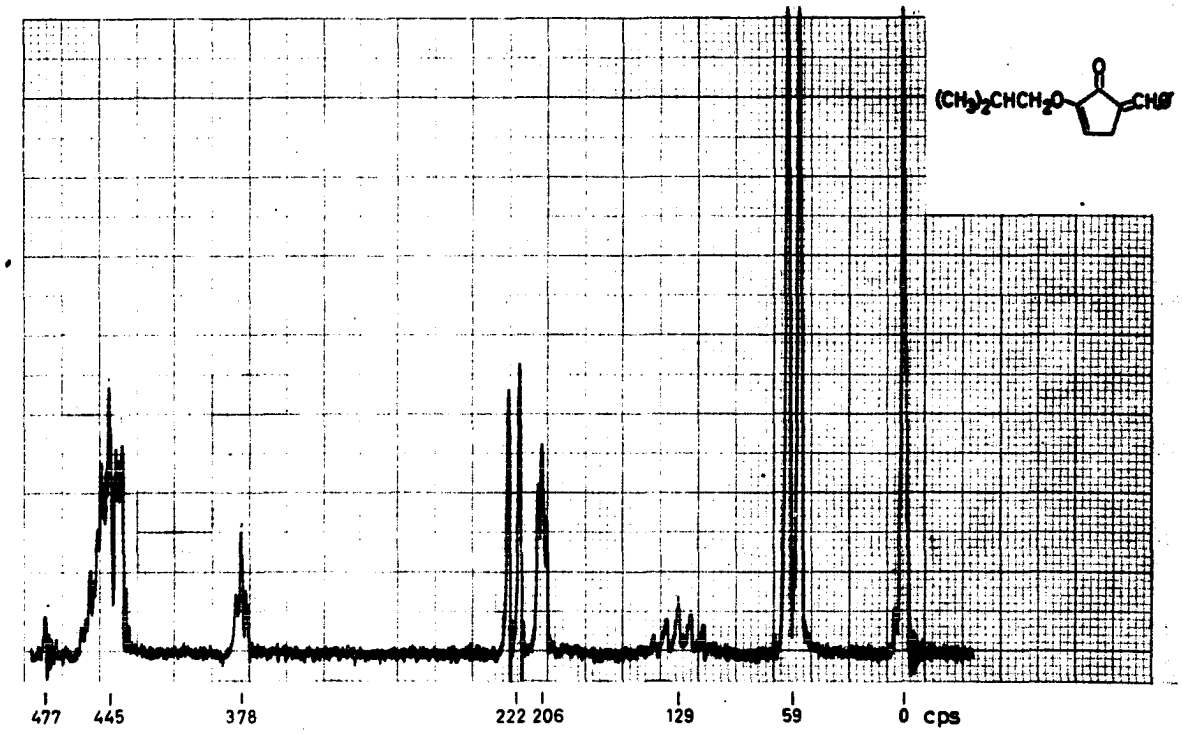
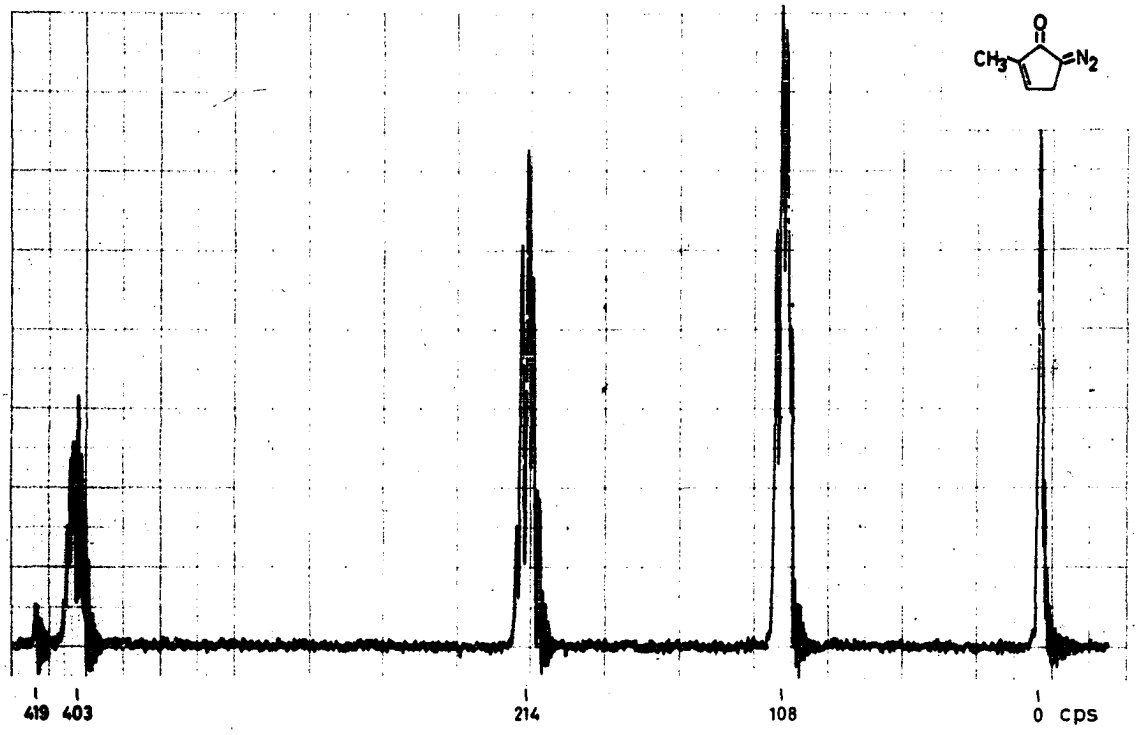

(CH3)2CHCH2O
CHØ
477
445
378
222 206
129
59
0 cps

Figure 24. NMR spectrum of 5-diazo-2-methylcyclopent-2-enone (XVI)

Figure 25. NMR spectrum of 5-benzylidene-2-isobutoxy-cyclopent-2-enone (XXIX) after exchange


419
403
214
108
0 cps

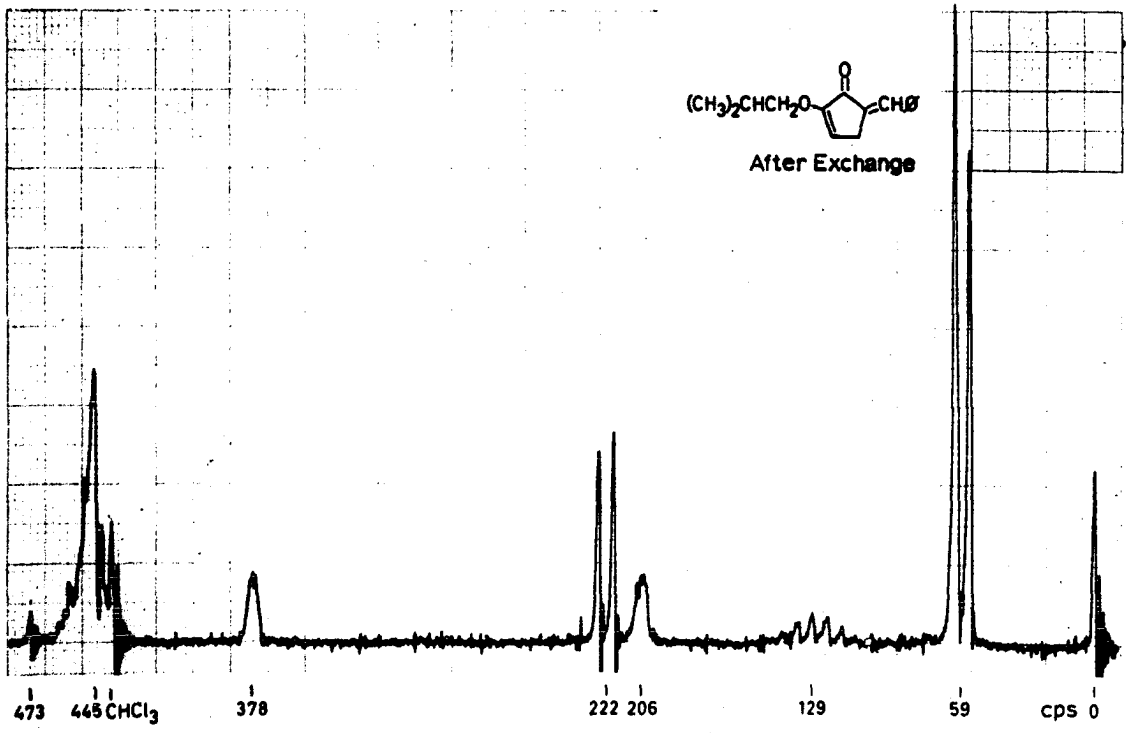
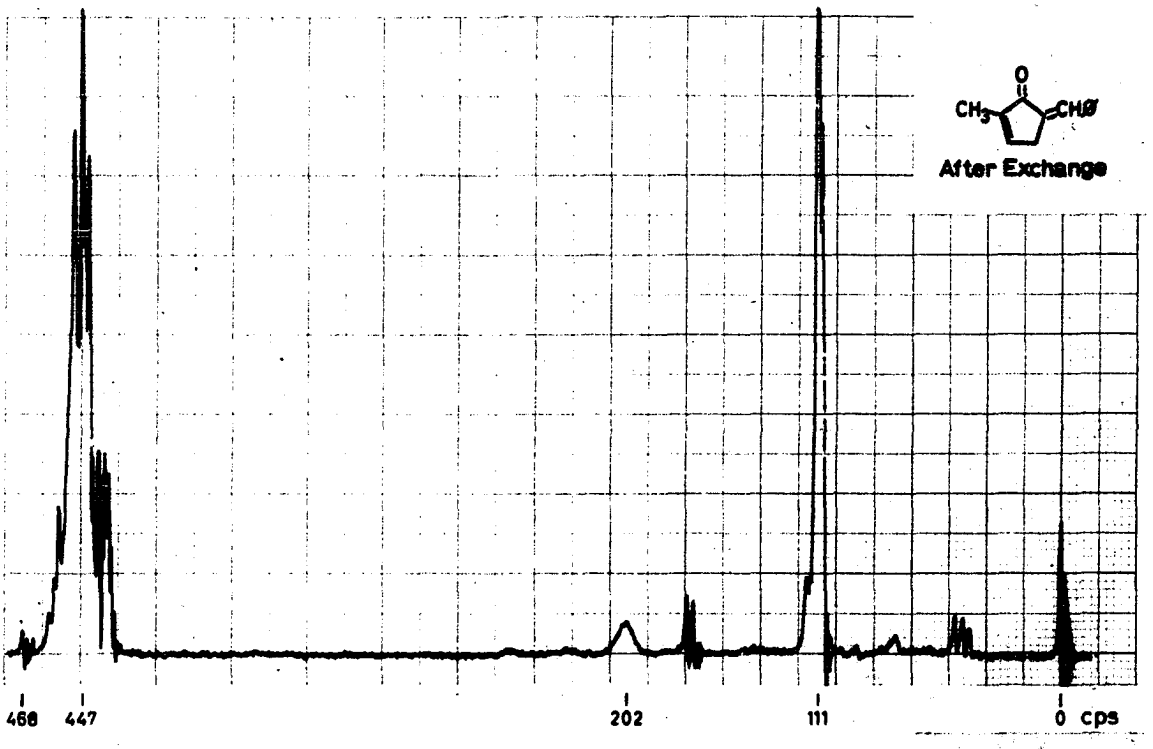
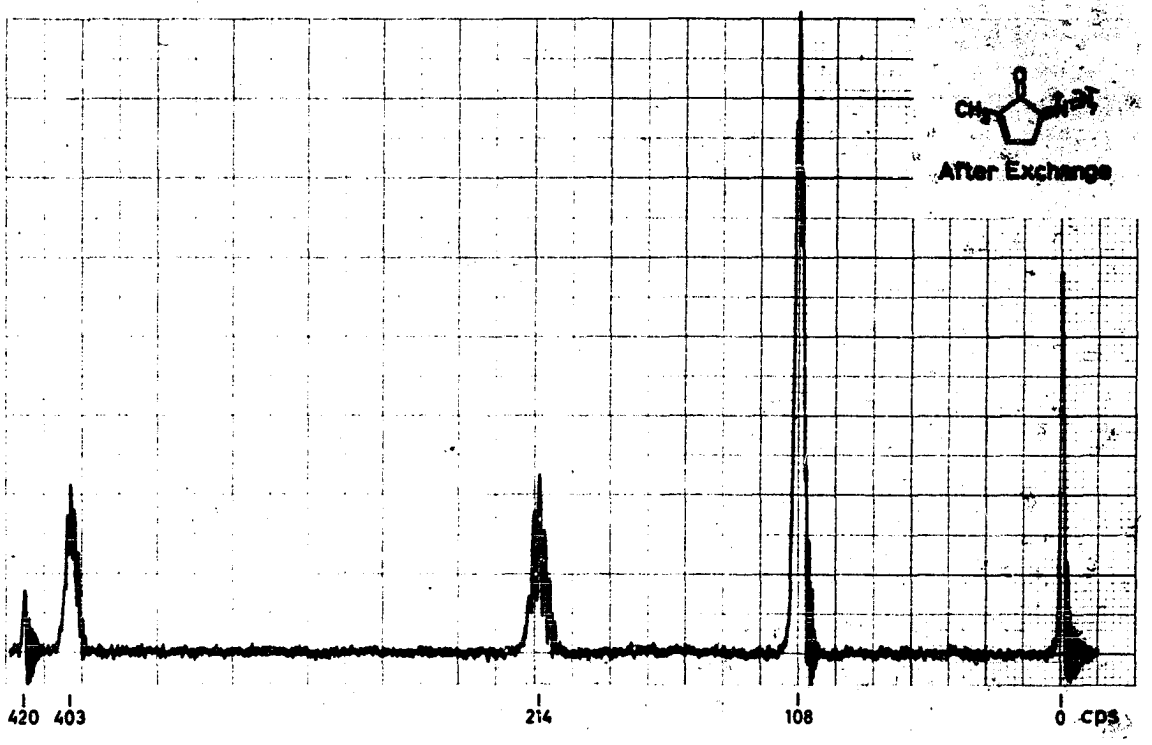

After Exchange
473
445
CHCl3
378
222
206
129
59
cps 0

Figure 26. NMR spectrum of 5-benzylidene-2-methylcyclopent-2-enone (XIV) after exchange

Figure 27. NMR spectrum of 5-diazo-2-methylcyclopent-2-enone (XVI) after exchange


After Exchange
468
447
202
111
0 cps


After Exchange
420
403
214
108
0 cps