ABSTRACT

PHOTOCHEMICAL REARRANGEMENT OF α,β-EPOXY KETONES. AN ELABORATION OF THE MECHANISM

by Charles S. Markos

A study of the photochemical rearrangements of a number of α,β-epoxy ketones was undertaken to elaborate the mechanism of the shift of a β-substituent to form a β-dicarbonyl compound.

The order of migratory aptitudes found for β-substituents is: benzhydryl and benzyl > hydrogen > methylene > methyl >> phenyl. With the exception of hydrogen, this order parallels the stability of the corresponding radical, and radical characteristics are suggested for intermediates or transition states in the mechanism.

Although a β-benzyl substituent is partly diverted to free radical products (*eg*., dibenzyl), the stereospecificity of the rearrangement, the migratory aptitude of β-hydrogen and the formation of a strained rearrangement product (2-acetyl-1-hydroxycyclobutene from 3-methyl-2,3-epoxycyclopentanone) all argue against a general fragmentation-recombination mechanism for the rearrangement. The 1,3-diradical intermediate proposed for these rearrangements must be very short lived, since the pulegone oxide stereoisomers rearrange stereospecifically faster than they isomerize.

Studies with triplet state quenchers (piperylene) and sensitizers (acetophenone) indicate that the rearrangement

occurs only from the first excited singlet state [S_1] of the epoxy ketone. An alternate explanation for the rearrangement of a β-hydrogen substituent was ruled out by the absence of bimolecular hydrogen abstraction involving a triplet excited state [T_1].

4-Methyl-3,4-epoxy-2-pentanone was rapidly photoreduced by tri-_n_-butyl stannane ($\Phi = 0.65$). This reaction apparently proceeds _via_ the triplet state [T_1] since it was completely quenched by solvent piperylene, leaving only photorearrangement to 3-methyl-2,4-pentanedione ($\Phi = 0.03$).

PHOTOCHEMICAL REARRANGEMENT OF α,β-EPOXY KETONES.

AN ELABORATION OF THE MECHANISM

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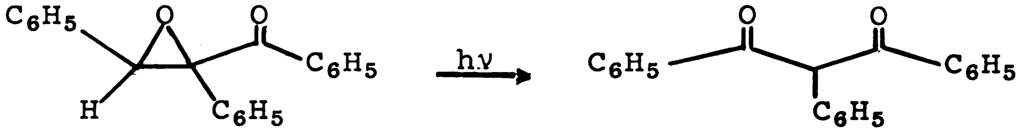
HISTORICAL AND INTRODUCTION

The photochemical rearrangement of α, β epoxy ketones has been known since 1918, when Bodforss (1) reported the conversion of chalcone oxide 1 to dibenzoyl phenylmethane 2 upon exposure to light (eq 1). More recently, Zimmerman (2) has shown that *trans*-dypnone oxide 3 is isomerized to the *cis*-isomer 4 photochemically (eq 2).

(1)



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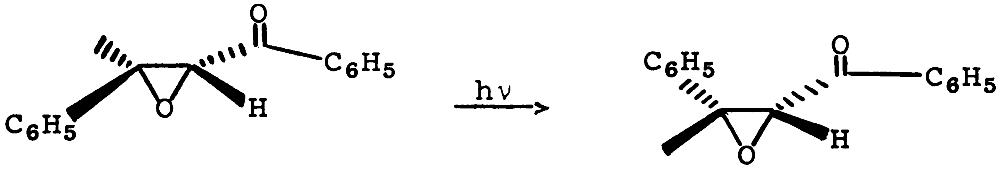
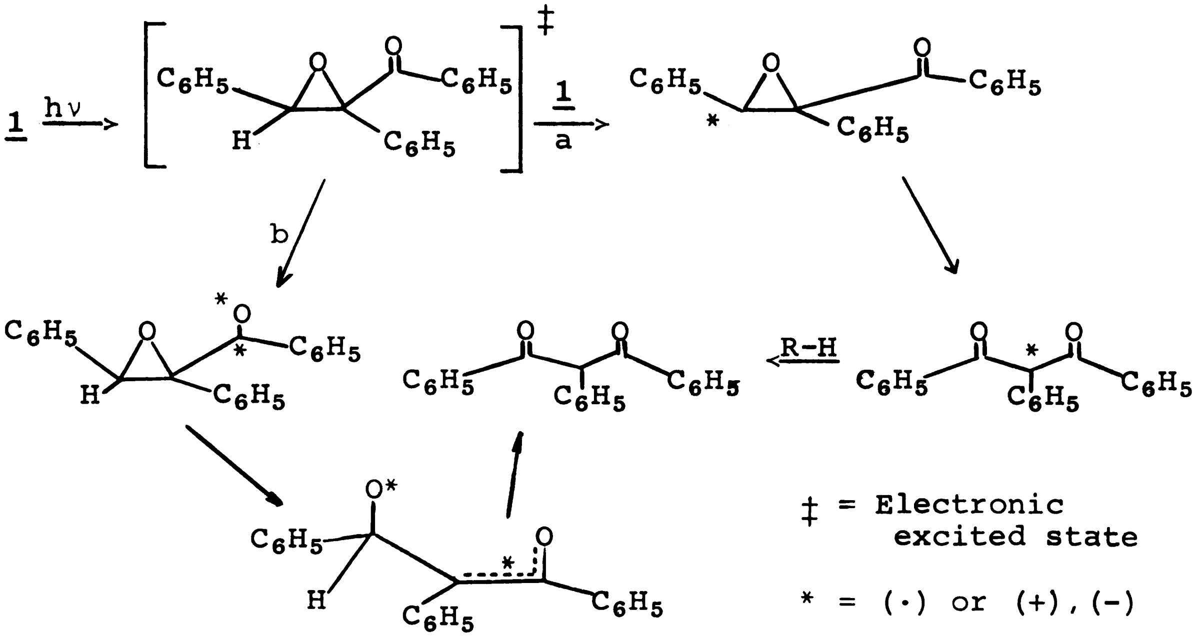


3 4

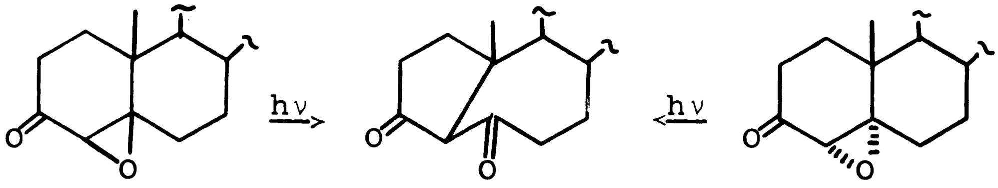
Several mechanistic interpretations of the reactions described by Bodforss and Zimmerman are possible. These may be classified as (a) intermolecular abstraction of a hydrogen atom, or (b) direct 1,2-hydrogen migration.

CHART I



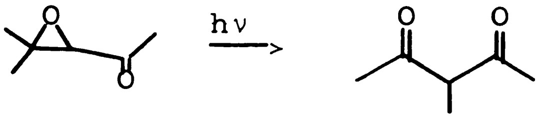
Jeger, Schaffner and Wehrli (3) then found that β-alkyl groups also shift in a similar manner (eq 3); consequently, mechanism (b) appeared to offer a more general rationale for the rearrangment.

(3)



Additional examples of alkyl group rearrangement were reported by Johnson, Dominy, and Reusch (4) (eq 4,5). These workers also noted a remarkable and unexpected preferential shift of a β-methylene over a phenyl group as illustrated in equation (6). Independent work by Zimmerman, Cowely, Tseng and Wilson (5) has disclosed a similar migrational order in the acyclic epoxy ketone 15 (eq 7).

(4)



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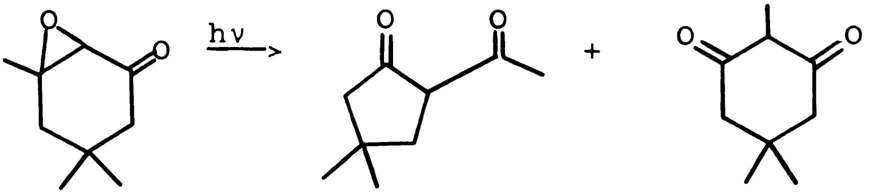
(5)



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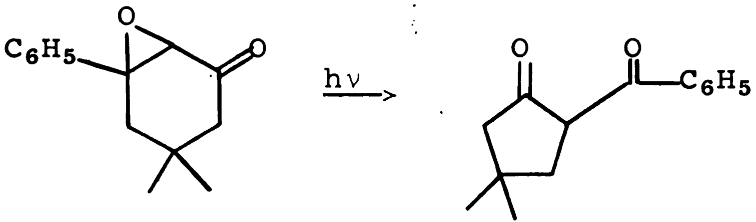
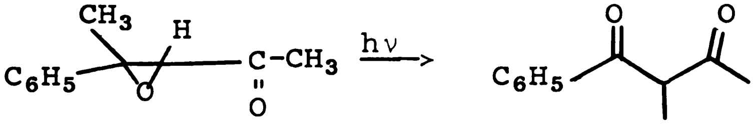
(6)



13 14

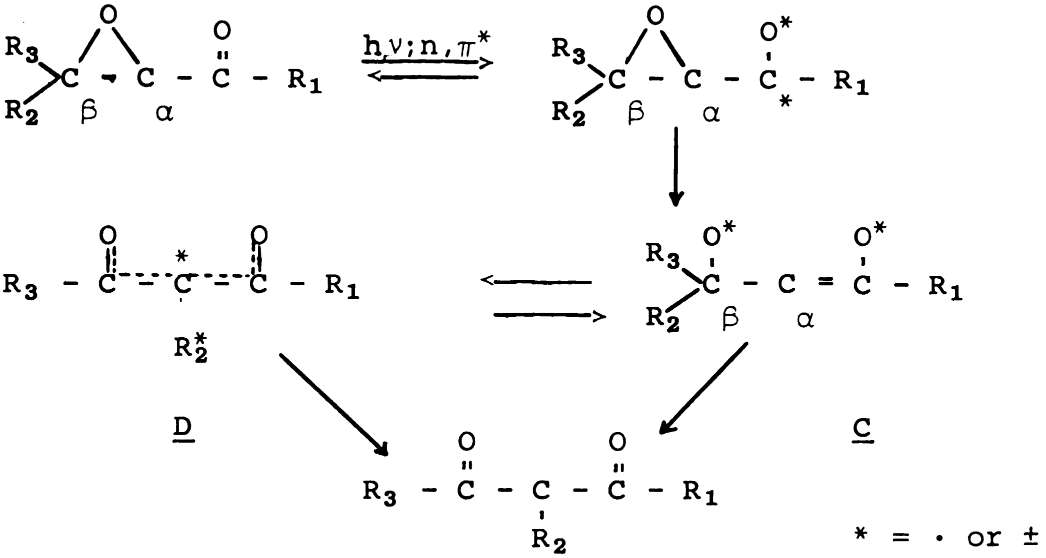
(7)



15 16

These facts led Reusch and Zimmerman to propose a mechanism (illustrated in Chart II) in which n, π^* excitation of the carbonyl group causes oxirane ring cleavage (5) to an intermediate C followed by rearrangment of a β-substituent.

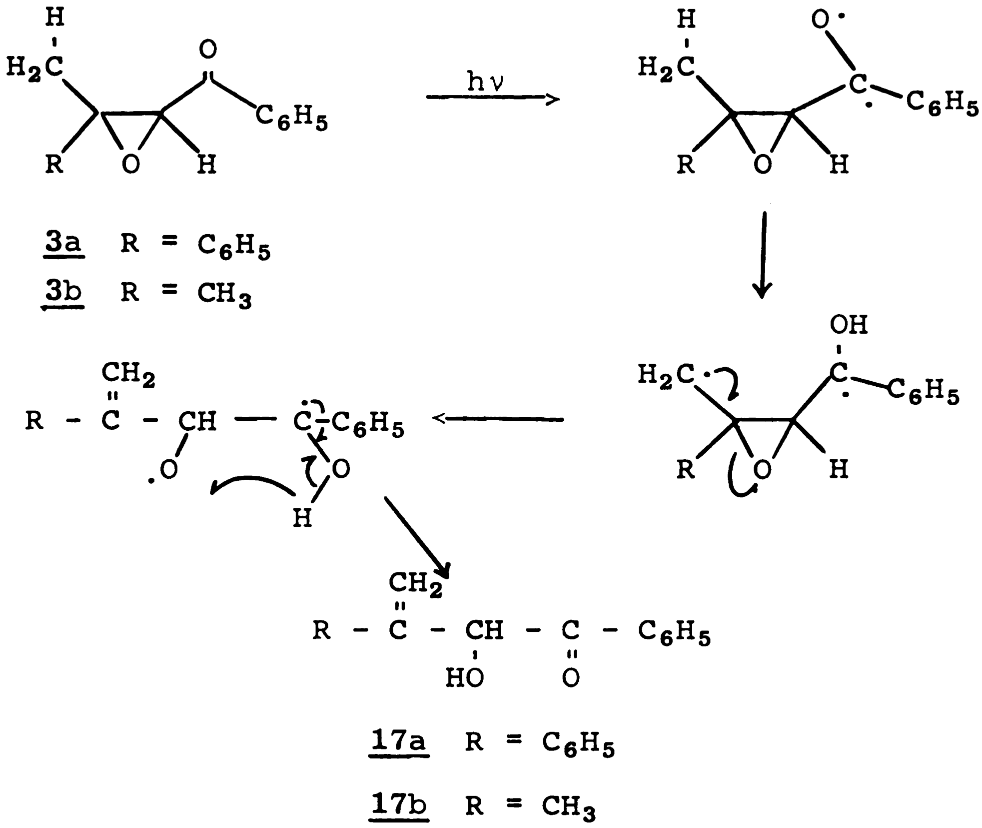
CHART II



This mechanism successfully rationalizes the effects of substituent variations. If R_1 = phenyl, oxirane ring opening to intermediate C is not favored because the reactive character of the excited carbonyl carbon would be delocalized by the phenyl group. In fact, Zimmerman and co-workers (5) have found that trans-dypnone oxide 3a gives 1,3-diphenyl-3-butene-2-ol-1-one 17a as the major photoproduct. Dimethyl acrylophenone 3b similarly gave 1-phenyl-3-methyl-3-butene-2-ol-1-one 17b. This transformation apparently proceeds via the well documented (6) abstraction of γ-alkyl hydrogen by the triplet state of an aryl ketone, as outlined in Chart III.

If R_1 is an alkyl group oxirane ring opening to intermediate C occurs, and the relative migrational aptitudes of the β-substituents must be determined in a subsequent step.

CHART III



3a R = C_6H_5

3b R = CH_3

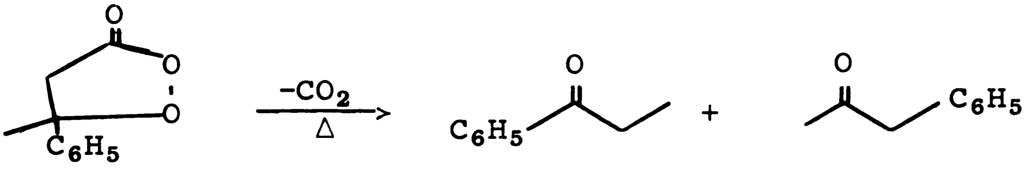
17a R = C_6H_5

17b R = CH_3

Lack of phenyl migration from intermediate C may be explained by assuming radical character in C, leading either to the radical pair D or to a transition state having more breaking of the C_β-R bond than making of C_α-R bond. In both cases, the migratory aptitude of the β-substituent should parallel the stability of the corresponding radical.

A fivefold preference for methyl migration *vs* phenyl in the thermal decomposition of β-methyl-β-phenyl-β-peroxypropiolactone (eq 8) was noted by Greene, Adam, and Knudsen (7) and a 1,3-diradical similar to intermediate C was suggested as an intermediate in this transformation.

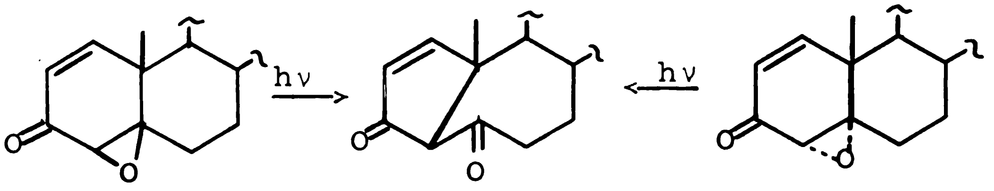
(8)



5 : 1

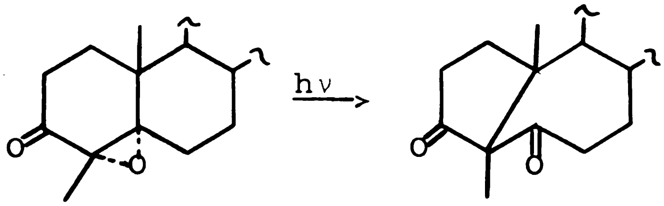
In stereochemically rigid steroidal epoxy ketones, Jeger and co-workers (3,8) have found similar 1,2-migrations of β-substituents to yield β-dicarbonyl compounds in yields ranging from 10 to 80% as shown in (eq 9-16).

(9)



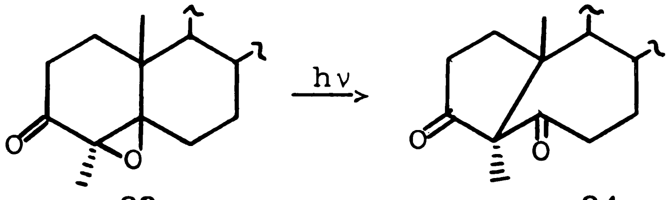
18 20 19

(10)



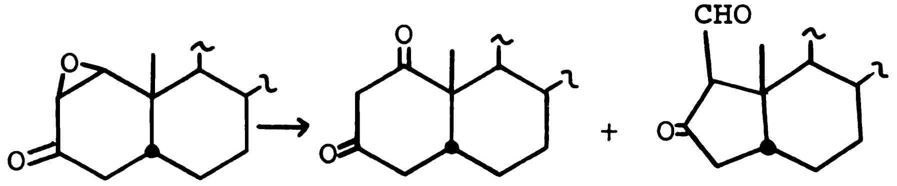
21 22

(11)



23 24

(12)



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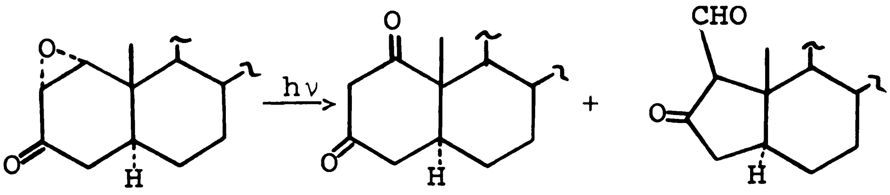
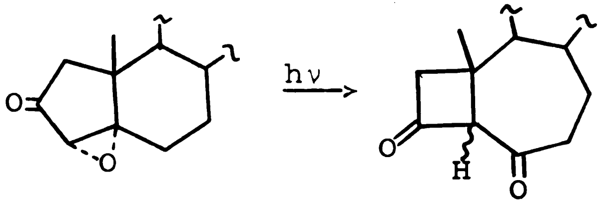
(13)



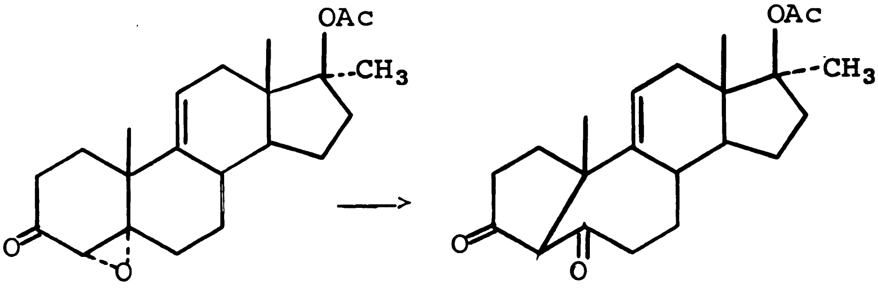
28 29 30

(14)



31 32

(15)



33 34

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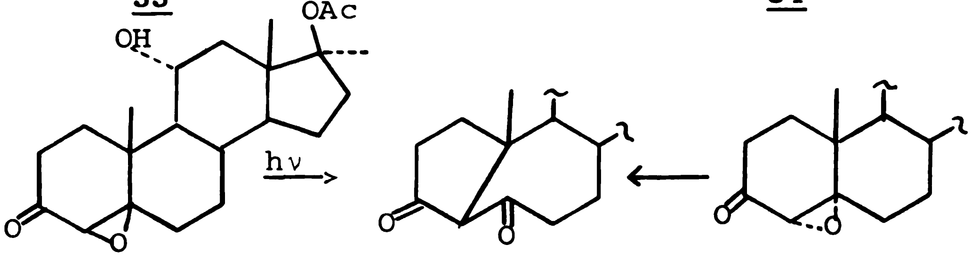
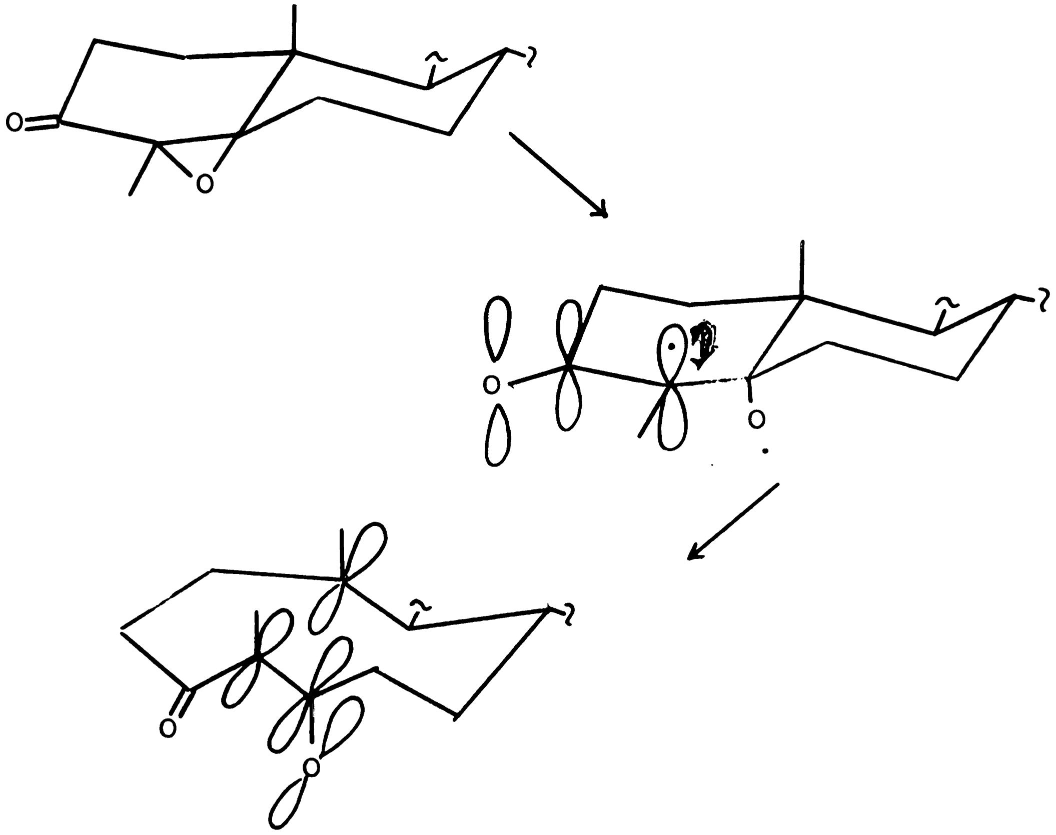


35 37 36

Rearrangement of the Δ^1-unsaturated epoxy ketones (18 and 19) was found to proceed only by exposure to 2537 Å light (π, π^* excitation) and not from irradiation with light of wavelengths greater than 3100 Å (n,π^* excitation).

The stereospecific rearrangment of epoxy ketones 21 and 23 has been cited (8) as evidence for a "synchronous" or "concerted" process (Chart IV) as opposed to a two step fragmentation mechanism. However, the conformational restrictions of medium sized rings may prevent facile equilibration of a diradical intermediate of type D (Chart II).

CHART IV



Our objectives in this research were: (a) To determine the existence and nature of intermediate C by investigating the effect of radical scavengers, triplet quenchers and sensitizers on the rearrangement. (b) To determine whether the migration of a β-substituent is truly concerted. (c) To elaborate the migrational aptitudes of various β-substituents.

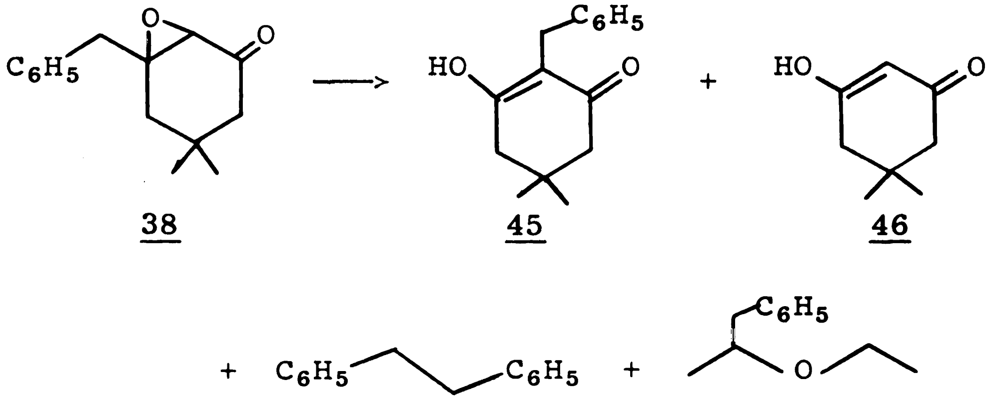
RESULTS

I. PHOTOPRODUCTS OF α,β-EPOXY KETONES

The photochemical transformations described here were effected by a medium pressure mercury lamp equipped with a Corex filter. The yields are not optimum conversions as it was desired to obtain relatively pure materials uncontaminated by secondary products and polymers.

A. Photolysis of 3-benzyl-5,5-dimethyl-2,3-epoxycyclohexanone:

(17)



38 45 46 47 48

Irradiation of an 0.029M ether solution of 3-benzyl-5,5-dimethyl-2,3-epoxycyclohexanone for 4 1/2 hr gave a single rearrangement isomer, benzyl dimedone, in 19.4% yield. The identity of this material was demonstrated by comparison (infrared spectrum and melting point, 155-157°) with authentic benzyl dimedone, prepared by alkylation of dimedone (9). Inspection of the vpc chromatogram before and after basic extraction of the photomixture indicated that two base-soluble compounds were present; the second proved to be dimedone, isolated as formalin dimedone in 11.7% yield.

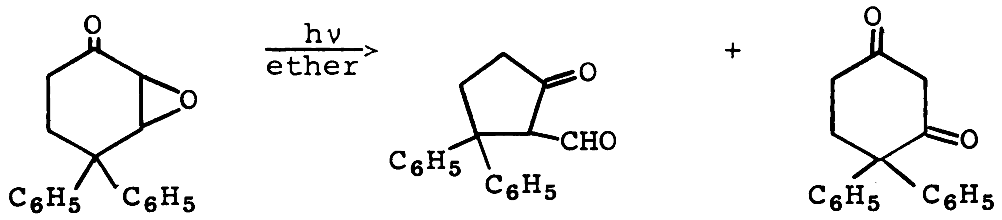
Base-insoluble compounds isolated from the photomixture were unchanged epoxy ketone (28.6%), dibenzyl (21.0%), and α-benzyl diethylether (6.5%). These were purified by a combination of column and preparative vapor phase chromatography. The identities of the latter compounds were established by a comparison of the melting points and infrared spectra with authentic dibenzyl, and by comparing the infrared and nmr spectra with those from independently synthesized α-benzyldiethyl ether.

Irradiation of <u>38</u> in pentane gave the same product mixture with the exception of the substituted ether. Products having similar vpc retention times were assumed to be benzyl pentane isomers. Irradiation of neat samples of <u>38</u> gave the stoichiometrically expected ratio of dimedone to dibenzyl of 2:1.

An ether solution of benzyl dimedone (0.007M) remained essentially unchanged after being irradiated under the same conditions used above.

B. Photolysis of 4,4-diphenyl-2,3-epoxycyclohexanone:

(18)



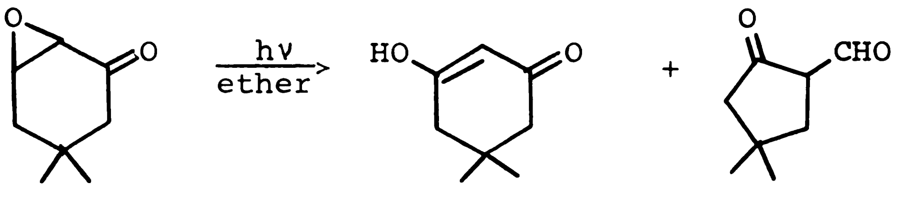
Irradiation of an 0.025M ether solution of 4,4-diphenyl-2,3-epoxycyclohexanone for 3 1/2 hours gave a 47% yield of base soluble material which proved to ba a 5:1 mixture of two components: 3,3-diphenyl-2-hydroxymethylenecyclopentanone, mp 94-96^{0}, and 4,4-diphenyl-1,3-cyclohexanedione, mp 193^{0} (dec.). Unchanged epoxy ketone was recovered in 50% yield from the base insoluble residue.

3,3-Diphenyl-2-hydroxymethylenecyclopentanone was characterized by a satisfactory C, H micro analysis, infrared (Fig. 5) and nmr (Fig. 4) spectra and a crystalline copper chelate mp 131-133^{0}. The infrared spectrum of the copper chelate exhibits absorption at $\bar{\nu}_{max}$ (CCl$_4$) 1600, 1463 and 1340 cm^{-1}.

4,4-Diphenyl-1,3-cyclohexanedione was characterized by a satisfactory C, H analysis, and by its formaline derivative which has a similar infrared spectrum to that of formalin dimedone in the carbonyl region.

C. Photolysis of 5,5-dimethyl-2,3-epoxycyclohexanone:

(19)



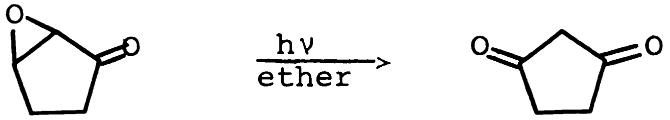
40 46 51

Irradiation of an 0.048M ether solution of 5,5-dimethyl-2,3-epoxycyclohexanone for 1 1/2 hr gave *ca*. 34% of a 10:1 mixture of dimedone and 4,4-dimethyl-2-hydroxymethylenecyclopentanone. Unchanged epoxy ketone accounted for 42% of the starting material.

The structure of 4,4-dimethyl-2-hydroxymethylene-cyclopentanone was determined from the nmr (Fig 8) and infrared (Fig 7) spectra. Base catalyzed degradation of this compound gave a single base-insoluble compound, identified as 3,3-dimethylcyclopentanone by comparing its infrared spectrum with that of an authentic sample.

D. Photolysis of 2,3-epoxycyclopentanone:

(20)

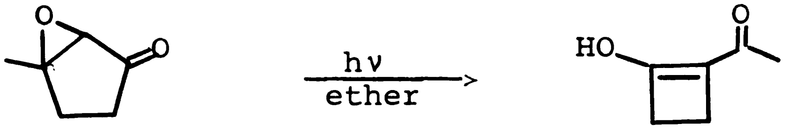


41 52

Irradiation of an 0.092M ether solution of 2,3-epoxycyclopentanone for 1/2 hr gave a precipitate in 4.7% yield, mp. 149-151^0, which proved to be cyclopentane-1,3-dione (10). Spectroscopic examination was not particularly informative as this compound is quite insoluble in suitable solvents, however, absorption characteristic of a cyclic enolized β-diketone is observed at 1580 and 1660 cm^{-1}.

E. Photolysis of 3-methyl-2,3-epoxycyclopentanone:

(21)



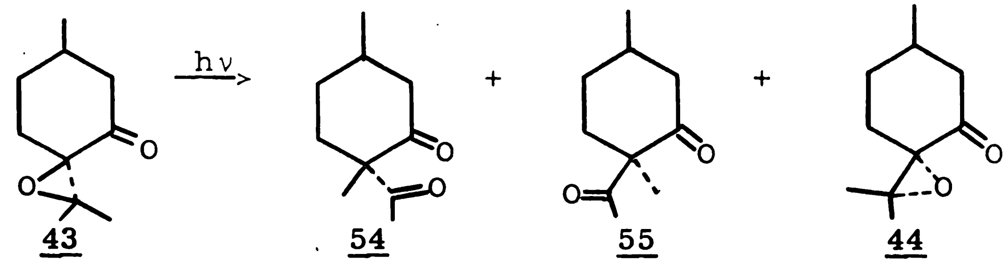
42 53

Irradiation of an 0.132M ether solution of 3-methyl-2,3-epoxycyclopentanone for three hr gave a 40% yield of 2-acetyl-1-hydroxycyclobutene mp 104-104.5^{0}, provided continuous extraction of the product was in effect throughout the reaction. If continuous extraction was not employed, the only base-soluble material isolated after long irradiation periods (over 2 hr) was acetic acid. However, 2-acetyl-1-hydroxycyclobutene was shown to be photochemically inert under equivalent conditions.

The rearranged product was characterized by microanalysis, infrared, nmr, and mass spectra. Positive iodoform and ferric chloride tests were also obtained. Treatment with ethereal diazomethane gave 1-acetyl-1-methoxycyclobutene, and the nmr spectrum of this derivative (Fig 13) displayed a quartet for the four methylene protons in contrast to the broad singlet observed with the enol precursor.

F. Photolysis of β-pulegone oxide:

(22)

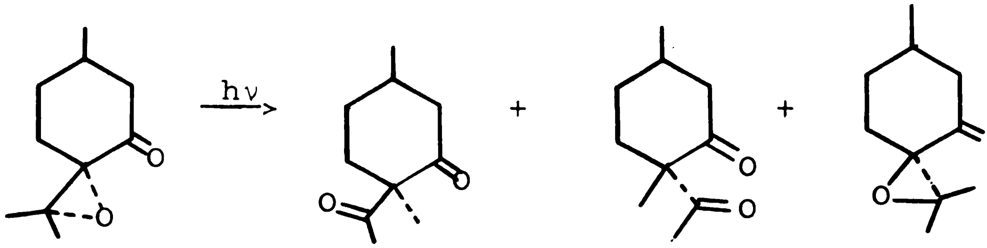


Irradiation of a 0.057M solution of β-pulegone oxide in ether for three hours gave three products: α-pulegone oxide, and the diasteromic 2,5-dimethyl-2-acetylcyclohexanones. Unchanged β-pulegone oxide represented more than 90% of the product mixture.

α-Pulegone oxide was identified by vpc retention time only. The two rearrangement isomers were isolated by removing the solvent and distilling the residue at 5mm, collecting _ca_ 500 mg of forerun. Preparative vpc gave two isomers having identical infrared spectra to authentic samples prepared by ozonolysis of a 4-methyl-_iso_-pulegone isomer mixture (11), configurations of which have been recently established (12).

G. Photolysis of α-pulegone oxide:

(23)

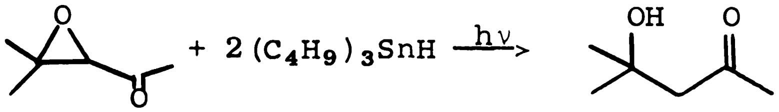


44 55 54 43

Irradiation of a 0.25M solution of α-pulegone oxide in acetonitrile (_ca_ 3 ml) gave β-pulegone oxide and the same two rearrangement isomers described above. These assignments rested on a comparison of vpc retention times with authentic samples.

H. Photoreduction of 4-methyl-3,4-epoxy-2-pentanone with tri-_n_-butyl stannane:

(24)



A 0.1 molar pentane solution of 4-methyl-3,4-epoxy-2-pentanone containing an equivalent of tri-*n*-butyl stannane was irradiated for 2 hr under an atmosphere of nitrogen. Column chromatography of the products gave a 93% yield of diacetone alcohol as the only isolated product, identified by comparison (infrared spectrum) with authentic diacetone alcohol.

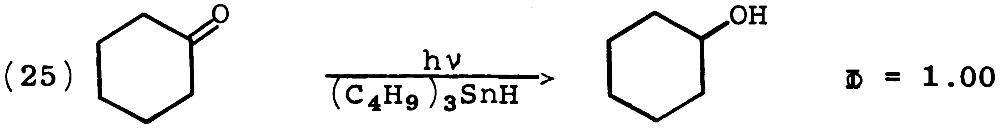
A similar chromatographic separation of the epoxy ketone and tri-*n*-butyl stannane showed that no reduction occurred on the column.

II. Relative Rates of Photochemical Reactions

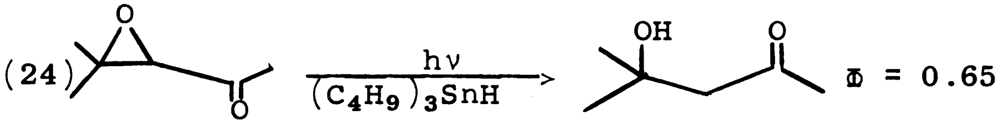
All solutions were degassed and irradiated in sealed pyrex ampules, using a merry-go-round apparatus (13). An inert internal standard was added to the solutions as an aid to vpc integration. The data thus obtained is presented in Tables 1-5.

A. Relative quantum yields.

A comparison of the rates of rearrangment and tri-*n*-butylstannane photoreduction of 4-methyl-3,4-epoxy-2-pentanone with the stannane photoreduction of cyclohexanone to cyclohexanol ($\Phi = 1.00$ assumed) gave relative quantum yields of 0.65 and 0.03 respectively for photoreduction and rearrangement of the epoxy ketone.



57 58



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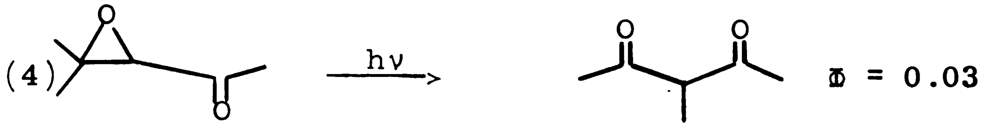


8 59

The quantum yield for 3-methyl-2,4-pentanedione 59 formation was not affected by solvent changes (piperylene, pentane, acetonitrile, ether) or the presence of air. However, photoreduction of 8 with tri-*n*-butyl stannane was completely quenched by 6M piperylene leaving only rearrangement to 3-methyl-2,4-pentanedione (Φ = 0.03). Thus it appears that photoreduction of 4-methyl-3,4-epoxy-2-pentanone proceeds only through a triplet [T_1] excited state, and photorearrangment of the epoxy ketone occurs only from the singlet [S_1] excited state.

Additional evidence excluding a triplet [T_1] state intermediate in the rearrangement is seen in the failure of acetophenone (E_t = 73.6 kcal) to sensitize the rearrangement of isophorone oxide or of 5,5-dimethyl-2,3-epoxycyclohexanone. This fact contrasts with a report (14) of triplet sensitization of certain steroidal epoxy ketones by compounds of lower triplet energy than acetophenone (triphenylene, biacetyl, β-dicarbonyl compounds). Sensitized stannane photoreduction of these substrates was also observed.

B. Solvent variations

A simultaneous irradiation of 3-benzyl-5,5-dimethyl-2,3-epoxycyclohexanone in ether, acetonitrile, and 2,5-dimethyl-2,4-hexadiene demonstrated that the rate of reaction was essentially the same in all three solvents. The fragmentation product, dibenzyl, was also produced at approximately the same rate in all three solvents. This insensitivity to solvent variations, including triplet state quenchers, was also noted for the β-hydrogen rearrangment in 5,5-dimethyl-2,3-epoxycyclohexanone, and again implies the rearrangement proceeds only from the singlet excited state [S_1].

A comparison of the rearrangement rates for 3-benzyl-5,5-dimethyl-2,3-epoxycyclohexanone (λ_{max} 2850 Å) and 4-methyl-3,4-epoxy-2-pentanone (λ_{max} 3000 Å) is not meaningful, as the absorption spectra of these two compounds are markedly different.

All preparative scale photolyses of epoxy ketones were not affected in any detectable manner by degassing. Furthermore, addition of piperylene, a triplet state quencher, to ether solutions of 3-benzyl-5,5-dimethyl-2,3-epoxycyclohexanone or isophorone oxide did not affect product ratios or the overall yield.

C. The pulegone oxides

Simultaneous irradiation of acetonitrile solutions of β-pulegone oxide and α-pulegone oxide gave a stereospecific rearrangement to stereoisomeric 2,5-dimethyl-2-acetylcyclohexanones as well as isomerization to the stereoisomeric pulegone oxide. The combined rate of rearrangement to β-diketones was greater than the rate of isomerization in all cases. A temperature difference of <u>ca</u> 30^0 had no apparent effect on the course of the reaction.

Table 1. Effect of acetophenone on photolysis[a] of isophorone oxide.

System	Ketone(s),(M)	Solvent	Time (min)	% Reaction
1	isophorone,(0.3)	acetonitrile	267	trace[c]
			754	0.31[b]
			1396	0.83
2	isophorone,(0.3) acetophenone,(0.5)	acetonitrile	267	none
			754	none
			1396	none
3	acetophenone,(0.3)	toluene	30	3.4[d]
			60	6.0
			90	8.9
			120	11.3

[a] 450 watt mercury lamp filtered by pyrex, 0.1M naphthalene in cyclohexane, and soft glass.

[b] Product: 4,4-dimethyl-2-acetylcyclopentanone from comparison of vpc retention times (20% SE-30) with an authentic sample. Chlorobenzene was added as an internal standard.

[c] A ferric chloride test proved more sensitive than vpc.

[d] Determined by disappearance of 3200 Å maximum in u.v.

Table 2. Photolysis[a] of 3-benzyl-5,5-dimethyl-2,3-epoxycyclohexanone in different solvents.

Solvent	Time(hr)	Concentration[b] (M) x 10^2
Ether	0	8.83
	2	7.89
	4	7.53
Acetonitrile	0	8.96
	2	8.35
	4	7.75
2,5-dimethyl-2,4-hexadiene	0	8.88
	2	7.75
	4	7.23

[a] 200 watt mercury lamp, Corex filter.

[b] Analysis by vpc (4% QF-1) with triphenylcarbinol added as an internal standard.

Table 3. Photolysis of 4-methyl-3,4-epoxy-2-pentanone; rearrangement *vs* reduction by tri-*n*-butyl stannane: effect of 2,4-pentadiene.

Light source	Ketone, (M)	Solvent (adducts, M)	Time (min)	Concentration (M) (ketone)	Concentration (M) (product)
200 watt[a]	**8**, (.06)	cyclohexane,	0	0.060	0.00
		(piperylene, 6)	15	0.058[b]	0.0016[b,c]
			30	0.064	0.0032
			45	0.059	0.0045
			60	0.055	0.0055
3130 Å[d]	**8**, (.12)	cyclohexane,	0	0.121[b]	0.000
		(stannane, .0685)	60	0.100	0.017
			120	0.077	0.038
3130 Å[d]	**8**, (.12)	cyclohexane,	0	0.121[b]	0.000
		(stannane, .0689)	120	0.117	0.0025[b,c]
		(piperylene, 6)	240	0.116	0.0038
3130 Å[d]	**8**, (.12)	cyclohexane,	0	0.120[b]	0.000
		(piperylene, 6)	120	0.119	0.0016[b,c]
			240	0.117	0.0033
3130 Å[d]	**8**, (.12)	cyclohexane	0	0.120	0.000
			120	0.116	0.0014[b,c]
			240	0.117	0.0033
3130 Å[d]	**8**, (.503)	pentane			0.0173[b,e,g]
		(stannane, .201)	60	--	±0.0001
3130 Å[d]	**8**, (.12)	cyclohexane	60	--	0.0169[b,e,g]
		(stannane, .0685)			±0.0001

Table 3. (Continued)

Light source	Ketone, (M)	Solvent (adducts, M)	Time (min)	Concentration (M)	
				(ketone)	(product)
3130 Å[d]	cyclo- (.50) hexanone	pentane (stannane, .2)	60	--	0.0265[b,f,g] ±0.0005

---

[a] Pyrex filter.

[b] Analysis by vpc (15% FFAP) with chlorobenzene added as an internal standard.

[c] Product: 3-methyl-2,4-pentandione.

[d] We are grateful to Dr. P. J. Wagner for the use of a merry-go-round apparatus (13).

[e] Product: diacetone alcohol.

[f] Product: cyclohexanol.

[g] Average of two samples.

Table 4. Photolysis[a,b] of the pulegone oxides.

Ketone	Temp °C	Time (min)	Reaction %	$\frac{[55]}{[54]}$	$\frac{[55+54]}{[\text{isomerization}]}$
43 (.25M)	45-50	0	0[c]	-	-
		100	0.16	1.00	-
		200	2.16	1.91	1.50
		300	2.20	4.60	1.04
		400	3.69	2.61	1.04
43 (.25M)	18-20	0	0[c]	-	-
		100	0.92	2.00	1.87
		200	2.56	1.43	1.14
		300	3.00	1.58	1.08
44 (.25M)	45-50	0	0[c]	-	-
		100	1.40	0.39	2.50
		200	2.36	0.34	1.95
		300	3.20	0.34	2.20
		400	3.80	0.24	1.44
44 (.25M)	18-20	0	0[c]	-	-
		100	1.24	0.31	1.22
		200	2.40	0.35	1.07
		300	2.72	0.31	1.11

[a] 200 watt mercury lamp filtered by pyrex.

[b] Acetonitrile solution.

[c] Analysis by vpc (4% QF-I) with biphenyl added as internal standard. A small amount of impurities (ca 1%) with the same retention times as the rearrangement products made exact measurement difficult.

Table 5. Effect of acetophenone and 2,4-pentadiene on photolysis[a] of 5,5-dimethyl-2,3-epoxycyclohexanone.

Ketone(s), (M)	Solvent	Time (hr)	%Reaction[b]
40, (0.30)	2,4-pentadiene	6	14.3[c]
40, (0.30)	benzene	6	19.0
40, (0.28) Acetophenone, (0.42)	benzene	6	0.00[d]

[a] 450 watt lamp, pyrex filter.

[b] Disappearance of starting material was noted. Products did not give satisfactory analysis at concentration used.

[c] Analysis by vpc (4% QF-I) with menthol added as internal standard.

[d] Analysis by vpc with acetophenone as standard.

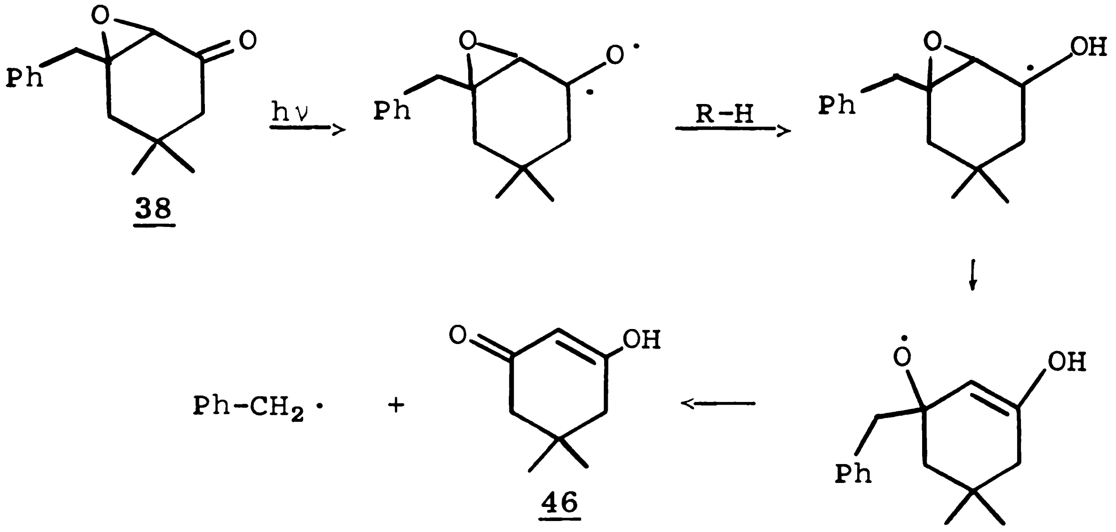
DISCUSSION

I. Radical Character of the Rearrangement

A consideration of the β-dicarbonyl products produced by photolysis of the α,β-epoxy ketones studied in this investigation, combined with those reported previously,(1, 3,4,5) leads to the following order of migratory aptitudes for β-substituents: benzhydryl and benzyl > hydrogen > methylene > methyl >> phenyl. With the exception of hydrogen, this order parallels the stability of the corresponding radicals and suggests that the β-group assumes radical characteristics during its migration.

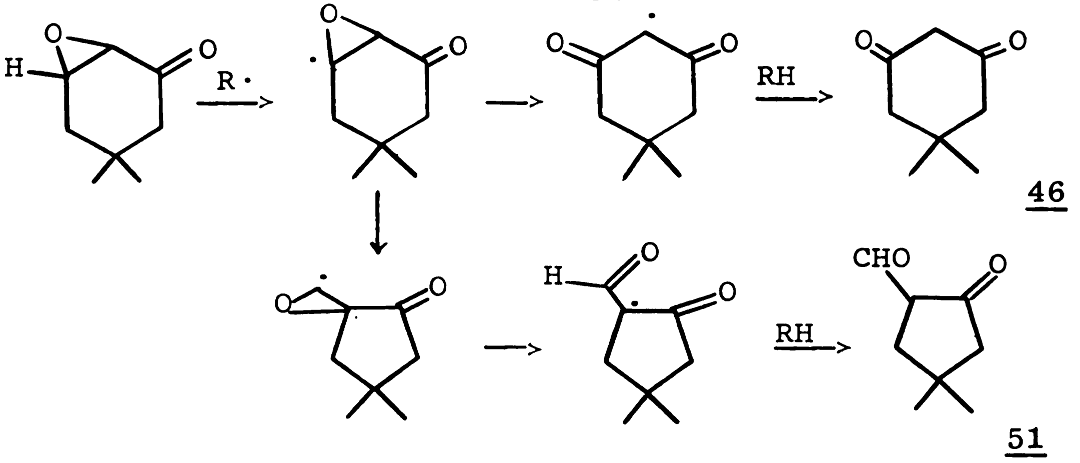
Additional support for this view is found in the fragmentation products, dibenzyl, dimedone, and α-benzyl diethylether, obtained from 3-benzyl-5,5-dimethyl-2,3-epoxycyclohexanone. The implication here is that the rearrangement either proceeds <u>via</u>, or is diverted to a radical pair; and that in this case the relatively stable benzyl radical escapes the solvent cage.

This homolytic fragmentation of a β-group can be interpreted in another manner, as illustrated for the case of 3-benzyl-5,5-dimethyl-2,3-epoxycyclohexanone:



However, photolysis of this epoxy ketone in acetonitrile, a poor hydrogen atom source, gave essentially the same rate of reaction and just as much dibenzyl as photolysis in ether. Also, fragmentation products are still observed when triplet quenching dienes (0.1-9M) are added to the photolysis sample. Since bimolecular hydrogen abstraction by singlet excited states has been shown not to occur (15), this alternate mechanism may be discounted.

The position of hydrogen in the order of migratory aptitudes argues against a general fragmentation mechanism, as hydrogen atoms are not normally formed in radical reactions. In the photolysis of 5,5-dimethyl-2,3-epoxycyclohexanone, an alternate mechanism involving abstraction of a β-hydrogen could lead to the observed products.



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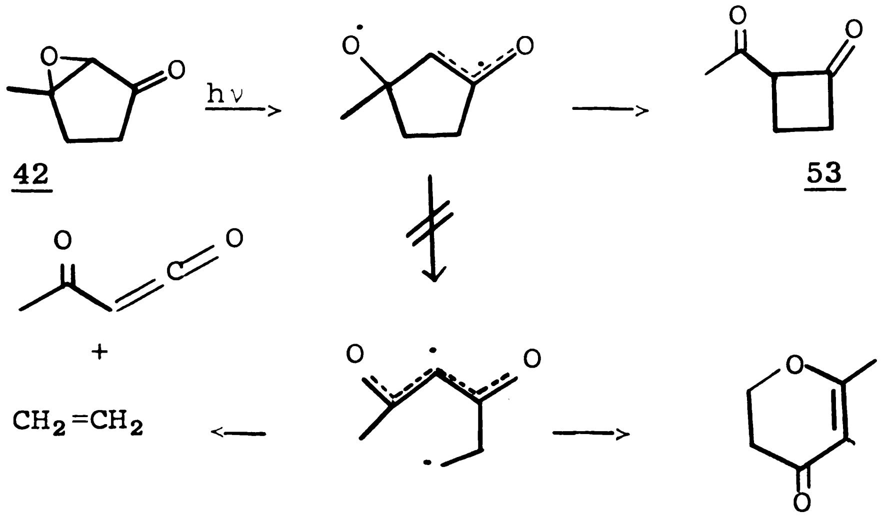
The most likely radical initiating species in this mechanism is an excited carbonyl compound. Since photolysis in piperylene gave approximately the same rate of epoxy ketone disappearance as in benzene, and since no reaction occurred when acetophenone was used in an attempt to sensitize the reaction, there is no support for this mechanism.

A two step radical reaction in the photolysis of 3-methyl-2,3-epoxycyclopentanone should favor either formation of a six-membered heterocyclic compound or fragmentation rather than the strained cyclobutane derivative.



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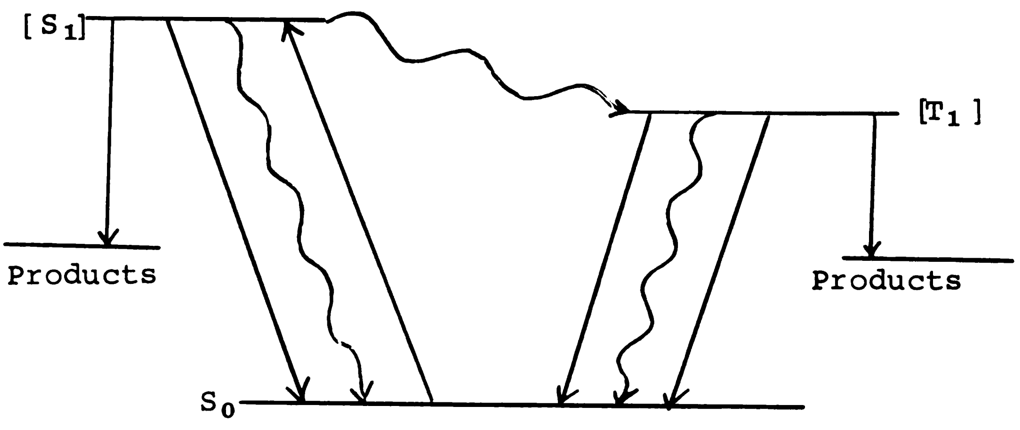
Stereospecific rearrangement of steroidal epoxy ketones 25 and 28 as well as 21 and 23 has also been cited (8) as evidence for a concerted mechanism rather than a two step radical fragmentation, which would be expected to lead to epimerization of C_{10} in 25 and 28, and C_4 in 21 and 23. The stereospecific photorearrangement of the pulegone oxides reported here offers the most convincing evidence for a concerted mechanism, since in this substrate the steric course of the reaction is less likely to be controlled by conformational barriers in the rest of the molecule. This is illustrated in greater detail on page 32.

II. Photochemistry of the Rearrangement

In recent years, several authors (16,17,18) have advanced theories to account for photochemical transformations of carbonyl compounds. There is general agreement that n,π^* excitation of a carbonyl group produces excited singlet states which rapidly cascade to the zero vibrational level of the lowest excited singlet state [S_1]. This excited state may be deactivated through chemical reactions, conversion to the ground state S_0 by fluorscence, internal conversion and bimolecular energy transfer. In the photochemistry of carbonyl compounds, the most important mode of n,π^* singlet state deactivation is intersystem crossing to the first excited triplet [T_1]. The triplet state in turn may be deactivated through chemical transformations, conversion to S_0 by intersystem crossing, phosphorescence, or bimolecular quenching.



The true photochemistry in the rearrangement of α,β-epoxy ketones centers about the formation of diradical intermediate <u>C</u> <u>vs</u> the various modes of deactivation of excited states. Within these bounds, the most important competing paths should be intersystem crossing from both the triplet and singlet excited states:

$$[T_1] \rightsquigarrow S_0 + \text{heat}$$

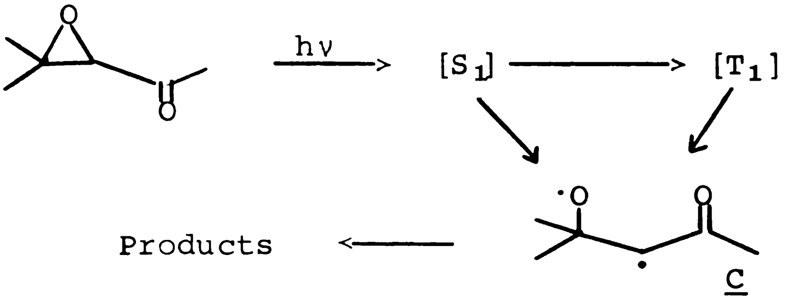
$$[S_1] \rightsquigarrow [T_1] + \text{heat}$$

and bimolecular quenching of the excited triplet state:

$$[T_1] + Q \longrightarrow S_0 + Q^* .$$

All other modes of deactivation are too slow to compete with these (19).

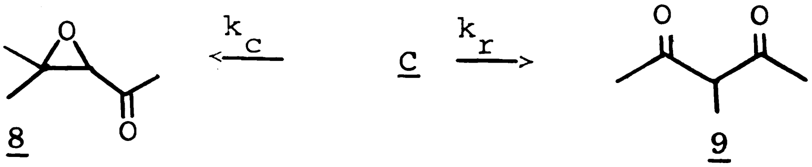
Both $[S_1]$ and $[T_1]$ appear to be theoretically acceptable precursors for <u>C</u>. From our attempts to quench or sensitize a triplet reaction, it would appear that intermediate C is produced only from [S_1]. However, other workers have reported (3,8,14) that photochemical rearrangement of steroidal epoxy ketones is both sensitized (triphenylene, biacetyl, and β-dicarbonyl compounds were used), and to some extent quenched by piperylene. These results suggest that intermediate C is produced from both [S_1] and [T_1].



The same workers (14) have also investigated tri-n-butyl stannane photoreduction of their epoxy ketone substrates, and report that solvent piperylene completely quenches the rapid reduction of substrate as well as the slower rearrangment. This contrasts strikingly with irradiation in piperylene in the absence of stannane, which gave the rearrangement product in 15% yield.

Our experiments with tri-n-butyl stannane photoreduction of 4-methyl-3,4-epoxy-2-pentanone show that photoreduction of the epoxy ketone occurs only from the triplet excited state, a fact in accord with recent work on a similar photoreduction of acetone (15). The quantum yield for rearrangement of this epoxy ketone ($\Phi = 0.03$) was unchanged by irradiation in cyclohexane, piperylene, or in piperylene and stannane.

Using the quantum yield for photoreduction ($\Phi = 0.65$) as a measure of intersystem crossing ($[S_1] \rightsquigarrow [T_1]$ + heat) in epoxy ketones, demonstrates that 35% of the excited singlets must be deactivated by other means. Since the value of Φ_{isc} is low in comparison to acetone ($\Phi_{isc} > 0.99$) (15), formation of C from $[S_1]$ is left as the only attractive alternative for deactivation of $[S_1]$. If the quantum yield for $[S_1] \longrightarrow$ C is 0.35, the low quantum yield for rearrangment ($\Phi = 0.03$) is probably due to unfavorable competition between rearrangement and closing of the oxirane ring ($k_c > k_r$).



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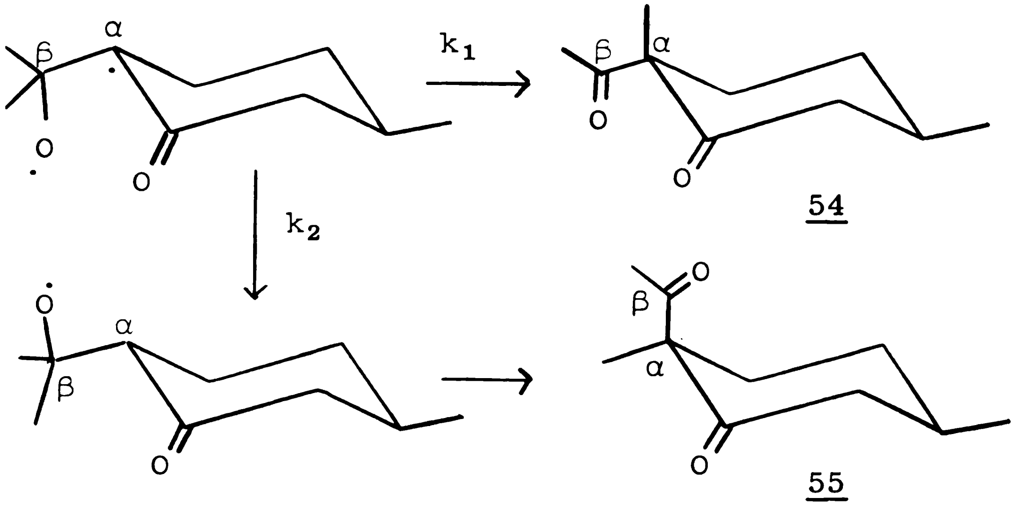
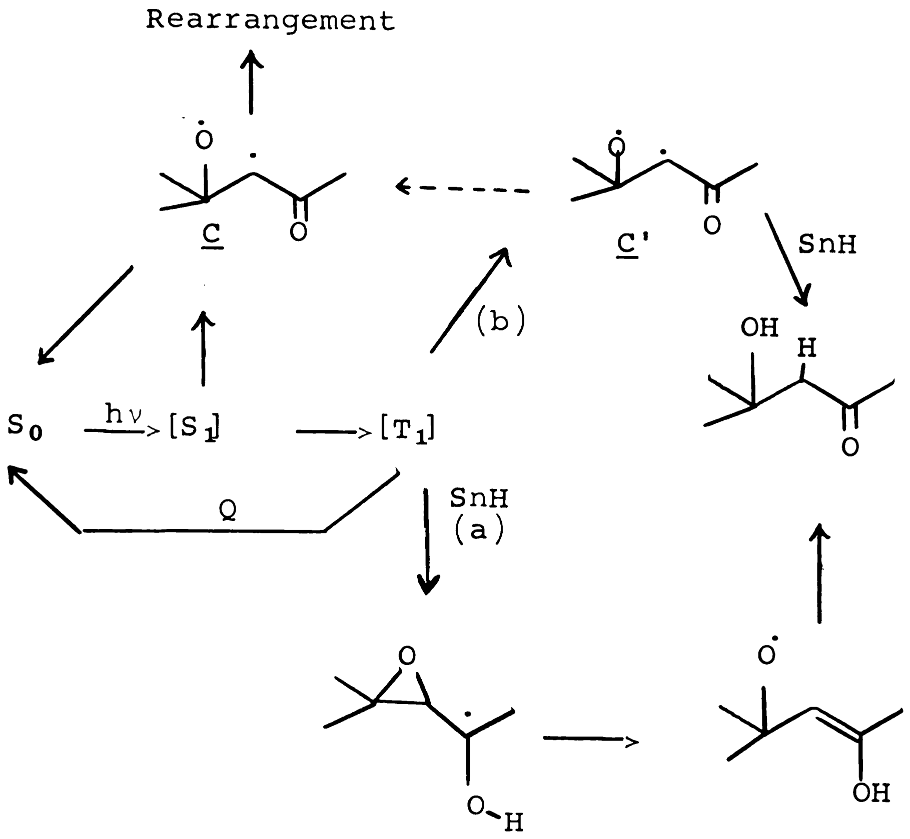
Our original objective in using tri-n-butyl stannane was to trap diradical intermediate C. But as photolysis of 4-methyl-3,4-epoxy-2-pentanone in piperylene and stannane gave no reduction, one can only assume that if C exists, its lifetime is too short to permit bimolecular reactions. Good evidence for a short lived intermediate, or for a concerted process, is seen in the stereospecific rearrangement of the pulegone oxides where oxirane opening must be immediately followed by β-methyl migration before much rotation about the C_α-C_β bond can occur ($k_1 > k_2$).



The usual course of photochemical reductions of carbonyl compounds begins with hydrogen abstraction by the excited state of the carbonyl oxygen, which has been attributed to its oxy-radical character (15). Hydrogen abstraction by an oxy-radical followed by oxirane ring opening is plausible in view of the radical reduction of epibromohydrin by stannane to give allyl alcohol in high yield (20).

The photoreduction of α,β-epoxy ketones does not, however, necessarily follow this path, as $[T_1]$ could give a triplet intermediate C' which could subsequently undergo reduction by stannane (path b).



If this latter mechanism (path b) operates, then intermediate C' is generated regardless of the presence of stannane. The facts presented in this thesis greatly restrict the subsequent reactions of C', and in fact argue against a significant contribution by path b. Thus, C' can not react with dienes since no products of this nature are observed and epoxy ketone is not consumed by unknown reactions; C' can not be converted to C, since this would represent a triplet state precursor to rearrangement products; finally C' would have to be very short lived (for a triplet state intermediate) to account for the slow isomerization of the pulegone oxides.

EXPERIMENTAL

I. General Procedures

A. Apparatus

All infrared spectra were obtained on a Perkin-Elmer Model 237B recording spectrophotometer, using sodium chloride cells. The ultraviolet spectra were determined in 1 cm quartz cells using a Unicam SP.800 spectrophotometer. Nuclear magnetic resonance spectra were determined in solution or neat using a Varian, A-60, high resolution spectrometer or a JEOL Co. C-60H high resolution instrument. All spectra were obtained at 60Mc using tetramethylsilane as an internal standard. Mass spectra were taken on a Consolidated Electrodynamics Corp. Mass Spectrometer Type 21-103C.

Vapor phase chromatography analyses were made using three different instruments: Aerograph A-90P and A-90P3 instruments with thermal conductivity detectors using 1/4" x 6' columns, and a Varian Aerograph series 1200 Hy-Fi III instrument with a flame ionization detector using 1/8" x 6' columns.

B. Melting Points

Melting points were determined on a Koefler hot-stage and are uncorrected.

C. Microanalysis

All microanalyses were performed by the Spang Microanalytical Laboratory, Ann Arbor, Michigan.

II. Preparation of α,β-epoxy Ketones

A. Preparation of 3-benzyl-5,5-dimethyl-2,3-epoxycyclohexanone

1. Preparation of 5,5-dimethyl-3-methoxy-2-cyclohexene-1-one.

A solution of dimedone (100 g, 0.715 mole) in 700 ml anhydrous methanol and 30 ml concentrated sulfuric acid was stirred under gentle reflux for 19 hours. Approximately 600 ml of the methanol was removed on a rotary evaporator. The residual solution was poured into one liter of 6% sodium hydroxide solution and extracted with three 300 ml portions of USP ether. The combined ether layers were washed with water until the wash was neutral and dried over magnesium sulfate. Filtration and removal of the ether left 65.7 grams of crude product. The aqueous portion was acidified with concentrated sulfuric acid and cooled in an ice-water bath whereupon unchanged dimedone crystallized. The crystals were collected by suction filtration, washed with water and dried in the air (yield 25 grams).

5,5-dimethyl-3-methoxy-2-cyclohexene-1-one was distilled under reduced pressure and 55 g (50%) of pure product was obtained, bp 72-74°/1.0 mm. $\bar{\nu}_{max}$ (CCl_4) 1662, 1610 cm^{-1}.

2. Preparation of 3-benzyl-5,5-dimethyl-2-cyclohexene-1-one.

Into a three-necked, 250 ml round-bottom flask equipped with a magnetic stirrer, reflux condenser and dropping funnel and having all outlets protected by drying tubes, was placed magnesium turnings (3.94 g, 0.162 mole) in 50 ml of anhydrous ether. Benzyl chloride (20.5 g, 0.162 mole) in 50 ml of anhydrous ether was added slowly until a spontaneous reaction began. The flask was then placed in an ice-water bath and the remainder of the benzyl chloride solution was added dropwise. The Grignard complex was heated under gentle reflux (heating mantle) for 1/2 hour after the spontaneous reaction had subsided. The flask was then cooled in an ice-water bath and 50 ml of an ether solution containing 5,5-dimethyl-3-methoxy-2-cyclohexene-1-one (25 g, 0.162 mole) was added dropwise with rapid stirring. The reaction mixture was stirred at reflux temperature for an additional 2 hours, cooled and poured into a solution of 40 ml concentrated sulfuric acid in 200 ml of ice water. The ether layer was separated and the aqueous phase extracted twice more with 100 ml portions of ether. The combined ether layers were washed with three 75 ml portions of water and dried over magnesium sulfate. The solvent was removed on a rotary evaporator to yield 32.96 g of crude product. Vapor phase chromatography (5' x 1/4" 4% QF-1 column, 195^0, 50 cc/min) of the crude product showed peaks having retention times of 0.44 min (ether and toluene), 2.84 min (the enol ether), 12.8 minutes (desired product) and three other peaks at 2.06 to 4.9 minutes which were later shown to be dibenzyl and the two dehydration products of the initial Grignard adduct. Integration of the chromatogram indicated a yield of 58%.

The product was purified *via* Girard's T derivative (22), taking care to keep the reaction mixture at ice-water temperature while extracting all non-ketonic material. Hydrolysis of the derivative left an orange oil which was further purified by distillation under reduced pressure to yield 15.4 g, bp $110^{0}/0.2$ mm; 43% of theory. $\bar{\nu}_{Max}$ (CCl_4) 1670 cm^{-1}.

3. Preparation of 3-benzyl-5,5-dimethyl-2,3-epoxycyclohexanone

5,5-Dimethyl-3-benzyl-2,3-epoxy-1-cyclohexanone was prepared from pure 5,5-dimethyl-3-benzyl-2-cyclohexene-1-one by the method of Wasson and House (23). An 80% yield of material distilling at $100\text{-}105^{0}/0.05$ mm was obtained. $\bar{\nu}_{Max}$ (CCl_4) 1720 cm^{-1}. Nmr spectrum (Figure 1).

B. Preparation of 4,4-diphenyl-2,3-epoxycyclohexanone

1. Preparation of stilbene glycol (24)

Benzoin (100 g, 0.48 mole) was added to 500 ml of 95% ethanol and warmed slightly to aid solution. Ten grams of sodium borohydride was added in small portions (exothermic reaction with foaming). The solution was then heated on a steam bath for 20 minutes, 500 ml of water was added and the solution was boiled for five minutes on a hot plate and filtered through a glass-wool plug into one liter of water. The glycol crystallized upon cooling and was collected by suction filtration and washed with water, mp 135-136°.

2. Preparation of diphenylacetaldehyde

Diphenylacetaldehyde, bp 125-130°/0.5 mm, was prepared from the crude, wet glycol by the method of Henze and Leslie (25), i.e., in refluxing 25% sulfuric acid. Yield: 15.5% from benzoin.

3. Preparation of 4,4-diphenyl-2-cyclohexene-1-one

4,4-Diphenyl-2-cyclohexene-1-one, mp 91-92.5°, was prepared from diphenylacetaldehyde and methyl vinyl ketone in 53% yield by the method of Bordwell and Wellman (26).

4. Preparation of 4,4-diphenyl-2,3-epoxycyclohexanone

4,4-Diphenyl-2-cyclohexene-1-one (9.0 g, 0.0363 mole) was dissolved in fifty ml of 50% acetone and methanol. Hydrogen peroxide (10.5 ml of 30% solution) was added to the solution and the temperature rose from 20° to 32°. The solution was stirred in a water bath at 20° while one milliliter of 6N sodium hydroxide solution was added. After a total reaction time of 1 1/2 hours, analysis by micro tlc (silica G, benzene) showed no remaining starting material. The mixture was worked up as usual to yield a clear oil which was taken up in hot ligroin (60-90°) and benzene. Slow cooling of the solution produced only an oil, but rapid cooling caused a granular white solid to precipitate, 8.0 g (83%), mp 87-89.5°. Further attempts to purify this material gave only the oil again. The infrared spectrum was identical to that of another sample (mp 72-73°) from a previous preparation purified by column chromatography and recrystallization from ligroin. $\bar{\nu}_{\text{Max}}$ (CCl_4) 1713 cm^{-1}.

C. Preparation of 5,5-dimethyl-2,3-epoxycyclohexanone

1. Preparation of 5,5-dimethyl-2-cyclohexene-1-one

5,5-Dimethyl-3-methoxy-2-cyclohexene-1-one (15.4 g, 0.10 mole) was reduced with 1.9 g of lithium aluminum hydride by the method of Gannon and House (27) to yield 10.7 g (87%) of 5,5-dimethyl-2-cyclohexene-1-one, bp 63°/7.5 mm. $\bar{\nu}_{\text{Max}}$ (CCl_4) 1675 cm^{-1}.

2. Preparation of 5,5-dimethyl-2,3-epoxycyclohexanone

5,5-Dimethyl-2-cyclohexene-1-one (10.7 g, 0.087 mole) was oxidized with 20 ml of 30% hydrogen peroxide by a modification (total reaction time was 1.5 hr at 8-12°) of the method of Wasson and House (23) to yield 10.05 g (83%) of 5,5-dimethyl-2,3-epoxy-1-cyclohexanone, bp 80°/8 mm. $\bar{\nu}_{\text{Max}}$ (CCl_4) 1720 cm^{-1}.

D. Preparation of 2,3-epoxycyclopentanone

1. Preparation of 2-cyclopentene-1-one

The procedure devised by Garbish (28) was used to prepare 2-cyclopentenone via the 2-bromo ethylene ketal of cyclopentanone in 26% yield. $\bar{\nu}_{Max}$ (CCl_4) 1707 cm^{-1}.

2. Preparation of 2,3-epoxycyclopentanone

2-Cyclopentene-1-one (20.5 g, 0.25 mole) was dissolved in 230 ml of methanol and cooled to 4^0 in an ice-bath. One milliliter of 6N sodium hydroxide solution was added and 26 ml of 30% hydrogen peroxide was added over a period of 35 minutes, keeping the temperature between 5-10^0. The ultraviolet spectrum at this time showed no alpha-beta unsaturated ketone (λ_{max} 218 mμ, ϵ 9500). After the temperature had dropped back to 4^0, the mixture was poured into 300 ml of water containing 95 g of sodium chloride. The aqueous mixture was extracted with three portions of ether and the combined ether extracts were washed with two 50 ml portions of saturated sodium chloride solution followed by one 50 ml portion of water. The ether solution was then dried over magnesium sulfate, filtered and the solvent removed by distillation. The residue was distilled on the spinning band column at 30 mm and gave the following fractions:

1.	24-46°	(cyclopentenone)	1.1g
2.	46-74°		
3.	74-79°		
4.	79-82°		2.0 g (contains some cyclopentenone)
5.	82°		3.0 g
6.	82°		2.5 g

(overall yield 30.5%) fractions 4-6.
$\bar{\nu}_{Max}$ (CCl_4) 1750 cm^{-1}.

E. Preparation of 3-methyl-2,3-epoxycyclopentanone

1. Preparation of 3-methyl-2-cyclopentene-1-one

3-Methyl-2-cyclopentenene-1-one, bp 80-82°/18 mm, was prepared from 120 g of acetonylacetone in 52% yield by the method of Acheson and Robinson (29). The only modification was the use of saturated sodium chloride solutions for all extractions and washes. Vpc retention times of the starting material and product were the same on 4% QF-1 and 20% SE-30 columns. $\bar{\nu}_{Max}$ (CCl_4) 1707 cm^{-1}.

2. Preparation of 3-methyl-2,3-epoxycyclopentanone

3-Methyl-2-cyclopentene-1-one (4.8 g, 0.05 mole) was dissolved in 45 ml of methanol, twelve drops of 6N sodium hydroxide solutions was added and the solution was cooled in an ice-bath; 30% hydrogen peroxide was added in portions and ultraviolet spectra were taken after each addition by taking aliquots of 0.5-0.6 microliters and diluting these to 5 ml in methanol.

Time (min)	H_2O_2 added (ml)	NaOH added	Aliquot (μl)	Absorbance
5	0.00	12 drops	0.50	1.95
20	3.00	---------	0.53	0.88
40	5.00	---------	0.55	0.60
60	7.00	---------	0.56	0.34
80	9.00	---------	0.58	0.22
100	11.00	16 drops	0.60	0.10
120	---	---------	0.60	0.06
140	---	---------	0.60	0.005

The reaction mixture was poured into 100 ml of saturated sodium chloride solution, extracted with three portions of ether and the combined ether extracts were washed with saturated sodium chloride and dried over magnesium sulfate. The ether was removed by distillation to yield 4.6 g of crude product. Analysis by vpc (20% SE-30, 135°) showed only one peak at 4.8 min.

Following the above procedure, 24 g (0.25 mole) of 3-methyl-2-cyclopentene-1-one gave 14 g (51%) of 3-methyl-2,3-epoxy-1-cyclopentanone distilled on a spinning band column at reduced pressure and pure according to vpc analysis. $\bar{\nu}_{Max}$ (CCl_4) 1745 cm^{-1}.

F. Other epoxy ketones

Samples of the pulegone oxides (30), isophorone oxide (31), and 4-methyl-3,4-epoxy-2-pentanone (32) were supplied by Dr. William Reusch.

III. Photolysis of 3-benzyl-5,5-dimethyl-2,3-epoxycyclohexanone

A degassed solution of 3-benzyl-5,5-dimethyl-2,3-epoxycyclopentanone in 300 ml of anhydrous ether was irradiated for 4 hr with a 450 watt mercury lamp filtered by Corex. Base soluble materials were extracted with cold 5% sodium hysroxide solution. Treatment of the basic extracts with 6N hydrochloric acid gave a white precipitate (0.39 g) which was recrystallized from acetone and water, needles mp 155-157°.

Analysis of the photomixture by vpc (4% QF-I) before and after basic extraction showed two base soluble compounds, unchanged epoxyketone and several smaller peaks.

A. Photoproducts from 3-benzyl-5,5-dimethyl-2,3-epoxycyclohexanone

1. Benzyl dimedone <u>45</u>

The crystalline base soluble material, mp 155-157°, was shown to be 2-benzyl dimedone by an undepressed mixed melting point with authentic 2-benzyl dimedone. The photoproduct also had an infrared spectrum identical to that of the authentic material.

2. Dimedone <u>46</u>

Extraction of the ether photomixture from a similar photolysis of 3-benzyl-5,5-dimethyl-2,3-epoxycyclohexanone

(2.0 g) with three 20 ml portions of 1M sodium acetate solution followed by treatment of the combined extracts with 2.5 ml of concentrated hydrochloric acid, 25 ml water, and 10 ml of 38% formaldehyde solution gave an immediate precipitate which was collected after 16 hrs to yield 0.1173 g of formalin dimedone, identified by a comparison of melting point (188.5-190^0) and infrared spectra with authentic material.

3. Dibenzyl <u>47</u>

The base insoluble photoproducts were chromatographed on silica gel and gave dibenzyl in the first fractions eluted with hexane. The product was further purified by sublimation and found identical to authentic dibenzyl by mixed melting point and comparison of infrared spectra.

4. α-benzyl diethylether <u>48</u>

The base insoluble photoproducts were fractionated in a micro distillation apparatus equipped with a dry-ice trap. Analysis of the distilled material by vpc showed a mixture of dibenzyl and a more volatile compound. The latter was collected on a DEGS column at 160^0 and proved to be α-benzyl diethylether identical to an authentic sample in its infrared and nmr spectra (Figures 2 and 3).

B. Photolysis of neat samples

Samples of 3-benzyl-5,5-dimethyl-2,3-epoxycyclohexanone (ca. 5 μl) were placed between two glass microscope slides (optical density: 95% transmittance at 3400 Å, 40% at 3000 Å, 0% at 2800 Å). The slides were then attached to a vycor lamp holder with rubber bands and irradiated with a 450 watt lamp through a Corex filter.

At intervals of 1/2 hr the slides were removed, washed down with ether, and the solution checked by vpc (4% QF-1, 190°). All chromatograms showed a ratio of dibenzyl to dimedone of approximately 1:2.

The residues from four of the slides were dissolved in ether, extracted with cold 5% sodium hydroxide solution, washed with water and dried over magnesium sulfate. Analysis of the base-insoluble ether solution by vpc showed that the peaks corresponding to dimedone and benzyl dimedone had disappeared.

C. Separation of a dimedone and benzyl dimedone mixture

Solutions of dimedone and benzyl dimedone in 100 ml of ether were prepared as follows:

Sample	dimedone (g)	benzyldimedone (g)
I	0.1134	none
II	0.1075	0.1612
III	none	0.1655

Each ether solution was extracted with three 20 ml portions of 1M sodium acetate solution, followed by one 30 ml portion of cold 5% sodium hydroxide solution. To the sodium acetate extracts from each sample was added 2.5 ml of 12N (conc) hydrochloric acid, 25 ml of water, and 10 ml of 38% formaldehyde solution. Samples I and II gave almost immediate precipitates upon the addition of formaldehyde while sample III gave no precipitate after 24 hours.

The sodium hydroxide extracts were acidified with 6N hydrochloric acid. Sample I gave no precipitate, Samples II and III gave immediate precipitates.

The formalin dimedone precipitates were collected from samples I and II, washed with water and set to dry in the air. Sample I gave 0.0935 g (78.3%). Sample II gave 0.0899 g (80.1%). Melting point of the formalin dimedone prepared in this way was 188.5-190°. Infared spectra of the two samples were identical.

D. Photolysis in other solvents

1. Photolysis in pentane

3-Benzyl-5,5-dimethyl-2,3-epoxycyclohexanone (2.0 g) was irradiated in 300 ml of pentane for 4 1/2 hr with a 450 watt mercury lamp filtered by Corex. A precipitate on the walls of the apparatus was shown to be a mixture of dimedone and benzyl dimedone using the procedure under C. There was no base soluble material in the pentane solution. Vpc analysis of base insoluble residues showed dibenzyl,

starting epoxyketone and materials of approximately the same retention time as α-benzyl diethyl ether (assumed to be benzyl pentane isomers).

2. Photolysis in 0.1M piperylene

Irradiation of an ether solution 0.015M in epoxy ketone and 0.1M in piperylene gave essentially the same product mixture as before according to vpc analysis.

E. Mass-balance of photo-products from 3-benzyl-5,5-dimethyl-2,3-epoxy-1-cyclohexanone in diethyl ether.

Integration of the vpc chromatogram gives the following results:

Compound	38	45	48	47	46
M.W.	230	230	164	182	140
Grams Isolated	---	0.3891	---	---	0.1424[a]
Integrated Area (Rel.)	630	428	145	233	254
Moles Present	0.00249	0.00169	0.00057	0.000092	0.00102
Grams Present	0.57	0.3891	0.093	0.167	0.1424
Yield (%)[b]	28.6	19.4	6.5	21.0	11.7

[a] Dimedone analysis: The amount of dimedone isolated (calculated from formalin dimedone) was actually 0.1140 grams but the procedure has been shown to yield only about 80% of the theoretical amount. Dividing 0.1140 by 0.80 results in the value of 0.1424 which is in good agreement with the vpc integration ratios.

[b]These data account for 75.5% of the starting material. Unidentified materials are estimated to account for 15-20% of the starting material (vpc analysis).

IV. Photolysis of Benzyl Dimedone

A. Preparation of benzyl dimedone

A solution of dimedone (5 g, 0.036 mole) in 8 ml of 20% potassium hydroxide containing potassium iodide (0.25 g) was alkylated with benzyl chloride (4.5 g, 0.036 mole) according the method of Stelter, Kesseler, and Meisel (9).

After heating under reflux for 1 1/2 hr the mixture was cooled, poured into 53 ml of 3% sodium hydroxide, extracted with ether, and the basic layer treated with 6N hydrochloric acid to yield a yellow-white precipitate. This was collected, washed with water and recrystallized from acetone and water; yield: 6.3 g (76%), needles, mp 155-157°.

B. Photolysis of benzyl dimedone

An ether solution of benzyl dimedone (0.4954 g, 0.00216 mole) under a nitrogen atmosphere was irradiated for 4 hr with a 450 watt mercury lamp filtered by Corex. The solution was extracted with five 40 ml portions of cold 3% sodium hydroxide solution, washed with water, and dried over magnesium sulfate.

Base soluble extracts were treated with 6N hydrochloric acid and a white precipitate was collected and shown to be unchanged 1-benzyl dimedone.

Removal of the ether from the base insoluble layer gave a small amount of residue which was combined with that from previous photolyses and micro distilled. The distillate gave (ca. 10 μl) α-benzyl diethyl ether by preparative vpc (4% QF-I, 148°), identified by its infrared spectrum.

V. Photolysis of 4,4-diphenyl-2,3-epoxycyclohexanone

An ether solution of 4,4-diphenyl-2,3-epoxycyclohexanone (2.0 g) was irradiated for 3 1/2 hr with a 450 watt mercury lamp filtered by Corex. The solution was extracted with four 50 ml portions of cold 5% sodium hydroxide. The combined basic extracts were saturated with sodium chloride and washed with ether, then treated with 6N hydrochloric acid to yield 0.93 g of precipitate. The base insoluble ether layer was washed with water, dried over magnesium sulfate and the solvent removed to yield 0.97 g of a yellow oil which crystallized on standing. This material was identified by infrared and vpc analysis as the unchanged epoxy ketone.

A. Photoproducts from 4,4-diphenyl-2,3-epoxycyclohexanone

1. 4,4-Diphenyl-1,3-cyclohexanedione

The base soluble precipitate was crushed under 7 ml hot carbon tetrachloride and filtered to give 0.167 g of precipitate. The filtrate yielded a brown oil (0.78 g).

The carbon tetrachloride insoluble precipitate was recrystallized from acetone and water to yield needles m.p. 191-193° (dec).

<u>Anal</u>. Calc'd for $C_{18}H_{16}O_2$: C, 81.79; H, 6.10%

Found: C, 81.80; H, 6.13%

2. 3,3-Diphenyl-2-hydroxymethylenecyclopentanone

The carbon tetrachloride soluble filtrate was chromatographed on 10 g silica gel with 75 ml of methylene chloride. The effluent yielded a solid substance which was recrystallized from acetone and water, needles, mp 94-96°. The infrared spectrum of this compound, 3,3-diphenyl-2-hydroxymethylenecyclopentanone, is shown in Figure 5.

<u>Anal</u>. Calc'd for $C_{18}H_{16}O_2$: C, 81.79; H, 6.10%

Found: C, 81.63; H, 6.15%

B. Derivatives of the photoproducts

4,4-diphenyl-2,3-epoxycyclohexanone (1.0068 g) was irradiated for 2 1/2 hr as before. The basic extracts were made neutral to pH paper with 6N hydrochloric acid. Half of the cloudy suspension was treated with formaldehyde solution to give a formalin derivative (0.0131 g, 2.6%) with an identical infrared spectrum (Figure 6) to that of the formalin derivative prepared from 4,4-diphenyl-1,3-cyclohexanedione.

One fourth of the neutral suspension was treated with 2 ml of copper acetate solution containing 0.2632 meq Cu^{++}. The chelate was filtered and the filtrate iodometrically determined to contain 0.2221 meq Cu^{++}. Thus, the sample contained 0.0411 meq of chelating β-dicarbonyl compound and the yield of 3,3-diphenyl-2-hydroxymethylenecyclopentanone was calculated as 43%.

In a separate experiment, 3,3-diphenyl-2-hydroxymethylenecyclopentanone was treated with excess copper acetate and gave a green precipitate, mp 131-133°. The infrared spectrum of this compound exhibits absorption at $\bar{\nu}_{max}(CCl_4)$ 1600, 1463 and 1340 cm^{-1}.

VI. Photolysis of 5,5-dimethyl-2,3-epoxycyclohexanone

Irradiation of an ether solution of 5,5-dimethyl-2,3-epoxycyclohexanone for 90 min with a 450 watt mercury lamp filtered by Corex gave the following compounds according to vpc analysis (4% QF-I, 138°):

Compound	Retention Time(min)	Relative Area
51	2.3	0.058
40	3.4	1.00
46	8.8	0.595

The volume of solvent was reduced to approximately 20 ml and precipitated dimedone was collected by suction filtration. The filtrate was then extracted with cold 5% sodium hydroxide solution. The basic extract was treated with 6N hydrochloric acid and the aqueous suspension extracted with ether. The ether extract was washed with sodium chloride solution and dried over magnesium sulfate.

A. Photoproducts from 5,5-dimethyl-2,3-epoxycyclohexanone

1. Dimedone

The precipitate from the photolysis was identified as dimedone by a comparison of its infrared spectrum eith that of authentic material, yield: 0.44 g, 25%. In another experiment the yield of formalin dimedone by extraction with sodium acetate solutions was 31%.

2. 4,4-Dimethyl-2-hydroxymethylenecyclopentanone

The ether solution of base soluble photoproducts gave an oil which upon sublimation at reduced pressure yielded crystals, mp 85-88^{0}(dec), identified as 4,4-dimethyl-2-hydroxymethylene <u>51</u> by infrared spectrum (Figure 7) and nmr spectrum (Figure 8). This compound also exhibited a positive ferric chloride test.

3. Basic cleavage of 4,4-dimethyl-2-hydroxymethylenecyclopentanone (33)

4,4-Dimethyl-2-hydroxymethylenecyclopentanone (200 mg) was placed in 20 ml 10% sodium hydroxide solution and heated at reflux for 1/2 hr. The solution was cooled, extracted with ether, and the ether extract was washed with saturated sodium chloride solution, and dried over magnesium sulfate. Removal of the solvent left a residue containing only one component by vpc analysis. The product was shown to be 3,3-dimethylcyclopentanone by comparison of its infrared spectrum with that of authentic material.

VII. Photolysis of 2,3-epoxycyclopentanone

An ether solution of 2,3-epoxycyclopentanone (2.7 g, 0.0276 mole) was irradiated for 1/2 hr with a 450 watt mercury lamp filtered by Corex. A considerable amount of white precipitate had collected on the walls of the apparatus making a longer irradiation time impractical. The precipitate was collected to give 0.1260 g of material (4.7%), mp 149-151°.

The clear ether filtrate was extracted with cold 5% sodium hydroxide and gave an orange basic solution, which upon treatment with 6N hydrochloric acid gave an orange suspension. This suspension was filtered and extracted with ether. The ether extract was washed with saturated sodium chloride solution and dried over magnesium sulfate. Removal of the solvent left approximately 1 g of an orange oil.

A. Photoproducts of 2,3-epoxycyclopentanone

1. Cyclopentane-1,3-dione

The precipitate mp 149-151° has the same melting point as that reported for cyclopentane-1,3-dione (10). An infrared spectrum of this material shows $\nu_{max}^{CHCl_3}$ 1590 cm^{-1} and 1650 cm^{-1} indicative of a β-dicarbonyl compound.

2. Unknown compound "X"

The base soluble oil was microdistilled and the volatile material showed a major peak upon vpc inspection.

Preparative vpc gave enough compound for an infrared spectrum (Figure 9) and nmr spectrum (Figure 10) but no structure has been assigned from this data.

VIII. Photolysis of 3-methyl-2,3-epoxycyclopentanone

An ether solution of 3-methyl-2,3-epoxycyclopentanone (3.9 g, 0.035 mole) was irradiated for 2 hr with a 450 watt mercury lamp filtered by Corex. The ether solution was extracted with cold 5% sodium hydroxide solution. The basic extract was washed with ether and treated with 6N hydrochloric acid. The aqueous phase was then extracted with ether, the ether extracts washed with saturated sodium chloride solution and dried over magnesium sulfate. Removal of the solvent left 1.25 g residue.

When a similar epoxy ketone solution was irradiated for 4 hr, only acetic acid was found as a base soluble product.

In another photolysis, the product was continuously extracted by a 100 ml layer of 2% sodium hydroxide during the irradiation period. A 40% yield of base soluble material was obtained by the previous workup.

A. Photoproducts from 3-methyl-2,3-epoxycyclopentanone

1. Acetic acid

The base soluble material from a 4 hr irradiation of 3-methyl-2,3-epoxycyclopentanone was distilled at reduced pressure to yield volatile material from which acetic acid was collected by vpc. Identification was by comparison of infrared and nmr spectra with authentic acetic acid.

2. 2-Acetyl-1-hydroxycyclobutene

The base soluble residue from photolysis of 3-methyl-2,3-epoxycyclopentanone was sublimed at reduced pressure yielding white crystals, mp 104-104.5°. This compound was not 2-methyl-1,3-cyclopentanedione, reported mp 214-215° (34).

The compound gave positive ferric chloride and iodoform tests. When an alcohol solution of the compound was treated with an excess of copper acetate solution, a color change from blue to green was noted, but no precipitate formed.

An nmr spectrum (Figure 11) infrared spectrum (Figure 12) and mass spectrum (Table 6):

Table 6. Mass spectrum of 2-acetyl-1-hydroxycyclobutene

m/e	Rel. Abund.	m/e	Rel. Abund.
27	83	55	89
39	60	69	89
41	100	83	46
43	71.5	112	46

all support 2-acetyl-1-hydroxycyclobutene as the structure of this compound.

Anal. Calc'd for $C_6H_{10}O_2$: C, 64.27; H, 7.19%

Found: C, 64.33; H, 7.23%

B. Preparation of 1-methoxy-2-acetylcyclobutene

An ether solution of 2-acetylcyclobutanone (0.5 g, 0.0045 mole) was treated with an excess of ethereal diazomethane. After the yellow color had disappeared from the solution, a few drops of acetic acid were added and the solution was extracted with cold 5% sodium hydroxide, washed with saturated sodium chloride solution and dried over magnesium sulfate.

The solvent was removed leaving a residue showing only one peak according to vpc analysis. Preparative vpc gave enough pure compound for an infrared spectrum (Figure 14) and nmr spectrum (Figure 13). These spectra support the structure of the methylated photoproduct as 1-methoxy-2-acetylcyclobutene.

IX. Photolysis of 2-acetyl-1-hydroxycyclobutene

2-Acetyl-1-hydroxycyclobutene (0.050 g, 0.00044 mole) was placed in a pyrex test tube and dissolved in approximately 3 ml of anhydrous ether. After the solution was flushed briefly with nitrogen, the tube was stoppered and attached to a vycor immersion lamp holder. Irradiation for 1 1/2 hr gave no reaction as determined by vpc inspection. Evaporation of the solvent left a residue of pure white crystals mp 104°.

X. Photolysis of the Pulegone Oxides

A. Photolysis of β-pulegone oxide

A solution of β-pulegone oxide (2.9 g, 0.0172 mole) in 300 ml ether was irradiated for three hours with a 450 watt mercury lamp filtered by Corex. Analysis on a 4% QF-I column (135°) indicated approximately 5% conversion to products. The solvent was removed and the residue distilled on a short-path apparatus at 5 mm up to 90°. The condenser was rinsed with ether and combined distillates purified by preparative vpc to yield several unidentified low boiling fractions and two photorearrangement products.

B. Photoproducts of β-pulegone oxide

1. 2-Acetyl-2,5-dimethylcyclohexanone stereoisomers

The two rearrangement isomers were collected from a 4% QF-I column at 130°, retention times 4.3 and 5.4 min. The infrared spectrum (Figure 16) of the compound with a retention time of 4.3 min was identical to that of the minor ozonolysis product <u>55</u> of a 4-methyl-<u>iso</u>-pulegone isomer mixture (11). The infrared spectrum (Figure 15) of the compound with a retention time of 5.4 min was identical to the major ozonolysis product <u>54</u>. Retention times of the ozonolysis products were the same as the photoproducts.

2. α-Pulegone oxide

α-Pulegone oxide was not isolated from the photomixture. Identification was made by a comparison of vpc retention time with authentic α-pulegone oxide.

C. Photolysis of α-pulegone oxide

A solution of α-pulegone oxide 0.25M in 3 ml acetonitrile was irradiated in a sealed pyrex tube for 6 hr. Analysis by vpc demonstrated the presence of compounds having the same retention times as β-pulegone oxide and both stereoisomeric rearrangement products. The extent of reaction was approximately 3%.

XI. Photoreduction of 4-methyl-3,4-epoxy-2-pentanone with tri-n-butyl stannane

(a) A solution of 4-methyl-3,4-epoxy-2-pentanone (1.23 g, 0.0108 mole) and tri-n-butyl stannane (5.82 g, 0.020 mole) in 90 ml of anhydrous ether was irradiated for 2 1/4 hr with a 450 watt mercury lamp fitted with a Corex filter. The solution was agitated by a continuous stream of nitrogen.

After filtering the solution, the solvent was removed by a rotary evaporator and the residue was washed with three portions of water (both diacetone alcohol and the starting epoxy ketone are water soluble). The combined water washes were filtered, saturated with sodium chloride and extracted with ether to yield ca. one gram of product. This was distilled and purified by vpc (4% QF-I). Two components were present; the major (ca. 80%) was diacetone alcohol identified by its infrared spectrum, and the minor was unchanged starting material.

(b) A solution of 4-methyl-3,4-epoxy-2-pentanone (1.14 g, 0.01 mole) and tri-n-butyl stannane (5.82 g, 0.02 mole) in 90 ml of pentane was irradiated as above for two hours.

The solvent was removed and the residue was chromatographed on a silica gel column 4.5 cm in diameter by 3.5 cm in depth. The butyl tin compounds were eluted with pentane and the remaining organic material was eluted with 300 ml of ether. Most of the ether was removed on a rotary evaporator to yield 1.2 g of residue which upon vpc inspection (4% QF-I, 115°) contained only ether (ca. 10%) and diacetone alcohol.

XII. Preparation of 3,3-dimethylcyclopentanone (11)

A. 3,3-dimethylcyclohexanol

3,3-Dimethylcyclohexanol was prepared by the method of Doering (35). Dimedone (94 g) was dissolved in 100 ml of purified acetic acid and reduced over platinum oxide to give 50 g (58.5%) of the alcohol, bp 85°/13mm.

B. β,β-dimethyladipic acid

β,β-dimethyladipic acid was prepared by the nitric acid oxidation of 3,3-dimethyl-cyclohexanol according to the procedure of Ellis (36). A 59% yield was obtained, mp 80-84°.

C. 3,3-Dimethylcyclopentanone

3,3-Dimethylcyclopentanone was prepared by the method of Pines (37). β,β-Dimethyl adipic acid (40 g) and 2 g of barium hydroxide were heated to 285°. The distillate gave 14.2 g (55%) of the cyclopentanone bp 29°/5 mm. n_D^{24} 1.4322.

XIII. Preparation of α-benzyl Diethylether

A. 1-Phenyl-2-propanol (38)

Reduction of phenylacetone (26.8 g, 0.20 mole) by an excess of lithium aluminum hydride in anhydrous ether gave 1-phenyl-2-propanol bp 98°/10 mm in 75% yield.

B. α-Benzyldiethylether

Ethyl iodide (10 g, 0.065 mole) was added to an anhydrous tetrahydrofuran suspension of the sodium salt of 1-phenyl-2-propanol (6.8 g - prepared by adding an equivalent of sodium hydride to the alcohol) to yield the desired ether contaminated by the starting alcohol. After removing the solvent and a crude distillation, α-benzyl diethyl ether was collected by preparative vpc (20% DEGS, 160°). An infrared spectrum (Figure 2) and nmr spectrum (Figure 3) were identical to those of the photoproduct.

XIV. Preparation of tri-*n*-butylstannane (39)

Treatment of tri-*n*-butyl tin chloride (112 g, 0.345 mole) in 400 ml of ether with lithium aluminum hydride

(5.0 g, 0.13 mole) gave tri-n-butyl stannane distilling at 71-74°/0.5 mm; 80 g, 80% yield.

XV. Quantitative Measurements of Photolysis Rates

Samples of the material(s) to be irradiated were accurately weighed and solutions made up volumetrically to insure known concentrations. A known quantity of a substance having a suitable vpc retention time and absorbtion spectrum was usually added as an internal standard for vpc analysis.

Piperylene and 2,5-dimethyl-2,3-hexadiene were purified by distillation, while other hydrocarbon solvents were purified by treatment with concentrated sulfuric acid followed by distillation from phosphorus pentoxide. Acetonitrile was Fisher certified grade and ether was Fisher anhydrous grade.

Solutions were prepared for irradiation by placing ca 3 ml into 13 mm pyrex tubes which were then degassed and sealed.

Irradiation was in a light equilibrating water bath (13) using either a 200 or 450 watt Hanovia medium pressure mercury lamp equipped with appropriate filters in a water cooled (or heated) vycor or quartz immersion well.

Conversion to products was kept small as some of them exhibit photochemical instability.

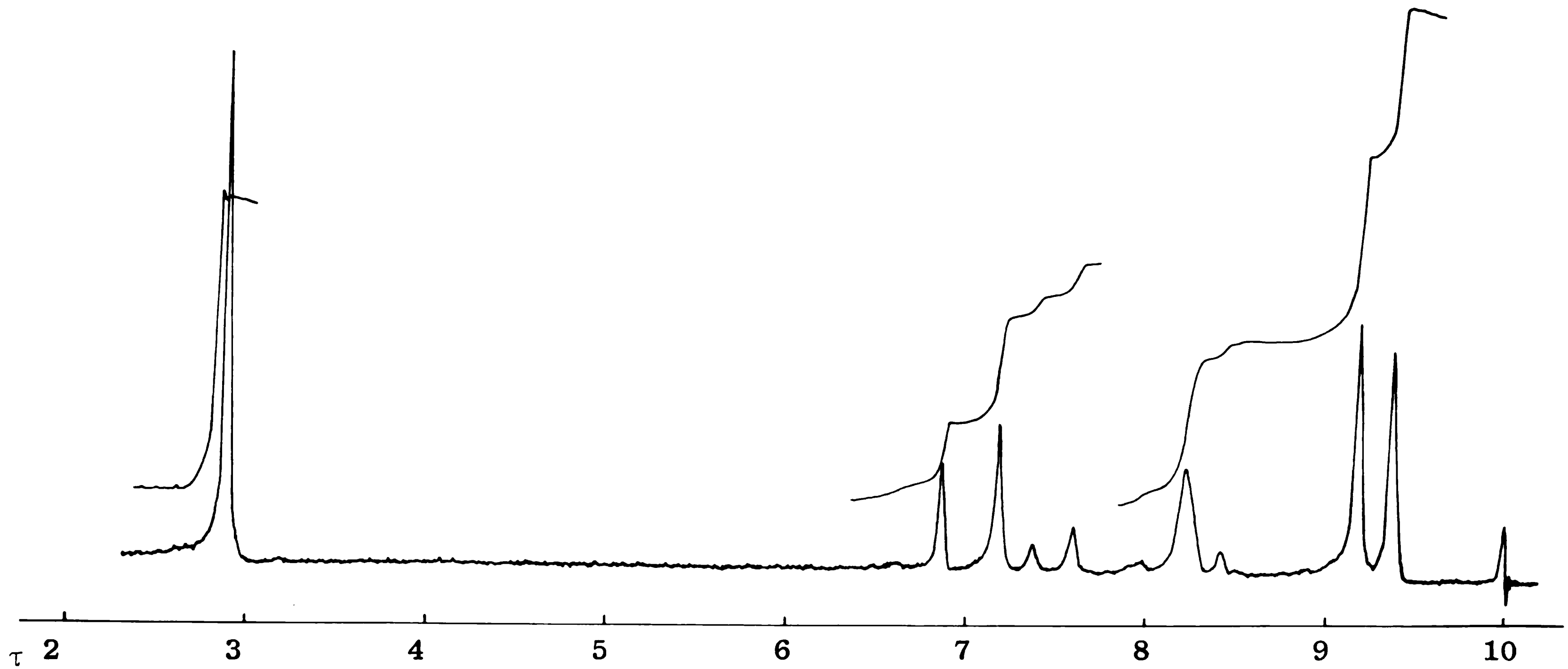


Figure 1. Nmr Spectrum of 3-benzyl-5,5-dimethyl-2,3-epoxycyclohexanone.

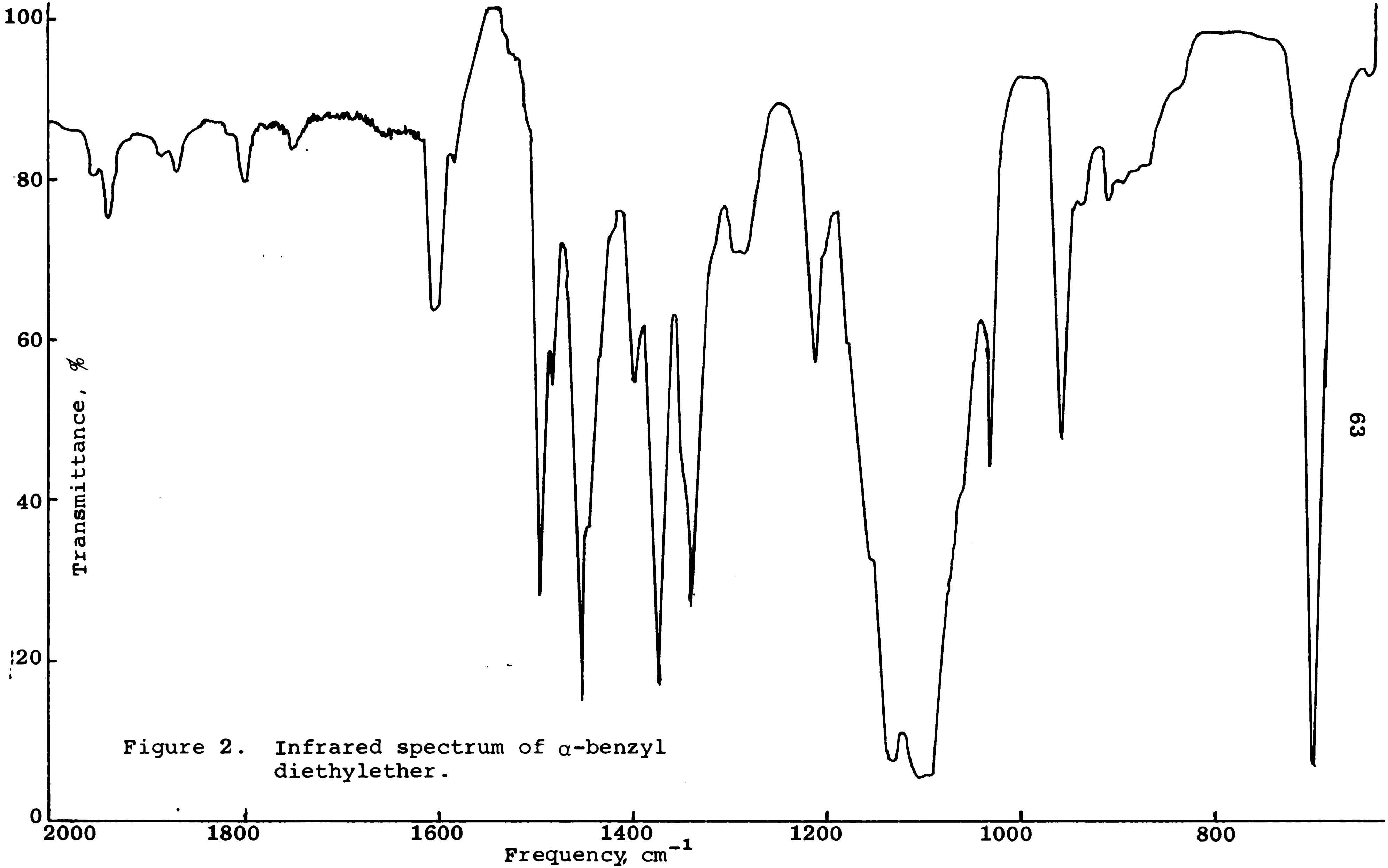


Figure 2. Infrared spectrum of α-benzyl diethylether.

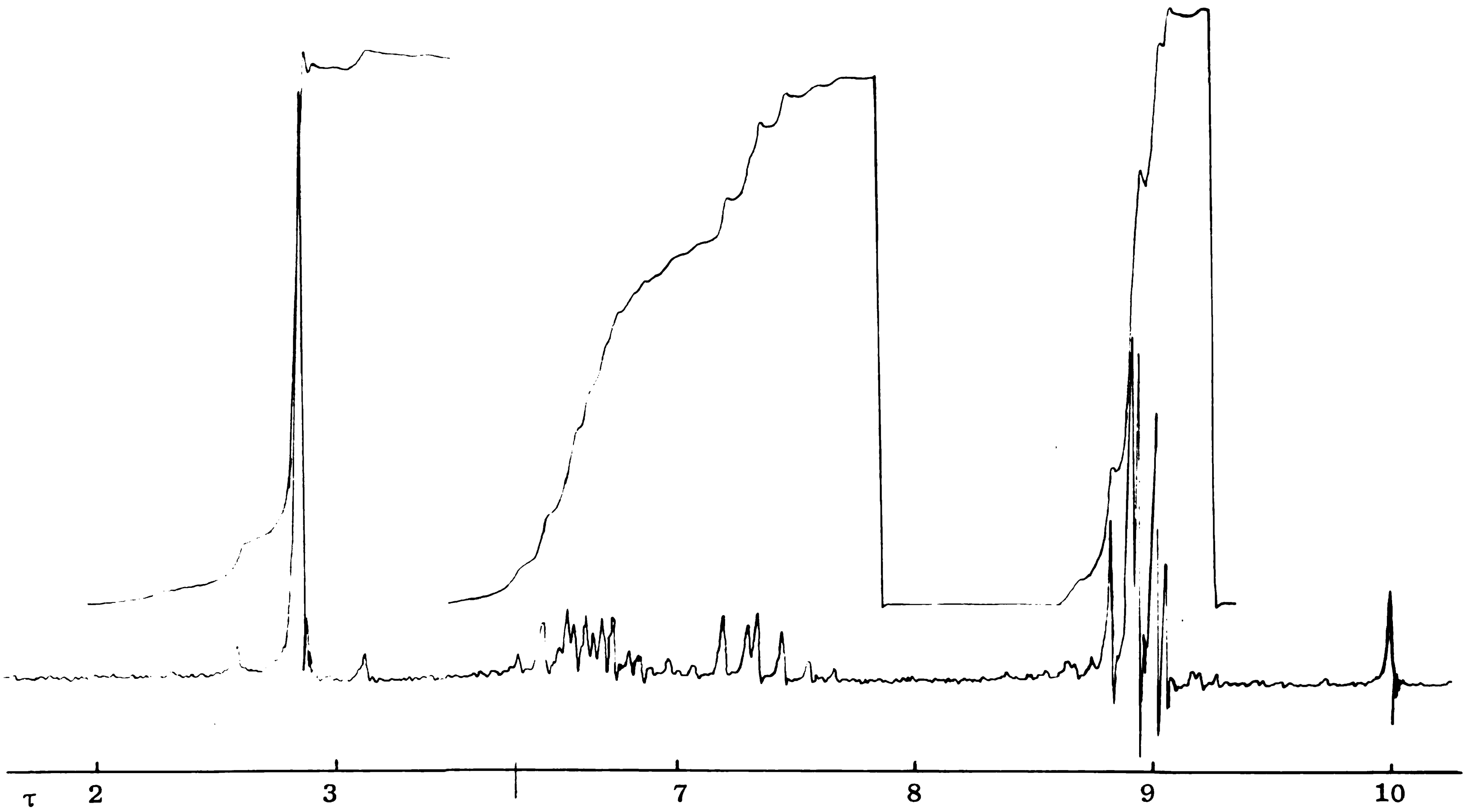


Figure 3. Nmr spectrum of α-benzyl diethylether.

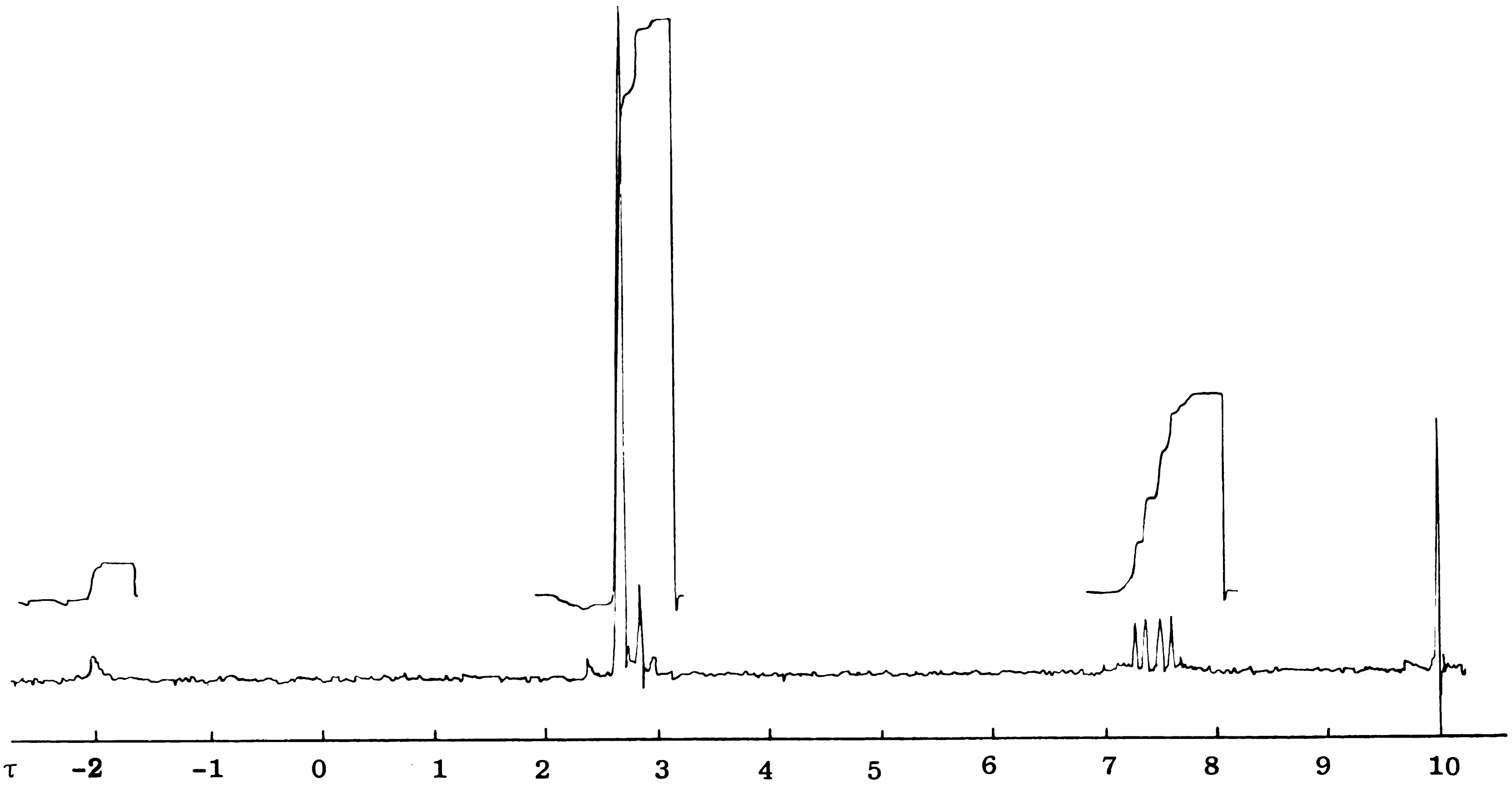


Figure 4. Nmr spectrum of 3,3-diphenyl-2-hydroxymethylenecyclopentanone.

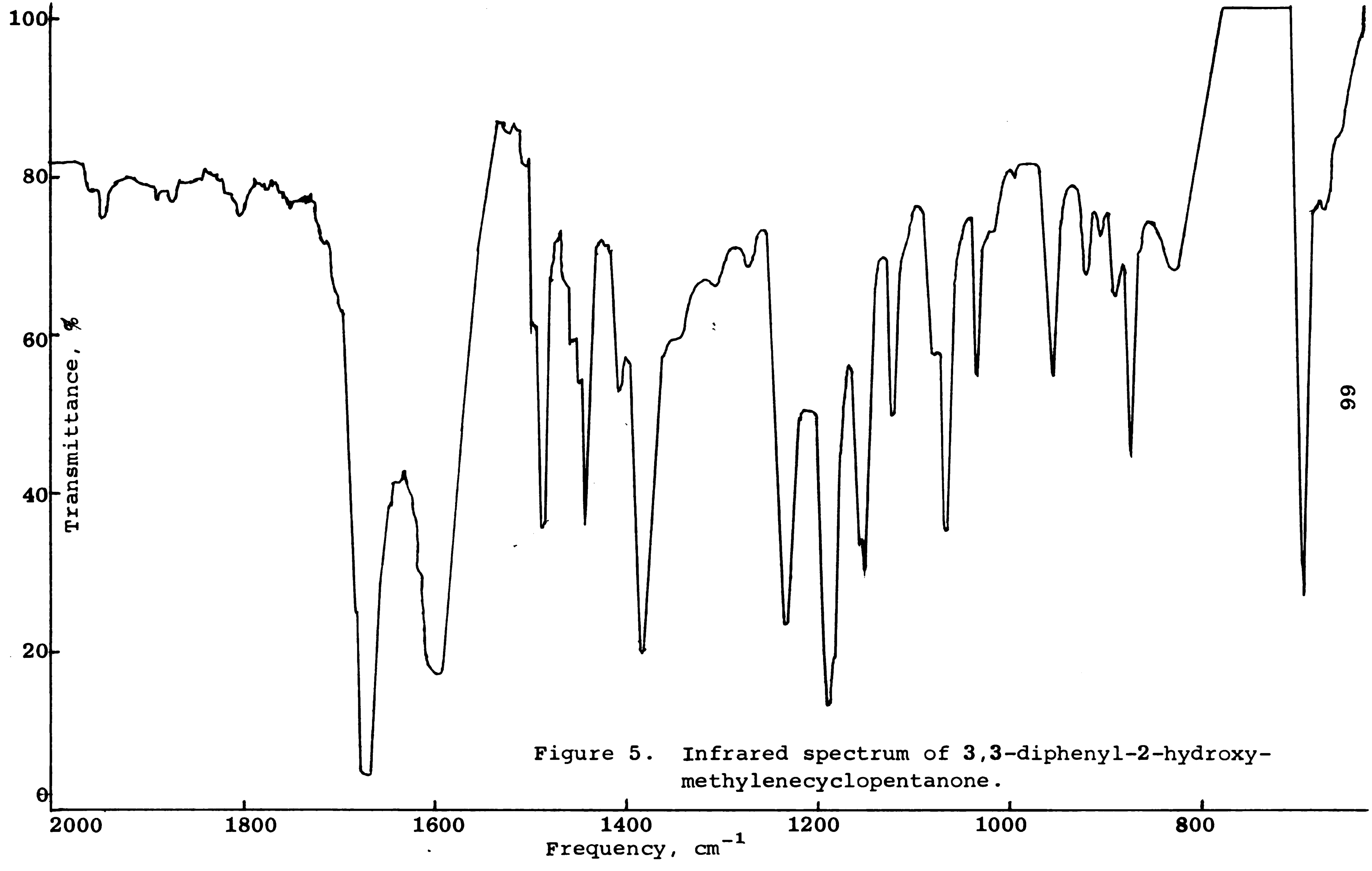


Figure 5. Infrared spectrum of 3,3-diphenyl-2-hydroxymethylenecyclopentanone.

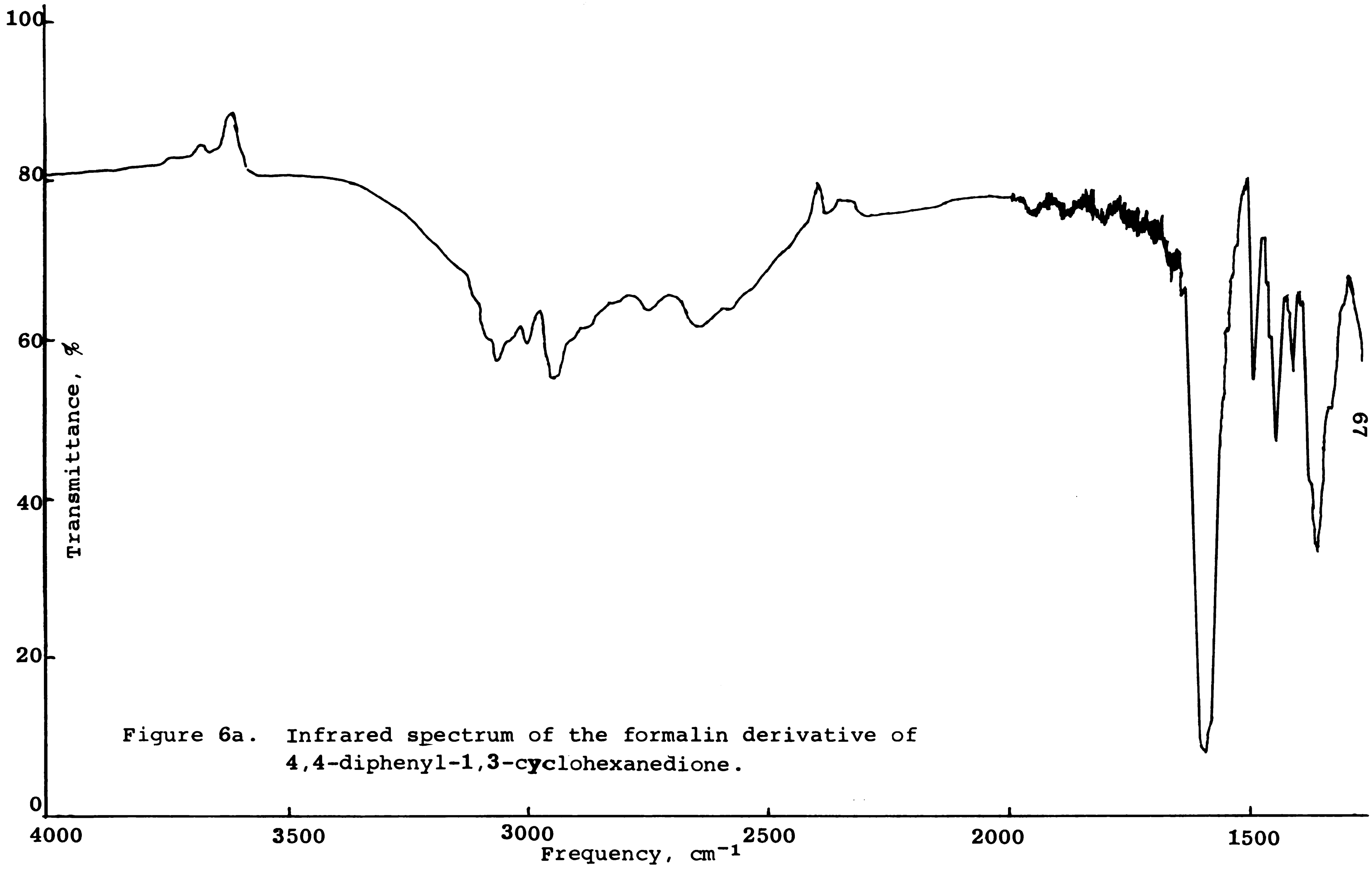


Figure 6a. Infrared spectrum of the formalin derivative of 4,4-diphenyl-1,3-cyclohexanedione.

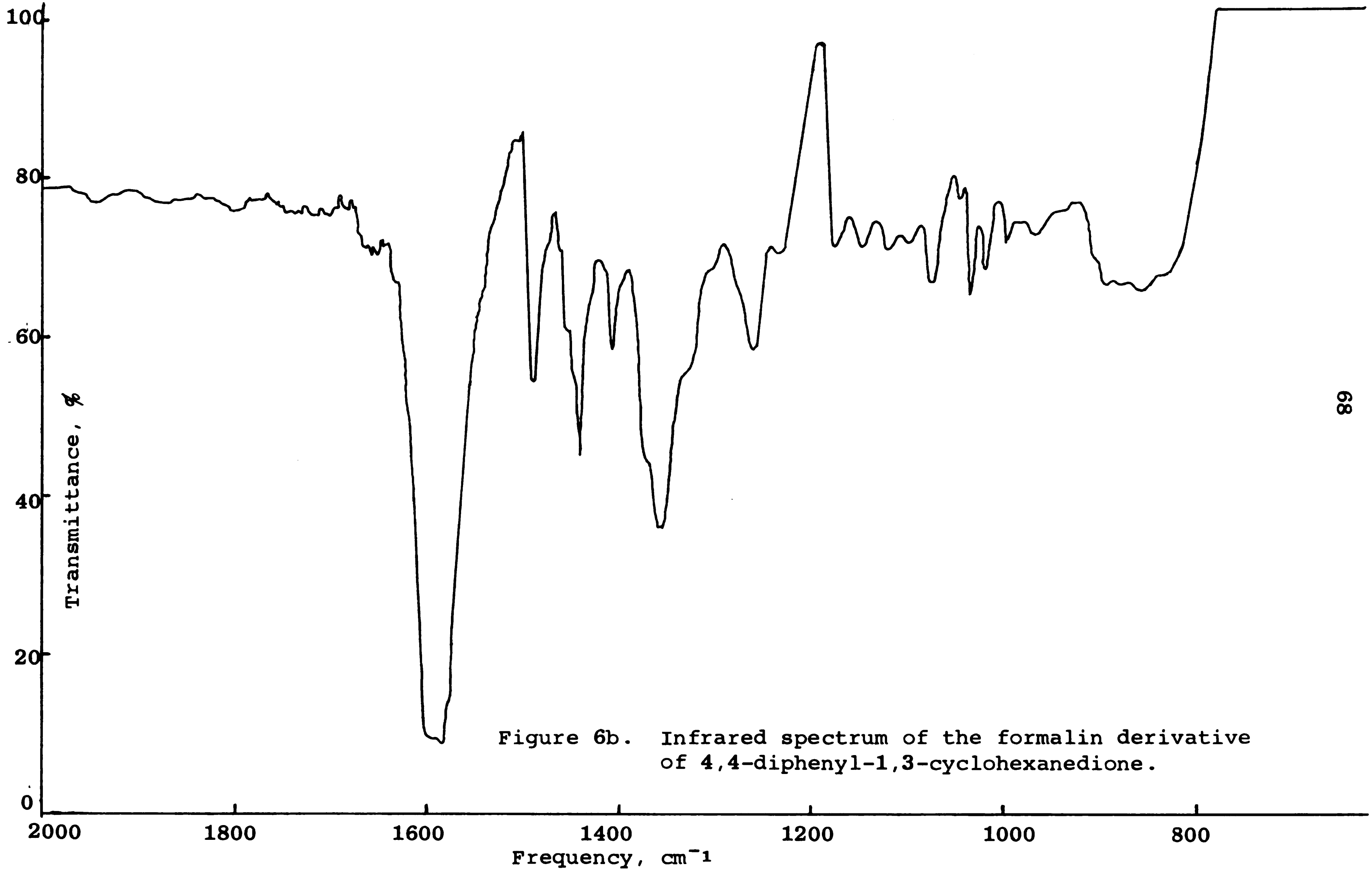


Figure 6b. Infrared spectrum of the formalin derivative of 4,4-diphenyl-1,3-cyclohexanedione.

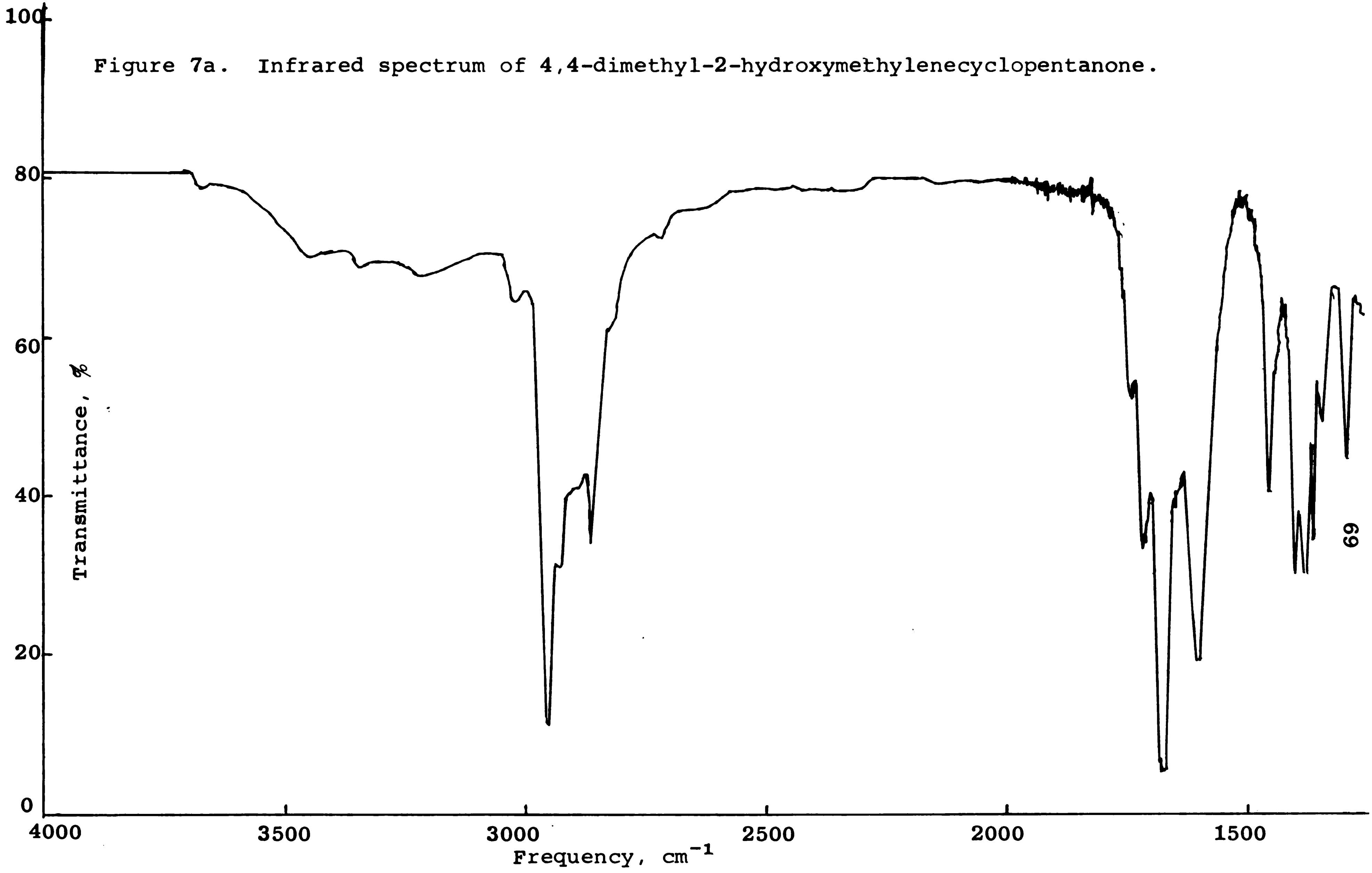


Figure 7a. Infrared spectrum of 4,4-dimethyl-2-hydroxymethylenecyclopentanone.

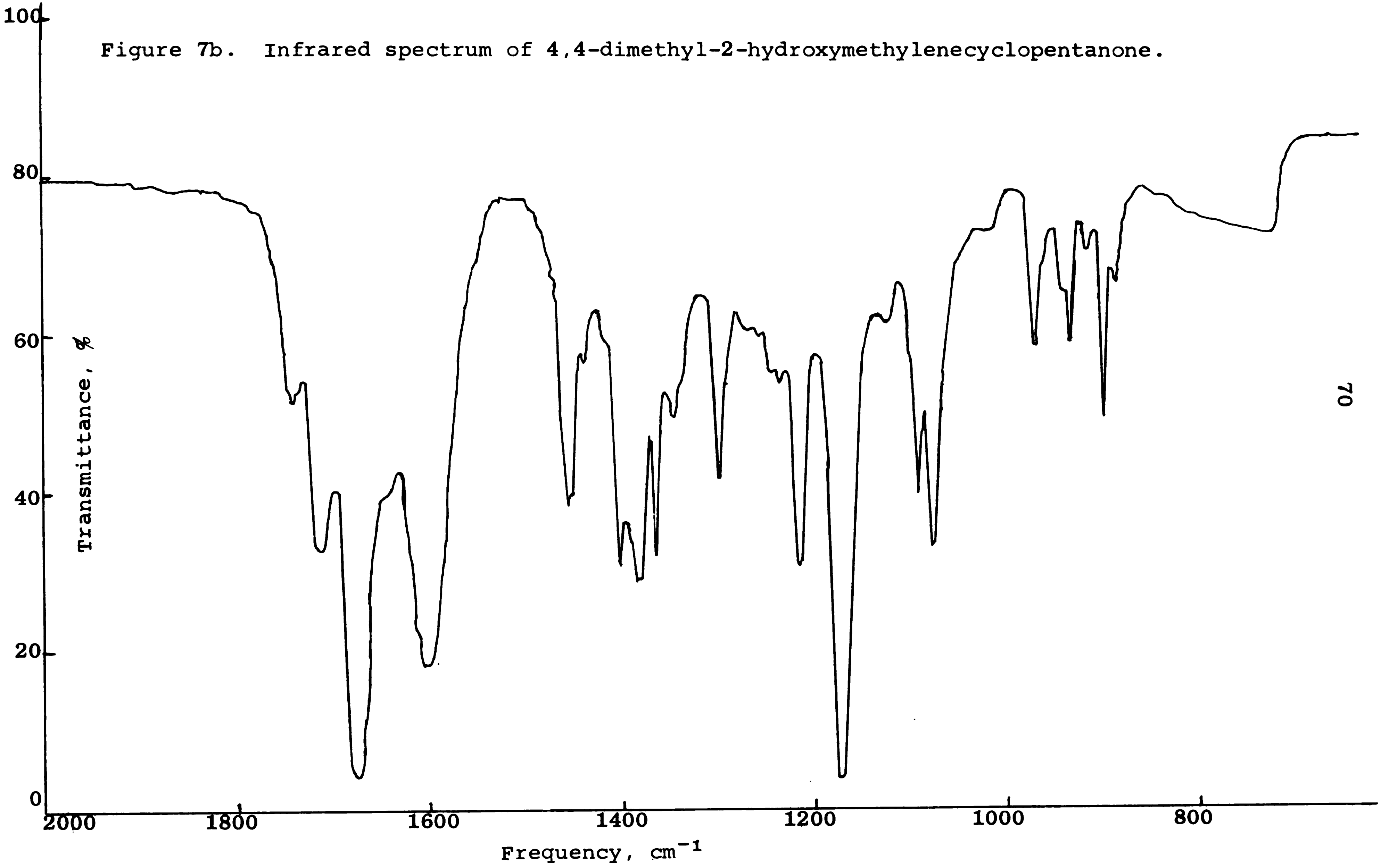


Figure 7b. Infrared spectrum of 4,4-dimethyl-2-hydroxymethylenecyclopentanone.

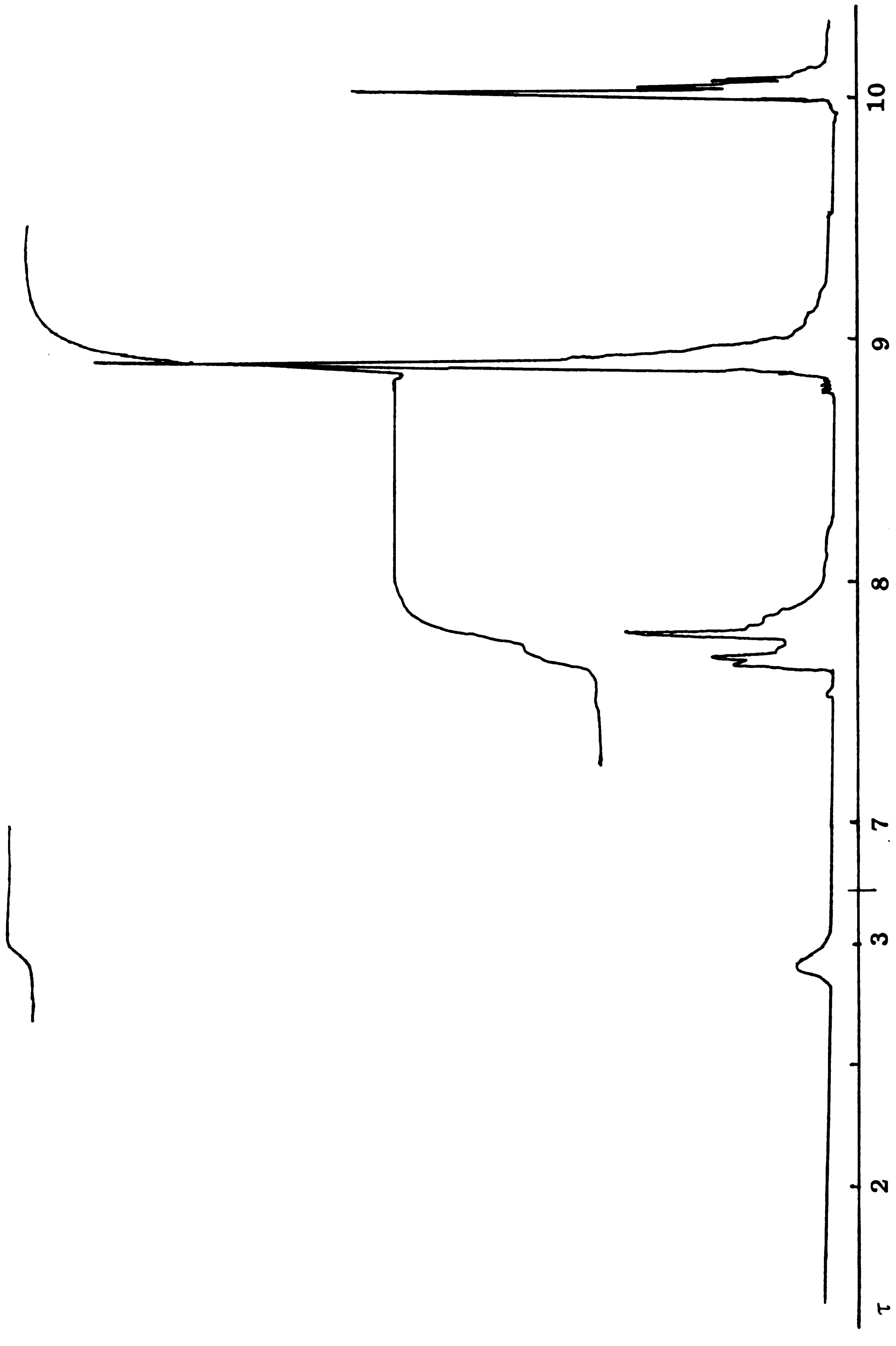


Figure 8. Nmr spectrum of 4,4-dimethyl-2-hydroxymethylenecyclopentanone.

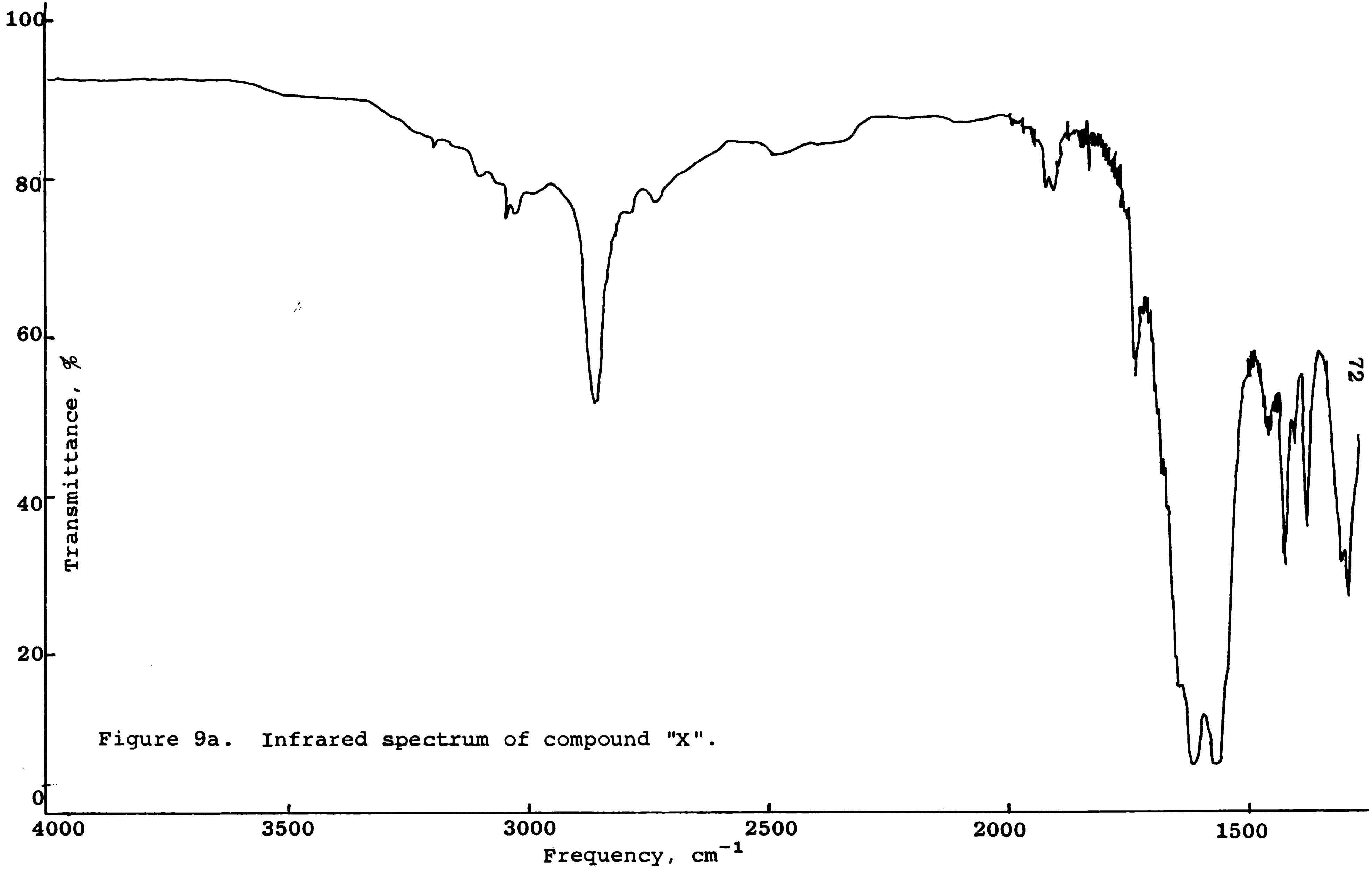


Figure 9a. Infrared spectrum of compound "X".

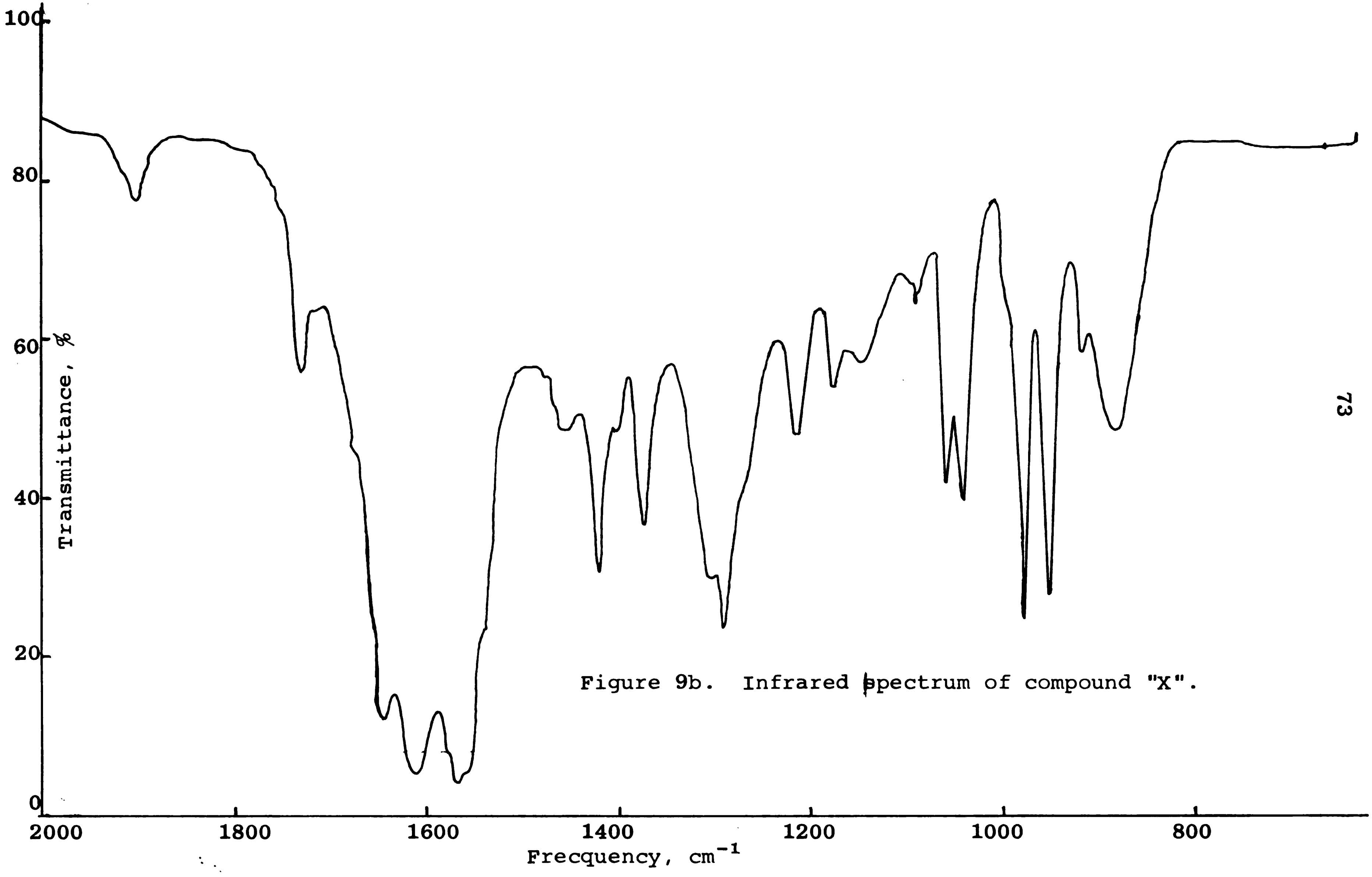


Figure 9b. Infrared spectrum of compound "X".

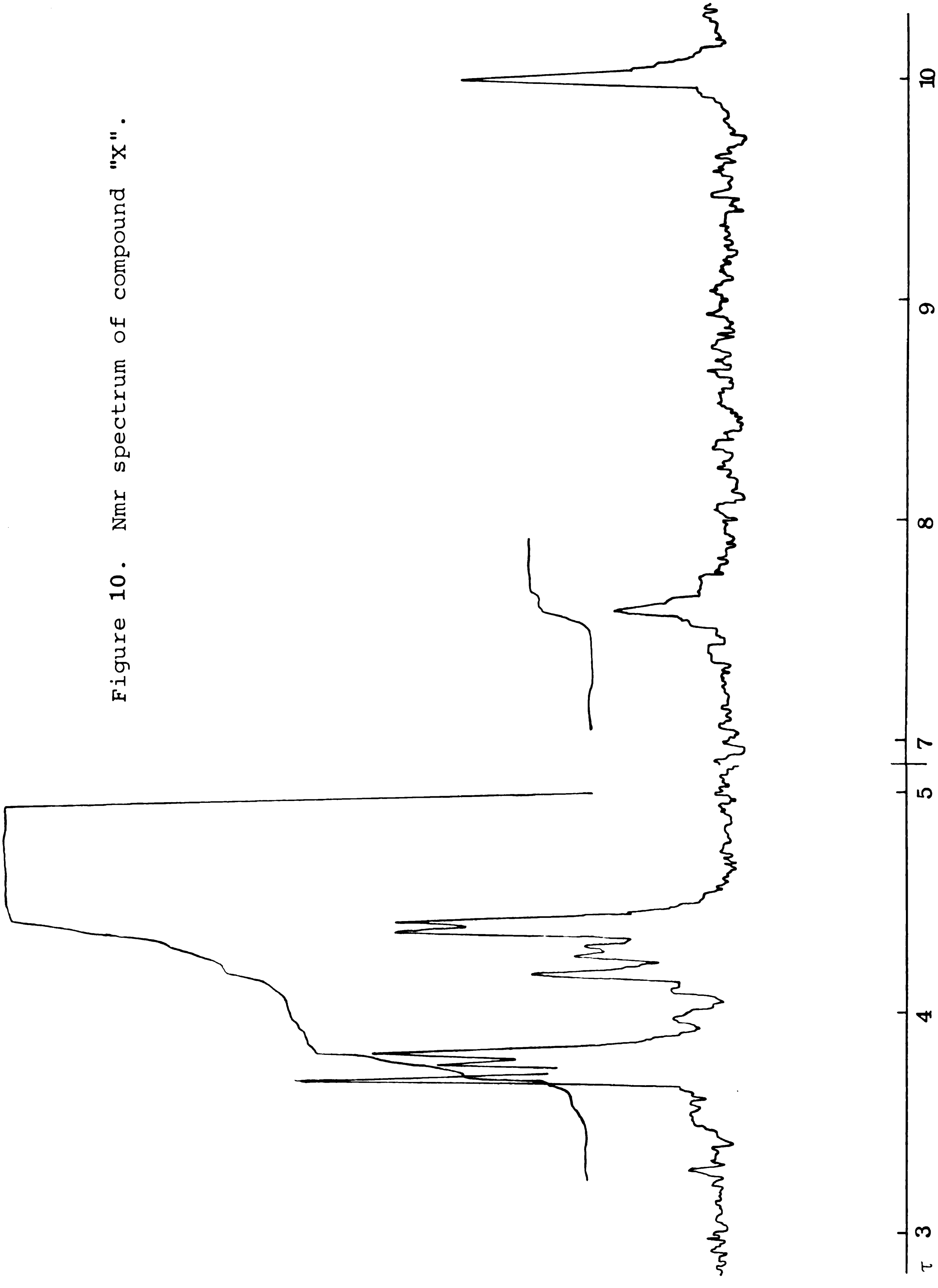


Figure 10. Nmr spectrum of compound "X".

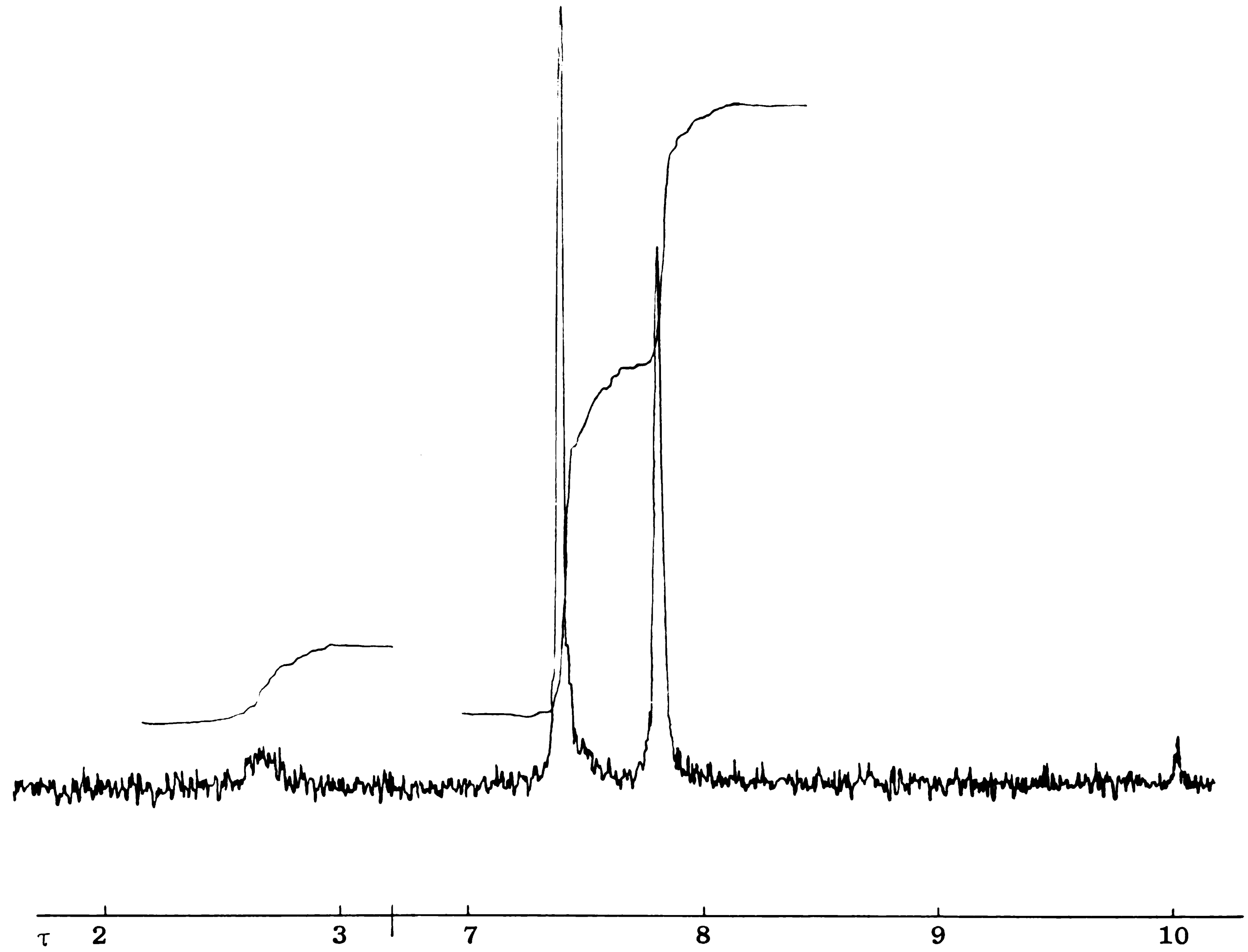


Figure 11. Nmr spectrum of 2-acetyl-1-hydroxycyclobutene.

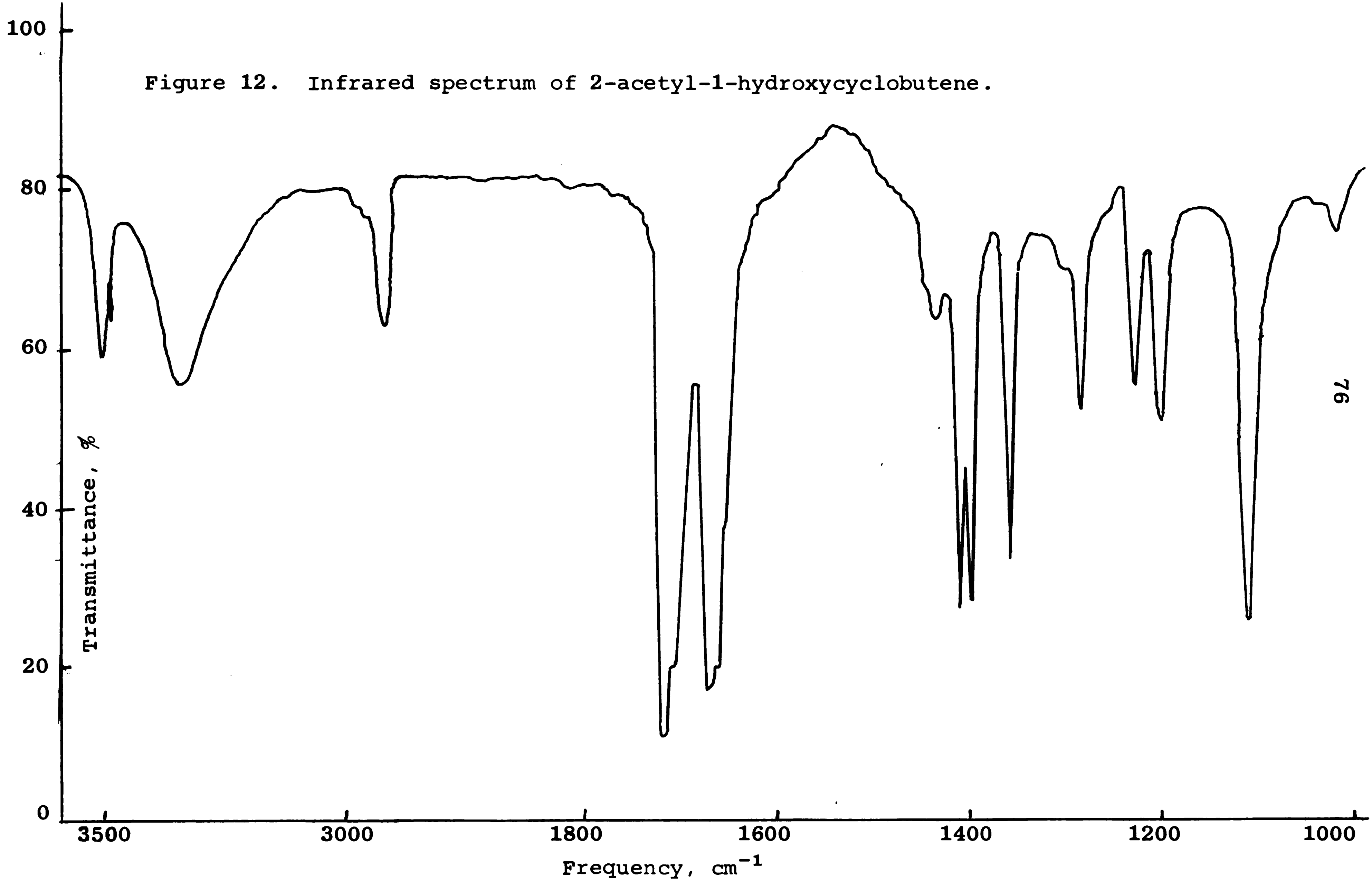


Figure 12. Infrared spectrum of 2-acetyl-1-hydroxycyclobutene.

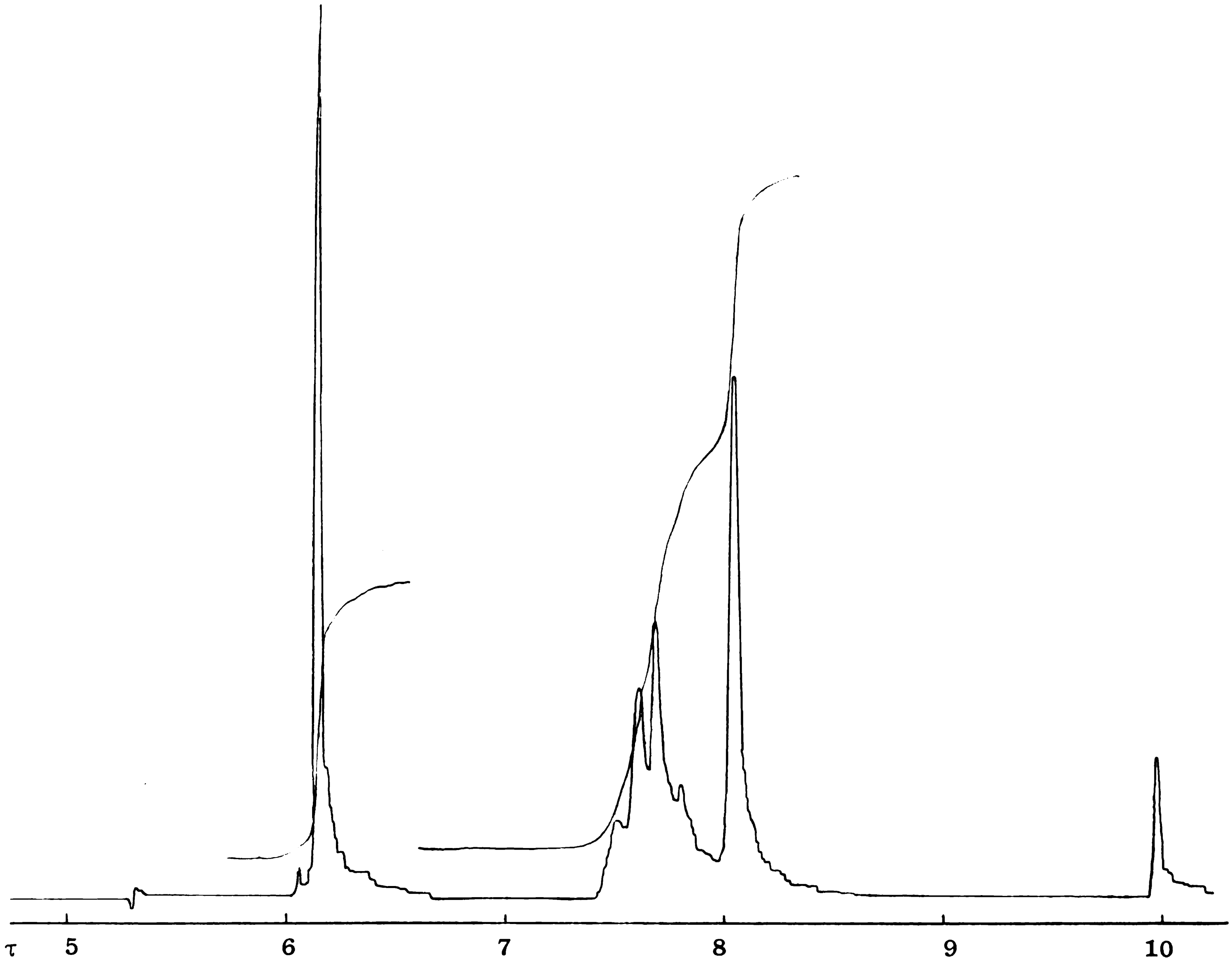


Figure 13. Nmr spectrum of 2-acetyl-1-methoxycyclobutene.

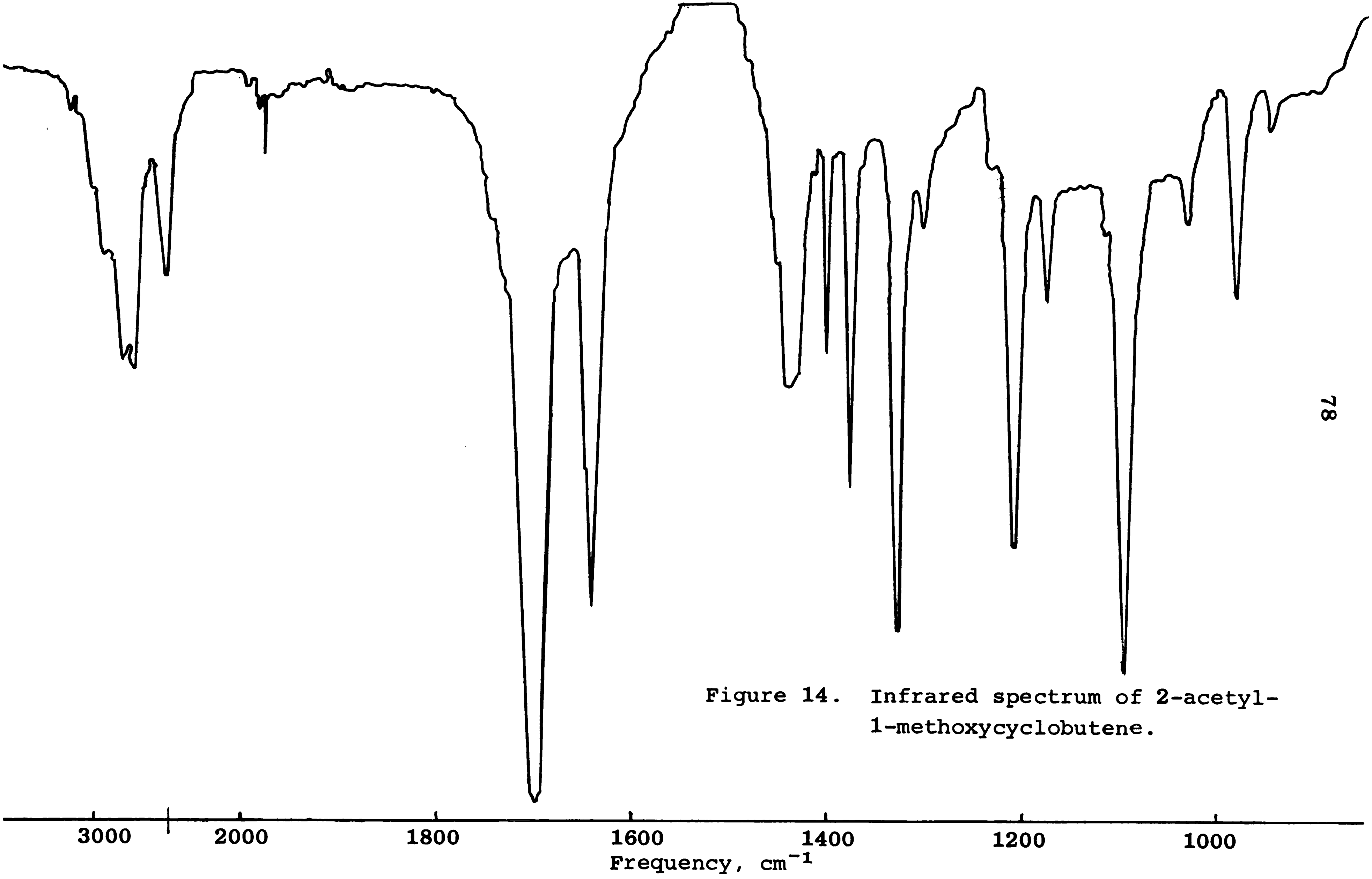


Figure 14. Infrared spectrum of 2-acetyl-1-methoxycyclobutene.

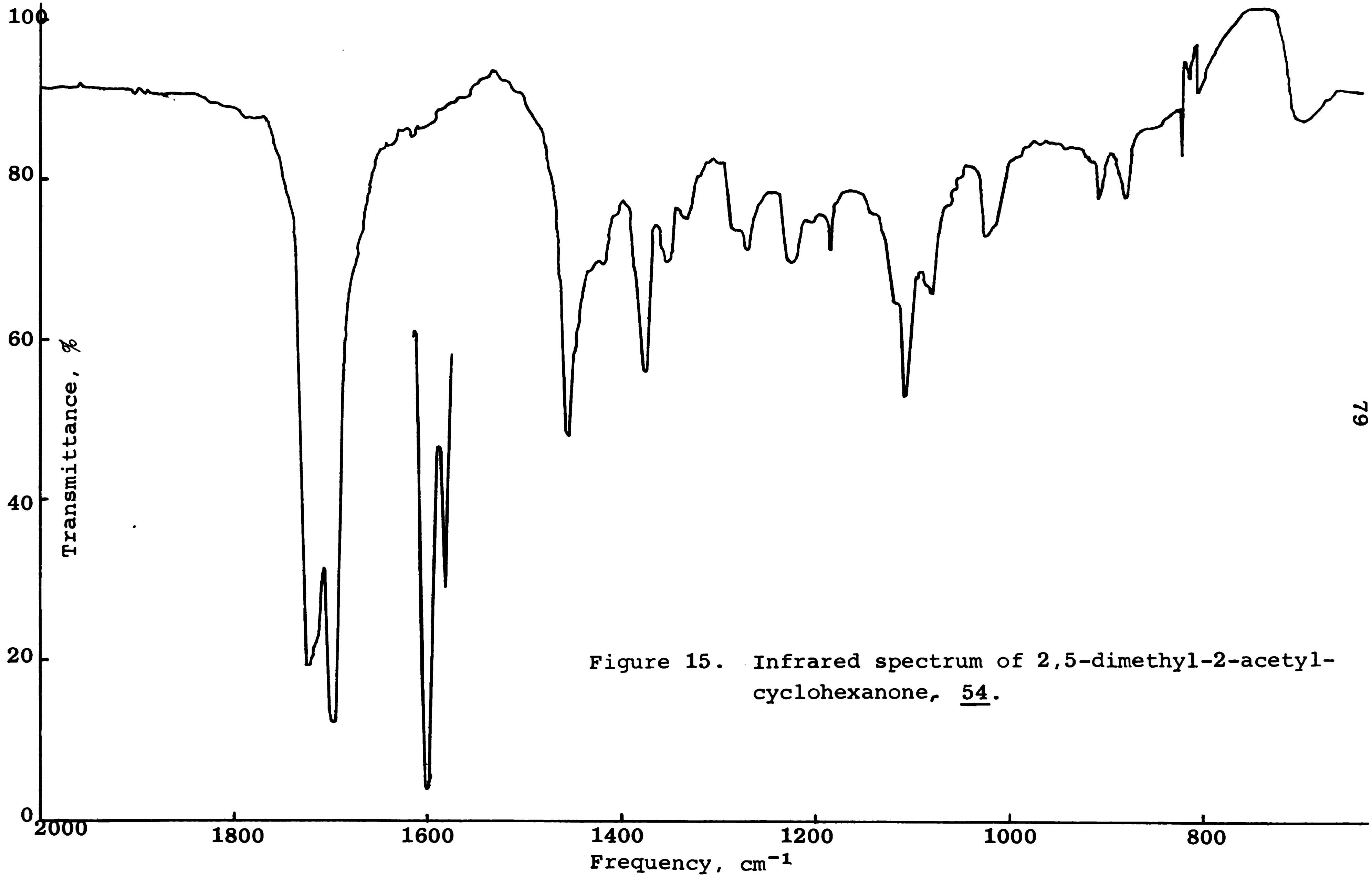


Figure 15. Infrared spectrum of 2,5-dimethyl-2-acetylcyclohexanone, 54.

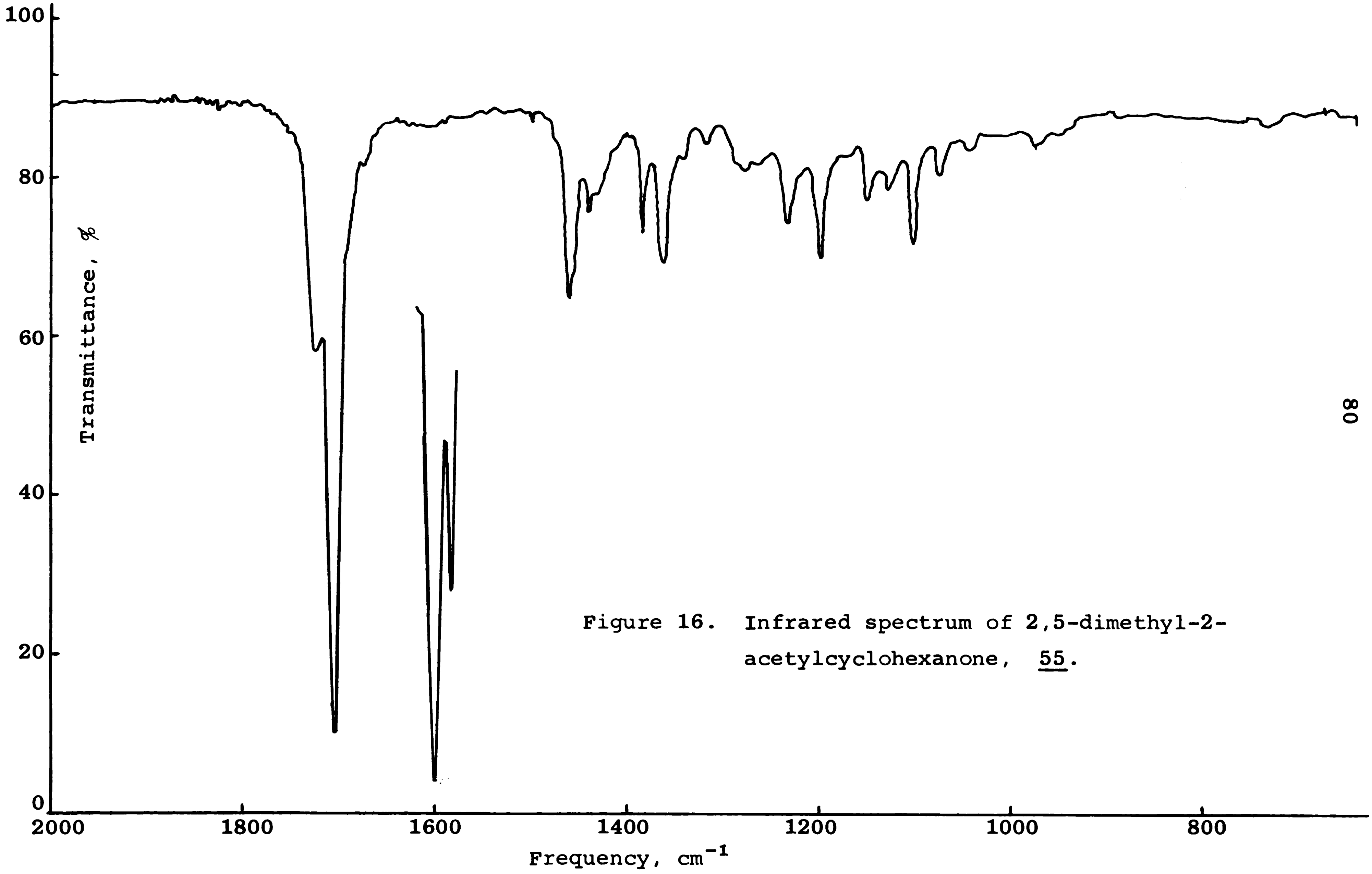


Figure 16. Infrared spectrum of 2,5-dimethyl-2-acetylcyclohexanone, <u>55</u>.

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