ABSTRACT

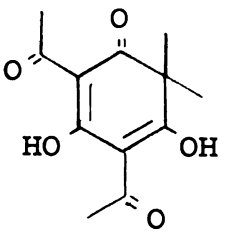
THE PHOTOISOMERIZATION AND PHOTO-OXIDATION OF SOME SUBSTITUTED DIENONES

by Robert H. Young

The purpose of this research was to investigate the effect of substituents on the photolysis of 2,4-cyclohexadienones. Substituents used were acetyl and hydroxyl groups.

Diacetylfilicinic acid (2,4-diacetyl-3,5-dihydroxy-6,6-dimethyl-2,4-cyclohexadienone, 1) was prepared from 1,3-diacetylphloroglucinol, 2, by treatment with methyl iodide and sodium methoxide in methanol. Phloroglucinol and acetic anhydride were refluxed with an acid catalyst to give the 1,3-diacetylphloroglucinol.

Acetylfilicinic acid (2-acetyl-3,5-dihydroxy-6,6-dimethyl-2,4-cyclohexadienone, 3) was obtained by refluxing diacetylfilicinic acid in methanol-sodium methoxide or by allowing the reaction mixture to stand at room temperature for more than two weeks. A number of other related substituted 2,4- and 2,5-cyclohexadienones were also prepared to aid structural assignments. Spectral data including uv spectra at different acid and base concentrations were used to assign definite structures to these compounds.



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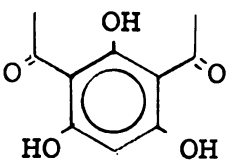

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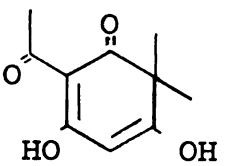

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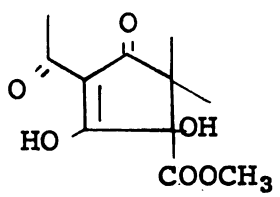
Diacetylfilicinic acid, 1, was inert when irradiated through Pyrex with a Hanovia L 450 watt or a Hanovia S 200 watt lamp in methanol under nitrogen. However, in alkaline methanol under oxygen it did undergo an interesting photo-oxidation and rearrangement to 2-acetyl-3,4-dihydroxy-4-carbomethoxy-5,5-dimethyl-2-cyclopentenone, 4. This compound was identified by its spectral properties and its conversion to the known 2-acetyl-3,4-dihydroxy-5,5-dimethyl-2-cyclopentenone, 5, using 2N sodium hydroxide at 100^0. Spectral data confirmed the structure of the latter compound. A mechanism was postulated for the formation of the photo-oxidation product, which involved the reaction of the enolate anion of 1 with singlet oxygen as a key step. The photo-oxidation could be sensitized by dyes known to produce singlet oxygen. The same photo-oxidation product, 4, was also obtained thermally, using (singlet) oxygen from the peroxide of 9,10-diphenylanthracene.

Acetylfilicinic acid, 3, was photo-oxidized in the same way as diacetylfilicinic acid to give not only the same product, 4, but in addition some of the decarboxylated compound, 5, probably via a new route. Thus the reactions of enolate anions with singlet oxygen may be general; the study of further examples seems desirable.



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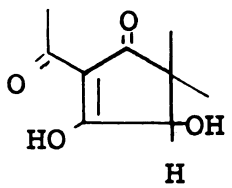

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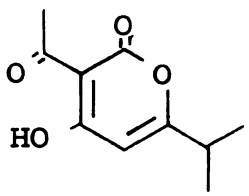

6

Acetylfilicinic acid, 3, underwent a photolytic rearrangement in neutral media, unlike diacetylfilicinic acid. The product was a pyrone, 3-acetyl-4-hydroxy-6-i-propyl-2H-pyrone, 6. The formation of the pyrone may be rationalized by photolytic ring opening of 3 to a ketene, followed by intramolecular attack by the 5-hydroxyl substituent on the ketene.

Some kinetic experiments showed that the photo-oxidation was independent of the oxygen and base concentrations, except when the base concentration was low. The chemical rate depended only upon the efficiency with which the excited state was formed followed by reaction with oxygen resulting in singlet oxygen.

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By

Robert H. Young

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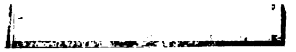

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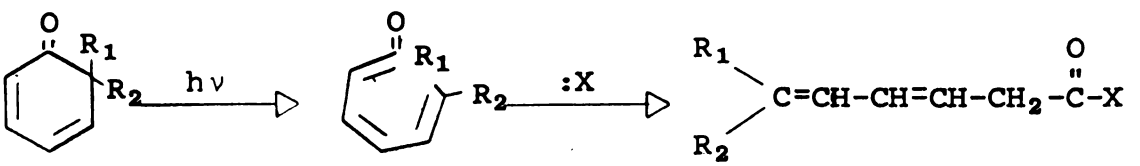
INTRODUCTION

Until recently the normal photochemical reaction for 2,4-cyclohexadienones in solvents containing a nucleophile was a ring opening to give esters, amides, or acids depending upon whether the nucleophile was an alcohol, amine or water (1,2,3). The photochemical product is known to be a ketene, which then reacts thermally with the nucleophile. An example is outlined in the scheme:



1

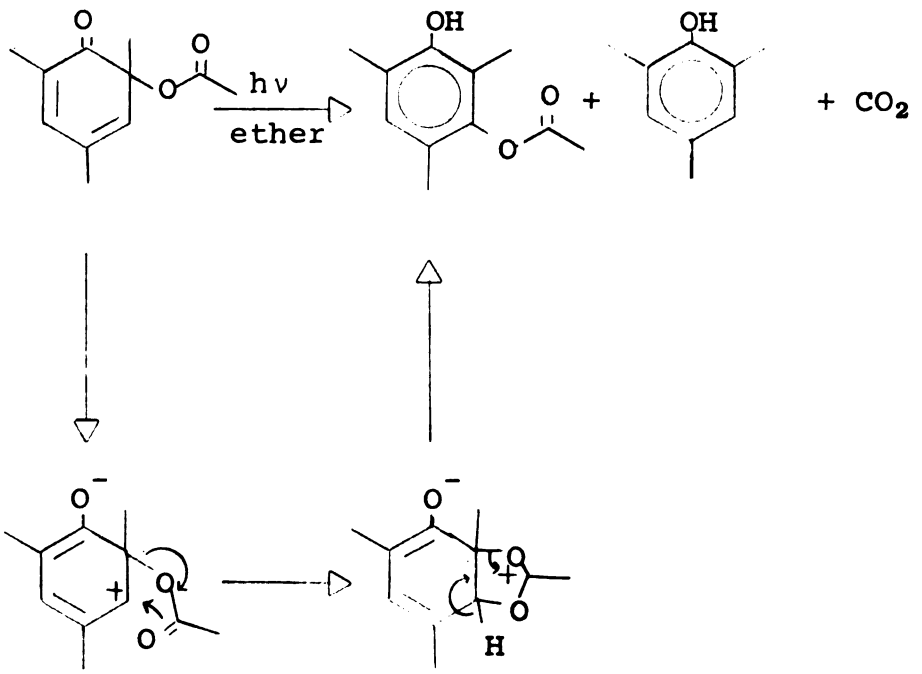
X: = nucleophile

a. $R_1 = R_2 = CH_3$

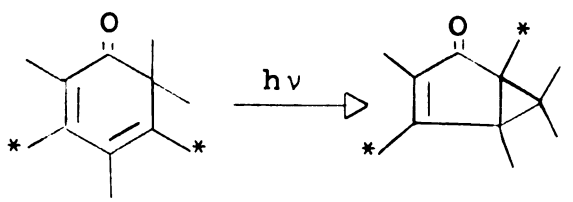
b. $R_1 = R_2 = OAc$

c. $R_1 = CH_3$; $R_2 = OAc$

Alternate modes of rearrangement include expulsion of a heteroatom from the C-6 position or migration of a substituent from C-6 to C-5 to give a phenol (3).

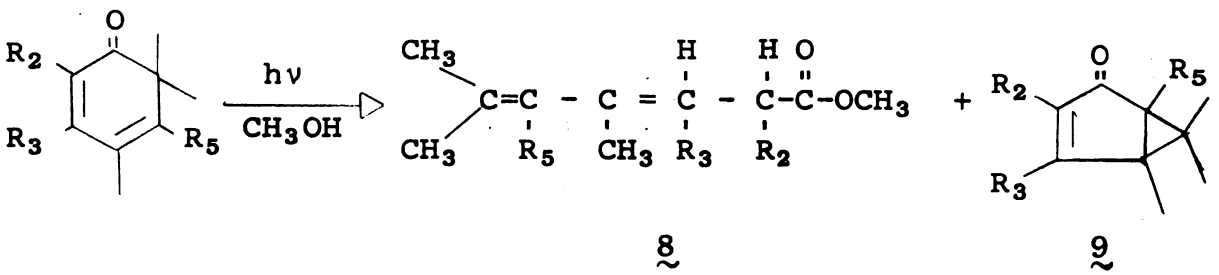


Recently Hart et al. (4) have shown that a fourth alternative is possible. Hexamethyl-2,4-cyclohexadienone, 2, rearranged in the presence of ultraviolet light to a bicyclic isomer, 3. In a later paper (5) they discussed the mechanism which was elucidated through labeling experiments; no migration of methyl groups occurred.



2 3

Hart and Collins (6) prepared and photolyzed a series of methyl-substituted 2,4-cyclohexadienones, and found that the reaction course depends critically on the number and positions of the substituents. A mechanism involving two separate routes with two different types of transition states to account for the two products was favored. They suggested that additional work is necessary to determine the nature of the excited state for each reaction.



8 + 9

2 ($R_2 = R_3 = R_5 = CH_3$) $\xrightarrow{h\nu}$ 9

4 ($R_2 = R_3 = CH_3$; $R_5 = H$) $\xrightarrow{h\nu}$ 9

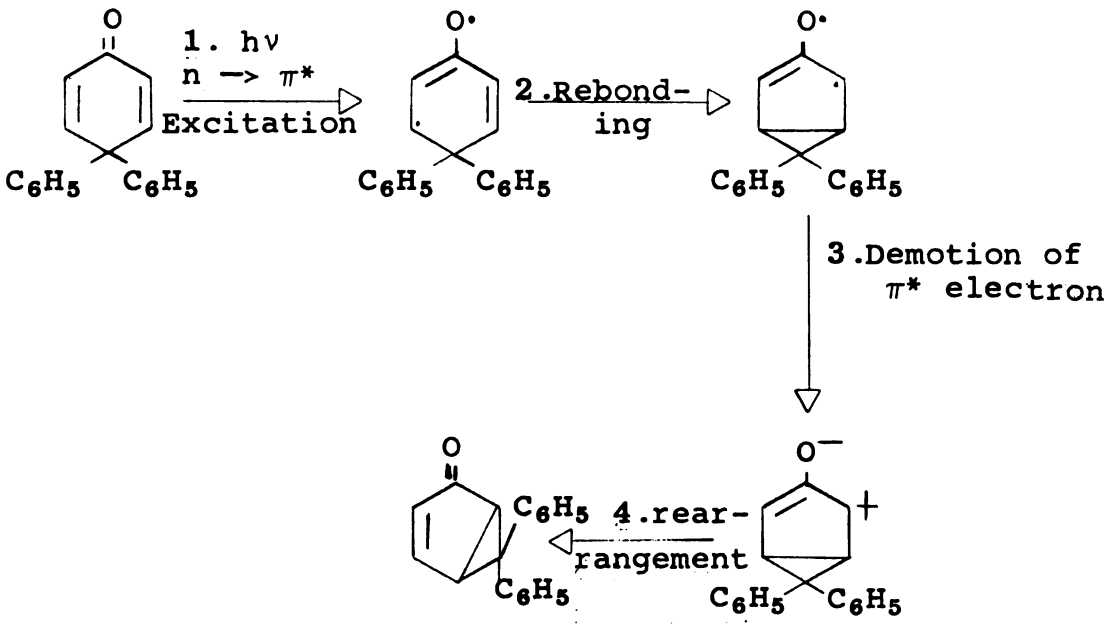
5 ($R_2 = H$; $R_3 = R_5 = CH_3$) $\xrightarrow{h\nu}$ 8

6 ($R_2 = R_5 = H$; $R_3 = CH_3$) $\xrightarrow{h\nu}$ 8

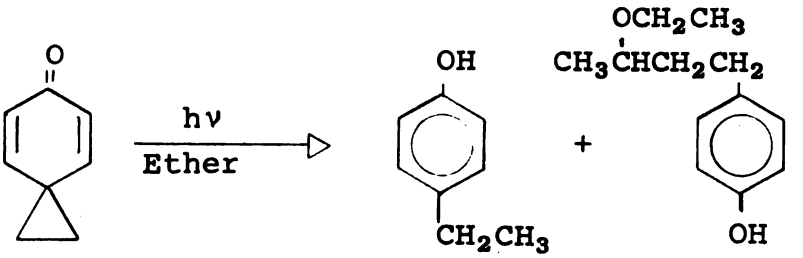
7 ($R_2 = R_5 = CH_3$; $R_3 = H$) $\xrightarrow{h\nu}$ 8 + 9

The photoisomerizations of 2,5-cyclohexadienones have been studied more intensively than those of their 2,4-isomers. Chapman first proposed dipolar excited states (7), and Fisch applied these to explain the photorearrangement of 2,5-cyclohexadienones to bicyclic compounds (8). Zimmerman later proposed a more plausible diradical excited state (9). Zimmerman's mechanism involved four steps:

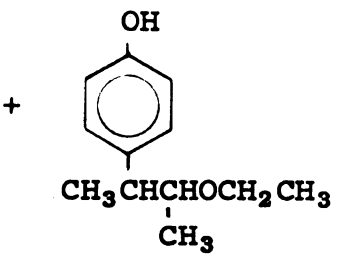
(1) excitation, (2) rebonding, (3) demotion of the π^* electron, and (4) rearrangement of the resulting charge-separated species. This scheme is outlined below.

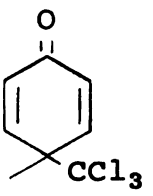


More recent experimental evidence favoring this mechanism has been advanced by Schuster and shows that radicals must be involved in the excited state in order to get the fragmentation products in the photolysis of 10 (10). Fragmentation must occur before the electron demotion step in the previously mentioned scheme. He also showed the importance of this mechanism in the photolysis of 11 (11). Photolysis of 11 carried out in ether gave 12 by radical fragmentation followed by hydrogen abstraction. Photolysis in benzene gave 13.

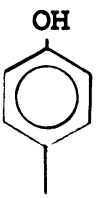

O
hν
Ether
OH
CH2CH3
OCH2CH3
CH3CHCH2CH2
OH

10

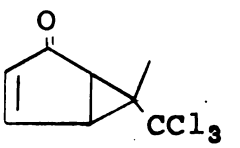

OH
CH3CHCHOCH2CH3
CH3


O
CCl3

11

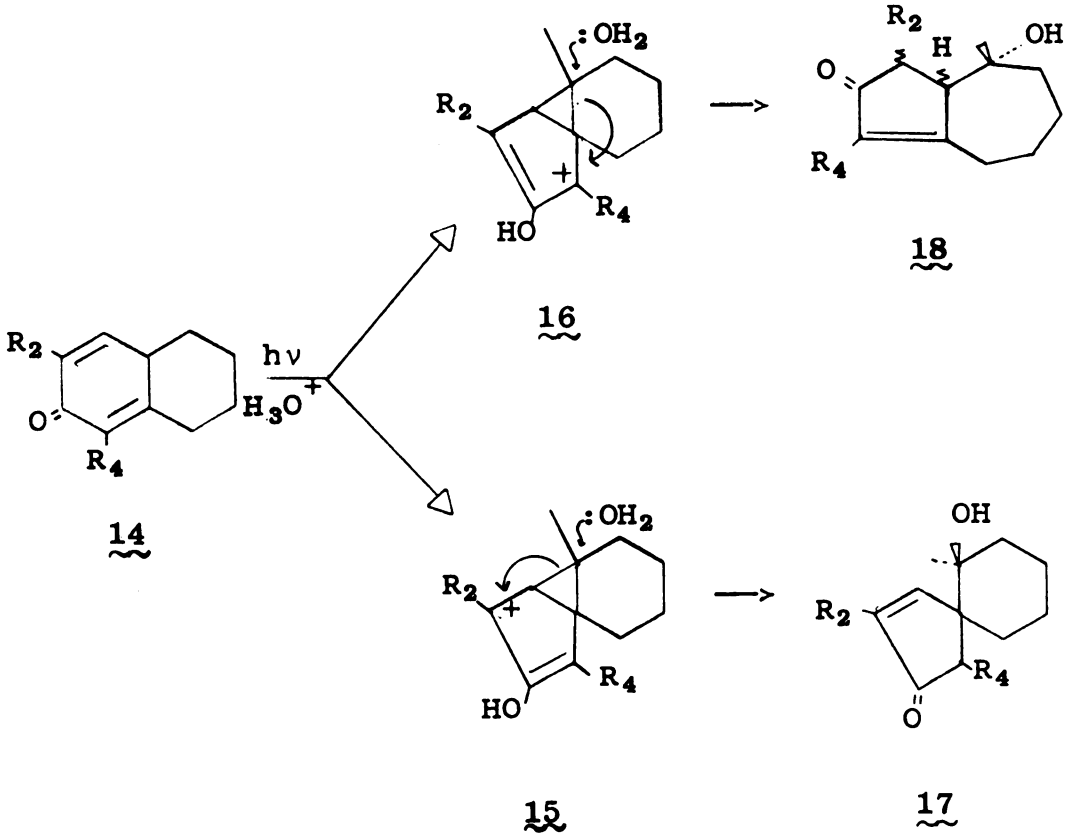

OH

12


O
CCl3

13

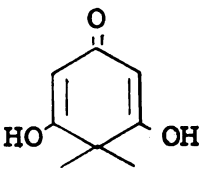
Some work has also been carried out on the mechanistic interpretation of the photolyses of 2,5-cyclohexadienones by the use of substituent groups in other than the 4 position of the molecule. The reaction as outlined here was taken from Chapman's, Organic Photochemistry (3). When both R_2 and R_4 are hydrogens, then both 17 and 18 are formed. When R_2 is electron donating (R_2 = CH_3 ; R_4 = H), then the intermediate 15 is favored and the product is 17. When R_4



is electron donating (R_4 = CH_3 ; R_2 = H) then 18 is formed. However, when R_2 is electron withdrawing (R_2 = CHO or COOH ; R_4 = H) then 15 is unfavorable as an intermediate and products are formed from intermediate 16.

Both of these intermediates could result from electron demotion after the initial photochemical reaction and not necessarily have any effect on the excited state of the molecule or the bond crossing mechanism.

Except for the work on the different methyl-substituted 2,4-cyclohexadienones (6) little work has been done on the effects of different substituents in these compounds. For this reason 2,4-cyclohexadienones substituted by electron-donating and/or electron-withdrawing groups were irradiated. Filicinic acid, which has been represented in the literature as 19 (12,13,14) and as 20 (13,15), was chosen as an initial



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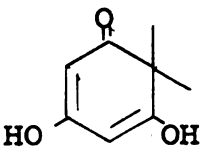

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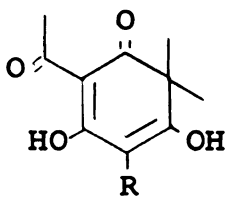
example. Not only can the substituent effect of the hydroxyl groups be studied, but also the substance has the interesting option of behaving as a 2,4- or 2,5-cyclohexadienone. Due to the initial difficulties in acquiring a quantity of filicinic acid and because its structure was found to be a 2,5-cyclohexadienone, work was concentrated on the photolysis of 2,4-diacetyl-3,5-dihydroxy-6,6-dimethyl-2,4-cyclohexadienone (diacetylfilicinic acid, 21) a readily available precursor in the synthesis of filicinic acid.

Although this particular compound, 21, did not undergo any direct photolysis reaction for reasons which will be discussed later, it did experience a novel and interesting photo-oxidation. The preparation and structural determination of filicinic acid, 19, and its derivatives will be presented and discussed, as will those of a number of related compounds. New photoisomerizations and photo-oxidations of two of these compounds, 2,4-diacetyl-3,5-dihydroxy-6,6-dimethyl-2,4-cyclohexadienone (diacetylfilicinic acid, 21) and 2-acetyl-3,5-dihydroxy-6,6-dimethyl-2,4-cyclohexadienone (acetylfilicinic acid, 22), were discovered and studied in detail. The mechanism and general implications



21, R = $CH_3-\overset{O}{\overset{\|}{C}}-$

22, R = H

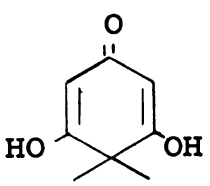
of these photoreactions will be discussed with the aid of kinetic results.

RESULTS AND DISCUSSION

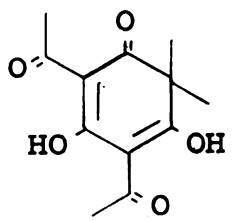
I. Preparation of Substituted Dienones

A. Preparation of Filicinic Acid and Related Derivatives

3,5-Dihydroxy-4,4-dimethyl-2,5-cyclohexadienone (filicinic acid, 19) and its diacetyl precursor, 2,4-diacetyl-3,5-dihydroxy-6,6-dimethyl-2,4-cyclohexadienone (diacetylfilicinic acid, 21) were prepared according to the method used by Riedl (12). Although definite structures are given



19



21

for these compounds at this time, other tautomers are possible. Because of the interrelation of the structures of a number of these filicinic acids and related products, (Fig. I and Fig. II) proof of structures will be delayed until all the spectral evidence has been presented.

Dry phloroglucinol, 23, in acetic acid was treated with boron trifluoride for about one hour. An 81.5% yield of 1,3-diacetylphloroglucinol, 24, was obtained. This compound was identified by its mp of 167.5-169^0 after recrystallization and sublimation (lit., 168^0 (12)). Its

Figure I. Outline of products synthesized from phloroglucinol, 23.

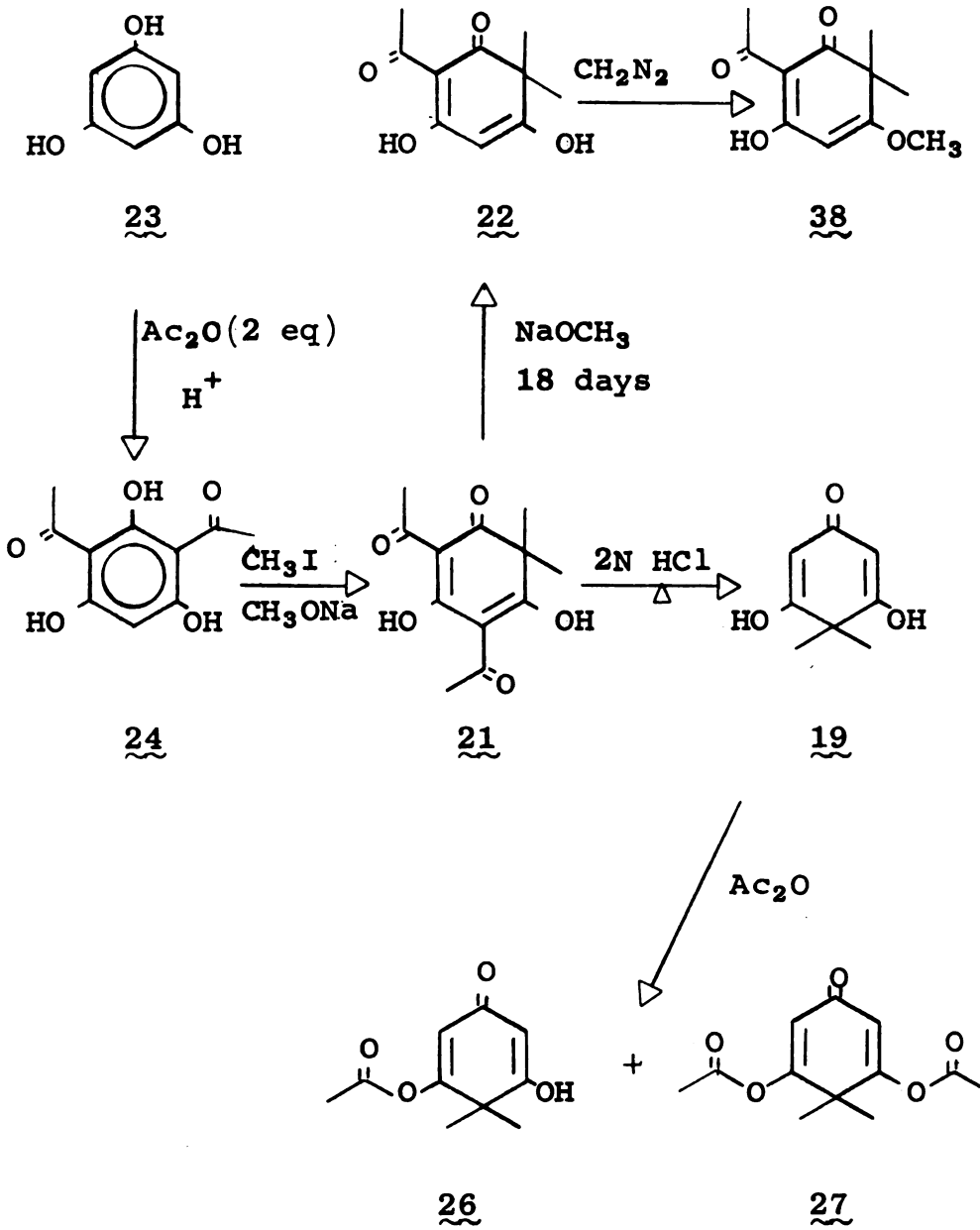


Figure I. (Cont.)

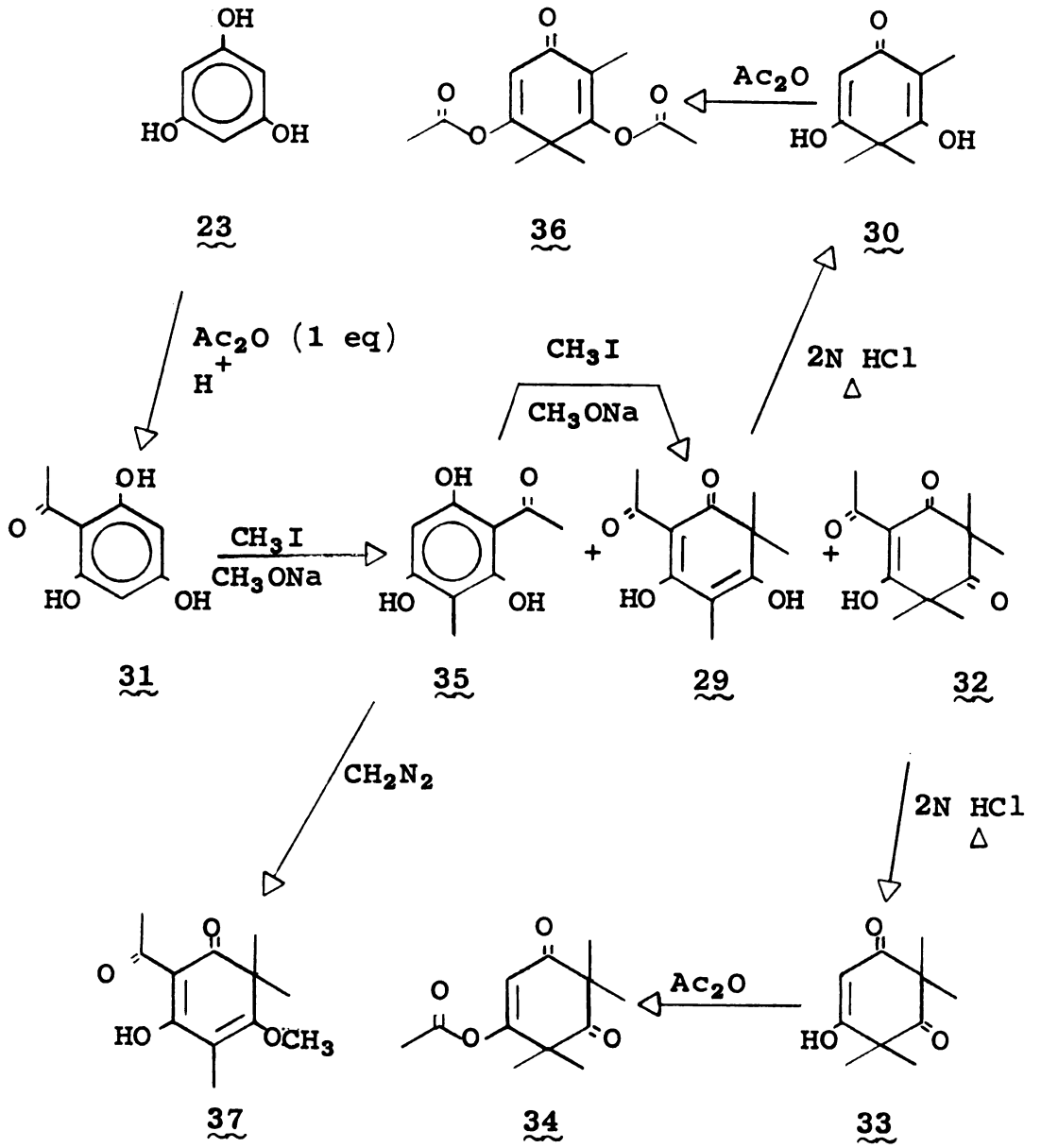
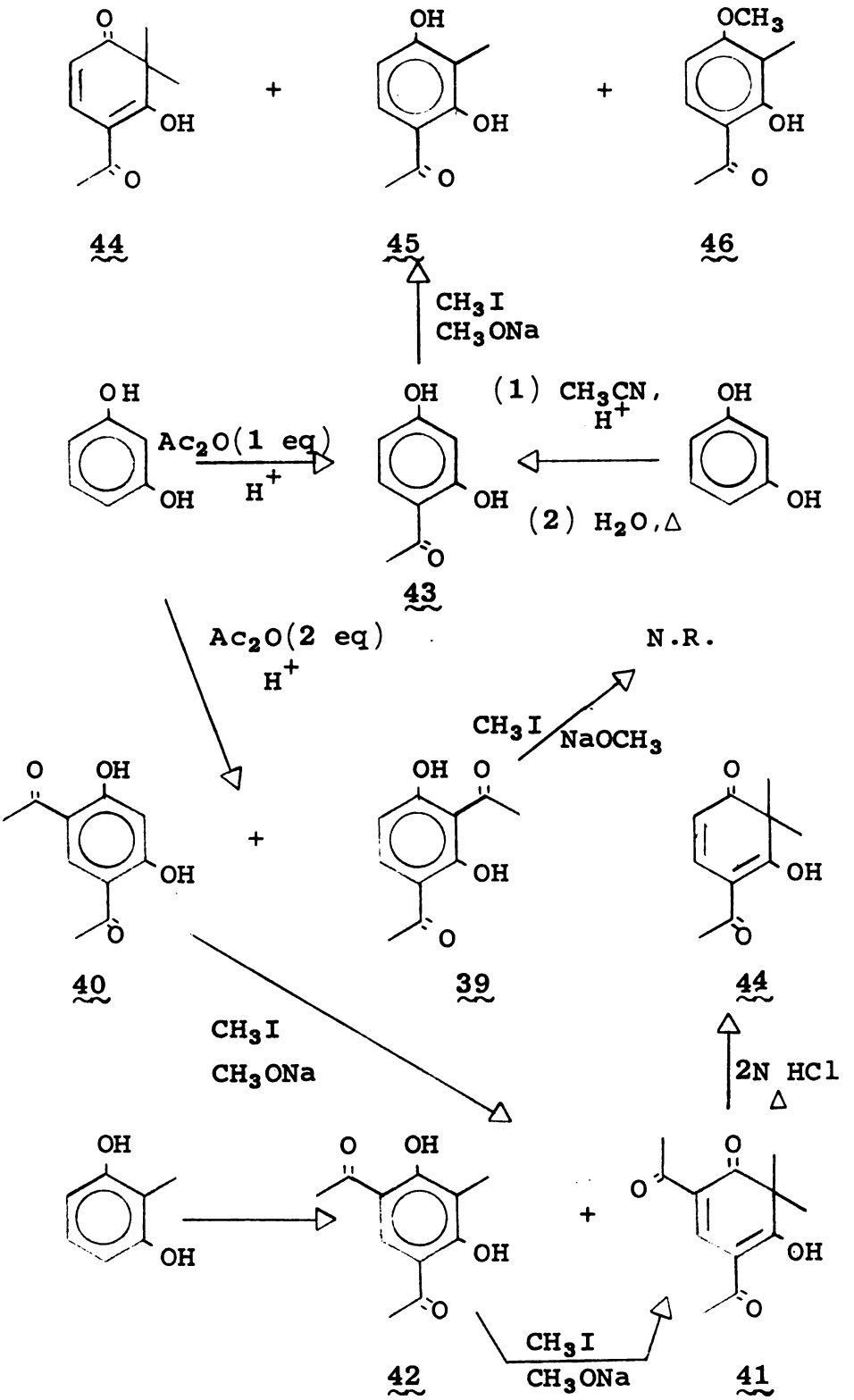
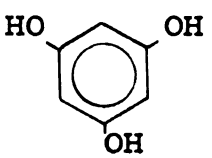


Figure II. Outline of products synthesized from resorcinol.



ir spectrum had bands at 1610 cm^{-1} for a conjugated intramolecularly hydrogen-bonded (chelated) carbonyl group, at 3000 cm^{-1} for chelated hydroxyl groups, and at 3450 cm^{-1}



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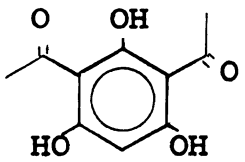

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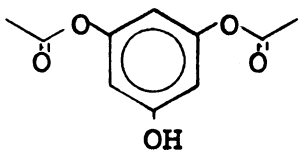

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for the non-chelated phenolic hydroxyl group. This preparation was found useful only for small scale reactions. The temperature required for the Fries rearrangement of the diacetoxy intermediate, 25, to 24 was unobtainable for larger scale reactions with this method.

A preparation related to that used by Israelstram (16) was found not only more suitable for larger scale reactions but also quicker and gave almost as good yields (61.5% yield on a scale four times as large as that used in the boron trifluoride reaction). In this method oven dried (110^0) phloroglucinol was suspended in twice its molar equivalent of acetic anhydride. After the addition of sulfuric acid the phloroglucinol dissolved and the solution was refluxed at 135^0 for a few minutes. Work up afforded a compound which was identical to 24 by its mp after sublimation.

Diacetylfilicinic acid, 21, was prepared from 24 by methylating with methyl iodide and sodium methoxide

in anhydrous methanol. It was important to use dry sodium methoxide and anhydrous methanol in order to obtain the product. Diacetylfilicinic acid, 21, was identified by its ir spectrum which had a band at 1560 cm^{-1} assigned to the conjugated, chelated carbonyls of the acetyl groups, and a band at 1665 cm^{-1} assigned to the conjugated carbonyl group of the ring. The nmr spectrum, given in Table I, indicates the presence of two acetyl methyl groups (τ 7.47 and 7.37), a gem dimethyl group (τ 8.59) and two chelated hydroxyl hydrogens (τ -8.45 and -8.85). The nmr spectrum also indicated the presence of about 15% of a tautomer (with methyl peaks at τ 8.46 and 7.38; the relative amounts were determined by integration of the peak observed for the gem dimethyl group at τ 8.46 compared to τ 8.59 for 21).

Filicinic acid, 19, was prepared by refluxing diacetylfilicinic acid, 21, with 2N hydrochloric acid, whereupon a good yield (67%) of filicinic acid was obtained. The compound was identified by its mp of 215-217° (sublimed 220-221°, lit., 212-215° (12)). The ir spectrum had bands at 1630 cm^{-1} assigned to a conjugated carbonyl group and at 2500-3500 cm^{-1} for the intermolecularly hydrogen-bonded enol hydroxyl groups. The nmr spectrum (Table I) in sodium deuteroxide and deuterium oxide had only one peak at τ 8.83, the other hydrogens being exchanged very rapidly with deuterium.

Table I. Nuclear magnetic resonance spectra* of filicinic acid and related compounds

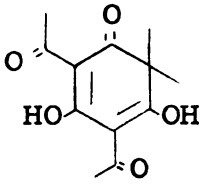
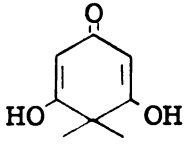
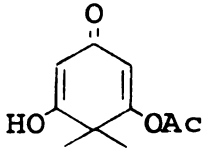
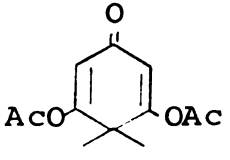
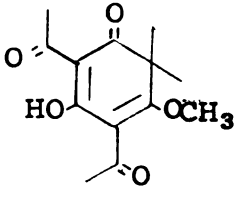
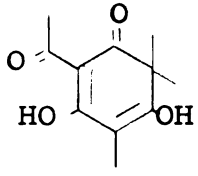
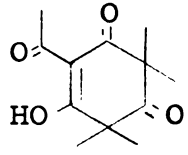
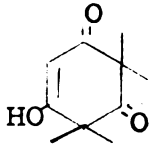
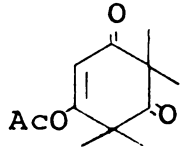
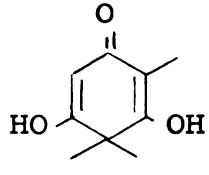
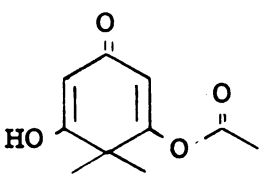
Compound		Solvent	$CH_3\!>\!C\!<\!CH_3$	CH_3-C=O	$-OCH_3$	-OH	Vinyl H	Other
	21	CCl_4	8.59	7.47 7.34		-8.45 -8.85		
		$DMSO(d_6)$	8.64	7.40				
	19	NaOD D_2O	8.83					
	26	Acetone (d_6)	8.62	7.72			4.54 4.06	
	27	CCl_4	8.68	7.75			3.99	
	28	CCl_4	8.68	7.51 7.43	6.19			

Table I. (Cont.)

Compound		Solvent	$CH_3\!>\!C\!<\!CH_3$	CH_3-C=O	$-OCH_3$	-OH	Vinyl H	Other
	29	DMSO(d_6)	8.68	7.50				8.20 Ring Methyl
	32	CCl_4	8.69 8.59	7.44				
	33	NaOD	8.76					
	34	CCl_4	8.69 8.65	7.73			4.02	
	30	NaOD D_2O	8.80					8.35 Ring Methyl

*All peaks are singlets unless otherwise noted.

This compound was further identified by preparing both the monoacetate and diacetate, by treatment of 19 with acetic anhydride and pyridine. The two acetates were separated by recrystallization from carbon tetrachloride, from which the monoacetate precipitated (mp 142-144°). The ir spectrum was consistent with structure 26. It had bands at 1660 cm^{-1} (conjugated carbonyl group) and at 1775 cm^{-1} (acetyl carbonyl). The nmr spectrum is given in Table I and shows the presence of one acetyl methyl group at τ 7.72, a gem dimethyl group at τ 8.62 and two vinyl hydrogens at



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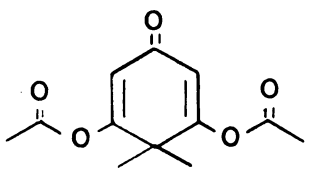
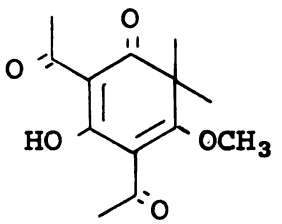


27

τ 4.06 and 4.54. The residue from the carbon tetrachloride mother liquor contained largely the diacetate of filicinic acid, 27. This compound was recrystallized from a mixture of ethyl ether-petroleum ether and gave a mp of 85° (lit. 82-85° (17)). The structure was confirmed by its ir spectrum which had absorption bands at 1660 cm^{-1} for a conjugated carbonyl group and 1775 cm^{-1} for the ester carbonyl groups. The nmr spectrum (Table I) indicates the presence of two equivalent acetate methyl groups at τ 7.75, a gem dimethyl group at τ 8.68, and only one peak at τ 3.99 for the two equivalent vinyl hydrogens.

An attempt to identify diacetylfilicinic acid, 21, in a similar manner by formation of its diacetate was unsuccessful. Attempts to prepare the methyl ether(s) by treatment of 21 with diazomethane yielded a crude reaction product whose nmr spectrum (Table I) showed the presence of a methyl ether (peak at τ 6.19). On work up, this compound, 28, hydrolyzed back to the more stable chelated starting material, 21.

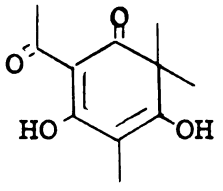


28

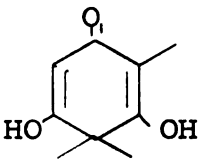
In order to learn more about the structures of the previously mentioned compounds other similar compounds were prepared for use as spectroscopic models. Two selected were 2-acetyl-3,5-dihydroxy-4,6,6-trimethyl-2,4-cyclohexadienone (acetylmethylfilicinic acid, 29) and 2-methyl-3,5-dihydroxy-2,5-cyclohexadienone (methylfilicinic acid, 30).

The precursor to 29, acetylphloroglucinol, 31, was prepared in two ways. The first was similar to the method developed by Robinson (18). Phloroglucinol was treated with acetonitrile using hydrogen chloride gas and zinc chloride as catalysts. This yielded (81.6%) the

acetophloroglucinol with a mp of 215-218° (lit. 218-219° (18)).



29



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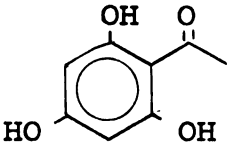
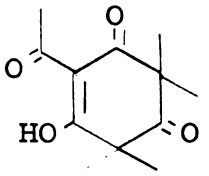


31

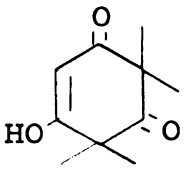
A second method involved treatment of phloroglucinol with one molar equivalent of acetic anhydride under reflux for 2 min with concentrated sulfuric acid as a catalyst. Although the yield was not as good (41%) the method proved faster and more feasible. The ir spectrum of 31 had absorption bands at 1610 cm^{-1} for the chelated hydroxyl group, and 3550 cm^{-1} for the unassociated hydroxyl groups.

Acetylmethylfilicinic acid, 29, was prepared from 31 by treatment with methyl iodide and sodium methoxide in methanol at room temperature using the method of Riedl (15). The product was identified by its mp of 157° (lit. 160-161° (15)) and its ir spectrum which had bands at 1600 cm^{-1} for a conjugated carbonyl and 3300 cm^{-1} (broad) caused by an intermolecularly associated enolic hydroxyl group. The nmr spectrum (Table I) showed the presence of a gem dimethyl group with a peak at τ 8.68, and acetyl methyl group at τ 7.50, and a ring methyl group at τ 8.20. Since the nmr spectrum was carried out in dimethyl sulfoxide-d_6 no hydroxyl hydrogen signals were observed.

Riedl also isolated 2-acetyl-3-hydroxy-4,4,6,6-tetramethyl-2-cyclohexene-1,5-dione, 32, from the benzene soluble portion and this fact was verified. Compound 32 was identified by its ir spectrum which had bands at 1560 cm^{-1}



32



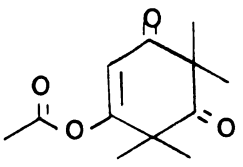
33

(conjugated carbonyl group) and at 1710 cm^{-1} (nonconjugated carbonyl group). The nmr spectrum of 32 (Table I) indicated the presence of two different gem dimethyl groups at τ 8.69 and 8.59. A peak at τ 7.44 for one acetyl methyl group was also found.

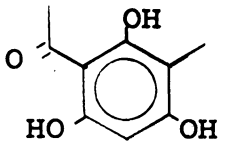
To further prove the identity of 32, the compound was refluxed in 2N hydrochloric acid for five hours. 3-Hydroxy-4,4,6,6-tetramethyl-2-cyclohexen-1,5-dione, 33, was obtained. This compound was identified by its mp of 192-193° (lit. 187-190° (15)) and its ir spectrum which had bands at 1610 cm^{-1} for the conjugated carbonyl group, 1700 cm^{-1} for the non-conjugated carbonyl group and 3000 cm^{-1} for the enolic hydroxyl group. The nmr spectrum in sodium deuteroxide and deuterium oxide (Table I) showed only one peak for the two gem dimethyl groups, as expected for the corresponding symmetrical anion.

The acetate derivative, 34, (mp 54-57°) was formed from 33 and its structure confirmed by its ir spectrum which had absorption bands at 1660 cm^{-1} for the conjugated carbonyl group, 1710 cm^{-1} for the non-conjugated carbonyl group and 1770 cm^{-1} for the carbonyl of the ester group. The nmr spectrum of 34 (Table I) had peaks indicating the presence of two different gem dimethyl groups at τ 8.69 and τ 8.65, one acetate methyl group at τ 7.73 and a vinyl hydrogen at τ 4.02.

From the original ether layer in the preparation of acetylmethylfilicinic acid, 29, methylacetylphloroglucinol, 35, was obtained. The crude material had a mp of 185-205°



34



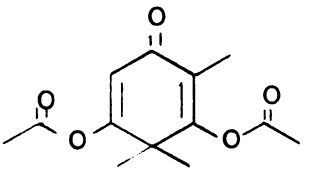
35

(lit. 211° (15)). This compound was further treated with methyl iodide and sodium methoxide to give an additional quantity of 29.

Methylfilicinic acid, 30, was prepared from 29 by refluxing in 2N hydrochloric acid for five hours. A yield of 64% was obtained. The compound had a mp of 174-177° (lit. 180° (15)). The ir spectrum of 30 had absorption bands at 1650 cm^{-1} (conjugated carbonyl group) and 3100 cm^{-1}

(broad); (intermolecular hydrogen-bonded hydroxyl groups). The nmr spectrum (Table I) in deuterium oxide and sodium deuteroxide had peaks at τ 8.80 indicating the presence of a gem dimethyl group and τ 8.35 for a methyl on a double bond.

A diacetate of methylfilicinic acid, 36, was prepared



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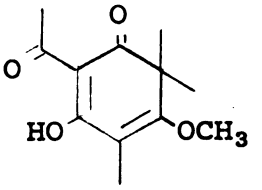


37

from 30 and acetic anhydride using concentrated sulfuric acid as a catalyst. The nmr spectrum (Table II) had peaks at τ 8.77 showing the presence of a gem dimethyl group, τ 7.77 for two acetate methyl groups, τ 8.42 for the methyl on the double bond and τ 3.94 for the vinyl hydrogen.

The monomethyl ether of acetylmethylfilicinic acid, 37, was prepared from acetylmethylfilicinic acid, 29, using diazomethane. The ir spectrum of 37 indicated two conjugated carbonyls with bands at 1635 and 1655 cm^{-1}. The nmr spectrum (Table II) had peaks at τ 8.67 assigned to the hydrogens of the gem dimethyl group, τ 8.08 for the methyl group on the double bond, τ7.43 for the acetyl methyl and τ 6.08 for the methoxyl group. The uv spectrum (and structure proof, i.e., position of the double bonds) is related to

Table II. Nuclear magnetic resonance spectra

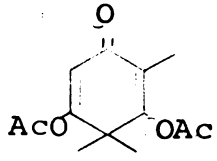
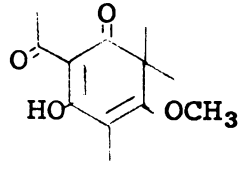
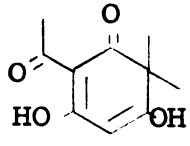
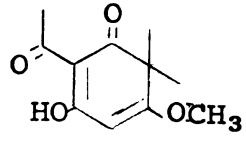
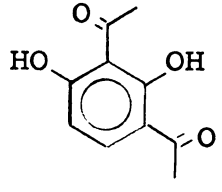
Compound		Solvent	$CH_3\!\!>\!\!C\!\!<\!\!CH_3$	$CH_3\text{-}\overset{\overset{O}{\|}}{C}\text{=}O$	$-OCH_3$	$-OH$	Other	
	36	CCl_4	8.77	7.77			3.94 Vinyl H 8.42 Ring Methyl	
	37	CCl_4	8.67	7.43	6.08		8.08 Ring Methyl	
	22	Acetone (d_6)	8.62	7.50		-7.6	4.49 Vinyl H	
	38	CCl_4	8.70	7.47	6.17	-8.6	4.65 Vinyl H	
	39	CCl_4		7.48 7.30		-3.92 -4.56	3.83 (J = 9 cps) 3.65 2.48 (J= 9 cps) 2.21	Aromatic H

Table II. (Cont.)

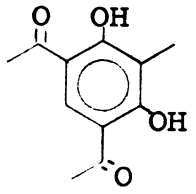
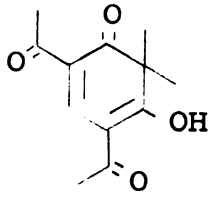
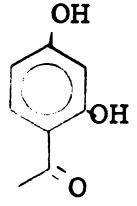
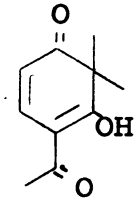
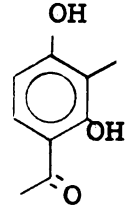
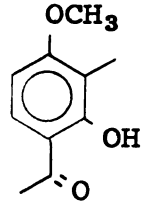
Compound		Solvent	$CH_3\diagdown C \diagup CH_3$	$CH_3-\overset{\|}{C}=O$	$-OCH_3$	$-OH$	Other
	42	CCl_4		7.48		-3.0	2.08 Aromatic H 8.02 Ring Methyl
	41	CCl_4	8.62	7.60 7.50			1.27 Vinyl H
	43	Acetone		Not Observed	1.10 -2.59		4.27, 4.22, 4.07, 4.03 and 2.87, 2.73 Aromatic H

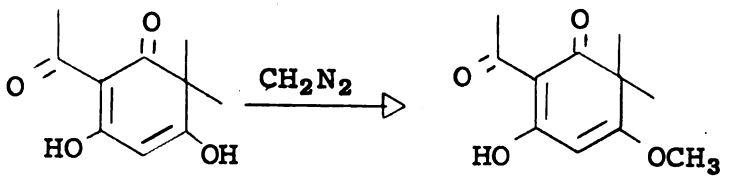
Table II. (Cont.)

Compound		Solvent	$CH_3 \diagdown C \diagup CH_3$	$CH_3-\overset{\|}{C}=O$	$-OCH_3$	-OH	Other	
	44	CCl_4	8.71	7.71			4.45 4.28 (J = 10 cps) 2.74 2.57	Vinyl H
	45			7.42		-3.14	4.15 4.00 (J = 9 cps) 3.01 2.86 7.76 Ring Methyl	Aromatic H
	46	CCl_4		7.64	6.19	-3.22	3.83 3.67 (J = 9.6 cps) 2.67 2.50 8.00 Ring Methyl	Aromatic H

that of the methyl ether of acetylfilicinic acid, 38, which will be discussed later.

2-Acetyl-3,5-dihydroxy-6,6-dimethyl-2,4-cyclohexadienone (acetylfilicinic acid, 22) was prepared by treating diacetylfilicinic acid, 21, with sodium methoxide in methanol at reflux for eighteen hours or at room temperature for eighteen days. The product was identified by its mp of 170-172.5^0 (lit. 174-176^0 (19) and 177-178^0 (20)). The ir spectrum had absorption bands at 1540-1580 cm^{-1} for the conjugated chelated carbonyl group, 1630 cm^{-1} for the cyclohexadienone carbonyl and 2600-3000 cm^{-1} for the intermolecular hydrogen-bonded enol hydroxyl group. The nmr spectrum (Table II) had peaks at τ 8.62 for the gem dimethyl, τ 7.50 for the acetyl methyl, τ 4.49 for the vinyl hydrogen and τ -7.6 for the chelated hydroxyl group. The hydrogen of the other hydroxyl was not located. The uv spectrum and further structure proof will be presented later.

The monomethyl ether of acetylfilicinic acid, 38, was prepared from acetylfilicinic acid, 22, and diazomethane. It was identified by its uv spectrum (see later discussion) and its ir spectrum which had absorption bands at 1620 and 1660 cm^{-1} for the conjugated carbonyl groups. The large band (2600-3000 cm^{-1}) for the intermolecularly hydrogen-bonded hydroxyl groups that was characteristic of 22 was not present. The nmr spectrum (Table II) had peaks at



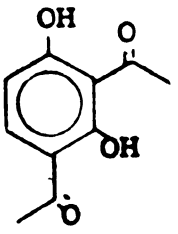
22 38

τ 8.70 for the gem dimethyl, τ 7.47 for the acetyl methyl, τ 6.17 for the methoxyl methyl, τ 4.65 for the vinyl hydrogen and τ -8.6 for the chelated hydroxyl hydrogen. See Fig. I for an outline of the products synthesized from phloroglucinol, 23

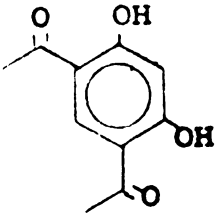
B. Preparation of Related Compounds from Resorcinol

The reaction of resorcinol with acetic anhydride and concentrated sulfuric acid as a catalyst yielded a mixture of 2,4-diacetylresorcinol, 39, and 4,6-diacetylresorcinol, 40. These compounds were separated by recrystallization from acetone, from which pure 40 was obtained (mp 179-181°) (lit. 182° (21)).

2,4-Diacetylresorcinol, 39, was obtained from the acetone mother liquor and after fractional sublimation had a mp of 87-89° (lit. 92° (21)). The nmr spectrum of 39 (Table II) had peaks at τ 7.48 and 7.30 for the two different acetyl methyl groups and an AB pattern for the two aromatic hydrogens centered at τ 3.05 (J = 9 cps). The low



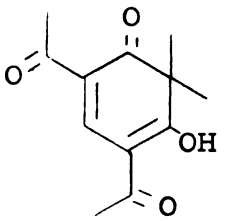
39



40

field doublet was assigned to the hydrogen adjacent to the acetyl group.

2,4-Diacetyl-5-hydroxy-6,6-dimethyl-2,4-cyclohexadienone, 41, was prepared from 40 by treating it with methyl iodide and sodium methoxide in anhydrous methanol for four days at room temperature. The methanol was evaporated, water added, then the solution neutralized and extracted with ethyl ether. From a potassium bicarbonate extract of the ether a 15.5% yield of 41 was obtained. The compound had a mp of 134-137° after recrystallization, reprecipitation from base and sublimation. Its ir spectrum had absorption bands at 1560 cm^{-1} for the chelated carbonyl and 1670 cm^{-1} for the conjugated carbonyls. The nmr spectrum (Table II) had peaks at τ 8.62 for the gem dimethyl group, τ 7.60 for one acetyl methyl group, τ 7.50 for the chelated acetyl methyl group and τ 1.27 for the vinyl hydrogen between the two acetyl groups. There was no sign of the chelated hydroxyl hydrogen. The compound analyzed well for $C_{12}H_{14}O_4$.



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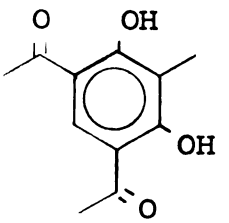


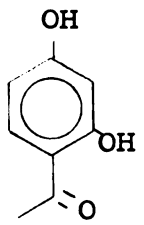
42

From the ether layer 2-methyl-4,6-diacetylresorcinol, 42, (mp 132-133.5°) was isolated. This compound was identified by its nmr spectrum (Table II) which had peaks at τ 8.02 for the aromatic methyl group, τ 7.48 for the two acetyl methyl groups, τ 2.08 for the aromatic hydrogen and τ -3.0 for the two hydroxyl hydrogens.

This compound was also prepared by treating 2-methylresorcinol with acetic anhydride (two molar equivalents) using concentrated sulfuric acid as a catalyst. A 63.6% yield of 42 was obtained. 2-Methyl-4,6-diacetylresorcinol, 42, was treated with methyl iodide and sodium methoxide in methanol for one week and the reaction was worked up as in the preparation of 41. A 56% yield of 2,4-diacetyl-5-hydroxy-6,6-dimethyl-2,4-cyclohexadienone, 41, was obtained.

4-Acetylresorcinol, 43, was prepared from resorcinol and acetic anhydride (one molar equivalent) by refluxing for ten minutes with concentrated sulfuric acid as a catalyst. A 63.6% yield of 43 was obtained with a mp of 145° (lit.

147° (18)). The nmr spectrum (Table II) had peaks in the aromatic region at τ 4.27, 4.22, 4.07 and 4.03 (for two hydrogens) due to the hydrogen at atom 2 between the hydroxyl groups and the hydrogen at carbon 6 adjacent to one hydroxyl group. This latter hydrogen was coupled to the hydrogen ortho to it (J = 9 cps) and also to the hydrogen meta to it (J = 2.0-2.5 cps). The nmr spectrum also had a quartet at τ 2.80 assigned to the hydrogen adjacent to the acetyl group and coupled to the adjacent hydrogen (J = 9 cps) and to the hydrogen para to it (J = 0.8-1.0 cps). Peaks for the hydroxyl hydrogens were found at τ 1.10 and -2.59.



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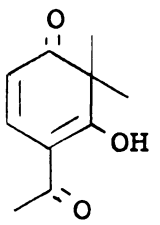
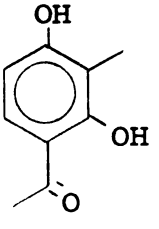


44

4-Acetyl-5-hydroxy-6,6-dimethyl-2,4-cyclohexadienone, 44, was prepared in two ways. 2,4-Diacetyl-5-hydroxy-6,6-dimethyl-2,4-cyclohexadienone, 41, was refluxed in 2N hydrochloric acid to give 44. Alternatively, 43 was methylated with methyl iodide in sodium methoxide and methanol. In neither case was the yield very good nor the product very pure. It was an oily substance which had ir absorption bands at 1605 and 1660 cm^{-1} for the chelated and conjugated

carbonyl groups respectively. The nmr spectrum had peaks at τ 8.71 for the gem dimethyl group, τ 7.71 for the acetyl methyl (note the possibility of the acetyl carbonyl being less chelated than the cyclohexadienones mentioned previously), and a multiplet at τ 3.51 for an AB pattern caused by the vinyl hydrogens, with a coupling constant of 10 cps. The down field peak was assigned to the vinyl hydrogen adjacent to the acetyl group.

Methylation of 43 gave largely two compounds, a sodium bicarbonate-soluble compound, 2-methyl-4-acetylresorcinol, 45, and an ether-soluble compound which dissolved in 2N sodium hydroxide with difficulty, identified as 2-methyl-3-hydroxy-4-acetylanisole, 46. Compound 45 was identified



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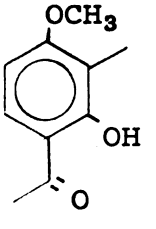


46

by its mp of 151-155^0 (lit. 156-157^0 (22)) and ir spectrum which had absorption bands at 1620 cm^{-1} for the acetyl carbonyl and 3000 and 3300 cm^{-1} for the chelated and non-chelated hydroxyl groups respectively. The nmr spectrum as given in Table II was consistent with this structure. Compound 46 was also identified by its mp of 78^0 (lit. 82-83^0

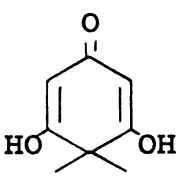
(22)), nmr (Table II) and ir spectra.

Attempted methylation of 2,4-diacetylresorcinol, 39, with methyl iodide in sodium methoxide and methanol resulted in recovered starting material.

See Fig. II for an outline of the compounds synthesized from resorcinol.

II. Discussion of the Structures of Filicinic Acid and Related Compounds

The question of the structure of filicinic acid actually began some time ago when Boehm suggested 19 or 20 as possible structures (13,23). He found that oxidation



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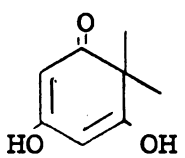
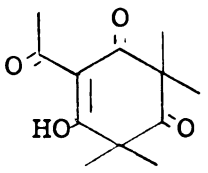


20

of filicinic acid with potassium permanganate gave carbonic acid, isobutyric acid and dimethylmalonic acid. Since the tautomers can probably rapidly interconvert during a chemical reaction, the results obtained may not be reliable in determining which structure is better.

With the use of more recent spectrometric methods of analysis such as ir, uv and nmr, it is possible to examine molecules without disturbing their structure appreciably. In order to have suitable standards, several compounds such

as 32, 33 and 41 were used for comparative purposes. There can be little doubt as to the structures of these compounds.



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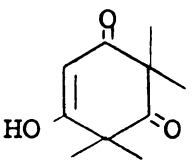

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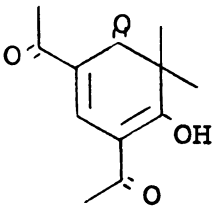

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The uv spectra of each of these, along with filicinic acid, diacetylfilicinic acid, methylfilicinic acid, and acetylmethylfilicinic acid, were determined at varying acid and base concentrations. Their changing absorption intensities at given wavelengths were plotted against the concentration of the acid or base added to the solvent (water). These graphs are presented in the next few pages. Each of these will be discussed in connection with other spectral evidence to assign a definite structure to each compound and its anion(s).

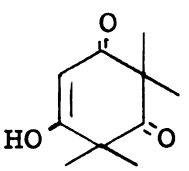
The uv spectra reported for these compounds in the literature vary considerably in wavelength and intensity of absorption. The reason for this is that different acid and base concentrations were used by different workers. The uv spectra they measured were of compounds for which different and undetermined concentrations of the various anions and neutral or protonated forms were present. By

carrying out the uv spectral determinations at different base concentrations each absorption band was identified and assigned to a particular structure.

Although there are structures in the literature for each of these compounds they vary depending upon the author. For this reason all of the compounds with questionable structures were given an independent proof.

A. The Structure of Filicinic Acid

The structure of filicinic acid has been given as 19 (10,12,13,23,24,25) and 20 (23,25). For a recent review of related compounds see reference 25. As the ir spectrum did not indicate any non-conjugated carbonyls, poly-keto structures which could conceivably be present can be eliminated from consideration. This applies also to the other related compounds to be discussed later. In all cases the fully enolized structures are the most probable.



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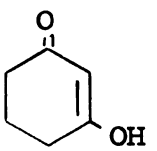

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The uv spectra at various concentrations of acid and base for filicinic acid are given in Fig. III. The uv spectrum of the neutral compound had a band at 250 mμ. This compares favorably with the band at 258 mμ for compound 33 (Fig. IV) and 260 mμ for compound 47 (dihydroresorcinol)(26).

Fig. III. UV spectra of filicinic acid .

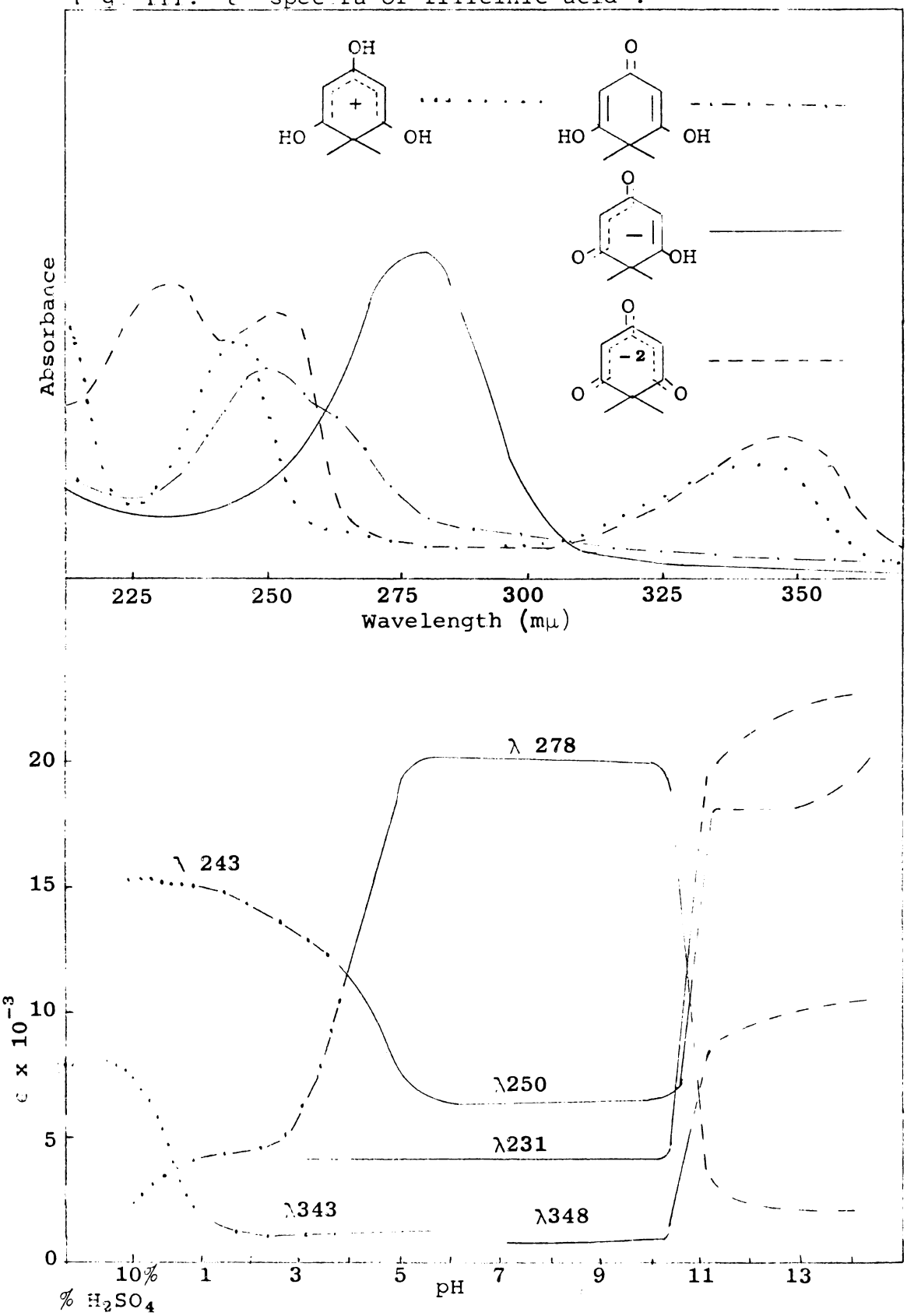
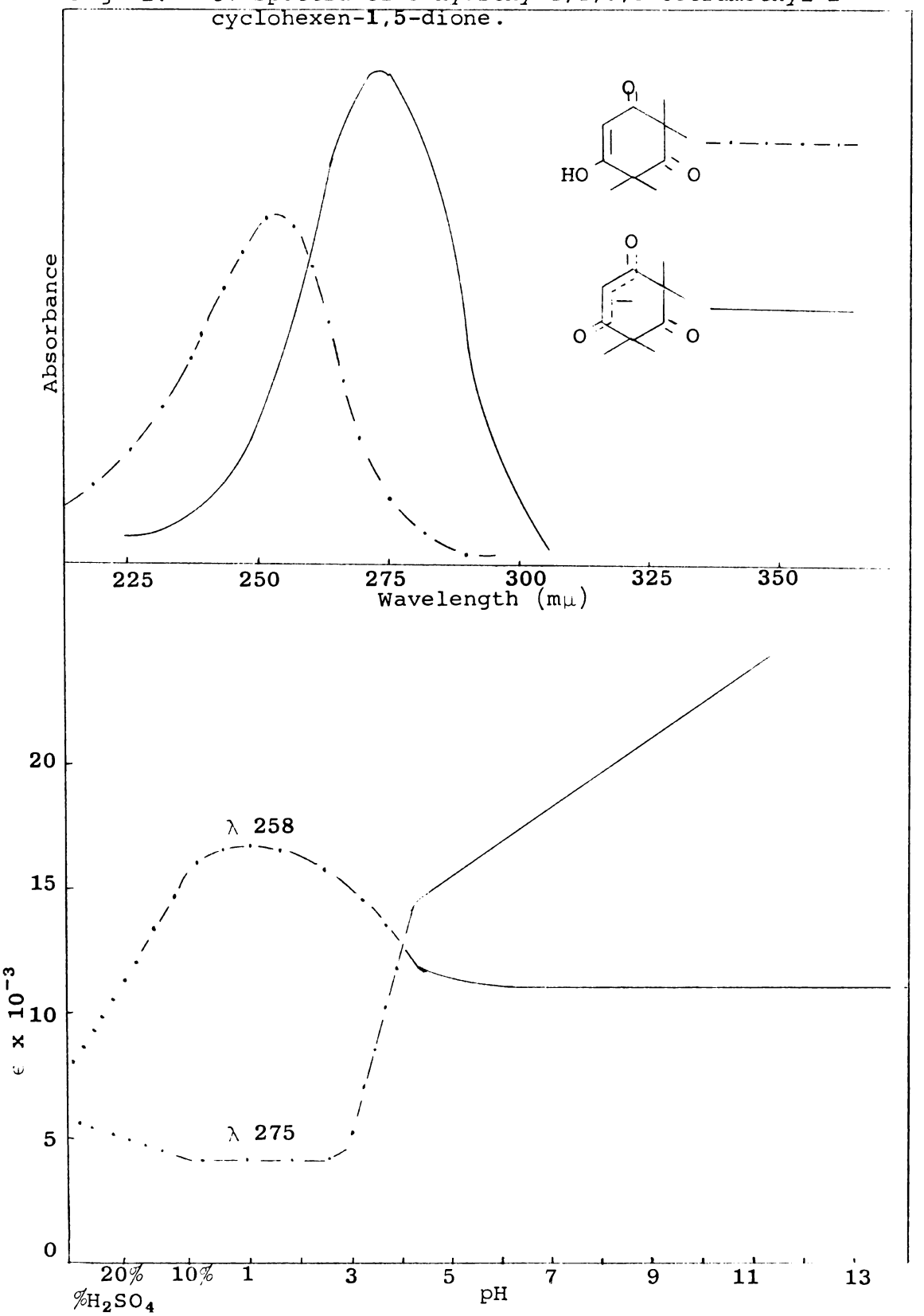
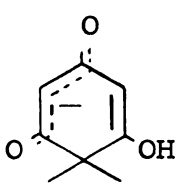


Fig. IV. Uv spectra of 3-hydroxy-4,4,6,6-tetramethyl-2-cyclohexen-1,5-dione.



This comparison indicates that filicinic acid has the cross conjugated structure, 19. The fully conjugated form, 20, would be expected to have a uv absorption band in the region of 300 mμ, as observed for other fully conjugated structures discussed later.

The anion of filicinic acid can have two forms, 48 and 49. Schwarzenbach (26) explained the changes and differences in intensities of various uv bands at different base concentrations to different concentrations of the two possible forms of filicinic acid. He found that the uv spectrum of 50 had uv absorption bands at 360 mμ and 290 mμ.



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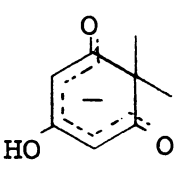

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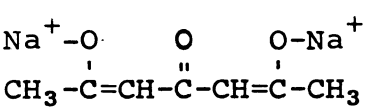
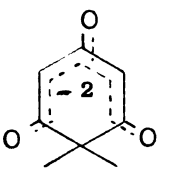


50

However, the uv spectrum of the monoanion of filicinic acid (Fig. III) had a band a 278 mμ, comparable to bands at 275 mμ and 280 mμ for the anions of 33 and 47 respectively. This would indicate that 48 was the form of the monoanion.

In Figure III there was a sharp change in intensities of absorption wavelengths at pH of 10-11. When the base concentration became large enough, presumably the dianion of filicinic acid formed. It had uv absorption bands at 348, 250, and 231 mμ. This ion can be represented by structure 51. The monoprotonated form 52 was formed in strong acid solutions (pH < 1)



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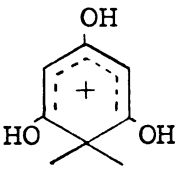
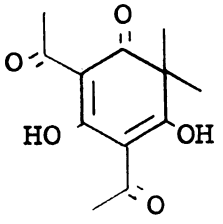


52

Some experimental evidence for the structure of filicinic acid came from the preparation of its mono- and diacetates, 26 and 27. If 20 were the structure, the diacetate would be expected to have two nonequivalent acetyl methyl groups and two different vinyl hydrogens. Due to the symmetry of the diacetate of 19, only one peak for the acetyl methyl groups and one for the vinyl hydrogens would be present in the nmr spectrum. This was found as the nmr spectrum (Table I) had one peak at τ 7.75 integrating for six hydrogens and one peak at τ 3.99 integrating for two hydrogens. This indicates that the structure of filicinic acid is 19.

B. The Structure of Diacetylfilicinic Acid

There are two structural possibilities for diacetylfilicinic acid. Structure 53 has been used recently (12) for this compound, although 21 is now believed to be the correct structure. Evidence for this form came from comparison of its uv spectrum (Fig. V) with those of 32, (λ_{max} 277 and 241 mμ) (Fig. VI) and 41 (λ_{max} 310-345 mμ) (Fig. VII). The cross-conjugated form, 53, would be expected to have a uv spectrum similar to that of 32. However the neutral compound actually had absorption bands at λ_{max} 300-315 mμ, which suggests that the structure is the fully conjugated form, 21.



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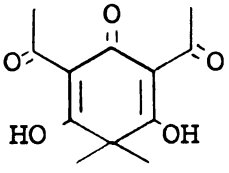

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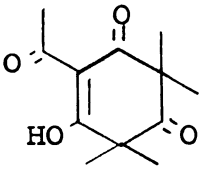

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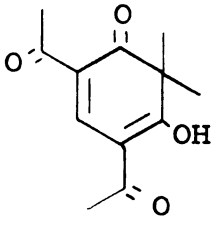

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In addition the acetyl and hydroxyl groups are equivalent in structure 53, and would be expected to have only one peak in its nmr spectrum for the acetyl methyl groups and one for the hydroxyl hydrogens. The nmr spectrum actually had peaks for two different acetyl methyl groups (Table I) at τ 7.47 and 7.34, and two peaks for two different hydroxyl hydrogens at τ -8.45 and -8.85. This

Fig. V. Uv spectra of diacetylfilicinic acid

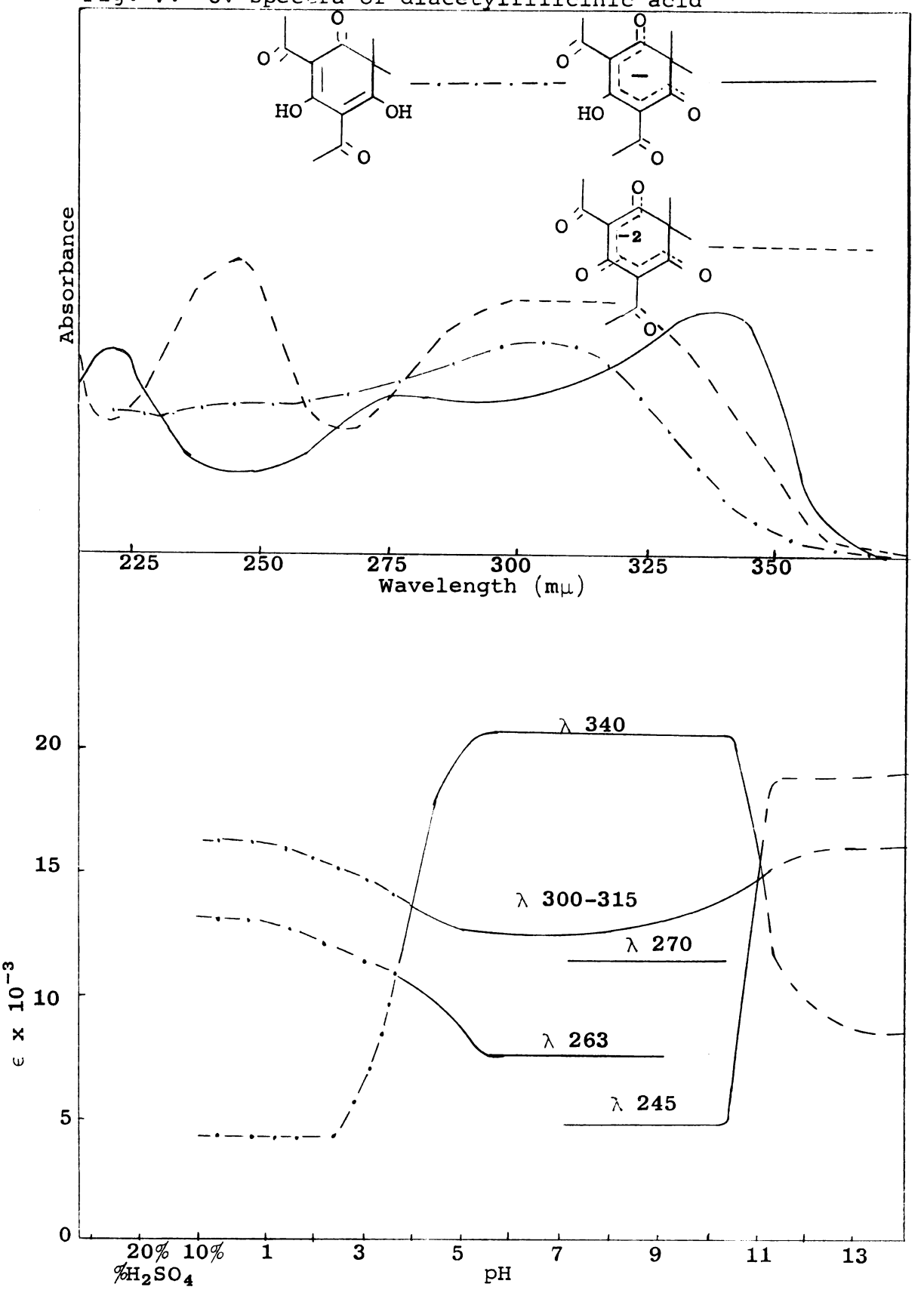


Fig. VI. Uv spectra of 2-acetyl-4,4,6,6-tetramethyl-2-cyclohexen-1,5-dione.

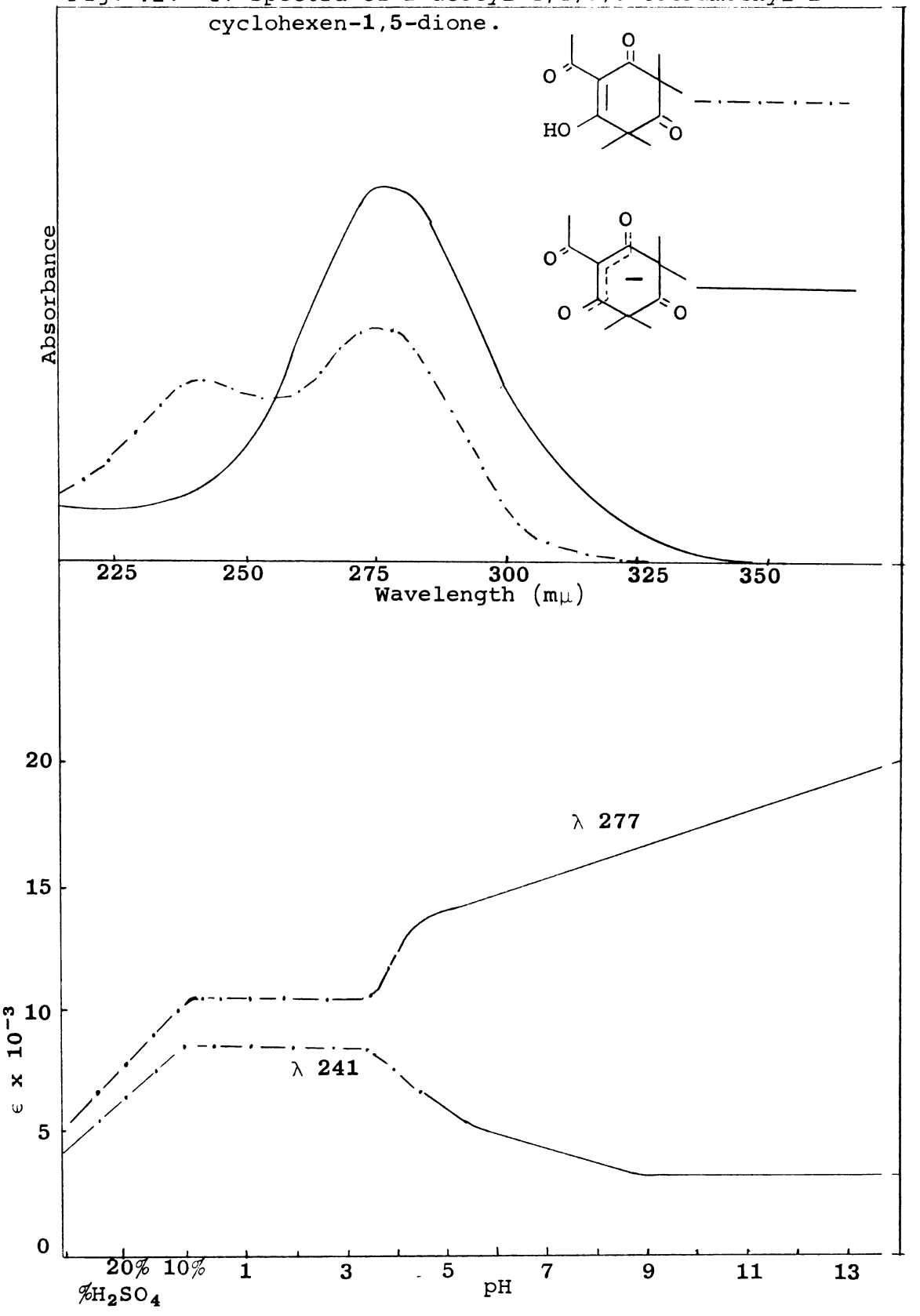
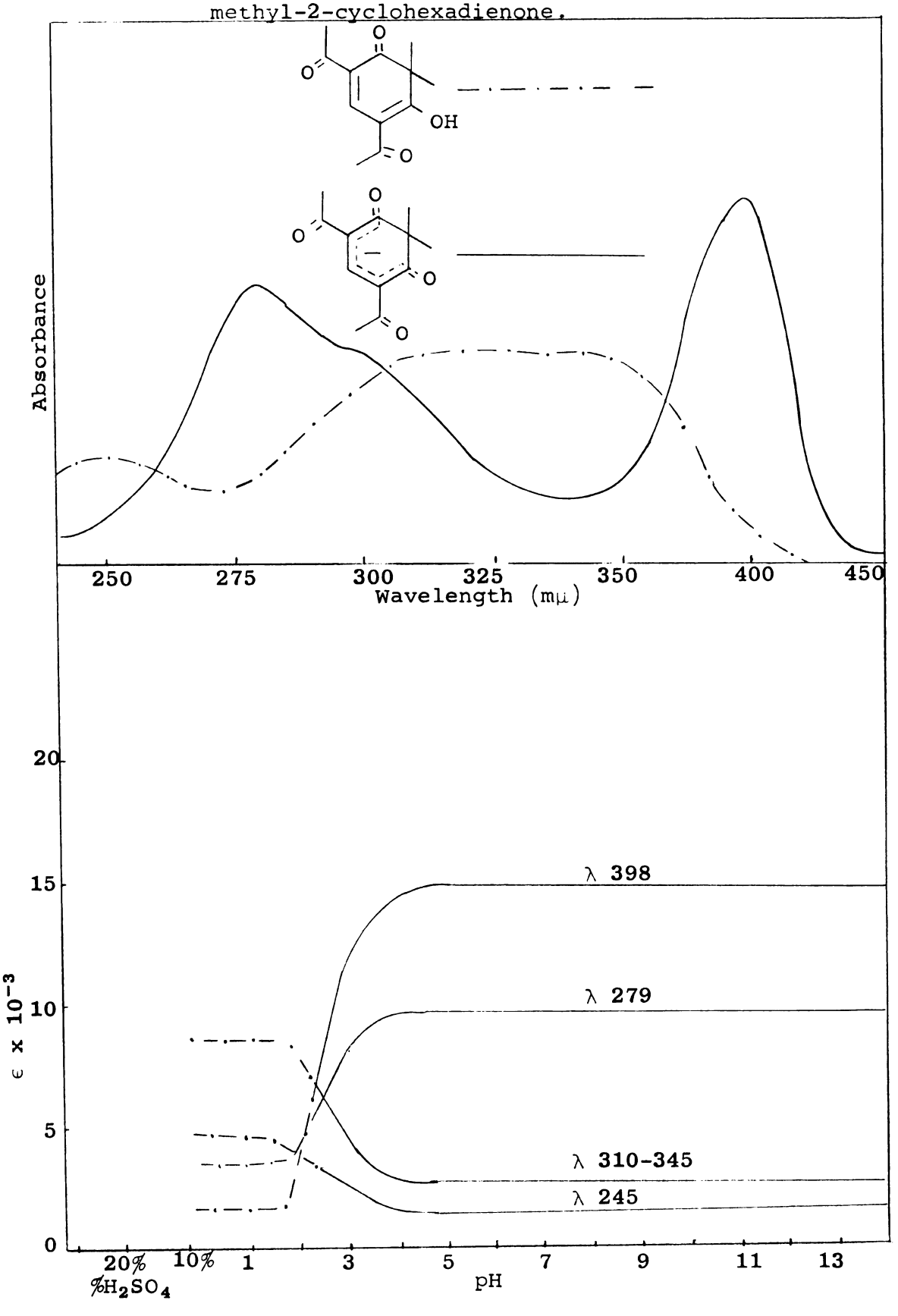


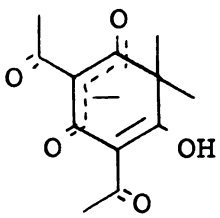
Fig. VII. Uv spectra of 2,4-diacetyl-5-hydroxy-6,6-dimethyl-2-cyclohexadienone.



corresponded to 85% of the material with an additional 15% of another isomer, perhaps 53. The nmr spectrum thus confirms the structure of diacetylfilicinic acid to be 21. The upfield acetyl methyl group (τ 7.47) was assigned to the group adjacent to the carbonyl on carbon 1. The other acetyl methyl (τ 7.34) was assigned to the group between the two hydroxyl groups, on carbon 4. These assignments were based on a comparison with the nmr spectrum of 32 which had its acetyl methyl group at τ 7.44. Also a comparison showed that the gem dimethyl group for 32, between the carbonyl and hydroxyl groups, had an nmr peak at τ 8.59 consistent with that for 21 (τ 8.59). The upfield nmr peak of 32 (τ 8.69) was assigned to the gem dimethyl group between the two carbonyl groups.

The possibility for two different monoanions of diacetylfilicinic acid also existed, as represented by 54 and 55. Anion 54 would be expected to show a hypsochromic shift in the anionic form from the absorption of the neutral compound (see later arguments). Structure, 55, on the other hand would be expected to show a bathochromic shift from the neutral molecule in the uv absorption and this in fact was observed. There was a shift from 315 mμ to 340 mμ (Fig. V). Comparison of this to the uv spectrum of 41 (Fig. VII) shows agreement in the trend of the shift but not in its magnitude. That is, in going from 41 to 56 there was a bathochromic shift from 310-345 mμ (broad) to 398 mμ. The anion of diacetylfilicinic acid cannot be 54 since this

should have a uv spectrum similar to the monoanion of 32, which must have structure 57. This anion, however, had its long wavelength absorption at 277 mμ.



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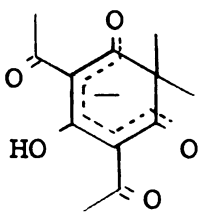

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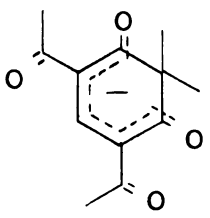

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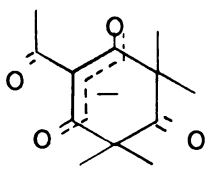

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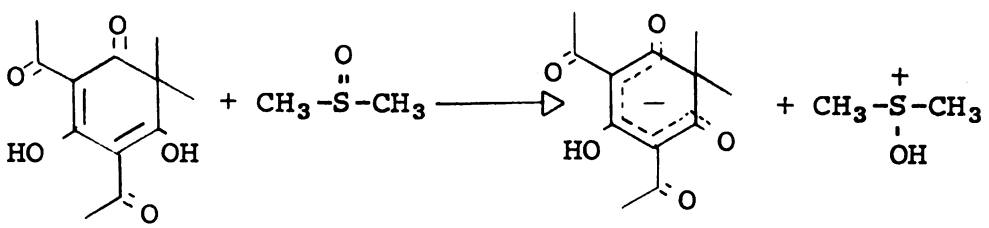
Additional evidence came from the nmr spectrum of 21 in dimethylsulfoxide-d_6, in which there was only one peak for the acetyl methyl groups (τ 7.40). In this solvent 21 was probably present as its monoanion, due to the basicity



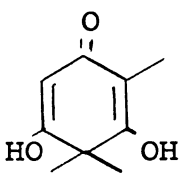
21 55

of the solvent. Structure 55 is symmetrical, whereas 54 might be expected to show two acetyl methyl peaks. Other less likely explanations are possible; for example 53 might

be the major component in this solvent, or there might be rapidly interconverting structures between 21 and 53, causing the acetyl methyl groups to become equivalent.

C. The Structure of Methylfilicinic Acid

Methylfilicinic acid was assigned structure 30 because its uv spectrum (Fig. VIII) was similar to that of filicinic acid, 19. There was a slight bathochromic shift from that of 19 because of the extra methyl group.



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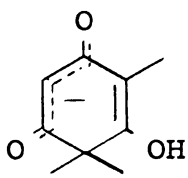

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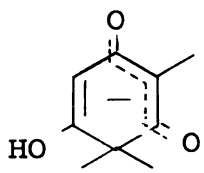

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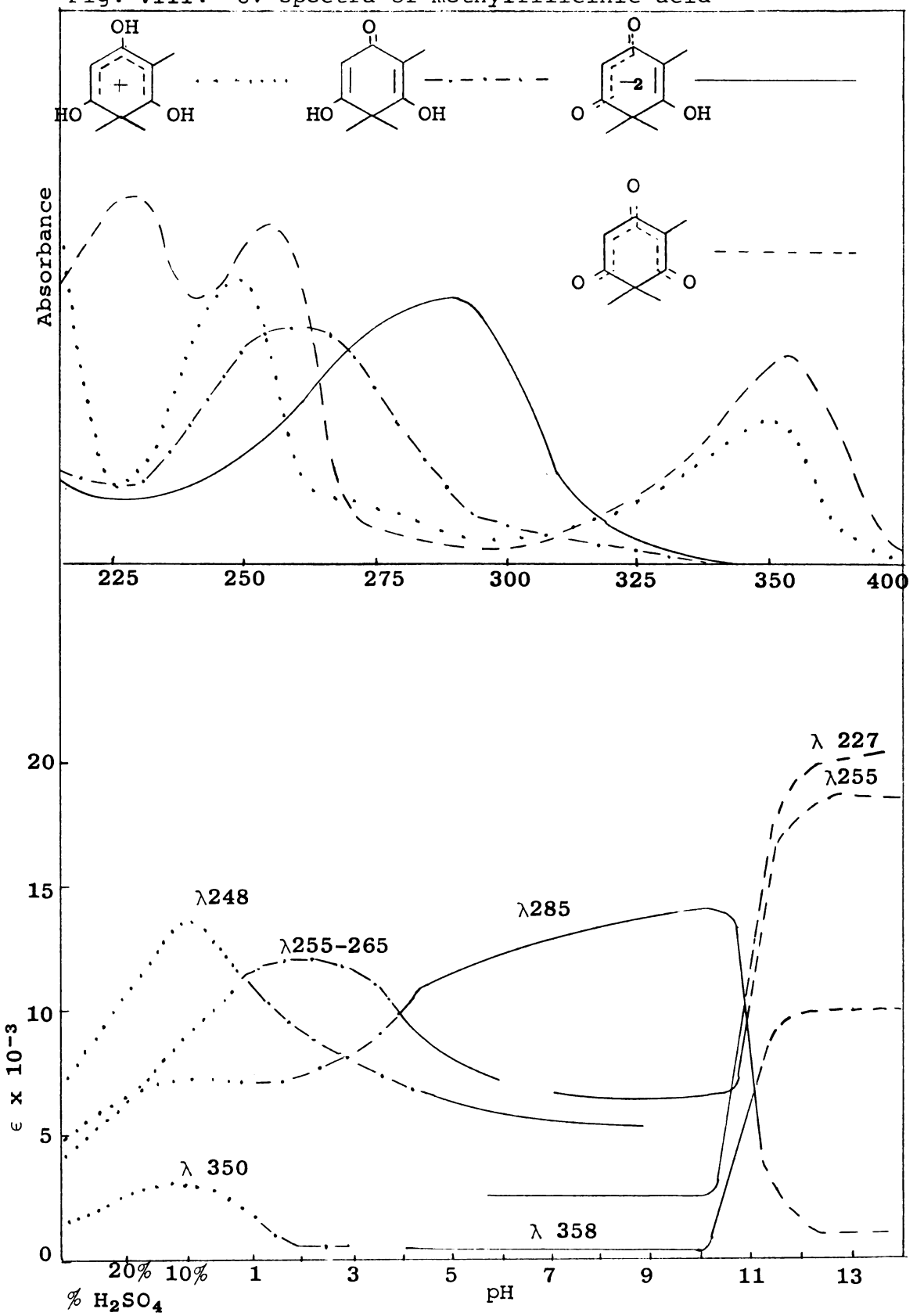
Methylfilicinic acid, 30, has three possible monoanionic forms, but because the uv spectra were similar to those of filicinic acid (Fig. III) the monoanion was assigned a cross-conjugated structure. Of the two possible such anions (58 or 59), structure 58 would be more probable since there is little or no increase in negative charge on the carbon atom bearing the extra methyl group.

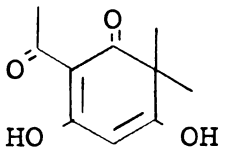
D. The Structure of Acetylfilicinic Acid

Acetylfilicinic acid may have a cross-conjugated structure and two different fully conjugated forms.

Fig. VIII. Uv spectra of methylfilicinic acid



Because its uv spectra (λ_{max} 330 mμ (acid) and λ_{max} 345 mμ (basic)) were similar to those of diacetylfilicinic acid, 21, (λ_{max} 300 mμ (acid) and λ_{max} 340 mμ (basic)) its structure was thought to be either 22 or 60. The latter has appeared in the literature (15) as has the cross-conjugated



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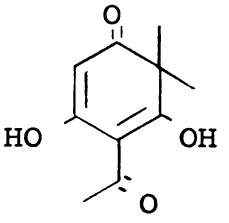
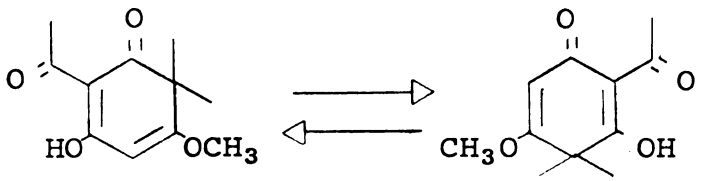


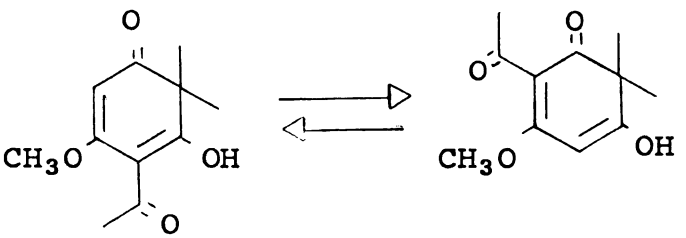
60

form (12). However, it is probable that 22 is the correct structure. The nmr spectrum of acetylfilicinic acid (Table II) has a peak for an acetyl methyl group at τ 7.50 which agrees with other examples of acetyl groups between a carbonyl and hydroxyl group, chelated to the hydroxyl hydrogen. The vinyl hydrogen was at τ 4.49.

To show further that structure 22 was correct, the monomethyl ether, 38, was prepared. Forsen and Nilsson (27) have previously prepared this compound and have argued that 38 was the structure. They based their choice on the fact that methylation of acetylfilicinic acid could give several methyl ethers, only two of which are capable of giving enols with strong intramolecular hydrogen bonds, 38 and 61. They are both interconvertable to other forms, 62 and 63.



38 62



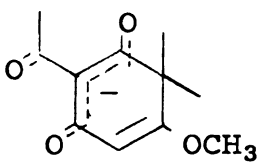
61 63

Forsen and Nilsson say that 63 would be unlikely since it does not have the additional stabilization to be gained from an intramolecular chelated hydrogen bond. However, they observed two distinctly different forms in the nmr which were interconvertable as shown by a ratio of 1:6 in carbon tetrachloride solution and a ratio of 1:8 in benzene solution. They therefore felt that the correct structure must be of the type 38 or 62.

The uv spectrum of the methyl ether (λ_{max}^{EtOH} (acidic), 315 and 235 mμ) compared with that of acetylfilicinic acid (λ_{max}^{EtOH} (acidic) 330, 271, 235 and 204 mμ), indicates that the larger fraction must have structure 38. Additional evidence for this structure was provided by its nmr spectrum

(Table II). The acetyl methyl (τ 7.47) had not shifted from that of acetylmethylfilicinic acid, 22, (τ 7.50), but both the vinyl hydrogen (τ 4.65) and the gem dimethyl group (τ 8.70) had shifted (from τ 4.49 and 8.62) indicating that the methoxy group must be between the vinyl hydrogen and the gem dimethyl group, as in 38.

In addition the uv spectrum in base showed a hypsochromic shift (from λ_{max} 315 mμ to λ_{max} 305-310 mμ) as consistent for the anion 64. This was compared to the bathochromic shift for the anion of acetylfilicinic acid, 65,



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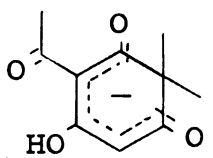


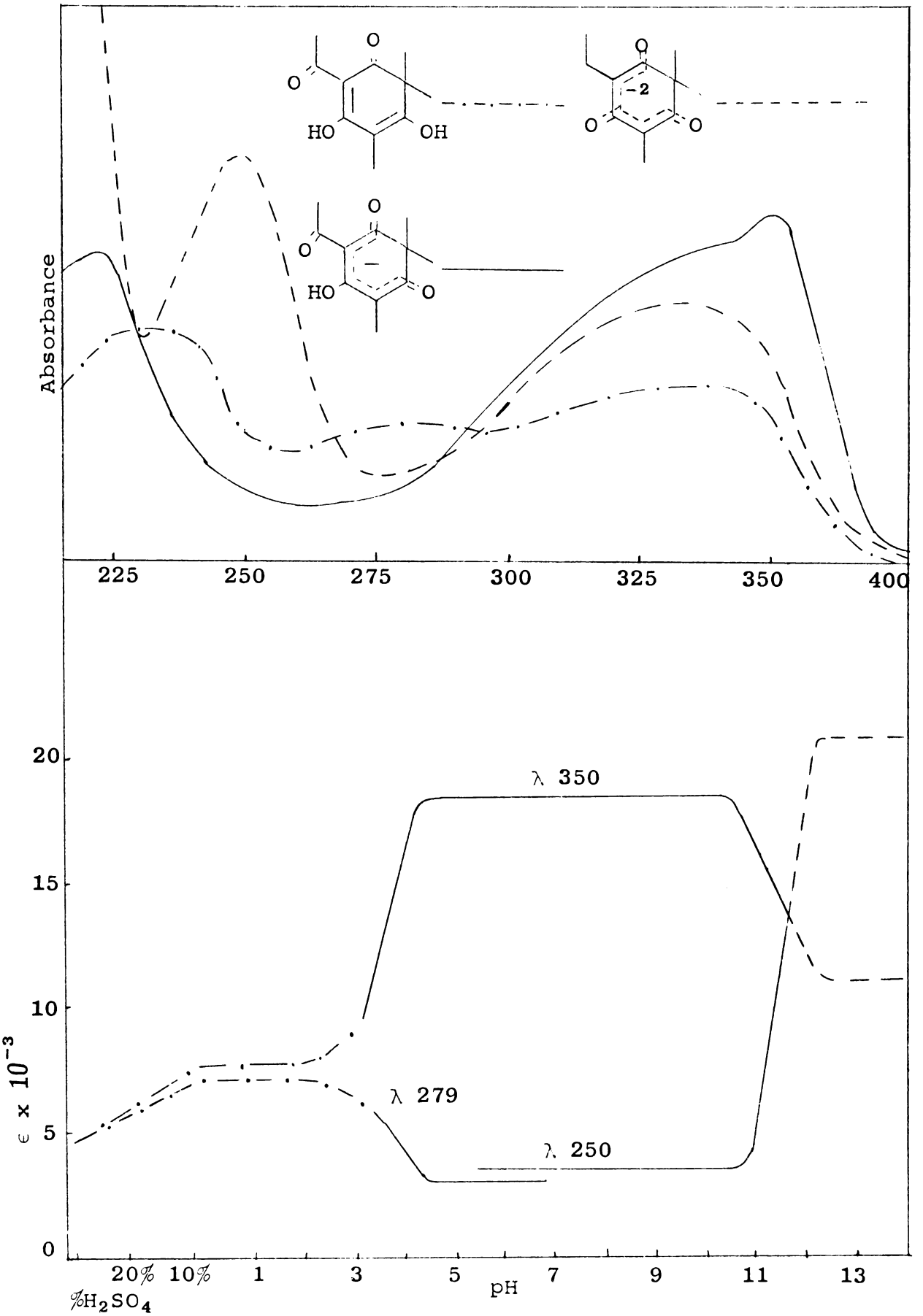
65

(λ_{max} 345 mμ) from that of the parent compound 22 (λ_{max} 330 mμ). This would be consistent with structure 38 for the neutral compound and 64 for its monoanion.

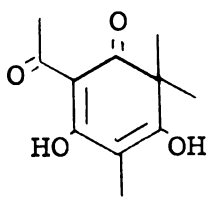
E. The Structure of Acetylmethylfilicinic Acid

Acetylmethylfilicinic acid has three possible neutral structures. As the uv spectrum (λ_{max} 334 mμ) (Fig. IX) was like that of acetylfilicinic acid, 22, (λ_{max} 330 mμ) only the fully conjugated structures 29 and 66 will be

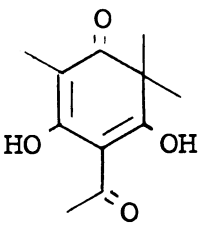
Fig. IX. Uv spectra of acetylmethylfilicinic acid.



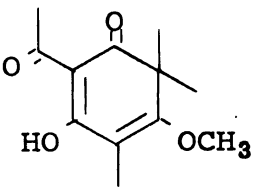
considered. An nmr spectrum (Table I) of acetylmethylfilicinic acid was consistent with structure 29, indicating a gem dimethyl at τ 8.68 and an acetyl substituent between a carbonyl and hydroxyl group at τ 7.50. Structure 29 is the most probable since the monomethyl ether prepared from 29 can be assigned structure 37. This structure was con-



29



66



37

firmed by its nmr spectrum (Table II) which had peaks at τ 7.43 for an acetyl methyl between a carbonyl and hydroxyl group. The uv spectra (λ_{max} 323-340 mμ (neutral) and 285-310 mμ (basic)) were similar to those of 22, and show the bathochromic shift expected for 37.

III. Photolysis and Photo-oxidation of Diacetylfilicinic Acid

A. Direct Photolysis of Diacetylfilicinic Acid

Recently Hart and co-workers (4,6) have shown that some methyl-substituted 2,4-cyclohexadienones undergo a photo-rearrangement to give bicyclo[3.1.0]hexenones in much the same way as 2,5-cyclohexadienones (2,3). This

rearrangement was unusual, for 2,4-cyclohexadienones usually cleave to open chain compounds or phenols (1,2,3).

Since diacetylfilicinic acid, 21, was shown to exist in the 2,4-cyclohexadienone form, it was decided to study the photolysis of this and related compounds to ascertain the effect of acetyl and hydroxyl substituents on the reaction course.

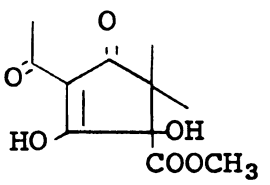
Diacetylfilicinic acid was photolyzed using a Hanovia L 450 watt lamp under a variety of conditions through Pyrex. No noticeable reaction in ethyl ether or in methanol under nitrogen was observed. There also was no reaction when 21 was photolyzed in methanol under oxygen, nor in the presence of alkaline methanol under nitrogen.

Thus diacetylfilicinic acid appears to be photochemically inert, at least with respect to radiation > 300 mμ, despite its absorption band in that region. It was noted, however, that irradiation of alkaline solutions of diacetylfilicinic acid (i.e., the monoanion) in the presence of air resulted in a gradual change in the absorption spectrum of the solution. Since no similar change occurred in a nitrogen atmosphere, it was concluded that a photo-oxidation was involved, and this reaction was studied in detail, as described below.

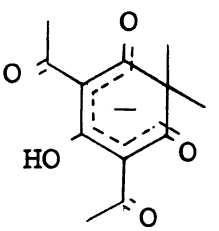
B. Photo-oxidation of Diacetylfilicinic Acid

Diacetylfilicinic acid, 21 (0.03 molar solution) was irradiated in about 0.1 N sodium methoxide in methanol,

while bubbling air through the solution. It was smoothly converted to a new crystalline product, mp 77.5-79°, $C_{11}H_{14}O_6$, to which the structure 2-acetyl-3,4-dihydroxy-4-carbomethoxy-5,5-dimethyl-2-cyclopentenone, 67, is assigned. The reaction was followed by the appearance of new uv absorption bands at λ_{max} 271 and 250 mμ in place of the band at λ_{max} 340 mμ (due to the monoanion of diacetylfilicinic acid, 55).



67



55

Compound 67 was identified by its spectral properties and chemical behavior. It gave a parent m/e of 242 in its mass spectrum. Its nmr spectrum (Table III and nmr Spectrum I) indicated the presence of two methyl groups probably due to a gem dimethyl group, since rearrangement of one of the methyl groups of 21 (or 55) seemed rather unlikely. These methyls had nmr peaks at τ 8.76 and 8.71. There might be four reasons for the presence of two methyl peaks rather than one: (1) restricted rotation in an open chain compound, (2) coupling with another hydrogen, (3) location adjacent to an asymmetric carbon, or (4) presence of tautomeric isomers.

Table III. Nuclear magnetic resonance spectra results of photo-oxidation products and related compounds

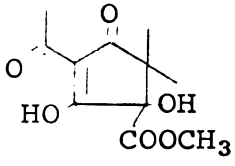
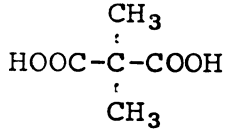
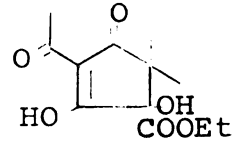
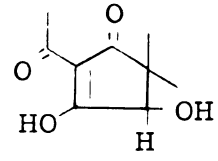
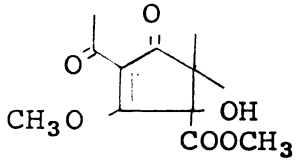
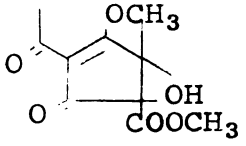
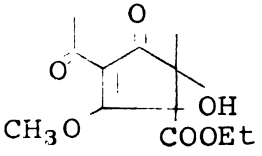
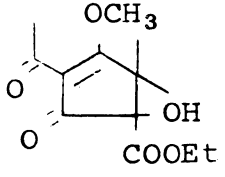
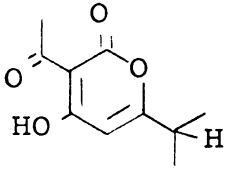
Compound		Solvent	$CH_3 \diagdown C \diagup CH_3$	$CH_3-\overset{\prime}{C}=O$	$-OCH_3$	-OH	Other
	67	$CDCl_3$	8.76 (3) 8.71 (3)	7.49	6.23	0.46	
		Acetone (d_6)	8.58			0.37 (2)	
	69	CCl_4	8.80 (Two singlets very close)	7.51		0.52	8.88 5.96 8.77 5.84 (J = 7.2) 8.65 5.72 5.60 Ethyl Group
	70	$CDCl_3$	8.77 (3) 8.61 (3)	7.47		0.45	5.85 Methyne Hydrogen
	81	CCl_4	8.84 (3) 8.75 (3)	7.58	6.25 5.93		

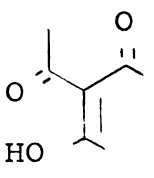
Table III. (Cont.)

Compound		Solvent	$CH_3 \diagdown C \diagup CH_3$	$CH_3-\overset{\|}{C}=O$	$-OCH_3$	-OH	Other
	82	CCl_4	9.00 (3) 8.84 (3)	7.58	6.19 6.01		
	83	CCl_4	8.85 (3) 8.73 (3)	7.58	5.94		5.97 8.85 5.87 8.73 5.75 (J = 6-7) 8.61 5 65 Ethyl Group
	84	CCl_4	8.95 (3) 8.85 (3)	7.58	5.98		5.93 8.85 5.80 (J = 7.2) 8.72 5.68 8.60 5.53 Ethyl Group
	89	Acetone (d_6)	8.81 (3) 8.75 (3)	7.42	6.65		
	90	$CDCl_3$	8.81 (J=7) 8.79	7.48		-6.9	7.34 (m) (J = 7) 4.28 Vinyl Hydrogen

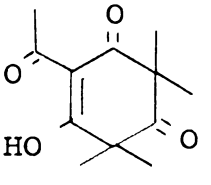
Restricted rotation was unlikely because there was no change in the relative positions of the methyl resonance peaks as the temperature was varied from 35^0 to 60^0. However the peaks did look sharper and better separated at the higher temperatures (Nmr Spectrum 1).

The methyls were probably not part of an isopropyl group, because the difference between the two peaks was only 3 cps instead of the expected coupling constant of 7-10 cps. Long range coupling was ruled out by determining the nmr spectrum at 100 Mc. In this case the methyl peaks were separated by 5 cps; there would have been no change if the difference had its origin in coupling to another hydrogen. The conclusion was that the chemical shift difference of these peaks was either caused by a difference in methyl environment due to a ring structure with an asymmetric center, or by the presence of equal concentrations of two tautomeric forms.

The nmr spectrum had a singlet at τ 7.49 probably due to an acetyl methyl between two carbonyls of an enolized β-diketone (see Table I for other examples such as 21, 22, and 32). Therefore the photoproduct contained the partial structure given below.



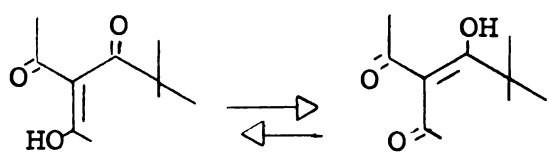
Partial structure



32

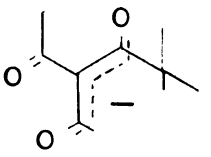
This partial structure was supported by the uv spectrum of the photoproduct which had absorption bands at λ_{max} 273 mμ in its neutral form and λ_{max} 271 and 250 mμ in its monoanion form. These spectra were not unlike those of compound 32 (λ_{max} 277 and 241 mμ (acid) and λ_{max} 277 mμ (basic)).

Photo-oxidation of 21 in aqueous alkali yielded a small amount of a compound which had an ir spectrum identical to that of dimethylmalonic acid and an nmr spectrum (Table III) which substantiated this structure. This indicated that the gem dimethyl group remained intact during the photo-oxidation, and that the partial structure for the photo-oxidation product must have been as shown, with two tautomeric forms possible.



The existence of two tautomers could explain the presence of two methyl peaks in the nmr spectrum. However, an nmr spectrum of the photoproduct in deuterium oxide and sodium deuteroxide solution still indicated two distinct methyl groups (difference of 1 cps), rather than a combination of these two to form one peak as expected for the anion of the two tautomeric forms, 68. Thus the difference in the methyls must be due to a difference

in environment caused by the groups on an adjacent carbon atom. The deuterium oxide, sodium deuteroxide nmr spectrum

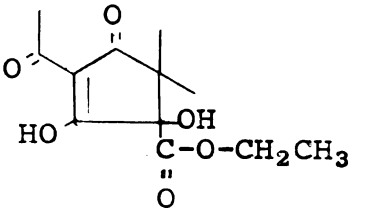


68

also indicated the presence of two easily exchangeable hydrogens, other than those of the acetyl methyl group which also exchanged, but slowly. This suggests that there are two hydroxyl groups in the photo-oxidation product.

The nmr spectrum of the photoproduct also showed a three proton signal at τ 6.25, assigned to the methyl hydrogens of a carbomethoxy group. The presence of an ester was confirmed by a band at 1740 cm^{-1} in the ir spectrum (Infrared Spectrum 1).

By carrying out the photo-oxidation in slightly basic 95% ethanol a different photoproduct, mp 80-81°, $C_{12}H_{16}O_6$, was obtained to which the structure 2-acetyl-3,4-dihydroxy-4-carboethoxy-5,5-dimethyl-2-cyclopentenone, 69, was ultimately assigned. The nmr spectrum (Table III and Nmr



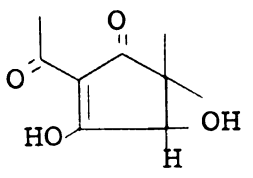
69

Spectrum 2) indicated the presence of a carboethoxy group in place of the carbomethoxy group. This showed clearly that one acetyl group was lost from diacetylfilicinic acid, 21, and that a solvent molecule was added, probably as an ester group.

When either 67 or 69 was heated in 2N sodium hydroxide at 100^0 for sixteen to twenty hours a single product with the molecular formula $C_9H_{12}O_4$ formed in 79% yield. This represents the loss of $C_2H_2O_2$ or $C_3H_4O_2$ due to saponification of the ester and decarboxylation as expected for a β-keto acid. Possibly the alkaline cleavage of the ester group was direct, rather than via saponification and decarboxylation. This possibility was strengthened when 70 was prepared by refluxing 67 with sodium methoxide in methanol.

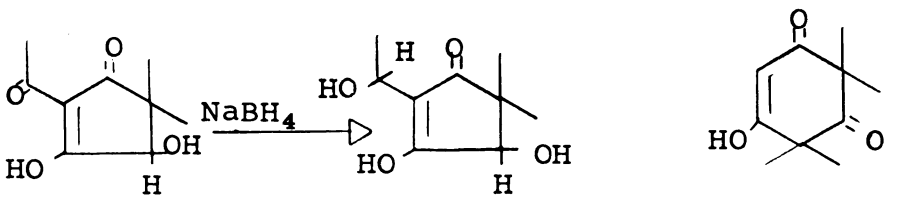
An ir spectrum of the photo-oxidation product, 67 showed the presence of an unassociated hydroxyl at 3450 cm^{-1}.

All the evidence presented here was combined to deduce structures 67 and 69 for the photo-oxidation products, and structure 70 for the degraded compound.



70

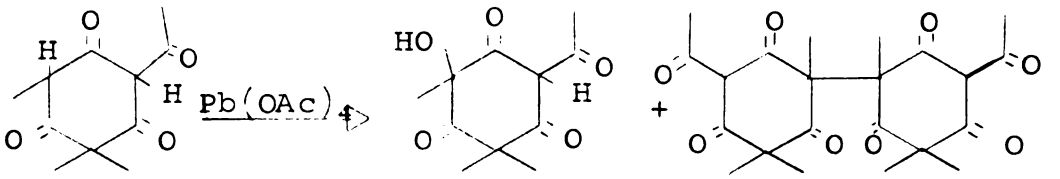
The nmr spectrum (Table III and Nmr Spectrum 3) of 2-acetyl-3,4-dihydroxy-5,5-dimethyl-2-cyclopentenone, 70, indicated the presence of a gem dimethyl group adjacent to an asymmetric center (τ 8.73 and 8.61), an acetyl group (τ 7.47), a methyl hydrogen (τ 5.85) and an hydroxyl hydrogen (τ 0.45). The ir spectrum (Infrared Spectrum 2) was similar to that of 67 except for the band at 1740 cm^{-1} which was absent. In addition the acetyl carbonyl of 70 was reduced with sodium borohydride to give a compound with a uv absorption (λ_{max} (acidic) 248 mμ, (basic) 276 mμ) similar to the uv absorption of compound 33 (λ_{max} (acidic) 258 mμ, (basic) 279 mμ).

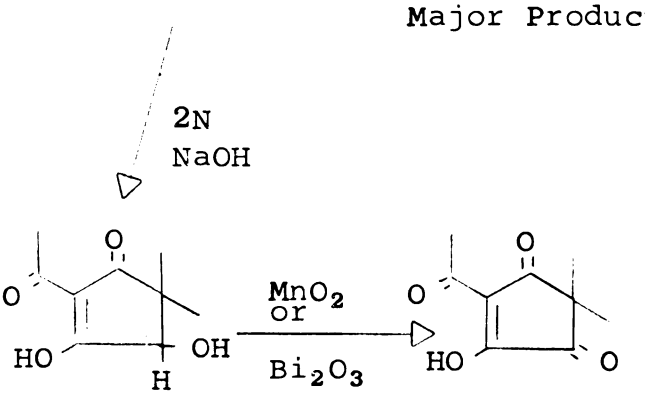


70 33

The nmr spectrum of 70 in deuterium oxide and sodium deuteroxide indicated the presence of two easily exchanged hydrogens due to two hydroxyl groups. The peak at τ 5.85 did not exchange and must be due to a methyl hydrogen adjacent to an electron withdrawing group(s). It appeared at too high a field to have been a vinyl hydrogen. There was no noticeable change in the relative positions of the two different methyl groups in this solution, as compared to the nmr in deuterated chloroform. This indicated, as

before, that the different methyl peaks were not due to two tautomeric forms. The mp of 70 was 104-105° which agreed with that of the known compound (104-106°) which had been prepared by Stevens (28) in the following manner:





70 71

To further identify 70 it was oxidized with manganese dioxide and also with bismuth oxide to 71 in a manner similar to that used by Stevens. A yellow crystalline compound was obtained with a mp of 87-88° (lit. 87° (28)). The uv spectrum was similar to that obtained by Stevens.

C. Dye-sensitized Photo-oxidations

The mechanism for the photo-oxidation of diacetylfilicinic acid, 21, was most likely via a self-sensitized

reaction which produced singlet oxygen. Singlet oxygen has been postulated recently as being involved in numerous sensitized photo-oxidations (29,30,31).

Schönberg (32) had originally proposed that self-sensitized photo-oxidations occur via a "moloxide" intermediate (·S-O-O·) which then transferred the oxygen to a second molecule of reactant (A). The existence of this "moloxide" was based partially on the fact that anthracene was photo-oxidized to a peroxide faster in the presence of diphenylanthracene than in its absence. This would indicate that there was a transfer of oxygen from the diphenylanthracene "moloxide" to the anthracene molecule.

This mechanism for photo-oxidation was adopted by Schenck (33) for dye-sensitized photo-oxidations, and can be summarized as follows:

$$S + h\nu \longrightarrow \cdot S \cdot^*$$

$$\cdot S \cdot^* + O_2 \longrightarrow \cdot S\text{-}O\text{-}O \cdot^*$$

$$\cdot S\text{-}O\text{-}O \cdot^* + A \longrightarrow S + AO_2$$

In a solution without an added sensitizer, S = A. Schenck used kinetic, spectroscopic and chemical data to support this mechanism.

Kasche and Lindquist (34) considered that the triplet state of the sensitizer was responsible for its photochemical activity, although possibly the sensitizer might react via its singlet state. In addition to the short-lived "moloxide" they suggested two additional mechanisms. One

involved reduction of the photo-excited dye by the oxidizable reactant to a semireduced dye radical, followed by reoxidization to the ground state by the oxygen present in solution. The other is one in which the photo-excited dye is oxidized by oxygen to a semi-oxidized dye radical, which is then reduced to the ground state by the oxidizable reactant. They based the latter mechanism on the formation of a semi-oxidized dye species in the photo-oxidation of fluorescein.

More recently it has been proposed that singlet oxygen is formed during the reaction and this subsequently reacts with the reagent to give the photo-oxidation products. Foote (29) proposed the mechanism:

$$\text{Sens.} \xrightarrow{h\nu} {}^1\text{Sens.}$$

$${}^1\text{Sens.} \xrightarrow{\text{isc.}} {}^3\text{Sens.}$$

$${}^3\text{Sens.} + 3O_2 \longrightarrow \text{Sens.} + {}^1O_2$$

$${}^1O_2 + A \longrightarrow AO_2 \text{ (product)}$$

He based this mechanism on the similarity of products obtained from dye-sensitized photo-oxidations and from oxidations of the same compounds by singlet oxygen formed from sodium hypochlorite. Corey (31) produced singlet oxygen using gaseous oxygen subjected to an electrodeless discharge at 6.7 Mc. He then bubbled this through various solutions and found oxidation products identical to those obtained from photo-oxidation reactions. Compounds compared included anthracene, 9,10-dimethylanthracene and some reactive 1,3-dienes.

McKeown (31) produced singlet oxygen by the reaction of alkaline hydrogen peroxide with either sodium hypochlorite or bromine and also by decomposition of alkaline solutions of organic peracids. He allowed the singlet oxygen thus produced to react with derivatives of anthracene and obtained peroxides identical to those formed by photo-oxidations.

Thus the more recent evidence supports a singlet oxygen mechanism for these photo-oxidations.

Similar techniques were used in the present work to explore the scope and mechanism of the photo-oxidations of the enolate anions of 1,3,5-cyclohexanetriones.

Diacetylfilicinic acid, 21, was photo-oxidized by irradiating an alkaline methanol solution, under air, with a 200 watt tungsten lamp using a variety of dyes (Rose Bengal was found to be the best) as sensitizers. A good yield of the photo-oxidation product, 67, was obtained. Other dyes used besides Rose Bengal were fluorscein and methylene blue; however, these were found difficult to work with due to problems in separating the dye from the product.

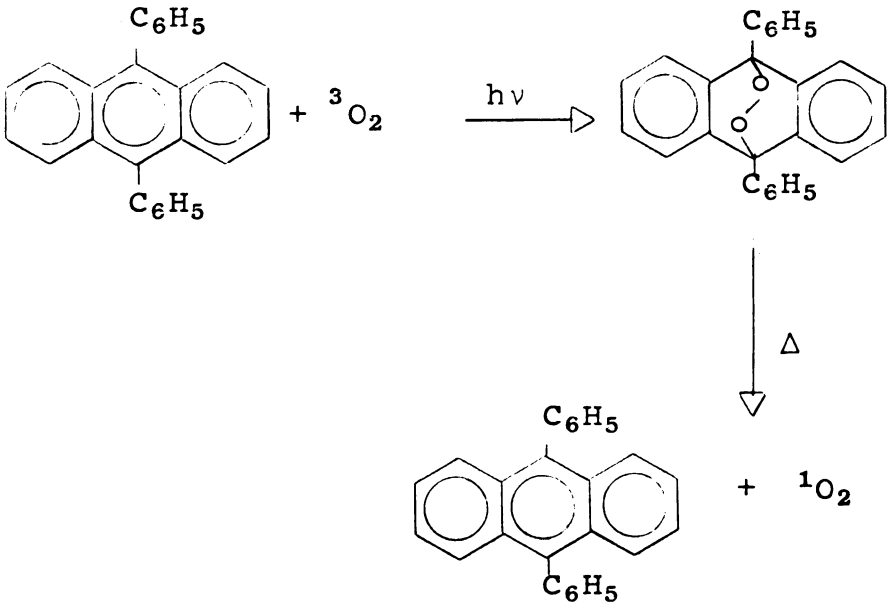
In a standard reaction, photo-oxidation of the mono-anion of diacetylfilicinic acid, 55, without a dye sensitizer, gave only 4% reaction in two hours. On the other hand, in the presence of Rose Bengal (0.0002%) a 98.8% yield of 67 (as measured by uv spectroscopy, 73.8% isolated yield) was obtained after thirty-five minutes of irradiation.

Additional evidence that singlet oxygen was responsible for the photo-oxidation of 55 was obtained by allowing

chemically prepared singlet oxygen to react with the anion.

Wasserman (35) decomposed the peroxide of 9,10-diphenylanthracene by heating it in benzene or chloroform in the presence of such reagents as 2,3,4,5-tetraphenylfuran. He postulated that the peroxide decomposed to give the parent hydrocarbon plus singlet oxygen; the products isolated were similar to those formed in typical photo-oxidation reactions.

When an alkaline solution of diphenylanthracene peroxide in methanol was refluxed with 55 a good yield of 67 was obtained. The 9,10-diphenylanthracene-9,10-cyclic peroxide was prepared by passing air through an ether solution of 9,10-diphenylanthracene while irradiating through Pyrex with a Hanovia L 450 watt lamp. The reaction was followed by observing the disappearance of uv absorption bands in the region of λ 350-400 mμ and the appearance of a band at λ_{max} 210 mμ. On completion of the photo-oxidation the ethyl ether solution was concentrated and added to an alkaline methanolic solution of 21. When this solution was refluxed in the absence of light, singlet oxygen was produced and subsequently afforded the photo-oxidation product, 67. However, because the 9,10-diphenylanthracene peroxide did not seem to decompose very rapidly in a standard reaction (see also Ref. 35) it is possible that the reaction of 55 with the peroxide might be proceeding other than via singlet oxygen.



In conclusion the function of the anion of diacetylfilicinic acid, 55, as as sensitizer can be replaced by dyes known to produce singlet oxygen, or 55 can be oxidized by singlet oxygen formed from diphenylanthracene peroxide.

D. Mechanism of the Photo-oxidation of Diacetylfilicinic Acid

The photo-oxidation of the anion of diacetylfilicinic acid, 55, probably occurred via a self-sensitized photo-oxidation. A reasonable scheme based on that presented by Foote (29) would be:

$$\underset{\sim}{55} \xrightarrow{h\nu} {}^1(\underset{\sim}{55})^*$$

$${}^1(\underset{\sim}{55})^* \xrightarrow{isc} {}^3(\underset{\sim}{55})^*$$

$${}^3(\underset{\sim}{55})^* + {}^3O_2 \longrightarrow \underset{\sim}{55} + {}^1O_2$$

$$\underset{\sim}{55} + {}^1O_2 \longrightarrow \underset{\sim}{67}$$

In order to determine which position of anion 55 would be most susceptible to attack by singlet oxygen, the charge densities in the anion were calculated using molecular orbital theory (ω-technique). Molecular orbital calculations were performed using a program written by Professor R. S. Schwendeman of Michigan State University (see Appendix II). This employed a variation of the ω-technique which allows for the changes in molecular orbital energies caused by the introduction of the oxygen heteroatoms. Values for the coulomb and resonance integrals for the carbonyl and hydroxyl oxygen atoms were taken from Quantum Organic Chemistry (36). When calculations were carried out on anions, appropriate ratios of these values were used depending upon the relative contributions of the carbonyl and hydroxyl groups. The parameters are given in Table IV. Molecular orbital calculations of the anion of diacetylfilicinic acid, 55, showed a relatively high negative charge at carbon atoms 2 and 4 (which are equivalent). It is reasonable that attack by singlet oxygen, which can be represented by the structure below, should occur at the most negative site. This representation for the charged

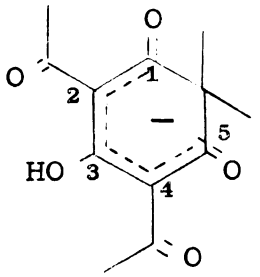
$$^{+}O - O^{-}$$

Table IV. Parameters for the oxygen heteroatom in molecular orbital calculations

Group(s)	h	k
C=O	1.2	2.0
C-O-H	2.0	0.9
1 C=O 1 C-OH	1.6	1.45
2 C=O 1 C-OH	1.46	1.62
1 C=O 2 C-OH	1.72	1.26
3 C=O 1 C-OH	1.4	1.77

Table V. Charge densities of the anion of diacetylfilicinic acid

Atom	Charge
1	0.1313
2	-0.2035
3	0.0605
4	-0.2035
5	0.1313



55

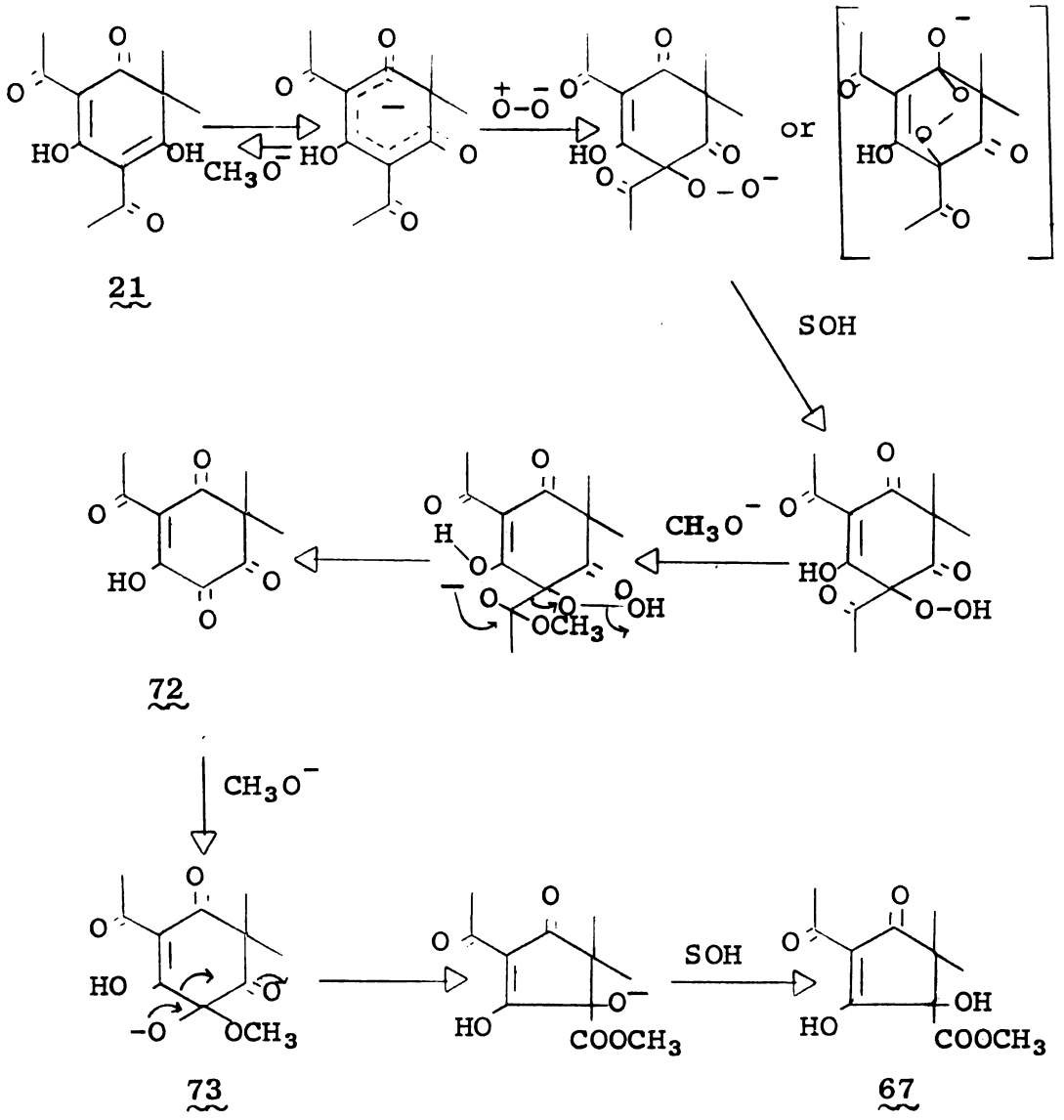
separated oxygen molecule has been used for the base catalyzed oxidations of enolizable ketones (37). A second formulation for singlet oxygen also has been used (31), and can be written as:

O=O

This would indicate its structural resemblance to ethylene, and explain the reactivity of singlet oxygen as a dienophile, capable of immediate addition to conjugated 1,3-dienes and to anthracenoid hydrocarbons. This formulation better explains the diradical character of singlet oxygen when reacting with olefins (33). The evidence indicates that singlet oxygen behaves very much like dienophiles and as such their reactions with dienes may involve a charge transfer process.

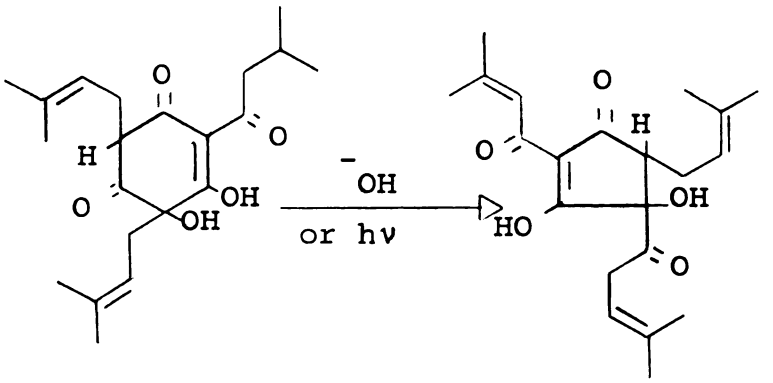
Although the monoanion of acetylfilicinic acid, 65, underwent a similar photo-oxidation to the monoanion of diacetylfilicinic acid, 55, it was shown that 65 was not formed under the conditions of the photo-oxidation of 55 (but in the absence of air or oxygen) in the time that 55 could photo-oxidize to 67.

A plausible mechanism for formation of the peroxide intermediate and the resulting photoproduct, 67, is given here.



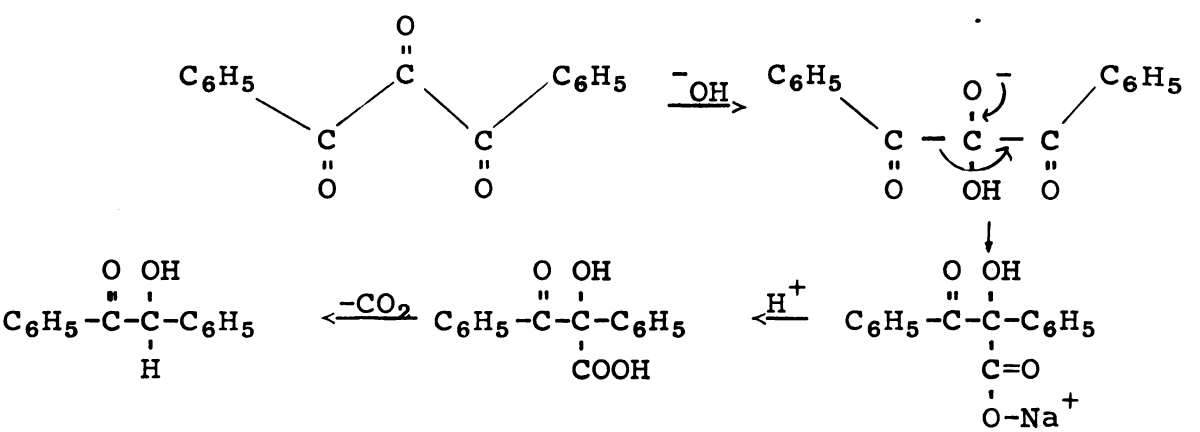
Rearrangement of intermediate 73 is similar to the rearrangement of humulone, 74, to isohumulone, 75, and to rearrangements of related compounds (38). This rearrangement

of 74 to 75 has been carried out using either dilute base or uv irradiation. The latter method (39) required a long reaction time (thirty-six hours). Due to the rapid rate of the present photo-oxidation and rearrangement, the rearrangement of 73 to 67 was probably base-catalyzed and not light-catalyzed.

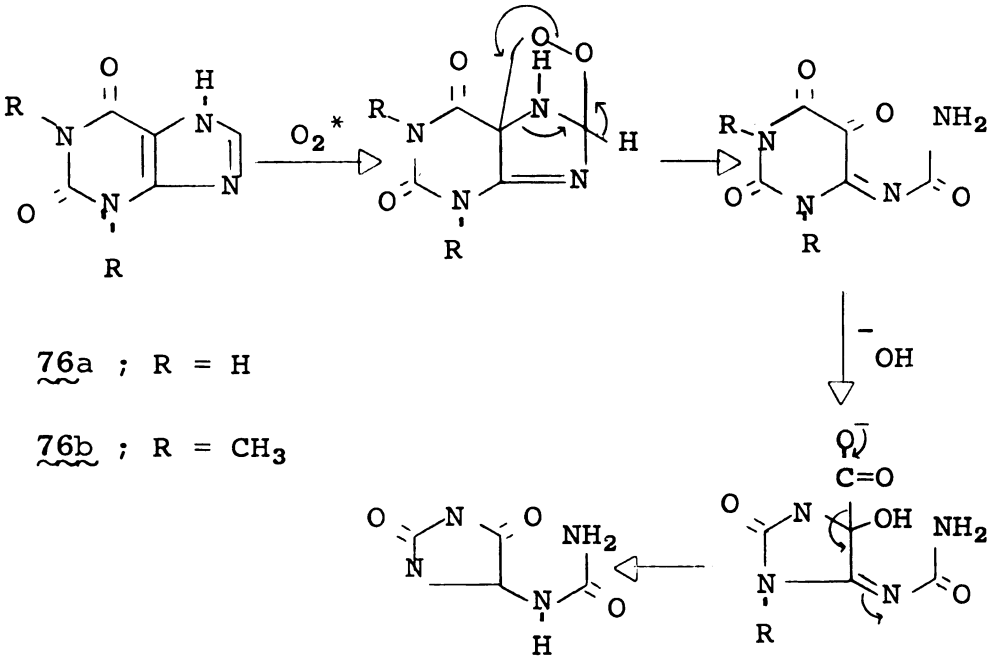


76 77

This rearrangement is not unexpected in light of the work of Roberts (40). He found by using isotopic labeling that a benzoyl shift occurred rather than a phenyl shift in the decomposition of 1,3-diphenyl-triketopropane. This would be similar to the rearrangement of 72 to the photo-oxidation product, 67.



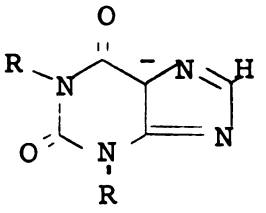
A related photo-oxidation has been carried out by Matsuura and Saito (**41**). They photo-oxidized xanthine, **76a**, and its dimethyl derivative, 76b, in an alkaline water solution. After an initial Diels-Alder type addition of an oxygen molecule to the diene, cleavage of the peroxide followed by a benzilic acid-type rearrangement was postulated to account for the product. In the absence of a sensitizer no product was formed.



76a ; R = H

76b ; R = CH_3

A suggested anion structure given here, 77, could be the species attacked by singlet oxygen. This would be consistent with the photo-oxidation of the monoanion of diacetylfilicinic acid, 55.



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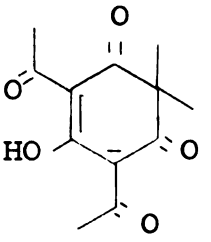
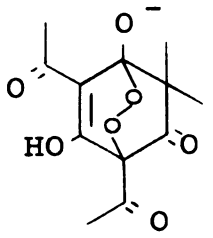
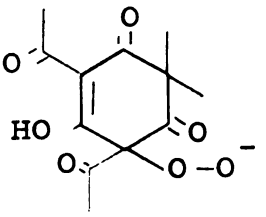


55

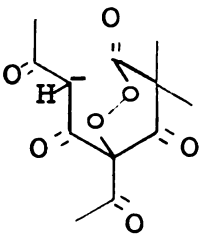
Whether the intermediate peroxide in the photo-oxidation of 55 is 78 or 79 is inconclusive. However at this time structure 79 is favored as cleavage of the C_1-C_2 bond



78



79



80

in 78 might be favorable due to the stable anion, 80, which would form. Products arising from this type of ring opening were not observed.

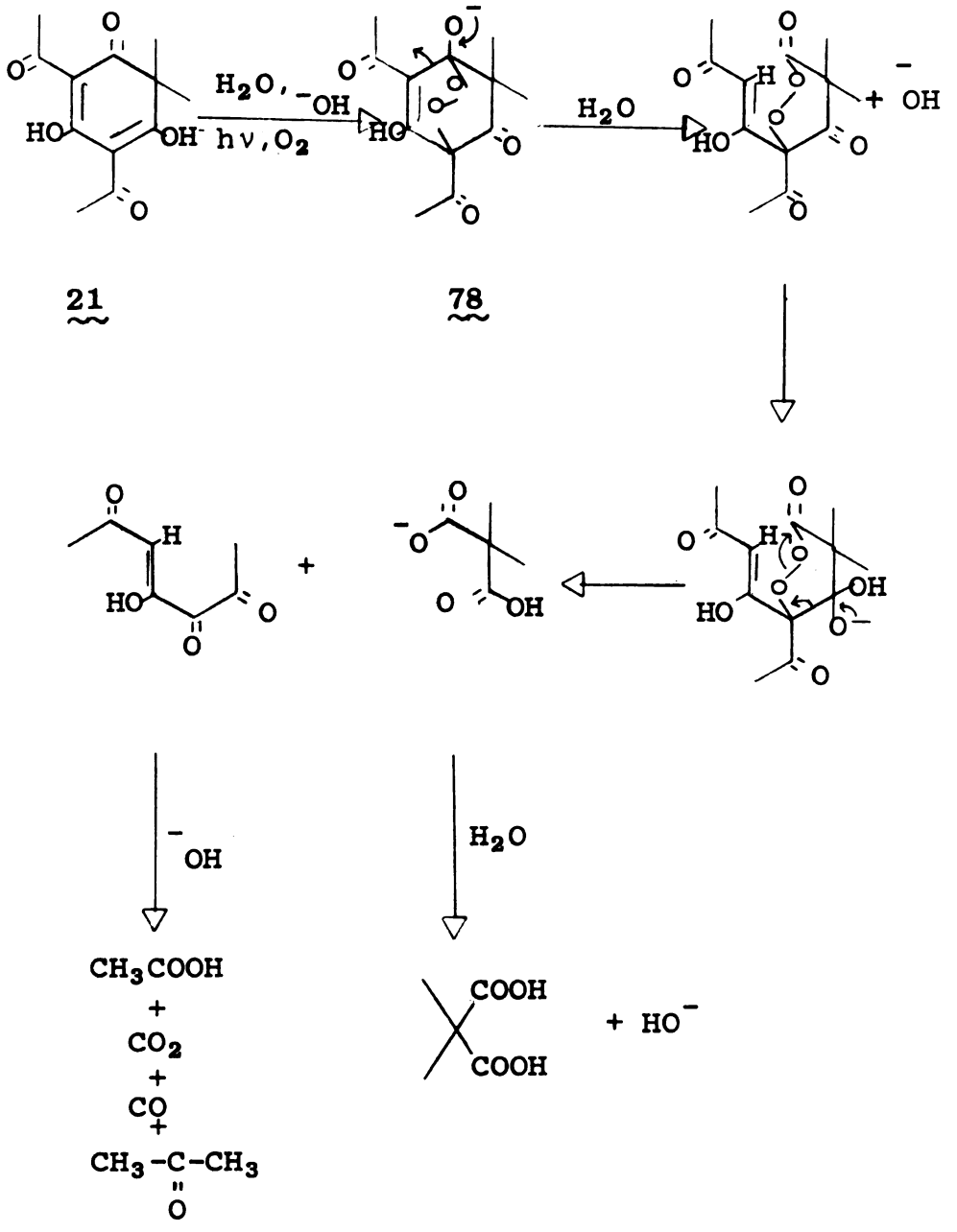
E. The Formation of Dimethylmalonic Acid

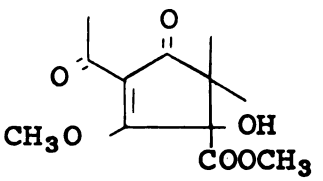
It was mentioned previously that dimethylmalonic acid formed when diacetylfilicinic acid, 21, was irradiated through Pyrex with a Hanovia L 450 watt lamp, under air,

in an alkaline water solution. The formation of dimethylmalonic acid was used as evidence that cleavage of the C_1-C_6 and C_5-C_6 bonds of 21 did not occur in the photo-oxidation of 21 in alkaline methanol. Since the methanol photoproduct, 67, and the degraded compound 70 were found to be inert under the conditions of the photolysis and photo-oxidation, they cannot be intermediates in the photo-oxidation of 21 to dimethylmalonic acid. Thus the formation of dimethylmalonic acid must occur through a change in the mechanism prior to the rearrangement to 67. A suggested intermediate for the formation of dimethylmalonic acid could be 78, which could form if cleavage of the acetyl group was slow. This becomes probable when the concentration of base is low. One possible mechanism for this reaction is outlined on the following page.

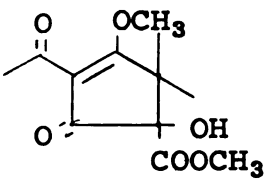
F. The Methyl Ethers of the Photo-oxidation Products

Some interesting results were obtained when the photo-oxidation product , 67, was treated with diazomethane. Two different methyl ethers, obtained in good and equal yield, had identical uv spectra. The two methyl ethers could not be separated by vapor phase chromatography, the peaks being only separated enough to tell that there were two compounds present. However it was possible to distinguish the two isomers by their nmr spectra (Table III). The two methyl ethers were identified as 81 and 82. The assignments of the nmr peaks were made on the assumption that the chemical


H2O, -OH
hν, O2
H2O
21
78
+ OH
- OH
H2O
CH3COOH
+
CO2
+
CO
+
CH3-C-CH3
O
COOH
COOH
+ HO-



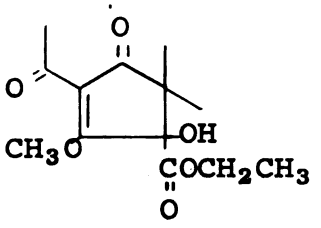
81



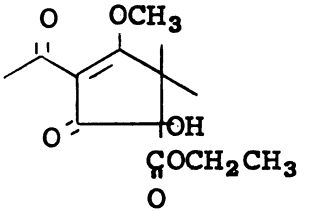
82

shifts of the gem dimethyl group in 81 (τ 8.84 and 8.75) would not vary much from those of 67 (τ 8.76 and 8.71), whereas those for 82 (τ 9.00 and 8.84) would be expected to change due to the altered environment. The band at τ 6.25 was assigned to the methyl ester group of 81 and the band at τ 5.93 to the methoxy group on the double bond.

For 82 the ester methoxyl was considered to give rise to the nmr peak at τ 6.19, whereas the methoxyl on the double bond was responsible for the peak at τ 6.01. The relative assignments were obtained by comparison not only with 67, which showed the upfield methoxyl peaks to be due to the ester groups, but also by comparison with the two methyl ethers, 83 and 84, similarly obtained from 71. Although 83 and 84 were not separated, relative assignments of the peaks in their nmr spectra were possible because the compounds were produced in a 1:2 molar ratio. The compound in least abundance, 83, showed the least change in chemical shift of the gem dimethyl group (τ 8.85 and 8.73) in comparison to the starting material, (τ 8.80). Thus by taking



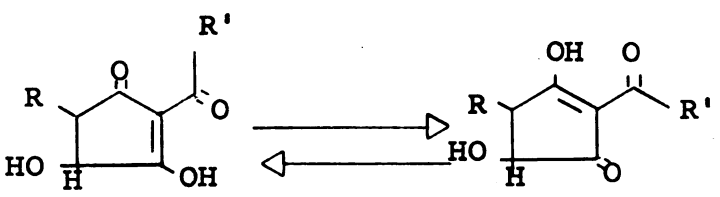
83



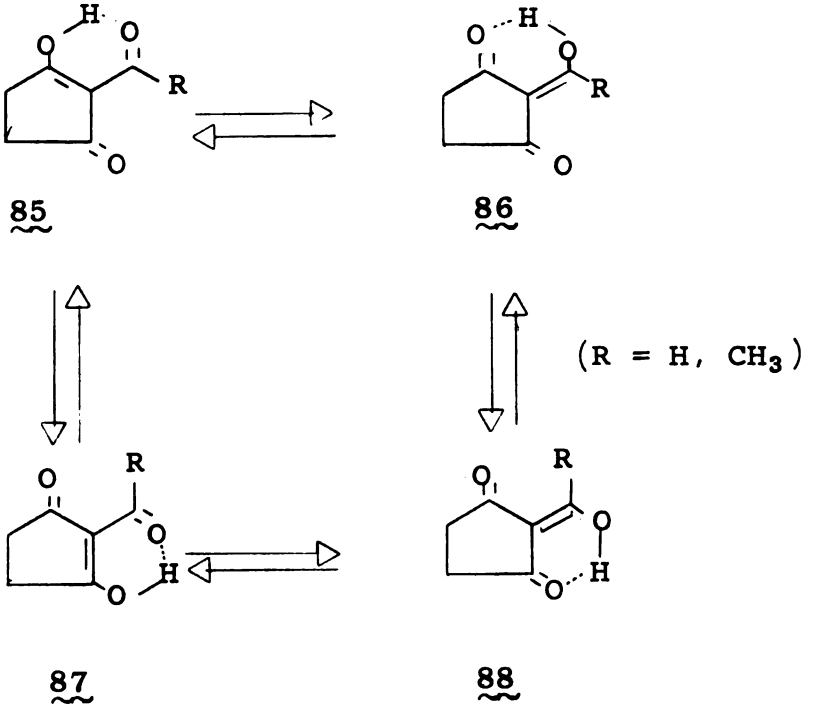
84

the lower intensity peaks throughout it was possible to assign peaks in the nmr spectrum as given in Table III. It was noted that the low field methylene hydrogens of the ethoxy group were due to compound 84, which had the methoxy adjacent to the gem dimethyl group. For this reason the compound having the low field peak due to the ester methoxyl (τ 6.19) in the previous pair was taken as 82. In the same manner the position for the methoxyl on the double bond was assigned as indicated in Table III.

Since it has been previously shown (42) that an equilibrium such as that outlined here exists for this type of compound, it is not too surprising that two different methyl ethers were obtained in each case. For example,



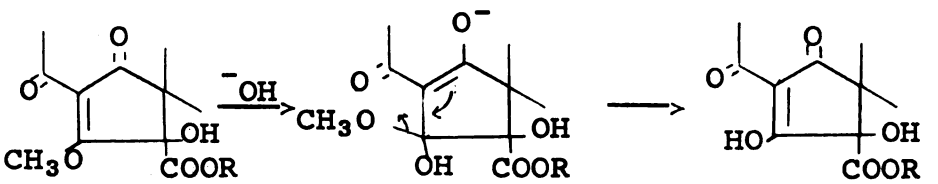
Nilsson has shown (43) that of the four possible enol tautomers, shown below, of the 2-acetyl or 2-formylcyclopentane-1,3-diones only 85 and 87 are probable when R = H. Because of the distinct AB pattern of the methylene



hydrogens in the nmr spectrum, these two interconvert only slowly relative to the nmr time scale. Structures 86 and 88 were ruled out as there was no noticeable coupling between the vinyl hydrogen and the expected hydroxyl hydrogen, when R = H. Nilsson stated that the ir and uv spectra of the compound where R = CH_3 were similar to those where R = H; thus forms 85 and 87 would also be preferable for the acetyl derivative.

Evidence that a similar equilibrium was also important for 67 was the broadening of the nmr peaks for the methyl hydrogens of the gem dimethyl group (Nmr Spectrum 1). Because the peaks for the chelated hydroxyl hydrogens could not be found in the nmr spectra of 67 and 69 this indicated that these hydrogens might be broadened due to enol-keto tautomerism.

When the methyl ethers, 81 and 82 or 83 and 84, were placed in alkaline solution, 67 or 69 were recovered. This reaction occurred very rapidly with only a trace of base in 95% ethanol. The driving force for this reaction could be the formation of a more stable compound since 67 and 69 have an intramolecularly hydrogen-bonded hydroxyl group.



81; R = CH_3

82; R = $-CH_2CH_3$

67; R = CH_3

69; R = $-CH_2CH_3$

IV. The Photolysis and Photo-oxidation of Acetylfilicinic Acid

A. Photo-oxidation of Acetylfilicinic Acid

To extend the photochemical study to related substituted 2,4-cyclohexadienones, the behavior of monoacetylfilicinic acid, 22, was examined. When an alkaline solution

of 22 was irradiated through Pyrex using a Hanovia L 450 watt lamp, under air, a very rapid photo-oxidation occurred. Work-up afforded a 50:50 mixture of 67 and 70 as determined by nmr spectral analysis. Repetition of the reaction gave a mixture of 51 mole % 67 and 35 mole % 70. Recrystallization from hexane–ethyl ether gave a 14% isolated yield of 67 identified by its ir spectrum.

Acetylfilicinic acid, 22, was also photo-oxidized using a 200 watt tungsten lamp with Rose Bengal as the sensitizer. The photolysis was completed within an hour and an nmr spectrum of the product mixture indicated it to be 83% compound 67.

The photo-oxidation product, 67, is postulated to form in an analogous manner to that given before for the photo-oxidation of the anion of diacetylfilicinic acid, 55. Instead of the cleavage of an acetyl group, a proton is lost.

The charge densities at the carbon atoms of acetylfilicinic acid monoanion, 65, were calculated using the molecular orbital method described previously. The results are given in Table VI.

This indicates that singlet oxygen should attack primarily at carbon atom 4, the most negative position (although carbon 2 carries nearly as much negative charge). The major product formed, 67, can be accounted for by the scheme shown, initial attack being at carbon 4.

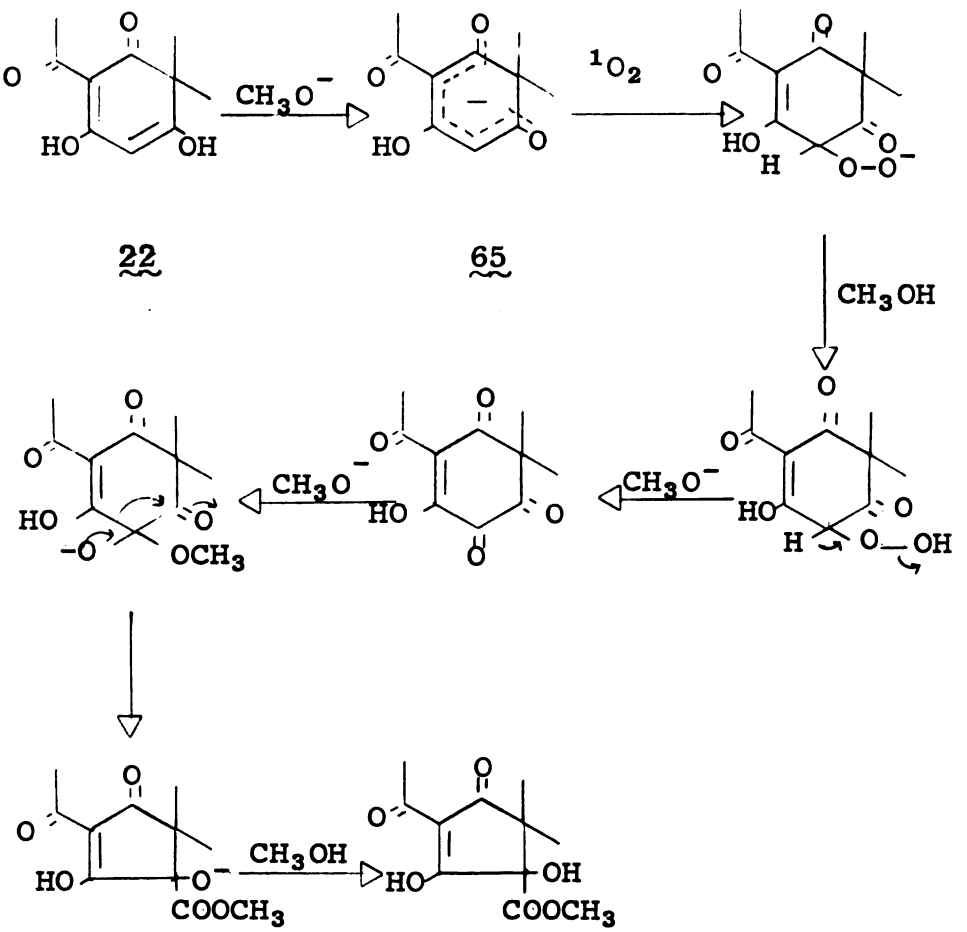
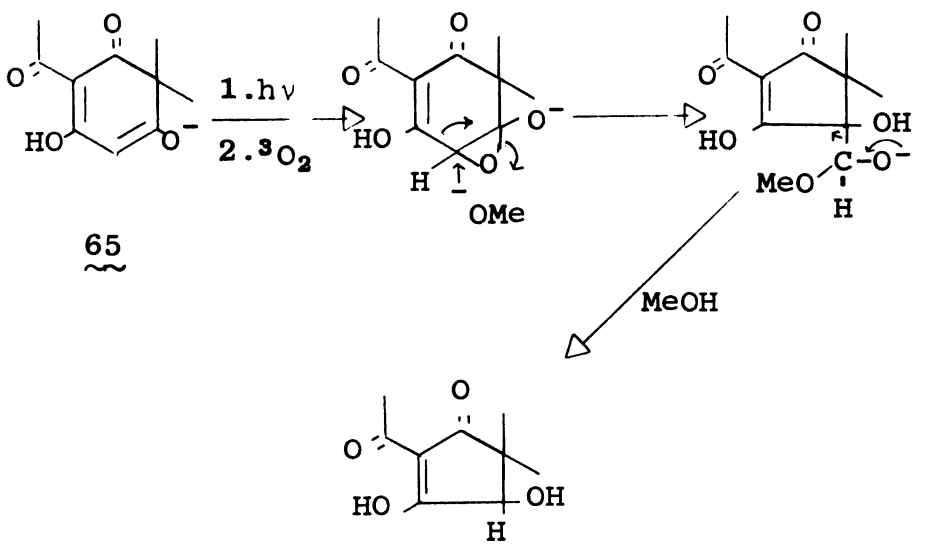


Table VI. Charge densities of the anion of acetylfilicinic acid (65)

Atom	Charge
1	0.1288
2	-0.1990
3	0.0420
4	-0.2082
5	0.1106

Although it was possible to prepare 70 from 67 under alkaline conditions it does not seem likely that the temperature of the photolysis (25-35^0) was high enough, the base concentration (0.1 N) strong enough, nor the reaction time long enough (two hours) for cleavage to have occurred to give 70 from 67 during the photo-oxidation. Also, compound 67 does not photorearrange to 70 under similar conditions. Thus there must be a new mechanism operating for the photo-oxidation of acetylfilicinic acid, not operative for diacetylfilicinic acid which allows the direct formation of 70.

One possible mechanism given here for the formation of 70 involves direct reaction of triplet oxygen with the

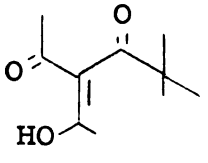


65

70

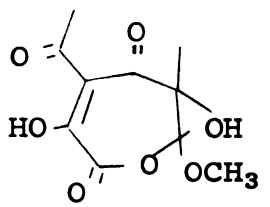
excited state of the monoanion of acetylfilicinic acid, 65, since it was found that 65 did not give 70 on reaction with singlet oxygen formed in a dye-sensitized photo-oxidation.

Still a third product was obtained when 22 was photo-oxidized through Pyrex using a Hanovia L 450 watt lamp in methanol containing only one molar equivalent of sodium methoxide. The reaction was slower than before. On work-up a small amount of a carbon tetrachloride-insoluble compound (mp 179-181°) was obtained, in addition to 67. The compound analyzed for the empirical formula $C_{11}H_{14}O_7$. Its nmr spectrum (Table III and Nmr Spectrum 4) indicated the presence of a gem dimethyl group at τ 8.81 and 8.75, an acetyl group at τ 7.42 and a methoxyl group at τ 6.65. The uv spectra were similar to those of 67. The ir spectrum had absorption bands at 1580 (broad), 1670, 1755 and 3000-3500 cm^{-1} (Ir Spectrum 4). The nmr spectrum of this compound in sodium deuteroxide and deuterium oxide still showed two distinct peaks for the gem dimethyl group. This would indicate that the two peaks were not due to the presence of two tautomeric forms but due to the gem dimethyl group being adjacent to an asymmetric center in a closed ring system. An unequivocal structure assignment cannot yet be made for this compound. From the combined evidence a partial structure can be drawn:



$+ -OCH_3 + -OH + C_2O_2$

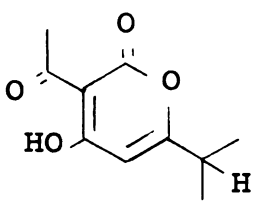
Structure 89 is one possibility for this compound which is consistent with the evidence.



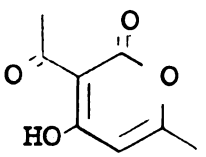
89

B. Photoisomerization of Acetylfilicinic Acid

When acetylfilicinic acid was irradiated in methanol or ether, under a nitrogen atmosphere, for 32-48 hours with a Hanovia L 450 watt lamp, a new compound was obtained. This compound was identified as 3-acetyl-4-hydroxy-6-i-propyl-2H-pyrone, 90. It analyzed correctly ($C_{10}H_{12}O_4$) for an isomer of 22. The nmr spectrum of 90 (Table III



90



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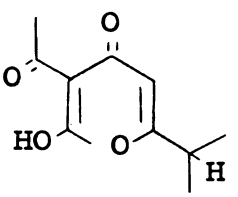


92

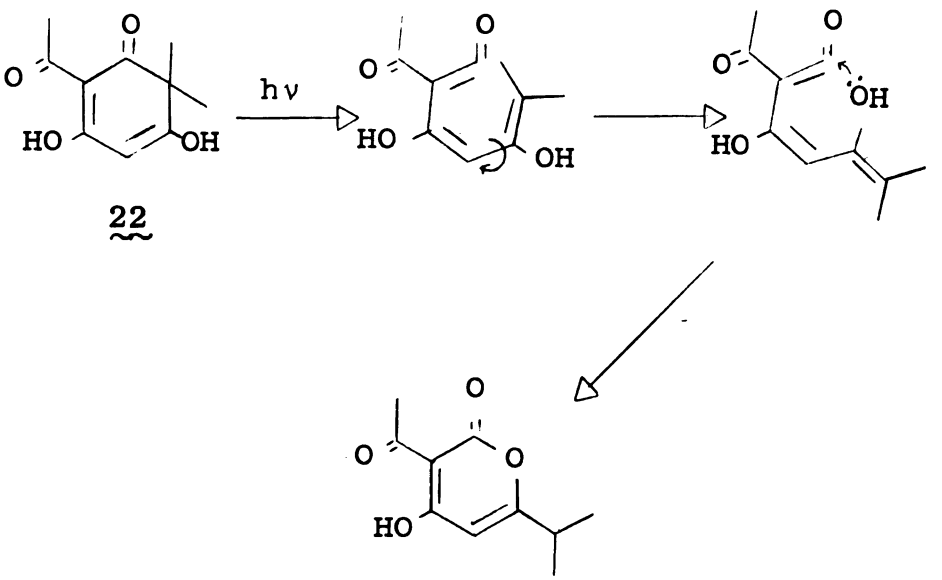
and Nmr Spectrum 5) indicated that the compound had an acetyl methyl group (τ 7.48), a chelated hydroxyl proton (τ -6.9), a vinyl proton (τ 4.28), and an isopropyl group (a six-proton doublet at τ 8.75, J = 7 cps and a one-proton multiplet centered at τ 7.34, J = 7 cps). Its uv and ir spectra

resembled those of dehydroacetic acid, 91. The uv spectra had absorption maxima at λ 309, 223 and 203 mμ in acidic ethanol and at λ 291, 229 and 204 mμ in basic ethanol. With dehydroacetic acid similar uv maxima appeared at λ 310 and 225 mμ in neutral solution, and at λ 294 mμ in basic solution. This would not be likely for the other possible tautomeric structure 92, which should show a bathochromic shift as observed for the related compound 32.

The ir spectrum of 90 in KBr (1555, 1635, 1710, 1730 cm^{-1}) (Ir Spectrum 5a) was different from that in carbon tetrachloride solution (1575 (small), 1610 (sh), 1635, 1710 (sh) and 1725 cm^{-1}) (Ir Spectrum 5b), but almost identical to the ir spectrum of dehydroacetic acid both in potassium bromide (1550, 1635 and 1715 (broad) cm^{-1}) (Ir Spectrum 6a) and carbon tetrachloride (1615 (sh), 1640 and 1724 cm^{-1}) (Ir spectrum 6b). The difference in ir spectra of 90 in carbon tetrachloride and potassium bromide may be due to different concentrations of the two possible pyrone structures, 90 and 92. The similarity of ir spectra of the pyrone to the ir spectra of dehydroacetic acid indicates that the two must have almost identical structures.

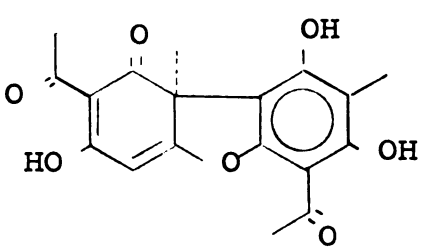
A possible mechanism for the formation of 90 is outlined below, the key intermediate being ketene 93. The intramolecular reaction of the postulated ketene intermediate is apparently faster than attack by the nucleophilic solvent, methanol, since no open-chain unsaturated esters which might result from such attack were isolated.

Such products are common from the photolysis of 2,4-cyclohexadienones which do not have substituents which may act intramolecularly as nucleophiles (1,2,3,6). Barton (1) has shown that usnic acid, 94, racemized by uv light in



22 90

dioxane solution and he postulated a similar ketene intermediate which then reclosed in either of the two possible manners to give a racemic mixture of the starting compound.

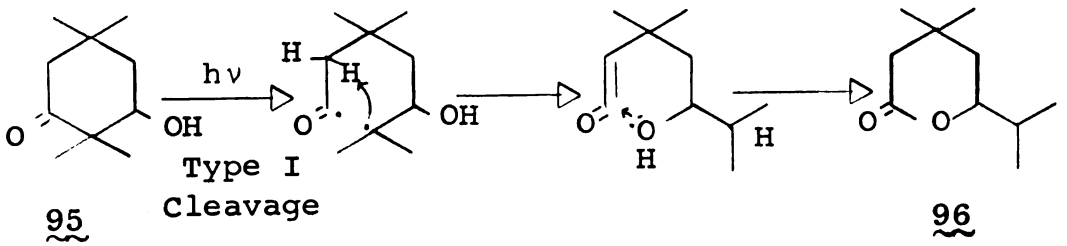


94

The monomethyl ether of acetylfilicinic acid, 38, failed to photo-oxidize under conditions where acetylfilicinic acid was readily oxidized to 67. Ether 38 also did not photoisomerize to a pyrone under neutral conditions. These facts lend some support to the proposed mechanisms for each of these photoreactions of acetylfilicinic acid. Compound 38 did not photo-oxidize as it could not give the required anion at carbon 4. Although ring-opening to a ketene (on irradiation of 38 in neutral solution) could have occurred, this must have reclosed as in the Barton photolysis of usnic acid, because isomerization to a pyrone would have required the loss of a methyl cation. It is perhaps surprising that a ring-opened, unsaturated methyl ester was not obtained by solvent capture of the ketene.

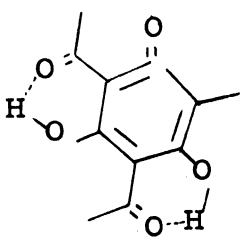
A possibly related example for this type of ring-opening and recyclization has been presented by Cookson (44), who suggested that the photochemical rearrangement of 95 to 96 involved a hydrogen migration, possibly *via* a ketene. This reaction involves an α-cleavage (Type I) of a ketone, whereas the photoisomerization of acetylfilicinic acid, 22, can be visualized as involving either a Type I or a Type II cleavage.

A rationalization is required for the observation that acetylfilicinic acid underwent photoisomerization to a pyrone in neutral solution, whereas diacetylfilicinic



95 96

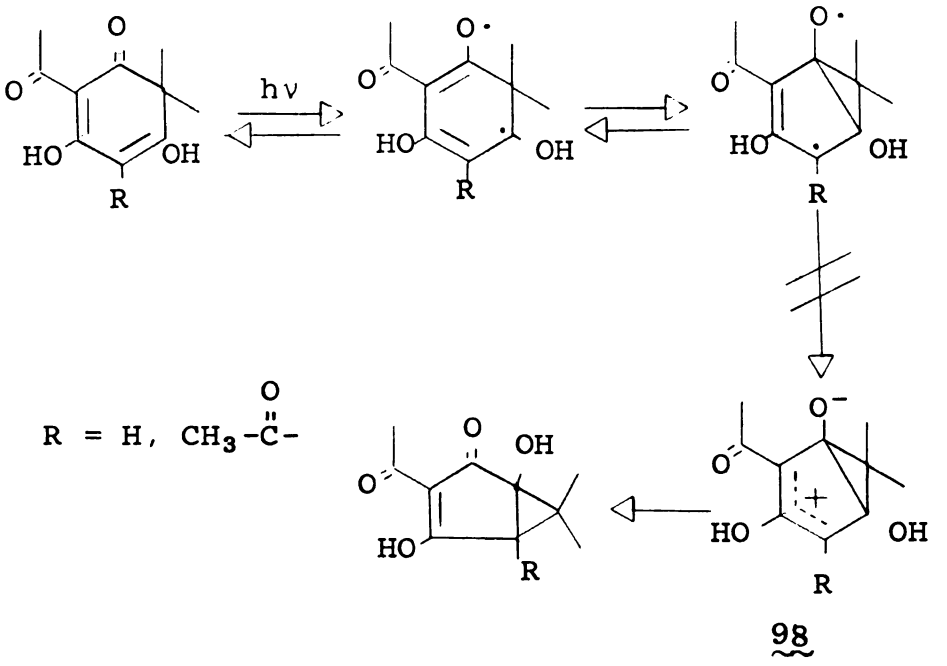
acid, treated similarly, was photochemically inert. Perhaps cleavage to a ketene intermediate occurs in both cases. However, the rotation necessary for internal ring closure to give the pyrone is less likely with diacetylfilicinic acid, since it requires disruption of the internal chelated structure, 97. Ring closure to give the original starting compound would result in no observable change.



97

Photoisomerization of mono- or diacetylfilicinic acid to a bicyclo[3.1.0]hexenone (the major photochemical path for hexamethyl-2,4-cyclohexadienone; see page 3) was not observed. One possible reason could be the instability of

the intermediate, 98, which would occur after electron demotion. This intermediate would be unstable due to the location of the positive charge adjacent to the acetyl group(s).



V. Results and Discussion of Kinetic Experiments

A series of kinetic experiments was undertaken to ascertain the effect of various conditions upon the photo-oxidation rates. Such information would hopefully prove useful in understanding the photo-oxidation reaction mechanism. The reactions were followed using the uv spectra of small aliquots. All reaction conditions were maintained

constant except the one being varied. In the first series of reactions 0.0105 molar diacetylfilicinic acid was used and the concentration of base was varied. The results of these experiments are plotted in Fig. X, and the steady state reaction rates of these zero order reactions are given in Table VII. There was very little change in rate as the base concentration increased from 0.05 N sodium methoxide to 0.40 N sodium methoxide.

Table VII. Series I reaction rates (methanol at room temp.)

Experiment	$NaOCH_3$ (molarity)	Conditions	Rate (mole/l/hr) (x 10^3)
IV A1	0.05	Air	3.3
IV A2	0.20	Air	3.6
IV A3	0.40	Air	3.6
IV A4	0.05	Oxygen	3.3
IV A5	0.05	Saturation with air for 3 hrs before irradiation	3.1
IV A6	0.05	Air, 0.0026 mole of diacetylfilicinic acid	4.3
IV A7	0.05	Air, 0.00255 mole of acetylfilicinic acid	17.3

In a second series of reactions 2,5-dimethylfuran, which is known to react with singlet oxygen (45), was added to both dye-sensitized and self-sensitized photo-oxidation reactions of diacetylfilicinic acid. If the singlet oxygen is intercepted by dimethylfuran in the self-sensitized

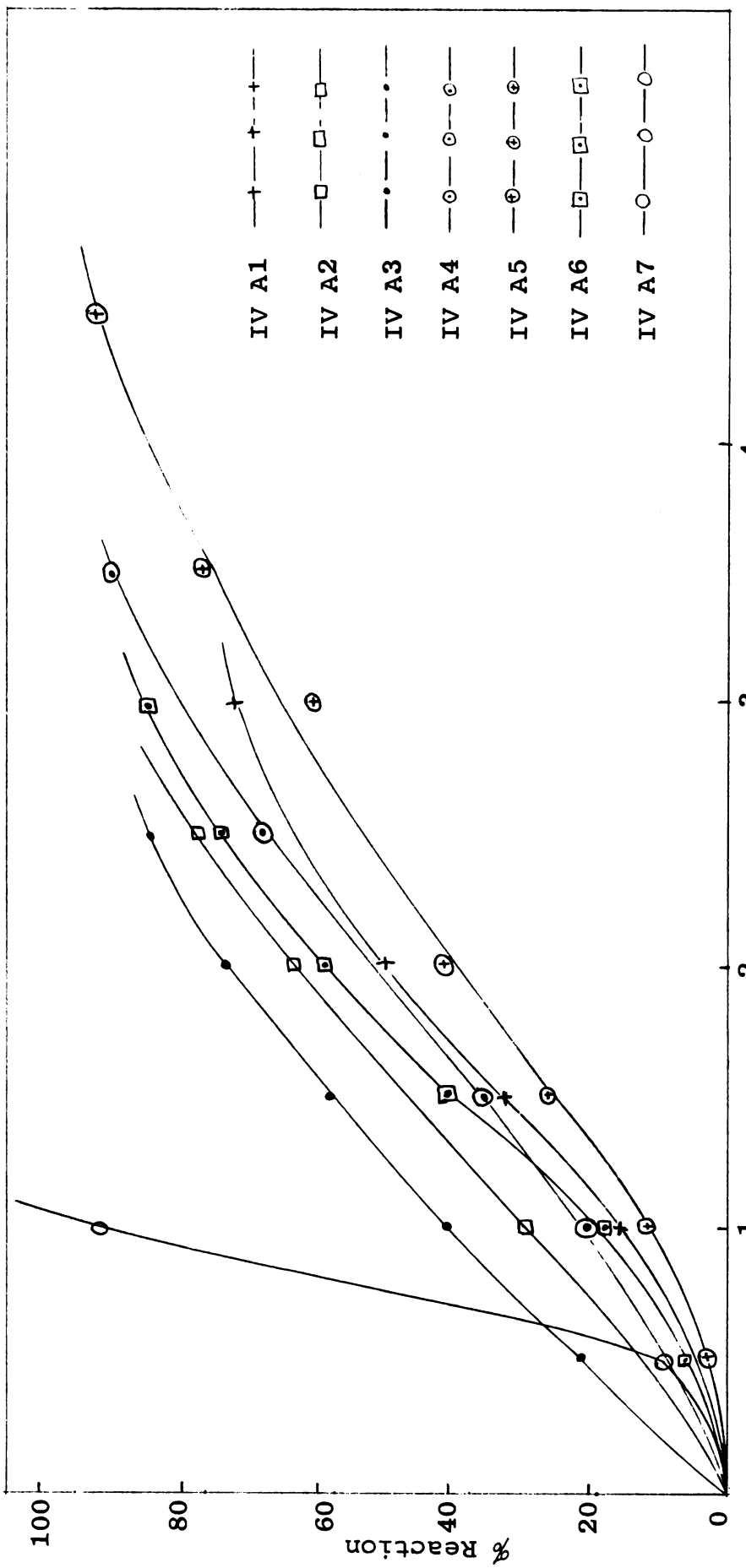


Fig. X. Graphic results of kinetics; Series I.

photo-oxidation as well as in the dye-sensitized photo-oxidation, then this would be evidence for the formation of singlet oxygen in both reactions. In these reactions an 0.00525 molar solution of diacetylfilicinic acid in 200 ml of methanol was photo-oxidized with a Hanovia L 450 watt lamp. Results were plotted (Fig. XI) and the rates are given in Table VIII. When dimethylfuran was added (Exp. IV B5, IV B9), an initial rapid trapping of singlet oxygen occurred. However, the subsequent photoreaction appeared to occur relatively quickly. The dimethylfuran, or its photo-oxidation product(s) were thought to react with the diacetylfilicinic acid under the influence of uv radiation. Schenck and Foote (45) have shown that the photo-oxidation of dimethylfuran yielded a cyclic peroxide which was hydrolyzed in acid to 3-hexene-2,5-dione.

A similar reaction was carried out to check the reactivity of singlet oxygen to 2,5-dimethylfuran in alkaline methanol. A change in the uv absorption from λ 217 mμ to λ 213 and 282 mμ occurred on photo-oxidation of the 2,5-dimethylfuran. This was followed by a decrease in intensity of these absorption bands which were replaced by an absorption band at λ 230 mμ. This phenomenon is interpreted to mean that the dimethylfuran was photo-oxidized to cis-3-hexene-2,5-dione (uv λ_{max}^{EtOH} 223 (6600) and 292(174)mμ (46)). which subsequently isomerized to the trans isomer (uv λ_{max}^{EtOH} 228(14,400) and 324 (70) mμ (46)). Conceivably the cis or trans form of 3-hexen-2,5-dione was reacting with the

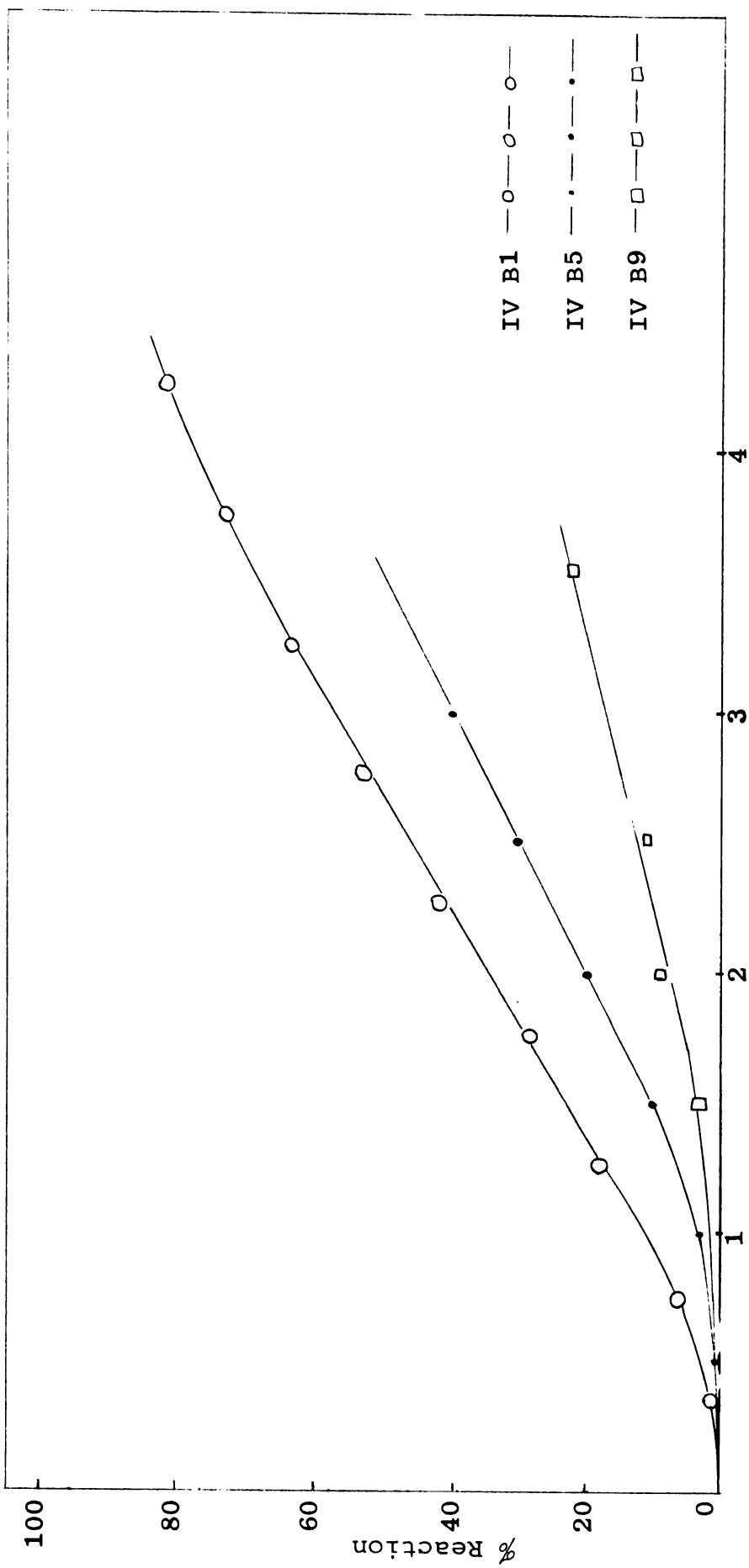


Fig. XI. Graphic results of kinetics; Series II, with Hanovia L 450 watt lamp.

Table VIII. Series II reaction rates using diacetylfilicinic acid, 21, in methanol

Exp. No.	Reaction	Lamp	$NaOCH_3$ (mole in 200 ml)	Dimethylfuran (mole in 200 ml)	Conditions	Rate (moles/l/hr) (x 10^{3})
IV B1	Unsens.	Han. 450 watt	0.0093		air	1.35
IV B2	Unsens.	200 watt tungsten	0.0093		air	0.08
IV B3	Dye-sens.	200 watt tungsten	0.0093		air	9.60
IV B5	Unsens.	Han. 450 watt	0.0093	0.0104	air	1.23
IV B6	Dye-sens.	200 watt tungsten	0.0093	0.0104	air	2.9
IV B7	Dye-sens.	200 watt tungsten	0.0093	0.0104	oxygen	2.9
IV B8	Dye-sens.	200 watt tungsten	0.0372		air	10.9
IV B9	Unsens.	Han. 450 watt	0.0093	0.104	air	0.51
IV B10	Dye-sens.	200 watt tungsten	0.0093	0.104	air	0.80

diacetylfilicinic acid to give unidentified product(s).

For the dye-sensitized reactions using Rose Bengal a marked decrease in rate was noticed on the addition of 2,5-dimethylfuran (Exp. IV B6, IV B10). The photo-oxidation rate in the presence of 0.0104 mole of the dimethylfuran was initially slow, then increased, then slowed down after approximately an hour. This would fit the tentative explanation that the rate increased as the concentration of dimethylfuran decreased by reacting with the singlet oxygen. The rate then decreased as the isomerization from the cis to trans 3-hexen-2,5-dione occurred (see Fig. XIV for a plot of the absorption at λ 282 mμ versus time). This isomerization may be causing the quenching of the triplet state of the dye, or the singlet oxygen moiety, resulting in a rate retardation.

When a large amount of furan was used to trap singlet oxygen the rate was slower by a factor of 12 (Exp. IV B10). This indicates that the singlet oxygen was reacting with the furan rather than the diacetylfilicinic acid.

Although furan caused a rate retardation in the dye-sensitized photo-oxidation, the same effect was not observed in the non-sensitized photo-oxidation of diacetylfilicinic acid (Exp. IV B5, IV B9). Singlet oxygen was trapped only in the initial stages of the latter reaction, as can be seen in Fig. XI.

An increase in the base concentration caused only a slight increase in the dye-sensitized photo-oxidation rate

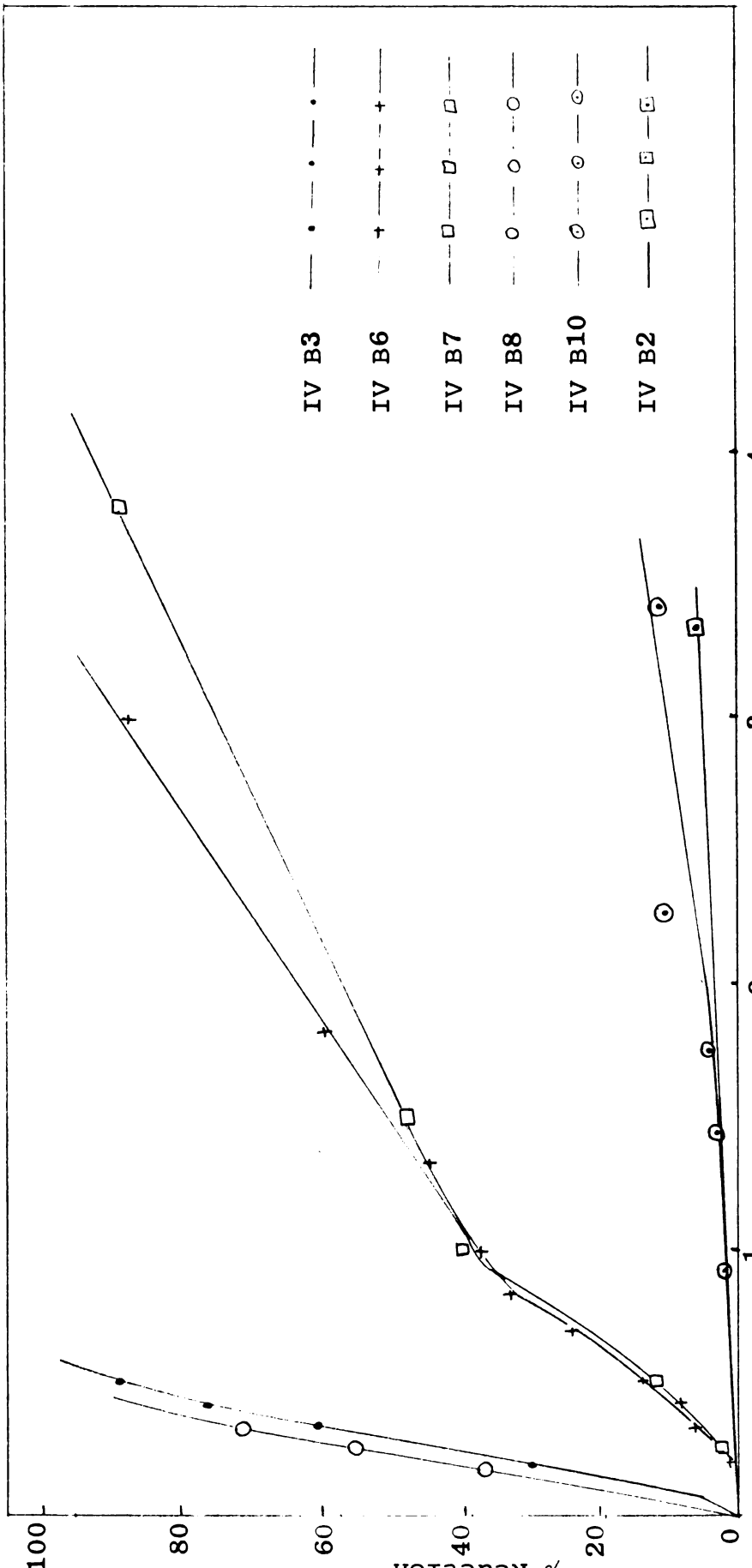


Fig. XII. Graphic results of kinetics; Series II, dye-sensitized photo-oxidation.

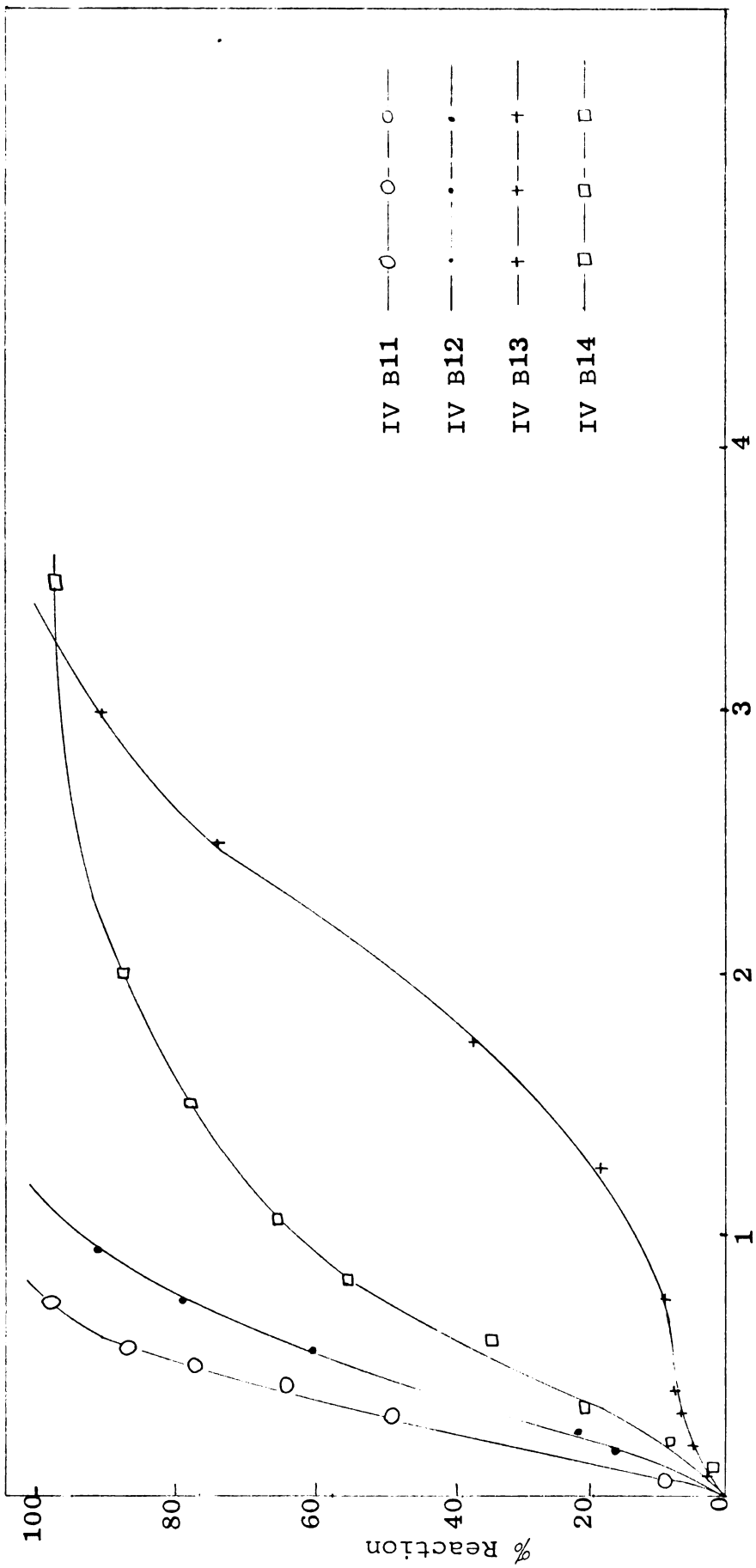


Figure XIII. Graphic results of kinetics; Series II, acetylfilicinic acid.

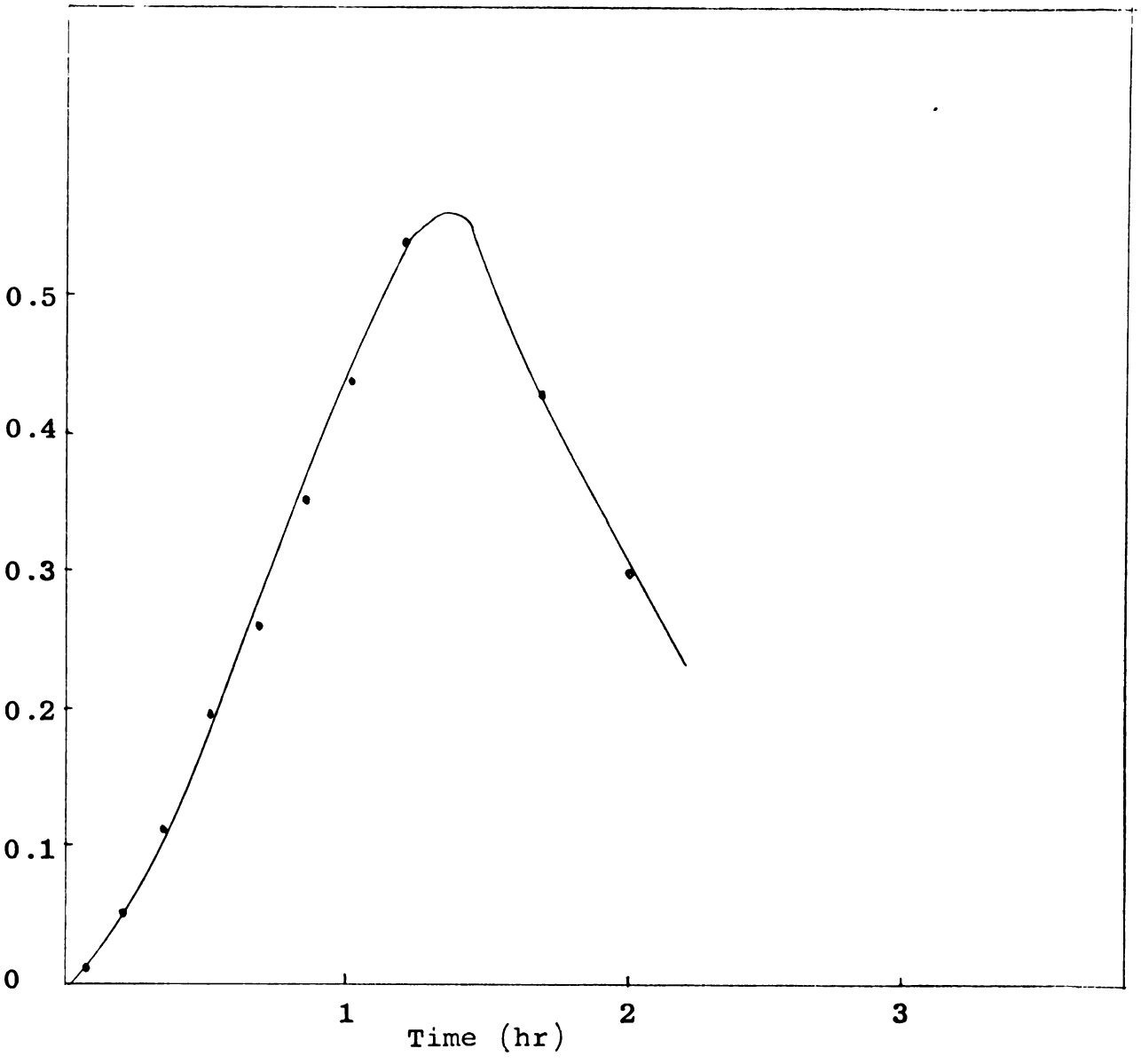


Fig. XIV. Plot of ultraviolet absorption of 3-hexene-2,5-dione during the photo-oxidation of dimethylfuran (at λ_{max} 282mμ).

of diacetylfilicinic acid (from 9.6×10^{-3} moles/l/hr to 10.9×10^{-3} moles/l/hr)(Exps. IV B3 and IV B8).

The photo-oxidation of acetylfilicinic acid was faster by a factor of 6.2 than the photo-oxidation of diacetylfilicinic acid, when using a Hanovia L 450 watt lamp (Exp. IV B11). This could result from a more favorable excited state for acetylfilicinic acid than diacetylfilicinic acid.

Table IX. Series II reaction rates using acetylfilicinic acid in methanol

Exp. No.	Reaction	Lamp	$NaOCH_3$ (mole in 200 ml)	Rate (mole/l/hr) ($\times 10^{-3}$)
IV B11	Unsens.	Han. 450 watt	0.0093	8.1
IV B12	Dye-sens.	200 watt tungsten	0.0093	5.9
IV B13	Unsens.	Han. 450 watt	0.000128	2.35
IV B14	Dye-sens.	200 watt	0.000128	3.8

The rate of the dye-sensitized photo-oxidation of 22 using a 200 watt tungsten lamp (5.9×10^{-3} moles/l/hr) was only slightly less than the equivalent rate for diacetylfilicinic acid (9.6×10^{-3} moles/l/hr) (Exps. IV B12 and IV B3). These comparable rates might be expected as the reaction only depends upon the rate of production of singlet oxygen, which would be constant in both reactions, and the subsequent attack of this species on the enol anions.

When the base concentration was decreased to one molar equivalent a marked decrease in the rate (3.45 times slower) for the direct photo-oxidation of acetylfilicinic acid occurred (Exp. IV B13). This reaction not only gave the normal photo-oxidation product, 67, but also a new product, 89. For the dye-sensitized photo-oxidation at low base concentration, the rate was only slightly decreased (1.55 times) and only the normal photoproduct, 67, was obtained (Exp. IV B14).

A question which remains regarding these reactions was the determination of the rate-determining step. If S represents both the anion and sensitizer then the reaction can be expressed by the following series of equations:

$$S + h\nu \xrightarrow{\Phi} {}^1S$$

$${}^1S \xrightarrow{k_{isc}} {}^3S$$

$${}^3S + {}^3O_2 \xrightarrow{k_1} {}^3S\ldots{}^3O_2$$

$${}^3S\ldots{}^3O_2 \xrightarrow{k_2} S + {}^1O_2$$

$$S + {}^1O_2 \xrightarrow{k_{r_1}} SO_2$$

$$SO_2 \xrightarrow{k_{r_2}} \text{products}$$

$$(\text{Furan} + {}^1O_2 \xrightarrow{k_t} \text{Furan peroxide} \longrightarrow \text{Furan products})$$

Three factors are likely candidates for the slow step in the reaction. These are the photochemical step, the rate of diffusion of oxygen in the solution, or the subsequent chemical reaction, one step of which is the cleavage of the

acetyl group from diacetylfilicinic acid or the hydrogen from acetylfilicinic acid.

As the rate for the direct photo-oxidation of diacetylfilicinic acid did not change very much with increasing base concentration, cleavage of the acetyl group by base could not be the rate-determining step (see Table VII). Also the dye-sensitized photo-oxidation rate was much faster than the self-sensitized rate, showing that cleavage by base was not rate-limiting.

When oxygen was used in the place of air, effectively increasing the oxygen content by about five times, no major change in the rate of the photo-oxidation occurred. Thus it is unlikely that the rate of diffusion of oxygen through the solution is the controlling factor. The most probable rate-controlling step is the initial quantum yield, which would involve the initial excitation and intersystem crossing to the triplet state, in a manner suggested in Section III.

For the previously mentioned series of equations it can be shown that in the steady state the rate of photo-oxidation can be represented by:

$$\frac{d(\text{product})}{dt} = I_a \Phi \ .$$

However if the base concentration were to become low enough the rate of cleavage of the acetyl group, or loss of a proton might become slow enough to be the rate-determining step of the reaction. This was observed in the photolysis of acetylfilicinic acid (Table IX).

The results of these kinetic reactions can be summarized as follows:

1. Acetylfilicinic acid undergoes direct photo-oxidation faster than diacetylfilicinic acid.
2. Diacetylfilicinic acid undergoes dye-sensitized photo-oxidation slightly faster than acetylfilicinic acid.
3. The effect of changing the base concentration was almost unnoticeable unless the basic concentration was low.
4. The rate of photo-oxidation of diacetylfilicinic acid was decreased by adding 2,5-dimethylfuran.
5. The rate of reaction was independent of the oxygen concentration.

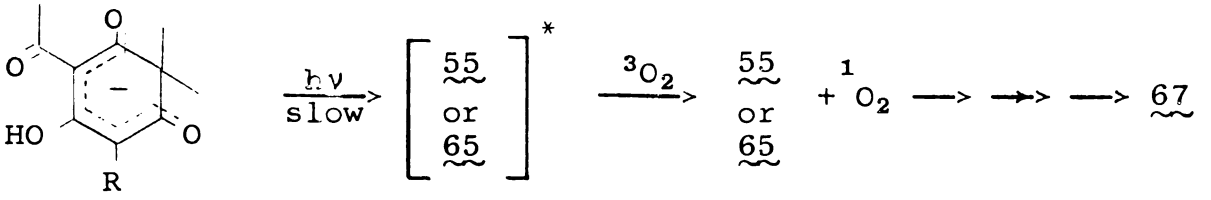
The conclusions which can be drawn from these results are:

1. The photochemical step(s) in the self-sensitized photo-oxidation of acetylfilicinic acid, 22, is better than in the self-sensitized photo-oxidation of diacetylfilicinic acid, 21, perhaps because of a more favorable excited state.

2. The cleavage of the acetyl group in the mechanism (page 70) is unlikely to be the rate-determining step of the reaction under the normal conditions.

3. When dimethylfuran was added to the reaction it preferentially reacted with the singlet oxygen.

A mechanism which is consistent with these results is outlined here.



55 R = $CH_3-\overset{O}{\overset{\|}{C}}$

65 R = H

EXPERIMENTAL

I. General Procedures

All ultraviolet spectra were measured with a Unicam Model SP-800 recording spectrophotometer in 95% ethanol solution unless otherwise stated. When spectra are referred to as having been measured in base or acid, the basic solutions were obtained by addition of a small amount of sodium methoxide, and the acidic solutions by the addition of one or two drops of 2N hydrochloric acid to the ethanol. The term pH refers to the value calculated from the amount of acid (H_2SO_4) or base (NaOH) added to a water solution. Unless otherwise stated, all uv λ_{max} are reported as mμ, with the extinction coefficient, ϵ, given in parentheses. The infrared spectra were obtained on a Unicam Model SP-200 spectrophotometer, calibrated with polystyrene. The nuclear magnetic resonance spectra were obtained on a Varian A-60, a Varian HA-100 or a Jeolco C-60H spectrometer, with tetramethylsilane as an internal reference. Melting points were taken with a Gallenkamp melting point apparatus and are uncorrected. The photolyses were carried out with a Hanovia L 450 watt or a Hanovia S 200 watt lamp with a Pyrex filter. Photo-oxidations under air or oxygen were obtained by bubbling air or oxygen through the reaction solution. The dye-sensitized photo-oxidations were carried out with a 200 watt tungsten lamp in a 250-ml 3-necked flask equipped with a

reflux condenser and a gas inlet tube. Elemental analyses were performed by Spang Microanalytical Laboratories, Ann Arbor, Michigan. Sublimations were carried out at 0.5 mm of mercury a few degrees below reported melting points. Reactions followed by uv were sampled with a 50 μl syringe; a constant amount of reaction mixture was injected into 3 ml of solvent (95% ethanol) in a 1 cm quartz cell. The disappearance of absorption bands of the reactant and/or the appearance of absorption bands for the product(s) were monitored. For example the uv absorption wavelengths used for the monoanion of diacetylfilicinic acid, 55, was λ_{max} 340 mμ; for the monoanion of acetylfilicinic acid, 65, λ_{max} 345 mμ; for acetylfilicinic acid, 22, λ_{max} 330 mμ; and for the photo-oxidation product 2-acetyl-3,4-dihydroxy-4-carbomethoxy-5,5-dimethyl-2-cyclopentenone, 67, λ_{max} 270 and 250 mμ in basic ethanol. When reaction percentages are quoted, these were calculated from the relative intensities of the longest wavelength absorption bands obtained from spectra at the beginning and at the end of the reaction.

II. Preparation of Filicinic Acid and Derivatives

A. Preparation of 1,3-Diacetylphloroglucinol, 24

1. Using Boron Trifluoride as Catalyst

In a 100-ml 3-necked flask equipped with a gas inlet tube and a reflux condenser were placed 10 g (0.0795 mole) of phloroglucinol and 50 ml of glacial acetic acid. The

phloroglucinol was dissolved by warming the mixture. Without cooling, boron trifluoride gas was bubbled through the solution for one hour with stirring. The reaction mixture was poured into about 400 ml of water and allowed to stand several hours. Filtration afforded 13.6 g (81.5%) of crude 1,3-diacetylphloroglucinol, 24. This crude material was recrystallized from 50% aqueous methanol. After sublimation at 150° and 1 mm of mercury white crystals of the product were obtained (mp 167.5-169°, lit. 168° (12)).

The infrared spectrum of 24 had absorption bands at ν_{max} 1610, 3000 and 3450 cm^{-1}.

2. Using Concentrated Sulfuric Acid as Catalyst

a. Small Scale Reaction.- Ten grams (0.0795 mole) of oven dried (110°) phloroglucinol was added to 16.16 g (0.158 mole) of acetic anhydride. After the addition of 1.5 ml of concentrated sulfuric acid the temperature rose to 97°. The reaction mixture was refluxed at 135° for five minutes, then 40 ml of 30% concentrated hydrochloric acid in methanol was carefully added. The mixture was poured into 300 ml of cold water. Crystals precipitated immediately and filtration gave 12.2 g of crude product (mp 100-107°). Recrystallization from 50% methanol in water yielded 6.3 g (37.7%) of an orange crystalline product (mp 160-166°). After sublimation at 150° and 1 mm of mercury the mp rose to 168-170°.

b. Large Scale Reaction.- In a 250-ml 3-necked flask equipped with a reflux condenser was placed 40 g (0.317 mole) of dry phloroglucinol. Acetic anhydride (64.3 g, 0.63 mole) was added followed by 4 ml of concentrated sulfuric acid. The temperature rose to 95° after which the mixture was refluxed at 135° for five minutes. A 50 ml mixture of 50:50 concentrated hydrochloric acid and methanol was added carefully to the hot reaction mixture. After the mixture was poured into one liter of water, the orange solid which separated was filtered. Recrystallization from 50% aqueous methanol yielded 40.2 g (61.5%) of 1,3-diacetylphloroglucinol. It had a mp of 168-170° after sublimation.

B. Preparation of 2,4-Diacetyl-3,5-dihydroxy-6,6-dimethyl-2,4-cyclohexadienone(Diacetylfilicinic Acid, 21

A solution of 20 g (0.37 mole) of sodium methoxide and 200 ml of anhydrous methanol was cooled in an ice-water bath. Methyl iodide (40 g, 0.282 mole) was added slowly, followed by 20 g (0.095 mole) of 1,3-diacetylphloroglucinol in one portion. The mixture was allowed to stand with occasional stirring from two to four days at room temperature. The methanol was removed under water vacuum and the residue dissolved in 200 ml of water. After acidification, this mixture was extracted twice with ethyl ether. The ether solution was extracted several times with 50-ml portions of saturated potassium bicarbonate solution until a clear extract was obtained. The sodium bicarbonate solution was

neutralized and allowed to stand until the reddish-brown oil crystallized. After filtration, the reddish-brown solid was triturated with 30 ml of cold benzene and filtered. The filtered solid was identified as recovered starting material by its uv spectrum. The benzene mother liquor was evaporated under water vacuum on a rotary evaporator and the residue recrystallized from methanol. After vacuum distillation (170^0 and 0.5 mm pressure) yields varying from 30% to 60%, based on reacted starting material, were obtained in a series of reactions with about 50% conversion. For example in one reaction 12.3 g of starting material was recovered and 5.7 g (65.5%) of recrystallized and distilled diacetylfilicinic acid was obtained. After sublimation the diacetylfilicinic acid had a melting point of $63-66^0$ (lit. $65-66^0$ (12)).

Infrared spectra: ν_{max}^{KBr} 1560 and 1665 cm^{-1}

$\nu_{max}^{CCl_4}$ 1580 and 1660 cm^{-1}

$\nu_{max}^{CHCl_3}$ 1560 and 1660 cm^{-1}

Ultraviolet spectra: λ_{max}^{EtOH}, acidic, 300 (13,800) and 245 (12,350)

λ_{max}^{EtOH}, basic, 340 (20,600), 275 (11,600) and 220 (15,200).

The nuclear magnetic resonance spectrum is given in Table I.

1. Attempted Preparation of a N-Phenylmaleimide Derivative of Diacetylfilicinic Acid, 21

Diacetylfilicinic acid (1 g, 0.0042 mole) and 0.73 g (0.0042 mole) of N-phenylmaleimide were refluxed in ethyl ether overnight. Only 21 was recovered as identified by its melting point and nmr spectrum.

2. Attempted Acetylation of Diacetylfilicinic Acid, 21

a. Using Acetyl Chloride.- Diacetylfilicinic acid (1 g, 0.0042 mole) and 1 g of acetyl chloride were heated on a steam bath for 15 minutes. After water was added, unchanged 21 crystallized from the solution. The yield of recovered starting material was 0.8 g; it was identified by its melting point.

b. Using Acetic Anhydride.- Acetic anhydride (5 ml) and 0.8 g of diacetylfilicinic acid were mixed in a 4" test tube. After the addition of one drop of concentrated sulfuric acid the mixture was heated on a steam bath, then added to water. Only starting material was isolated, and identified by its melting point and nmr spectrum.

C. Preparation of 3,5-Dihydroxy-4,4-dimethyl-2,5-cyclohexadienone (Filicinic Acid, 19)

Diacetylfilicinic acid (5 g, 0.021 mole) was refluxed for six hours in 120 ml of 2N hydrochloric acid. When most of the oil had dissolved the hot solution was filtered and concentrated to 10-20 ml under a water vacuum on a rotary

evaporator. A solid product crystallized from the solution on standing overnight. The precipitate was filtered and washed with a few ml of ethyl ether, yielding 2.7 g (67%) of filicinic acid (mp 215-217°, after sublimation 220-221°, lit. 212-215° (12)).

Infrared spectrum: ν_{max}^{KBr}, 1630 and 2500-3000 cm^{-1}

Ultraviolet spectra: $\lambda_{max}^{H_2O}$, pH = 11, 348(9340), 250 (18,000) and 231(21,300).

$\lambda_{max}^{H_2O}$, pH = 5-10, 278(20,000)

$\lambda_{max}^{H_2O}$, pH = 1.5-3, 251(14,300)

$\lambda_{max}^{H_2O}$, 10% sulfuric acid, 343(7550) and 243(16,100).

The nuclear magnetic resonance spectrum is given in Table I.

D. Preparation of the Diacetates of Filicinic Acid

One gram (0.0065 mole) of filicinic acid and 6.2 g (0.0608 mole) of acetic anhydride with two drops of pyridine were heated in a test tube on a steam bath for 14 hours. The excess acetic anhydride and acetic acid was removed under water vacuum on a rotary evaporator. The residue was vacuum distilled at 185° and 0.5 mm pressure to give 0.95 g of crude material. One half of this material was recrystallized from carbon tetrachloride and 0.1 g of the monoacetate of filicinic acid, 26, was obtained (mp 142-144°).

Infrared spectrum: $\nu_{max}^{CCl_4}$ 1660 and 1775 cm^{-1}.

The nuclear magnetic resonance spectrum is given in Table I.

After the carbon tetrachloride was evaporated from the mother liquor of the filicinic acid monoacetate, the residue obtained was recrystallized from petroleum ether-ethyl ether to yield 0.1 g of filicinic acid diacetate, 27 (mp 85°, lit. 82-85° (17)).

Infrared spectrum: ν_{max}^{KBr} 1660 and 1775 cm^{-1}.

The nuclear magnetic resonance spectrum is given in Table I.

E. Reaction of Diacetylfilicinic Acid with Diazomethane

A solution of 30 ml of ethyl ether and 12 ml of 30% potassium hydroxide was cooled in an ice-salt bath to less than 5° and 1.5 g N-nitrosomethylurea was added slowly. After this decomposed to form a yellow ethereal solution of diazomethane, the ether layer was decanted into an erlenmeyer flask containing 1 g of diacetylfilicinic acid in 10 ml of ethyl ether. When the evolution of nitrogen ceased and the solution remained yellow the excess ether was evaporated. An nmr spectrum of the residue indicated the presence primarily of the monomethyl derivative of diacetylfilicinic acid. A uv spectrum had absorption bands in neutral 95% ethanol at λ_{max} 320, 278 and 235 mμ and in basic ethanol at λ_{max} 305, 278 and 215 mμ.

When an ether solution of this material was extracted with concentrated aqueous potassium bicarbonate and 10% aqueous sodium carbonate solutions, the product isolated had an nmr spectrum identical to diacetylfilicinic acid.

F. Preparation of Acetylphloroglucinol, 31

1. From Phloroglucinol and Acetonitrile

Anhydrous phloroglucinol (20 g, 0.158 mole) was mixed with 13 g (0.317 mole) of anhydrous acetonitrile, 80 ml of anhydrous ethyl ether and 4 g of anhydrous zinc chloride. The mixture was cooled in an ice-salt bath while hydrogen chloride was passed through for two hours. The mixture was placed in a refrigerator for three days, then filtered and the solid washed twice with 20-ml portions of ethyl ether. The solid was refluxed for 3.5 hr in 1 liter of water, then cooled to give 21.6 g (81.6%) of acetylphloroglucinol (mp 215-218^0, lit. 218-219^0 (18)).

2. From Phloroglucinol and Acetic Anhydride

Phloroglucinol (10 g, 0.079 mole) was added to 8 g (0.079 mole) of acetic anhydride. When 8 drops of concentrated sulfuric acid were added in one portion the temperature rose to 100^0. The mixture was refluxed at 135-140^0 for 2-3 min, then 10 ml of concentrated hydrochloric acid in 30 ml of methanol was carefully added. After the mixture was poured into 400 ml of water, 6.0 g of crude product precipitated (mp 195-208^0). Recrystallization from 50% aqueous methanol yielded 5.5 g (41%) of orange colored crystals. Sublimation gave white crystals of acetylphloroglucinol (mp 213-218^0, lit. 218-219^0 (18))

Infrared spectrum: $\nu_{max}^{CHCl_3}$ 1610, 3200 and 3550 cm^{-1}.

G. Preparation of 2-Acetyl-3,5-dihydroxy-4,6,6-trimethyl-2,4-cyclohexadienone (Acetylmethylfilicinic Acid, 29)

Acetylphloroglucinol (18 g, 0.107 mole) and 17.2 g (0.319 mole) of sodium methoxide in 150 ml of anhydrous methanol was cooled in an ice bath while 91.4 g (0.64 mole) of methyl iodide was added slowly. The mixture was stirred for 5 days at room temperature. The methanol was removed under water vacuum on a rotary evaporator, and the residue dissolved in a mixture of 150 ml of water and 50 ml of ether. After neutralization with hydrochloric acid the aqueous layer was extracted twice with ethyl ether. The ether portions were combined and extracted with eight 30-ml portions of saturated potassium bicarbonate solution. Neutralization gave 9.55 g of a solid material which was washed with 180 ml of cold benzene to yield 8.2 g (36%) of acetylmethylfilicinic acid (mp 157°, lit. 160-161° (15)).

Infrared spectrum: ν_{max}^{KBr} 1600, 1660 and 3300 (broad) cm^{-1}.

Ultraviolet spectra: $\lambda_{max}^{H_2O}$, pH less than 2.5, 240 (9120), 279 (7000) and 335 (12,100).

$\lambda_{max}^{H_2O}$, pH = 4.5 to 10, 350 (18,500), and 222 (16,000).

$\lambda_{max}^{H_2O}$, pH greater than 12, 331 (13,400) and 250 (21,000).

The nuclear magnetic resonance spectrum is given in Table I.

The benzene mother liquor was evaporated and yielded 1.4 g of a material identified as 2-acetyl-3-hydroxy-4,4,6,6-tetramethyl-2-cyclohexen-1,5-dione, 32.

Infrared spectrum: $\nu_{max}^{CHCl_3}$ 1560, 1660, 1710 and 3400 cm^{-1}.

Ultraviolet spectra: $\lambda_{max}^{H_2O}$, acidic, 277(10,700) and 241(8500).

$\lambda_{max}^{H_2O}$, basic, 277(17,400).

The nuclear magnetic resonance spectrum is given in Table I.

This compound was refluxed in 2N hydrochloric acid for 5 hr to give 0.6 g of 3-hydroxy-4,4,6,6-tetramethyl-2-cyclohexen-1,5-dione, 33 (mp 189°, after sublimation 192-193.5°, lit. 187-190° (15)).

Infrared spectrum: ν_{max}^{KBr} 1610, 1700 and 3000 cm^{-1}

Ultraviolet spectra: $\lambda_{max}^{H_2O}$, acidic, 258(16,200).

$\lambda_{max}^{H_2O}$, basic, 279(17,850).

The nuclear magnetic resonance spectrum is given in Table I.

Compound 33 (0.8 g, 0.0036 mole) was mixed with 2 ml of acetic anhydride and 4 drops of pyridine in a small test tube, then heated on a steam bath for 5 min. The mixture was dissolved in ethyl ether and washed with aqueous solutions of saturated potassium bicarbonate and 2N hydrochloric acid. The ether solution was dried with sodium sulfate. Evaporation gave 0.55 g of the acetate derivative (56%).

After sublimation at 50°, 0.5 mm, a white crystalline solid was obtained (mp 54-57°).

Infrared spectrum: $\nu_{max}^{CHCl_3}$ 1660, 1710 and 1770 cm^{-1}.

The nuclear magnetic resonance spectrum is given in Table I.

The original ether layer in the preparation of acetylmethylfilicinic acid was extracted with eight 50-ml portions of 10% aqueous sodium carbonate. Neutralization of the basic solution gave 7.0 g of acetylmethylphloroglucinol, 35 (mp 185-205°, lit. 211° (15)). This material was treated with sodium methoxide and methyl iodide in methanol as before to give, after work-up, an additional 2.6 g of acetylmethylfilicinic acid (mp after sublimation, 158-162°).

H. Preparation of 2,4,4-Trimethyl-3,5-dihydroxy-2,5-cyclohexadienone (Methylfilicinic Acid, 30)

Acetylmethylfilicinic acid, 29 (8.2 g, 0.039 mole) was added to 100 ml of 2N hydrochloric acid. The mixture was refluxed for 5 hrs, filtered while hot and extracted with ethyl ether. After the ethereal layer was dried and evaporated 4.2 g (64%) of crude methylfilicinic acid was obtained. Sublimation afforded a white crystalline material with a mp 174-177° (lit. 180° (15)).

Infrared spectrum: ν_{max}^{KBr} 1650 and 3100 (broad) cm^{-1}.

Ultraviolet spectra: $\lambda_{max}^{H_2O}$, pH greater than 11, 358(10,100), 255(18,800) and 227(20,300).

$\lambda_{max}^{H_2O}$, pH 5-10, 285(13,000).

$\lambda_{max}^{H_2O}$, pH 0.8-3.3, 265 (11,300) and 255 (11,200).

$\lambda_{max}^{H_2O}$, greater than 10% sulfuric acid, 350 (7030), 285 (2580) 248 (8300) and 208 (19,100).

The nuclear magnetic resonance spectrum is given in Table I.

One gram of methylfilicinic acid was dissolved in 5 ml of acetic anhydride and 5 drops of concentrated sulfuric acid. The temperature rose to 70° and the mixture was allowed to stand for 5 min. After the mixture was poured into water and extracted with ethyl ether, the organic layer was washed with water and 10% aqueous sodium carbonate solution. The ether layer was dried and evaporated to give a small amount of residue which, judging by its nmr spectrum (Table II), was the diacetate of methylfilicinic acid, 36.

I. Preparation of 2-Acetyl-3-hydroxy-5-methoxy-4,6,6-trimethyl-2,4-cyclohexadienone, 37.

An ether solution of diazomethane was prepared by adding 2.5 g of N-nitrosomethylurea to a mixture of 15 ml of 30% potassium hydroxide and 30 ml of ethyl ether cooled to below 0° in an ice-salt bath. The yellow diazomethane-ethyl ether solution was decanted into a methanol-ether solution containing 1 g of acetylmethylfilicinic acid. The diazomethane solution was added until the nitrogen evolution ceased. After one hour the excess ether was evaporated.

The residue was found to be the desired monomethyl ether, 37.

Infrared spectrum: $\nu_{max}^{CCl_4}$ 1635 and 1655 cm^{-1}.

Ultraviolet spectra: λ_{max}^{EtOH}, acidic and neutral, 323-340.

λ_{max}^{EtOH}, basic, 285-310.

The nuclear magnetic resonance spectrum is given in Table II.

J. Preparation of 2-Acetyl-3,5-dihydroxy-6,6-dimethyl-2,4-cyclohexadienone (Acetylfilicinic Acid, 22)

1. Standing Eighteen Days at Room Temperature

Diacetylfilicinic acid (10 g, 0.042 mole) was added to 1 liter of methanol and 10 g (0.185 mole) of sodium methoxide. After 18 days at room temperature the methanol was evaporated under water vacuum on a rotary evaporator. The residue was dissolved in water, neutralized with concentrated hydrochloric acid and extracted with ethyl ether. The ether layer was dried with anhydrous sodium sulfate and evaporated. The residue was triturated with carbon tetrachloride and filtered to yield 5.27 g (94% based on reacted starting material) of acetylfilicinic acid (mp 170-172.5°, lit. 174-176° (19)). Evaporation of the carbon tetrachloride yielded 3.23 g of recovered diacetylfilicinic acid.

Infrared spectrum: ν_{max}^{KBr} 1540-80, 1630 and 2600-3000 cm^{-1}.

Ultraviolet spectra: λ_{max}^{EtOH}, acidic, 330(10,100), 271 (9,290), 235(15,500) and 204 (13,200).

λ_{max}^{EtOH}, basic, 345(18,000), 310sh (14,200) and 218(18,600).

The nuclear magnetic resonance spectrum is given in Table II.

2. From Refluxing Methanol and Sodium Methoxide

Diacetylfilicinic acid (2.5 g, 0.0105 mole) was added to 3 g (0.0555 mole) of sodium methoxide in 600 ml of anhydrous methanol. The mixture was refluxed for 18 hrs and worked up as before to give 1.45 g (70%) of acetylfilicinic acid. The product was contaminated with a trace of the completely deacetylated product, filicinic acid, as determined by removal of the acetylfilicinic acid by sublimation at 160-170° and 0.5 mm of mercury. The residual filicinic acid was identified by its mp of 205-215°. Higher base concentrations or longer reaction times increased the amount of filicinic acid produced.

K. Preparation of 2-Acetyl-3-hydroxy-5-methoxy-6,6-dimethyl-2,4-cyclohexadienone (Monomethyl Ether of acetylfilicinic Acid)

An ether solution of diazomethane was prepared by adding 2 g of N-nitrosomethylurea to an ice-cold mixture of 6 ml of 40% aqueous potassium hydroxide and 20 ml of ethyl ether. The diazomethane-ether solution was decanted into

an ether solution of 0.7 g of acetylfilicinic acid. After 20 hrs the ether was evaporated and gave 0.6 g of a substance which was 97% one component as shown by gas liquid phase chromatography. This was identified as the monomethyl ether of acetylfilicinic acid (mp 103°, lit. 107-109° (27)).

Infrared spectrum: $\nu_{max}^{CCl_4}$ 1620 and 1660 cm^{-1}

Ultraviolet spectra: λ_{max}^{EtOH}, acidic, 315 and 235.

λ_{max}^{EtOH}, basic, 305-10, 278(sh) and 235.

The nuclear magnetic resonance spectrum is given in Table II.

L. Preparation of 2,4- and 4,6-Diacetylresorcinols

Resorcinol (11 g, 0.1 mole) was dissolved in 25 g (0.245 mole) of acetic anhydride and 3 ml of concentrated sulfuric acid. The mixture was refluxed for 10 min, then treated with 40 ml of methanol and concentrated hydrochloric acid (2:1). On addition of water, a mixture of the two diacetylresorcinols crystallized out. The solid material was recrystallized from about 30 ml of hot acetone to yield 1.7 g of crude brown crystals (mp 179-181°, lit. 182° (21)) of the 4,6-diacetylresorcinol. A second crop of 1.3 g was obtained from the mother liquor for a total yield of 3.0 g (15.5%). The residue obtained by evaporation of the acetone mother liquor yielded, after fractional sublimation, mainly

2,4-diacetylresorcinol, (1.0 g (5%), mp 87-90°, lit. 92° (21)) as identified by its nuclear magnetic resonance spectrum (Table II).

M. Preparation of 2,4-Diacetyl-5-hydroxy-6,6-dimethyl-2,4-cyclohexadienone, 41

Methyl iodide (7.1 g, 0.05 mole) was dropped into an ice cold solution of sodium methoxide (3.55 g, 0.066 mole) and 30 ml of anhydrous methanol. 4,6-Diacetylresorcinol (2.5 g, 0.05 mole) was added in one portion. After 4 days at room temperature with occasional stirring, the methanol was removed under water vacuum on a rotary evaporator. The residue was dissolved in a mixture of 150 ml of water and 50 ml of ethyl ether, neutralized with concentrated hydrochloric acid and extracted twice with ethyl ether. The ether layer was extracted eight times with 40-ml portions of saturated potassium bicarbonate solution. After evaporation of the ether, 1.15 g of a light yellow material remained, identified as primarily 2-methyl-4,6-diacetylresorcinol by its nuclear magnetic resonance spectrum (Table II).

Neutralization of the potassium bicarbonate fraction yielded 1.15 g (40%) of 2,4-diacetyl-5-hydroxy-6,6-dimethyl-2,4-cyclohexadienone. The compound was recrystallized from ethanol-water, redissolved in base and reprecipitated, and sublimed (mp 134-137°).

Infrared spectrum: ν_{max}^{KBr} 1670 and 1560 cm^{-1}.

Ultraviolet spectra: λ_{max}^{EtOH}, acidic, 320(12,650) and 340(5,930).

λ_{max}^{EtOH}, basic, 400(22,600) and 278(15,900).

The nuclear magnetic resonance spectrum is given in Table II.

Anal. Calcd. for $C_{12}H_{14}O_4$: C, 64.85; H, 6.35.

Found: C, 64.91; H, 6.24.

N. Preparation of 2-Methyl-4,6-diacetylresorcinol, 42

2-Methylresorcinol (5 g, 0.04 mole)(Aldrich Chemical Co.) was added to 8.22 g (0.08 mole) of acetic anhydride and 2 ml of concentrated sulfuric acid. The mixture was refluxed at 140° for 10 min then treated with 30 ml of methanol and concentrated hydrochloric acid (1:1). This mixture was poured into 200 ml of water. After one hour, filtration afforded 5.3 g (63.6%) of a reddish brown solid. Sublimation yielded white crystals of 2-methyl-4,6-diacetylresorcinol (mp 132-133.5°). It was identified by the nuclear magnetic resonance spectrum given in Table II.

O. Preparation of 2,4-Diacetyl-5-hydroxy-6,6-dimethyl-2,4-cyclohexadienone, 41, from 2-Methyl-4,6-diacetylresorcinol

Sodium methoxide (3.22 g, 0.06 mole) and 50 ml of anhydrous methanol were cooled with ice water and stirred as 6.3 g (0.0445 mole) of methyl iodide was added dropwise.

2-Methyl-4,6-diacetylresorcinol (3.1 g, 0.015 mole) was added in one portion. After one week the mixture was worked up as in Experiment II-M. From the saturated potassium bicarbonate fraction 0.65 g (56% based on the reacted starting material) of 2,4-diacetyl-5-hydroxy-6,6-dimethyl-2,4-cyclohexadienone was obtained. This compound was identified by its nuclear magnetic resonance spectrum (Table II) as in Experiment II-M. Evaporation of the ether fraction yielded 2.0 g of recovered 2-methyl-4,6-diacetylresorcinol.

P. Preparation of 4-Acetylresorcinol, 43

Resorcinol (30 g, 0.272 mole), 12 g of anhydrous zinc chloride, 18 g (0.44 mole) of acetonitrile and 150 ml of anhydrous ethyl ether were stirred with a mechanical stirrer as hydrogen chloride was bubbled in for 70 minutes. After 12 hrs the solid material was filtered, washed with ether and refluxed in 500 ml of water for 2.5 hrs. 4-Acetylresorcinol (17 g, 41%) precipitated from the aqueous solution after several hours (mp 145°, lit. 147° (18)). It was identified by its nuclear magnetic resonance spectrum, given in Table II.

Q. Preparation of 4-Acetyl-5-hydroxy-6,6-dimethyl-2,4-cyclohexadienone, 44

1. From 2,4-Diacetyl-5-hydroxy-6,6-dimethyl-2,4-cyclohexadienone, 41

2,4-Diacetyl-5-hydroxy-6,6-dimethyl-2,4-cyclohexadienone

(1 g, 0.0045 mole), 3 ml of methanol and 30 ml of 2N hydrochloric acid were refluxed for 3.5 hrs. Starting material (0.2 g) crystallized on cooling the aqueous phase. Extraction of the water with ethyl ether resulted in a small amount of crude oily material identified as 4-acetyl-5-hydroxy-6,6-dimethyl-2,4-cyclohexadienone.

Infrared spectrum: ν_{max}^{Neat} 1660 and 1605 cm^{-1}

The nuclear magnetic resonance spectrum is given in Table II.

2. By Methylation of 4-Acetylresorcinol

To an ice-cold solution of 23 g (0.425 mole) of sodium methoxide and 120 ml of anhydrous methanol was added 61 g (0.43 mole) of methyl iodide. 4-Acetylresorcinol (16.2 g, 0.108 mole) was added in one portion. After three days at room temperature the methanol was evaporated under water vacuum on a rotary evaporator. The residue was dissolved in a mixture of 150 ml of water and 50 ml of ethyl ether, neutralized with concentrated hydrochloric acid, and extracted twice with ethyl ether. The ether fraction was extracted twice with 40-ml portions of saturated potassium bicarbonate solution. Neutralization and extraction with ether gave 0.25 g (1.3%) of a crude oil which was identified as 4-acetyl-5-hydroxy-6,6-dimethyl-2,4-cyclohexadienone, 44, by its nmr (Table II) and ir spectra.

The ether layer was extracted 8 times with 50-ml portions of 10% sodium carbonate solution. Neutralization

yielded 4.0 g of a material identified as 2-methyl-4-acetylresorcinol. It was recrystallized from carbon tetrachloride, and a sublimed sample gave a mp of 151-155° (lit. 156-7° (22)).

Infrared spectrum: $\nu_{max}^{CHCl_3}$ 1620, 3000 and 3300 cm^{-1}.

The nuclear magnetic resonance spectrum is given in Table II.

R. Attempted Methylation of 2,4-Diacetylresorcinol

A solution of 3.55 g (0.06 mole) of sodium methoxide and 50 ml of methanol was cooled in an ice bath as 7.1 g (0.05 mole) of methyl iodide was added. 2,4-Diacetylresorcinol (2.5 g, 0.013 mole) was added in one portion and the mixture stirred for 3 days at room temperature. The methanol was removed under water vacuum on a rotary evaporator. The residue was dissolved in water, neutralized with concentrated hydrochloric acid and extracted twice with ethyl ether. Two grams of starting material were recovered.

III. Photolyses and Photo-oxidations

A. The Photolysis and Photo-oxidation of 2,4-Diacetyl-3,5-dihydroxy-6,6-dimethyl-2,4-cyclohexadienone (Diacetylfilicinic Acid, 21)

1. The Photolysis of Diacetylfilicinic Acid in Ethyl Ether

Fifteen milligrams of diacetylfilicinic acid and 6 ml of anhydrous ethyl ether were placed in a small quartz test

tube. After one day of irradiation through Pyrex with a Hanovia L 450 watt lamp, a uv spectrum of a sample indicated only the presence of starting material. After irradiation for 52 hours with a Hanovia S 200 watt lamp a uv spectrum denoted only starting material.

2. Photolysis of Diacetylfilicinic Acid in Methanol under a Nitrogen Atmosphere

a. Small Scale.- A solution of 30 mg of diacetylfilicinic acid in 8 ml of methanol was placed in a small Pyrex test tube. Nitrogen was passed through for a few minutes and the test tube sealed with a rubber serum cap. The mixture was irradiated for 44 hours with a Hanovia L 450 watt lamp. A uv spectrum of a sample indicated no change in the reaction solution.

b. Large Scale.- The above reaction was repeated using 1 g of diacetylfilicinic acid and 1 g of sodium methoxide in 700 ml of methanol. The solution was irradiated through Pyrex for 24 hours with a Hanovia L 450 watt lamp, under nitrogen. The methanol was evaporated and the residue was dissolved in water, neutralized with hydrochloric acid and extracted with ether. On evaporation of the ether the residue had identical ir and uv spectra to those of diacetylfilicinic acid. There was no indication in the ir spectrum of the presence of 2-acetyl-3,5-dihydroxy-6,6-dimethyl-2,4-cyclohexadienone (acetylfilicinic acid, 22).

3. Photolysis of Diacetylfilicinic Acid in Methanol with an Oxygen Atmosphere

A solution of 30 mg of diacetylfilicinic acid in 8 ml of methanol was irradiated for 44 hours with a Hanovia L 450 watt lamp, under oxygen. A uv spectrum of a sample indicated no change in composition of the reaction solution.

4. Photolysis of Diacetylfilicinic Acid in Alkaline Methanol, Using a Nitrogen Atmosphere

One gram of diacetylfilicinic acid, 1 g of sodium methoxide and 700 ml of methanol were placed in a 700-ml photolysis well. The solution was irradiated for 46 hrs with a Hanovia L 450 watt lamp using a Pyrex filter and under nitrogen. A uv spectrum of a sample indicated only the presence of starting material.

Oxygen was passed through the solution for 30 min. The photolysis was continued by irradiation through Pyrex for 13 hours with a Hanovia S 200 watt lamp and 12 hours with a Hanovia L 450 watt lamp. A uv spectrum indicated the loss of the uv absorption band at λ 340 mμ and the appearance of two absorption bands at λ 272 and 250 mμ. Work-up of the reaction as outlined in the next experiment afforded 2-acetyl-3,4-dihydroxy-4-carbomethoxy-5,5-dimethyl-2-cyclopentenone, 67, as identified by ir and nmr spectra.

5. Photolysis of Diacetylfilicinic Acid in Alkaline Methanol, Air Atmosphere

Diacetylfilicinic acid (5 g, 0.021 mole), 5 g(0.093 mole) of sodium methoxide and 700 ml of anhydrous methanol

were irradiated through Pyrex with a Hanovia L 450 watt lamp for 24 hours, under air. The methanol was removed under water vacuum in a rotary evaporator and the residue dissolved in water. The aqueous mixture was neutralized, extracted twice with ethyl ether and the ether evaporated. The residue was recrystallized from cyclohexane-ethyl ether to give 3.47 g (68%) of 2-acetyl-3,4-dihydroxy-4-carbomethoxy-5,5-dimethyl-2-cyclopentenone, 67. A mp of 77.5-79° was obtained after two sublimations.

Infrared spectrum (Ir Spectrum 1): ν_{max}^{KBr} 1560, 1640, 1705, 1740 and 3450 cm^{-1}.

Ultraviolet spectra: λ_{max}^{EtOH}, acidic, 273(9,800) and 225(9,960).

λ_{max}^{EtOH}, basic, 271(15,700), 250 (18,600) and 207(11,350).

The nuclear magnetic resonance spectrum is given in Table II and Nmr Spectrum 1.

Anal. Calcd. for $C_{11}H_{14}O_6$: C, 54.54; H, 5.83.

Found: C, 54.56; H, 5.76.

A mass spectrum indicated a parent mass of m/e 242.

6. Photolysis of Diacetylfilicinic Acid in Alkaline Ethanol (95%) with an Air Atmosphere

The previous reaction was repeated with 2 g (0.0084 mole) of diacetylfilicinic acid and 2 g (0.037 mole) of sodium methoxide in 700 ml of 95% ethanol. The mixture was irradiated through Pyrex for 22 hrs with a Hanovia L

450 watt lamp under air. Work-up in a manner similar to that used in the previous experiment resulted in 1.1 g (51%) of 2-acetyl-3,4-dihydroxy-4-carboethoxy-5,5-dimethyl-2-cyclopentenone, 69 (mp 80-81° after sublimation).

Infrared spectrum: $\nu_{max}^{CCl_4}$ 1600, 1640, 1715, 1740 and 3600 cm^{-1}. (Ir Spectrum 3)

Ultraviolet spectra: λ_{max}^{EtOH}, acidic, 273(10,600) and 223(11,000).

λ_{max}^{EtOH}, basic, 272(17,000) and 250(20,600).

The nuclear magnetic resonance spectrum is given in Table III, and Nmr Spectrum 2.

Anal. Calcd. for $C_{12}H_{16}O_6$: C, 56.24; H, 6.29.

Found: C, 55.94; H, 6.23.

7. Photolysis of Diacetylfilicinic Acid in Water with an Air Atmosphere

Experiment III A5 was repeated with 1 g (0.0042 mole) of diacetylfilicinic acid, 1 g (0.0186 mole) of sodium methoxide and 700 ml of water. The solution was irradiated through Pyrex with a Hanovia L 450 watt lamp, under air. The reaction mixture was worked up as in previous experiments. Trituration of the ether residue with carbon tetrachloride gave 0.67 g (12%) of dimethylmalonic acid (mp 188-189°, lit. 186° (47), 192-193° (48)) as the only isolated product. Its ir spectrum was identical to that of dimethylmalonic acid (47).

The nuclear magnetic resonance spectrum is given in Table III.

8. Dark Reaction of Diacetylfilicinic Acid in Alkaline Methanol in an Air Atmosphere

A solution of 1 g of diacetylfilicinic acid, 1 g of sodium methoxide and 700 ml of anhydrous methanol were placed in a 700-ml photolysis well, wrapped in aluminum foil and stored in the dark under air. After 6 days a uv spectrum indicated little change, and that no photo-oxidation products had formed. Work-up yielded 0.5 g (61%) of acetylfilicinic acid (mp 174-176°, lit. 177-178° (20)).

B. Preparation of 2-Acetyl-3,4-dihydroxy-5,5-dimethyl-2-cyclopentenone, 70.

1. With 2N Sodium Hydroxide

2-Acetyl-3,4-dihydroxy-4-carbomethoxy-5,5-dimethyl-2-cyclopentenone (1 g, 0.0041 mole) in 50 ml of 2N sodium hydroxide was heated on a steam bath for 16 hrs. The mixture was neutralized with concentrated hydrochloric acid and extracted twice with ethyl ether. Evaporation of the ether and recrystallization of the residue from carbon tetrachloride gave 0.6 g (79%) of 2-acetyl-3,4-dihydroxy-5,5-dimethyl-2-cyclopentenone (mp 96-97°, and after sublimation 104-105°, lit. 104-106° (29)).

Infrared Spectrum: ν_{max}^{KBr} 1570, 1630, 1705 and 3500 cm^{-1}.

Ultraviolet spectra: λ_{max}^{EtOH}, acidic, 264(10,500), and 223(13,250).

λ_{max}^{EtOH}, basic, 269(19,200), 249 (21,700) and 205(14,400).

The nuclear magnetic resonance spectrum is given in Table III (Nmr Spectrum 3).

Anal. Calcd. for $C_9H_{12}O_4$: C, 58.69; H, 6.57.
Found: C, 58.77; H, 6.44.

2. With 2N Hydrochloric Acid

A solution of 0.5 g of 2-acetyl-3,4-dihydroxy-4-carbomethoxy-5,5-dimethyl-2-cyclopentenone in 50 ml of 2N hydrochloric acid was refluxed for 3 hrs, then extracted with ethyl ether. The ether solution was evaporated and the residue fractionally sublimed. The first fraction contained both 2-acetyl-3,4-dihydroxy-5,5-dimethyl-2-cyclopentenone, 70, and starting material. The second fraction had a mp of 98° and an ir spectrum (KBr) identical to that of authentic 72.

3. With Sodium Methoxide

A solution of 0.5 g of 2-acetyl-3,4-dihydroxy-4-carbomethoxy-5,5-dimethyl-2-cyclopentenone and 2 g of sodium methoxide in 100 ml of methanol was refluxed for 12 hrs. The methanol was removed under water vacuum on a rotary evaporator and the residue dissolved in water. Neutralization and extraction with ethyl ether afforded on evaporation a compound (mp 96-101°) with an ir spectrum ($CHCl_3$)

similar to that of 2-acetyl-3,4-dihydroxy-5,5-dimethyl-2-cyclopentenone.

4. From 2-Acetyl-3,4-dihydroxy-4-carboethoxy-5,5-dimethyl-2-cyclopentenone and 2N Sodium Hydroxide

2-Acetyl-3,4-dihydroxy-4-carboethoxy-5,5-dimethyl-2-cyclopentenone (0.2 g) in 40 ml of 2N sodium hydroxide was heated on a steam bath for 20 hrs. The reaction mixture was neutralized and worked up as in the previous experiments. An ir spectrum of the residue indicated only the presence of 72.

C. Preparation of 2-Acetyl-3-hydroxy-4-keto-5,5-dimethyl--2-cyclopentenone, 71

1. Oxidation of 2-Acetyl-3,4-dihydroxy-5,5-dimethyl-2-cyclopentenone with Manganese Dioxide

A mixture of 2.0 g of activated manganese dioxide and 0.4 g (0.00217 mole) of 2-acetyl-3,4-dihydroxy-5,5-dimethyl-2-cyclopentenone in 15 ml of chloroform were stirred for 45 min. The mixture was filtered and the chloroform evaporated to give starting material. The filtered residue was washed with 50 ml of hot methanol. The methanol was evaporated and the residue recrystallized from petroleum ether. A small amount of yellow solid formed. A fractional sublimation yielded starting material, 72 (mp 99-101°) and an impure yellow crystalline solid.

The manganese dioxide residue was rewashed with 200 ml of hot methanol. The methanol was evaporated and the

residue sublimed resulting in 30 mg (7.6%) of a compound (mp 82-86°, lit. 87° (28)) which had a uv spectrum identical to that reported for 2-acetyl-3-hydroxy-4-keto-5,5-dimethyl-2-cyclopentenone, 71 (28).

Ultraviolet spectra: λ_{max}^{EtOH}, acidic, 282(7,150).

λ_{max}^{EtOH}, basic, 323(7,880) and 252(11,100).

2. Oxidation of 2-Acetyl-3,4-dihydroxy-5,5-dimethyl-2-cyclopentenone with Bismuth Oxide

A mixture of 90 mg of 2-acetyl-3,4-dihydroxy-5,5-dimethyl-2-cyclopentenone, 180 mg of bismuth oxide and 10 ml of glacial acetic acid were refluxed for 24 hrs. The acetic acid was evaporated under water vacuum on a rotary evaporator and a small amount of dilute hydrochloric acid was added to the residue. The aqueous mixture was extracted with ethyl ether and the ether layer separated, dried and evaporated. Fractional sublimation yielded 2 mg of 71 (mp 87-88°).

D. Dye-sensitized Photo-oxidations

1. Standard Reactions Without Dye

a. In a Pyrex Photolysis Well.- Diacetylfilicinic acid (0.5 g), 0.5 g of sodium methoxide and 190 ml of methanol were irradiated with a 200 watt tungsten lamp under air, while cold water circulated through the inner well

jacket. After 18 hrs 92% of the starting material remained, as indicated by the difference in the uv spectra of aliquots at the beginning and the end of the reaction.

b. In a 250-ml 3-necked Flask.- Diacetylfilicinic acid (0.25 g, 0.00105 mole), 0.5 g (0.0093 mole) of sodium methoxide and 200 ml of methanol were placed in a 250-ml 3-necked flask equipped with a reflux condenser, a gas inlet tube and covered with aluminum foil. After one day of irradiation with a 200 watt tungsten lamp, under air, 90% of the starting material had reacted. A uv spectrum indicated that a compound with a uv spectrum identical to that of 2-acetyl-3,4-dihydroxy-4-carbomethoxy-5,5-dimethyl-2-cyclopentenone, 67, was formed in 75% yield. The methanol was evaporated, the residue dissolved in water, neutralized with hydrochloric acid and extracted with ethyl ether. Evaporation of the ether yielded 0.16 g of a yellow solid. A compound with an ir spectrum identical to that of 2-acetyl-3,4-dihydroxy-5,5-dimethyl-2-cyclopentenone, 70, was obtained after sublimation.

2. Dye-sensitized Photo-oxidations of Diacetylfilicinic Acid

a. With Fluorescein.- Fluorescein (0.120 g) was added to the solution of Experiment III D 1a which contained 92% unreacted diacetylfilicinic acid. The solution was irradiated with a 200 watt tungsten lamp, under air. After 22 hrs 83% of the diacetylfilicinic acid had reacted as

indicated by a uv spectrum. The reaction was worked up by evaporation of the methanol, addition of water to the residue, followed by neutralization and extraction with ethyl ether. The residue from the ether layer had uv absorption bands at 250 and 271 mμ in basic ethanol solution which was characteristic of 2-acetyl-3,4-dihydroxy-4-carbomethoxy-2-cyclopentenone, 67. Its ir spectrum had absorption bands at 1600, 1640, 1710 and 1740 cm^{-1} similar to the ir spectrum of 67, but also showed a band at 1660 cm^{-1} due to the dye and/or the starting diacetylfilicinic acid.

b. With Methylene Blue.- A solution of 0.5 g of diacetylfilicinic acid, 0.5 g of sodium methoxide and 0.20 g of methylene blue in 190 ml of methanol was irradiated with a 200 watt tungsten lamp, under air. After two hours 60% of the starting material had reacted, and also 70% of the methylene blue. Irradiation for an additional 2.75 hrs resulted in complete reaction of the methylene blue and no increase in the photo-oxidation of the diacetylfilicinic acid. The reaction was worked up as in the previous experiment. The residue had ir and uv spectra similar to a 60:40 mixture of 1-acetyl-3,4-dihydroxy-4-carbomethoxy-5,5-dimethyl-2-cyclopentenone, 67, and diacetylfilicinic acid.

c. With Rose Bengal.- A solution of 0.5 g (0.0021 mole) of diacetylfilicinic acid, 0.5 g (0.0093 mole) of sodium methoxide, 0.030 g of Rose Bengal and 200 ml of methanol was irradiated for 3.3 hrs with a 200 watt tungsten

lamp, under air. The reaction was followed by uv spectra which indicated a 98.8% yield of 2-acetyl-3,4-dihydroxy-4-carbomethoxy-5,5-dimethyl-2-cyclopentenone. The methanol was evaporated under water vacuum on a rotary evaporator, the residue dissolved in water, neutralized with acid and extracted with ethyl ether. The ethyl ether was evaporated and the residue recrystallized from cyclohexane-ethyl ether to give 0.375 g (73.8%) of 2-acetyl-3,4-dihydroxy-4-carbomethoxy-5,5-dimethyl-2-cyclopentenone. This was identified by its ir spectrum.

E. Reaction of Diacetylfilicinic Acid with Singlet Oxygen Prepared from 9,10-Diphenylanthracene Peroxide

1. Standard Experiment

A solution of 0.33 g of 9,10-diphenylanthracene in 190 ml of ethyl ether was irradiated for 0.5 hr with a Hanovia L 450 watt lamp, under air. The photo-oxidation was followed by observing the decrease in uv absorption bands of diphenylanthracene at λ 350-400 and 258 mμ, and the increase in intensity of the uv absorption band at λ 210 mμ due to the diphenylanthracene peroxide. The ether solution was concentrated to 10 ml and added to 0.075 g of diacetylfilicinic acid in 40 ml of methanol. The reaction mixture was refluxed for 4 hrs in the dark. There was no change in a uv spectrum of an aliquot which indicated no change in the composition of the reaction mixture. Sodium methoxide (0.2 g) was added and after 0.5 hr reflux 78% of

the diacetylfilicinic acid had reacted to give 2-acetyl-3,4-dihydroxy-4-carbomethoxy-5,5-dimethyl-2-cyclopentenone, 67, as identified by a uv spectrum.

2. Preparation of 2-Acetyl-3,4-dihydroxy-4-carbomethoxy-5,5-dimethyl-2-cyclopentenone from the Peroxide of 9,10-Diphenylanthracene

A solution of 0.5 g of 9,10-diphenylanthracene in 190 ml of ethyl ether was irradiated with a Hanovia L 450 watt lamp for 2.5 hrs, under air. The reaction was followed by observing the decrease in intensity of the uv absorption bands of diphenylanthracene at λ 350-400 mμ. The ether was concentrated to 10 ml and added to a solution of 40 ml of methanol, 0.075 g of diacetylfilicinic acid and 0.150 g of sodium methoxide. The uv absorption band at λ 340 mμ for the diacetylfilicinic acid monoanion disappeared after 1.75 hrs reflux. Subtraction of the uv absorption bands for diphenylanthracene and its peroxide from a uv spectrum of the reaction solution resulted in bands at λ 250 and 270 mμ characteristic of the photo-oxidation product, 2-acetyl-3,4-dihydroxy-4-carbomethoxy-5,5-dimethyl-2-cyclopentenone, 67. The methanol was removed under water vacuum on a rotary evaporator and the residue dissolved in water. The solution was neutralized with acid and extracted with ethyl ether. Evaporation of the ether yielded 0.0564 g (74%) of 67. It was identified by its ir and uv spectra.

F. Preparation of Methyl Ethers of the Photo-oxidation Products

In all cases diazomethane was prepared by the addition of N-nitrosomethylurea to an ice cold 30-40% aqueous potassium hydroxide and ethyl ether mixture. When the N-nitrosomethylurea had completely decomposed, the yellow diazomethane-ethyl ether phase was decanted into an ice cold ether solution of each compound. At least 70% conversion of the N-nitrosomethylurea was assumed in all cases and an excess of the N-nitrosomethylurea beyond this was used.

1. Reaction of 2-Acetyl-3,4-dihydroxy-4-carbomethoxy-5,5-dimethyl-2-cyclopentenone with Diazomethane

An excess of diazomethane in ether was prepared from 2.5 g of N-nitrosomethylurea and 10 ml of 30% potassium hydroxide. The ether layer was decanted into 10 ml of ether containing 1 g of 2-acetyl-3,4-dihydroxy-4-carbomethoxy-5,5-dimethyl-2-cyclopentenone, 67. After one hour the ether and excess diazomethane was evaporated. Vpc analysis indicated a 67% yield of equal concentrations of two methyl ethers, 2-acetyl-3-methoxy-4-hydroxy-4-carbomethoxy-5,5-dimethyl-2-cyclopentenone, 81, and 2-acetyl-3-methoxy-4,4-dimethyl-5-hydroxy-5-carbomethoxy-2-cyclopentenone, 82, identified by a nmr spectrum (Table III).

Infrared spectrum: $\nu_{max}^{CCl_4}$ 1600, 1675, 1700, 1735 and 3550 cm^{-1}.

Ultraviolet Spectrum: λ_{max}^{EtOH} 250 mμ.

An ether solution of 81 and 82 was extracted with a saturated potassium bicarbonate solution. Neutralization and ether extraction of the aqueous phase resulted in recovered 67 as identified by ir and uv spectra.

2. Reaction of 2-Acetyl-3,4-dihydroxy-4-carboethoxy-5,5-dimethyl-2-cyclopentenone with Diazomethane

Diazomethane was prepared by the addition of 1.3 g of N-nitrosomethylurea to an ice cold mixture of 5 ml of 30% aqueous potassium hydroxide and 10 ml of ethyl ether. The yellow diazomethane-ethyl ether solution was decanted into an ether solution of 0.5 g of 2-acetyl-3,4-dihydroxy-4-carboethoxy-5,5-dimethyl-2-cyclopentenone, 69. The ether solution was evaporated after one hour. An nmr spectrum of the residue indicated the presence of two methyl ethers which were assigned the structures 2-acetyl-3-methoxy-4-hydroxy-4-carboethoxy-5,5-dimethyl-2-cyclopentenone, 83, and 2-acetyl-3-methoxy-4,4-dimethyl-5-carboethoxy-5-hydroxy-2-cyclopentenone, 84, in a 1:2 ratio. The mixture had a uv absorption band at λ_{max}^{EtOH} 250 mμ. The nuclear magnetic resonance spectrum is given in Table III.

The mixture of the two methyl ethers was dissolved in 20 ml of 2N sodium hydroxide, then neutralized immediately with concentrated hydrochloric acid. Extraction with ethyl ether and evaporation of the ether layer gave only 69 as identified by its ir spectrum.

G. Reaction of 2-Acetyl-3,4-dihydroxy-5,5-dimethyl-2-cyclopentenone with Sodium Borohydride

2-Acetyl-3,4-dihydroxy-5,5-dimethyl-2-cyclopentenone, 70 (0.3 g, 0.0016 mole), 0.6 g (0.016 mole) of sodium borohydride and 30 ml of 95% ethanol were stirred for 1.75 hrs. The uv absorption bands of a sample changed to λ 248 mμ in acidic ethanol and λ 276 mμ in basic ethanol, from those of 70 which had uv absorption bands at λ 270 and 250 mμ in basic ethanol and λ 264 and 223 mμ in acidic media.

Dilute hydrochloric acid was added to the reaction mixture and the aqueous mixture was extracted with ether. The ether layer was evaporated and an ir spectrum of the residue had absorption bands at ν 1710, and 1640 cm^{-1}, indicating that the acetyl carbonyl group of 70 may have been reduced.

H. Photolysis and Photo-oxidation of 2-Acetyl-3,5-dihydroxy-6,6-dimethyl-2,4-cyclohexadienone (Acetylfilicinic Acid, 22)

1. Photo-oxidation of Acetylfilicinic Acid in Alkaline Methanol with an Air Atmosphere

Acetylfilicinic acid (0.35 g, 0.0018 mole) and 0.35 g (0.0065 mole) of sodium methoxide in 400 ml of methanol were irradiated through Pyrex with a Hanovia L 450 watt lamp for two hours, under air. The methanol was evaporated under water vacuum on a rotary evaporator. The residue was dissolved in water, neutralized and extracted with ether. Evaporation of the ether gave a residue which contained 50%

of 2-acetyl-3,4-dihydroxy-4-carbomethoxy-5,5-dimethyl-2-cyclopentenone, 67, and 50% 2-acetyl-3,4-dihydroxy-5,5-dimethyl-2-cyclopentenone, 70, as determined by an nmr spectrum. The mixture was recrystallized from hexane-ethyl ether to give 0.062 g (14%) of 67 as identified by an ir spectrum.

The reaction was repeated with 0.25 g of 22, 0.5 g of sodium methoxide in 200 ml of methanol. The result was 0.1772 g of material which contained 51 mole % of 67 and 36 mole % 70 as determined by integrating the area under the peaks assigned to the gem dimethyl groups in the nmr spectrum.

2. Photolysis of Acetylfilicinic Acid with one Equivalent of Sodium Methoxide and an Air Atmosphere

A solution of 0.25 g (0.00127 mole) of acetylfilicinic acid, 22, and 69 mg (0.00127 mole) of sodium methoxide in 200 ml of methanol was irradiated through Pyrex with a Hanovia L 450 watt lamp for 3 hrs, under air. The reaction was worked up as in the previous experiment. Carbon tetrachloride was added to the ether residue and 45 mg (mp 179-181°) of an unknown compound precipitated.

Infrared spectrum: (ν_{max}^{KBr} 1580(broad), 1670, 1755 and 3000-3500(broad) cm^{-1} (Ir Spectrum 4)

Ultraviolet spectra: λ_{max}^{EtOH}, acidic, 273(9,130) and 220(7,060).

λ_{max}^{EtOH}, basic, 265(15,700), 250 (15,700)and 207(13,200)

The nuclear magnetic resonance spectrum is given in Table III (Nmr Spectrum 4).

Anal. Calcd. for $C_{11}H_{14}O_7$: C, 51.16; H, 5.47.
Found: C, 50.85; H, 5.42.

The residue from evaporation of the carbon tetrachloride was primarily 2-acetyl-3,4-dihydroxy-4-carbomethoxy-5,5-dimethyl-2-cyclopentenone, 67, plus a small amount of the unknown compound as indicated by an ir spectrum. The residue had ir absorption bands at $\nu_{max}^{CCl_4}$ 1600, 1640, 1710, and 1740 cm^{-1}. The band at 1740 cm^{-1} was slightly larger than the others, due to the presence of the unknown compound which has an ir absorption band at 1755 cm^{-1}.

3. Photolysis of Acetylfilicinic Acid

a. In Ethyl Ether Under a Nitrogen Atmosphere.- A solution of 0.67 g (0.0034 mole) of acetylfilicinic acid in 190 ml of anhydrous ethyl ether was irradiated through Pyrex for 48 hrs with a Hanovia S 200 watt lamp, under nitrogen. The ethyl ether was evaporated and yielded 3-acetyl-4-hydroxy-6-i-propyl-2H-pyran-2-one, 90 (83% as measured by vpc). On sublimation of a collected sample a white crystalline compound was obtained (mp 54-55°).

Infrared spectra: ν_{max}^{KBr} 1555, 1635, 1700 and 1730 cm^{-1} (Ir Spectrum 5a)

$\nu_{max}^{CCl_4}$ 1575(small), 1610(sh), 1635,

1710(sh), and 1725 cm^{-1}

(Ir Spectrum 5b)

Ultraviolet spectra: λ_{max}^{EtOH}, acidic, 309(13,200), 223 (11,300) and 203(8,300).

λ_{max}^{EtOH}, basic, 291(11,200), 229 (20,200) and 204(26,900).

The nuclear magnetic resonance spectrum is given in Table III (Nmr Spectrum 5).

Anal. Calcd. for $C_{10}H_{12}O_4$: C, 61.21; H, 6.17.

Found: C, 60.92; H, 6.28.

b. In Methanol under a Nitrogen Atmosphere.- Acetylfilicinic acid, 22, (2.0 g, 0.01 mole) in 700 ml of methanol was irradiated through Pyrex for 32 hrs with a Hanovia L 450 watt lamp, under nitrogen. The methanol was evaporated and distillation of the residue (110^0, 1 mm) gave 0.66 g (33%) of 3-acetyl-4-hydroxy-6-i-propyl-2H-pyran-2-one, 90 (mp $54.5-55^0$) as identified by an ir spectrum.

A dark reaction of about the same concentration (15 mg of 22 in 3 ml of methanol) underwent no change on standing for 10 days.

An attempt was made to make a Diels-Alder adduct with 0.2 g of 89 and 0.1 g of maleic anhydride in 30 ml of anhydrous ethyl ether. The solution was refluxed for two days but there was no change in the uv spectrum of a sample of the reaction mixture.

I. Photolysis of 2-Acetyl-3-hydroxy-5-methoxy-6,6-dimethyl-2,4-cyclohexadienone

1. In Ethyl Ether

2-Acetyl-3-hydroxy-5-methoxy-6,6-dimethyl-2,4-cyclohexadienone, 38 (15 mg) was dissolved in 2-3 ml of ethyl ether in a small Pyrex test tube. The tube was sealed with a serum cap and the solution irradiated with a Hanovia L 450 watt lamp for 45 hrs. A uv absorption spectrum of a sample of the reaction solution showed no change.

2. In Alkaline Methanol with an Air Atmosphere

Air was passed through a solution of 15 mg of 38, and 15 mg of sodium methoxide in 2-3 ml of methanol. The tube was sealed with a serum cap and irradiated through Pyrex with a Hanovia L 450 watt lamp for 45 hrs. A uv absorption spectrum of a small amount of the solution indicated no change.

J. Miscellaneous Photolysis Reactions

1. Attempted Photolysis of 3-Acetyl-4-hydroxy-6-i-propyl-2H-pyran-2-one.

3-Acetyl-4-hydroxy-6-i-propyl-2H-pyran-2-one, 90 (15 mg), 15 mg of sodium methoxide and 2.5-3 ml of methanol were placed in a Pyrex test tube. The tube was sealed with a rubber serum cap and the solution irradiated for 48 hrs with a Hanovia L 450 watt lamp, under air. A uv spectrum detected no change.

2. Attempted Photolysis of 2-Acetyl-3,4-dihydroxy-5,5-dimethyl-2-cyclopentenone

a. In Methanol.- 2-Acetyl-3,4-dihydroxy-5,5-dimethyl-2-cyclopentenone, 70 (15 mg) and 2.5-3 ml of methanol were irradiated through Pyrex with a Hanovia L 450 watt lamp for 22 hrs. Only 70 was recovered as indicated by an ir spectrum of the residue obtained on evaporation of the methanol.

b. In Alkaline Methanol under an Air Atmosphere.- The above reaction was repeated with 15 mg of sodium methoxide also present. The tube was sealed with a serum cap and the solution irradiated with a Hanovia L 450 watt lamp for 22 hrs, under air. This produced no reaction as indicated by an ir spectrum after work-up.

c. In Alkaline Water under an Air Atmosphere.- A solution of 0.5 g of 70, and 1.0 g of sodium methoxide in 600 ml of water were irradiated through Pyrex with a Hanovia L 450 watt lamp, under air. A uv spectrum of an aliquot indicated no change after 19 hrs.

3. Photolysis of 2-Acetyl-3,4-dihydroxy-4-carbomethoxy-5,5-dimethyl-2-cyclopentenone

A solution of 2-acetyl-3,4-dihydroxy-4-carbomethoxy-5,5-dimethyl-2-cyclopentenone, 67 (0.5 g) and 0.5 g of sodium methoxide in 500 ml of water was irradiated through Pyrex with a Hanovia L 450 watt lamp, under air, for 16 hrs.

A uv spectrum of an aliquot indicated no change. The mixture was worked up by evaporation of the methanol, addition of water, neutralization with acid and extraction with ethyl ether. The residue obtained on evaporation of the ethyl ether layer had an ir spectrum identical to that of the starting material, 67.

IV. Kinetic Reactions on the Photo-oxidation of Diacetylfilicinic Acid, 21, and Acetylfilicinic Acid, 22

A. Series 1

This series of reactions was carried out under a single set of conditions. Diacetylfilicinic acid (0.5 g, 0.00191 mole, 0.01050 molar) in 190 ml of methanol was used unless otherwise stated. A Hanovia L 450 watt lamp was used to irradiate the solutions through Pyrex for the indicated length of time. Reactions were carried out under air in all cases except one reaction in which oxygen was used. The reactions were monitored by uv spectral analysis as outlined in the General Procedure. The results were plotted graphically and are presented in the Results and Discussion.

1. Photo-oxidation with Sodium Methoxide (0.00930 mole)

Time(hr)	21 (%)
0	100
1	83.6
2	49.6
3	28.3

2. Photo-oxidation with Sodium Methoxide(0.037 mole)

Time(hr)	21 (%)
0	100
1	70.7
2	37.1
2.5	23.5

3. Photo-oxidation with Sodium Methoxide(0.074 mole)

Time(hr)	21 (%)
0	100
0.5	78.3
1	58.6
1.5	42.4
2	27.8
2.5	16.4

4. Photo-oxidation with Sodium Methoxide (0.0093 mole), Under Oxygen

This reaction was carried out to test the effect of oxygen concentration on the reaction rate.

Time(hr)	21 (%)
0	100
0.5	91.7
1	79.2
1.5	64.8
2.5	34.1
3.5	10.2

5. Photo-oxidation with Sodium Methoxide (0.0093 mole); Solution Saturated with Air Before Irradiation

This reaction was carried out to test the effect of

saturation of the methanol solution with air for three hours before irradiation.

Time(hr)	21 (%)
0	100
0.5	96.6
1	87.9
1.5	74.4
2	58.7
3	35.1
4	14.8
4.5	8.1

6. Photo-oxidation with Sodium Methoxide (0.0093 mole) and Diacetylfilicinic Acid (0.000497 mole)

Time(hr)	21 (%)
0	100
0.5	93.6
1	78.8
1.5	58.2
2	41.2
2.5	25.9
3	15.6

7. Photo-oxidation with Sodium Methoxide (0.0093 mole) and Acetylfilicinic Acid (0.00255 mole)

Time(hr)	22 (%)
0	100
0.5	91
1	8.8

B. Series II

In this group of kinetic reactions 0.25 g of diacetylfilicinic acid, 21, 0.5 g of sodium methoxide and 200 ml of methanol were used unless otherwise stated. All reactions were irradiated through Pyrex with a Hanovia L 450 watt lamp, or a 200 watt tungsten lamp when 0.015 g of Rose Bengal was used as a sensitizer. All reactions were carried out under air unless otherwise indicated. The reactions were followed by uv spectral analysis as outlined in the General Procedures. Unless otherwise noted the reactions were not worked up and the product, 67, was identified only by its characteristic uv absorption spectrum in basic ethanol (λ_{max}, 270 and 250 mμ).

1. Standard Photo-oxidation with a Hanovia L 450 Watt Lamp

Time(hr,min)	21 (%)
0, 0	100
0, 20	98.8
0, 44	93.8
1, 15	82
1, 45	71.9
2, 15	58.9
2, 45	47.1
3, 15	36.7
3, 45	27.2
4, 17	18.0

2. Standard Photo-oxidation with a 200 Watt Tungsten Lamp

This reaction was carried out using a 200 watt tungsten lamp but without any dye-sensitizer present.

Time(hr, min)	21 (%)
0, 00	100
3, 20	94
6, 00	90.3
12, 00	59
23, 15	10.5

See Experiment III D 1b for the work-up and products for this reaction.

3. Dye-sensitized (Rose Bengal) Photo-oxidation

Rose Bengal (15 mg) was used in the reaction and irradiated with a 200 watt tungsten lamp (otherwise, conditions are the same as in Experiment 2 immediately preceding).

Time(min)	21 (%)
0	100
10	71
20	39.4
30	13
50	0

4. Photo-oxidation of 2,5-Dimethylfuran

2,5-Dimethylfuran (1.0 g) in 200 ml of methanol containing 0.5 g of sodium methoxide was irradiated with a

200 watt tungsten lamp, under air, in the presence of 15 mg of Rose Bengal. The uv absorption band at 217 mμ (due to the furan) decreased in intensity, while an absorption band at λ 282 mμ increased in intensity. However, the band at λ 282 mμ increased to a maximum after 1 hr 20 min, then decreased in intensity. This was due to the formation of 2-hexen-2,5-dione (cis) (λ_{max} 282 and 213 mμ (45)), followed by isomerization to the more stable trans structure (λ_{max} 228 and 324 mμ (45)).

5. Photo-oxidation with 2,5-Dimethylfuran as a Singlet Oxygen Trapping Agent

In this reaction 1.0 g of dimethylfuran was used and the solution was irradiated with a Hanovia L 450 watt lamp.

Time(hr, min)	21 (%)
0	100
0, 30	99 4
0, 57	97.3
1, 30	89.8
2, 00	80.7
2, 32	70.1
3, 00	60.2

6. Photo-oxidation with 2,5-Dimethylfuran as a Singlet Oxygen Trapping Agent in a Dye-sensitized Reaction

In this reaction 1.0 g of dimethylfuran was used, and the solution was irradiated with a 200 watt tungsten lamp.

Time(min)	21 (%)
0	100
33	78
60	58.2

This reaction was repeated to test the reproducibility and to get intermediate values.

Time(hr, min)	21 (%)
0, 0	100
0, 5	100
0, 10	99
0, 15	97.5
0, 20	94
0, 25	91.3
0, 30	86.2
0, 40	76
0, 50	67.5
1, 00	63.4
1, 20	55.7
1, 50	39.9
3, 00	12.7

The values in this reaction gave good agreement with those obtained in the first reaction.

7. Photo-oxidation with 2,5-Dimethylfuran (0.0104 mole) as a Singlet Oxygen Trapping Agent, in a Dye-sensitized Reaction under Oxygen

Time(hr, min)	21 (%)
0, 00	100
0, 05	100
0, 15	98
0, 30	78.2

7. (Continued)

Time(hr, min)	21 (%)
1, 00	61.2
1, 30	52.5
3, 50	12.0

8. Photo-oxidation with Sodium Methoxide (0.037 mole) in a Dye-sensitized Reaction

Time(min)	21 (%)
0	100
10	63.8
15	45.3
20	29.2
25	23.8

9. Photo-oxidation with 2,5-Dimethylfuran (0.104 mole) as a Singlet Oxygen Trapping Agent

Time(hr, min)	21 (%)
0, 00	100
0, 30	100
1, 00	98
1, 30	97
2, 00	91
2, 35	89
3, 35	77.5
5, 20	59
7, 15	45
19, 45	0

In this reaction the photo-oxidized furan products probably reacted with diacetylfilicinic acid, 21.

10. Photo-oxidation with 2,5-Dimethylfuran (0.104 mole) as a Singlet Oxygen Trapping Agent in a Dye-sensitized Reaction

Time(hr, min)	21 (%)
0, 00	100
0, 10	100
0, 30	100
0, 55	97
1, 25	96.3
1, 45	95.5
2, 17	91
3, 24	90.5
5, 49	---*

*The uv absorption intensity at λ340 mμ increased after 5 hrs instead of decreasing. This was caused by the formation of the cis-3-hexen-2,5-dione, which has a uv absorption band at λ 282 mμ. This increase can be corrected for throughout by using data obtained from Exp. IV B4 and IV B9. For example, the value of 91% would change to 86.5% with a corresponding change of the other values. The values in this table are all uncorrected, as in the early stages of the reaction there would be little change.

11. Photo-oxidation of Acetylfilicinic Acid, 22

Time(min)	22 (%)
0	100
20	52
25	36.2
30	23.5
35	14
45	0

The methanol was evaporated and the residue was dissolved in water, neutralized with hydrochloric acid, then

extracted with ethyl ether. Evaporation of the ether yielded 0.177 g of a mixture, which consisted of 51% of 67 and 35% of 72 (mole percentages), as determined by integration of the peaks due to the gem dimethyl groups. The relative absorption band heights in an ir spectrum of the mixture indicated a composition of 55-65% 67 and 35-45% 72.

12. Photo-oxidation of Acetylfilicinic Acid, 22, with a Dye-sensitizer

Time (min)	22 (%)
0	100
5	91.3
10	84.3
15	78.3
25	61.4
35	39.8
45	21.2
55	8.7
∞	0

This reaction was worked up as in the previous experiment. An nmr spectrum indicated only the presence of 67 (83%).

13. Photo-oxidation of Acetylfilicinic Acid, 22, with One Molar Equivalent of Sodium Methoxide Present

In this reaction 69 mg of sodium methoxide was used.

Time(hr, min)	22 (%)
0, 00	100
0, 05	96.4
0, 10	95.3
0, 20	94.7
Adjustment of air flow at this point as air flow had stopped	
0, 30	94
0, 45	91.8
1, 16	79.8
1, 45	63.7
2, 30	26.2
3, 00	8.9

This reaction was worked up as given in Experiment III H 2. The products are also discussed in this previous experiment.

14. Photo-oxidation of Acetylfilicinic Acid, 22, with one Molar Equivalent of Sodium Methoxide in a Dye-sensitized Reaction

In this reaction 69 mg of sodium methoxide was used.

Time(hr, min)	22 (%)
0, 00	100
0, 05	96.3
0, 10	91
0, 20	79.3
0, 35	66.3
0, 50	46.6
1, 05	35.0
1, 30	22
2, 00	13
2, 30	4

A uv spectrum of a sample of the solution indicated an 84.5% yield of 67. The methanol was evaporated, the residue was dissolved in water, neutralized with concentrated hydrochloric acid, and extracted with ethyl ether. Evaporation of the ether afforded 0.3131 g (containing some of the dye) which had an ir spectrum identical to that of 67. The ir spectrum showed no evidence for the presence of 70 or the unknown compound, 89.

SUMMARY

1. 2,4-Diacetyl-3,5-dihydroxy-6,6-dimethyl-2,4-cyclohexadienone (diacetylfilicinic acid, 21) was prepared in two steps from phloroglucinol with an overall yield of 40%. Phloroglucinol was acetylated with acetic anhydride and concentrated sulfuric acid. The resulting 1,3-diacetylphloroglucinol, 24, was treated with methyl iodide using sodium methoxide in methanol and afforded compound 21.

2. Monoacetylfilicinic acid (2-acetyl-3,5-dihydroxy-6,6-dimethyl-2,4-cyclohexadienone, 22) was prepared from 21. Other related 2,4- and 2,5-substituted cyclohexadienones were prepared for comparative purposes. These included acetylmethylfilicinic acid (2-acetyl-3,5-dihydroxy-4,6,6-trimethyl-2,4-cyclohexadienone, 29), methylfilicinic acid (3,5-dihydroxy-4,4,6-trimethyl-2,5-cyclohexadienone, 30), filicinic acid (3,5-dihydroxy-4,4-dimethyl-2,5-cyclohexadienone, 19), 2-acetyl-3-hydroxy-4,4,6,6-tetramethyl-2-cyclohexen-1,5-dione, 32, 3-hydroxy-4,4,6,6-tetramethyl-2-cyclohexen-1,5-dione, 33, 2,4-diacetyl-5-hydroxy-6,6-dimethyl-2,4-cyclohexadienone, 42, and others.

3. Ultraviolet, ir and nmr spectra of the 2,4- and 2,5-cyclohexadienones and their methoxy and acetate derivatives were used to determine the most probable structures. The structures were assigned as indicated above.

4. Diacetylfilicinic acid, 21, was found to be photo-inert in ethyl ether and methanol under nitrogen or oxygen, and in alkaline methanol under nitrogen. A photo-oxidation reaction occurred on irradiation of 21 in an alkaline methanol solution, under air or oxygen, to give 2-acetyl-3,4-dihydroxy-4-carbomethoxy-5,5-dimethyl-2-cyclopentenone, 67. A mechanism for this oxidation and rearrangement was given. Identification of 67 was based on its spectral properties and on its conversion to the known compound, 2-acetyl-3,4-dihydroxy-5,5-dimethyl-2-cyclopentenone, 72, by treatment of 67 with 2N sodium hydroxide at 100^0. The formation of singlet oxygen in the initial stages of the photo-oxidation is postulated. This is based on the fact that the photo-oxidation could be dye-sensitized. Also, thermal decomposition of the peroxide of 9,10-diphenylanthracene in the presence of 21 in alkaline solution yielded the same photo-oxidation product, 67.

5. Acetylfilicinic acid, 22, was photo-oxidized to give 67, and in addition some of the decarboxylated product 72, probably by a second mechanism. Acetylfilicinic acid was irradiated in either ethyl ether or methanol to give a crystalline isomer of 22 (83%) to which a pyrone structure was assigned (3-acetyl-4-hydroxy-6-i-propyl-2H-pyrone, 89. It is postulated that 89 was formed by ring opening of 22 to give an intermediate ketene, followed by rotation and intramolecular attack of the 5-hydroxyl group on the

ketene function. The structure of **89** rests on its spectral data and comparison to the known pyrone, dehydroacetic acid.

6. Several kinetic runs on the photo-oxidations were carried out. The concentrations of sodium methoxide and oxygen were found to have little effect on the rate of the photo-oxidation. The rate seems to depend only on the efficiency of the formation of the excited state and subsequent formation of singlet oxygen.

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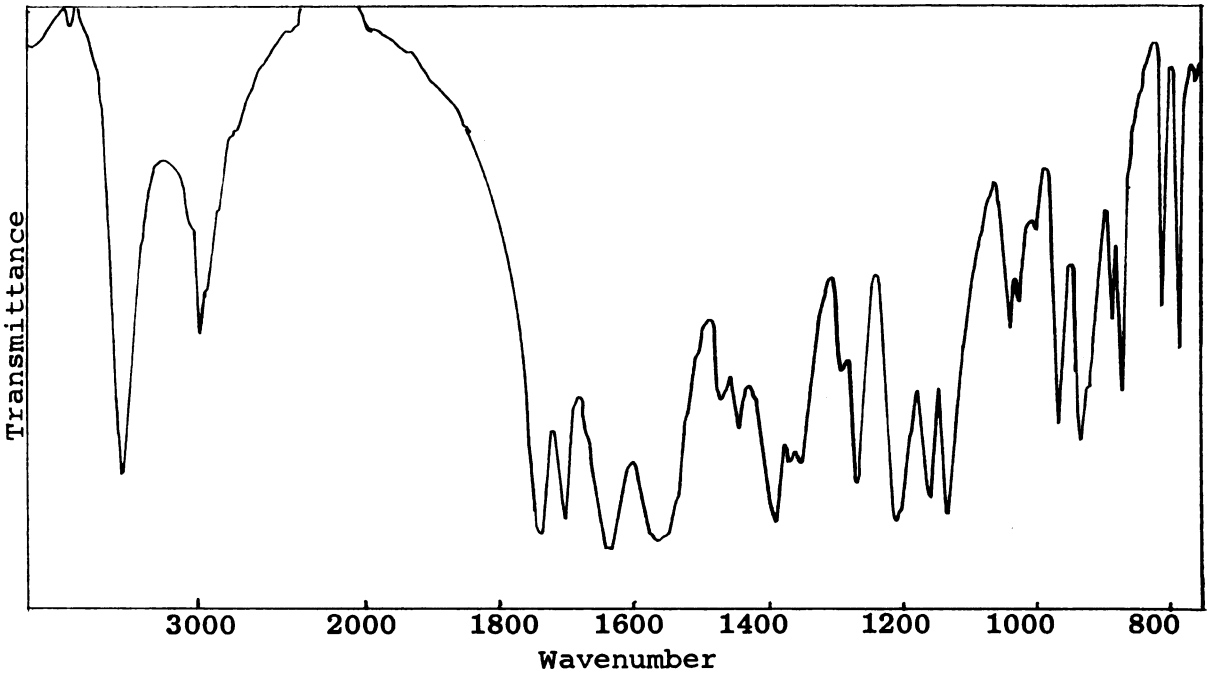
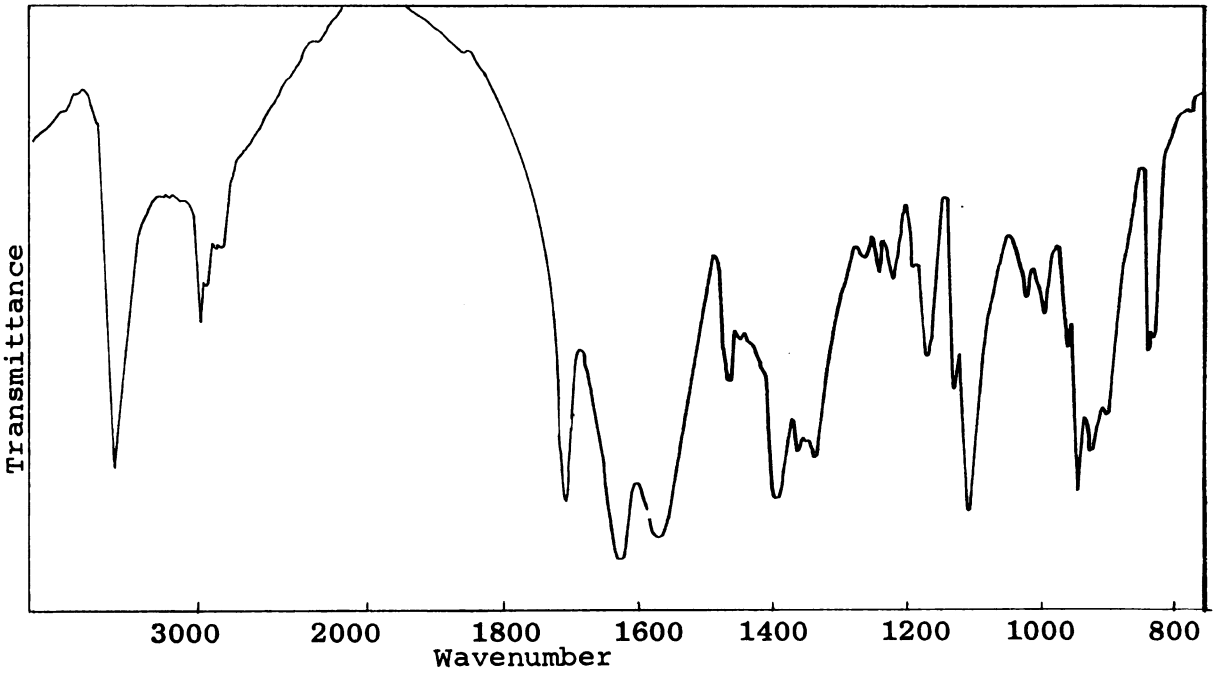
APPENDIX I

Ir and Nmr Spectra

Ir Spectrum 1. 2-Acetyl-3,4-dihydroxy-4-carbomethoxy-5,5-dimethyl-2-cyclopentenone, 67 (KBr).



Ir Spectrum 2. 2-Acetyl-3,4-dihydroxy-5,5-dimethyl-2-cyclopentenone, 70 (KBr).



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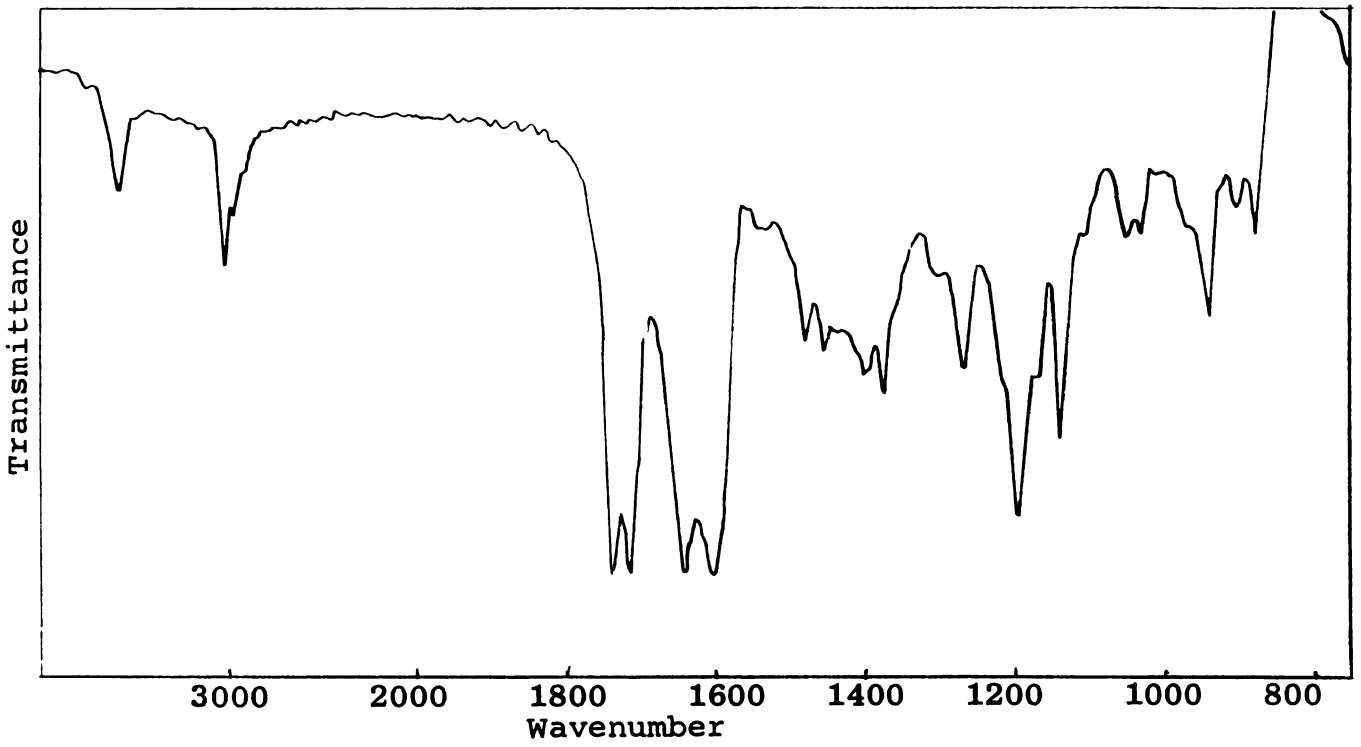

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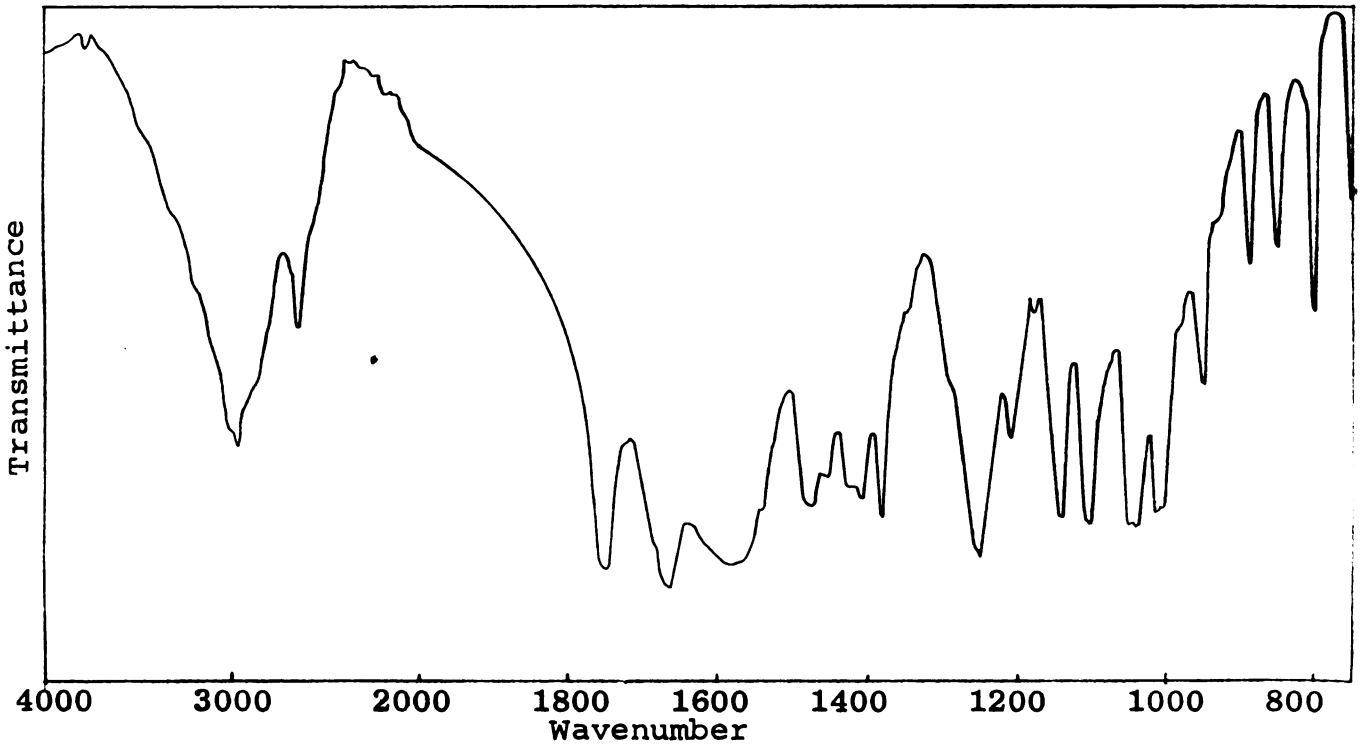
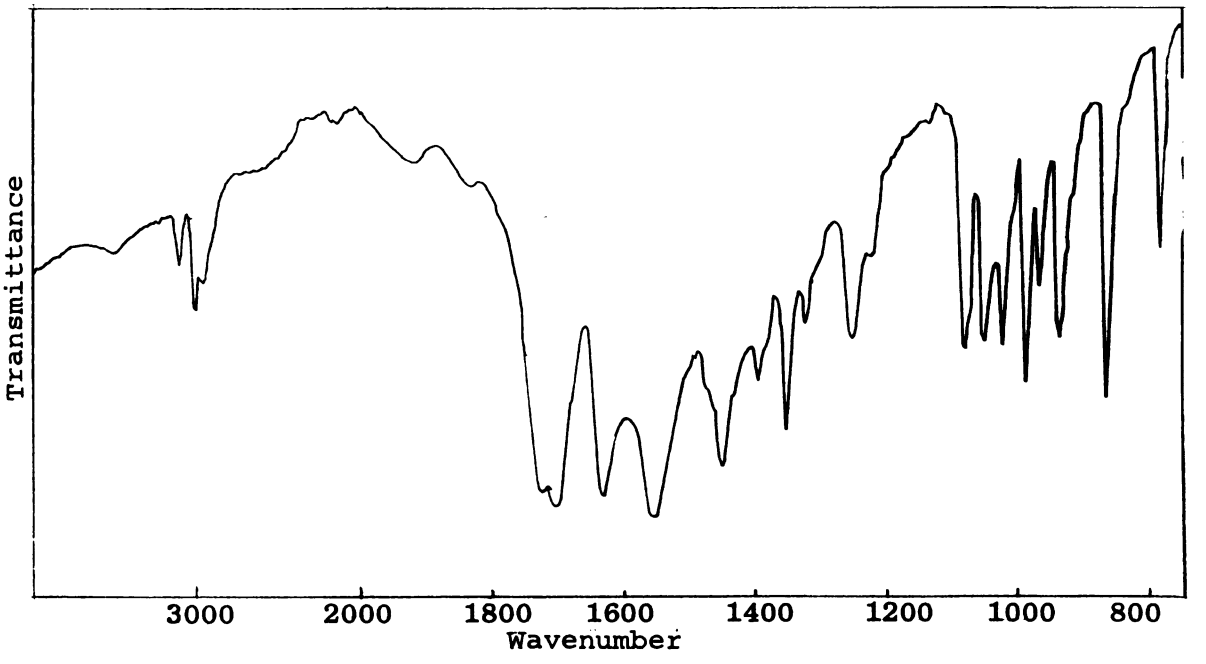
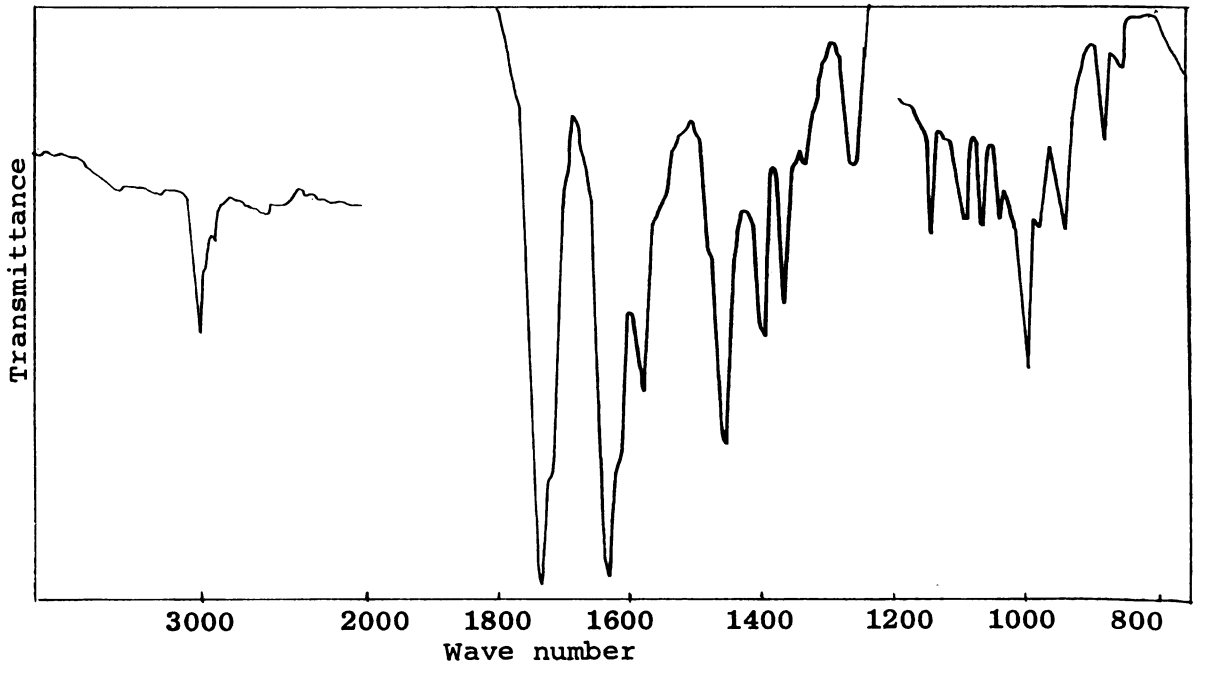


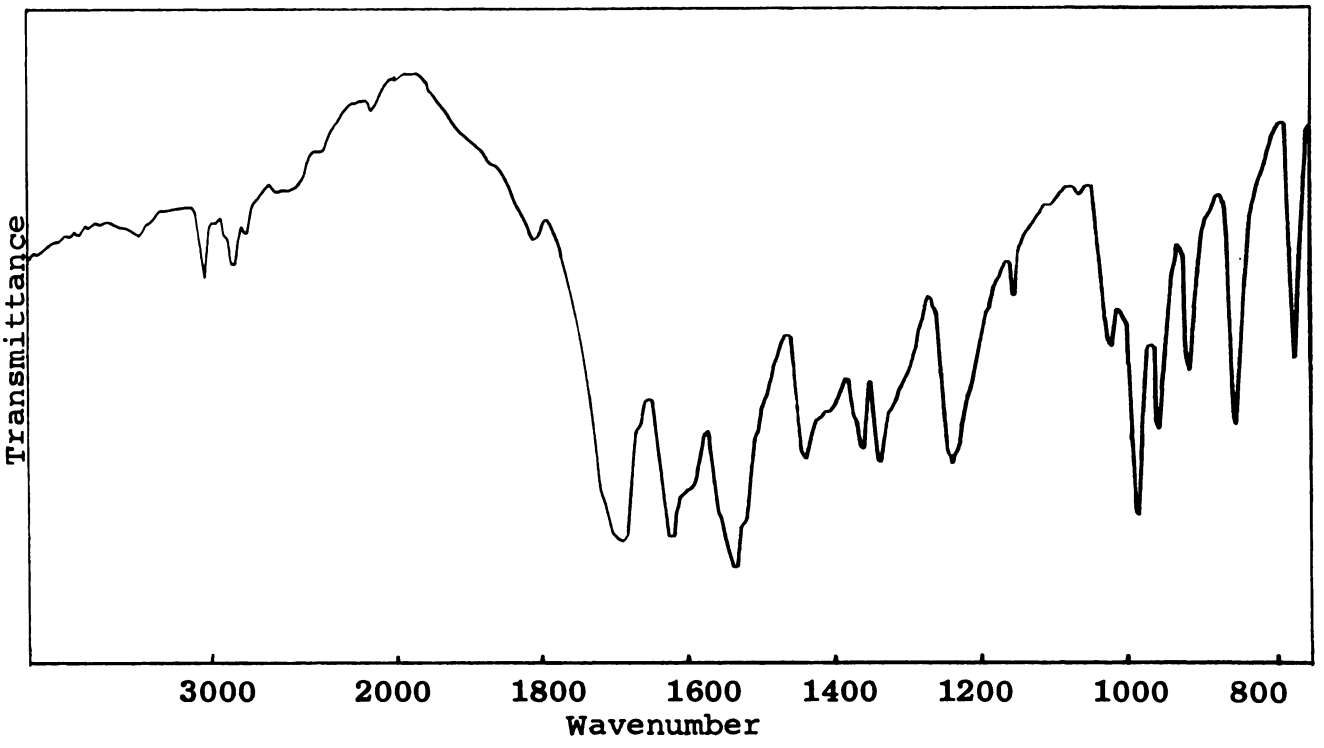
Ir Spectrum 5a. 3-Acetyl-4-hydroxy-6-i-propyl-2H-pyrone, 90 (KBr).



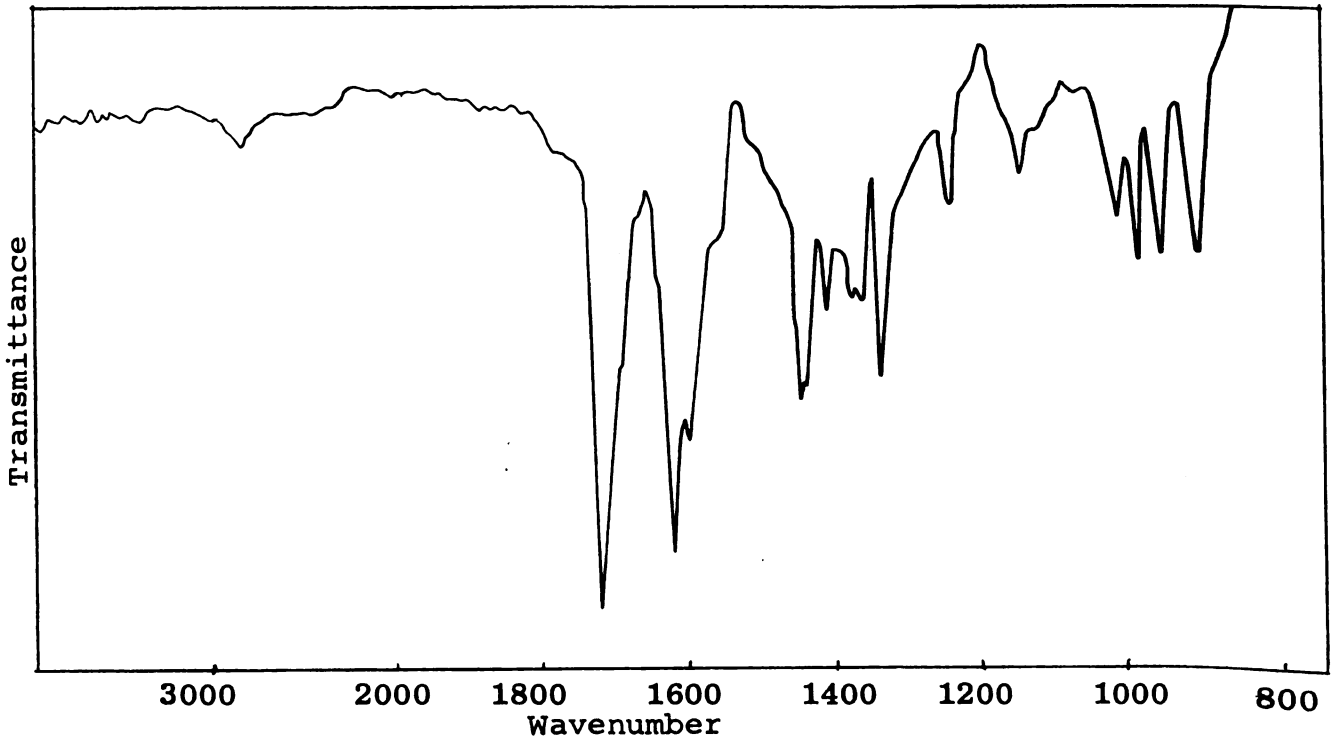
Ir Spectrum 5b. 3-Acetyl-4-hydroxy-6-i-propyl-2H-pyrone, 90 (CCl_4).



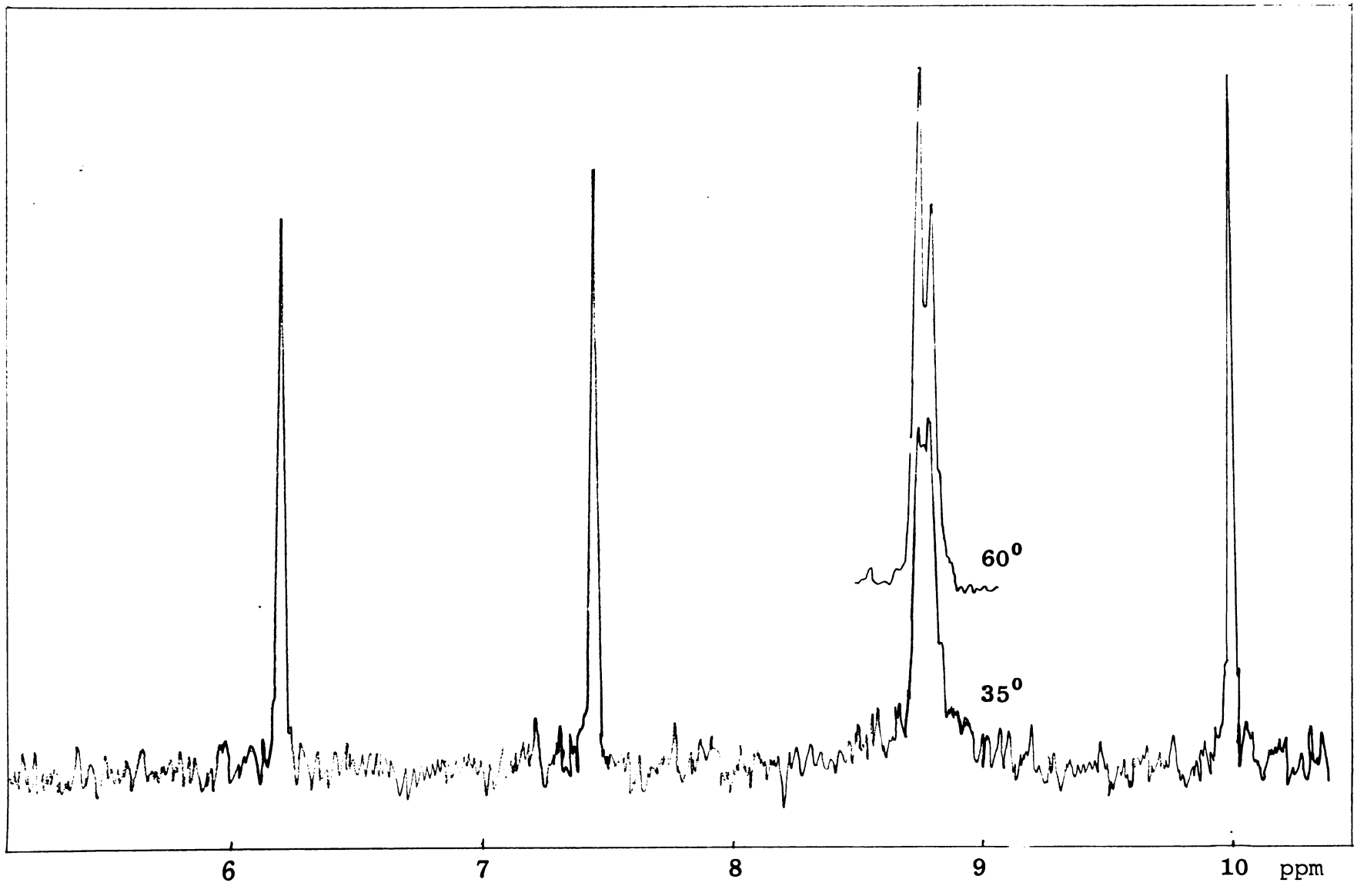
Ir Spectrum 6a. Dehydroacetic Acid, 91 (KBr)



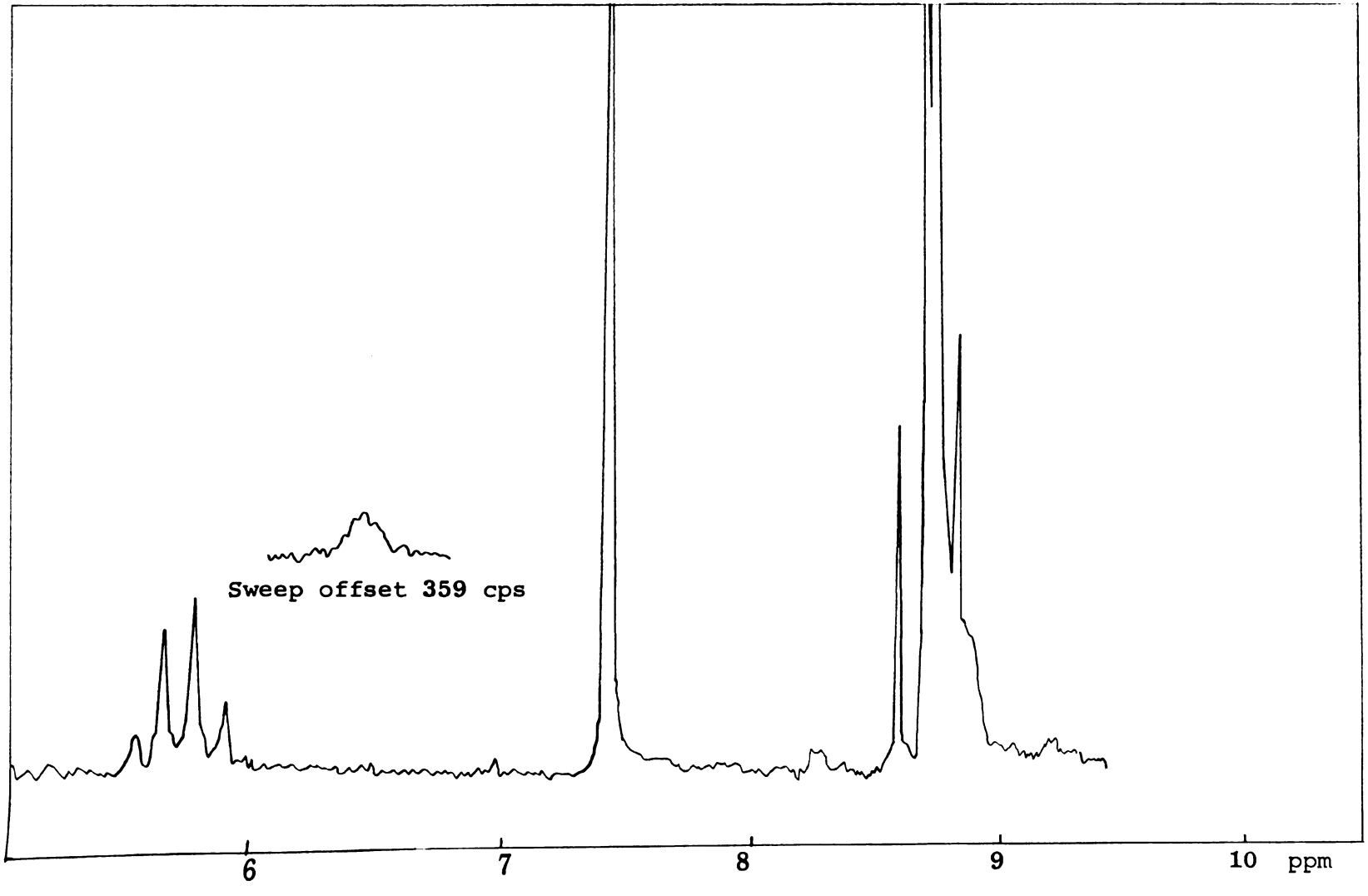
Ir Spectrum 6b. Dehydroacetic Acid, 91 (CCl_4)

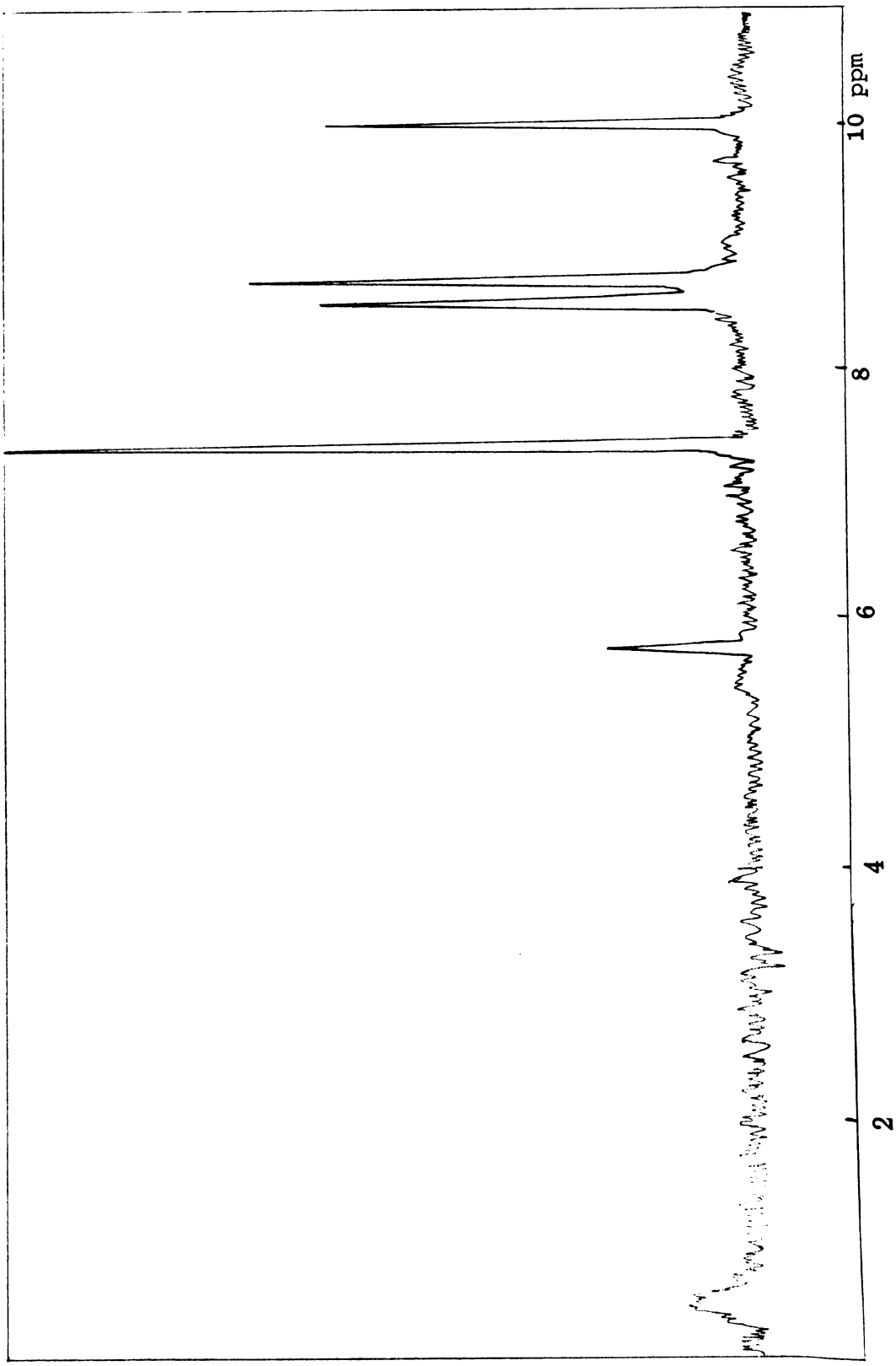


Nmr Spectrum 1. 2-Acetyl-3,4-dihydroxy-4-carbomethoxy-5,5-dimethyl-2-cyclopentenone.

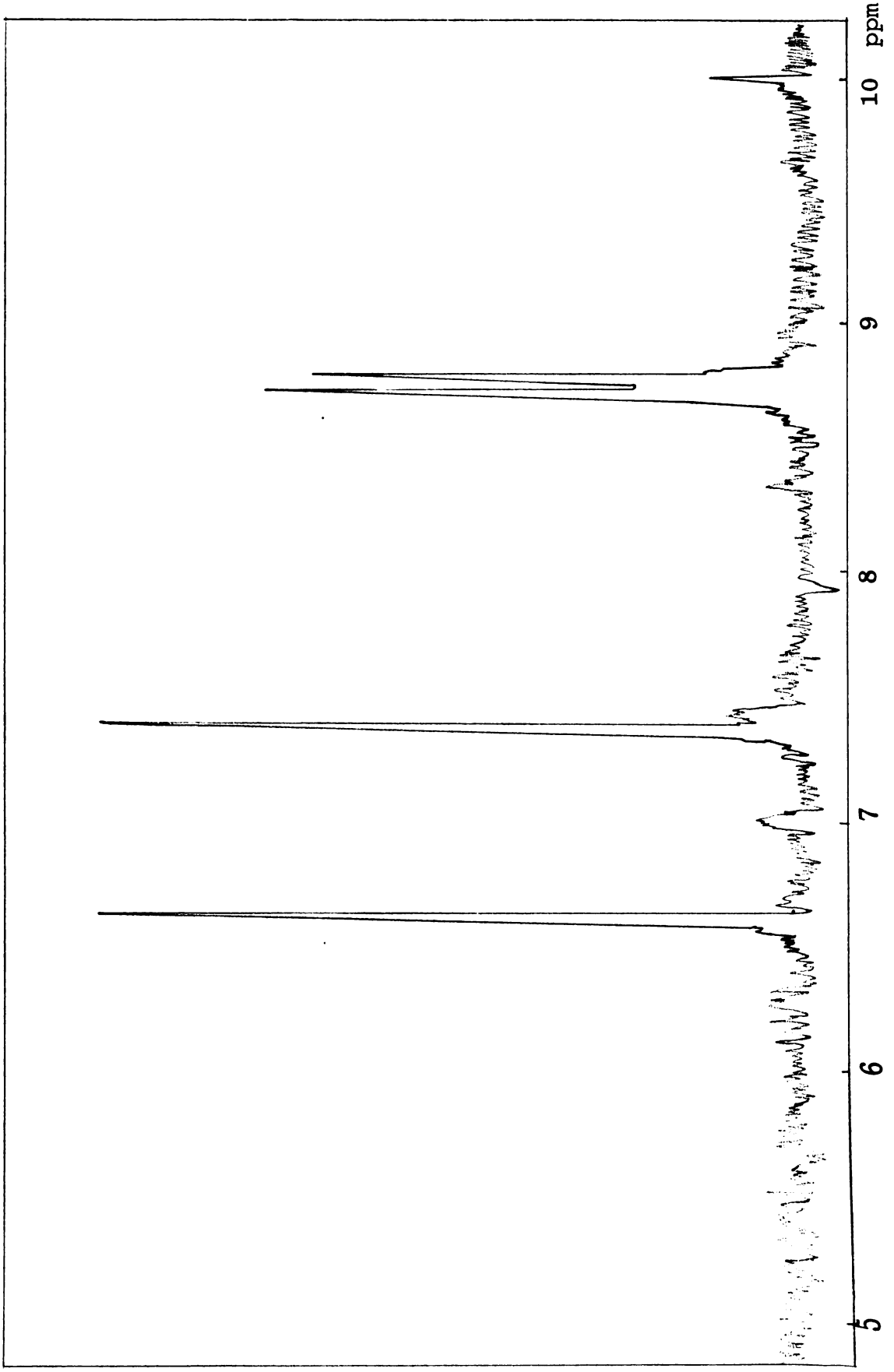


Nmr Spectrum 2. 2-Acetyl-3,4-dihydroxy-4-carboethoxy-5,5-dimethyl-2-cyclopentenone.

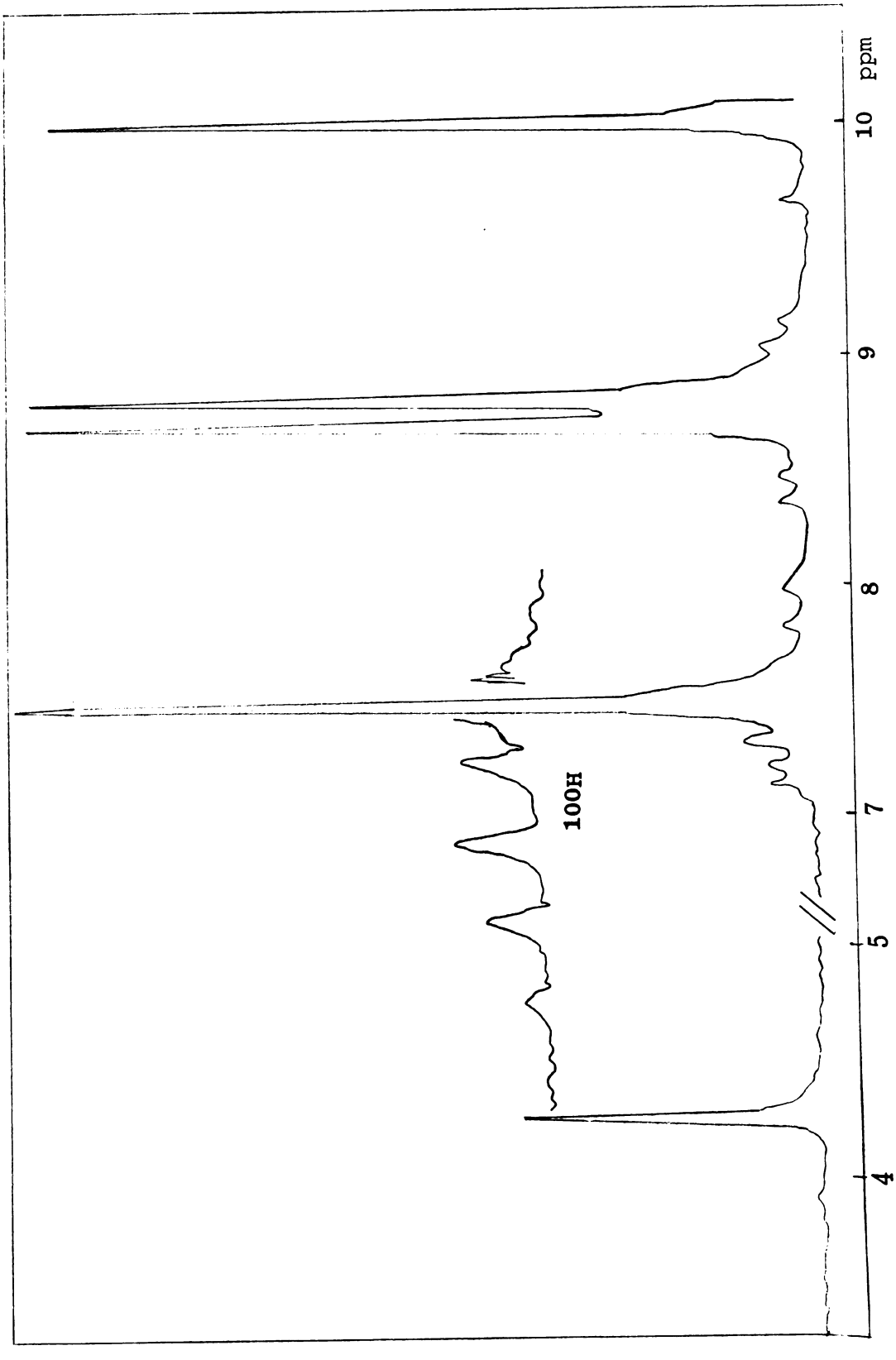




Nmr Spectrum 3. 2-Acetyl-3,4-dihydroxy-5,5-dimethyl-2-cyclopentenone.



Nmr Spectrum 4. Unknown Compound, 89.



Nmr Spectrum 5. 3-Acetyl-4-hydroxy-6-i-propyl-2H-pyrone.

APPENDIX II

Molecular Orbital Calculations (ω-Technique)

APPENDIX II

Molecular Orbital Calculations (ω-Technique)

Although much work has been done on the photolysis of 2,4-cyclohexadienones (2,3,9), no quantitative experimental work has been done to explain why some 2,4-cyclohexadienones give ring-opened products and others rearrange to bicyclo[3.1.0]hexenones when irradiated. In Sections III and IV it was found that molecular orbital calculations were useful in predicting the position of attack by singlet oxygen on two carbon anions. Molecular orbital calculations might also provide some explanation for the two different reaction paths observed in the photolysis of 2,4-cyclohexadienones. Also calculations could provide a rationale for the preferred stability of one tautomeric form of a 2,4- or 2,5-cyclohexadienone over another as assigned in Sections I and II.

A. The Method

Molecular orbital calculations were carried out with a 3600 Control Data Computer using a program written by Professor R. S. Schwendeman of the Chemistry Department of Michigan State University.

The method used was a variation of the Hückel molecular orbital method known as the "ω-technique" (49). Normally the values of the coulomb integral are taken as a

constant value, "α" for carbon. It is a function of the nuclear charge of the atom. The resonance integral, β, is related to the degree of overlap and is constant for a given overlap between two carbon "p" orbitals at a given distance. A change in the atomic number of an atom effects both the coulomb and resonance integrals. The relationships for new values of these integrals can be expressed by:

$$\alpha = \alpha_0 + h\beta_0 \qquad 1$$

$$\beta = k\beta_0 \qquad 2$$

Where α_0 and β_0 are the values for carbon, and h and k are constants which depend upon the heteroatom which replaces carbon. Values of these constants for a carbonyl oxygen and a hydroxyl oxygen were taken from the text Quantum Organic Chemistry (36). Because the anions of some of the compounds in this research are resonance hybrids containing several carbonyl and hydroxyl groups, a direct ratio of values for h and k was used. These values are given in Table IV in Section III.

The "ω-technique" allows the coulomb integral to be adjusted for changes in the charge on each atom. It has been suggested (49) that the value of α should be linearly related to the charge and may be formulated as:

$$\alpha = \alpha_0 + (1 - q_r)\ \omega\beta_0 \qquad 3$$

Where "ω" is a dimensionless parameter whose value may be chosen (the recommended intermediate value of 1.4 was used here) to give the best agreement with experiments. The

charge on the atoms was taken as q_r, defined in the usual way as:

$$q_r = \Sigma N c_i^2 \qquad 4$$

Where N is the number of electrons in the molecular orbital, and c_i is the coefficient of the "i"th atom. The sum is taken over all the occupied molecular orbitals. After each calculation the charges can be recalculated from the coefficients. The new charges can then be put into equation (3) and the molecular orbital calculations repeated. This process is continued until the values for the molecular orbital energy levels and charges on the atoms converge to constant values. The program does this automatically, it being necessary only to put in the desired number of iterations.

The input data were written up as:

Input for HMOWM

Name Card:

1	, C, A, R, B, O, N, Y, L, , G, R, O, U, P, , ,

Name can be from column 2 to 55

Parameter Card:

, 2	, 2	, , 4	, , , ,	,	, , , , , , , , ,
No. Atoms	No. Electrons	No. Iterations 100 x ω		No. Pairs	

Data Cards:

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20,21
i_i,	i	,	j	,	k	,	l	$100M_{ij}$			,	$100M_{ik}$		,	$100M_{il}$		,	$100M_{ii}$	
1			2					2	0	0								1	2
2																			
3																			
4																			

An explanation of the input data follows. In the Name Card, if column one is left blank, the program operates normally. This means that the atom-atom polarizabilities are calculated only once and these values are used in successive iterations. Although this procedure may cause slight inaccuracies, it saves computer time. When a 1 is placed in this column, the atom-atom polarizabilities are recalculated for each iteration. This may aid in convergence of the molecular orbital energy values and the charges on the atoms. Any desired name may be placed on the rest of the card.

The second card is the parameter card. In the first two columns the number of atoms in the system is placed. The next two spaces are for the total number of electrons, and the following two spaces are for the desired number of iterations. Normally three to four iterations are sufficient for convergence to occur. The value for 100ω is put in the next four places. Normally "ω" equals 1.4 so 140 would placed here. This program is written such that

if "ω" equals 1.4 it is not necessary to put this value in. However, if a different value for "ω" is used then it must be put in these columns.

The next series of cards are the actual data cards, one for each atom of the molecule. In the first two columns the atom number of the molecule is placed. The next three places are for the atom number(s) that this atom is connected to. It is not necessary to indicate the interrelation between any two atoms more than once, although all atom numbers must appear in the first two columns. Consider, for example, an ethylene group. A number 1 would be placed in column 2 and a number 2 would be placed in column 4, signifying that atom 1 is connected to atom 2. In a second card a 2 would be placed in column 2 and nothing else is needed as it has already been indicated on the first card that atom one is connected to atom two.

Under the columns labeled $100M_{ij}$, $100M_{ik}$ and $100M_{il}$ are placed the relationship of the resonance integral between atoms "i" and "j", atoms "i" and "k" and atoms "i" and "l" respectively, if different from one. This would be the value of k from equation 2, x 100.

In column 19 the value of h (Equation 1) for the coulomb integral begins, if it differs from the normal 1 for carbon atoms. An example is written out for the carbonyl group using the values of h and k taken from Table IV in Section III. Note that only two data cards are needed and only a 2 in the second column will be needed

on the second card

2 1
C - O

Calculations of compounds with a larger number of atoms can be carried out in a similar manner.

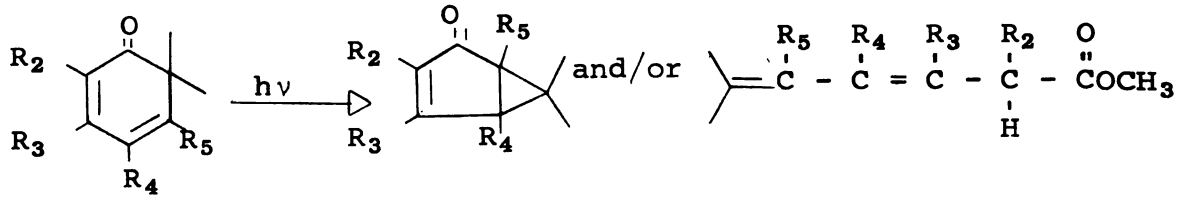
At times it may be desirable to carry out simple Hückel calculations with the same program. This will be done automatically if there is no charge on the molecule. However, the program was designed to spread any charge evenly over all the atoms in the first calculation so as to be one step towards the actual solution and save computor time. To obtain the simple Hückel molecular orbital energy levels it is necessary to add or subtract from each molecular orbital energy level the amount which the diagonal value of the topological matrix deviates from the normal α value. This normal value would be 1 for a carbon atom and h for the heteroatoms. For charged hydrocarbons this would turn out to be the fraction of the charge expected on each atom.

The molecular orbital calculations were used to calculate the charges on the atoms, not only in the ground state but in excited states as well. The ground state charges were obtained directly from the output data sheet. To get the n-π^* excited states, extra charges were added to each of the atoms using equation 4 and the coefficients of the lowest unoccupied molecular orbital.

For the π - π^* excited states a difference of the squares of the coefficients for the lowest unoccupied molecular orbital and the highest occupied molecular orbital were added to each of the ground state charges. This gave the charges on each atom for this excited state.

B. <u>The Effect of Substituents on the Photolysis of 2,4-Cyclohexadienones</u>

It seemed desirable to try to use molecular orbital theory to examine the effect of substituents on the photolysis of 2,4-cyclohexadienones in an attempt to understand why ring-opened products are obtained in some cases and bicyclic products in others.



Hart (6) found that a methyl substituent at carbon 5 does not effect the course of the photolysis. When the substituents (R_2, R_3, R_4) are all methyls then a bicyclic product was obtained. If R_3 was a hydrogen then both the bicyclic and ring-opened products were obtained. In the case where R_2 was hydrogen or R_2 and R_5 were hydrogens then only the open chain compound was formed.

Examination of the coefficients of the lowest unoccupied molecular orbital and the highest occupied molecular orbital (Table XI) of 2,4-cyclohexadienone showed that the greatest increase in electron density for n - π^* excitation would be at C_2 and C_5. Such an increase at these carbons should facilitate α-cleavage between the carbonyl carbon and C_6 due to the increased ease with which double bonds might be formed at these positions.

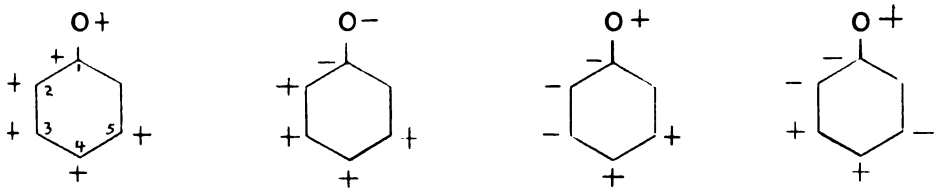
Table XI. Coefficients of the highest occupied and lowest unoccupied molecular orbitals and charges on ring atoms of 2,4-cyclohexadienone (ω-technique)

	Coefficients		Charges		
Atom	m + 1	m	Ground State	n - π^*	π - π^*
O	0.3223	0.2785	-0.2119	-0.316(+0.684)*	-0.2359
C_1	-0.2183	-0.0340	0.1430	0.0955	0.0964
C_2	-0.5024	-0.5726	-0.0066	-0.2586	0.0684
C_3	0.4404	-0.3488	0.0399	-0.1521	-0.0321
C_4	0.2790	0.3621	0.0079	-0.0699	0.0609
C_5	-0.5694	0.5836	0.0277	-0.2953	0.0437

*Indicates actual charge on the oxygen atom after accounting for the loss of one "p" electron on n - π^* excitation.

Most of the difficulty in predicting the photolysis course for 2,4-cyclohexadienones when substituents are present, is the result of a lack of knowledge regarding the photochemistry of the reaction(s). It is not known whether the photolysis occurs <u>via</u> n - π^* or π - π^* excitation or is a singlet or a triplet reaction. Hart (6) has shown

that the reactions are not quenched by piperylene, and says the question of singlet or triplet remains open for both types of photoisomerizations. For this reason both types of excitation were considered in the molecular orbital calculations (see Table X). The ground state for 2,4-cyclohexadienone has the following molecular orbitals:



m-2 m-1 m m+1

It can be seen that the m - 2 orbital favors the C_1 - C_5 bonding while the other two do not. The first excited state (m + 1) also favors bonding between C_1 and C_5. This is necessary if bond crossing at this point is involved in the mechanism as outlined here to give the bicyclic product.

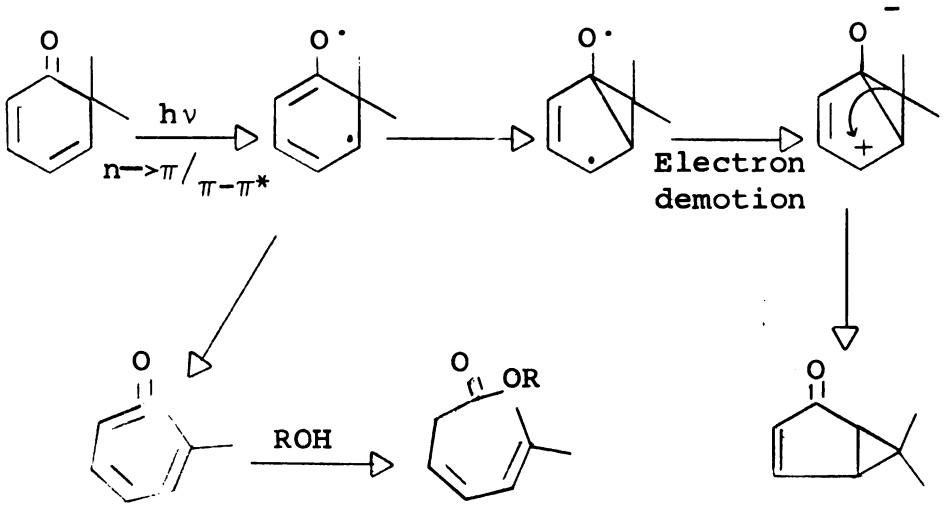
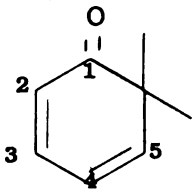
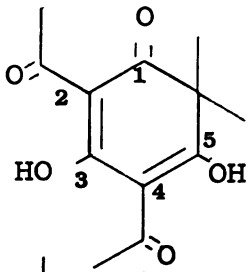
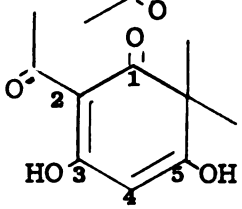
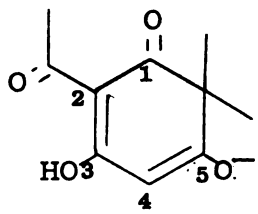
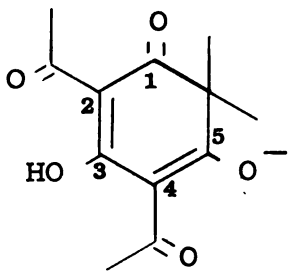


Table X. Parameters for molecular orbital calculations of 2,4-cyclohexadienones

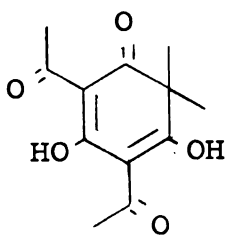
Compound		C=O		C-C		C-OH		C-O⁻	
		h	k	h	k	h	k	h	k
		1.2	2.0	1	1				
	21	1.2	2.0	1	1	2.0	0.9		
	22	1.2	2.0	1	1	2.0	0.9		
	65	1.46	1.62	1	1	2.0	0.9	1.46	1.62
	55	1.4	1.77	1	1	2.0	0.9	1.4	1.77

Zimmerman gives a similar argument in explaining the bond-crossing of 2,5-cyclohexadienones to give a similar bicyclic product (50). If the photo excitation is n - π^* to the m + 1 molecular orbital, then there is increased electron density at C_2 and C_5 which is favorable for the formation of ring-opened compounds and also for increased bonding between C_1 and C_5, which favors bicyclic products. However, it is known that bicyclic products are only formed when certain substituents are present. One possible explanation is that n - π^* excitation causes the formation of ring-opened products, whereas π - π^* excitation favors bicyclic products. This is consistent with the calculations. An n - π^* excitation increases electron density at C_2 and C_5 whereas π - π^* excitation would not change the electron density at these carbons very much. It can be seen from Table XI that the coefficients for the m and m + 1 orbitals at C_2 and C_5 are similar. Therefore π - π^* excitation would not be particularly favorable for the formation of ring-opened product. However, π - π^* excitation would be favorable for bond-crossing, leading to a bicyclic product. Not only are the signs of the coefficients correct for C_1 - C_5 bond formation in the m + 1 state but one electron would be removed from the m level, which is unfavorable for such bonding. In all cases disrotatory bond formation of the cyclopropane ring is assumed.

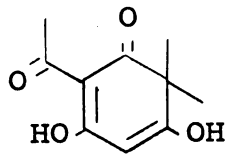
The n - π^* excitation results in increased negative charge at all the carbon atoms. Methyl substituents, which

would not favor such an increase, would be expected to destabilize the n - π^* excited state. However, in the π - π^* excited state there is an increase in positive charge at C_2, C_4 and C_5, the largest increase being at C_2 and C_4. This is consistent with the observation that bicyclic product was formed only when methyls were at both of these positions (6). Methyl substituents should favor the n - π^* excited state and lower the energy of the m + 1 level, perhaps low enough so that the π - π^* absorption could occur at a wavelength (330 mμ) longer than that of the n - π^* absorption.

It was of interest to examine the effect of other substituents on the 2,4-cyclohexadienone. If the above conclusions are valid then the type of substituent is important in determining which excited state is obtained. It would be expected that electron-withdrawing groups at C_2 and C_4 should not favor π - π^* excitation. This expectation was supported when it was found that neither diacetylfilicinic acid, 21, nor acetylfilicinic acid, 22, gave a bicyclic product in ethyl ether or methanol on irradiation under a nitrogen atmosphere.



21



22

Acetyl groups at C_2 and/or C_4 should favor the n - π^* excited state as they would stabilize the increased negative charge. In order to examine this in more detail, molecular orbital calculations were carried out for both 21 and 22. The results are given in Tables XII and XIII.

For acetylfilicinic acid, calculations show an increased electron density especially at carbons 2, 3 and 5 for n - π^* excitation. Increased electron density at C_2 and C_5 should favor bond-breaking to give ring-opened product.

Table XII. Coefficients of the highest occupied and lowest unoccupied molecular orbitals and charges on ring atoms of acetylfilicinic acid (ω-technique)

	Coefficients		Charges		
Atom	m + 1	m	Ground State	n - π^*	π - π^*
O	0.2250	0.2934	-0.2626	-0.3136(+0.6864)*	-0.2276
C_1	-0.1724	-0.0848	0.1214	0.0918	0.0990
C_2	-0.3002	-0.5939	-0 1824	-0.2724	0.0796
C_3	0.4780	-0.1330	0.0607	-0.1683	-0.1506
C_4	0.1679	0.4036	-0 1163	-0.1445	0.0179
C_5	-0.5682	0.3012	0.0637	-0.2593	-0.1697

*Indicated actual charge on the oxygen atom after accounting for the loss of one "p" electron on n -π^* excitation.

An overall increase in negative charge was found at all the carbon atoms for n - π^* excitation. This is favorable at carbon 2 where the acetyl group is located but probably not favorable at the 3 and 5 carbons where there are hydroxyl substituents. Thus the n - π^* excited state

for acetylfilicinic acid may not be as stable as the n - π^* excited state of 2,4-cyclohexadienone. This may explain why the ring opening does occur for 22 but requires such long reaction times (32 to 48 hours).

Table XIII. Coefficients of the highest occupied and lowest unoccupied molecular orbitals and charges on ring atoms of diacetylfilicinic acid(ω-technique)

	Coefficients		Charges		
Atom	m + 1	m	Ground State	n - π^*	π - π^*
O	0.2317	-0.2275	-0.2416	-0.2951(+0.7049)*	-0.2433
C_1	-0.1577	0.0557	0.1318	0.1070	0.1254
C_2	-0.3556	0.4654	-0.1212	-0.2474	-0.0304
C_3	0.4327	0.1406	0.0768	-0.1102	-0.0904
C_4	-0.4249	-0.5635	-0.1032	-0.2842	0.0338
C_5	0.3384	-0.2239	0.0447	-0.0703	-0.0203

*Indicates actual charge on the oxygen atom after accounting for the loss of one "p" electron on n - π^* excitation.

For the π - π^* excitation there is an increase in positive charge at carbons 2 and 4, and an increase of negative charge at carbons 3 and 5, both of which work against the stability of this excited state. In addition it can be seen that the electron density at carbon 2 would actually decrease and the density at carbon 5 would only increase slightly over that of the ground state, which would not favor ring cleavage. For these reasons the π - π^* excited state was thought to be unstable relative to the n - π^* excited state, which, via ring-opening to a ketene,

can give the pyrone, 90 .

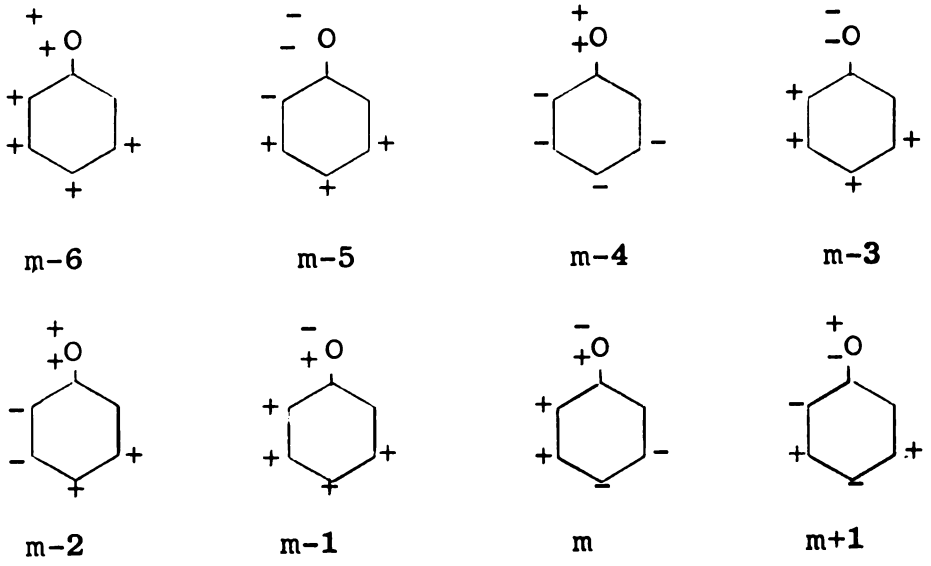
Calculations for the molecular orbitals and charge densities for diacetylfilicinic acid, 21, are given in Table XIII. It can be seen that although the n - π^* excited state would be stabilized with negative charges on the atoms where the acetyl groups are located, there are negative charges on the atoms containing hydroxyl substituents. The increase in electron density at carbon 5 (0.1150) is much less than that for acetylfilicinic acid, 22, (0.319) and for 2,4-cyclohexadienone (0.323) both of which undergo ring-opening. This might be an explanation why diacetylfilicinic acid, 21, gives no ring-opened compound.

For the π - π^* excitation the charges are unfavorable for stabilization of the excited state, as with acetylfilicinic acid, and the increased electron density at carbons 2 and 5 (0.0908, 0.0650) would not favor ring cleavage. Also in this case π - π^* excitation does not enhance the possibility of bond-crossing, which is seen to be unfavorable both in the m and m + 1 molecular orbitals.

On the whole there are only three molecular orbitals that favor bond-crossing for diacetylfilicinic acid, 21, whereas four do not. When one adds the fact that π - π^* excitation does not increase the possibility for bond crossing, it is not unreasonable that no bicyclic product is formed.

In order to seek a reason for the relative rates of the self-sensitized photo-oxidations of acetylfilicinic

acid, 22, (8.1×10^{-3} mole/l/hr) and diacetylfilicinic acid, 21, (1.35×10^{-3} mole/l/hr) molecular orbital calculations were carried out on the mono-anions of these compounds (Table XIV and Table XV).



Molecular orbitals of Diacetylfilicinic acid, 21.

The only major difference is the fact that in the $\pi - \pi^*$ excited state there are two acetyl groups destabilizing the excited state for diacetylfilicinic acid and only one destabilizing the excited state for acetylfilicinic acid. On this basis the $\pi - \pi^*$ excited state for acetylfilicinic acid may be less unstable.

The acetyl groups should stabilize the $n - \pi^*$ excited states for both monoanions, whereas the hydroxyl groups should destabilize it. The only other factor which may be

important in connection with the faster photo-oxidation rate of acetylfilicinic acid is that the increase in electron density at C_5 for acetylfilicinic acid (0.192) is greater than the increase at the equivalent carbon atom for diacetylfilicinic acid (0.0628).

Table XIV. Coefficients of the highest occupied and lowest unoccupied molecular orbitals and charges on ring atoms of monoanion of acetylfilicinic acid (ω-technique)

	Coefficients		Charges		
Atom	m + 1	m	Ground State	n - π^*	π - π^*
O	0.2216	-0.3055	-0.3923	-0.4413(+0.5587)*	-0.3483
C_1	-0.2475	0.1455	0.1288	0.0676	0.1688
C_2	-0.0917	0.4889	-0.1990	-0.2074	0.0311
C_3	0.5520	-0.0868	0.0420	-0.2630	-0.2555
C_4	-0.1847	-0.5918	-0.2082	-0.2422	0.0738
C_5	-0.4397	-0.1681	0.1106	-0.0814	-0.0536

Indicated actual charge on the oxygen atom after accounting for the loss of one "p" electron on n - = excitation.

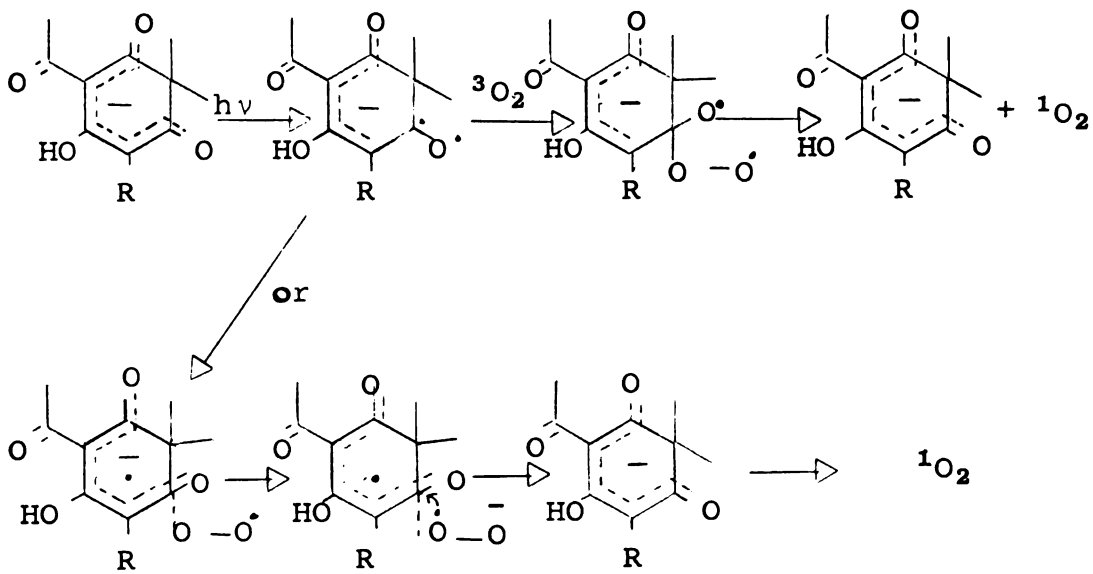
Table XV. Coefficients of the highest occupied and lowest unoccupied molecular orbitals and charges on ring atoms of the monoanion of diacetylfilicinic acid (ω-technique)

	Coefficients		Charges		
Atom	m + 1	m	Ground State	n - π^*	π - π^*
O	0.2452	-0.3023	-0.3467	-0.4067(+0.5933)*	-0.3157
C_1	-0.2516	0.1250	0.1313	0.0685	0.0213
C_2	-0.1610	0.5348	-0.2035	-0.2294	0.0317
C_3	0.6025	-0.0000	0.0605	0.0243	-0.0119
C_4	-0.1610	-0.5348	-0.2035	-0.2294	0.0317
C_5	-0.2516	-0.1250	0.1313	0.0685	0.0213

*Indicated actual charge on the oxygen atom after accounting for the loss of one "p" electron on n - π^* excitation.

Schenck says (33) that in his opinion the singlet and triplet states of the sensitizer react with oxygen to form a sensitizer-oxygen adduct, rather than to produce excited oxygen molecules by mere physical energy transfer. This adduct may be interpreted as a Mulliken charge-transfer complex. He also suggested later that if the excited molecule has biradical character then it could behave chemically in the manner of free radicals. Therefore reactions with oxygen should not only be very efficient in quenching the excited state but also lead to a new biradical molecule in which the oxygen is attached to a former radical site by a normal chemical bond.

It is possible that the two carbanions studied here might form singlet oxygen by the following mechanism(s).



R = CH_3-C(=O)- , H

If this is the case then the rate of singlet oxygen formation may be related to the electron density at C_5 in the excited state; this may be the basis for the rate difference of the self-sensitized photo-oxidations of acetylfilicinic acid, 22, and diacetylfilicinic acid, 21,.

The rate of the dye-sensitized photo-oxidation of acetylfilicinic acid (5.9×10^{-3} mole/l/hr) and diacetylfilicinic acid (9.6×10^{-3} mole/l/hr) are more comparable and the difference here could be due to the fact that there are two equivalent positions in the diacetylfilicinic acid anion which can be attacked whereas there is only one for acetylfilicinic acid anion.

In conclusion molecular orbital calculations suggest that for an unsubstituted 2,4-cyclohexadienone, n - π^* excitation might lead to a ring-opened product. If the n - π^* excited state is destabilized and the π - π^* excited state is stabilized by substituents such as methyl groups, then the π - π^* excited state could become more favorable. Calculations show that the π - π^* excited state would favor bond-crossing to give a bicyclic product, in preference to a ring-opened product.

On extending this idea to other substituents such as acetyl and hydroxyl groups, calculations show that acetylfilicinic acid, 22, would be more likely to form a reactive n - π^* excited state than diacetylfilicinic acid, 21. This offers an explanation for the fact that acetylfilicinic acid undergoes ring-opening on photolysis, whereas diacetylfilicinic acid is photochemically inert. Molecular

orbital calculations also show that the π-π^* excited state in both cases are unfavorable for bond-crossing and give a reason for the lack of bicyclic compound formation.

The reason for the more rapid photo-oxidation of acetylfilicinic acid over that of diacetylfilicinic acid is not as clear. The results indicated that acetylfilicinic acid was more efficient in reacting with oxygen to produce singlet oxygen. This could be due to a more stable excited state or, as suggested by molecular orbital calculations, due to a higher electron density at C_5. This would enable more facile quenching of the excited state by triplet oxygen, if the quenching reaction was visualized as a free radical type reaction.

C. The Relative Stability of Tautomeric Structures as Predicted by Molecular Orbital Calculations

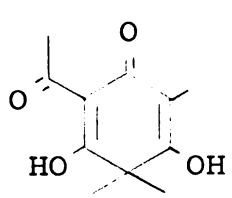
Molecular orbital calculations were carried out to determine relative stabilities of different isomeric structures of the substituted 2,4- and 2,5-cyclohexadienones given in Sections I and II. The values of the energy of the systems (in terms of β) obtained from simple Hückel calculations and using the "ω-technique" are recorded in Table XVI. Calculations for a number of possible structures were carried out for some compounds. Also recorded are the difference in β values between the highest occupied molecular orbital and lowest unoccupied molecular orbital for each structure.

Table XVI. Molecular orbital calculation results on tautomeric structures of substituted dienones.

Structure	Total π Energy (β) Hückel	Total π Energy (β) "ω" technique	(m+1)-(m) (β)	Longest absorption wave length (mμ)	Deviation from Line (β)	Symbol
19	18.6946	13.7767	1.2347	251	0.32	•
20	18.8341	13.8946	0.9757	251	0.57	□
48	18.3715	13.5924	1.0059	278		○
49	18.4434	13.6649	0.9385	278		ϕ
51	18.1674	13.4411	0.9949	348		o^{-2}
52	18.1674	13.4411	0.9949	343		
21	30.2735	25.1604	0.8714	300-315	0.08	•
53	29.8206	24.7198	1.1800	300-315	0.23	□
55	30.1330	25.2904	1.0841	340		○
54	29.6742	24.8082	1.0572	340		ϕ
29 and 22	24.0557	19.6138	0.9536	R=CH_3 335 R=H 330	0.13	•
66 and 60	24.0089	19.5578	0.9518	R=CH_3 335 R=H 330	0.13	□
99	24.4449	19.4572	1.1800	R=CH_3 335 R=H 330	0.36	□

Table XVI. (Continued)

Structure	Total π Energy (β) Hückel	"ω" technique	(m+1)-(m) (β)	Longest absorption wavelength (mμ)	Deviation from Line (β)	Symbol
65	24.0141	19.2077	1.2116	R=CH_3 350 R=H 345		
100	23.4303	19.1367	1.0388	R=CH_3 350 R=H 345		
33	12.0472	9.5472	1.3696	258		
101	11.6344	9.3015	1.2431	279		
32	17.7960	15.2207	1.2948	277 241		
41	26.0268	23.3759	0.8959	310-345		
56	25.8128	23.4274	0.9539	398		
57	17.2177	14.8503	1.4469	277		



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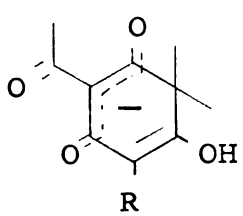

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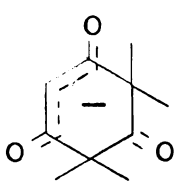

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The calculations (Table XVI) agree extremely well with the structures assigned on the basis of spectroscopic evidence. The only exception is filicinic acid itself. In this case the fully conjugated structure, 20, was predicted by calculations to be more stable than the cross-conjugated structure, 19; the latter was assigned on the basis of spectral evidence. For all the other compounds, that structure predicted by molecular orbital calculations to be most stable was the structure which predominated, as deduced experimentally. The agreement for anion structures was also good, with the exception of the monoanion of filicinic acid.

Additional evidence for structure assignments were obtained by plotting the difference in energy, Δm, (in terms of β) between the highest occupied and lowest unoccupied molecular orbitals against the longest uv absorption wavelength for each compound (Fig. XV). These were compared to a curve obtained by plotting similar values for a series of related compounds with known structures, (Table XVII); see Fig. XVI. For most of these compounds there was quite good agreement between absorption wavelength and Δm. The compounds from Table XVI were plotted in a similar way. The assigned structures for the neutral compounds gave good agreement with the line obtained in the previous graph. By taking the deviation from the line in terms of β, structure preferences were obtained (Table XVI). The structure which had the smallest deviation would be preferred. As

Table XVII Molecular orbital calculation results on standard compounds containing oxygen atoms

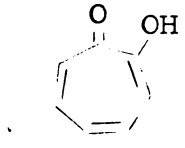
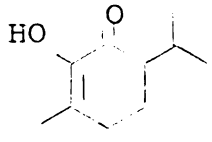
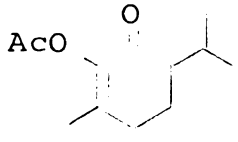
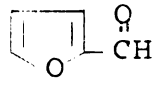
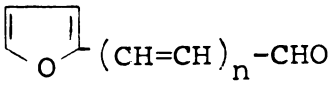
Compound	m	UV absorption (mμ)	Symbols
$CH_3(CH{=}CH)_n{-}\overset{O}{\overset{\|}{C}}{-}H$			
n = 1	1.7130	220	.
n = 2	1.1106	271	.
n = 3	0.8202	315	.
n = 4	0.6499	351(353)	.
n = 5	0.5381	377	.
n = 6	0.4591	399	.
n = 7	0.4003	424	.
$CH_3{-}\overset{OH}{\overset{\|}{C}}{=}CH{-}\overset{O}{\overset{\|}{C}}{-}OEt$	1.4226	245	o
	0.8641	380	o
	1.2635	274	o
	1.3107	240	o
	1.5032	270	x

Table XVII. (Continued).

Compound	m	UV absorption (mμ)	Symbols
			
n = 1	1.0131	312	x
n = 2	0.7613	346	x
n = 3	0.6092	366	x
n = 4	0.5076	389	x
n = 5	0.4350	412	x
n = 6	0.3806	429	x

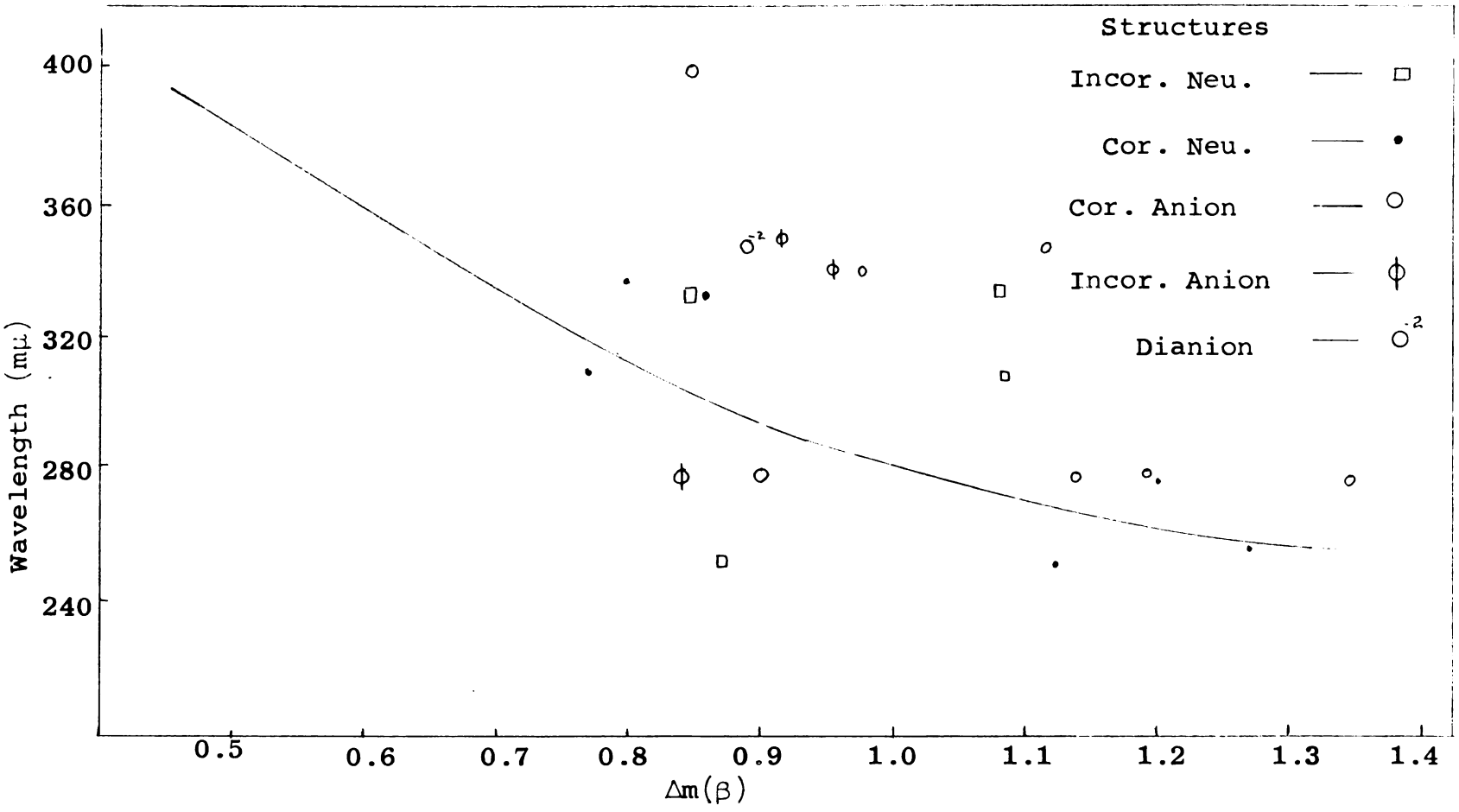


Fig. XV. Plot of absorption wavelength vs difference in energy of highest occupied and lowest unoccupied molecular orbitals of substituted cyclohexadienones.

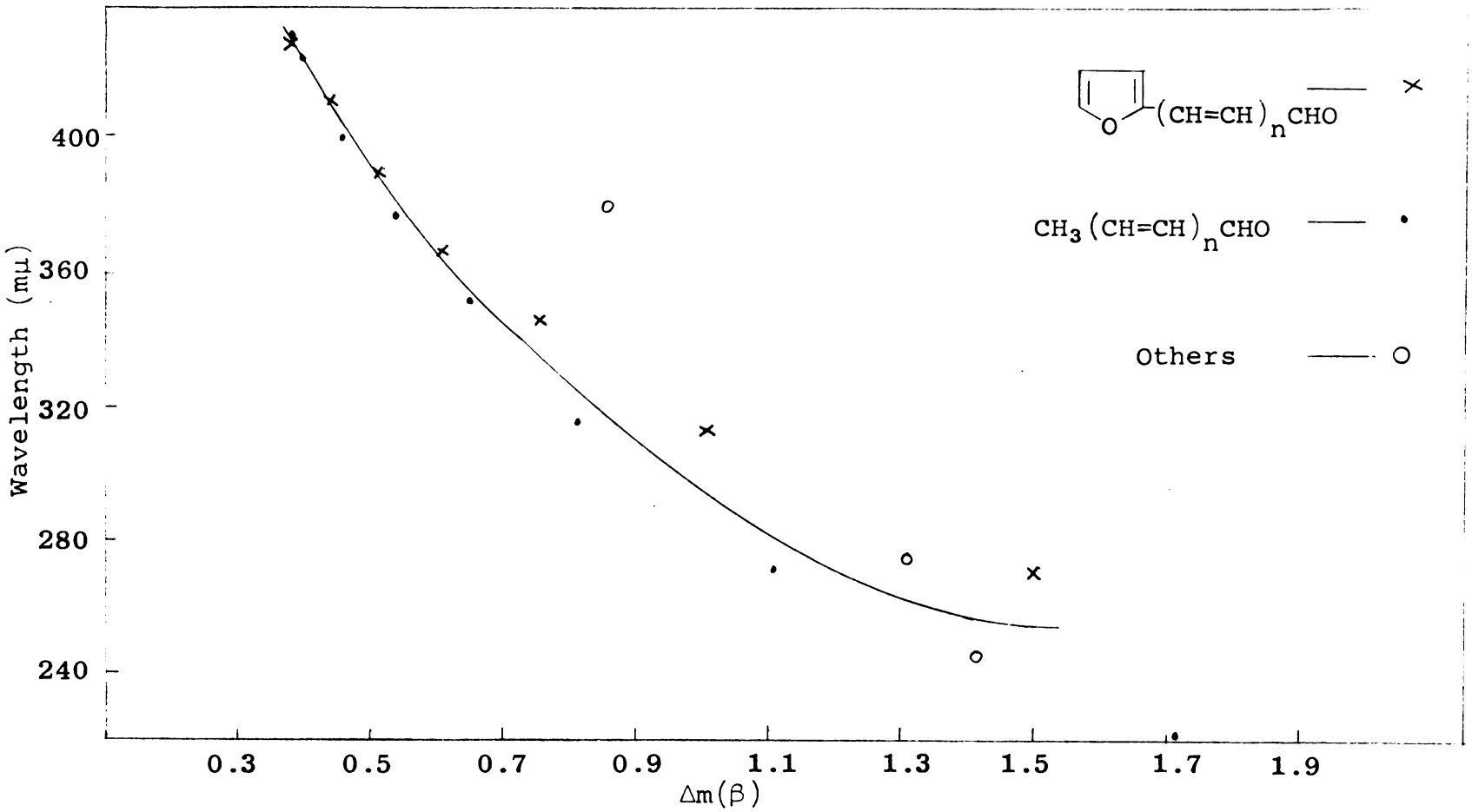


Fig. XVI. Plot of absorption wavelength vs difference in energy of highest occupied and lowest unoccupied molecular orbitals of standard compounds containing oxygen atoms.

can be seen from Table XVI structure 19 (for filicinic acid) was favored over that of 20. For diacetylfilicinic acid 21 was favored over 53. Both agree with the spectroscopically assigned structures. For acetylfilicinic acid (and acetylmethylfilicinic acid) this method did not distinguish between the two fully conjugated systems, 22, 60 and 29, 66, but did favor these over the cross-conjugated structures. For the anions most points appeared to be above the line, and perhaps should have a relation of their own, different from the neutral compounds. Most of the calculations for the anions are inconclusive using this method as they do not distinguish between structures.

On the whole, there was good agreement between the molecular orbital calculations and the structures assigned for the derivatives of filicinic acid and related compounds.