Control Oxidations.—An experiment identical with that described for photosensitized oxidation of cholesterol was run except that no photosensitizer was added. From 2.005 g of cholesterol 1.635 g of unaltered cholesterol was recovered, together with 48.4 mg of I, 1.6 mg of IIa, and 1.0 mg of IIIa, all isolated by the same means previously described. Chromatographic examination of mother liquors following recovery of I, IIa, and IIIa indicated that traces of IV, V, 3β-hydroxycholest-5-en-7-one, cholesta-3,5-dien-7-one, cholest-5-ene-3β,7α-diol, and cholest-5-ene-3β,7β-diol were present, all at much less than 1% levels. A control oxidation including photosensitizer but carried out completely in the dark gave a quantitative recovery of unaltered cholesterol.

Control oxidations carried out in cyclohexane instead of in pyridine were run similarly. A cyclohexane solution of 1.9835 g of cholesterol was irradiated for 22 hr and then processed as previously described. Crystalline cholesterol free of other demonstrable sterols was obtained in four crops (total 1.8035 g) and mother liquors after preparative thin layer chromatography gave 23.5 mg of amorphous sterols which contained IV and V in approximately 1:1 proportions but which did not contain any demonstrable IIa or IIIa. A similar control irradiation (23 hr) of 1.9753 g of cholesterol and 32.4 mg of added I was worked up in the same manner to give 1.8042 g of pure crystalline cholesterol free of other demonstrable sterols. Preparative thin layer chromatography of the mother liquors afforded 47.3 mg of sterol hydroperoxides as amorphous solids containing I, IV, and V in approximately equal proportions but which did not contain any demonstrable amounts of IIa or IIIa.

Pyrolysis Experiments.—Saturated solutions containing 2 mg of IIa, IIIa, VIII, or IX in acetone were injected onto a preparative 2% OV-210 column and material eluted from the column up to 30 min (containing minor components with t_R 0.40, 0.78, and 1.55 and IIb and IIIb if present) was collected in a capillary; material eluted between 30 and 120 min (containing VI and VII) was collected in a second capillary. Sterols were rinsed with acetone from the collecting capillaries and chromatographed on thin layer chromatoplates irrigated several times with ethyl acetate–benzene (1:1) to resolve major components. In no case did VIII or IX survive gas chromatography, both being completely converted to VI and VII.

5α-Cholestane-3,6-dione (VI).—Material eluted between 30 and 120 min from injections of IIa, IIIa, VIII, or IX was resolved by thin layer chromatography into two ultraviolet light absorbing zones at R_f 0.70 and 0.76. Material from the less mobile zone (R_f 0.70) was eluted with acetone and recrystallized from acetone, yielding pure VI: mp 169° (lit.[20] mp 168–172°); $\bar{\nu}_{max}^{KBr}$ 1715 cm^{-1}; R_f 0.70 in ethyl acetate–benzene (1:1); yellow color with 50% aqueous sulfuric acid; t_R 7.14 on 2% OV-210, 6.65 on 3% SP-2401; identical in these properties with authentic samples of VI prepared from VIII[13a] and by alkaline isomerization of IX.[13b]

Cholest-4-ene-3,6-dione (VII).—The more mobile zone (R_f 0.76) containing ultraviolet light absorbing material obtained on thin layer chromatograms from which VI had been isolated (from pyrolysis of IIa, IIIa, VIII, or IX) was eluted with acetone and recrystallized from methanol, yielding pure VII: mp 120–123° (lit.[20] mp 122–125°); $\bar{\nu}_{max}^{KBr}$ 1685, 1600 cm^{-1}; $\lambda_{max}^{CHCl_3}$ 253 nm (lit.[21] $\lambda_{max}^{CHCl_3}$ 252 nm); R_f 0.76 in ethyl acetate–benzene (1:1); yellow color with 50% aqueous sulfuric acid; t_R 7.80 on 2% OV-210, 7.13 on 3% SP-2401; identical in these properties with an authentic sample of VII.

Isomerization of 6β-Hydroxycholest-4-en-3-one (IX).—A solution of 6.3 mg of IX in 10 ml of 10% methanolic KOH was heated at 75° for 99 min. The cooled solution was neutralized and extracted into diethyl ether, the ether extract was evaporated under vacuum, and the residue was chromatographed on a chromatoplate irrigated twice with ethyl acetate–benzene (1:1). The more mobile zone (R_f 0.76) was eluted with acetone and recrystallized from methanol, yielding pure VII, mp 121–124°. The more polar zone (R_f 0.70) eluted with and recrystallized from acetone yielded pure VI, mp 166–170°, identical in physical properties with a sample of VI prepared from VIII.[13a]

Registry No.—IIa, 41209-87-4; IIb, 570-88-7; IIIa, 41209-89-6; IIIb, 15013-60-2; VI, 2243-09-6; VII, 984-84-9; IX, 570-89-8; cholesterol, 57-88-5.

(21) L. Dorfman, *Chem. Rev.*, **53**, 47 (1953).

A Ring Enlargement Reaction of Phenylmethoxycyclopropenone. A Regiospecific Mass Spectrometric CO Extrusion in Phenylmethoxycyclobutenedione

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Isonitriles have been reported to react with small ring unsaturated ketones to give ring enlarged derivatives. Thus, 2,6-dimethylphenylisonitrile reacts with diphenylcyclopropenone (**1**) to give 4,5-bis(2,6-dimethylphenylimino)-2,3-diphenylcyclopenten-1-one (**2**), which can be hydrolyzed to diphenylcyclopentenetrione.[1] In the presence of triphenylphosphine, **1** is converted into diphenylcyclobutenedione by way of 4-(2,6-dimethylphenylimino)-2,3-diphenylcyclobuten-1-one (**3**).[2] We would like to report the results of similar experiments with phenylmethoxycyclopropenone (**4**)[3] including the structure of the intermediate 4-(2,6-dimethylphenylimino)-3-methoxy-2-phenylcyclobuten-1-one (**5**) and two interesting processes which were discovered during the course of elucidating the structure of **5**: a regiospecific loss of CO from phenylmethoxycyclobutenedione (**6**) upon electron impact and a regioselective incorporation of ^{18}O in phenylhydroxycyclobutenedione (**7**) involving the enolate ion (**7b**).

Treatment of **4** with an excess of 2,6-dimethylphenylisonitrile in refluxing benzene overnight under a nitrogen atmosphere afforded a dark solution which, after removal of the solvent and isonitrile under vacuum, slowly crystallized. Recrystallization from hexane afforded 4-(2,6-dimethylphenylimino)-3-methoxy-2-phenylcyclobuten-1-one (**5**) as yellow crystals. The gross structural features of **5** were established by hydrolysis to phenylmethoxycyclobutenedione[4] (**6**) and 2,6-dimethylaniline, isolated as the hydrochloride, in 80% yield. Compound **6** was identified by comparison to a sample prepared from squaric acid.[5] The nuclear magnetic resonance spectrum of **5** was in agreement with the proposed structure, exhibiting resonances congruous with aromatic protons (8 H), methoxyl protons (3 H), and aromatic methyls (6 H). The mass spectrum of **5**, although consistent with the proposed structure, did not give any additional structural information.

In contrast to **1**, phenylmethoxycyclopropenone (**4**) does not yield cyclopentenetrione derivatives when treated with 2,5-dimethylphenylisonitrile.[1] Carrying out the reaction at room temperature for 20 hr in the presence of trace amounts of triphenylphosphine, conditions which convert **1** into **3**,[2] afforded a mixture of

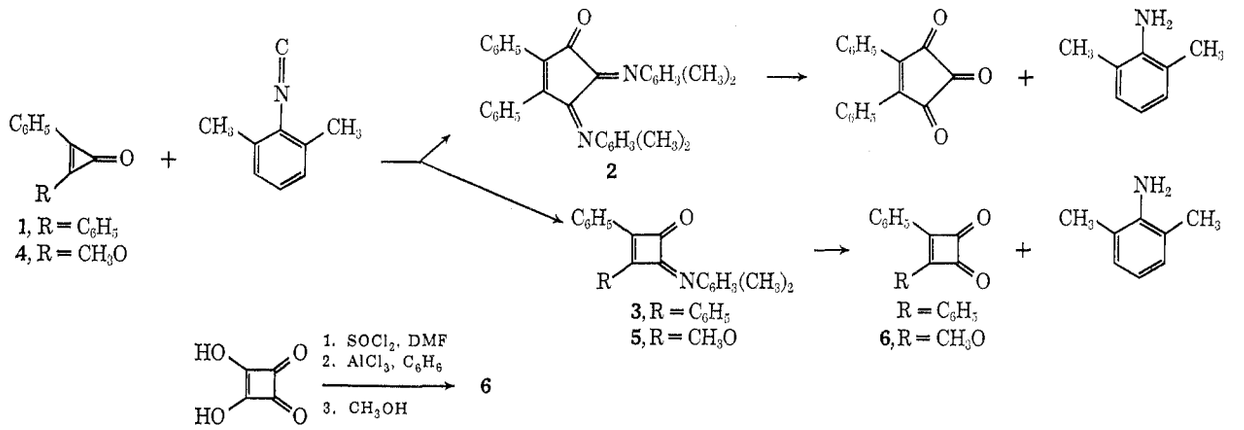
(1) T. Takizawa, N. Obata, Y. Suzuki, and T. Yanagida, *Tetrahedron Lett.*, 3403 (1969).

(2) N. Obata and T. Takizawa, *Tetrahedron Lett.*, 2231 (1970).

(3) (a) D. G. Farnum, J. S. Chickos, and P. Thurston, *J. Amer. Chem. Soc.*, **88**, 3075 (1966); (b) R. West, J. S. Chickos, and S. Osawa, *ibid.*, **90**, 3885 (1968); J. S. Chickos, L. Patton, and R. West, manuscript in preparation.

(4) E. J. Smutny, M. C. Caserio, and J. D. Roberts, *J. Amer. Chem. Soc.*, **82**, 1793 (1960).

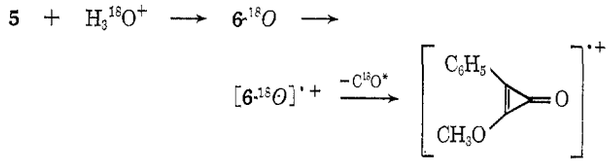
(5) R. C. De Selms, C. J. Fox, and R. C. Riordan, *Tetrahedron Lett.*, 781 (1970).



starting materials and **5**. Heating the reaction mixture increased the conversion into **5**, which could be isolated by column chromatography. The fate of the triphenylphosphine was not determined.

The structure of **5** was completed by mass spectroscopic ^{18}O-labeling experiments performed on **6**. The 70-eV mass spectrum and major fragmentation pattern of **6** are shown in Figure 1 and Scheme I, respectively.[6,7] The fragmentation pathway is based on the labeling experiments and the observation of appropriate metastable ions (*).

Acid-catalyzed hydrolysis of **5** in ^{18}O-enriched water led to the incorporation of only one ^{18}O-labeled oxygen. The single label was identified by the presence of a P + 2 parent molecular ion (29% of the molecular ion intensity) in the mass spectrum of **6**. It was further observed that 99 ± 5% of this label was absent in the P − CO^+ molecular ion, and that metastables corresponding to the loss of $C^{16}O$ and $C^{18}O$ from the parent molecular ion were observable.



To establish which of the three oxygens was specifically being lost, the following experiments were performed. First, to determine whether ^{18}O could be incorporated into **6** by exchange, phenylhydroxycyclobutenedione (**7**, pK_a[4] 0.37), dioxane, and enriched $H_2{}^{18}O$ (38 mol %) were heated for 15 min at 70°. Following methylation with diazomethane, the isotopic distribution associated with the parent P − CO^+ and P − $2CO^+$ ions was found to be consistent with a statistical ^{18}O distribution (29% enrichment; see Experimental Section). As a control experiment, **6**, statistically labeled with ^{18}O, was dissolved in H_2O–dioxane and allowed to stand 30 min at room temperature. Mass spectral analysis revealed that the ^{18}O content of the P^+, P − CO^+, and P − $2CO^+$ ions was approximately the same. Furthermore, unlabeled **6**, dissolved in dioxane–$H_2{}^{18}O$–HCl, for 30 min did not

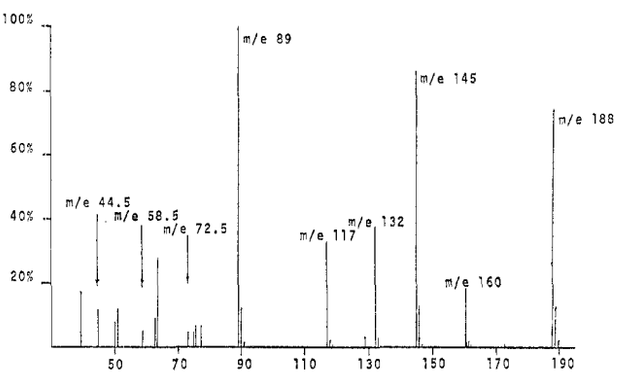
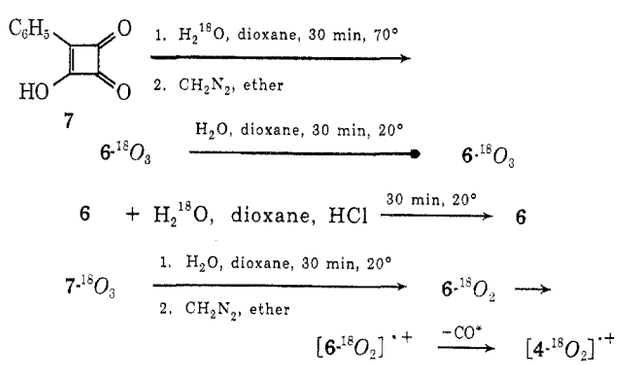


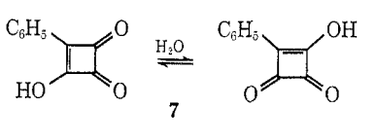
Figure 1.—The mass spectrum of phenylmethoxycyclobutenone (**6**).

incorporate any significant amount of ^{18}O, demonstrating the identity of the position of attachment of the label obtained from hydrolysis of **5** in $H_2{}^{18}O$ and the position of attachment of the imino group in **5**.

Treatment of **7** with $H_2{}^{18}O$–dioxane for 30 min at room temperature followed by methylation, led to incorporation of only one ^{18}O in the parent molecular



ion, 90 ± 5% of which was lost in the P − CO^+ ion. Alternatively, statistically labeled **7**, dissolved in H_2O–dioxane, for 30 min at room temperature followed by methylation afforded **5** in which the parent and P − CO^+ ions contained approximately the same amount of ^{18}O.

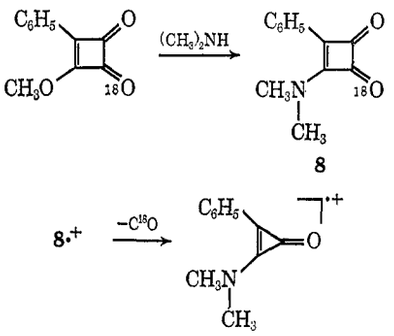


The equivalency of positions 1 and 3 on the time scale employed due to tautomerism in **7** would require loss of

(6) The mass spectrum of **3** was practically superimposable on the spectrum of **5** below *m/e* 160, suggesting common ions and fragmentation pathways.

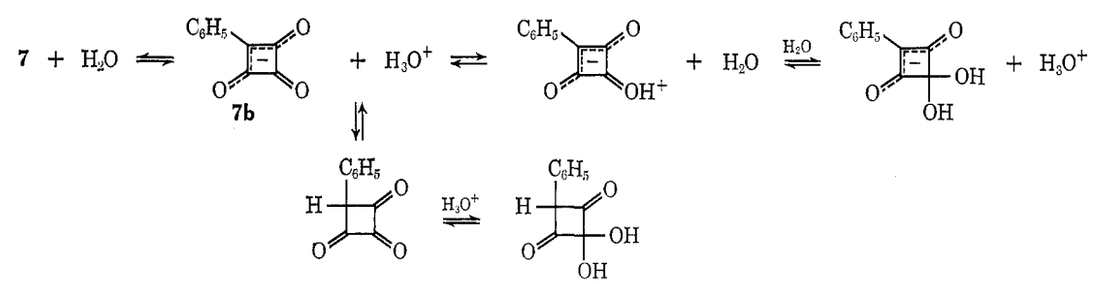
(7) A similar sequential loss of carbon monoxide has also been observed in the oxocarbons, rhodizonic, croconic, and squaric acids: S. Skujins, J. Delderfield, and G. A. Webb, *Tetrahedron*, **24**, 4805 (1968).

only 50% of the ^{18}O label in the P − CO^+ ion if the oxygen at these positions was lost. On the basis of these experiments therefore, it can be concluded that the 2,6-dimethylphenylimino grouping in **5** is attached at position 4 of the ring as shown.



To test the generality of the regiospecific CO extrusion observed in the mass spectrum of **6**, phenyl-*N*,*N*-dimethylaminocyclobutenedione (**8**), labeled with ^{18}O in the 4 position, was prepared as shown. A similar specificity in extruding CO was also observed here. Methylhydroxycyclobutenedione[8] showed a similar selectivity in incorporating ^{18}O by exchange and specificity in extrusion of CO.

The failure to observe ^{18}O exchange in **6** with rates comparable to those in which one label is introduced in **7** suggests that acid-catalyzed ^{18}O exchange of the carbonyl group is occurring *via* the enolate anion as shown. Consistent with this interpretation was the failure to observe any significant change in the rate of ^{18}O incorporation into **7** with added mineral acid. Two possible pathways, protonation at carbon to yield phenylcyclobutanetrione or at oxygen to give a dipolar ion, appear likely. A distinction between these two tautomeric possibilities is not presently possible.



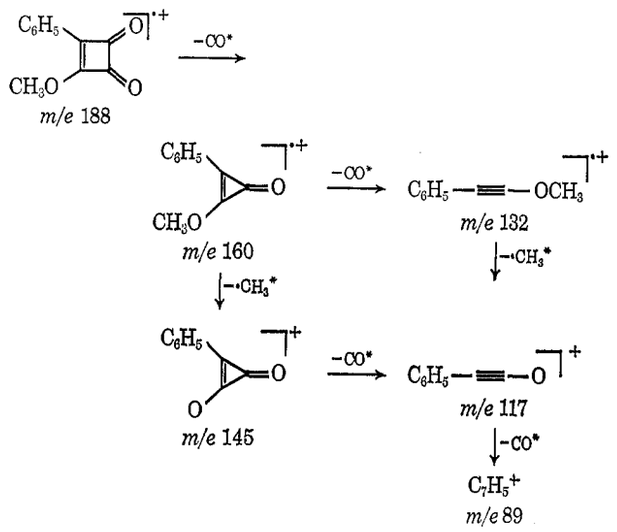
Similar results involving only the enolate ion and not the neutral enol have recently been reported in a study of the keto-enol tautomerism of 3-hydroxy-2,4-dimethylcyclobutenone.[9] It appears that those factors which promote the strong acid character of these compounds also destabilize protonation of the neutral enols to an extent that prototropic tautomerism by way of the enolate becomes the energetically preferred pathway.

Experimental Section

Melting points were taken on a Hoover Thomas melting point apparatus and are uncorrected. Microanalyses were determined by Galbraith Laboratories, Knoxville, Tenn. Infrared spectra were recorded on a Perkin-Elmer Infracord, Model 137; nmr spectra were recorded on a Varian T-60 spectrometer and Perkin-Elmer R-20 60MHz spectrometer equipped with a variable temperature probe. Mass spectra were recorded on an AEI MS 12 spectrometer. ^{18}O analyses were obtained by measurement of line intensities at 70 eV and are normalized to 100%. The error associated with measurement of each molecular ion approximates ±1% of the recorded value. The $H_2{}^{18}O$ (38% ^{18}O enrichment) was obtained from Diaprep, Inc., Atlanta, Ga.

SCHEME I

THE MAJOR MASS SPECTROMETRIC FRAGMENTATION PATHWAYS OF PHENYLMETHOXYCYCLOBUTENEDIONE



Preparation of 4-(2,6-Dimethylphenylimino)-3-methoxy-2-phenylcyclobuten-1-one (5).—Phenylmethoxycyclopropenone, prepared as reported[3] (1.4 g, 8.75 mmol), mp 44–47° (lit.[3a] 54–57), was refluxed in benzene under nitrogen with an excess of 2,6-dimethylphenylisonitrile[10] (3.44 g, 26.3 mmol) for several hours. The solution slowly darkened. Evaporation of the solvent followed by fractional sublimation afforded unreacted isonitrile (2.0 g). The residue, which slowly crystallized, was purified by recrystallization from hexane to afford yellow crystals of **5** (2.05 g, 80%): mp 97–99°; ν_{max} (Nujol) 1780, 1695, and 1590 cm^{-1}; nmr (30°, $CDCl_3$, TMS) τ 7.83 (s, 6 H), 5.28 (broad s, $w_{1/2}$ = 4 Hz, 2.9 H), 3.0 (broad s, 3 H), 2.64 (m, 3 H), 2.15 (m, 2 H); a sharp absorption ($w_{1/2}$ = 1 Hz) for the resonance at 5.28 was observed at −10 and 68°.

Anal. Calcd for $C_{19}H_{17}NO_2$: C, 78.35; H, 5.84, O, 10.99; mol wt, 291. Found: C, 77.98; H, 5.68; O, 10.65; *m/e*, 291.

Hydrolysis of 4-(2,6-Dimethylphenylimino)-3-methoxy-2-phenylcyclobuten-1-one (5).—A solution containing **5** (1.87 g, 6.42 mmol), acetone (30 ml), and hydrochloric acid (2.5 *N*, 25 ml) was warmed to 40° briefly, and then a stream of nitrogen was used to remove the solvent. The residue (2.37 g) was extracted with methylene chloride leaving a white crystalline solid behind (1.01 g, 82%) identified as 2,6-dimethylaniline hydrochloride by comparison with an authentic sample. The methylene chloride was evaporated, affording crude **6** (1.11 g, 92%): mp 140–150°; recrystallized (CH_3OH, 640 mg), mp 150–151° (lit.[4] 151–152°). Compound **6** was identical with a sample of material isolated from methanolysis of phenylchlorocyclobutenedione, prepared by the

(8) J. S. Chickos, *J. Amer. Chem. Soc.*, **92**, 5749 (1970).

(9) J. S. Chickos and R. E. K. Winter, *J. Amer. Chem. Soc.*, **95**, 506 (1973).

(10) I. Ugi, U. Fetzer, U. Eholzer, H. Krupfer, and K. Offermann, *Angew. Chem.*, **77**, 492 (1965); *Angew. Chem., Int. Ed. Engl.*, **4**, 472 (1965); R. Meyer, *Chem. Ber.*, **93**, 239 (1960).

reaction of dichlorocyclobutenedione with benzene and aluminum chloride.[5] Hydrolysis of **6** (640 mg, 3.4 mmol) afforded **7** (400 mg, 68%), mp 206–208° (lit.[4] 208–211°).

Reaction of Phenylmethoxycyclopropenone (4) with 2,6-Dimethylphenylisonitrile in the Presence of Triphenylphosphine.—Phenylmethoxycyclopropenone (200 mg, 1.25 mmol), 2,6-dimethylphenylisonitrile (164 mg, 1.25 mmol), and triphenylphosphine (16 mg) were dissolved in benzene and allowed to stand overnight under an atmosphere of nitrogen. Analysis of the reaction mixture by nmr indicated the presence of approximately 15% **5** and the remainder unreacted **4**. Heating the mixture for several hours afforded mainly **5** (according to nmr analysis). Chromatography of the residue on silica gel (CH_2Cl_2) after removal of the solvent afforded **5** (154 mg, 42%). The fate of the triphenylphosphine was not determined.

Hydrolysis of 4-(2,6-Dimethylphenylimino)-3-methoxy-2-phenylcyclobuten-1-one (5) with $H_2{}^{18}O$.—A solution prepared by dissolving **5** (52 mg, 0.18 mmol), $H_2{}^{18}O$ (47 mg, 2.53 mmol of 38% ^{18}O content), dioxane (787 mg), and concentrated hydrochloric acid (23 mg, 0.205 mmol) was allowed to stand at room temperature. After 30 min the solution was evaporated *in vacuo* and the residue partitioned between methylene chloride–water. Next the organic phase was dried over $MgSO_4$ and evaporated. Sublimation of the residue afforded ^{18}O-labeled **6** (mp 140–150°, 31 mg): recrystallized from methanol, mp 150–151° (18 mg). It was observed that no label was lost during the recrystallization process.

^{18}O Analysis. Found: P, *m/e* 188, 70.2%; P + 2, 29.1%; P + 4, 0.6%; P − CO, *m/e* 160, 98.8%; P + 2, 1.2%. Calcd for P (based on 29% ^{18}O enrichment, 1 ^{18}O incorporated): *m/e* 188, 71%; P + 2, 29%; P − CO (based on natural isotopic abundance), *m/e* 160, 99.1%; P + 2, 0.9%.

Stereoselective ^{18}O Incorporation into Phenylhydroxycyclobutenedione (7).—Compound **7** (31 mg, 0.178 mmol) was dissolved in dioxane (54 mg) containing $H_2{}^{18}O$ (40 mg, 2.1 mmol) and allowed to stand 30 min at room temperature. The solvent was removed *in vacuo* and the residue dissolved in ether, treated with excess anhydrous diazomethane,[11] and then evacuated. Recrystallization of the residue from heptane followed by sublimation afforded **6** (28 mg, 84%), mp 149–151°.

^{18}O Analysis. Found: P, *m/e* 188, 73%; P + 2, 25.9%; P + 4, 1.1%; P − CO, *m/e* 160, 95%; P + 2, 5%. Calcd for stereospecific incorporation of ^{18}O and stereospecific loss of $C^{18}O$: P − CO, *m/e* 160, 99%; P + 2, 1%. Calcd for a 10% statistical incorporation of ^{18}O: P, *m/e* 188, 72.9%; P + 2, 24.3%; P + 4, 2.7%; P + 6, 0.1%; P − CO, *m/e* 160, 81%; P + 2, 18%; P + 4, 1%.

Statistical ^{18}O Incorporation into Phenylhydroxycyclobutenedione (7).—Compound **7** (30 mg, 0.16 mmol), dioxane (30 mg), and $H_2{}^{18}O$ (58 mg, 3.1 mmol) were heated to 70° for 15 min. Evaporation of the solution followed by reaction with diazomethane, recrystallization (heptane), and sublimation gave **6** (25 mg), mp 149–152°. Theoretical equilibrium ^{18}O incorporation calcd, 32.7%; found, 29%.

^{18}O Analysis. Found: P, *m/e* 188, 36%; P + 2, 43.2%; P + 4, 18%; P + 6, 2.7%; P − CO, *m/e* 160, 53.8%; P + 2, 37.3%; P + 4, 8.9%; P − 2CO, *m/e* 132, 73.2%; P + 2, 26.8%. Calcd for 29% ^{18}O statistically distributed: P, *m/e* 188, 35.8%; P + 2, 43.6%; P + 4, 17.9%; P + 6, 2.4%; P − CO, *m/e* 160, 50.4%; P + 2, 41.2%; P + 4, 8.4%; P − 2CO, *m/e* 132, 71%; P + 2, 29%.

Stereoselective ^{18}O Hydrolysis from Statistically Labeled Phenylhydroxycyclobutenedione-$^{18}O_3$ (7).—Compound **7** (12 mg, 0.069 mmol), dioxane (48 mg), and $H_2{}^{18}O$ (23 mg, 1.22 mmol) were heated to 70° for 15 min. The solvent was evaporated *in vacuo*. The residue was dissolved in dioxane (55 mg) and H_2O (53 mg, 2.95 mmol) and kept at room temperature for 30 min. Evaporation of the solvent, reaction with diazomethane, recrystallization, and sublimation afforded **6** (6 mg), mp 148–150°. The ^{18}O distribution could best be accounted for by ^{18}O substitution at positions 1 and 3 and ^{16}O at position 4, assuming a regiospecific loss of CO from position 4.

^{18}O Analysis. Found: P, *m/e* 188, 63.2%; P + 2, 31.6%; P + 4, 5.3%; P − CO, *m/e* 160, 66.3%; P + 2, 29.8%; P + 4, 3.9%; P − 2CO, *m/e* 132, 82%; P + 2, 18%. Calcd assuming a 14% statistical distribution of ^{18}O: P, *m/e* 188, 63.5%; P + 2, 31.1%; P + 4, 5%; P + 6, 0.3%; P − CO, *m/e* 160, 74%; P + 2, 24%; P + 4, 2%; P − 2CO, *m/e* 132, 86%; P + 2, 14%. Calcd assuming a 19% ^{18}O content at positions 1 and 3 and 100% ^{18}O content at position 4 and a regiospecific loss of CO from position 4: P, *m/e* 188, 65.6%; P + 2, 30.8%; P + 4, 3.6%; P − CO, *m/e* 160, 65.6%; P + 2, 30.8%; P + 4, 3.6%; P − 2CO, *m/e* 132, 81%; P + 2, 19%.

Attempted ^{16}O Exchange in Statistically Labeled Phenylmethoxycyclobutenedione-$^{18}O_3$ (6).—Statistically labeled **6**, from **7** (14 mg, 0.08 mmol) and $H_2{}^{18}O$ (21 mg, 1.12 mmol) in dioxane (29 mg), was prepared as previously described. Next, 2.5 *N* HCl (32 mg) and dioxane (438 mg) were added; the solution was allowed to stand for 30 min and then evacuated. The residue was recrystallized (heptane) and sublimed giving **6** (10 mg): mp 140–150°; recrystallized (CH_3OH), mp 148–150°. The ^{18}O content remained the same (within experimental error) after recrystallization from methanol. Less than 10% of the ^{18}O in the carbonyl group at position 4 was lost as indicated by mass spectroscopy.

Anal. Found: P, *m/e* 188, 37.5%; P + 2, 43%; P + 4, 17%; P + 6, 2.5%; P − CO, *m/e* 160, 50.5%; P + 2, 40%; P + 4, 9.3%; P − 2CO, *m/e* 132, 70.7%; P + 2, 29.4%.

Attempted ^{18}O Exchange in Unlabeled Phenylmethoxycyclobutenedione (6).—A solution containing **6** (7 mg, 0.021 mmol), dilute HCl (2.5 *N*, 10 mg), $H_2{}^{18}O$ (38% ^{18}O, 10 mg), and dioxane (138 mg) was allowed to stand 30 min at room temperature. Evaporation of the solvent followed by sublimation of residue afforded **6** (4 mg), mp 140–148°; recrystallized (methanol), mp 148–150°.

Anal. Found: P, *m/e* 188, 87%; P + 1, 10.8%; P + 2, 2.2%; P − CO, *m/e* 160, 89.2%; P + 1, 10%; P + 2, 2.5%. Calcd for natural isotopic abundance: P, *m/e* 188, 88.2%; P + 1, 10.8%; P + 2, 1.12%; P − CO, *m/e* 160, 89.2; P + 1, 10%; P + 2, 0.8%. Calcd for incorporation of 1 ^{18}O (theoretical): P, *m/e* 188, 73.2%; P + 1, 8.1%; P + 2, 16.7%; P + 3, 1.8%.

Preparation of Phenyl-*N*,*N*-dimethylaminocyclobutenedione (8).—To a solution of **6** (100 mg, 0.532 mmol) in ether was added an excess of dimethylamine gas. A yellow crystalline solid (**8**) was isolated by filtration (100 mg, 93%): mp 132–134° (heptane); ν max (Nujol) 1785, 1730, and 1610 cm^{-1}; nmr ($CDCl_3$, TMS, 30°) τ 6.83, 6.53 (broad s, 6 H, coalescence temp 39°), 2.6 (m, 5.1 H).

Anal. Calcd for $C_{12}H_{11}NO_2$: C, 71.63; H, 5.51; N, 6.96; mol wt, 201.21. Found: C, 71.84; H, 5.61; N, 6.82; *m/e*, 201.

Preparation of ^{18}O-Labeled Phenyl-*N*,*N*-dimethylaminocyclobutenedione (8).—Compound **6** (10 mg, 0.053 mmol) specifically labeled at the 4 position with ^{18}O (26% ^{18}O enrichment) was treated with anhydrous dimethylamine in anhydrous ether affording **8** (10 mg, 93%), mp 130–132°.

^{18}O Analysis. Found: P, *m/e* 201, 75%; P + 2, 25%; P − CO, *m/e* 173, 86.2%; P + 1, 12%; P + 2, 1.8%. Calcd for P − CO (natural isotopic abundance): *m/e* 173, 88%; P + 1, 11%; P + 2, 0.8%.

Incorporation of ^{18}O in Methylhydroxycyclobutenedione (9).—Compound **9**[8] (25 mg, 0.223 mmol) was dissolved in $H_2{}^{18}O$ (36 mg, 1.8 mmol) and heated to 70°. Evaporation of the solvent followed by sublimation afforded **9** (24 mg), mp 160–163° (lit.[8] 162–164).

^{18}O Analysis. Found: P, *m/e* 112, 34.1%; P + 2, 43.2%; P + 4, 18.9%; P + 6, 2.7%; P − CO, *m/e* 84, 50.7%; P + 2, 42%; P + 4, 7.2%. Calcd (statistical distribution, 30% ^{18}O enrichment): P, *m/e* 112, 34.3%; P + 2, 44.2%; P + 4, 18.9%; P + 6, 2.7%; P − CO, *m/e* 84, 49%; P + 2, 42%; P + 4, 9%.

Compound **9** (11 mg, 0.1 mmol, 30% ^{18}O enrichment, statistical distribution), dissolved in $H_2{}^{18}O$ (27 mg, 1.4 mmol) for 30 min at room temperature followed by evaporation of the solvent *in vacuo* and sublimation afforded **9** (8 mg), mp 160–163°.

^{18}O Analysis. Found: P, *m/e* 112, 51.2%; P + 2, 40%; P + 4, 9%; P − CO, *m/e* 84, 51.5%; P + 2, 40%; P + 4, 8.6%. Calcd for 28.5% ^{18}O enrichment at positions 1 and 3 and stereospecific loss of CO at position 4: P, P − CO; P, 51.2%; P + 2, 40.6%; P + 4, 8.1%.

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Registry No.—**4**, 6460-83-9; **5**, 41328-60-3; **6**, 711-78-4; **6**-^{18}O, 41328-63-6; **6**-$^{18}O_2$, 41391-12-2; **6**-$^{18}O_3$, 41328-64-7; **7**, 708-10-1; **7**-$^{18}O_3$, 41328-66-9; **8**, 22118-96-4; **8**-^{18}O, 41328-68-1; **9**, 29769-75-3; **9**-$^{18}O_2$, 41328-70-5; 2,6-dimethylphenylisonitrile, 2769-71-3.

Abnormal Michael Reaction. The Reaction between 2-Cyclohexenone and Diethyl Methylmalonate

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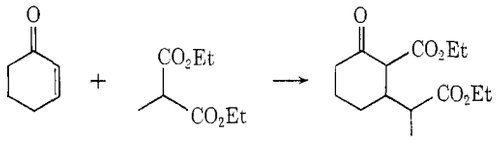
Although the abnormal Michael reaction has been investigated for a number of years, the synthetic aspects of this reaction have not been studied.[1-7] Recently, we have been interested in developing new syntheses of the sesquiterpene series, and thought that the reaction between 2-cyclohexenone and diethyl methylmalonate under these conditions would afford, if successful, the β-keto ester **1**, which could be a potential precursor for the synthesis of the cadalene family.



1

On investigating this reaction, we found that the reaction failed under the usual abnormal Michael conditions.[2] Distillation of the reaction mixture afforded only starting materials. Extending the reaction time did not affect the reaction course; however, when the concentrations of both reactants were increased, a reaction did occur. Under these modified conditions, the reaction mixture gave a positive ferric chloride test, and distillation of this mixture afforded ethyl propionate, diethyl methylmalonate, and 2-(3-oxocyclohexyl)-2-cyclohexenone (**2**). We were unable to distill any substance which displayed a positive ferric chloride test from the mixture.

Thick layer chromatographic analysis of the remaining oil afforded a band which gave the enol test. Extraction of this band with methanol and subsequent 2,4-dinitrophenylhydrazone formation yielded a crystalline compound which analyzed for $C_{21}H_{24}N_4O_7$. Based upon nmr analysis, the hydrazone appears to be a derivative of 2-(2-ethoxycarbonyl-3-oxocyclohexyl)-2-cyclohexenone (**3**). In addition to the characteristic signals due to the protons of the 2,4-dinitrophenyl nucleus, the derivative has a complex series of signals at δ 1.5–2.5, a quartet centered at δ 4.05, and a complex multiplet at δ 7.42. The upfield portion of the spectrum and the signal in the vinyl region are very similar to the signals in the spectrum of 2-(3-oxocyclohexyl)-2-cyclohexenone.

(1) A. Michael, *J. Prakt. Chem.*, **35**, 349 (1887).
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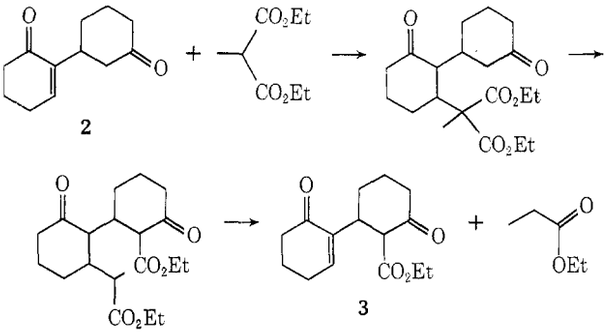
The isolation of **2** and **3** suggests the following conversion.



2

3

In order to test this reaction scheme, we prepared 2-(3-oxocyclohexyl)-2-cyclohexenone[8] and subjected it to abnormal Michael conditions. Analysis of this mixture revealed the presence of the same reaction products as in the 2-cyclohexenone reaction. Distillation afforded ethyl propionate, diethyl methylmalonate, and **2**; thick layer chromatography of the residue yielded a single positive ferric chloride band which gave a 2,4-dinitrophenylhydrazone identical with the one produced from the 2-cyclohexenone sequence.

Thus, it appears that the facile conversion of 2-cyclohexenone into **2** precludes the employment of the abnormal Michael reaction in the synthesis of cyclic terpenoid systems.

Experimental Section

Reaction of Diethyl Methylmalonate with 2-Cyclohexenone with a Minimum of Solvent.—Diethyl methylmalonate (8.7 g, 0.05 mol) and 2-cyclohexenone (4.8 g, 0.05 mol) were refluxed in a solution of sodium (1.15 g, 0.05 mol) in absolute ethanol (25 ml) for 24 hr under nitrogen. The reaction mixture was neutralized, taken up in ether (100 ml), and washed with water (2 × 50 ml). The ether was dried and concentrated to give a crude oil (10.0 g). Distillation of this oil gave ethyl propionate (0.2 g, 22%), diethyl methylmalonate (2.8 g, 32%), and 2-(3-oxocyclohexyl)-2-cyclohexenone (**2**): 1.1 g (23%); bp 132–134° (4 mm); ir (CCl_4) 5.82 (C=O), 5.95 μ (α,β-unsaturated C=O); uv max (95% EtOH) 233 mμ; nmr ($DCCl_3$) δ 6.74 (t, 1). Chromatography of the crude oil (silica; elution with 3% ethyl acetate in heptane) followed by extraction of the enolic band with methanol gave a yellow oil (0.050 g): 2,4-dinitrophenylhydrazone mp 182–184°; nmr ($DCCl_3$) δ 9.11 (d, 1), 8.30 (d, 1), 7.94 (d, 1), 7.42 (m, 1), 4.05 (m, 2).

Anal. Calcd for $C_{21}H_{24}N_4O7$: C, 56.76; H, 5.41; N, 12.61. Found: C, 56.58; H, 5.55; N, 12.97.

Preparation of 2-(3-Oxocyclohexyl)-2-cyclohexenone.—2-Cyclohexenone (9.6 g, 0.1 mol) was treated with a solution of sodium (0.23 g, 0.01 mol, in 100 ml of ethanol) at 0° for 72 hr. Neutralization and concentration gave a crude mixture, which was taken up in diethyl ether (100 ml) and washed with water (2 × 50 ml). The ether layer was dried (Na_2SO_4) and concentrated. The resulting oil afforded 3-ethoxycyclohexanone (0.8 g, 6%) and 2-(3-oxocyclohexyl)-2-cyclohexenone (**2**) (3.2 g, 33%) which was identical with the compound produced in the reaction between diethyl methylmalonate and 2-cyclohexenone.

Anal. Calcd for $C_{12}H_{16}O_2$: C, 75.00; H, 8.33. Found: C, 75.18; H, 7.99.

Reaction between 2-(3-Oxocyclohexyl)-3-cyclohexenone and Diethyl Methylmalonate.—2-(3-Oxocyclohexyl)-2-cyclohexenone (7.7 g, 0.08 mol) and diethyl methylmalonate (13.9 g. 0.08 mol) in absolute ethanol (20 ml) were refluxed in the presence of sodium (1.8 g, 0.08 mol) for 24 hr under nitrogen. The reaction mixture was neutralized, taken up in ether, and washed with water. The ethereal solution was dried (Na_2SO_4) and concentrated. Subsequent distillation of the oil yielded ethyl propionate, diethyl methylmalonate, and 2-(3-oxocyclohexyl)-2-cyclohexenone. Chromatography of the pot residue and subsequent treatment of the enol component with 2,4-dinitrophenyl-

(8) J. E. Englehart and J. R. McDivitt, *J. Org. Chem.*, **36**, 367 (1971).