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New Photoisomerization Paths for Epoxy-2,4-cyclohexadienones and a General Mechanistic Scheme for the Photoisomerization of α,β-Unsaturated γ,δ-Epoxy Ketones

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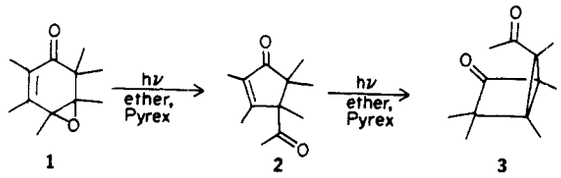
Two new reaction paths not previously observed in the irradiation of 2,4-cyclohexadienone 4,5-epoxides are described. Irradiation of 6,6-dimethyl-2,4-cyclohexadienone 4,5-epoxide (**5**) through Pyrex gave mainly the enol lactone **6**. The proposed mechanism, supported by isotopic labeling, involves as an intermediate the cyclopropanone aldehyde G (also implicated as the precursor of **6** in the singlet oxygen oxidation of dimethylfulvene). The photoisomerization of **5** to **6** involves a triplet excited state ($E_T \simeq 50$–60 kcal/mol). Irradiation of 2,3,4,6,6-pentamethyl-2,4-cyclohexadienone 4,5-epoxide (**19**) through Pyrex gave, among other products, the Δ^2-butenolide **22** (27%), a product best accounted for if the first bond-breaking step is cleavage of the C(1)–C(6) bond in **19**. This is the first example of α-cleavage in the irradiation of epoxy enones of this type. A general mechanism is proposed for the photoisomerization of 2,4-cyclohexadienone 4,5-epoxides. The first step following excitation is either α-cleavage (rare) or cleavage of the C(4)–O bond of the epoxide ring (common) to give diradical D, which may isomerize in one or more of four different ways depending on methyl substitution. Experimental examples of each path are given. A general mechanistic scheme is proposed which summarizes to date the observed photoisomerizations of α,β-unsaturated γ,δ-epoxy ketones.

We recently reported that the epoxy ketone **1** is converted by irradiation to **2** and then **3**.[1] In this paper, we will describe

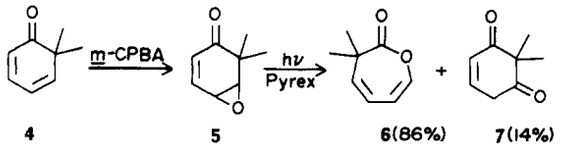


1 **2** **3**

the photochemistry of analogues of **1** containing fewer methyl substituents. These studies disclosed novel photoisomerization paths not previously observed with such epoxy ketones, for one of which we propose a cyclopropanone intermediate.[2] Following a description of these new reactions and evidence for their mechanisms, we will present a general mechanistic scheme which summarizes the known photochemistry of α,β-unsaturated γ,δ-epoxy ketones to date, and which places the new reactions in perspective.

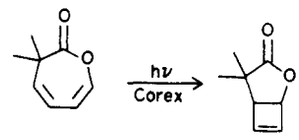
Results and Discussion

Photochemistry of 6,6-Dimethyl-2,4-cyclohexadienone 4,5-Epoxide (5). The epoxy ketone **5** was obtained in high yield by oxidizing the corresponding dienone **4**[3] with *m*-chloroperbenzoic acid (*m*-CPBA).



4 **5** **6(86%)** **7(14%)**

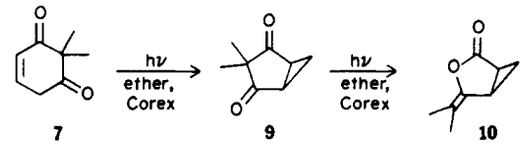
Irradiation of **5** (0.01 M in ether, Pyrex) gave two photoisomers in quantitative yield. The major product (86%) was the enol lactone **6**, a compound which has recently been ob-



6 **8**

tained[4] as the major product from the reaction of singlet oxygen with 6,6-dimethylfulvene (Scheme II). Irradiation of **6** through Corex converted it to the isomeric lactone **8**.[5]

The minor product (14%) was assigned the unsaturated β-diketone structure **7** on the basis of its spectra and further transformations. In particular, irradiation of **7** through Corex gave in succession the known β-diketone **9**[6b] and unsaturated lactone **10**.[6b] The first of these photoisomerizations is an



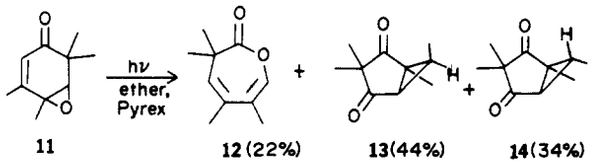
7 **9** **10**

oxa-di-π-methane rearrangement,[7] and the second involves the typical α-cleavage of a cyclic nonenolizable β-diketone.[6]

It is clear from the product structures that the methyl

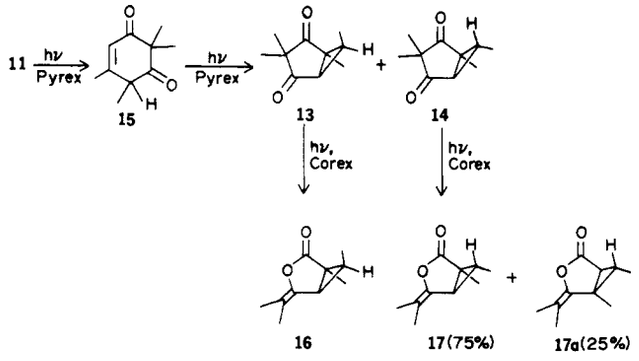
substituents play an important part in determining the photoisomerization paths of **1** and **5**. Before discussing the mechanism by which **6** and **7** are formed from **5**, and before trying to rationalize the different photoisomerization paths of **1** and **5**, it will be helpful to summarize the results obtained by irradiating dienone epoxides with an intermediate number of methyl substituents.

Photochemistry of Other 2,4-Cyclohexadienone Epoxides. The epoxy ketones **11**, **19**, and **24** were prepared from the corresponding dienones by oxidation with *m*-CPBA. Ir-



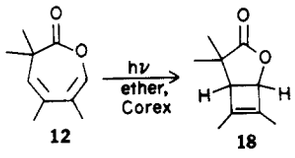
11 **12** (22%) **13** (44%) **14** (34%)

radiation of **11** (0.06 M in ether, Pyrex) gave the enol lactone **12** and the epimeric β-diketones **13** and **14**. The latter two compounds are secondary products derived from the primary photoproduct **15** (analogous to the formation of **9** from **7**). The methyl substituents must enhance this reaction, thus preventing us from observing **15**.[8] The structures of **13** and **14** were confirmed by their conversion to the lactones **16**–**17** on irradiation through a Corex filter.[9]



16 **17** (75%) **17a** (25%)

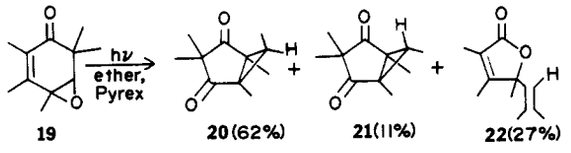
The structure of the enol lactone **12** was established as follows. Its IR and UV spectra were similar to those of **6**. The NMR spectrum showed a sharp singlet for the *gem*-dimethyl group, two vinyl protons (not coupled to each other) and two vinyl methyl groups. The exact location of the methyl groups was established by further irradiation of **12** through a Corex filter. The resulting **18** had no vinyl protons, but two mutually



12 **18**

coupled aliphatic protons at δ 2.82 and 4.67 (J = 4 Hz), the latter being the proton adjacent to the oxygen. This result required that the vinyl protons in **12** be at the termini of the diene moiety. The remainder of the NMR spectrum of **18** was consistent with this assignment.

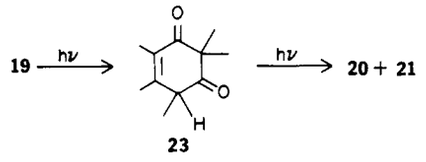
Except for quantitative aspects, the photochemistry of **5** and **11** appears to be identical, the primary products being an enol lactone (**6** and **12**, respectively) and an α,β-unsaturated



19 **20** (62%) **21** (11%) **22** (27%)

β-diketone (**7** and **15**, respectively). Differences appeared when one more methyl substituent was added.

Irradiation of **19** (0.01 M in ether, Pyrex) gave the epimeric β-diketones **20** and **21** and the butenolide **22**. The first two compounds are again secondary products, derived from the further photoisomerization of the unsaturated β-diketone **23**.

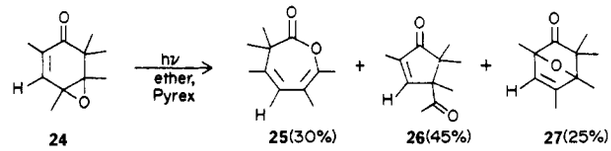


23

As with the formation of **15** (vide supra), it was not possible to detect the primary product **23**. However, we were able to obtain **23** through the treatment of **19** with trifluoroacetic acid.[10] Irradiation of **23** under the same conditions used with **19** gave a quantitative yield of **20** and **21**, in the same ratio as they were formed by irradiating **19**.

The structure of the butenolide **22** is based on its spectra. Its IR and UV spectra were nearly identical with those of the known analogue in which the vinyl hydrogen is replaced by a methyl group.[11] The NMR spectrum of **22** showed one aliphatic methyl singlet (δ 1.23), four vinyl methyls in the region δ 1.74–1.80 and one vinyl proton as a multiplet at δ 5.40. Decoupling by irradiation in the vinyl methyl region sharpened the vinyl proton signal to a singlet. Europium-shift data (see Experimental Section) and deuterium labeling experiments further support the structure. We consider **22** and **23** to be the direct photoproducts of **19**.[12]

The third epoxy ketone whose photochemistry we will describe in this section is **24**.[13] Irradiation of **24** (0.01 M in ether,

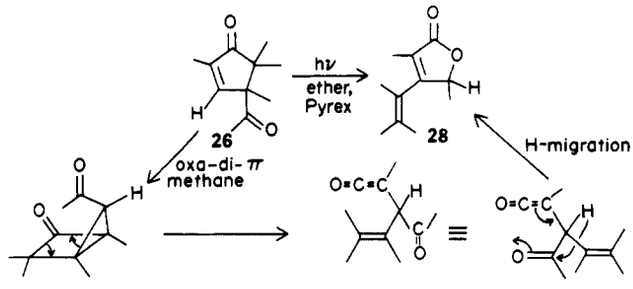


24 **25** (30%) **26** (45%) **27** (25%)

Pyrex) gave the enol lactone **25**, the acetyl cyclopentenone **26**, and the bicyclic ketone **27**.

The gross structure of **25** was clear from the similarity of its IR, UV, and NMR spectra to those of **6** and **12**. Since the vinyl proton in **24** occupies a position corresponding to a methyl group in **11** (and therefore in **12**) the proton in **25** must be located on one of the two central carbons of the butadiene moiety. Of the two alternative structures, only **25** was consistent with the europium and chemical-shift data, and with the results of labeling experiments (vide infra).[14]

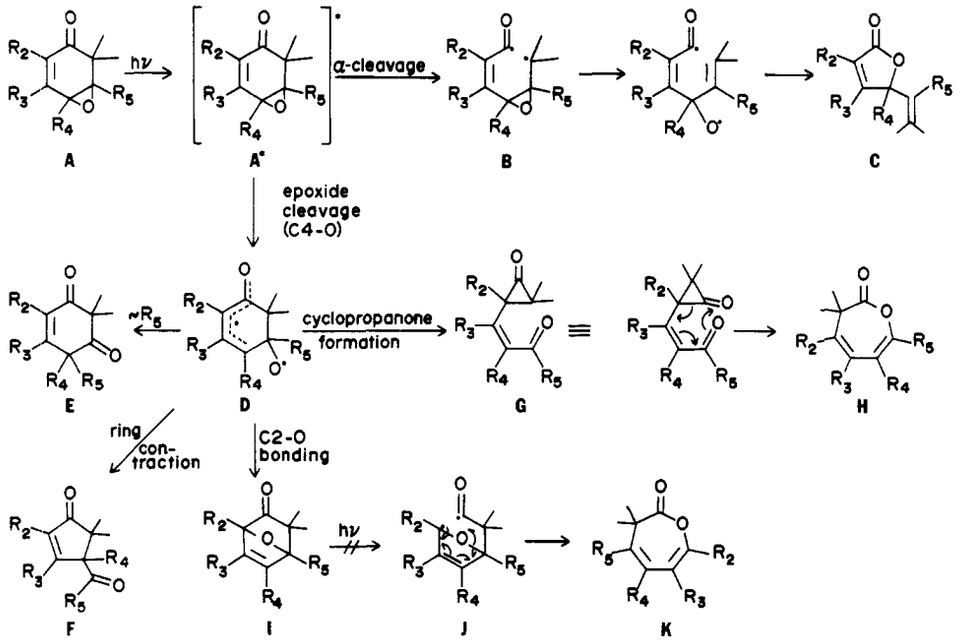
Compound **26** was analogous to **2**; their IR, UV, and NMR spectra (except for the vinyl proton) were nearly identical. Although **26** was an initial photoproduct of **24**, prolonged ir-



radiation converted it quantitatively to an isomer, the butenolide **28**. This conversion has a direct analogy[1,15] and undoubtedly proceeds via the bicyclic and ketene intermediates shown.

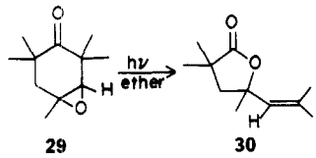
The third photolysis product of **24** had a carbonyl band at 1740 cm^{-1} typical of a five-membered-ring ketone, and the UV spectrum showed only end absorption. The NMR spectrum of **27** showed one vinyl proton (δ 5.56), coupled with an adjacent vinyl methyl (δ 1.72, J = 2 Hz), and four aliphatic

Scheme I



methyls, two gem (δ 1.12, 1.14) and two bridgehead (δ 1.30, 1.32), requiring a bicycle structure such as that shown. The remainder of the structural assignment (i.e., relative positions of the groups on the 2-carbon bridges) is based on mechanistic grounds and labeling results (vide infra).

Mechanisms for the Photoisomerization of 2,4-Cyclohexadienone 4,5-Epoxides. Scheme I summarizes the mechanisms we considered to rationalize our results. Following excitation to A* there are two options, α-cleavage to give B, or epoxide cleavage to give D. α-Cleavage has not been observed in any previous photochemical studies on α,β-unsaturated γ,δ-epoxy ketones, but we include the path A* → B → C to rationalize the formation of **22** from **19**. This minor reaction pathway has some precedent. Compound **29**, a close saturated analogue of **19**, gave the lactone **30** as the sole photoisomerization product.[16]



29 **30**

The predominant pathway following excitation to A* is epoxide cleavage at the C(4)–O bond to give the diradical D. Four options for this diradical are shown in Scheme I. 1,2-Migration of R_5 will give the unsaturated β-diketone E, a path which is particularly important when R_5 = H (as in the formation of **7** from **5**, **15** from **11**, and **23** from **19**). Type E products may not be observable, however, since they contain nearly the same chromophore as the starting epoxy ketone A. Consequently E may compete effectively with A for the light and rearrange further. This was true of **15** and **23**, which were detectable only as their oxa-di-π-methane rearrangement products (**13** and **14** from **15**; **20** and **21** from **23**).

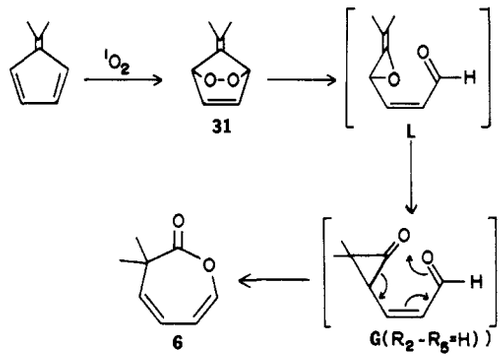
If R_5 is not hydrogen but methyl, then ring contraction is favored over R_5 migration, to give the cyclopentenone F. For example, this was the principal path in the photoisomerization of **1** (to **2**) and of **24** (to **26**). Once again the chromophore in this type of product (F) is similar to that of the starting epoxy ketone A, and further photoisomerizations may occur. In the examples studied, an oxa-di-π-methane rearrangement occurs (**3** from **2**, and **28** from **26**); however, this reaction usually is slow enough so that the initial photoproducts of type F can be isolated.

A third option open to biradical D is formation of cyclopropanone G. This reaction can be regarded as analogous to the ring contraction to F, except that a 1,4 instead of a 1,2 shift occurs. The reaction could be stepwise or concerted. The cyclopropanone G must be formed with cis geometry at the C(3)–C(4) double bond; consequently, a rapid subsequent six-electron electrocyclic reaction to form the seven-membered ring enol lactone H is possible.

A cyclopropanone intermediate of this type was proposed[4] to rationalize the formation of **6** from the reaction of singlet oxygen with dimethylfulvene (Scheme II). Cleavage of the O–O bond in the initial adduct **31** and rebonding was postulated to give the allene-oxide **L**, a precursor and valence tautomer of the cyclopropanone aldehyde G (R_2–R_5 = H).[17]

A plausible alternate route to the seven-membered ring enol lactones is also shown in Scheme I. The first step involves collapse of the diradical D to the bicyclic ether ketone I. In-

Scheme II



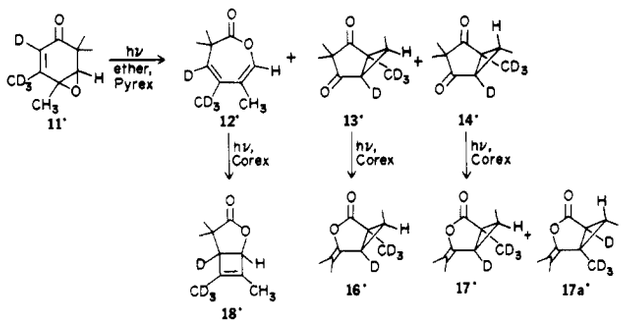
deed, a product of this type (**27**) was formed in the irradiation of **24**. Subsequent irradiation of I could cause α-cleavage to J, which on bond reorganization as shown in the scheme could lead to the enol lactone K.

This route to the enol lactones can be safely discarded on two grounds. First, irradiation of **27** (0.014 M in ether, Pyrex) under the same conditions which led to the enol lactone **25** from **24** gave no enol lactone whatever, only recovered starting material. Second, it will be noted that enol lactone derived from the cyclopropanone route (H) has the substituents R_2–R_5 arranged in the reverse order from enol lactone (K) derived from the two-photon route. The following deuterium-labeling

Table I. Substitution Pattern and Mechanistic Paths

Registry no.	Epoxy ketone	R_2	R_3	R_4	R_5	% R_5 migration	% ring contraction	% cyclopropanone formation	% C(2)–O bonding	% α-cleavage
63449-05-8	**5**	H	H	H	H	14	0	86	0	0
52898-22-3	**11**	H	CH_3	CH_3	H	78	0	22	0	0
63449-06-9	**19**	CH_3	CH_3	CH_3	H	73	0	0	0	27
50506-42-8	**1**	CH_3	CH_3	CH_3	CH_3	0	100	0	0	0
63449-07-0	**24**	CH_3	H	CH_3	CH_3	0	45	30	25	0

experiment was carried out to distinguish between these alternatives.



Irradiation of 11* (A, R_2 = D, R_3 = CD_3, R_4 = CH_3, R_5 = H) gave **12***. The NMR spectrum of unlabeled **12** has vinyl proton signals at δ 5.13 and 6.13 and a six-proton vinyl methyl signal at δ 1.80. In **12*** the signal at δ 5.13 was absent and the peak at δ 1.80 was reduced in area to three protons. If the lower field vinyl proton in **12** is adjacent to the oxygen, the label can be assigned as shown in **12***. To confirm this assignment, **12*** was irradiated in Corex to give **18***. The methine protons in unlabeled **18** appear at δ 2.82 and 4.67, the lower field proton clearly being the one adjacent to the oxygen. In **18***, the methine signal at δ 2.82 was absent, establishing the label pattern as shown on the structures. This result shows that the correct structural relationship between the epoxy ketone A and the enol lactone is as shown in H, not K (Scheme I), and supports the mechanism which involves the cyclopropanone intermediate G. Another labeling experiment, using deuterated **24**, verified this conclusion (see Experimental Section). The labeling pattern in the other products (for example **13*** and **14***) was also consistent with the mechanisms proposed in Scheme I.

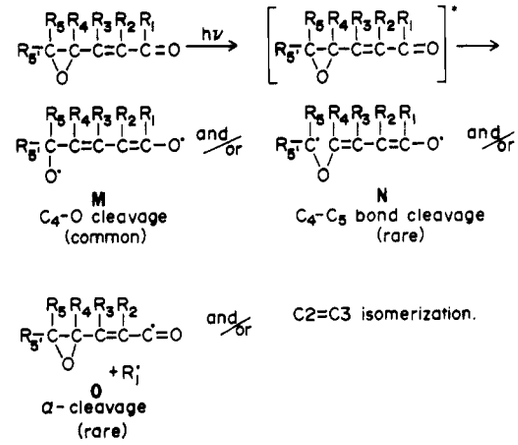
Table I summarizes the mechanistic paths in Scheme I that are followed by the simple cyclohexadienone epoxides studied thus far. Different products derived from the same path were summed (for example, **13 + 14, 20 + 21**) to get the values in the table. Examination of the results in this way permits us to draw a few conclusions regarding the way in which methyl vis-a-vis hydrogen substituents influence the reaction course. Only when R_5 is hydrogen do we see the R_5-migration path; only when R_5 is methyl do we see ring contraction. The comparison between **19** and **1**, where this is the only structural change, is most striking. The sequence hydrogen migration > ring contraction > methyl migration is characteristic for the photorearrangement of α,β-epoxy ketones and α,β-epoxyalkenes.[18] Cyclopropanone formation appears to be dimished by substitution of methyl for hydrogen at R_2 (compare **11** and **19**) or at R_3 (compare **24** and **1**, or **5** and **11**). α-Cleavage was only observed when R_2 = CH_3, R_5 = H (**19**; see also **29**).

Since the highest yield of enol lactone was obtained from the unsubstituted epoxy ketone **5**, we studied its photochemistry in somewhat greater detail. The photoisomerization of **5** could be sensitized with either acetophenone or benzophenone. Although the reaction could not be quenched with piperylene, it was efficiently quenched by *trans*-1,3,5-hexatriene (E_T = 47 kcal/mol[19]). These results suggest that the photoisomerization of **5** occurs via a triplet excited state with an energy of about 50–60 kcal/mol.[20]

We tried to detect or trap the cyclopropanone intermediate G [R_2–R_5 = H]. After a 4-h irradiation of **5** in acetone-d_6 at −78 °C, a fairly strong multiplet was observed at δ 9.7 (aldehyde proton), which slowly disappeared on warming. This peak may have been due to G [R_2–R_5 = H],[21] though we were unable to definitely connect its disappearance with the appearance of peaks due to **6**. Infrared studies were similarly indicative but not conclusive. Irradiation of **5** in THF at −105 °C caused a weak band to appear at 1815 cm^{-1} which could be attributed to the cyclopropanone intermediate.[22] Its intensity decreased when irradiation was stopped, but its decay could not be associated directly with the appearance of bands due to **6**. Irradiation of **5** in CD_3OD at −78 °C, with the hope of trapping the cyclopropanone as a ketal, gave only **6** and **7** in the same ratio as in ether. Consequently, the aldehyde cyclopropanone intermediate G remains a plausible but not proven intermediate in the photoisomerization of A to H (Scheme I).[23]

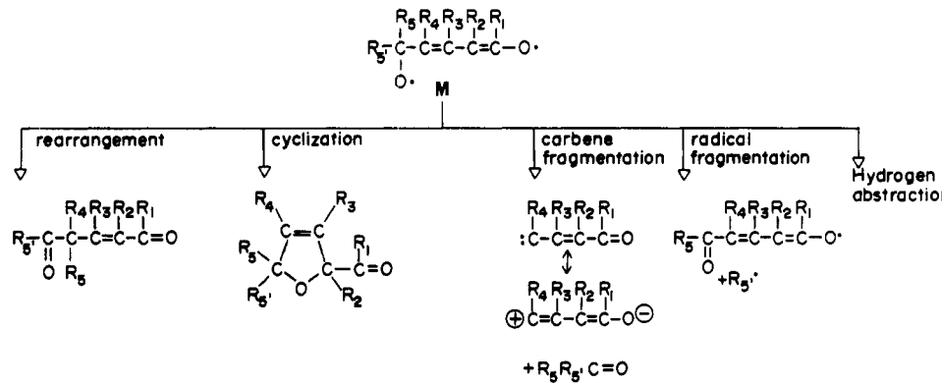
A General Mechanistic Scheme for the Photoisomerization of α-Unsaturated γ,δ-Epoxy Ketones. The cyclohexadienone epoxides whose photochemistry we have described here and summarized in Scheme I belong to the more general class of compounds, α,β-unsaturated γ,δ-epoxy ketones, many of which have been irradiated in recent years by Jeger, Schaffner, and co-workers.[24] We think it useful to summarize in one scheme the many types of reactions which have been observed to date following excitation of this interesting class of compounds (Schemes III and IV, no stereochemistry implied). The various alternatives are illustrated below with specific examples.

Scheme III

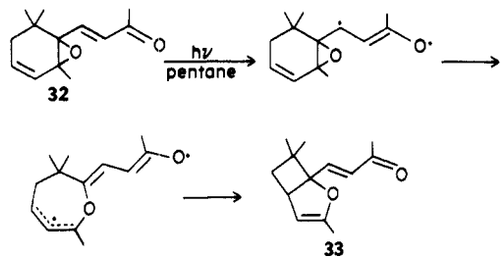


Following initial excitation (the reactive state is usually a triplet) one of three-bond-cleavage processes usually occurs. Carbon–carbon cleavage of the epoxide ring (to give N) has been observed[24e,h] when the groups at C(5) can stabilize the resulting radical (in **32**, R_5 = vinylic, R_5 = methyl).[25,26] The only example of α-cleavage (to give O) reported thus far is the formation of **22** from **19** reported in this paper (vide supra). In acyclic systems, $E \rightleftharpoons Z$ isomerism at the C(2)–C(3) double bond of the enone moiety is also known.[24d,g,h]

Scheme IV

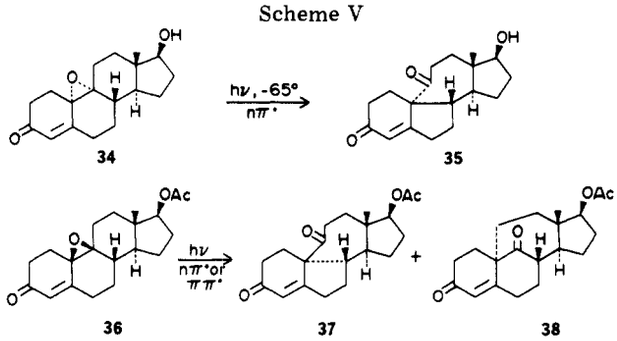


By far the most common reaction observed in these systems is cleavage of the epoxide ring at the C(4)–O bond.[1,24a-d,f-h] Scheme IV summarizes the types of subsequent reactions

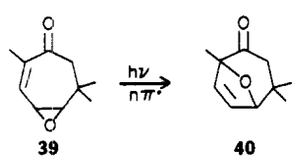


which have been observed for the resulting diradical M. Rearrangement of a group R_5 from C(5) to C(4) occurs frequently, and the group which migrates may be a hydrogen,[24a,f] methyl,[24h] or other carbon fragment.[1,24a-c] Although the precursor to these rearrangements has been written in Scheme IV as a diradical, the migration may in fact be stereospecific,[24b,c] as in Scheme V.

Scheme V

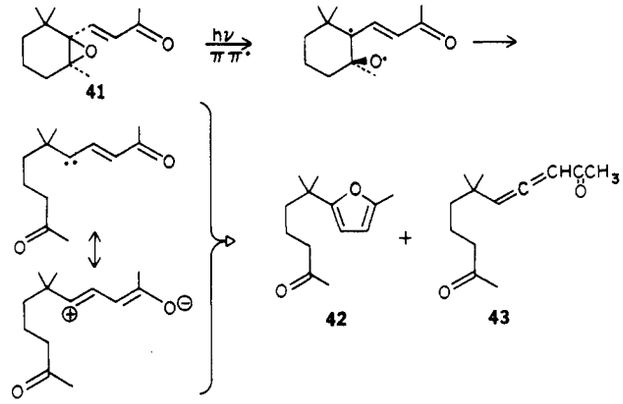


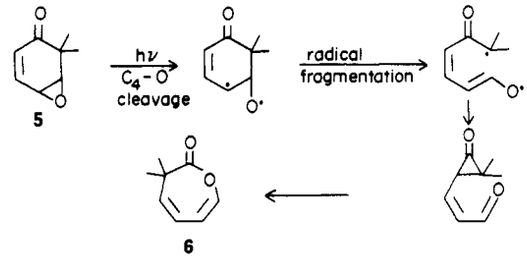
Cyclization to form a dihydrofuran by bond formation between the epoxide oxygen and C(2), as exemplified in this paper by the formation of **27** from **24** (vide supra), has precedent,[24d,f,h] the best example being eucarvone epoxide **39**.[24f]



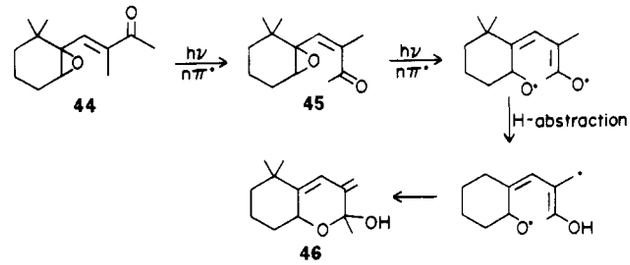
The diradical M may fragment by cleavage of the C(4)–C(5) bond to give a carbonyl compound and a carbene (or dipolar ion), as illustrated by the formation of **42** and **43** on irradiation of *trans*-β-ionone epoxide **41**.[24d,h,27,28]

The formation of the cyclopropanone G (Scheme I), and ultimately the enol lactone H reported in this paper (vide supra) can be visualized as a radical fragmentation of the diradical M (Scheme IV). This is shown specifically for the formation of **6** from **5**. This type of diradical fragmentation has not been observed previously in the photoisomerization of α,β-unsaturated γ,δ-epoxy ketones.[1,24,29]





Finally, the diradical intermediates M and N (Scheme III) may abstract hydrogen atoms, particularly from favorably located intramolecular positions.[24g,h] A good example is the predominant formation of the bicyclic alcohol **46** on nπ* excitation of **44**.



The reactions shown in Scheme I for cyclohexadienone epoxides constitute a subgroup of the more general Schemes III and IV. Certain reactions in Scheme III (C(4)–C(5) bond cleavage and *E*–*Z* isomerization) have not been observed or are precluded by the cyclic structure of this type of epoxy enone. One path in Scheme III (α-cleavage) is thus far unique to cyclohexadienone epoxides. Of the five alternatives open to the diradical M which results from C(4)–O bond cleavage (Scheme IV), three (rearrangement, cyclization, radical

fragmentation) are known with cyclohexadienone epoxides, the last of these being so far unique to this class of epoxy enones. Schemes III and IV provide a framework for studying structural effects on the photochemistry of epoxy enones; most of the various possible reaction paths have probably now been delineated, and further progress may rest on more quantitative studies.

Experimental Section

General Procedures. Analytical gas chromatography (VPC) was carried out on a Varian Aerograph Model 1400 (flame-ionization detector) and preparative VPC was performed with a Varian Aerograph Auto Model 700 instrument (thermal-conductivity detector).

NMR spectra were measured in $CDCl_3$ or CCl_4 solutions on a Varian Associates T-60 or HA-100 spectrometer using Me_4Si as an internal standard. Low-temperature NMR spectra were obtained on an A56-60 spectrometer. Spectra are reported in δ units. Numbers adjacent to protons in structures refer to chemical shifts of these protons. Numbers in brackets beside the chemical shifts are "europium-shift numbers" obtained by adding small increments of $Eu(fod)_3$. Shift numbers are the ratios obtained by dividing the shift of each signal in the spectrum by the shift of the least-shifted signal.

IR spectra were recorded on a Unicam SP-200 spectrometer except for the low-temperature study, in which a Perkin-Elmer 237 grating spectrophotometer was used. They were calibrated against a polystyrene film. UV spectra were recorded on a Unicam-800 spectrometer. Mass spectra were obtained with a Hitachi Perkin-Elmer RMU-6 operated at 70 eV; we are indebted to Mrs. Ralph Guile for this service. Melting points were determined with a Thomas-Hoover melting-point apparatus and are uncorrected. Analyses were performed by Spang Microanalytical Laboratories, Ann Arbor, Mich., and by Clark Microanalytical Laboratories, Urbana, Ill.

Analytical chromatographic columns used in this work are as follows: column A: 5 ft × 0.125 in., 20% SE-30 on chromosorb W, AW-DMCS 80/100; column B: same, 10% Carbowax 20 M; column C: same, 10% FFAP; column D: same, 5% SE-30; column E: same, 20% FFAP. Preparative chromatographic columns used in this work are as follows: column F: 10 ft × 0.25 in., 20% SE-30 on chromosorb W, AW-DMCS 80/100; column G: 6 ft × 0.25 in., 10% FFAP on chromosorb W, AW-DMCS 80/100; column H: same as G, but 5 ft × 0.25 in.; column I: same as F but 20% FFAP; column J: same as I, but 5 ft × 0.25 in.

General Photolysis Procedures. Solutions of compounds to be irradiated were placed in septum-capped Pyrex tubes or NMR tubes and purged of oxygen by bubbling dry, oxygen-free nitrogen through them for 30 min prior to photolysis. Irradiations were carried out with a 450-W Hanovia Type L medium-pressure mercury vapor lamp with the appropriate filter. The tubes were fastened to an immersion well which was immersed in water at ambient temperature. Alternatively, a Rayonet photochemical chamber reactor or Type RS preparative photochemical reactor was used. Photolyses were monitored by withdrawing small (<1 μL) aliquots and injecting them into the analytical gas chromatograph.

6,6-Dimethyl-2,4-cyclohexadienone 4,5-Epoxide (5). To a solution of 2.5 g (0.02 mol) of 6,6-dimethyl-2,4-cyclohexadienone 4[3] in 20 mL of methylene chloride was added at 0 °C a solution of 3.54 g (0.02 mol) of *m*-chloroperbenzoic acid in 20 mL of methylene chloride. The mixture was stirred at room temperature for 8 h, precipitated *m*-chlorobenzoic acid was removed by filtration, and the solvent was removed by rotary evaporation. Petroleum ether (bp 30–60 °C) was added, the filtrate was washed with aqueous sodium bicarbonate and saturated sodium chloride solution, dried ($MgSO_4$), and evaporated to give 2.37 g of a light yellow oil (86%). The crude product was chromatographed on Florisil (60–200 mesh) using ether–hexane (1:10) as eluent, to give **5**. Analytical VPC (column A, 130 °C, 30 mL of N_2/min) gave a retention time of 3 min; preparative VPC (column F, 100 °C, 60 mL of He/min, retention time 22 min) gave pure **5**: IR (neat) 3000 (s), 1680 (s), 1480 (m), 1385 (m), 1380 (w), 1295 (m), 1250 (m), 1225 (w), 1180 (m), 1118 (s), 1065 (m), 940 (m), 860 (m), 830 (s) cm^{-1}; UV (MeOH) λ_{max} 235 nm (ϵ 35 370) 280 (4080); NMR (CCl_4) see footnote 30; mass spectrum *m/e* (rel intensity) 138 (7), 123 (10), 122 (29), 109 (45), 95 (44), 82 (100), 79 (60), 77 (30), 70 (20), 67 (20), 55 (40), 54 (25).

Anal. Calcd for $C_8H_{10}O_2$: C, 69.54; H, 7.30. Found: C, 69.54; H, 7.26.

Irradiation of 5. A degassed solution of VPC collected **5** (100 mg, 0.73 mmol) in 50 mL of anhydrous ether was irradiated through Pyrex with a 450-W Hanovia lamp at room temperature. The photolysis, followed by VPC and NMR, was complete in 7 h. Analytical VPC (column B, 109 °C, 30 mL of N_2/min) showed two components, **6** (86%, retention time 17 min) and **7** (14%, 24 min). Preparative VPC (column G, 105 °C, 60 mL of He/min) gave pure **6** and **7**.

For **6** (3,3-dimethyl-2(3*H*)oxepinone): IR (neat) 1740 cm^{-1} ($\nu_{C=O}$), 1640 and 1603 cm^{-1} ($\nu_{C=C}$); UV (EtOH) λ_{max} 243 nm (ϵ 6460); NMR (CCl_4, 60 MHz) δ 1.30 (s, 6 H) and multiplets (4 H) between δ 5.47 and 6.39. The NMR spectrum (CCl_4, 100 MHz) showed four sets of vinyl protons at δ 5.47, 5.63, 6.02 and 6.39 ($J_{1,2}$ = 6.7 Hz, $J_{2,3}$ = 6.2 Hz, $J_{3,4}$ = 10.2 Hz); mass spectrum *m/e* (rel intensity) 138 (12) 109 (2), 95 (100), 81 (5), 79 (6), 77 (4), 68 (2), 67 (19), 66 (1), 65 (5), 55 (3), 52 (1), 50 (2), 43 (2), 42 (2), 40 (45), 39 (30), 38 (3). All spectral data were identical to the literature reports.[4]

For **7** (6,6-dimethyl-2-cyclohexene-1,5-dione): IR (neat) 2990 (m), 1720 (s), 1675 (s), 1640 (w), 1530 (m), 1385 (m), 1340 (w), 1300 (m), 1170 (2), 830 (m) cm^{-1}; UV (MeOH) λ_{max} 228 nm (ϵ 7000); NMR (CCl_4) δ 1.23 (s, 6 H, *gem*-dimethyl), 3.17 (br, 2 H, methylene), 5.80–6.20 [d, 1 H, J = 9 Hz, C(2) vinyl], and 6.57–7.03 [m, 1 H, C(3) vinyl]; mass spectrum *m/e* (rel intensity) 138 (42), 123 (1), 110 (12), 95 (22), 77 (4), 70 (100), 68 (55).

Anal. Calcd for $C_8H_{10}O_2$: C, 69.54; H, 7.30. Found: C, 69.60; H, 7.39.

Identical results were obtained as when carbon tetrachloride, benzene, methanol, *tert*-butyl alcohol, or acetone was used as the solvent for irradiation of **5** through Pyrex. Irradiation of **5** through a uranyl glass filter gave an almost quantitative yield of **6**; no **7** was isolated.

Irradiation of 6. A degassed solution containing 60 mg of **6** in 15 mL of anhydrous ether was irradiated through Corex with a 450-W Hanovia lamp. The photolysis was followed by analytical VPC (column B, 100 °C, 30 mL of N_2/min). As the reaction proceeded, the peak with a retention time of 12 min (corresponding to **6**) decreased in intensity and a peak with a retention time of 15 min due to **8** appeared. After a 20-h irradiation, preparative VPC (column G, 105 °C, 60 mL of He/min) allowed collection of the single photoproduct, 4,4-dimethyl-2-oxabicyclo[3.2.0]hept-6-en-3-one (**8**)[5]: IR (neat) 2980 (m), 2940 (2), 1770 (s), 1540 (m), 1390 (w), 1360 (m), 1350 (w), 1300 (w), 1270 (m), 1170 (m), 1140 (s), 1095 (s), 1015 (s), 970 (m), 930 (w), 910 (w), 860 (m), 800 (s) cm^{-1}; UV (MeOH) λ_{max} 220 nm (ϵ 235); NMR (CCl_4) δ 1.16 (s, 6 H; europium shift reagent showed that the two methyl groups are not identical), 3.13 [m, 1 H, C(5) methine], 4.98 [m, 1 H, C(1) methine], 6.30 (m, 2 H, vinyl protons); mass spectrum *m/e* (rel intensity) 138 (1.5), 123 (2), 110 (15), 109 (36), 95 (100), 93 (10), 91 (11), 83 (12), 81 (33), 79 (66), 77 (35), 67 (28), 53 (22), 51 (11).

Irradiation of 7. A degassed solution containing 40 mg of **7** in 10 mL of anhydrous ether was irradiated through Corex with a 450-W Hanovia lamp. The photolysis was followed by analytical VPC (column B, 100 °C, 30 mL of N_2/min). As the reaction proceeded, the peak with a retention time of 29 min corresponding to **7** decreased in intensity and the peak due to the product **9** appeared at 39 min. After complete reaction (2 h), preparative VPC (column H, 125 °C, 60 mL of He/min) allowed collection of the single photoproduct **9**[6] in 95% yield: IR (neat) 3001 (w), 1750 (w), 1710 (s), 1480 (m), 1400 (w), 1307 (w), 1290 (m), 1241 (w), 1190 (m), 1160 (w), 1010 (m), 900 (m) cm^{-1}; UV (ethanol) λ_{max} 215 nm (ϵ 550), 280 (190); NMR (CCl_4) see footnote 31; mass spectrum *m/e* (rel intensity) 138 (47), 123 (9), 110 (21), 109 (16), 97 (17), 95 (70), 93 (6), 91 (7), 83 (6), 82 (10), 81 (15), 79 (24), 77 (8), 70 (100), 69 (19), 68 (69), 67 (55).

Irradiation of 9. A degassed solution containing 35 mg of compound **9** in 10 mL of anhydrous ether was irradiated through Corex, or 30 mg of compound **9** in 10 mL benzene was irradiated through Pyrex with a 450-W Hanovia lamp. The photolysis was followed by NMR (benzene-d_6) and analytical VPC (column B, 153 °C, 30 mL of N_2/min). The reaction was complete within 30–45 min in Corex and within 2 h with the Pyrex filter. As the reaction proceeded, the peak with a retention time of 18 min corresponding to **9** decreased in intensity and the peak due to the product **10** appeared with a retention time 23 min. Preparative VPC (column G, 105 °C, 60 mL of He/min) allowed collection of the single photoproduct **10**[6] in 90% yield: IR (neat) 3100 (m), 1795 (s), 1720 (s), 1680 (w), 1480 (w), 1380 (w), 1238 (w), 1210 (m), 1150 (m), 1100 (m) cm^{-1}; UV (methanol) showed end absorption; NMR (CCl_4) see footnote 32; mass spectrum *m/e* (rel intensity) 138 (50), 123 (18), 110 (15), 109 (20), 96 (18), 95 (80), 79 (35), 77 (25), 70 (100), 68 (80), 67 (62).

Irradiation of 5 with 254-nm Light. Irradiation of an 0.01 M ether solution of **5** at 254 nm (Rayonet MGR-100) or with a Hanovia 450-W lamp and Corex filter gave **6** and **7** in a ratio 7:1 after 2 h. Further irradiation for 7 h followed by VPC (column C, 125 °C, 30 mL of N_2/

min) gave the following products (%, retention time in min): **6** (38, 6), **7** (46, 9.5), **9** (12, 17), and **10** (4, 30).

Irradiation of 5 at Low Temperatures. A degassed solution of **5** (25 mg) in 0.5 mL of acetone-d_6 was irradiated in a Pyrex NMR tube with a 450-W Hanovia lamp at −78 °C. The photolysis was followed by NMR and by VPC. After a 4-h irradiation, besides the strong product signals of **6** and **7**, an aldehyde proton peak at δ 9.7 was observed. When the solution stood at the same temperature for 3 h, the intensity of the aldehyde proton signal gradually decreased. Following a similar separate irradiation, the solution was warmed slowly (8 h) to room temperature, and the signal due to the aldehyde disappeared. Replacement of the acetone by methanol-d_4 gave identical results.

A solution of 20 mg of **5** in 0.1 mL of tetrahydrofuran was placed in a sodium chloride cavity cell (0.2-mm path length) held in a lead block and cooled to −105 °C. A beam from a 1000-W Hanovia mercury lamp was filtered through Pyrex and diverted into the cavity cell. Examination of the IR spectrum after irradiation for 10 min indicated a decrease in the intensity of the carbonyl absorption at 1680 cm^{-1} due to **5** and the appearance of a sharp intense absorption at 1740 and 1720 cm^{-1}, attributed to photoproducts. A weak peak also appeared at 1815 cm^{-1}. When the solution was warmed to room temperature, the band at 1815 cm^{-1} gradually disappeared.

Sensitization and Quenching Studies with 5. Analytical grade benzene was purified by stirring with concentrated sulfuric acid for several days, washing (10% sodium hydroxide, water, sodium chloride), drying (calcium hydride), and distilling (from potassium, middle cut). Methanol and acetophenone was purified by distillation, and benzophenone and hexamethylbenzene were purified by recrystallization from ethanol. *trans*-1,3,5-Hexatriene and piperylene were used as purchased from Aldrich Chemical Co.

In benzene: 110 mg of **5** and 64 mg of hexamethylbenzene (to serve as a VPC reference) were dissolved in 40 mL of benzene to give an 0.02 M standard solution of **5.** For sensitization, a 3 M solution of acetophenone was prepared by dissolving 3.6 g of acetophenone in 10 mL of the standard solution. For quenching, a 2.6 M solution of *trans*-1,3,5-hexatriene was prepared by dissolving 1 g of the triene in 5 mL of the standard solution.

Aliquots (2.8 mL) of each solution were sealed in Pyrex tubes after five freeze-thaw cycles (<0.005 Torr). Samples were irradiated in a merry-go-round apparatus with a 450-W Hanovia lamp and Pyrex filter. After varying times (to 7 h), samples were removed and analyzed by VPC (column B, 155 °C, 30 mL of N_2/min). At 7 h, the blank showed a single peak at 8.5 min due to **6;** the acetophenone solution gave the same result, but the triene solution showed only 10% **6** and 90% **5** (10.5).

In methanol: the standard solution of **5** was prepared as in benzene (vide supra). The sensitization solution was 2 M in benzophenone (3.5 g in 10 mL of standard solution). The quenching solution was 5 M in piperylene (3.4 g in 10 mL of standard solution). Irradiation as described for the benzene solutions and VPC analysis (column D, 131 °C) showed after 7 h only one peak due to **6** (2 min) in all three solutions.

3,4,6,6-Tetramethyl-2,4-cyclohexadienone-4,5-epoxide (11). To a solution containing 5.0 g (0.033 mol) of 3,4,6,6-tetramethyl-2,4-cyclohexadienone[33] in 25 mL of methylene chloride was added at 0 °C a solution of *m*-chloroperbenzoic acid (5.9 g, 0.034 mol) in 50 mL of the same solvent. The reaction, which was followed by NMR, was complete in about 1 h, during which time *m*-chlorobenzoic acid precipitated from solution. The precipitate was removed by filtration, the solvent was removed by rotary evaporation, and the residue, which consisted mainly of the desired epoxy ketone **11** contaminated with a trace of *m*-chlorobenzoic acid (NMR), was chromatographed on a short column of Florisil (80–100 mesh) using ethyl ether as eluent. The yield of **11**, which was identified by comparing its IR and NMR spectra[30] with those of an authentic sample,[34] was nearly quantitative.

2-Deuterio-3-trideuteriomethyl-4,6,6-trimethyl-2,4-cyclohexadienone 4,5-Epoxide (11*). To a solution of **11** (500 mg, 3.01 mmol) in dimethyl-d_6 sulfoxide (15 mL) was added with stirring and under N_2 370 mg (3.30 mmol) of potassium *tert*-butoxide. The mixture was stirred at room temperature for 3 h and then quenched with ice–water and extracted with ether. The combined organic layers were dried (Na_2SO_4) and the solution was evaporated to give a nearly quantitative yield of **11***. The NMR spectrum was identical to that of **11**,[30] except that the peaks at δ 2.08 (3 H) and 5.72 (1 H) were absent.

Irradiation of 11. A degassed solution containing 300 mg (1.81 mmol) of **11** in 30 mL of anhydrous ether was irradiated through Pyrex with a 450-W Hanovia lamp. The photolysis was followed by analytical VPC (column C, 140 °C, 30 mL of N_2/min). The reaction was complete in about 8 h. VPC showed that there were three products, **13** (44%, retention time 8.5 min), **14** (34%, 12.5 min), and **12** (22%, 16.5 min). The products were isolated by preparative VPC (column H, 150 °C). A similar irradiation in methanol gave the same result.

For **12** (4,5,7,7-tetramethyl-2-oxacyclohepta-3,5-dien-1-one): IR (CCl_4) 1745 (s), 1145 (w), 1085 (w) cm^{-1}; UV (MeOH) λ_{max} 240 nm (ϵ 3225); NMR (CCl_4) δ 1.25 (s, 6 H, *gem*-dimethyl), 1.80 (m, 6 H, separates to two doublets, J = 1 Hz, with Eu shift reagent), 5.13 [br, 1 H, C(6) vinyl], 6.13 [br, 1 H, C(3) vinyl]; mass spectrum *m/e* (rel intensity) 167 (5), 166 (40), 138 (78), 124 (35), 123 (100), 109 (22), 96 (10), 95 (37), 91 (15), 77 (22), 67 (57), 55 (35), 53 (28), 51 (13).

Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.25; H, 8.37.

For **13** (*endo*-6-methyl-1,3,3-trimethylbicyclo[3.1.0]hexane-2,4-dione): IR (CCl_4) 3000 (m), 1745 (w), 1710 (s), 1465 (w), 1385 (w), 1300 (w), 1140 (w) cm^{-1}; UV (MeOH) λ_{max} 215 nm (ϵ 2590); NMR (CCl_4) see footnote 31; mass spectrum *m/e* (rel intensity) 167 (9), 166 (77), 151 (29), 138 (14), 124 (15), 123 (55), 107 (20), 105 (10), 96 (100), 95 (27), 91 (17), 81 (19), 70 (23), 68 (64), 67 (65), 53 (38).

Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.28; H, 8.49.

For **14** (*exo*-6-methyl-1,2,3-trimethylbicyclo[3.1.0]hexane-2,4-dione): IR (CCl_4) 3000 (m), 1740 (m), 1705 (s), 1465 (w), 1390 (w), 1280 (m), 1130 (w), 1095 (m) cm^{-1}; UV (MeOH) λ_{max} 225 nm (ϵ 1240); NMR (CCl_4) see footnote 31; mass spectrum (70 eV) *m/e* (rel intensity) 167 (9), 166 (58), 151 (19), 149 (16), 138 (18), 124 (20), 123 (59), 107 (28), 105 (15), 97 (10), 96 (100), 95 (35), 91 (20), 81 (20), 78 (17), 76 (11), 70 (20), 68 (78), 67 (83), 55 (21), 53 (58), 51 (15).

Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.32; H, 8.55.

Irradiation of 11*. The conditions and workup procedure were as described for **11** (ether). The NMR spectrum of the resulting **13*** was identical with that of **13**,[31] except that the signals at δ 1.40 and 2.22 were absent. The NMR spectrum of the resulting **14*** was identical with that of **14**,[31] except that the signals at δ 1.33 and 1.70 were absent. The NMR spectrum of the resulting **12*** was identical with that of **12,** except that the signal at δ 5.13 was absent and the area of the peak at δ 1.80 was reduced to 3 H and simplified to a doublet.

Irradiation of 12. A degassed solution containing 100 mg (0.60 mmol) of **12** in 10 mL of anhydrous ether was irradiated through Corex with a 450-W Hanovia lamp. The photolysis was followed by analytical VPC (column C, 135 °C, 30 mL of N_2/min). As the reaction proceeded, the peak with a retention time of 12.5 min (corresponding to **12**) decreased in area and a product peak appeared at 6 min. After 2 h, the reaction was complete and the product, 2,2,6,7-tetramethyl-4-oxabicyclo[3.2.0]hept-6-en-3-one (**18**), was collected by preparative VPC (column H, 180 °C): IR (CCl_4) 2960 (m), 2920 (w), 1780 (s), 1385 (w), 1330 (w), 1250 (w), 1160 (m), 1100 (s), 1060 (m), 1050 (m), 875 (s) cm^{-1}; UV (MeOH) λ_{max} 210 nm (ϵ 830); NMR (CCl_4) δ 1.10 [s, 3 H, C(2) methyl], 1.17 [s, 3 H, C(2) methyl], 1.68 [s, 6 H, C(6) and C(7) methyls, separate with Eu shift reagent], 2.82 [m, 1 H, C(1) methine], 4.67 [d, 1 H, J = 4 Hz, C(5) methine]; mass spectrum *m/e* (rel intensity) 166 (4), 148 (40), 123 (100), 109 (18), 107 (32), 91 (28), 79 (22), 77 (13), 67 (22), 55 (19), 53 (16). Since the mass spectrum showed that **18** was an isomer of **12,** it was not subjected to elemental analysis.

Irradiation of 12*. The conditions and workup procedure were as described for **12.** The resulting **18*** had an NMR spectrum identical with that of **18,** except that the signal at δ 2.82 was absent and the peak at δ 1.68 was reduced in area to 3 H.

Irradiation of 2,3,6,6-tetramethyl-2-cyclohexene-1,5-dione (15a). A degassed solution containing 200 mg of **15a**[8] in 15 mL of anhydrous ether was irradiated through Pyrex with a 450-W Hanovia lamp. The photolysis was followed by analytical VPC (column C, 160 °C, 30 mL of N_2/min). As the reaction proceeded, the peak with a retention time of 7.0 min (corresponding to **15a**) decreased in area and a product peak appeared at 2.0 min. After 3 h, the reaction was complete and the product, 1,3,3,5-tetramethylbicyclo[3.1.0]hexane-2,4-dione (**13a**), was collected by preparative VPC (column H, 170 °C): IR (CCl_4) 3000 (m), 1750 (m), 1710 (s), 1470 (w), 1390 (w), 1290 (m), 1070 (m) cm^{-1}; UV (MeOH) λ_{max} 225 nm (ϵ 1190); NMR (CCl_4) see footnote 31; mass spectrum *m/e* (rel intensity) 167 (4), 166 (38), 151 (10), 124 (20), 123 (53), 97 (7), 96 (100), 95 (14), 68 (38), 67 (35), 53 (15).

Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.23, H, 8.57.

Irradiation of **15a** labeled with a CD_3 group at C(3) under the same conditions gave labeled **13a** whose NMR spectrum had the peak at δ 1.33 reduced in area to 3 H.

Irradiation of 13a. A degassed solution containing 100 mg (0.60 mmol) of **13a** in 10 mL of anhydrous ether was irradiated through

Corex with a 450-W Hanovia lamp. The photolysis was followed by analytical VPC (column C, 160 °C, 30 mL of N_2/min). As the reaction proceeded, the peak with a retention time of 7.0 min (corresponding to **13a**) decreased in area and a product peak appeared at 16 min. After 1 h, the reaction was complete and the product, 1,5-dimethyl-4-isopropylidene-3-oxabicyclo[3.1.0]hexan-2-one (**10a**), was collected by preparative VPC (column H, 170 °C): IR (CCl_4) 3000 (m), 1780 (s), 1700 (m), 1350 (w), 1300 (w), 1150 (w), 1135 (w), 1070 (m), 1030 (m) cm^{-1}; UV (MeOH) λ_{max} 235 nm (ϵ 3780); NMR (CCl_4) see footnote 32; mass spectrum *m/e* (rel intensity) 167 (4), 166 (34), 151 (10), 124 (21), 123 (58), 97 (7), 96 (100), 95 (16), 69 (10), 68 (35), 67 (33), 53 (15).

Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.04; H, 8.34.

Irradiation of **13a** labeled at C(1) [C(5)] with a CD_3 group under the same conditions gave labeled **10a** whose NMR spectrum differed from that of **10a** in that the areas of the peaks at δ 1.28 and 1.45 were each reduced by 50%.

Irradiation of 13. A degassed solution containing 100 mg (0.60 mmol) of **13** in 10 mL of anhydrous ether was irradiated through Corex with a 450-W Hanovia lamp. The photolysis was followed by analytical VPC (column C, 140 °C, 30 mL of N_2/min). As the reaction proceeded, the peak with a retention time of 8.5 min (corresponding to **13**) decreased in area and a product peak appeared at 10.5 min. After 1.5 h, the reaction was complete and the product, *endo*-6-methyl-1-methyl-4-isopropylidene-3-oxabicyclo[3.1.0]hexan-2-one (**16**), was collected by preparative VPC (column H, 170 °C): IR (CCl_4) 3000 (m), 1780 (s), 1710 (m), 1450 (w), 1305 (w), 1140 (w), 1100 (m), 1050 (m), 970 (w), 870 (m) cm^{-1}; UV (MeOH) λ_{max} 230 nm (ϵ 3320); NMR (CCl_4) see footnote 32; mass spectrum *m/e* (rel intensity) 167 (5), 166 (46), 151 (29), 148 (31), 138 (19), 124 (22), 123 (76), 107 (20), 105 (15), 96 (100), 95 (29), 91 (21), 68 (41), 66 (50), 55 (22), 53 (21). Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.27; H, 8.46.

Irradiation of 13*. The conditions and workup procedure were as described for **13**. The NMR spectrum of the resulting **16*** was identical with that of **16**,[32] except that the signals at δ 1.37 and 2.38 were absent.

Irradiation of 14. A degassed solution containing 100 mg (0.60 mmol) of **14** in 10 mL of anhydrous ether was irradiated through Corex with a 450-W Hanovia lamp. The photolysis was followed by analytical VPC (column C, 140 °C, 30 mL of N_2/min). As the reaction proceeded, the peak with a retention time of 12.5 min (corresponding to **14**) decreased in area, and two product peaks appeared with retention times of 17.0 and 28.5 min in the ratio of 3:1. After 1.5 h the reaction was complete. Preparative VPC (column H, 170 °C) gave a major component, *exo*-6-methyl-1-methyl-4-isopropylidene-3-oxabicyclo-[3.1.0]hexan-2-one (**17**): IR (CCl_4) 3000 (m), 1780 (s), 1715 (m), 1450 (w), 1290 (w), 1140 (w), 1060 (m) cm^{-1}; UV (MeOH)λ_{max} 235 nm (ϵ 2400); NMR (CCl_4) see footnote 32; mass spectrum *m/e* (rel intensity) 167 (5), 166 (39), 151 (20), 138 (14), 124 (22), 123 (68), 107 (25), 96 (100), 95 (30), 91 (26), 79 (20), 68 (52), 67 (71), 55 (31), 53 (55).

Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.24; H, 8.57.

The minor component was *exo*-6-methyl-5-methyl-4-isopropylidene-3-oxabicyclo[3.1.0]hexan-2-one (**17a**): IR (CCl_4) 2980 (w), 2940 (w), 1785 (s), 1700 (m), 1460 (w), 1280 (m), 1250 (w), 1180 (m), 1140 (w), 1080 (w), 975 (w), 890 (w) cm^{-1}; UV (MeOH) λ_{max} 235 nm (ϵ 6150); NMR (CCl_4) see footnote 32; mass spectrum *m/e* (rel intensity) 167 (12), 166 (100), 151 (40), 138 (13), 124 (15), 123 (49), 107 (27), 97 (14), 96 (52), 95 (27), 91 (27), 81 (16), 79 (19), 70 (30), 69 (20), 68 (48), 67 (45), 55 (16), 53 (27), 51 (8). Since the mass spectra showed that **17** and **17a** were isomers, **17a** was not subjected to elemental analysis.

Irradiation of 14*. The conditions and workup procedure were as for **14**. The resulting **17*** had an NMR spectrum identical with that of **17**,[32] except that the peaks at δ 1.33 and 1.93 were absent. Insufficient **17a*** was isolated for an NMR spectrum.

2,3,4,6,6-Pentamethyl-2,4-cyclohexadienone 4,5-Epoxide (19). To a solution of 1.20 g (7.32 mmol) of 2,3,4,6,6-pentamethyl-2,4-cyclohexadienone[35] in 20 mL of methylene chloride was added, at 0 °C, a solution of 1.42 g (8.61 mmol) of *m*-chloroperbenzoic acid in 20 mL of methylene chloride. The mixture was stirred at room temperature for 3 h (NMR monitoring showed complete reaction at this time). *m*-Chlorobenzoic acid was removed by filtration, and the solvent was removed by rotary evaporation. Petroleum ether (bp 30–60 °C) was added, the filtrate was washed with aqueous sodium bicarbonate and saturated sodium chloride solution, dried ($MgSO_4$), and evaporated to give 1.20 g (91%) of **19** as a light oil. The crude produce was chromatographed on Florisil (60–200 mesh) using ether–hexane (1:5) as eluent, to give pure epoxide **19**: IR (neat) 3000 (s), 1674 (s), 1616 (m), 1480 (m), 1390 (m), 1320 (m), 1260 (m), 1090 (m), 1050 (m), 918 (m); UV (MeOH) λ_{max} 210 nm (ϵ 2970), 255 (8460), 325 (270); NMR (CCl_4) see footnote 30; mass spectrum *m/e* (rel intensity) 180 (50), 165 (35), 164 (15), 151 (26), 137 (100), 135 (52), 123 (34), 121 (31), 119 (25), 112 (35), 110 (55), 95 (20), 91 (20), 83 (15), 81 (30), 69 (24), 67 (50), 55 (26), 53 (30).

Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H. 8.95. Found: C, 73.24; H, 8.92.

3-Trideuteriomethyl-2,4,6,6-tetramethyl-2,4-cyclohexadienone 4,5-Epoxide (19*). To a solution containing 500 mg (2.77 mmol) of **19** in 10 mL of dimethyl-d_6 sulfoxide was added with stirring and under N_2, 310 mg (2.77 mmol) of potassium *tert*-butoxide. The mixture was stirred at room temperature for 1 h and then quenched with ice–water and extracted with ether. Organic layers were dried ($MgSO_4$) and the solution was evaporated to give a nearly quantitative yield of **19***. The NMR spectrum was identical to that of the starting material, except that the signal at δ 1.95 had disappeared.

Irradiaion of 19. A degassed solution of 100 mg (0.55 mmol) of **19** in 30 mL of anhydrous ether was irradiated through Pyrex with a 450-W Hanovia lamp at room temperature for 2 h. The photolysis was followed by VPC. Analytical VPC (column C, 160 °C, 30 mL of N_2/min) showed three components: **20** (62%, retention time 2.5 min), **21** (11%, 5 min), and **22** (27%, 25 min). Preparative VPC (column I, 140 °C, 60 mL of He/min) gave pure **20** (retention time 18 min), **21** (31 min), and **22** (over 1 h). Further purification of **22** with VPC (5 ft × 0.25 in. column J, 180 °C, 60 mL of He/min) gave pure **22** (retention time 12 min).

For **20** (*endo*-1,3,3,5,6-pentamethylbicyclo[3.1.0]hexane-2,4-dione): IR (KBr) 3000 (m), 1700 (s), 1462 (m), 1380 (m), 1360 (w), 1300 (m), 1205 (m), 1110 (w), 1090 (w), 1040 (m), 845 (m) cm^{-1}; UV (MeOH) λ_{max} 215 nm (ϵ 2610); NMR (CCl_4) see footnote 31; decoupling at δ 1.06–1.27 caused the doublet at δ 1.04 to sharpen to a singlet; mass spectrum *m/e* (rel intensity) 180 (42), 165 (20), 163 (10), 137 (60), 120 (11), 110 (100), 109 (22), 105 (15), 95 (25), 82 (22), 79 (13), 67 (80).

Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.29; H, 8.97.

For **21** (*exo*-1,3,3,5,6-pentamethylbicyclo[3.1.0]hexane-2,4-dione): IR (neat) 3000 (m), 1742 (w), 1701 (s), 1470 (m), 1398 (m), 1295 (m), 1101 (w), 1080 (m), 1040 (w), 845 (w) cm^{-1}; UV (MeOH) λ_{max} 215 nm (ϵ 1870); NMR (CCl_4) see footnote 31; decoupling at δ 1.46 caused the methyl signal at δ 1.13 to sharpen to a singlet; mass spectrum *m/e* (rel intensity) 180 (53), 165 (20), 162 (9), 138 (20), 137 (60), 121 (13), 120 (25), 110 (100), 109 (27), 105 (10), 95 (25), 82 (25), 81 (15), 67 (88), 55 (7), 54 (7).

Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.11; H, 8.98.

For **22:** IR (neat) 2985 (m), 1741 (s), 1680 (m), 1448 (m), 1382 (m), 1325 (m), 1281 (m), 1180 (w), 1140 (w), 1100 (m), 1005 (m), 760 (m) cm^{-1}; UV (MeOH) λ_{max} 225 nm (ϵ 7150); NMR ($CDCl_3$) δ 1.23 [s, 3 H, C(4) methyl], 1.74 (br s, 3 H), 1.76 (s, 3 H), 1.79 [s, 3 H, C(3) methyl], 1.80 [s, 3 H, C(2) methyl], 5.40 (m, 1 H, vinyl); decoupling at δ 1.74–1.80 caused the vinyl proton at δ 5.40 to sharpen to a singlet; europium shift slopes, respectively, 3.00, 1.00, 1.30, 2.57, 5.80, 4.28; mass spectrum *m/e* (rel intensity) 180 (60), 165 (92), 137 (30), 135 (80), 125 (20), 119 (25), 112 (21), 110 (35), 105 (20), 97 (100), 91 (19), 69 (65), 68 (25), 55 (40), 54 (40), 53 (30).

Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.11; H, 9.02.

Irradiation of 3-Trideuteriomethyl-2,4,6,6-tetramethyl-2,4-cyclohexadienone 4,5-Epoxide (19*). The conditions and workup procedure were as described for the unlabeled material. From **19*** the resulting **20*** had an NMR spectrum identical with that of **20**, except that the signal at δ 1.32 (s, 6 H) was reduced to half its area (s, 3 H). The spectrum of the resulting **21*** was identical with that of **21**, except that the signal at δ 1.20 (s, 6 H) was reduced to half its area (s, 3 H). The spectrum of the resulting **22*** was identical with that of **22**, except that the signal at δ 1.79 was absent.

Irradiation of 23. A degassed solution of **23** (50 mg, 0.27 mmol) in 25 mL of anhydrous ether was irradiation through Pyrex with a 450-W Hanovia lamp. The photolysis, followed by VPC and NMR, was complete in about 1 h. Analytical VPC (column C, 160 °C, 30 mL of N_2/min) showed two components: **20** (85%, retention time 2.5 min) and **21** (15%, 5 min). Preparative VPC (column I, 140 °C, 60 mL of He/min) gave pure **20** and **21** in the same ratio.

Irradiation of **23** labeled at C(3) with a CD_3 group gave, under the same conditions, **21*** and **22*** in the same ratio as obtained from **19***.

2,4,5,6,6-Pentamethyl-2,4-cyclohexadienone 4,5-Epoxide (24). To a solution of 2.10 g (12.8 mmol) of 2,4,5,6,6-pentamethyl-2,4-cyclohexadienone[35] in 40 mL of methylene chloride was added, at 0

°C, a solution of 2.20 g (12.8 mmol) of *m*-chloroperbenzoic acid in 60 mL of methylene chloride. The mixture was stirred at room temperature for 2 h (NMR monitoring showed complete reaction). During this time a white precipitate formed; it was removed by filtration. The solvent was removed by rotary evaporation, petroleum ether (bp 30–60 °C) was added, the filtrate was washed three times with 15% aqueous sodium sulfite, water, and saturated sodium chloride solution, dried ($MgSO_4$), and evaporated to give 2.24 g (97.4%) of a light yellow oil. The crude product was chromatographed on Florisil (60–200 mesh) using ether–hexane (1:10) as eluent, to give colorless epoxide **24.** When epoxide **24** was subjected to preparative VPC (column F, 180 °C, 60 mL of He/min, retention time 18 min), only 60% was recovered and 40% was converted to an isomeric alcohol due to thermal oxirane ring opening. For **24:** IR (neat) 3000 (s), 1680 (s), 1550 (w), 1480 (s), 1400 (s), 1380 (m), 1278 (m), 1200 (w), 1130 (m), 1100 (s), 1080 (m), 1060 (m), 1003 (m), 978 (m), 900 (s), 848 (m), 780 (w), 740 (m) cm^{-1}; UV (methanol) λ_{max} 208 nm (ϵ 3200), 250 (9560), 320 (500); NMR (CCl_4) see footnote 30; mass spectrum *m/e* (rel intensity) 180 (9), 165 (18), 137 (100), 112 (40), 110 (20), 109 (18), 97 (10), 69 (35), 67 (36).

Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.33; H, 9.02.

5-Trideuteriomethyl-2,4,6,6-tetramethyl-2,4-cyclohexadienone 4,5-Epoxide (24*). 2,4,5,6,6-Pentamethylcyclohexa-2,4-dienone[35] (1 g) was added to a solution of 0.30 g of potassium *tert*-butoxide in dimethyl-d_6 sulfoxide. The solution became deep red immediately and remained so. The mixture was stirred at room temperature for 5 h (NMR monitoring showed complete reaction). The red-brown solution was poured into 300 mL of methylene chloride and washed with ice–water (three 50-mL portions). After being dried, the solution was evaporated to an oil, which was distilled, and then further purified by VPC (column J, 148 °C, 60 mL of He/min, retention time 2 min). The NMR spectrum, which was consistent with deuteration at the C(5) methyl group, consisted of three signals at δ 1.12, 1.81, and 6.60 with relative 6:6:1, assigned respectively to the *gem*-dimethyls, the allylic methyls at C(2), C(4), and C(3) vinyl proton.

To a solution containing 120 mg (0.73 mmol) of the labeled cyclohexadienone in 2 mL of methylene chloride was added a solution of 148 mg (0.86 mmol) of *m*-chloroperbenzoic acid in 2 mL of methylene chloride. The mixture was stirred at room temperature for 2 h, and workup was as described for the preparation of **24.** The product **24*** had an NMR spectrum identical with that of **24,**[30] except that the signal at δ 1.40 was absent.

Irradiation at 24. A degassed solution of 100 mg (0.55 mmol) of **24** in 50 mL of anhydrous ether was irradiated through Pyrex with a 450-W Hanovia lamp. The photolysis was followed by VPC, and was complete in about 1 h. Analytical VPC (column E, 178 °C, 30 mL of N_2/min) showed three components: **27** (retention time 1 min), **26** (7 min), and **25** (9 min). Preparative VPC (column F, 120 °C, 60 mL of He/min) gave pure **27** (25%; retention time 8 min), **26** (45%; 25 min), and **25** (30%; 40 min).

For **25** [3,3,4,6,7-pentamethyl-2(3*H*)-oxepinone]: IR (neat) 3000 (s), 1750 (s), 1660 (m), 1460 (m), 1400 (m), 1340 (w), 1280 (w), 1260 (w), 1200 (m), 1150 (m), 1120 (w), 1100 (w), 1040 (w), 950 (w), 880 (w) cm^{-1}; UV (MeOH) λ_{max} 212 nm (ϵ 2700), 250 (10 570); NMR (100 MHz, CCl_4) δ 1.23 (s, 6 H, *gem*-dimethyl), 1.67 [br s, 3 H C(6) methyl], 1.83 [d, 3 H, J = 2 Hz, C(4) methyl], 1.89 (br s, 3 H, C(7) methyl], 5.60 (m, 1 H, vinyl); decoupling at δ 5.60 caused the doublet at δ 1.83 to become a singlet; europium shift slopes, respectively, are 3.76, 1.05, 2.03, 1.00, 1.92; mass spectrum *m/e* (rel intensity) 180 (61), 165 (7), 138 (30), 137 (98), 109 (100), 108 (71), 93 (75), 91 (32), 97 (34), 67 (50), 65 (20), 55 (15), 53 (20).

Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.21; H, 9.09.

For **26** (4-acetyl-2,4,5,5-tetramethyl-2-cyclopentenone): IR (CCl_4) 3000 (s), 1710 (s), 1660 (w), 1480 (w), 1460 (w), 1400 (w), 1373 (m), 1305 (w), 1300 (w), 1192 (w), 1160 (m), 1050 (m), 990 (m), 890 (m) cm^{-1}; UV (cyclohexane) λ_{max} 265 (ϵ 7000); NMR (CCl_4), δ 0.90 [s, 3 H, C(5) methyl], 1.03 [s, 3 H, C(5) methyl], 1.25 [s, 3 H, C(4) methyl], 1.75 [d, 3 H, J = 1.0 Hz, C(2) methyl], 1.95 (s, 3 H, acetyl methyl), 6.92 (q, 1 H, J = 1 Hz, vinyl); europium shift slopes, respectively, are 4.80, 3.40, 1.00, 3.00, 2.50, 2.80; mass spectrum *m/e* (rel intensity) 180 (6), 162 (5), 144 (5), 139 (26), 138 (100), 137 (35), 123 (62), 109 (43), 93 (7), 91 (7), 81 (8), 71 (10), 77 (9), 69 (8), 67 (60), 55 (15).

Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.14; H, 8.91.

For **27** (1,3,3,4,5-pentamethyl-7-oxabicyclo[2.2.1]hept-5-en-2-one): IR (neat) 3000 (s), 1740 (s), 1640 (w), 1470 (m), 1450 (m), 1392 (m), 1300 (w), 1220 (m), 1200 (m), 1180 (m), 1100 (s), 1020 (w), 1000 (s), 900 (w), 860 (w), 810 (s) cm^{-1}; UV (MeOH) λ_{max} 207 nm (ϵ 950) with a shoulder at 280 (ϵ 100); NMR (CCl_4) δ 1.12 [s, 3 H, C(3) methyl], 1.14 [s, 3 H, C(3) methyl], 1.30 [s, 3 H, C(4) methyl], 1.32 [s, 3 H, C(1) methyl], 1.72 [d, 3 H, J = 2 Hz, C(5) methyl], 5.56 (q, 1 H, J = 2 Hz, vinyl]; europium shift slopes are, respectively, 3.50, 3.37, 2.77, 2.98, 1.00, 1.93; mass spectrum *m/e* (rel intensity) 180 (14), 165 (5), 152 (5), 140 (100), 139 (42), 138 (35), 137 (75), 124 (20), 122 (76), 121 (83), 111 (11), 110 (84), 108 (15), 95 (40), 94 (62), 92 (15), 82 (64), 77 (77), 69 (12), 67 (25), 59 (60), 55 (20), 54 (68), 53 (31), 52 (10), 51 (15).

Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.34; H, 8.96.

Irradiation of 24*. The conditions and workup procedure were as for the unlabeled material. From **24*** the resulting **27*** had an NMR spectrum identical with that of **27,** except the signal at δ 1.30 was absent. The spectrum of the resulting **26*** was identical with that of **26,** except that the singlet at δ 1.95 was absent. The resulting **25*** was identical with that of **25,** except that the signal at δ 1.89 was absent and the peak at δ 1.67 sharpened to a singlet.

Irradiation of 26. A degassed solution of 50 mg (0.28 mmol) of **26** in 25 mL of anhydrous ether was irradiated through Pyrex with a 450-W Hanovia lamp at room temperature. The photolysis was followed by VPC and was complete in about 40 min. Analytical VPC (column C, 150 °C, 30 mL of N_2/min) showed two components with retention times of 3.5 and 19 min, respectively, in a ratio of 1:6. Preparative VPC (column I, 120 °C, 60 mL of He/min) allowed collection of the major product **28** with a retention time of 52.5 min. For **28:** IR (neat) 3000 (m), 1760 (s), 1662 (m), 1460 (m), 1396 (m), 1360 (w), 1330 (m), 1200 (w), 1120 (m), 1080 (m), 1040 (w), 940 (w) cm^{-1}; UV (MeOH) λ_{max} 222 (ϵ 7640), 263 (6250); NMR (CCl_4) δ 1.35 [d, 3 H, J = 6 Hz, C(4) methyl], 1.66 (s, 3 H, vinyl methyl), 1.68 [s, 3 H, C(2) methyl], 1.86 (homoallylic coupling, 6 H, terminal vinyl methyls), 4.85 [q, 1 H, J = 6 Hz, C(4) proton]; europium shift slopes are respectively 2.30, 1.00, 5.47, (1.50, 1.62), 4.37; mass spectrum *m/e* (rel intensity) 180 (60), 165 (4), 137 (100), 138 (30), 123 (10), 110 (17), 109 (85), 108 (50), 93 (50), 91 (20), 77 (20), 67 (40), 55 (10), 53 (14).

Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.33; H, 8.86.

Irradiation of 27. A degassed solution of **27** (25 mg, 0.14 mmol) in 10 mL of anhydrous ether was irradiated through Pyrex with a 450-W Hanovia Type L lamp. The reaction was followed by NMR. After 1 h the NMR spectrum showed no change and **27** was recovered.

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Registry No.—**4,** 21428-63-7; **6,** 34786-27-1; **7,** 63449-15-0; **8,** 63449-16-1; **12,** 63449-17-2; **15a,** 63449-18-3; **18,** 63449-19-4; **22,** 63449-20-7; **23,** 63449-21-8; **25,** 63449-22-9; **25a,** 63449-23-0; **26,** 63449-24-1; **27,** 63449-25-2; **28,** 63449-26-3; 2,4,5,6,6-pentamethyl-2,4-cyclohexadienone, 16336-75-7; 3,4,66-tetramethyl-2,4-cyclohexadienone, 14069-95-5; 2,3,4,6,6-pentamethyl-2,4-cyclohexadienone, 16395-18-9.

References and Notes

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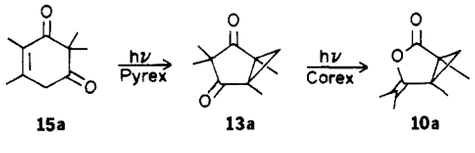
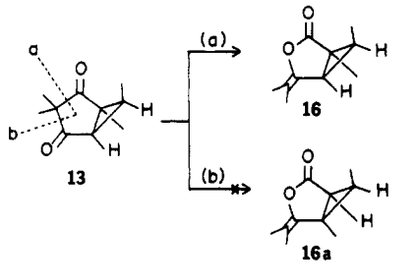
(6) (a) H. Nozaki, Z. Yamaguti, T. Okada, R. Noyori, and M. Kawanisi, *Tetrahedron,* **23,** 3993 (1967); (b) T. Okada, K. Kamogawa, M. Kawanisi, and H. Nozaki, *Bull. Chem. Soc. Jpn.,* **43,** 2908 (1970), and references cited therein.
(7) For reviews, see K. N. Houk, *Chem. Rev.,* **76,** 1 (1976); W. G. Dauben, G. Lodder, and J. Ipaktchi, *Fortschr. Chem. Forsch.,* **54,** 73 (1975).
(8) That such isomerizations do occur in Pyrex was established by irradiating **15a** (obtained from the acid-catalyzed rearrangement of **11;** details will



be described in a separate paper), which gave a quantitative yield of **13a**. Further irradiation through Corex gave **10a**.

(9) These rearrangements proceed through α-cleavage and rebonding at oxygen. There appears to be a strong preference for cleavage α to the carbonyl group that is adjacent to the methyl-bearing ring-juncture carbon. For example, with **13** cleavage occurs exclusively at a to give **16**; no **16a**



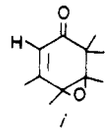
was formed. A similar (though not exclusive, but 3:1) preference was shown with **14**. We have no good explanation for this observation.

(10) Unpublished results, H. Hart and C.-t. Peng.

(11) Compound **10** in ref 1.

(12) Two Δ^1-butenolides and one Δ^2-butenolide were obtained[1] as a consequence of the thermal or photochemical isomerization of **3**, and it was conceivable that **19** photoisomerized to an aldehyde analogue of **3**, which could rearrange further to a butenolide. We therefore considered the butenolide structures that might have been obtained in this way, and were able to reject each structure as being inconsistent with the spectra of **22**.

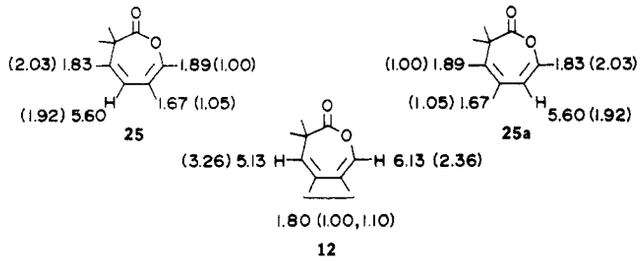
(13) Compound **24** does not logically belong in this sequence and it would have perhaps been more instructive to study the photochemistry of i, the missing member of the series **13**, **19**, i, **1**. Unfortunately, the necessary dienone



i

precursor of i is not accessible. However, the precursor of **24** was readily available from the same reaction that gave the precursor of **19**.

(14) The NMR spectrum of **25** showed that the vinyl proton (δ 5.60) was coupled with an adjacent vinyl methyl at δ 1.83 (J = 2 Hz); decoupling by irradiation of the vinyl proton collapsed the methyl signal to a singlet. The other two vinyl methyls were homoallylically coupled, at δ 1.67 and 1.89. The low-field vinyl methyls were at the termini of the butadiene moiety, limiting the possibilities to **25** and **25a**. The figures in parentheses are the relative europium-shift slopes. In **12**, where the assignment is unequivocal, the proton adjacent to the ether oxygen is at lowest field and has the *lowest* Eu-shift slope (coordination apparently occurs at the carbonyl, not the ether oxygen). By analogy, the lowest field, lowest Eu-shift methyl (δ, 1.89, slope 1.00) should be adjacent to the ether oxygen, as in **25**, not **25a**. Deuterium labeling results and mechanistic arguments confirm this assignment.



(15) D. A. Plank and J. C. Floyd, *Tetrahedron Lett.*, 4811 (1971); T. Mutsuura and K. Ogura, *J. Am. Chem. Soc.*, **89**, 3850 (1967); G. F. Burkinshaw, B. R. David, and P. D. Woodgate, *J. Chem. Soc. C*, 1607 (1970).

(16) R. K. Murray, Jr., T. K. Morgan, Jr., J. A. S. Polley, C. A. Andruskiewicz, Jr., and D. L. Goff, *J. Am. Chem. Soc.*, **97**, 938 (1975).

(17) Whereas the allene oxide is a precursor of the cyclopropanone aldehyde G in the singlet oxygen oxidation of dimethylfulvene, it is *not* a necessary precursor of G in the photoisomerization of dienone epoxides (Scheme I). Indeed, when the fulvene oxidation is carried out in methanol a variety of products are formed[4] in place of the enol lactone. These products must arise from the reaction of methanol with **31** or L, since the epoxy ketone photoisomerization gives **6** and **7** whether carried out in ether or methanol. It seems safe to conclude that the conversion of L to G is irreversible, or at least that the conversion of G to **6** is much faster than its reversion to L.

(18) C. S. Markos and W. Reusch, *J. Am. Chem. Soc.*, **89**, 3363 (1967); D. R. Paulson, G. Korngold, and G. Jones, *Tetrahedron Lett.*, 1723 (1972); for reviews, see N. R. Bertoniere and G. W. Girffin, *Org. Photochem.*, **3**, 115 (1973); A. Padwa, *ibid.*, **1**, 91 (1967); O. Jeger, K. Schaffner, and H. Wehrli, *Pure Appl. Chem.*, **9**, 555 (1964).

(19) S. L. Murov, "Handbook of Photochemistry", Marcel Dekker, New York, N.Y., 1973, p 27.

(20) This value compares favorably with the 55 kcal/mol estimated for the triplet energy of a related steroidal epoxy enone.[24a]

(21) An aldehyde signal at δ 9.77 was observed in an NMR study of the thermal isomerization of **9** to **6** (Scheme II). However, this peak persisted at room temperature and could not be attributed to either the allene oxide I or the cyclopropanone E.[4e]

(22) N. J. Turro, *Acc. Chem. Res.*, **2**, 25 (1969).

(23) Matrix isolation studies are being undertaken in collaboration with Professor O. L. Chapman.

(24) (a) J. A. Saboz, T. Iizuka, H. Wehrli, K. Schaffner, and O. Jeger, *Helv. Chim. Acta*, **51**, 1362 (1968); (b) M. Debono, R. M. Malloy, D. Bauer, T. Iizuka, K. Schaffner, and O. Jeger, *J. Am. Chem. Soc.*, **92**, 420 (1970); (c) D. Bauer, T. Iizuka, K. Schaffner, and O. Jeger, *Helv. Chim. Acta*, **55**, 852 (1972); (d) B. R. von Wartburg, H. R. Wolf, and O. Jeger, *ibid.*, **56**, 1948 (1973); (e) J. Ehrenfreund, Y. Gaoni, and O. Jeger, *ibid.*, **57**, 2704 (1974); (f) A. B. Alder and H. R. Wolf, *ibid.*, **58**, 1048 (1975); (g) B. R. von Wartburg, H. R. Wolf, and O. Jeger, *ibid.*, **59**, 727 (1976); (h) E. Eichenberger, H. R. Wolf, and O. Jeger, *ibid.*, **59**, 1253 (1976).

(25) There is evidence[24h] that C(4)–C(5) and C(4)–O cleavage of the epoxide ring may be associated with different excited states ($\pi\pi^*$ vs. $n\pi^*$) of the epoxy ketone.

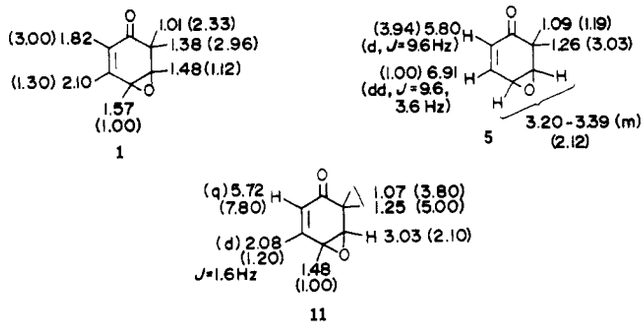
(26) There is ample precedent for carbon–carbon bond cleavage in epoxide photochemistry. For examples and leading references, see G. W. Griffin, K. Ishikawa, and I. J. Lev, *J. Am. Chem. Soc.*, **98**, 5697 (1976); V. Markowski and R. Huisgen, *Tetrahedron Lett.*, 4643 (1976).

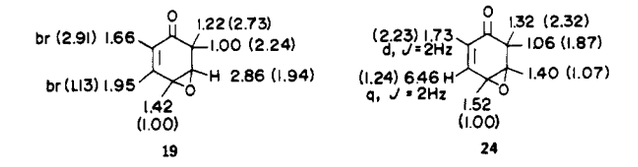
(27) Since both the C(4)–O and C(4)–C(5) bonds are broken in the overall reaction, the carbene may be derived by fragmentation of the diradical M as shown in Scheme IV, or by fragmentation of N (Scheme III).

(28) For other examples of fragmentation to a carbene in epoxide photochemistry, see P. C. Petrellis, H. Dietrich, E. Meyer, and G. W. Griffin, *J. Am. Chem. Soc.*, **89**, 1967 (1967); A. M. Torzzolo, W. A. Yager, G. W. Griffin, K. Kristinnsson, and I. Sarkar, *ibid.*, **89**, 3357 (1967); J. K. Crandall and D. R. Paulson, *Tetrahedron Lett.*, 2751 (1969).

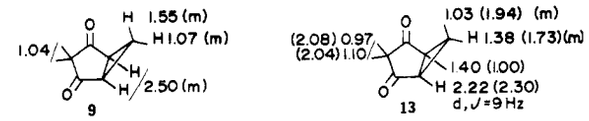
(29) This fragmentation is, of course, similar to what one could write as a stepwise path for the migration of a group R_5 from C(5) to C(4), and indeed similar migrations in the photoisomerization of α,β-epoxy ketones have been discussed in these terms [H. E. Zimmerman, B. R. Cowley, C.-Y. Tseng, and J. W. Wilson, *J. Am. Chem. Soc.*, **86**, 947 (1964)].

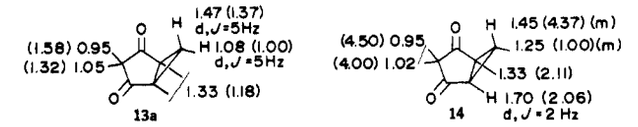
(30) Simple 4,5-epoxy-2,4-cyclohexadienones mentioned in this paper have the following NMR spectra (all peaks whose multiplicity is not indicated are singlets):

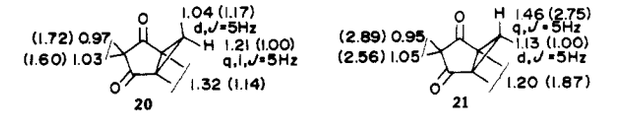




(31) The bicyclo[3.1.0]hexan-2,4-diones mentioned in this paper have the following NMR spectra (all peaks whose multiplicity is not indicated are singlets), where isomeric pairs (**13**, **14** and **20**, **21**) can be distinguished by the Eu-shift slopes and chemical shifts of the C(6) hydrogens and

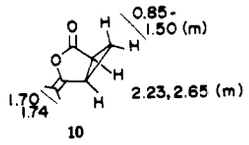




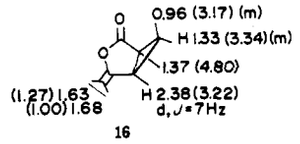


methyls. Registry no.: **9**, 15973-50-9; **13**, 63449-08-1; **14**, 63526-14-7; **20**, 63449-09-2; **21**, 63449-10-5; **13a**, 63449-11-6.

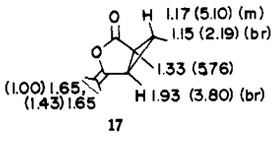
(32) The γ-lactones mentioned in this paper have the following NMR spectra (all peaks whose multiplicity is not indicated are singlets), where isomeric pair **16** and **17** can be distinguished by the Eu-shift slopes and chemical shifts of the C(6) hydrogens and methyls, and isomeric pair **17** and **17a** can be distinguished by similar examination of the C(1) and C(5) substituents. Registry no.: **10**, 29980-22-1; **16**, 63449-12-7; **17**, 63526-15-8; **17a**, 63449-13-8; **10a**, 63449-14-9.



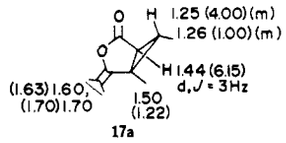
10



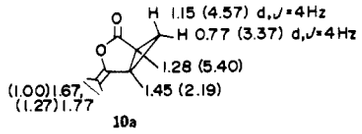
16



17



17a



10a

(33) H. Hart and R. M. Lange, *J. Org. Chem.*, **31**, 3776 (1966).
(34) H. Hart and P. Lavrik, *J. Org. Chem.*, **39**, 1793 (1974).
(35) H. Hart and P. M. Collins, *J. Chem. Soc. C*, 895 (1967).

Synthesis of 4aα-Phorbol 9-Myristate 9a-Acetate and Related Esters

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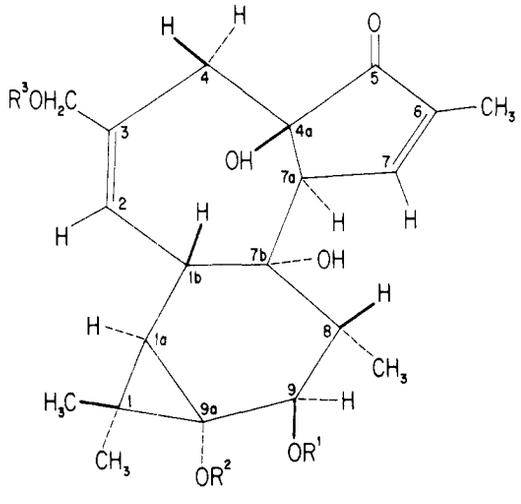
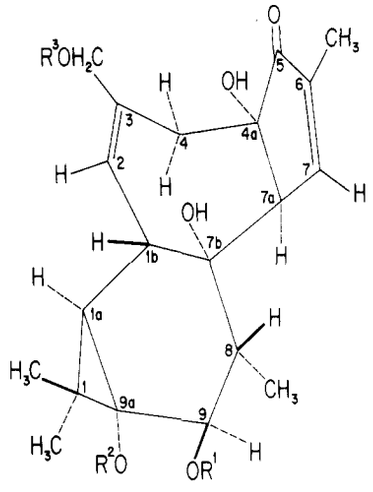
The stereoisomer of the most potent tumor-promoting agent phorbol 9-myristate 9a-acetate and its analogues have been synthesized and fully characterized. Phorbol isolated from croton oil was epimerized with 0.1 N sodium methoxide to 4aα-phorbol. Selective base-catalyzed esterification of 4aα-phorbol and selective acid-catalyzed hydrolysis of the resulting esters gave the desired compounds. They are: 4aα-phorbol 9-myristate 9a-acetate, 4aα-phorbol 9,9a-didecanoate, 3-decanoyl-4aα-phorbol 9,9a-didecanoate, 3-acetyl-4aα-phorbol 9,9a-diacetate, 3-acetyl-4aα-phorbol 9a-acetate, 4aα-phorbol 9a-acetate, 3-acetyl-4aα-phorbol 9-myristate 9a-acetate, 3-myristoyl-4aα-phorbol 9-myristate 9a-acetate, and 3-myristoyl-4aα-phorbol 9a-acetate.

Croton oil is a complex lipid mixture obtained by extraction or expression of the seeds of *Croton tiglium L.* This oil was first discovered to be a tumor promoter on mouse skin in two-stage carcinogenesis by Berenblum.[1] The subject of tumor promoters and cocarcinogens was recently reviewed.[2] The active principles of croton oil were isolated and characterized as the esters of the tetracyclic diterpene alcohol, phorbol[3,4] (**1a**). The structure and stereochemistry of **1a** was established from x-ray crystallographic studies.[5,6] Partial syntheses of phorbol esters have been reported.[7] We now wish to report the synthesis of 4aα-phorbol 9-myristate 9a-acetate (**2b**), which is the most important counterpart of the potent tumor promoter phorbol 9-myristate 9a-acetate[8] (**1b**), and the related



1a. $R^1=R^2=R^3=H$
b. $R^1=CO(CH_2)_{12}CH_3$; $R^2=COCH_3$; $R^3=H$
c. $R^1=R^2=CO(CH_2)_8CH_3$; $R^3=H$



2a. $R^1=R^2=R^3=H$
b. $R^1=CO(CH_2)_{12}CH_3$; $R^2=COCH_3$; $R^3=H$
c. $R^1=R^2=CO(CH_2)_8CH_3$; $R^3=H$
d. $R^1=R^2=R^3=CO(CH_2)_8CH_3$
e. $R^1=R^2=R^3=COCH_3$
f. $R^1=H$; $R^2=R^3=COCH_3$
g. $R^1=R^3=H$; $R^2=COCH_3$
h. $R^1=CO(CH_2)_{12}CH_3$; $R^2=R^3=COCH_3$
i. $R^1=R^3=CO(CH_2)_{12}CH_3$; $R^2=COCH_3$
j. $R^1=H$; $R^2=COCH_3$; $R^3=CO(CH_2)_{12}CH_3$

esters: 4aα-phorbol 9,9a-didecanoate (**2c**), 3-decanoyl-4aα-phorbol 9,9a-didecanoate (**2d**), 3-acetyl-4aα-phorbol 9,9a-diacetate (**2e**), 3-acetyl-4aα-phorbol 9a-acetate (**2f**), 4aα-phorbol 9a-acetate (**2g**), 3-acetyl-4aα-phorbol 9-myristate 9a-acetate (**2h**), 3-myristol-4aα-phorbol 9-myristate 9a-acetate (**2i**), and 3-myristol-4aα-phorbol 9a-acetate (**2j**). Com-