protons 4 and 7, and a multiplet at 6.01–6.13 (2 H) protons 3 and 8. When $CDCl_3$ was used as solvent the olefinic protons appeared as a triplet (J = 3.0 Hz). The mass spectrum showed a molecular ion at m/e 282.0907 (calcd for $C_{18}H_{10}N_4$: 282.0905).

Reaction of I with Dimethyl Acetylenedicarboxylate. A solution of I (0.30 g) and dimethyl acetylenedicarboxylate (0.30 g) in xylene (5 ml) was boiled under reflux for 48 hr. The xylene was removed under reduced pressure and the residue adsorbed on to an alumina plate (Merck, 1000 × 20 × 0.1 cm) and eluted with 30% ether–petroleum ether. Benzocyclooctatetraene (0.25 g) was obtained from the front-running band (which appeared as a dark band under ultraviolet light). A second band (which appeared as a bright-blue fluorescent band under short-wavelength ultraviolet light) was removed, extracted with chloroform and concentrated, to give the adduct XXXII (25 mg, 26%) as a pale yellow oil. This oil crystallized on standing to form very pale yellow prisms, mp 75–77°. The electronic spectrum (EtOH) had λ_{max} 213, 272, and 282 nm (ϵ 12,100, 3100, and 2200) and λ_{infl} 258 nm (ϵ 3400). The infrared spectrum ($CHCl_3$) had, *inter alia*, bands at 1725 (C=O), 1655, and 1590 (C=C) cm^{-1}. The nmr spectrum (60 MHz) exhibited a singlet at τ 2.86 (4 H) due to the aromatic protons, a hextet centered at 3.71 (2 H) protons 2 and 5, an asymmetric hextet at 4.35 (2 H) protons 3 and 4, a doublet centered at 5.76 (2 H, J = 8.5 Hz) due to protons 1 and 6, and a singlet at 6.26 (6 H) methoxyl protons. The mass spectrum had a molecular ion at m/e 296.1050 (calcd for $C_{18}H_{16}O_4$: 296.1049).

Photodimeric Cage Compounds. IV. Transformations of the Cyclobutenes Formed on Degradation of the Photodimers of 2,6-Dimethyl- and 2,6-Diethyl-4-pyrone[1]

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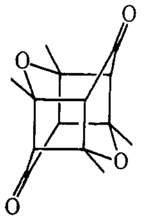
Contribution from the Departments of Chemistry, Harvard University, Cambridge, Massachusetts 02138, and the University of Toronto, Toronto, Ontario, Canada. *Received March 19, 1969*

Abstract: 3,4-Dihydroxy-2,4-dimethyl-1-cyclobutenecarboxylic acid (**3**), a degradation product from the photodimer of 2,6-dimethyl-4-pyrone, is converted by acid to 5,5-bis[2-(3,5-dimethylfuryl)]-4-methylpentanone (**4**), by pyrolysis to 1,6-dimethyl-3-[2-(4-oxopentyl)]-2,4-dioxabicyclo[3.2.0]hept-6-ene-7-carboxylic acid (**7**), and by base to 2-methyl-5-oxo-1-cyclopentenecarboxylic acid (**10**). The formation of the pyrolysis product and of an acetal on treatment with acetone establish that the cyclobutene is the *cis* isomer. On hydrogenation it gives two diastereomeric 2,3-dihydroxy-2,4-dimethylcyclobutanecarboxylic acids (**17**), whose stereochemistry is assigned on the basis of their conversion to the two diastereomers of 4-hydroxy-3-methyl-5-oxohexanoic acid lactone (**20**). These lactones were synthesized independently, and stereochemical assignments were made to them on the basis of equilibration studies. Analogous observations have been made on hydrogenation of the corresponding degradation product from the photodimer of 2,6-diethyl-4-pyrone.

The photodimer of 2,6-dimethyl-4-pyrone has been shown to have the cage structure **1**.[3] In the course of the structural elucidation **1** was converted to the dilactone **2**, which on hydrolysis gave 3,4-dihydroxy-2,4-dimethyl-1-cyclobutenecarboxylic acid, **3**. This compound, which combines several reactive functional groups in a small compass, undergoes a variety of interesting transformations, which we describe here.



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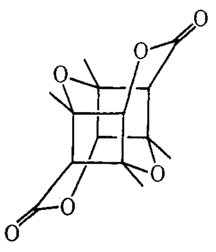

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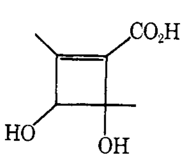

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Treatment of **3** with hot 10% hydrochloric acid gave a crystalline product with the empirical formula C_6H_8O. Its molecular formula was indicated to be $C_{18}H_{24}O_3$ by the fact that it formed a 2,4-dinitrophenylhydrazone, $C_{24}H_{28}N_4O_6$. The infrared spectrum of the compound $C_{18}H_{24}O_3$ showed bands at 5.86, 6.21 (w), 6.33 (w), and 7.33 μ. The ultraviolet spectrum of the 2,4-dinitrophenylhydrazone showed a long-wavelength maximum at 362 mμ (ϵ 22,900), demonstrating the presence of an unconjugated carbonyl group in the parent compound, which was also indicated by the band at 5.86 μ in the infrared spectrum of the latter. The band at 7.33 μ in this spectrum suggested that the carbonyl function was a methyl ketone, and this was confirmed by a positive iodoform test. The absence of a carbonyl band in the infrared spectrum of the 2,4-dinitrophenylhydrazone and of a hydroxyl stretching band in the infrared spectrum of the parent compound, led to the assignment of two of the oxygen atoms in the latter to ether linkages. The weak bands at 6.21 and 6.33 μ in the infrared spectrum of the parent compound, a maximum in its ultraviolet spectrum at 225 mμ (ϵ 14,000), and its resistance to catalytic hydrogenation favored the assignment of these two oxygen atoms to furan rings.[4–6] These con-

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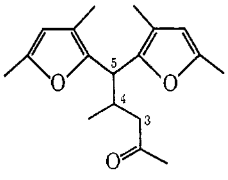
(1) Paper III: P. Yates, E. S. Hand, P. Singh, S. K. Roy, and I. W. J. Still, *J. Org. Chem.*, in press.

(2) (a) Lash Miller Chemical Laboratories, University of Toronto, Toronto, Ontario, Canada; Alfred P. Sloan Foundation Fellow, 1957–1960; (b) National Institutes of Health Fellow, Harvard University, 1957–1958; (c) Commonwealth Scholar, University of Toronto, 1963–1966.

(3) P. Yates and M. J. Jorgenson, *J. Amer. Chem. Soc.*, **85**, 2956 (1963).

(4) C. N. R. Rao, "Chemical Applications of Infrared Spectroscopy," Academic Press, New York, N. Y., 1963, p 324.

clusions regarding the functional groups and the origin of the compound $C_{18}H_{24}O_3$ led to the assignment to it of structure **4**.



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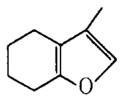
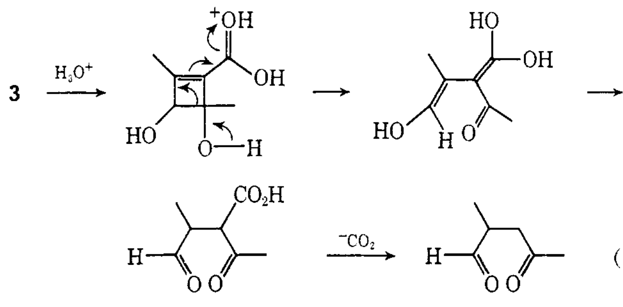


5

This structural assignment is in excellent accord with the observed ultraviolet spectrum [*cf.* the spectrum of the trisubstituted furan **5**: λ_{max} 222.5 mμ (ϵ 6300)[6]] and is corroborated by the nmr spectrum. This showed a three-proton doublet at δ 0.84 ppm (J = 6 Hz) which is assigned to the protons of the methyl group at C-4. A six-proton singlet at δ 1.88 ppm and a similar singlet at δ 2.21 ppm are assigned to the protons of the methyl groups at the β and α positions of furan rings, respectively.[7–9] A three-proton sharp singlet at δ 2.03 ppm is in accord with the presence of an acetyl methyl group. The singlet at δ 2.21 ppm is superimposed on a multiplet at δ 2.2–2.4 ppm; the group of signals as a whole corresponds to nine protons, and the multiplet can be assigned to the C-3 and C-4 protons. A one-proton doublet at δ 3.76 ppm (J = 11 Hz) is assigned to the proton at C-5; the large coupling constant can be attributed to the expected marked preference for the conformation of **4** in which the protons at C-5 and C-4 have a *trans* relationship. A two-proton broad singlet at δ 5.74 ppm is assigned to the furan ring protons: the position of this signal is in good accord with the assignment of a structure with these protons at the β position; had they been at the α position the signal would have appeared at lower field.[9,10]

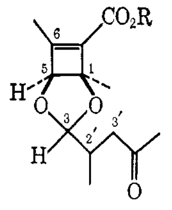
Compound **4** is considered to arise *via* conversion of **3** to 2-methyl-1,4-pentanedione (**6**) as in (1), for example. Acid-catalyzed dehydration of **6** could give 2,4-dimethylfuran;[11] acid-catalyzed condensation of this with compound **6** would be expected to occur preferentially at the α position of the furan rings to give **4**.[12,13] The involvement of the keto aldehyde **6** as an intermediate is corroborated by the fact that when **3** was treated with acid under milder conditions compound **6** could be isolated. It was identified by its spectra (see Experimental Section) and by its conversion to the corresponding bis-2,4-dinitrophenylhydrazone.[3]



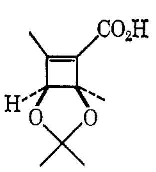
(1)

6

Pyrolysis of **3** at its melting point leads to gas evolution and the formation of a crystalline acidic compound, $C_{13}H_{18}O_5$. This showed bands in its infrared spectrum at 3–4 (br), 5.87, 5.92, 6.03 (w), and 7.37 μ (m) and an ultraviolet maximum at 213 mμ (ϵ 10,000). On mild acid-catalyzed hydrolysis it afforded 2-methyl-1,4-pentanedione (**6**). The relationship of its spectra to those of **3** [λ_{max}^{KBr} 3.02, 3–4, 5.92, and 5.99 μ (sh); λ_{max}^{EtOH} 213 mμ (ϵ 9330)] indicated that it possesses a closely related chromophore, but lacks free alcoholic hydroxyl groups. The bands at 5.87 and 7.37 μ in its infrared spectrum suggested the presence of a methyl ketone grouping (*cf.* **4** and **6**), which was also indicated by a positive iodoform test. On the basis of these data and its origin, the pyrolysis product is considered to have structure **7**.



7, R = H
8, R = CH_3



9

This structure readily accounts for the formation of **6** on hydrolysis [*cf.* (1)] and is corroborated by the nmr spectrum of the pyrolysis product. A three-proton singlet at δ 1.58 ppm and two singlets at δ 2.08 and 2.15 ppm that correspond together to six protons are assigned, respectively, to the C-1 methyl protons and the C-6 and acetyl methyl protons. A three-proton multiplet at δ 2.3–2.7 ppm is assigned to the methine and methylene protons at C-2′ and C-3′. A broad one-proton singlet at δ 4.51 ppm and a broad one-proton doublet at δ 4.83 are assigned to the methine protons at C-5 and C-3, respectively. The methyl group at C-2′ gives rise to a three-proton signal at δ 0.99 ppm that appears as a broad doublet with further splitting; this splitting pattern is considered to be due to virtual coupling[14,15] with the protons at C-3′ in addition to coupling with the C-2′ proton. Closely related effects have previously been observed for the methyl protons of 3-methylglutaric acid and 3-methylcyclohexanone.[14] Esterification of **7** with diazomethane gave a monomethyl ester which showed a similar signal at δ 0.97 ppm in its nmr spectrum making it unlikely that the complexity of the signal in the spectrum of **7** is attributable to lack of homogeneity. The other spectral features of the methyl ester, which include bands at 5.81 (sh), 5.84, and 6.02 μ (w) in its infrared spectrum and a three-proton

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(5) M. Fétizon and P. Baranger, *Bull. Soc. Chim. Fr.*, [5] **24**, 1311 (1957).

(6) H. Minato and T. Nagasaki, *J. Chem. Soc., C*, 377 (1966).

(7) P. Yates and I. W. J. Still, *J. Amer. Chem. Soc.*, **85**, 1208 (1963).

(8) J. R. Dyer, "Applications of Absorption Spectroscopy of Organic Compounds," Prentice-Hall, Inc., Englewood Cliffs, N. J., 1965, p 103.

(9) E. J. Corey, G. Slomp, S. Dev, S. Tobinaga, and E. R. Glazier, *J. Amer. Chem. Soc.*, **80**, 1204 (1958).

(10) L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, New York, N. Y., 1959, p 64.

(11) R. C. Elderfield and T. N. Dodd, Jr., in "Heterocyclic Compounds," Vol. 1, R. C. Elderfield, Ed., John Wiley & Sons, Inc., New York, N. Y., 1950, pp 127–128.

(12) A. R. Katritzky and J. M. Lagowski, "Heterocyclic Chemistry," John Wiley & Sons, Inc., New York, N. Y., 1960, pp 162, 166–167.

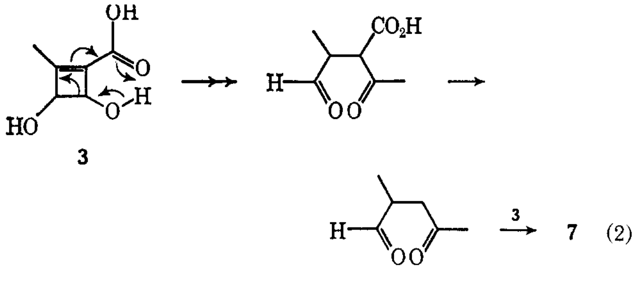
(13) P. Bosshard and C. H. Eugster, *Advan. Heterocyclic Chem.*, **7**, 402 (1966).

(14) F. A. L. Anet, *Can. J. Chem.*, **39**, 2262 (1961).

(15) J. I. Musher and E. J. Corey, *Tetrahedron*, **18**, 791 (1962).

signal at δ 3.77 ppm in its nmr spectrum, support the assignment to it of structure **8**.

The formation of **7** can be envisaged as occurring *via* formation of **6** from **3** as in (1) or (2) and acetal formation by reaction of this with **3** in the melt.

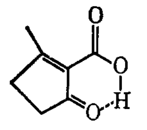


3

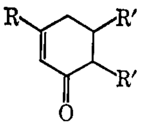
6

Although the crystalline sample of **7** that was isolated appeared to be a single diastereomer, its stereochemistry is unknown except in one respect—the *cis* fusion of the cyclobutene and ketal rings. This is in accord with the assignment of a *cis* relationship to the hydroxyl groups of **3**, as required by the mechanism proposed for its formation from **2**.[3] Independent confirmation of this stereochemistry for **3** was obtained by its conversion to the ketal **9** by reaction with acetone in the presence of anhydrous cupric sulfate.[16] The nmr spectrum of **9** showed the expected relationship with that of **7** with three-proton singlets at δ 1.63 and 2.10 ppm for the C-4 and C-2 methyl protons, respectively, and a one-proton singlet at δ 4.64 ppm for the methine proton at C-3. The signals due to the geminal methyl protons were superimposed and appeared as a six-proton signal at δ 1.44 ppm. The carboxylic acid proton signal, which was not recorded in the case of **7**, appeared as a broad singlet at δ 10.87 ppm.

Brief treatment of **3** with hot aqueous 2.5% sodium hydroxide followed by acidification gave a crystalline product, $C_7H_8O_3$. This showed bands in its infrared spectrum at 3–4.1, 5.73, 5.97, and 6.13 μ and an ultraviolet maximum at 232 mμ (ε 10,500); its nmr spectrum ($CDCl_3$) showed a complex multiplet at δ 2.6–2.9 ppm and a broad signal at δ 11.20 ppm. These spectra clearly indicated the presence of a carboxylic acid group, and this was corroborated by the solubility of the product in aqueous sodium bicarbonate. The compound formed a mono-2,4-dinitrophenylhydrazone, shown to be that of a conjugated carbonyl compound by a long-wavelength ultraviolet maximum at 376 mμ (ε 27,500). This evidence and the origin of the product, $C_7H_8O_3$, led to its formulation as **10**.



10

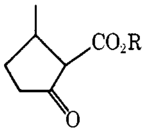


11, R = CO_2H; R′ = OH
12, R = CH_3; R′ = H

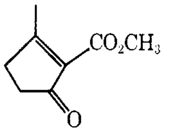
The infrared spectrum of the 2,4-dinitrophenylhydrazone showed the carbonyl-stretching band of the carboxylic acid group at 5.76 μ, strongly suggesting the assignment of the band at 5.73 μ in the spectrum of **10** to the carboxylic acid group and the band at 5.97 μ to the conjugated ketone group. This indicates that the acid **10** exists in the monomeric rather than the dimeric form,[17] a circumstance that can be attributed to the opportunity for strong intramolecular hydrogen bonding in the monomer as indicated in **10**. The bathochromic shift of the ketonic carbonyl-stretching band expected to result from this hydrogen bonding occurs, since 2-cyclopentenones normally absorb at *ca.* 5.85 μ.

Carboxylic acid groups appear to exert much the same effect as alkyl groups on the position of the $\pi \rightarrow \pi^*$ band in the ultraviolet spectra of α,β-unsaturated ketones when they are present as substituents on the ethylenic double bond: *cf.*, for example, **11** [$\lambda_{\max}^{\mathrm{EtOH}}$ 234 mμ (ε 12,100)][18] and **12** [$\lambda_{\max}^{\mathrm{EtOH}}$ 235 mμ (ε 12,900)].[19] Thus the position of the ultraviolet maximum for **10** is in good accord with this structure, since 2,3-dialkyl-2-cyclopentenones are reported to show maxima in the range 236 ± 5 mμ.[20] Although in the nmr spectrum of **10** in $CDCl_3$ the signals of all the protons except the carboxylic acid proton fall close together, it is possible to discern the signal due to the methyl protons at δ *ca.* 2.7 ppm. The spectrum of **10** in benzene shows a three-proton singlet at δ 2.30 ppm, assigned to the methyl group, and a four-proton multiplet at δ 1.8–2.0 ppm, assigned to the ring protons, together with a broad one-proton signal at δ 12.42 ppm. The position of the methyl proton signals in these spectra relative to those of the methylene protons must reflect the strong deshielding effect on them of the carbonyl group of the carboxylic acid.

The assignment of structure **10** was confirmed in the following ways. Hydrogenation of **10** proceeded with the uptake of one molar equivalent of hydrogen forming a liquid product that gave a positive ferric chloride test and whose spectra were in accord with its formulation as 5-methyl-2-oxocyclopentanecarboxylic acid (**13**). This on treatment with 2,4-dinitrophenylhydrazine reagent gave the 2,4-dinitrophenylhydrazone of 3-methylcyclopentanone, which was characterized by direct comparison with an authentic sample. Methylation of **10** gave the methyl ester **14**, which on hydrogenation gave the ester **15**, characterized as its semicarbazone. This was shown to be identical with the semicarbazone of an authentic sample of **15** prepared by ozonolysis of methyl pulegenate (**16**).



13, R = H
15, R = CH_3



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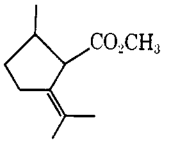

16

The formation of **10** from **3** is considered to occur by a route of the type shown in (3).

Hydrogenation of **3** over palladium-charcoal proceeded with the uptake of 1 molar equiv of hydrogen and gave a crystalline product and an oil in a 3:1 ratio. The former product was identical with the 2,3-dihy-

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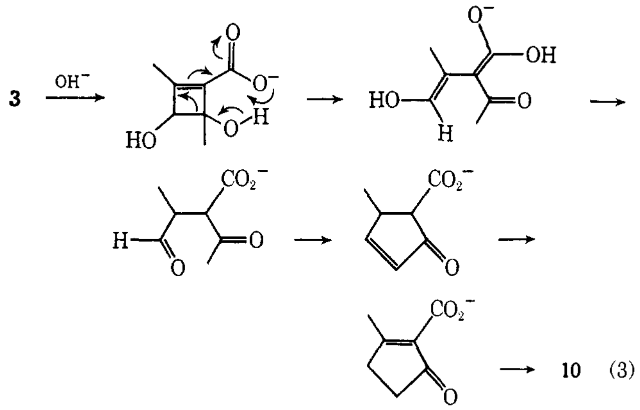
[16] *Cf.* I. Salamon and T. Reichstein, *Helv. Chim. Acta*, **30**, 1929 (1947); R. B. Woodward, F. Sondheimer, D. Taub, K. Heusler, and W. M. McLamore, *J. Amer. Chem. Soc.*, **74**, 4223 (1952).

[17] Reference 4, p 209; J. F. Grove and H. A. Willis, *J. Chem. Soc.*, 877 (1951).

[18] I. I. Salamon and B. D. Davis, *J. Amer. Chem. Soc.*, **75**, 5567 (1953).

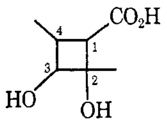
[19] L. K. Evans and A. E. Gillam, *J. Chem. Soc.*, 565 (1943).

[20] A. E. Gillam and T. F. West, *ibid.*, 811 (1941); 486 (1942); R. L. Frank, R. Armstrong, J. Kwiatek, and H. A. Price, *J. Amer. Chem. Soc.*, **70**, 1379 (1948); H. S. French, *ibid.*, **74**, 514 (1952).

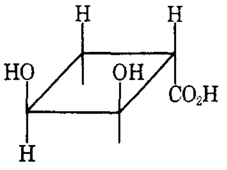


droxy-2,4- dimethylcyclobutanecarboxylic acid (**17**) previously obtained from this reaction.[3] It showed in its nmr spectrum in D_2O signals at δ 1.19 (d, J = 6.5 Hz, 3 H), 1.41 (s, 3 H), 2.6–3.2 (m, 2 H), and 3.89 ppm (br d, J = 8.5 Hz, 1 H), assignable to the C-4 methyl, C-2 methyl, C-1 and C-4 methine, and C-3 methine protons, respectively. It was stable at room temperature, but was converted to a lactone when heated with acid. The oily product showed infrared and nmr spectra that were similar to those of the crystalline product; it was very unstable and was converted to a lactone on standing at room temperature or on being chromatographed on silica. A completely pure sample of the oily product was not obtained since a very weak band in the infrared spectra of all samples showed contamination with a trace of lactonic impurity.

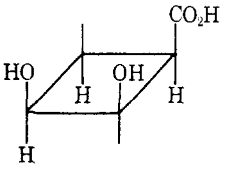
Hydrogenation of *cis*-**3** under mild conditions would be expected to give **18** and **19**, two diastereomers of **17**. The crystalline product is assigned structure **18** in which the carboxylic acid group is *trans* with respect to the hydroxyl groups, while the unstable oily product is considered to be its diastereomer, **19**, in which the carboxylic acid group is *cis* with respect to the hydroxyl groups. These assignments were confirmed by an examination of the lactones formed from the two hydrogenation products.



17

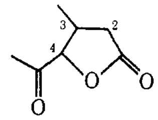


18



19

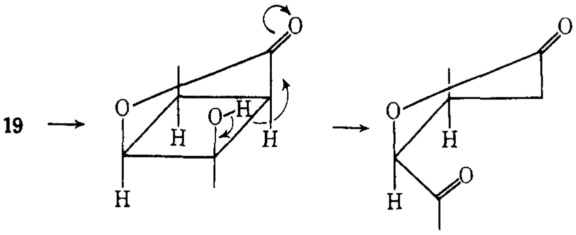
The lactone from the oily hydrogenation product showed bands in its infrared spectrum at 5.60, 5.82, and 7.35 μ (m) and was characterized as its 2,4-dinitrophenylhydrazone, which retained a band at 5.60 μ in its infrared spectrum. These data and its nmr spectrum suggested the assignment to it of the gross structure **20**.



20

The latter spectrum showed signals at δ 1.25 (d, J = 6.5 Hz, 3 H), 2.25 (s, 3 H), 2.35–2.85 (m, 3 H), and 4.40 (d, J = 6.5 Hz, 1 H) ppm assignable to the C-3 methyl, acetyl, C-2 methylene and C-3 methine, and C-4 methine protons, respectively. The position of the carbonyl-stretching band in the infrared spectrum is at somewhat shorter wavelength than normal for a simple γ-lactone. However, it is known that this band is shifted in this direction in the case of γ-lactones with electron-withdrawing substituents at C-4.[21,22] The position of the long-wavelength ultraviolet maximum (λ_{max} 352 mμ) of the 2,4-dinitrophenylhydrazone of **20** is also in good accord with this structural assignment. A hypsochromic shift of 8 mμ from the normal position at 362 mμ for the 2,4-dinitrophenylhydrazone of an unconjugated ketone has been found to be general for the 2,4-dinitrophenylhydrazones of α-acyloxy ketones.[23]

The facile formation of the lactone **20** from the oily hydrogenation product leads to the assignment of structure **19** to the latter, which is considered to give rise to **20** by the route shown in (4). This relationship requires that the lactone have the stereochemistry depicted in **21**. Its nmr spectrum and the relationship of this spectrum to that of its C-3 epimer can be interpreted in terms of the preponderance of **21a** as the preferred conformation of **21** (*vide infra*).



(4)

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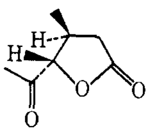

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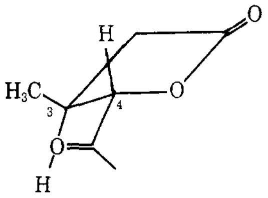


21a

As referred to above, the crystalline hydrogenation product from *cis*-**3** also can be converted to a lactone; the conversion, however, is much less facile than in the case of the oily hydrogenation product and requires treatment with aqueous acid or prolonged standing in ethanolic solution. The lactone thus formed is isomeric with **21**, as shown by the composition of its 2,4-dinitrophenylhydrazone. Its infrared spectrum and the infrared and ultraviolet spectrum of its 2,4-dinitrophenylhydrazone resemble closely those of **21**. The nmr spectra of the two lactones are also similar, that of the lactone from the crystalline hydrogenation product showing signals at δ 1.03 (d, J = 6.5 Hz, 3 H), 2.25 (s, 3 H), 2.3–3.05 (m, 3 H), and 4.89 (d, J = 7 Hz, 1 H) ppm. It is assigned structure **22**, epimeric with **21** at C-3, and is considered to exist predominantly in the conformation **22a**. The conformational assignments **21a** and **22a** permit reasonable interpretations of the nmr spectra of the two lactones. Thus the similarity of the coupling constants between the C-3 and C-4 protons is in accord

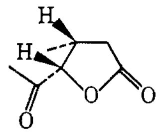
(21) R. B. Woodward and E. G. Kovach, *J. Amer. Chem. Soc.*, **72**, 1009 (1950).

(22) T. J. Mabry, H. E. Miller, H. B. Kagan, and W. Renold, *Tetrahedron*, **22**, 1139 (1966).

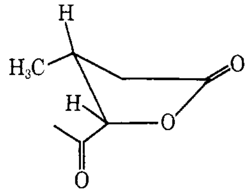
(23) F. Ramirez and A. F. Kirby, *J. Amer. Chem. Soc.*, **76**, 1037 (1954).

with the magnitudes of the dihedral angles between the corresponding C–H bonds. The fact that the C-3 methyl proton signal for **22a** is at significantly higher field than that for **21a** can be attributed to the different relationship of this group to the plane of the acetyl carbonyl group in the two structures.[24] Finally, the fact that the C-4 proton signal for **21a** is 0.5 ppm to higher field than that for **22a** can be accounted for in terms of both the deshielding effect of the carbonyl group in **22a** and the shielding effect of the C-3–methyl bond in **21a**.[25]

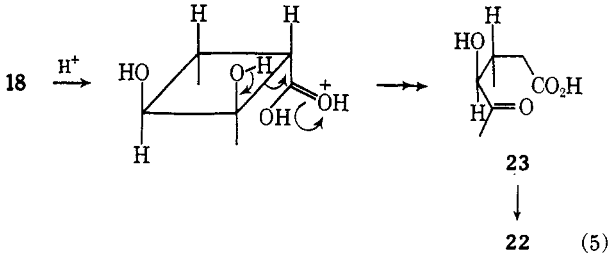
The formulation of the lactone from the crystalline hydrogenation product as **22** is in accord with the formulation of the latter product as **18**. Its formation could occur by the pathway shown in (5), provided that it is assumed that significant epimerization of the acyclic intermediate **23** does not occur under the reaction conditions. An alternative pathway could involve initial epimerization at C-1 in **18** followed by a reaction sequence analogous to (4) in which γ-lactone formation occurs prior to cleavage of the cyclobutane ring.



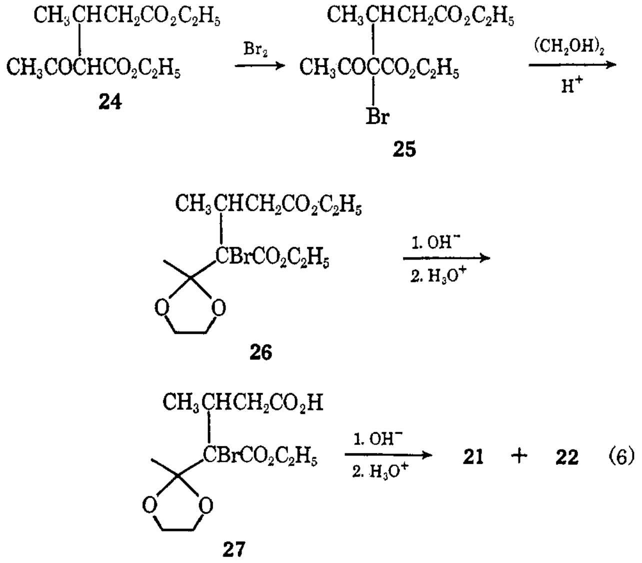
22



23a

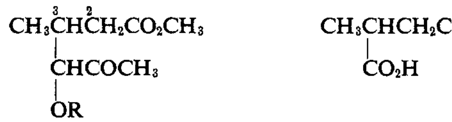


The assignment of structures **21** and **22** to the two lactones was confirmed by their independent synthesis by the route shown in (6). Bromination of the keto diester **24** gave the monobromo compound **25**; treatment of this with aqueous sodium hydroxide gave a product whose nmr spectrum showed the absence of an acetyl group, indicating that base-catalyzed cyclization had occurred. Compound **25** was therefore converted to the ketal **26** and this was treated with 2 molar equiv of aqueous sodium hydroxide for 10 hr followed by acidification. This treatment served only to hydrolyze the nonquaternary ester group to give the acid **27**; this was isolated as a sharp-melting crystalline solid that most probably corresponds to a single diastereomer of **27**. Prolonged treatment of **27** with boiling aqueous sodium hydroxide followed by acidification gave a mixture of the two lactones **21** and **22**; these were separated by chromatography and shown to be identical with the products obtained from the hydrogenation products of *cis*-**3**.



The individual stereochemical assignments to **21** and **22** were confirmed by the equilibration of the two lactones with potassium carbonate in xylene at reflux for 1 day.[26] Analysis of the product obtained from the lactone assigned structure **22** showed it to be a mixture of this lactone and the lactone assigned structure **21** in a *ca.* 1:8 ratio. Similar treatment of the latter lactone gave a mixture of lactones in which **22** and **21** were present in a *ca.* 1:7 ratio. These observations confirm the stereochemical assignments, since the lactone **21** with the *trans* disposition of the methyl and acetyl groups would be expected to be more stable than the lactone **22** with the *cis* disposition of these groups. The confirmation of these assignments also corroborates the stereochemical assignments **18** and **19** for the hydrogenation products of *cis*-**3**.

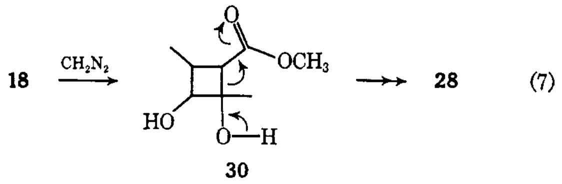
Treatment of the hydrogenation product **18** with methanolic ethereal diazomethane gave a product with bands at 2.85 (m), 5.76, 5.83, and 7.36 μ (m) in its infrared spectrum; this was characterized as its 2,4-dinitrophenylhydrazone, which showed a band at 5.78 μ in its infrared spectrum and a long-wavelength ultraviolet maximum at 359 mμ (ε 19,800). On prolonged standing at room temperature it was converted to a mixture of the lactones **21** and **22**. This product is assigned structure **28** on the basis of these data and its nmr spectrum which showed signals at δ 0.75 (d, $J = 6.5$ Hz, 3 H), 2.23 (s, 3 H), 2.4–3.0 (m, 3 H), 3.49 (br s, concentration dependent, 1 H), 3.70 (s, 3 H), and 4.27 (br s, 1 H) ppm, assigned to the protons of the C-3 methyl, acetyl methyl, C-2 methylene and C-3 methine, hydroxyl, methyl ester, and C-4 methine groups, respectively. This structural assignment was confirmed by



$$\begin{array}{l} \mathrm{CH_3\overset{3}{C}H\overset{2}{C}H_2CO_2CH_3} \\ \quad\mathrm{|} \\ \quad\mathrm{CHCOCH_3} \\ \quad\mathrm{|} \\ \quad\mathrm{OR} \end{array} \qquad \begin{array}{l} \mathrm{CH_3CHCH_2CO_2CH_3} \\ \quad\mathrm{|} \\ \quad\mathrm{CO_2H} \end{array}$$

28, R = H **29**

31, R = 3,5-$(NO_2)_2C_6H_3CO$



30

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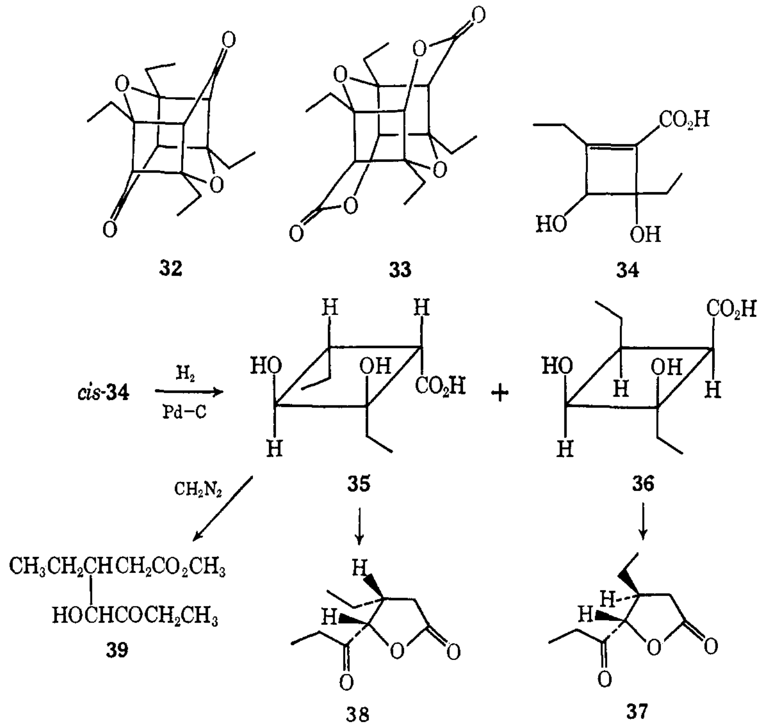
[24] *Cf.* M. J. Jorgenson, A. J. Brattesani, and A. F. Thacher, *J. Org. Chem.*, **34**, 1103 (1969).

[25] J. I. Musher, *J. Chem. Phys.*, **35**, 1159 (1961); G. Closs and J. J. Coyle, *J. Amer. Chem. Soc.*, **87**, 4270 (1965).

[26] *Cf.* W. Cocker, B. E. Cross, and C. Lipman, *J. Chem. Soc.*, 959 (1949); *Tetrahedron*, **8**, 181 (1960).

Scheme I



oxidation of **28** with chromic acid, which gave a product whose spectroscopic properties are in excellent accord with the assignment to it of structure **29**, followed by hydrolysis, which gave methylsuccinic acid. The fact that both lactones **21** and **22** are formed from **28** on standing indicates that epimerization occurs at C-4. Compound **28** is considered to arise *via* **30**, the methyl ester of **18**, as shown in (7). Treatment of **18** with ethereal diazomethane has previously been reported to give the ester **30**.[3] It is probable that the formation of **28** in the present case was due to catalysis of the conversion of **30** to **28** by either the methanol used as cosolvent or the silica used for chromatographic purification. It may be noted that treatment of **30** with 3,5-dinitrobenzoyl chloride and pyridine was found to give **31**, the 3,5-dinitrobenzoate of **28**.[3,27]

Treatment of the oily hydrogenation product **19** with methanolic ethereal diazomethane gave a crude product whose infrared spectrum showed both ester and lactone bands; chromatography gave only the lactone **21**. This was also formed, together with its epimer, **22**, when **19** was treated with 3,5-dinitrobenzoyl chloride and pyridine.

The photodimer of 2,6-diethyl-4-pyrone has been shown to have the head-to-tail cage structure **32**, analogous to **1**; it has been converted *via* the dilactone **33** to a dihydroxy acid assigned structure **34** in analogy to the formation of **3** from **1**.[1] This dihydroxy acid has been found to give a crystalline and an oily product, **35** and **36**, on hydrogenation whose spectral properties are entirely analogous to those of **18** and **19** (see Experimental Section). Furthermore, these products have been shown to give stereoisomeric lactones, **37** and **38**, that are the analogs of **21** and **22**, and the crystalline product has been found to give on treatment with diazomethane a product, **39**, analogous to **28**.[28] The structural assignment **34** is thus confirmed, and it can be designated as the *cis* isomer. Its transformation is summarized in Scheme I. The confirmation of structure **34** for the dihydroxy acid corroborates the assignment of the head-to-tail structure **32** to the photodimer, which has been made on other grounds.[1]

Experimental Section

Melting points and boiling points are uncorrected. Unless otherwise specified, solutions in organic solvents were dried over anhydrous magnesium sulfate.

Photodimer of 2,6-Dimethyl-4-pyrone (1).[29] A solution of 2,6-dimethyl-4-pyrone (225 g, 1.81 mol) in air-free distilled water (450 ml) was irradiated under nitrogen with a 450-W Hanovia medium-pressure mercury arc lamp contained in a water-cooled quartz well immersed in the solution. The irradiation was stopped from time to time and the solid was scraped from the cooling jacket. After 2 weeks, the solution had acquired a brown color, and irradiation was stopped. The solid was filtered, ground thoroughly with hot acetone, refiltered, washed with hot acetone, and dried in air to give **1** (47 g, 63% based on unrecovered monomer). Recrystallization from dimethylformamide gave the dimer as large needles, mp 282–284° dec (lit.[3] mp 281–284° dec); $\lambda_{max}^{CHCl_3}$ 5.88 μ; δ^{CDCl_3} 1.50 (s, 12) and 3.18 (s, 4).

The dark brown aqueous filtrate was concentrated to give colorless crystals; recrystallization from benzene–petroleum ether (bp 30–60°) gave 2,6-dimethyl-4-pyrone (150 g, 67%), mp 132–134°, identified by infrared and nmr spectral comparison.

Baeyer–Villiger Oxidation of 1. Formation of Dilactone 2.[3] A mixture of the dimer **1** (35.00 g, 0.141 mol), *m*-chloroperbenzoic acid (125 g, 0.727 mol), chloroform (900 ml), and methylene chloride (1 l.) was boiled under reflux. Aliquots were withdrawn at 2-hr intervals, worked up, and examined by infrared spectroscopy. After 14 hr the ketone band at 5.88 μ was completely replaced by the lactone band at 5.75 μ. The reaction mixture was then cooled

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[27] It cannot be excluded that the product previously assigned structure **30** contained compound **28**, since it was not fully characterized.

[28] A minor point of difference relates to the treatment of compound **39** with 2,4-dinitrophenylhydrazine reagent; the product isolated was the 2,4-dinitrophenylhydrazone of the lactone **38**, whereas in the case of **28**, the simple derivative was isolated. This difference most probably reflects the fact that in the case of **39** prolonged standing of an initially formed oily product was necessary before crystalline material was obtained; it may be surmised that contact with the reagent solution during this time led to acid-catalyzed lactone ring formation.

[29] An alternative procedure involving irradiation of the solid has been described previously.[3]

to give colorless crystals of dilactone **2** (16.86 g), which was filtered, washed thoroughly with aqueous 10% sodium carbonate and distilled water, and dried in an oven (90°). The filtrate was stirred with excess aqueous 10% sodium sulfite until the organic layer ceased to give coloration with starch–potassium iodide paper, when it was separated, washed three times with aqueous 5% sodium carbonate and once with water, and dried. Concentration of the solution to 1 l. furnished colorless crystals (1.50 g) of **2**. The combined crops of **2** (18.36 g, 47%) were recrystallized from dimethylformamide to give colorless prisms, mp 340–350° dec (lit.[3] mp 340–350° dec); $\lambda_{\max}^{\mathrm{CHCl_3}}$ 5.75 μ; $\delta^{\mathrm{CF_3CO_2H}}$ 1.65 (s, 12), 3.63 (d, J = 1.5 Hz, 2), and 4.53 (d, J = 1.5 Hz, 2).

Further concentration of the mother liquors from the original crystallization of **2** gave a mixture (7.50 g) of **2** and the corresponding unsymmetrical dilactone,[3] and pure unsymmetrical dilactone (11.50 g, 29%); the latter when recrystallized from chloroform–petroleum ether had mp 280–281° dec (lit.[3] mp *ca.* 280° dec); $\lambda_{\max}^{\mathrm{CHCl_3}}$ 5.75 μ; $\delta^{\mathrm{CDCl_3}}$ 1.59 (s, 6), 1.61 (s, 6), 3.57 (s, 2), and 4.22 (s, 2).

Base-Catalyzed Hydrolysis of 2. Formation of 3 and 3-Methyl-2-butenolide. The finely ground dilactone **2** (8.00 g, 0.029 mol) was stirred under nitrogen with aqueous 5% sodium hydroxide (200 ml) for 3 hr. The reaction mixture was maintained under nitrogen, cooled, and acidified with cold 10% hydrochloric acid. The unconsumed dilactone (3.00 g, 38%) was filtered, and the filtrate was saturated with ammonium sulfate and thoroughly extracted with ethyl acetate. Removal of the solvent from the dried extract gave a yellow paste (4.30 g), which upon trituration with chloroform and standing in the cold gave **3** as a white solid (1.425 g, 25%), mp 120–125°. One recrystallization from ethanol–chloroform gave colorless crystals, mp 131–132° dec (lit.[3] mp 132–134° dec); $\lambda_{\max}^{\mathrm{KBr}}$ 2.9–4.7 (complex), 5.5 (w), 6.0, 6.10 (sh), and 6.25 μ; $\delta^{\mathrm{D_2O}}$ 1.57 (s, 3), 2.13 (s, 3), 4.42 (br s, 1), and 4.83 (s, 1).

Removal of solvent from the aqueous filtrate gave a thick, dark brown oil (2.7 g) that showed eight overlapping spots on a silica tlc plate when developed with a mixture of carbon tetrachloride and methanol (4:1). The oil (23.0 g) obtained from several hydrolyses was dissolved in chloroform (200 ml), and the solution was washed thoroughly with aqueous 5% sodium bicarbonate and water. The chloroform layer was dried and stripped of solvent to give a brown paste (3.9 g). This was stirred with carbon tetrachloride and the mixture was filtered. Evaporation of carbon tetrachloride from the filtrate gave a brown liquid (2.0 g). The liquid was dissolved in benzene and chromatographed on silica gel in benzene; elution with 15% ether in benzene gave **3-methyl-2-butenolide**[30] (0.397 g) as a light brown liquid; $\lambda_{\max}^{\mathrm{CHCl_3}}$ 5.61, 5.72, 6.08 (w), and 11.25 μ (w); $\lambda^{\mathrm{CCl_4}}$ 5.60, 5.70 (m), 6.06 (m), and 11.35 μ (w); $\epsilon_{221}^{\mathrm{C_2H_5OH}}$ 2000; $\delta^{\mathrm{CDCl_3}}$ 2.15 (m, 3), 4.73 (m, 2), and 5.85 (m, 1).

Reaction of 3 with Acid. Formation of 4 and 6. A. The acid **3** (0.300 g) was heated with 10% hydrochloric acid (3 ml) on a steam bath for 15 min, when a faint red coloration appeared. The solution was cooled and extracted with chloroform; the extract was dried and stripped of solvent to give an oil (0.147 g). This was chromatographed on silica gel in benzene; elution with 5% ether in benzene gave **4** (70 mg, 39%) as an oil that solidified on standing. Two crystallizations from petroleum ether afforded needles, mp 61–62°; $\lambda_{\max}^{\mathrm{CHCl_3}}$ 5.86, 6.21 (w), 6.33 (w), and 7.33 μ (m); $\lambda_{\max}^{\mathrm{EtOH}}$ 225 mμ (ε 14,000); $\delta^{\mathrm{CDCl_3}}$ 0.84 (d, J = 6 Hz, 3), 1.88 (s, 6), 2.03 (s, 3), 2.21 and 2.2–2.4 (s and m, 9), 3.76 (d, J = 11 Hz, 1), and 5.74 (br s, 2).

Anal. Calcd for $C_{15}H_{24}O_3$: C, 74.97; H, 8.39. Found: C, 75.03; H, 8.28.

Compound **4** gave a precipitate of iodoform on treament with iodine and sodium hydroxide. It did not react with hydrogen over palladium–charcoal in ethanol.

The **2,4-dinitrophenylhydrazone of 4** was prepared by the method of Fieser.[31] It was chromatographed on silica gel in benzene. Elution with ether followed by two crystallizations from ethanol afforded yellow needles, mp 156–158°; $\lambda_{\max}^{\mathrm{CHCl_3}}$ 2.99 (w), 6.17, and 6.27 μ; $\lambda_{\max}^{\mathrm{EtOH}}$ 228 (ε 31,700) and 362 mμ (ε 22,900).

Anal. Calcd for $C_{24}H_{28}N_4O_6$: C, 61.52; H, 6.02; N, 11.96. Found: C, 61.56; H, 6.01; N, 11.83.

B. The acid **3** (0.100 g) was heated on a steam bath with 3% hydrochloric acid (5 ml). The reaction mixture became turbid and had a fragrant odor after 20 min. The turbid mixture was cooled and extracted with chloroform. The extract was washed with aqueous 10% sodium bicarbonate and water, dried, and stripped of solvent to furnish crude **6** (8 mg) as a liquid; $\lambda_{\max}^{\mathrm{CHCl_3}}$ 3.67 (w), 5.80 (sh), 5.83, and 7.32 μ (m); $\delta_{\max}^{\mathrm{CDCl_3}}$ 1.15 (d, J = 6 Hz), 2.20 (s), 2.5–3.0 (m), and 10.52 (br s) (signals due to **4** were also present).

The **bis-2,4-dinitrophenylhydrazone of 6,** prepared as above, was obtained as an orange solid, mp 198–204°. One recrystallization from acetone gave material, mp 204–208° (lit.[3] mp 211–213.5°), undepressed on admixture with an authentic sample.[3]

Pyrolysis of 4. Formation of 7. The acid **4** (0.290 g) was heated in an oil bath at 145° until gas evolution ceased. The reaction mixture was cooled and dissolved in chloroform, and the solvent was removed to give a thick oil (0.208 g) that solidified on standing. This was chromatographed on silica gel in benzene; elution with 50% ether–benzene gave crystalline **7** (0.180 g, 78%), mp 115–118°. Two recrystallizations from benzene–petroleum ether gave needles, mp 137–138.5°; $\lambda_{\max}^{\mathrm{KBr}}$ 3.0–4.0, 5.87, 5.92, 6.03 (m), 7.37 (m), and 9.40 μ (m); $\lambda_{\max}^{\mathrm{EtOH}}$ 213 mμ (ε 10,000); $\delta^{\mathrm{CDCl_3}}$ 0.99 (d, J = 7 Hz, with further splitting, 3), 1.58 (s, 3), 2.08 and 2.15 (s's, 6), 2.3–2.7 (m, 3), 4.51 (br s, 1), and 4.83 (d, J = 3.5 Hz, 1).

Anal. Calcd for $C_{13}H_{18}O_5$: C, 61.40; H, 7.14. Found: C, 61.21; H, 6.96.

Compound **7** gave a precipitate of iodoform on treatment with iodine and sodium hydroxide.

Treatment of 7 with Acid. Formation of 6. The pyrolysis product **7** (80 mg) was heated with 2.5% hydrochloric acid (10 ml) on the steam bath for a few minutes until it had dissolved and an oil had separated. The mixture was cooled and extracted with chloroform. The extract was dried and stripped of solvent to give **6** (33 mg) as a fragrant liquid; $\lambda_{\max}^{\mathrm{CHCl_3}}$ 3.67 (w), 5.80 (sh), 5.83, and 7.32 μ (m).

The **bis-2,4-dinitrophenylhydrazone of 6,** prepared as above, was obtained as yellow microcrystals, mp 208–211°; it was identified by mixture melting point and infrared and ultraviolet spectral comparison with an authentic sample.[3]

Esterification of 7 with Diazomethane. Formation of 8. The pyrolysis product **7** (90 mg) was dissolved in methanol and ethereal diazomethane was added until a faint yellow color persisted. The solution was dried and stripped of solvent. The residue (93 mg) was chromatographed on silica gel in benzene. Elution with 50% ether–benzene gave **8** as an oil (56 mg) whose spectra were unchanged on molecular distillation; $\lambda^{\mathrm{CHCl_3}}$ 5.81 (sh), 5.84, 6.02 (w), 7.37, and 9.5 μ (br); $\delta^{\mathrm{CDCl_3}}$ 0.97 (d, J = 7.0 Hz, with further splitting, 3), 1.58 (s, 3), 2.07 (s, 3), 2.13 (s, 3), 2.3–2.6 (m, 3), 3.77 (s, 3), 4.48 (br s, 1), and 4.80 (d, J = 3 Hz, 1).

Reaction of 3 with Acetone. Formation of 9. The acid **3** (0.150 g) in anhydrous acetone (100 ml) was stirred with anhydrous copper sulfate (3 g) for 8 days in a stoppered flask. The solution was filtered, and the filtrate was stripped of solvent to give a light brown crystalline solid (140 mg). This was dissolved in chloroform (10 ml), and the solution was cooled to −10° for 24 hr, when a crystalline solid (13 mg), mp 130–132°, was obtained. This was identified by mixture melting point as unconsumed **3**. The chloroform was removed from the mother liquid to give **9** as a crystalline solid (0.120 g, 67%). After recrystallization from cyclohexane, it had mp 153–154°; $\lambda_{\max}^{\mathrm{CHCl_3}}$ 2.8–4.1 (complex), 5.80 (sh), 5.88 (sh), 5.91, 6.01 (m), 7.25 (m), 7.29 (m), and 9.55 μ (br); $\lambda_{\max}^{\mathrm{EtOH}}$ 214 mμ (ε 8500); $\delta^{\mathrm{CDCl_3}}$ 1.44 (s, 6), 1.63 (s, 3), 2.10 (s, 3), 4.64 (br s, 1), and 10.87 (br s, 1).

Anal. Calcd for $C_{10}H_{14}O_4$: C, 60.60; H, 7.07. Found: C, 60.59; H, 7.07.

Treatment of 3 with Base. Formation of 10. A solution of the acid **3** (1.00 g) in aqueous 2.5% sodium hydroxide (40 ml) was boiled under reflux for 7 min, when the solution acquired a red coloration. The solution was cooled, acidified with 10% hydrochloric acid, and extracted with chloroform. The chloroform extract was washed with water, dried, and stripped of solvent to give **10** as an oil (0.36 g, 51%) that crystallized on standing. This was purified by chromatography on silica gel in benzene; elution with 50% ether–benzene furnished an oil that crystallized as needles (0.29 g) on standing. Recrystallization from petroleum ether gave colorless needles, mp 59–59.5°; $\lambda_{\max}^{\mathrm{CHCl_3}}$ 3.0–4.1, 5.73, 5.97, and 6.13 μ; $\lambda_{\max}^{\mathrm{EtOH}}$ 232 mμ (ε 10,500); $\delta^{\mathrm{CDCl_3}}$ 2.6–2.9 (m), 11.3 (br); $\delta^{\mathrm{C_6H_6}}$ 1.8–2.0 (m, 4), 2.30 (s, 3), and 12.42 (br s, 1).

Anal. Calcd for $C_7H_8O_3$: C, 59.99; H, 5.75; mol wt, 140. Found: C, 60.11; H, 5.88; mol wt (osmometry), 143.

Compound **10** was soluble in aqueous sodium bicarbonate.

The **2,4-dinitrophenylhydrazone of 10** was prepared as above. Four recrystallizations from acetone gave orange crystals, mp 219–221°; $\lambda_{\max}^{\mathrm{KBr}}$ 3.07 (w), 3.2–3.8 (br), 5.76, 6.18, and 6.28 μ; $\lambda_{\max}^{\mathrm{EtOH}}$ 218

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[30] Identified on the basis of analogy with the corresponding product formed from the photodimer of 2,6-diethyl-4-pyrone.[1]

[31] L. F. Fieser, "Experiments in Organic Chemistry," 3rd ed, D. C. Heath and Co., Boston, Mass., 1955, p 84.

(ε 18,200), 252 (ε 16,000), and 376 mμ (ε 27,500); $\delta^{\mathrm{C_5H_5N}}$ 2.22 (s, 3), 2.42 and 2.58 (s's, 4), and 10.11 (br s, 1).

Anal. Calcd for $C_{13}H_{12}N_4O_6$: C, 48.75; H, 3.78; N, 17.50. Found: C, 48.79; H, 3.94; N, 17.68.

Hydrogenation of 10. Formation of 13 and 3-Methylcyclopentanone. The acid **10** (0.120 g) was hydrogenated in ethanol over prereduced 5% palladium–charcoal (19 mg) at atmospheric pressure. Approximately 1 molar equiv of hydrogen was absorbed after 40 min and further uptake of hydrogen stopped (20.8 ml at NTP). Filtration of the solution and removal of ethanol at room temperature gave **13** as a colorless syrup (95 mg) that gave a violet-blue coloration with ferric chloride in chloroform and pyridine; $\lambda_{\max}^{\mathrm{CHCl_3}}$ 2.8–4.4, 5.70, 5.81, and 7.25 μ; $\delta^{\mathrm{CDCl_3}}$ 1.24 (d, J = 6 Hz), 2.0–3.0 (m), and 9.93 (br s). The syrup was chromatographed on silica gel in benzene; elution with 50% ether–benzene gave a liquid, whose infrared spectrum was identical with that of the original syrup.

Treatment of **13** with 2,4-dinitrophenylhydrazine reagent[31] gave a yellow solid, mp 117–121°. Repeated recrystallization from ethanol gave material, mp 121–124°; this melting point was not improved by chromatography on alumina, followed by recrystallization. This product was shown to be identical with the **2,4-dinitrophenylhydrazone of 3-methylcyclopentanone** by a mixture melting point with an authentic sample (*vide infra*).

Anal. Calcd for $C_{12}H_{14}N_4O_4$: C, 51.79; H, 5.07; N, 20.14. Found: C, 51.74; H, 5.25; N, 19.73.

3-Methylcyclopentanone 2,4-Dinitrophenylhydrazone. 3-Methylcyclopentanone was prepared by the method of Vogel;[32] bp 140–143°; $\lambda_{\max}^{\mathrm{CHCl_3}}$ 5.78 μ; $\delta^{\mathrm{C_4Cl}}$ 1.12 (d, J = 5.5 Hz, 3), and 1.5–2.4 (m, 7).

The 2,4-dinitrophenylhydrazone[31] was obtained after recrystallization from ethanol as a yellow solid mp 121–124° (lit.[33] mp 117–119°); $\lambda_{\max}^{\mathrm{CHCl_3}}$ 2.98 (m), 3.36 (w), 6.18, and 6.27 μ; $\lambda_{\max}^{\mathrm{EtOH}}$ 225 (ε 16,600), 260 (sh, ε 10,500), and 360 mμ (ε 21,000).

Esterification of 10 with Diazomethane. Formation of 14. The acid **10** (0.100 g) was dissolved in methanol and ethereal diazomethane was added until a faint yellow color persisted. The solution was dried and stripped of solvent. The residue (0.107 g) was chromatographed on silica gel in benzene; elution with 40% ether in benzene gave **14** as an oil (94 mg, 86%); $\lambda_{\max}^{\mathrm{CHCl_3}}$ 5.74 (sh), 5.85, and 6.15 μ (m); $\delta^{\mathrm{CDCl_3}}$ 2.4–2.85 (m, 7) and 3.82 (s, 3).

Hydrogenation of 14. Formation of 15. The ester **14** (50 mg) was hydrogenated in ethanol over prereduced 5% palladium–charcoal (6 mg) at atmospheric pressure. After 90 min 1 molar equiv of hydrogen had been absorbed, and hydrogen uptake stopped. Filtration of the solution and removal of the solvent gave a colorless liquid (32 mg, 63%) that gave a violet coloration with ferric chloride in methanol and was identified as **2-methoxycarbonyl-3-methylcyclopentanone (15)** by infrared and nmr spectral comparison with an authentic sample (*vide infra*).

The **semicarbazone of 15** was prepared as a colorless solid, mp 165–168°, by the method of Vogel.[34] After two recrystallizations from water it was obtained as colorless crystals, mp 169.5–170°; a mixture melting point with authentic semicarbazone (*vide infra*) was undepressed.

2-Methoxycarbonyl-3-methylcyclopentanone (15). Pulegenic acid was prepared by a modified version of the method of Rupe and Schäfer.[35] To a stirred and cooled solution of pulegone (50.0 g, 0.35 mol) in glacial acetic acid (100 ml) bromine (70.0 g, 0.38 mol) was added dropwise. After the addition of bromine was completed (*ca.* 45 min), the solution was stirred for a further 15 min and was then poured onto crushed ice. The oily layer was washed thoroughly with cold water and cold aqueous 10% sodium bicarbonate, and dried to give crude pulegone dibromide; $\lambda_{\max}^{\mathrm{CHCl_3}}$ 5.83 μ.

The crude pulegone dibromide was added dropwise with stirring to a boiling solution of sodium ethoxide (prepared from 25.0 g of sodium) in absolute ethanol (350 ml) under reflux. After the addition was completed, the solution was boiled under reflux for a further 4 hr. Most of the ethanol was removed, and the cooled mixture was acidified with 10% sulfuric acid. The mixture was extracted with ether, and the extract was dried and stripped of solvent to give a brown liquid (51.0 g). A solution of this liquid in ethanol (50 ml) was boiled under reflux with aqueous 10% sodium hydroxide (100 ml) for 1 hr, cooled, and acidified with 10% sulfuric acid. Most of the ethanol was distilled, and the organic layer was taken up in ether. The solution was dried and stripped of solvent. The residue was distilled to give pulegenic acid as a pale yellow liquid (24.0 g, 44%), bp 94–100° (1 mm); $\lambda_{\max}^{\mathrm{CHCl_3}}$ 2.8–4.2 (br), 5.89, 6.21 (sh), and 7.23 μ (w); $\delta^{\mathrm{CCl_4}}$ 1.07 (d, J = 6.5 Hz), 1.8–2.5 (m), 2.78–3.02 (m), and 10.83 (br s).

Pulegenic acid (15.50 g) was dissolved in ether, and ethereal diazomethane was added until a faint yellow color persisted. The solution was dried and stripped of solvent to give methyl pulegenate (**16**) as a very pale yellow liquid (12.30 g, 73%), bp 48–50° (0.4 mm) [lit.[36] bp 52–58° (0.70 mm)]; $\lambda_{\max}^{\mathrm{CHCl_3}}$ 5.80, 7.27 (w), and 7.43 μ (w); $\delta^{\mathrm{CCl_4}}$ 1.02 (d, J = 6 Hz, 3), 1.58 and 1.63 (s's, 6), 1.8–2.5 (m, 5), 2.85 (m, 1), and 3.42 (s, 3).

Ozonized oxygen was bubbled slowly (8 hr) through a solution of **16** (8.00 g) in dry carbon tetrachloride (60 ml) at −20° until the effluent gas liberated iodine from an acidified solution of potassium iodide.[37] Most of the solvent was removed under reduced pressure at room temperature, and the residue was heated under reflux for 1.5 hr with boiling water (52 ml). The mixture was cooled and extracted with ether. The ethereal solution was extracted very thoroughly with ice-cold aqueous 10% sodium hydroxide. The yellow aqueous layer was acidified with 10% cold acetic acid and extracted with ether. The ethereal extract was washed with saturated aqueous sodium bicarbonate and dried. Removal of the solvent gave **15** as a colorless liquid (1.20 g, 17%), bp 82° (3 mm) [lit.[37] bp 90–92° (12 mm)]; $\lambda_{\max}^{\mathrm{CHCl_3}}$ 5.70 and 5.79 μ; $\delta^{\mathrm{CDCl_3}}$ 1.19 (d, J = 6 Hz, 3), 2.0–2.9 (m, 6), and 3.74 (s, 3). Compound **15** gave a violet coloration with ferric chloride in methanol.

The **semicarbazone**[34] was obtained after recrystallization from water as colorless crystals, mp 169–170° (lit.[37] mp 176–177°); $\lambda_{\max}^{\mathrm{CHCl_3}}$ 2.81 (w), 2.91 (w), 2.95 (w), 5.79 (m), and 5.90 μ; further recrystallization failed to raise this melting point.

Hydrogenation of 3. Formation of 18, 19, and 21. Compound **3** (0.600 g, 3.4 mmol) was hydrogenated in ethanol over prereduced 5% palladium–charcoal (60 mg) at atmospheric pressure. After 30 min the hydrogen uptake was 1 molar equiv (82 ml at NTP). The solution was filtered and stripped of ethanol under reduced pressure at room temperature. A semisolid residue (0.584 g) was obtained, which on trituration with chlororoform gave **18** as a crystalline solid, mp 114–117°; cooling of the chloroform solution gave further crops of **18** (total yield 0.423 g, 75%). Two recrystallizations from ethanol–chloroform gave colorless microcrystals, mp 118–119° (lit.[3] mp 113–115°); $\lambda_{\max}^{\mathrm{KBr}}$ 2.98, 3.0–4.0 (complex), and 5.87 μ; $\delta^{\mathrm{D_2O}}$ 1.19 (d, J = 6.5 Hz, 3), 1.41 (s, 3), 2.6–3.2 (m, 2), 3.89 (d, J = 8.5 Hz, 1), 4.87 (HOD).

Removal of the chloroform at room temperature from the mother liquor gave **19** as an oil (0.103 g, 18%); $\lambda_{\max}^{\mathrm{CHCl_3}}$ 2.82–4.05 (complex) and 5.89 μ; $\delta^{\mathrm{CDCl_3}}$ 1.12 (d, J = 7 Hz), 1.42 (s), 2.2–3.0 (m), 3.69 (br d, J = 5.5 Hz), and 6.45 (br s, shifted upfield on dilution). The presence of a trace of lactonic impurity was indicated by a very weak infrared band at 5.60 μ. When this oil was allowed to stand at room temperature for 5 days, its infrared band at 5.60 μ became very strong, and its nmr spectrum now showed signals attributable to both **19** and **21** (*vide infra*).

The oil was chromatographed on silica gel in benzene. Elution with 30% ether in benzene gave **21** as an oil (50 mg); $\lambda_{\max}^{\mathrm{CHCl_3}}$ 5.60, 5.82, and 7.35 μ (m); $\delta^{\mathrm{CDCl_3}}$ 1.25 (d, J = 6.5 Hz, 3), 2.25 (s, 3), 2.35–2.85 (m, 3), 4.40 (d, J = 6.5 Hz, 1). The infrared and nmr spectra were identical with the corresponding spectra of authentic **21** (*vide infra*).

The **2,4-dinitrophenylhydrazone of 21** was obtained after three recrystallizations from ethanol as yellow, shining crystals, mp 176–177°; $\lambda_{\max}^{\mathrm{CHCl_3}}$ 2.99 (w), 5.60, 6.19, and 6.28 μ; $\lambda_{\max}^{\mathrm{EtOH}}$ 226 (ε 15,000), 250 (ε 12,000), and 353 mμ (ε 21,000); $\delta^{\mathrm{CDCl_3}}$ 1.27 (d, J = 7 Hz), 2.12 (s), 2.5–2.9 (m), 4.69 (d, J = 7 Hz), 7.87 (s), 8.02 (s), 8.30 (d, J = 2.5 Hz), 8.42 (d, J = 2.5 Hz), and 9.10 (d, J = 2.5 Hz). Its infrared and nmr spectra were identical with the corresponding spectra of the 2,4-dinitrophenylhydrazone of authentic **21**; a mixture melting point was undepressed.

Anal. Calcd for $C_{13}H_{14}N_4O_6$: C, 48.45; H, 4.38; N, 17.39. Found: C, 48.42; H, 4.46; N, 17.09.

Reaction of 18 with Acid. Formation of 22. The acid **18** (0.400 g) was heated on the steam bath with 5% hydrochloric acid (25 ml) for 30 min. The reaction mixture was cooled and extracted with

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[33] D. H. R. Barton, O. C. Böckman, and P. de Mayo, *ibid.*, 2263 (1960).

[34] A. I. Vogel, "Practical Organic Chemistry," 3rd ed, Longmans, London, 1956, p 344.

[35] H. Rupe and K. Schäfer, *Helv. Chim. Acta*, **11**, 463 (1928).

[36] J. Wolinsky and D. Chan, *J. Org. Chem.*, **30**, 41 (1965).

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chloroform. The chloroform extract was washed with aqueous 5% sodium bicarbonate and with water, dried, and stripped of solvent to give a colorless liquid (0.300 g), which was chromatographed on silica gel in benzene. Elution with 50% ether–benzene gave **22** as a colorless liquid (0.277 g, 79%); $\lambda_{max}^{CHCl_3}$ 5.60, 5.82, and 7.35 μ (m); δ^{CDCl_3} 1.03 (d, J = 6.5 Hz, 3), 2.25 (s, 3), 2.30–3.05 (m, 3), and 4.89 (d, J = 7 Hz, 1). The infrared and nmr spectra were identical with the corresponding spectra of authentic **22** (*vide infra*).

The **2,4-dinitrophenylhydrazone of 22** was obtained after three recrystallizations from ethanol as yellow microcrystals, mp 163–165.5°; $\lambda_{max}^{CHCl_3}$ 2.99 (w), 5.60, 6.18, and 6.27 μ; λ_{max}^{EtOH} 225 (ε 12,500), 252 (ε 9500), and 353 mμ (ε 17,000); δ^{CDCl_3} 1.08 (d, J = 6.5 Hz), 2.11 (s), 2.30–3.10 (m), 5.20 (d, J = 7 Hz), 7.83 (s), 8.00 (s), 8.25 (d, J = 2.5 Hz), 8.42 (d, J = 2.5 Hz), and 9.11 (d, J = 2.5 Hz). Its infrared and nmr spectra were identical with those of the corresponding spectra of the 2,4-dinitrophenylhydrazone of authentic **22**; a mixture melting point was undepressed.

Anal. Calcd for $C_{13}H_{14}N_4O_6$: C, 48.45; H, 4.38; N, 17.39. Found: C, 48.77; H, 4.68; N, 17.40.

Diethyl 2-Acetyl-2-bromo-3-methylglutarate (25). Diethyl 2-acetyl-3-methylglutaric acid (**24**) was prepared in 60% yield by the method of Smrt and Sǒrm;[38] it was obtained as a colorless liquid, bp 133–135° (2 mm) [lit.[38] 122–123° (2 mm)]; $\lambda_{max}^{CHCl_3}$ 5.76 (sh) and 5.81 μ; δ^{CCl_4} 0.97 (d, J = 7 Hz, 3), 1.23 and 1.27 (t's, J = 7.0 Hz, 6), 2.15 (s, 3), 2.30–2.80 (m, 3), 3.33–3.53 (d of d's, 1), and 4.08 and 4.20 (q's, J = 7 Hz, 4).

A solution of bromine (33.0 g, 0.201 mol) in carbon tetrachloride (40 ml) was added dropwise to a stirred solution of **24** (44.0 g, 0.193 mol) in dry carbon tetrachloride (80 ml) under nitrogen in a three-necked flask cooled in an ice–salt bath. The addition took 1 hr, and the mixture was stirred for a further 30 min. The pale yellow solution was washed with aqueous 10% sodium sulfite, cold aqueous 5% sodium bicarbonate, and water. The colorless organic layer was dried and stripped of solvent to give a colorless liquid (60.0 g), which was fractionally distilled. Compound **25** was obtained as the first fraction (43.0 g, 74%), bp 136–137° (0.75 mm); $\lambda_{max}^{CHCl_3}$ 5.77 and 7.37 μ (w); λ_{max}^{EtOH} 230 mμ (end absorption), and 289 mμ (ε 110); δ^{CCl_4} 0.95–1.45 (m, 9), 2.35 (s, 3), 2.50–3.05 (m, 3), and 3.90–4.45 (m, 4). The analytical sample was redistilled; bp 98–99° (0.06 mm).

Anal. Calcd for $C_{12}H_{19}BrO_5$: C, 44.58; H, 5.88; Br, 24.77. Found: C, 44.81; H, 5.93; Br, 24.66.

1-Ethyl 2-Acetyl-2-bromo-3-methylglutarate Ethylene Ketal (27). A stirred mixture of the bromo compound **25** (15.0 g), ethylene glycol (70 ml), *p*-toluenesulfonic acid (2.5 g), and dry benzene (50 ml) under nitrogen in a round-bottomed flask fitted with a Dean-Stark trap was boiled under reflux. After 2 days the reaction mixture was cooled, and the solution was made alkaline with methanolic 10% potassium hydroxide. The benzene layer was separated, and the glycol layer was extracted with chloroform (two 50-ml portions). The chloroform extracts and the benzene solution were combined, washed with water (25 ml), and dried. Removal of the solvent gave crude diethyl 2-acetyl-2-bromo-3-methylglutarate ethylene ketal (**26**) as a thick oil (10.2 g, 59%); $\lambda_{max}^{CHCl_3}$ 5.79, 7.30 (w), and 9.85 μ (m); δ^{CDCl_3} 0.95–1.45 (m, 9), 1.62 (s, 3), 2.20–2.70 (m, 3), and 3.90–4.50 (m, 8).

The ketal **26** (10.0 g), ethanol (50 ml), and aqueous 5% sodium hydroxide (50 ml) were boiled under reflux for 10 hr. Most of the ethanol was distilled, and the residue was washed with chloroform. The aqueous layer was cooled in ice and acidified (pH 6) with cold 2% hydrochloric acid, when the solution became turbid. The solution was extracted with chloroform (three 50-ml portions), and the chloroform extract was washed with water and dried. Removal of the solvent gave a brown paste (5.4 g) which was chromatographed on silica gel in benzene. Elution with 25% ether in benzene gave **27** as a thick oil (4.8 g, 52%) that crystallized on standing. Two recrystallizations from cyclohexane gave colorless microcrystals, mp 94–94.5°; $\lambda_{max}^{CHCl_3}$ 2.80–4.20 (br), 5.76, 5.84, and 9.30–9.80 μ (br); δ^{CDCl_3} 1.05 and 1.33 (d, J = 6 Hz, and t, J = 7 Hz, 6), 1.63 (s, 3), 2.00–3.33 (m, 3), 3.85–4.50 (m, 6), and 13.02 (br s).

Anal. Calcd for $C_{12}H_{19}BrO_6$: C, 42.47; H, 5.60; Br, 23.60. Found: C, 42.79; H, 5.68; Br, 23.46.

***trans*- and *cis*-4-Hydroxy-3-methyl-5-oxohexanoic Acid Lactones (21 and 22).** A. Compound **27** (4.50 g) was dissolved in aqueous 10% sodium hydroxide (80 ml), and the solution was boiled under reflux for 3 days. The reaction mixture was then cooled, acidified (pH 2) with concentrated hydrochloric acid, and heated for 2 hr on the steam bath. It was cooled and extracted with chloroform. The chloroform extract was washed with water, dried, and stripped of solvent to give a mixture of **21** and **22** as a liquid (1.20 g, 66%). The lactone mixture was chromatographed on silica gel in benzene and eluted with 20% ether in benzene. The earlier fractions gave **21** (0.732 g); 2,4-dinitrophenylhydrazone, mp 175–176.5°. The later fractions gave **22** (0.180 g); 2,4-dinitrophenylhydrazone, mp 163–165°.

B. The lactones **21** and **22** could also be obtained directly from **26** by the following procedure; the yield, however, was lower than that when the intermediate **27** was isolated as above. Compound **26** (0.750 g), ethanol (10 ml), and aqueous 80% potassium hydroxide (2 ml) were boiled under reflux for 6 days. The mixture was cooled, acidified (pH 2) with concentrated hydrochloric acid, and heated for 2 hr on the steam bath. The reaction mixture was cooled and extracted with chloroform. The chloroform extract was washed with water, dried, and stripped of solvent to give a mixture of **21** and **22** as a liquid (79 mg, 25%).

Equilibration of 21 and 22. Lactone **22** (0.170 g) and anhydrous potassium carbonate (0.200 g) were heated in boiling dry xylene (15 ml) under reflux for 24 hr; the reaction mixture was protected from atmospheric moisture with a calcium chloride tube. The mixture was cooled and filtered. Removal of solvent from the filtrate gave a liquid whose nmr spectrum showed it to be a mixture of lactones **21** and **22** (89 mg, 82%); the ratio of **21** to **22** was estimated to be 8:1 by measurement of the relative areas of the doublets at 1.25 and 1.03.

Under similar conditions the lactone **21** (0.107 g) gave a mixture of lactones **21** and **22** (80 mg, 72%) in the ratio of 7:1.

Reaction of 18 with Diazomethane in Ether–Methanol. Formation of 28. A solution of the acid **18** (0.410 g) in methanol was treated with ethereal diazomethane until a yellow color persisted. The solution was dried and stripped of solvent to give a colorless liquid (0.415 g). This was chromatographed on silica gel in benzene; elution with 50% ether–benzene gave **28** as a colorless liquid (0.385 g, 88%); $\lambda_{max}^{CCl_4}$ 2.85 (m), 5.76, 5.83, and 7.36 μ (m); δ^{CDCl_3} 0.75 (d, J = 6.5 Hz, 3), 2.23 (s, 3), 2.40–2.98 (m, 3), 3.49 (br s, 1; position concentration-dependent; absent after treatment with D_2O), 3.70 (s, 3), and 4.27 (br s, 1). The presence of a trace of lactonic impurity was indicated by a very weak band at 5.58 μ in the infrared spectrum; this impurity could not be removed by column chromatography or by fractional distillation. Compound **28** was unstable at room temperature and gave a mixture of lactones **21** and **22** on standing for 15 days, as indicated by infrared and nmr spectral data.

The **2,4-dinitrophenylhydrazone of 28** was obtained after three recrystallizations from ethanol as yellow crystals, mp 126–127°; λ_{max}^{KBr} 2.84 (m), 2.99 (w), 5.78, 6.19, and 6.28 μ; λ_{max}^{EtOH} 249 (ε 9900) and 359 mμ (ε 19,800).

Anal. Calcd for $C_{14}H_{18}N_4O_7$: C, 47.46; H, 5.08; N, 15.82. Found: C, 47.53; H, 5.07; N, 15.69.

Oxidation of 28 with Chromic Acid. Formation of 29 and Methylsuccinic Acid. Compound **28** was oxidized by the method of Brown and Garg.[39] A solution of sodium dichromate (0.60 g) in concentrated sulfuric acid (0.30 ml) and water (3.50 ml) was added over a period of 2 hr to a stirred solution of **28** (0.120 g) in ether (5 ml). The reaction mixture was boiled under reflux for 30 min, cooled, and extracted with ether. The ethereal extract was dried and stripped of solvent to give **29** as a colorless liquid (83 mg, 83%); $\lambda_{max}^{CCl_4}$ 2.85–4.20 (br), 5.74, and 5.84 μ; δ^{CDCl_3} 1.25 (d, J = 7 Hz, 3), 2.16–3.15 (m, 3), 3.68 (s, 3), and 10.37 (br s, 1). The presence of a trace of lactonic impurity was indicated by a very weak infrared band at 5.57 μ.

A solution of the ester **29** (80 mg) in ethanol (5 ml) was boiled under reflux with aqueous 5% sodium hydroxide (25 ml). After 8 hr the reaction mixture was cooled and acidified (pH 2) with 25% hydrochloric acid, and stripped of ethanol and water. The solid residue was boiled with benzene, and the mixture was filtered while hot. Removal of benzene from the filtrate under reduced pressure gave methylsuccinic acid as a colorless crystalline solid (46 mg, 60%). After recrystallization from benzene–petroleum ether it had mp 110–111° (lit.[40] mp 110–111°); λ_{max}^{KBr} 2.9–4.2 (br), 5.83 (sh), and 5.88 μ. It was identified by mixture melting point and infrared spectral comparison with an authentic sample (Aldrich Chemical Co.).

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(38) J. Smrt and F. Sǒrm, *Collect. Czech. Chem. Commun.*, **18**, 131 (1953).

(39) H. C. Brown and C. P. Garg, *J. Amer. Chem. Soc.*, **83**, 2952 (1961).

(40) G. B. Brown, "Organic Syntheses," Coll. Vol. III, John Wiley & Sons, Inc., New York, N. Y., 1955, p 615.

Reaction of 19 with Diazomethane in Ether–Methanol. Formation of 21. The acid **19** (52 mg) was dissolved in methanol (3 ml) and ethereal diazomethane was added until a yellow color persisted. The solution was dried and freed of the solvent at room temperature to give an oil; $\lambda_{\max}^{\mathrm{CHCl_3}}$ 5.60, 5.76, and 5.83 μ. This oil was chromatographed on silica gel in benzene; elution with 25% ether in benzene gave a liquid (45 mg) that was identified as the lactone **21** by infrared and nmr spectral comparison. Its 2,4-dinitrophenylhydrazone after two recrystallizations from ethanol had mp 173–174.5°, undepressed on admixture with an authentic sample of the 2,4-dinitrophenylhydrazone of **21**.

Reaction of 19 with 2,4-Dinitrobenzoyl Chloride. Formation of 21 and 22. The acid **19** (0.300 g) was treated with 2,4-dinitrobenzoyl chloride and pyridine by the method of Shriner, Fuson, and Curtin.[41] The mixture was extracted with chloroform and the extract was washed with 5% hydrochloric acid, aqueous 10% sodium bicarbonate, and water, and dried. Removal of the solvent gave a mixture of **21** and **22** as a pale brown liquid (0.200 g, 77%), identified by infrared and nmr spectral comparison. The ratio of **21** to **22** was 3:1.

Hydrogenation of 34. Formation of 35, 36, and 37. The unsaturated acid **34**[1] (1.50 g) was hydrogenated in ethanol (25 ml) over prereduced 5% palladium–charcoal (0.150 g) at atmospheric pressure. After 1.5 hr, 1 molar equiv of hydrogen had been taken up (180 ml at NTP), and further uptake of hydrogen stopped. The solution was filtered and stripped of solvent under reduced pressure at room temperature to give a semisolid residue (1.48 g). This was stirred with carbon tetrachloride, and the mixture was filtered, when **35** was obtained as a colorless crystalline solid (1.29 g, 85%), mp 143–147°. After three recrystallizations from ethanol–chloroform it had mp 156.5–158°; $\lambda_{\max}^{\mathrm{KBr}}$ 3.05, 3.3–4.2 (complex), 5.79 (sh), and 5.90 μ; $\delta^{\mathrm{D_2O}}$ 0.92 (t, J = 7.5 Hz, 6), 1.3–2.0 (m, 4), 2.32–2.92 (m, 1), 3.07 (d, J = 10 Hz, 1), and 4.02 (d, J = 8 Hz, 1).

Anal. Calcd for $C_9H_{16}O_4$: C, 57.45; H, 8.51. Found: C, 57.59; H, 8.51.

Removal of carbon tetrachloride from the filtrate under reduced pressure at room temperature afforded a mixture of **36** and **37** as a colorless oil (0.202 g); $\lambda_{\max}^{\mathrm{CHCl_3}}$ 2.85, 3.1–4.2 (complex), 5.60 (w), 5.82 (sh), 5.85, and 5.90 μ; $\delta^{\mathrm{CDCl_3}}$ 0.85–1.25 (m), 1.35–1.85 (m), 2.3–2.8 (m), 3.07 (dd, J = 10 and 2 Hz), 4.00 (dd, J = 6 and 2 Hz), and 6.63 (br s, absent after treatment with D_2O).

The oil was chromatographed on silica gel in benzene; elution with 10% ether in benzene gave **37** as a colorless liquid; $\lambda_{\max}^{\mathrm{CHCl_3}}$ 5.60, 5.82, and 7.22 μ (w); $\delta^{\mathrm{CDCl_3}}$ 0.95 and 1.10 (t's, J = 7 Hz, 6), 1.3–1.9 (m, 2), 2.1–2.6 and 2.63 (m and q, J = 7.5 Hz, 5), and 4.50 (d, J = 6 Hz, 1).

The **2,4-dinitrophenylhydrazone of 37** was obtained after three recrystallizations from ethanol as yellow crystals, mp 151–153°; $\lambda_{\max}^{\mathrm{CHCl_3}}$ 3.00 (w), 5.60, 6.18, and 6.27 μ; $\lambda_{\max}^{\mathrm{EtOH}}$ 227 (ϵ 9800), 252 (sh, ϵ 7000), and 352 mμ (ϵ 15,000).

Anal. Calcd for $C_{15}H_{18}N_4O_6$: C, 51.43; H, 5.14; N, 16.00. Found: C, 51.02; H, 5.61; N, 16.29.

Treatment of 35 with Acid. Formation of 38. The acid **35** (0.125 g) was heated on a steam bath for 30 min with 7% hydrochloric acid (6 ml). The solution was cooled and extracted with chloroform. Removal of the solvent from the dried extract gave a colorless liquid (0.107 g). This was purified by chromatography on silica gel in benzene; elution with 20% ether in benzene afforded **38** (82 mg, 74%); $\lambda_{\max}^{\mathrm{CHCl_3}}$ 5.60 and 5.82 μ; $\delta^{\mathrm{CDCl_3}}$ 0.85–1.65 and 1.01 (m and t, J = 7 Hz, 8), 2.4–2.9 and 2.55 (m and q, J = 7 Hz, 5), and 4.90 (d, J = 7 Hz, 1).

The **2,4-dinitrophenylhydrazone of 38** was first obtained as an orange liquid, which solidified on prolonged standing in the cold. After recrystallization from methanol it had mp 126–129°; $\lambda_{\max}^{\mathrm{CHCl_3}}$ 3.00 (w), 5.60, 6.18, and 6.26 μ; $\lambda_{\max}^{\mathrm{EtOH}}$ 216 (ϵ 14,000), 252 (ϵ 10,800), and 353 mμ (ϵ 20,000). A purer sample of this derivative was obtained indirectly from **35** (*vide infra*).

Reaction of 35 with Diazomethane in Ether–Methanol. Formation of 39. A solution of the acid **35** (0.102 g) in methanol was treated with ethereal diazomethane until a faint yellow color persisted. The solution was dried and stripped of the solvent to give **39** as a colorless liquid (90 mg, 81%); $\lambda_{\max}^{\mathrm{CHCl_3}}$ 2.85 (m), 5.77, and 5.82 μ; $\delta^{\mathrm{CDCl_3}}$ 0.85–1.35 and 1.13 (m and t, J = 7 Hz, 8), 2.35–3.75 and 2.53 (m and q, J = 7 Hz, 5), 3.54 (d, J = 5 Hz, 1; position concentration-dependent), 3.70 (s, 3), 4.95 (br d, J = 5 Hz, 1); the doublets at δ 3.54 and 4.95 appeared as broad singlets when the spectrum was taken in CCl_4, and the former was absent after treatment with D_2O.

Reaction of **39** with 2,4-dinitrophenylhydrazine reagent[31] gave an orange oil that solidified on prolonged standing in the cold. Two recrystallizations from methanol afforded yellow crystals, mp 129–130.5°, that were identified as the **2,4-dinitrophenylhydrazone of 38** by mixture melting point and infrared and ultraviolet spectral comparison.

Anal. Calcd for $C_{15}H_{18}N_4O_6$: C, 51.43; H, 5.14; N, 16.00. Found: C, 51.20; H, 5.35; N, 16.38.

Hydrolysis of 39 with Sodium Hydroxide. Formation of 37 and 38. A solution of the ester **39** (0.20 g) in methanol (5 ml) was treated with aqueous 1% sodium hydroxide (2 ml), and the mixture was allowed to stand for 20 min. It was then acidified (pH 6) and stripped of most of the methanol. The residue was extracted with chloroform, and the chloroform extract was washed with water. Removal of the solvent from the dried extract afforded an oil, which was identified as a mixture of lactones **37** and **38** (8:1) by infrared and nmr spectral comparison.

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[41] R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "The Systematic Identification of Organic Compounds," 4th ed, John Wiley & Sons, Inc., New York, N. Y., 1958, p 212.