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PHOTOCHEMISTRY OF ISOPIPERITENONE AND 4-ACETOXYISOPIPERITENONE. AN UNPRECEDENTED PHOTOCHEMICAL REACTION OF AN α,β-UNSATURATED KETONE*

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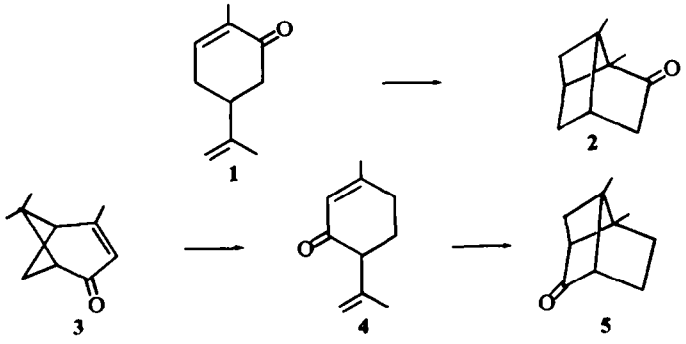
Abstract—Ultraviolet irradiation of (+)-isopiperitenone (**4**) and (±)-4-acetoxyisopiperitenone (**26**) in cyclohexane using a Pyrex filter afforded (+)-1,2-dimethyltricyclo[3.3.0.0^{2,7}]octan-6-one (**5**) in 35–42% yield and 5-acetoxy-1,2-dimethyltricyclo[3.3.0.0^{2,7}]octan-6-one (**28**) in 42% yield, respectively. Irradiation of (+)-**4** in methanol produced (+)-ketone **5** in 25% yield and (±)-5-carbomethoxymethyl-1,5-dimethylcyclohexene (**6**) in 49% yield. In methanol (±)-**26** was photochemically converted to **28** (15%) and 4-carbomethoxymethyl-1-acetoxy-2,4-dimethylcyclohexene (**29**) (65%). Hydrolysis of **28** yielded the alcohol derivative **30**. Treatment of **5** and **30** with hydrogen bromide produced the bromoketones **10** and **31**, respectively. A mechanism for production of the esters **6** and **28** is presented which involves an unprecedented cleavage of an α,β-unsaturated ketone.

INTRODUCTION

ALTHOUGH the photocycloaddition of carvone (**1**) to carvonecamphor (**2**) has been known since the turn of the century,[1–3] the intramolecular photoaddition of an isolated double bond to the double bond of an α,β-unsaturated ketone only recently has received much attention.† [4–9] In our study of the photochemical transformations of verbenone (**3**),[10] we reported the isolation of a tricyclic ketone—1,2-dimethylbicyclo[3.3.0.0^{2,7}]octan-6-one (**5**)—which, we concluded, was derived by photochemical cyclization of the initially produced isopiperitenone (**4**). In this paper we communicate our further studies on the photochemistry of isopiperitenone which confirm our original conclusions about the intermediacy of **4** in the production of **5** and unveil a second heretofore unprecedented photochemical transformation of an α,β-unsaturated ketone.



1 **2** **3** **4** **5**

* W. F. Erman and T. W. Gibson, Paper presented before the Division of Cellulose, Wood, and Fiber Chemistry, Symposium on Tall Oil and Turpentine, 153rd National Meeting of the Americal Chemical Society, Miami, Florida, 10–12 April 1967, Abstracts, D 51.

† For an excellent review and other examples of intromolecular cycloaddition reactions of α,β-unsaturated ketones see the Ph.D. Dissertation of R. A. Schneider, Cornell University, 1966.

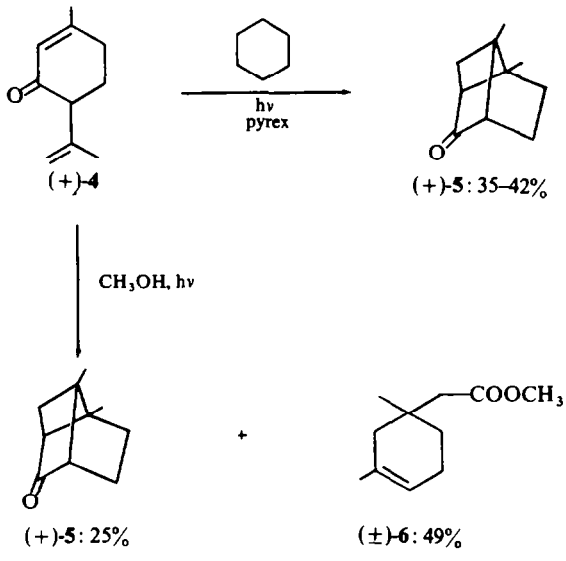
RESULTS

Photochemistry of isopiperitenone

Irradiation of (+)-isopiperitenone (**4**)[13] ($[\alpha]_D^{25}$ +48·7°) until complete consumption of the starting ketone* in cyclohexane solution using a Pyrex filter† afforded (+)-ketone **5**‡ of high optical rotation ($[\alpha]_D^{25}$ +147·0°) in 35–42% yield. When the irradiation was terminated at a point when about 70% of the isopiperitenone was consumed, the ketone **5** showed approximately the same rotation ($[\alpha]_D^{25}$ +147·2) and the recovered isopiperitenone (**4**) showed no loss in optical activity ($[\alpha]_D^{25}$ +48·7°).

The IR spectrum of the crude irradiation product from above gave evidence for the presence of a ketene (strong absorption at 4·72 μ) which could be trapped as the methyl ester derivative by irradiation of **4** in methanol. Thus irradiation of **4**, $[\alpha]_D^{25}$ +49°, in methanol afforded the ketone **5**, $[\alpha]_D^{25}$ +147°, in 25% yield and 5-carbomethoxymethyl-1,5-dimethylcyclohexene (**6**) $[\alpha]_D^{25}$ +0·0°, in 49% yield.

CHART 1



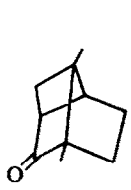
Although NMR structure analysis of the ketone **5** as previously presented seems invincible,[10] further confirmation of the structure is afforded by acid cleavage studies. Corey[12] has reported that the analogous tricyclic ketone, 3,8-cyclocamphor (**7**), on treatment with hydrogen bromide in methylene chloride cleaves to *cis*-π-bromo-

* Irradiations were monitored by gas chromatography; see the Experimental Section for details.

† Use of a Vycor or quartz filter led to rapid photochemical decomposition of the ketone **5**. Only polymeric products could be isolated at the point when complete consumption of isopiperitenone was observed under these conditions.

‡ The ketone **5** was spectroscopically and gas chromatographically identical with the tricyclic ketone **5** reported earlier.[10]

camphor (**8**). Similar cleavage of **5** would yield *cis*-π-bromo*epi*camphor (**9**), a material which could be easily converted to the known *epi*camphor.



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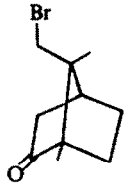

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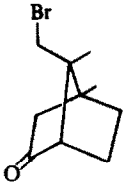
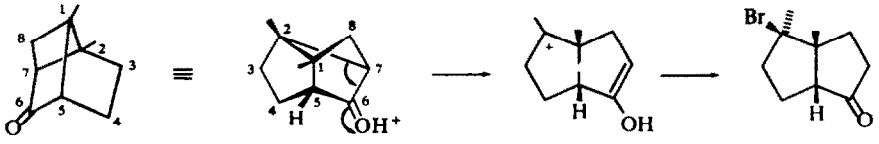


9

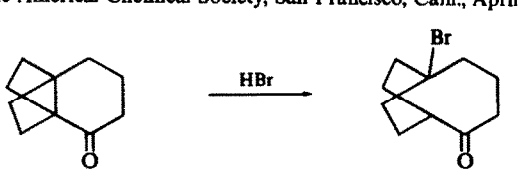
Treatment of **5** with hydrogen bromide following Corey's procedure[12] afforded a single crystalline bromide, the NMR spectrum of which clearly indicated a tertiary bromide of the structure **10** rather than the primary bromide **9**. The spectrum contained two singlets at τ 8·20 and 8·60, each of which integrated for 3 hydrogens; two noncoupled methyl groups are therefore necessarily present. The chemical shift of the one (τ 8·20) is characteristic of the protons of a methyl group attached to the same carbon atom as a bromo group.[13] The chemical shift of the protons of the second methyl was downfield (τ 8·60) relative to a normal tertiary methyl, suggesting the presence of a vicinal bromo function.[13] A tentative assignment of stereochemistry, as indicated by structure **10**, is based on the mechanistic assumption that addition of bromide (as HBr) to the intermediate carbonium ion **5a** occurs from the opposite side of the bond being cleaved concerted with bond rupture. Absolute assignment of stereochemistry will be reserved for a subsequent communication.



5 **5a** **10**

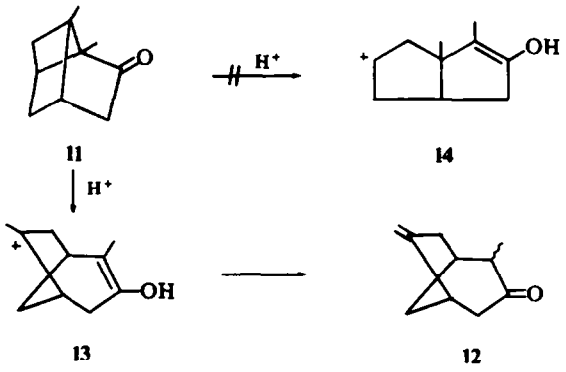
In retrospect the isomer **10**, rather than **9**, is the mechanistically anticipated acid cleavage product of **5**. To our knowledge the only other example of the cleavage of a strained cyclobutane ring adjacent to a ketone is that of the conversion of carvonecamphor (**11**) to 2-methyl-6-methylenebicyclo[3.2.1]octan-3-one (**12**).[2,*] In

* A second example recently has been supplied by Eaton who converted tricyclo[4.2.2.0^{1,6}]decan-2-one (i) to 1-bromobicyclo[4.2.2]decan-5-one (ii) on treatment with hydrogen bromide; P. E. Eaton, 155th National Meeting of the Americal Chemical Society, San Francisco, Calif., April 1968, Abstracts P-1.



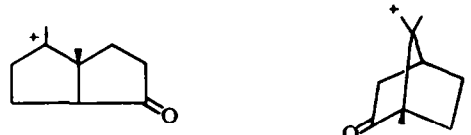
i ii

this example cleavage occurs in such a manner as to yield the more stable carbonium ion (i.e. via **13** rather than **14**). Similarly, cleavage of **5** to **10** via the tertiary carbonium



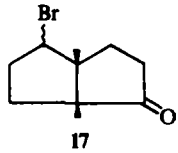
11 **14** **13** **12**

ion **15** should be favored over the conversion of **5** to **9** via **16**. In fact it was surprising that 3,8-cyclocamphor should undergo bond scission via a primary carbonium ion.



15 **16**

Consequently, we reinvestigated the latter cleavage. Treatment of **7** with hydrogen bromide using the exact conditions employed by Corey,[12] produced a single bromo derivative which possessed spectral and physical constants identical with the bromide reported by Corey and assigned the structure **8**. The NMR spectrum of the bromide, however, was inconsistent with the structure **8** and coincided with that predicted for the bicyclo[3.3.0]octanone system **17**. The two sets of methyl protons appeared as singlets at τ 8·88 and 8·97 and the proton which resides α- to the bromo group as a triplet, $J = 6{\cdot}5 \pm 0{\cdot}5$ Hz, at τ 6·16 in the relative ratio 3:3:1. Again the stereochemistry of the bromo group in **17** will be discussed in a separate communication.



17

The structure **6** was tentatively assigned to the ester product from the irradiation of **4** on the basis of the empirical formula $C_{11}H_{18}O_2$, the IR spectrum, which displayed carbonyl absorption at 5·74 μ, and the NMR spectrum, which was completely consistent with the assigned structure (see Experimental Section).

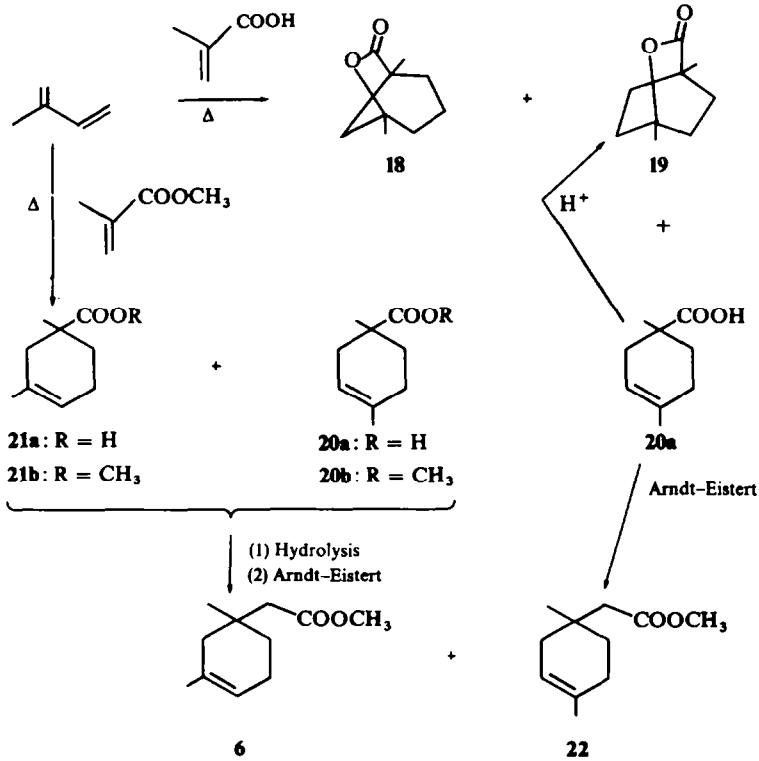
Final confirmation of structure **6** was made by an independent synthesis. Diels–Alder condensation of isoprene and methacrylic acid afforded 1,5-dimethyl-6-oxa-7-oxobicyclo[3.2.1]octane (**18**), 17%, 1,4-dimethyl-2-oxa-3-oxobicyclo[2.2.2]octane

(**19**), 17%, and 1,4-dimethylcyclohexen-4-carboxylic acid (**20a**), 17%. The structures of the two lactones were assigned on the basis of IR and NMR spectral data. The carbonyl absorption frequency of the lactone **18** was clearly that of a five-membered ring lactone (5·65 μ);[14] the NMR spectrum displayed single peaks at τ 8·60 and 8·82 for the noncoupled methyl protons, clearly indicating that the lactone ring was bridged between the two methyl groups.

The IR spectrum of **19** revealed carbonyl absorption at 5·72 μ for a six-membered ring lactone;[14] the NMR was recorded as a simple spectrum of three peaks at τ 8·29, 8·66 and 8·86 of relative ratio 8:3:3. Apparently the lactone function has little effect upon the environment of the methylene protons which occur as a single peak at τ 8·29. Again bridging of the lactone between the two methyl protons is assured by the noncoupled pattern of the methyl protons at τ 8·66 and 8·86.

The physical constants (m.p. and b.p.) of the acid **20a** were in close agreement with those previously reported.[15] However, the IR and NMR spectra of the acid and its methyl ester derivative were consistent with either structure **20** or **21** (see Experimental Section). Discrimination between **20** and **21** was made by acid catalyzed cyclization of the acid to the corresponding cyclic lactone. Since the six-membered lactone **19** was the product of this cyclization the structure **20a** must be assigned to the acid.

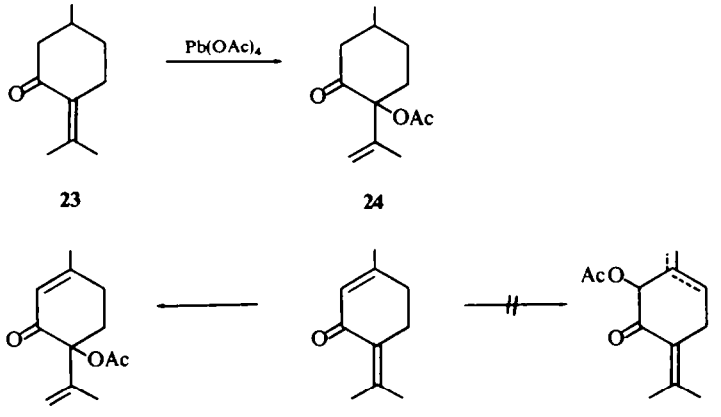
It is surprising, though ultimately experimentally gratifying, that the acid **21a** is almost completely converted to lactone **18** under the Diels–Alder conditions



before complete conversion of **20a** to **19** occurred. Lactonization was avoided by condensation of isoprene with methyl methacrylate as previously described by Nazarov *et al.*[15] The two esters **20b** and **21b**, produced in 18% and 10% yields, respectively, from this reaction could be analyzed by gas chromatography but could not be separated on a preparative scale. Hydrolysis of the ester mixture and Arndt–Eistert homologation of the subsequently formed acid chloride mixture afforded the homologous ester **22** (25% yield) and **6** (11% yield) which were readily resolved by preparative gas chromatography. Arndt–Eistert homologation of the acid chloride of pure acid **20a** produced an ester in 27% yield, the gas chromatographic retention time and spectral properties of which were identical with the ester **22** (formed in 25% yield) above. The spectral and physical properties of the second ester (formed in 11% yield from the previous homologation), which must possess the structure **6**, were identical with those of the ester assigned structure **6** from the photolysis of isopiperitenone.

Irradiation of 4-*acetoxyisopiperitenone* (**26**)

For reasons outlined in the Discussion Section we were impelled to study the irradiation of an isopiperitenone derivative with an oxygenated substituent at position 4. Zalkow's[16] observation that pulegone (**23**) undergoes exclusive conversion to 4-acetoxyisopulegone (**24**) on treatment with one mole of lead tetraacetate prompted us to attempt a similar oxidation of piperitenone (**25**). Even when **25** was treated with a 0·4 mole equivalent excess of lead tetraacetate the analogous (±)-4-acetoxyisopiperitenone (**26**)* was isolated in 34% yield with no evidence for the mono acetate derivative (**27**) which would have resulted from reaction at the ring double bond.

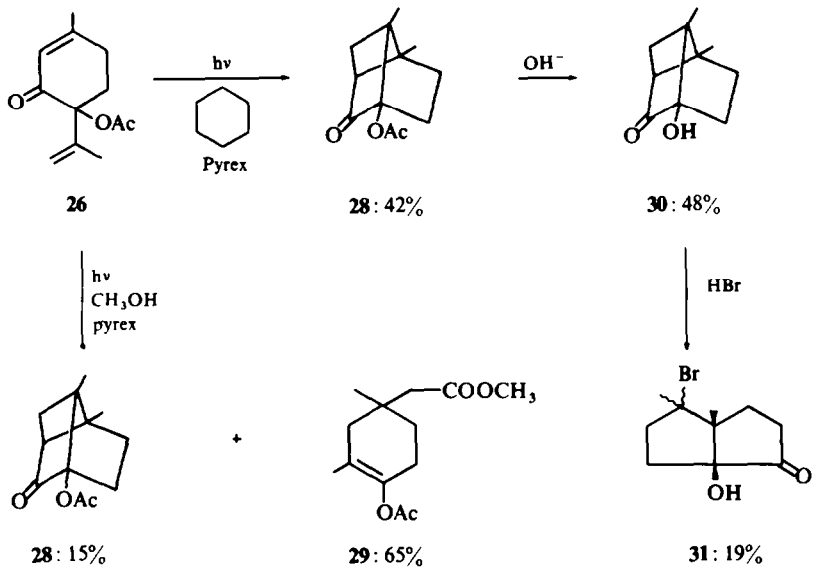


23 **24** **26** **25** **27**

Irradiation of (±)-**26** in cyclohexane afforded the ketone **28** in 42% yield. Again evidence for ketene absorption in the IR spectrum of the crude reaction product compelled us to perform the irradiation in methanol. In the latter solvent the yield of **28** was diminished to 15% while the ester **29** was isolated in 65% yield.

* The structure of **26** was clearly defined by its spectral properties (see Experimental Section).

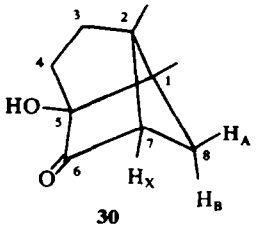
CHART 2



26 28: 42% 30: 48%

28: 15% 29: 65% 31: 19%

The structure of the ketone **28** was persuasively assigned by examination of the IR and NMR spectra of the acetate and the corresponding hydrolysis product **30**. The IR spectrum of **28** showed broad absorption in the 5·6–5·75 μ region which was reduced to a single well-defined band at 5·68 μ in the alcohol **30**; the presence of a strained 5-membered ring ketone and an acetate are thus assured. The well-defined ABX pattern of the C-7 and C-8 protons in the acetate and the alcohol paralleled that of the ketone **5**.[10] In the NMR spectrum of the alcohol **30**, for example, H_X occurs as a doublet (J_{AX} = 3·0 Hz, J_{BX} = 0) centered at τ 7·38, H_A as a quartet (J_{AB} = 8·5 Hz, J_{AX} = 3·0 Hz) at τ 7·78 and H_B as a doublet (J_{AB} = 8·5 Hz, J_{BX} = 0) at τ 8·23 (see the Experimental Section for a detailed analysis of the NMR spectrum of **28** and **30**) consistent with assignments previously applied to the ketone **5**.[10]

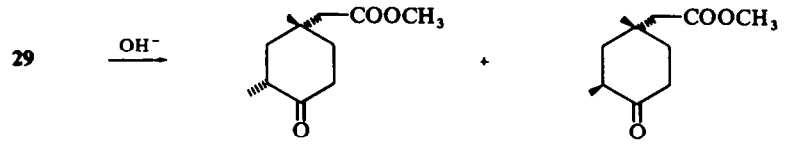


30

In a manner analogous to cleavage of the ketone **5**, **30** was converted to the bromoketone **31** in 19% yield on treatment with hydrogen bromide. Again structure assignment was based on spectral data (Experimental Section) and mechanistic arguments.

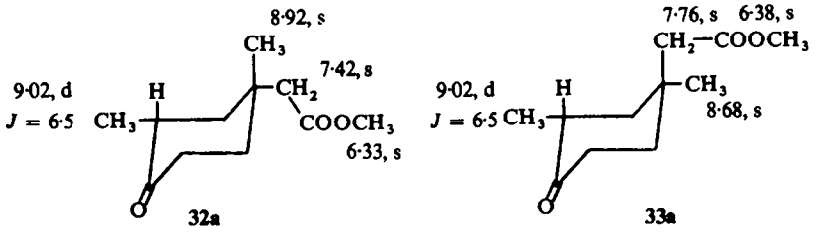
The structure of the ester **29** was revealed from the IR spectrum, which showed normal ester carbonyl absorption at 5·75 μ and characteristic acetate C—O stretching

at 8·2–8·4 μ;[17a] and the NMR spectrum, the analysis of which is presented in the Experimental Section. Hydrolysis of **29** and re-esterification of the acid function with diazomethane produced a mixture of the two epimeric ketones **32** and **33**. Both keto-esters.



32: *seqcis* **33**: *seqtrans*

which were only partially resolved by gas chromatography, displayed carbonyl absorptions at 5·74 μ for ester and 5·83 μ typical of a cyclohexanone.[17b] Tentative stereochemical assignment of the two isomers was made from the following arguments. Of the four possible conformations in which the two epimers can exist only **32a** and **33a** are devoid of 1,3-diaxial-alkyl interactions. The NMR spectra therefore should be a reflection of these two conformers. Although examples are sparse and the known cases difficult to relate to this example, an axial methyl may be expected to occur upfield in the NMR spectrum from an equatorial methyl.[18] On this basis the one isomer is assigned the *seqcis** structure **32** and the other isomer the *seqtrans* structure **33**. Thus, as outlined below, the C-4 methyl protons in **32** occur at 0·24 ppm higher field than the methyl protons in **33**.[19]



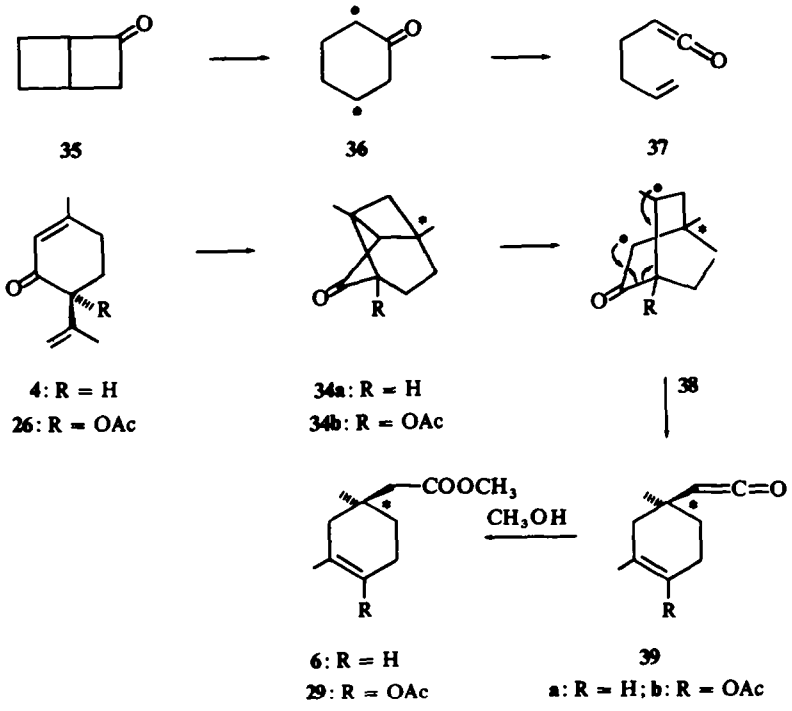
DISCUSSION

Two aspects of the photochemical reactions described above deserve attention. The first is the noticeable absence of the photocycloaddition product **34** which would have been produced by contrapositive addition of the isopropenyl double bond to the conjugated double bond, a subject which we have touched on previously.[10] The second is the mechanism for production of the ester products **6** and **29**. Since the latter has bearing on the former, this subject will be discussed first.

A priori it was tempting to suggest that the ketones **34a** and **34b** indeed were produced photochemically. Since even the less strained parent ketone (**35**) of the 4/4-fused ring system is highly unstable and undergoes rapid thermal decomposition at room temperature to 3-butenylketene (**37**),[19] probably via the intermediate diradical **36**, it was reasonable to assume that the structure **34** would decompose spontaneously.

* The *seqcis* and *seqtrans* terminology are used in accordance with rules suggested by R. S. Cahn, C. Ingold and V. Prelog, *Angew. Chem. Intern. Ed. Engl.* **5**, 385 (1966).

Thermal cleavage of **34** via the diradical **38** would yield the ketene **39**, the precursor of **6** and **29**.*



Since the above process does not affect the asymmetric center at the starred carbon, the ester **6** from irradiation of (+)-isopiperitenone should be *optically active*. In fact the ester **6** showed no rotation between 200–700 mμ. Since optically active saturated acids and esters show dispersion curves of significantly increased rotation in the 200–300 mμ region,† we must conclude that the ester **6** is clearly racemic. Therefore we suggest an alternative mechanism for production of **6** which involves initial cleavage of the C-3, C-4 bond of isopiperitenone. The intermediate optically inactive biradical **40** would undergo recoupling at the terminal carbon to produce the racemic ester **6**.

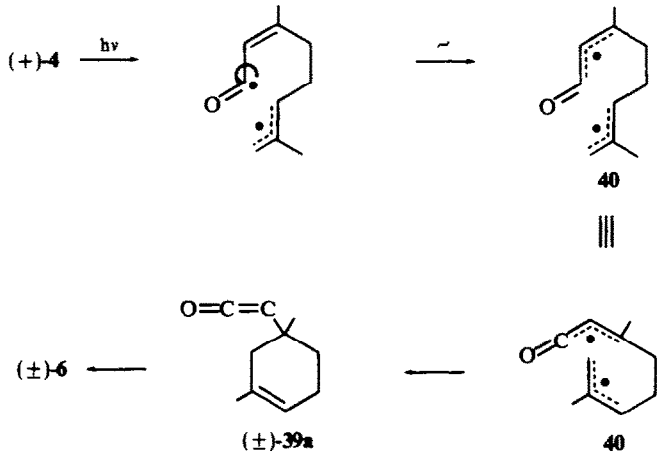
The formation of products by cleavage of the bond between the saturated carbon atom and the carbonyl carbon of a simple α,β-unsaturated ketone (i.e. cleavage of the 3,4-bond of the general structure A) is unprecedented.‡ In fact attempts to induce photoelimination reactions of alicyclic α,β-unsaturated ketones (which require initial cleavage of such a bond) were unsuccessful.§ Cleavage of β,γ-unsaturated ketones

* We should also emphasize that the biradical **38** could be produced directly from **4** as an intermediate in the photocycloaddition process.

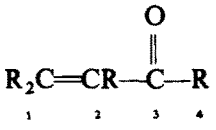
† See references listed in lit.[20a,b] and a single example recorded in lit.[20c]

‡ Two possible examples are the photochemical conversions of verbenone to methyl-3,7-dimethyl-3,6-octadienoate[10] and nootkatone to methyl-1-carbomethoxymethyl-2-*exo*-isopropenyl-2-*endo*-7,7-trimethylbicyclo[2.2.1]heptane.[21] However, alternative more plausible mechanisms can be proposed for these transformations.

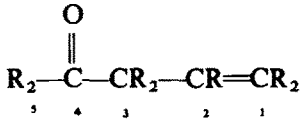
§ For explanations for the inefficiency of cleavage of alicyclic α,β-unsaturated ketones, see the publication of P. J. Wagner and G. S. Hammond, *J. Am. Chem. Soc.* **88**, 1245 (1966).



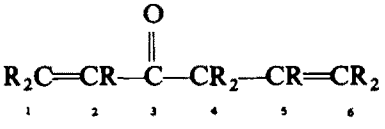
at the position allylic to the double bond (i.e. cleavage of the 3,4-bond of the general structure **B**) is a relatively efficient process due to stabilization of the incipient radical by the adjacent π-system of the double bond.* However, in alicyclic α,β-unsaturated ketones which contain β,γ-unsaturation, cleavage at the position allylic to the β,γ-double bond (i.e. cleavage of the 3,4-bond in structure **C**) has not be reported.



A



B

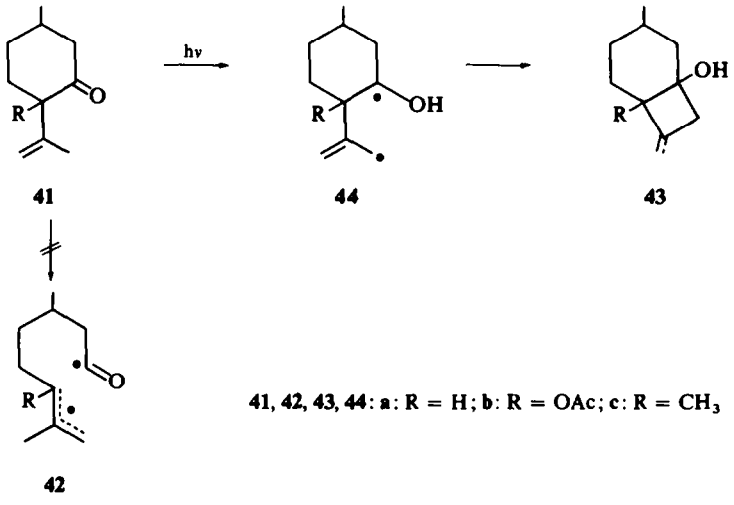


C

Finally, in contrast with the latter proposed course of reaction is the photochemical behavior of isopulegone and derivatives (**41**). Moroe,[22a] Sheehan,[22b] and Cookson[22c]

* For pertinent references see W. F. Erman, *J. Am. Chem. Soc.* **89**, 3828 (1967).

observed that **41a–c**, which might be expected to undergo facile photochemical cleavage to products via the diradicals **42a–c**, instead yielded the cyclobutanols **43a–c** on irradiation in methanol solution. As suggested by these authors, **43** is most likely produced via the intermediate biradical **44a–c**.



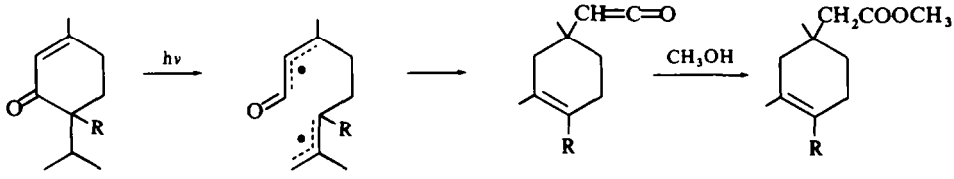
It was in search of evidence that the biradical **40** was involved as an intermediate in the production of **6** that we turned our attention to the photochemical behaviour of the acetoxyketone **26**. We reasoned that introduction of an oxygen function at the 4-position of isopiperitenone should stabilize an incipient radical developing at this position. The consequence should be an increase in the yield of the ester product at the expense of the cycloaddition product. Indeed introduction of an acetoxy group increased the yield of ester product in methanol solvent from 49 to 65% while the yield of cycloaddition product decreased from 25 to 15% (compare results in Charts 1 and 2, Results Section).

Surprisingly the yields of cycloaddition products **5** and **28** were approximately the same for unsubstituted and 4-substituted isopiperitenone when irradiations were performed in cyclohexane solvent. In fact, the yield of cycloaddition product was increased in going from methanol to cyclohexane in each instance.

The differences in yields of products in the two solvents could be explained by solvent effects on the cycloaddition process. Numerous workers have shown that yields and ratios of adducts produced by photodimerization of cyclic α,β-unsaturated ketones and cycloaddition of olefins to conjugated ketones are greatly influenced by solvent.[3, 6b, 23] In their detailed study of the photochemistry of carvone (**1**) Meinwald and Schneider observed a significant solvent effect on the rate of conversion of **1** to carvonecamphor (**2**). In this instance the use of the more polar solvent enhanced the rate of cycloaddition.[3] By analogy, the isopiperitenone photocycloaddition process might be expected to be enhanced in the more polar solvent. In actuality, the rate of formation of the tricyclic ketone **5**, as carefully monitored by gas chromatography,

was approximately the same in both cyclohexane ($0{\cdot}92 \times 10^{-7}$ moles/sec) and methanol ($0{\cdot}88 \times 10^{-7}$ moles/sec). We therefore assume that in methanol the increased yield of ester relative to tricyclic ketone is a result of enhancement of the α-cleavage process by methanol.

If we assume that the α-cleavage and radical recombination processes are reversible, then methanol could drive the reaction forward by trapping the ketene to produce the corresponding esters **6** and **29**. The argument for an overall reversible process is invalidated, however, by the observation that starting isopiperitenone is recovered with complete retention of configuration and the rotation of the cycloaddition product is approximately the same regardless of the solvent employed. If the overall process were reversible, the isopiperitenone would be expected to undergo racemization in cyclohexane and, consequently, the rotation of the cycloaddition product should be decreased in the latter solvent. Further experimentation is necessary in order to understand the solvent effect.[24]



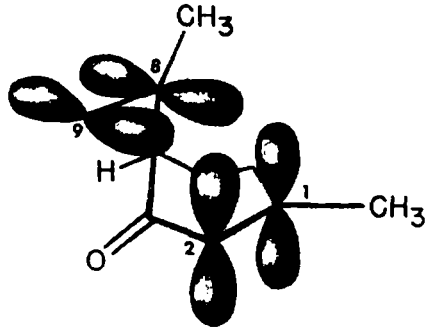
4: R = H
26: R = OAc

40

39

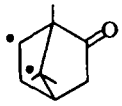
6: R = H
29: R = OAc

Since we have emphasized that the ester products are not produced from an intermediate ketone of structure **34**, we can now discuss the exclusive production of the one type adduct (i.e. **5** or **28**). Previously we rationalized this phenomenon using stereochemical arguments—i.e. regardless of how the isopropenyl group of isopiperitenone is rotated (when oriented in a pseudo axial position), the π-orbital of C-8 is better oriented for overlap with the C-1 than with the C-2 orbital; similarly the C-9 and C-2 orbitals are favorably oriented for overlap.[10] (See structure **4** below).



4

A second argument previously not discussed by us invokes a two-step process involving bicyclic intermediates. In their discussion of the formation of carvone-camphor (**2**) from carvone (**1**), Büchi and Goldman[6b] invoked the general rule that addition reactions proceed via the most stable biradical. Of the four biradicals **46–49**, **47** was clearly more stable than the others on the basis of inductive and resonance effects.



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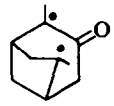

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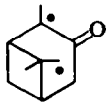
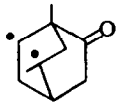
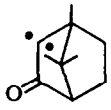


48



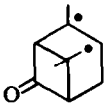
49

Of the four biradicals **50–53** anticipated for cycloaddition of isopiperitenone it would be difficult to chose between **51** and **53**. It is now generally recognized, however, that there is a preference for five-membered over six-membered ring formation in reactions of radicals with olefins.[25] On this basis **50** and **51** would be the preferred intermediates and the observed product is that predicted from the theory.

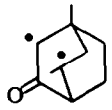


50

51



52



53

More recently Srinivasan[25e] has treated photocycloadditions as microscopically reversible processes in which the course of reaction is governed by the relative transition energies of both the biradical formation and final bond formation stages. Inherently the second step is dependent upon the relative strain energies of the cycloaddition products. On this basis, the less strained ketones **5** and **28** would be favored over the 4/4-fused structures of type **34**. In the specific example of isopiperitenone it would appear that the biradical formation step governs the course of reaction. If biradical **53** were produced competitively with **51** (or **50**), it would surely dissociate to ketene **39** (in analogy to the dissociation of **36** to **37**). Such a dissociation, as discussed earlier, would produce optically active ketene **39** instead of racemic **39**, as observed.

Thus steric arguments, as discussed earlier, appear to present the better rationale for product formation in this instance. Current studies on photocycloadditions in our laboratories suggest that *both* thermodynamic and stereochemical considerations are important in predicting the course of other photocycloaddition reactions.

EXPERIMENTAL

General

Melting points were determined on a Thomas–Hoover capillary melting point apparatus or on a micro hot stage and are corrected; boiling points are uncorrected. Infrared spectra were recorded on Perkin–Elmer 257 or 137 spectrophotometers as 5% solutions. Nuclear magnetic resonance spectra were obtained on an HA-100 spectrometer using sulfuric acid as an external reference. Chemical shifts are recorded as parts per million on the τ scale, coupling constants as Hz. Nuclear magnetic resonance data are recorded in the order: (solvent) chemical shift (multiplicity where s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, coupling constant, integration, interpretation). Gas chromatography separations were made on one of two columns: column 1, a 10 ft × 0·25 in. stainless steel column packed with 20% DC-200 silicone oil on 60–70 mesh Anakrom ABS; column 2, a 10 ft × 0·25 in. stainless steel column packed with 20% Reoplex-400 on 60–80 mesh Anakrom ABS-300.

Specific rotations were obtained using a Rudolph Model 70 precision polarimeter. Optical rotatory dispersion measurements were made using a Jasco Model ORD/UV/CD-5 spectropolarimeter. Microanalyses were performed by T. Atanovich and associates of these laboratories and by Spang Microanalytical Laboratories, Ann Arbor, Michigan.

The petroleum ether used in this work was purified by distillation, b.p. 30–60°. Magnesium sulfate was used for drying reaction mixtures. Photochemical reaction mixtures were flushed with argon for a period of 1 hr before irradiations; a steady stream of argon was bubbled through the mixture during the irradiations.

Preparation of 2-acetoxyisopiperitenone (**26**)

To a solution of 11·258 g (0·075 mole) of piperitenone (**25**)[26] b.p. 79° (1·5 mm), in 350 ml of benzene maintained at 64° was added 50·0 g (0·113 mole) of lead tetraacetate in portions over a period of 10 min. The mixture was heated at reflux for 16 hr, cooled to 25–26°, and filtered to remove the precipitated lead salts. The benzene filtrate was washed with two 50-ml portions of water, two 25-ml portions of sodium bicarbonate, and water, and dried. Evaporation of benzene under reduced pressure afforded 16·774 g of crude oil. Distillation from an 18 in. spinning band column afforded 4·7832 g of forerun, b.p. 45–104° (0·6–0·8 mm) (mixture containing principally piperitenone) and 5·429 g (34%) of 4-acetoxyisopiperitenone (**26**), b.p. 104° (0·6 mm), of 93% purity (GLPC). The 5·429 g of ketone **26** of 93% purity was dissolved in 200 ml of petroleum ether and decolorized with 6·1 g of activated charcoal. Filtration and evaporation of solvent afforded 3·726 g of crystalline **26**. Recrystallization from petroleum ether afforded 1·804 g (11%) of 4-acetoxyisopiperitenone (**26**) as colorless prisms: m.p. 52–53°; IR (CCl_4) 5·75 (acetate C=O), 5·95 (conj C=O), 6·12, 11·0, 11·25 (>C=CH_2), 8·12 (OAc), 9·6 μ (characteristic band); NMR ($CDCl_3$) τ 4·08 (s, 1, CH_3—C=C<u>H</u>—), 4·96 (s, 1, —C=C<u>H</u>$_2$), 4·22 (s, 1, —C=C<u>H</u>$_2$), 6·9–8·2 (m, methylene protons), 7·97 (s, C<u>H</u>$_3$COO—), 8·10, 8·15 (singlets, C<u>H</u>$_3$—C=CH— and C<u>H</u>$_3$—C=CH_2).

Anal Calcd for $C_{12}H_{16}O_3$: C, 69·21; H, 7·74. Found: C, 69·32; H, 7·89%.

Irradiation of isopiperitenone (**4**)

A. *Cyclohexane solvent; Complete consumption of* **4**. A solution of 1·002 g (0·007 mole) of isopiperitenone[11] [b.p. 98–99° (3·75 mm), $[\alpha]_D^{25}$ +49·0° (*c*, 0·96 in $CHCl_3$)] in 150 ml of spectroscopy grade cyclohexane was irradiated in a pyrex vessel as previosuly described[27] using a Hanovia 450 W mercury arc lamp for a period of 80 min. The cyclohexane was removed under reduced pressure. An IR spectrum of the residual liquid contained a sharp band at 4·72 μ (ketene) and at 5·68 μ (four-membered ring ketone or strained five-membered ring). The residual liquid was distilled to produce 382 mg (38%) of ketone **5** which solidified on standing. Recrystallization from petroleum ether afforded 60 mg of **5** as colorless crystals, m.p. 126–128°. Final purification by gas chromatography and sublimation at 53–73° (110 mm) afforded pure **5** as colorless camphoraceous plates: m.p. 133–134° [Lit.[10] m.p. 136–138°].

B. *Cyclohexane solvent. Partial consumption of* **4**. A solution of 499 mg (0·003 mole) of isopiperitenone[11] [b.p. 98–99° (3·75 mm), $[\alpha]_D^{25}$ +48·8° (*c*, 1·30 in $CHCl_3$)] in 50 ml cyclohexane was irradiated in a Pyrex flask as previously described[10,*] for a period of 90 min. The cyclohexane was removed by distillation and the crude product distilled from a modified Hickman still to afford 356 mg of distillate, b.p. 115–130° (3·75 mm) consisting of ketone **5** (60%; 42% yield) and ketone **4** (40%; 25% recovery). The ketone **5** was collected by preparative gas chromatography as previously described[10] and its identity revealed by comparison with a previously isolated sample of the ketone: m.p. 136–138°; $[\alpha]_D^{25}$ +147·2° (*c*, 1·26 in $CHCl_3$). The ketone **4** was collected by preparative gas chromatography on column 2 at 150° and 60 ml/min helium flow and identified by comparison of spectral parameters with starting material: $[\alpha]_D^{25}$ +48·8° (*c*, 1·52 in $CHCl_3$).

C. *Methanol solvent.* A solution of 503 mg (0·003 mole) of isopiperitenone (**4**)[11] [b.p. 98–99° (3·75 mm), $[\alpha]_D^{22}$ +49·0° (*c*, 0·96 in $CHCl_3$)] in 50 ml of absolute methanol contained in a Pyrex vessel was irradiated for a period of 85 min with UV light generated from a Hanovia 450 W mercury arc lamp.[7] Evaporation of solvent under reduced pressure and short path distillation afforded 380 mg of colorless liquid, b.p. 120–128° (7·0 mm), and 34·7 mg of liquid, b.p. 128–132° (7·0 mm). Analysis of the distillate b.p. 120–128° (7·0 mm) by GLPC on column 2 at 150° and 60 ml/min helium flow indicated the presence of two major peaks: *1,2-dimethyltricyclo*[3.3.0.0^{2,7}]*octan-6-one* (**5**), rel ret time 6·7 min, (32%; 25% yield) and *5-carbomethoxymethyl-1,5-dimethylcyclohexene* (**6**), rel ret time 11·3 min, (64%; 49% yield). The remaining 4% of the distillate consisted of a number of poorly resolved peaks.

The ketone **5** was collected by preparative GLPC on column 2 at 150° and 60 ml/min helium flow: m.p. 134–137° [Lit. m.p. 136–138°[10]]; $[\alpha]_D^{25}$ +147·2° (*c*, 1·31 in $CHCl_3$). The IR and NMR spectra and GLPC retention time of **5** were identical with those of an authentic specimen of **5**.[10]

The ester **6** was collected by preparative GLPC on column 1 as above and purified for analysis on column 2 at 150° and 60 ml/min helium flow: b.p. 125–126° (6·0 mm); $[\alpha]_D^{25}$ 0·0° (*c*, 1·33); IR (CCl_4) 5·74 μ (ester C=O); NMR ($CDCl_3$) τ 4·70 (m, 1, $CH_3-\underset{|}{C}=C\underline{H}-$), 6·42 (s, 3, $-COOC\underline{H}_3$), 7·8–8·7 (m, methylene protons), 7·80 (s, 2, $-C\underline{H}_2CO-$), 8·40 (s, $C\underline{H}_3C=CH-$), 9·01 (s, $C\underline{H}_3-\underset{|}{C}-CH_2COOCH_3$).

Anal Calcd for $C_{11}H_{18}O_2$: C, 72·49; H, 9·96. Found: C, 72·27; H, 9·75%.

The spectral properties and GLPC retention times of the ester **6** above and that prepared from 5-carbomethoxy-1,5-dimethylcyclohexene (**21b**), below, were identical. The ORD curve of the ester **6** showed no rotation between 200–700 mμ (*c*, 0·238 in EtOH).

Analysis of the distillate, b.p. 128–132° (7·0 mm), by GLPC as above indicated the presence of **5** (6%), **6** (38%) and isopiperitenone (44%). The isopiperitenone, isolated by preparative GLPC on column 2 at 150°, showed spectral properties consistent with those of the starting ketone **4**.

Irradiation of 4*-acetoxyisopiperitenone* (**26**).

A. *Cyclohexane solvent.* A solution of 4·006 g (0·0192 mole) of the ketoacetate (**26**) in 400 ml of cyclohexane was irradiated as above employing a Pyrex filter and 450 W Hanovia lamp for a period of 100 min. Removal of solvent and short-path distillation afforded 1·782 g of distillate, b.p. 115–130° (0·4 mm) and 55 mg distillate, b.p. 160° (0·5 mm). The fraction b.p. 115–130° (0·4 mm) consisted of ketone **28**, rel ret time 19·0 min (94%; 42% yield) and a mixture of unresolved peaks (6%). The fraction b.p. 160° (0·4 mm) consisted of starting ketoacetate **26** of 93% purity. The per cent compositions and rel ret times were based on analyses by GLPC on column 2 at 150° and 70 ml/min helium flow.

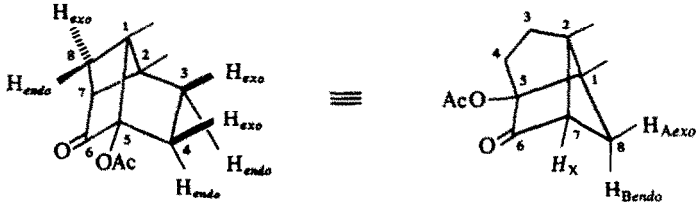
The ketone **28** was isolated as colorless crystals, m.p. 57–59°, by preparative GLPC on the same column above. Final purification for analysis was made on column 1 at 150° and 60 ml/min helium flow.

In a separate experiment irradiation of 1·500 g of ketoacetate **26** in 150 ml of cyclohexane afforded 1·7 g of residual oil after removal of the bulk of the solvent. The residue was dissolved in 100 ml of petroleum ether and adsorbed on 15·0 g of Davison 100–200 mesh silica gel. Elution with 400 ml of 5% ether in petroleum ether afforded 170 mg of crude ketone **28**. Further elution with 200 ml of 5% ether in petroleum ether afforded

* This run, in contrast to the above run, was performed in a Pyrex flask placed outside the Pyrex vessel used above. With this set-up the quantity of light transmitted to the solution is diminished; hence greater reaction periods are required.

519 mg (35%) of crystalline **28**, m.p. 57–59°. Elution with 200 ml of 25% ether in petroleum ether afforded 458 mg of crude **28** as an oil. Elution with 100 ml of ether gave 62 mg of recovered ketone **26**.

The 519 mg of **28**, m.p. 57–59°, was recrystallized from petroleum ether to afford 81 mg of 5-*acetoxy*-1,2-*dimethyltricyclo*[3.3.0.0^{2,7}]*octan*-6-*one* (**28**) as colorless crystals: m.p. 60–62°; IR (CCl_4) 5·68–5·75 (broad band) (ketone and ester C=O), 8·1 μ (broad band, acetate); NMR ($CDCl_3$) τ 7·32 (d, 1, J_{AX} = 3·0 Hz, C-7 H), 7·50 (d, 1, J_{AB} = 8·0 Hz, C-8-*endo*-proton) 7·7–8·1 (superimposed multiplets, 6, CH_3COO, C-3 and C-4-*exo*-H, C-8-*exo*-H; the acetate CH_3 and the C-8-*exo*-H are both centered at τ 7·97); 8·1–8·7 (C-3 and C-4-*endo*-H), 8·78 (s, 3, C-2 CH_3), 9·03 (s, 3, C-1 CH_3).



28

Anal Calcd for $C_{12}H_{16}O_3$: C, 69·39; H, 8·06. Found: C, 69·21; H, 7·74%.

5-*Hydroxy*-1,2-*dimethyltricyclo*[3.3.0.0^{2,7}]*octan*-6-*one* (**30**). A solution of 540 mg (0·003 mole) of ketoacetate **28** in 10 ml of 2M 95% methanolic potassium hydroxide solution was stored at 25–26° for 16 hr. After removal of the bulk of the methanol under reduced pressure, the residue was diluted with 10 ml of water and extracted with 150 ml of ether. The ethereal layer was washed with 4–10 ml portions of water and dried. Evaporation of solvent under reduced pressure afforded 209 mg (48%) of crystalline 5-hydroxy-1,2-dimethyltricyclo[3.3.0.0^{2,7}]octan-6-one (**30**) of 96% purity (analyzed by GLPC on column 1 at 150° and 60 ml/min helium flow). Recrystallization from petroleum ether afforded 22 mg of **30** as colorless crystals: m.p. 192–194°; IR (CCl_4) 2·92 (OH), 5·68 μ (C=O); NMR ($CDCl_3$) τ 6·40 (broad s, 1, OH), 7·38 (d, 1, J_{AX} = 3·0 Hz, C-7 H), 7·78 (q, 1, J_{AB} = 8·5 Hz, J_{AX} = 3·0 Hz, C-8 *exo*-H), 8·23 (d, J_{AB} = 8·5 Hz, C-8 *endo*-H), 7·9–8·7 (superimposed multiplets, C-3, C-4 protons), 8·80 (s, 3, C-2 CH_3), 9·01 (s, 3, C-1 CH_3).

Anal Calcd for $C_{10}H_{14}O_2$: C, 72·26; H, 8·49. Found: C, 71·92; H, 8·44%.

Irradiation of 4-*acetoxyisopiperitenone* (**26**)

B. *Methanol solvent.* A solution of 4·999 g (0·024 mole) of 4-acetoxyisopiperitenone (**26**) in 500 ml of absolute methanol was irradiated as above employing a Pyrex filter and 450 W Hanovia lamp for a period of 100 min. The methanol was removed under reduced pressure. Short-path distillation of the residual liquid afforded 4·003 g of colorless liquid, b.p. 119–124° (0·35–0·4 mm) consisting of ketoacetate **28** (19%; 15% yield) and 4-*carbomethoxymethyl*-1-*acetoxy*-2,4-*dimethylcyclohexene* (**29**) (81%; 65% yield). The per cent composition of each product was determined by GLPC on column 1 at 175° and 60 ml/min helium flow.

The ketoacetate **28** was isolated by preparative GLPC on the same column as colorless crystals, m.p. 57–59°. The NMR and IR spectra of this ketone were identical with those of the ketone isolated from the irradiation of **26** in cyclohexane, above.

The ester **29** was isolated by preparative GLPC on the same column as a colorless liquid: b.p. 119° (0·4 mm); IR (CCl_4) 5·75 (ester C=O), 8·2–8·4 μ (acetate); NMR ($CDCl_3$) τ 6·40 (s, 3, —$COOCH_3$), 7·6–8·6 (overlapping multiplets, methylene protons), 7·72 (s, —CH_2COOCH_3), 7·92 (s, CH_3COO—), 8·51 (s, CH_3—C=CH—), 8·94 (s, 3, CH_3C—CH_2COOCH_3).

Anal Calcd for $C_{13}H_{20}O_4$: C, 64·98; H, 8·39. Found: C, 64·85; H, 8·56%.

Preparation of 2-*bromo*-1,2-*endo*-*dimethyl*-*cis*-*bicyclo*[3.3.0]*octan*-6-*one* (**10**)

To a solution of 210 ml of methylene chloride saturated with anhydrous hydrogen bromide and maintained at 0–5° was added dropwise with stirring over a period of 15 min a solution of 340 mg (0·003 mole) of ketone **5** in 25 ml of methylene chloride. The mixture was stored at 25–26° for 16 hr and was washed with three 25 ml portions of sodium carbonate solution and 20 ml of saturated brine solution. Evaporation of methylene chloride afforded 482 mg of brown crystalline residue. The residue was dissolved in 5 ml of petroleum ether and decolorized with 10 mg of activated charcoal. Evaporation of solvent afforded 253 mg (49%) of crystalline ketone **10**. Recrystallization from petroleum ether afforded 27·9 mg of ketone

10 as colorless plates, m.p. 85–87°; IR (CH_2Cl_2) 5·72 μ (C=O); NMR ($CDCl_3$) τ 8·20 (s, 3, $C\underline{H}_3C(Br)$), 8·63 (s, 3, $C\underline{H}_3C$), 7·4–8·80 (overlapping multiplets, 9, methylene and methyne protons).

Anal Calcd for $C_{10}H_{15}BrO$: C, 51·95; H, 6·54. Found: C, 51·87; H, 6·42%.

The NMR spectrum of the crystalline residue obtained after removal of solvent from the mother liquors of the above recrystallization indicated the presence only of ketone **10** with traces of olefin (~5% olefin based on relative area of olefin peak at τ 4·76 and the methyl peak at τ 8·63). The crystalline residue was dissolved in 5 ml pyridine. The mixture was heated at reflux for 80 min, cooled to 25–27° and diluted with 150 ml of ether. The ethereal layer was washed with two 15-ml portions of water, 10 ml of 12N hydrochloric acid and four 15-ml portions of water. The ethereal layer was dried and the solvent removed under reduced pressure to afford 112 mg of crude olefin. Preparative GLPC first on column 2 at 125° and then on column 1 at 125° afforded 22 mg of *1,2-dimethylbicyclo*[3.3.0]*oct-2-en-6-one* (**54**) as a colorless liquid; IR (neat) 5·73 (C=O), 12·51 μ (trisubstituted olefin); NMR ($CDCl_3$) τ 4·76 (m, 1, $CH_3C=C\underline{H}$—), 8·38 (s, 3, $C\underline{H}_3C=CH$—), 7·4–8·3 overlapping multiplets, methylene and methyne protons), 8·80 (s, 3, CH_3C—).

Preparation of 3-*bromo*-5-*hydroxy*-1,2-endo-*dimethyl*-cis-*bicyclo*[3.3.0]*octan*-6-*one* (**31**).

A solution of 439 mg (0·003 mole) of ketone **30**, m.p. 192–194°, in 30 ml of methylene chloride was added dropwise over a 15 min period to a solution of methylene chloride saturated with anhydrous hydrogen bromide and maintained at 0–5°. The mixture was stored at room temperature for 16 hr. The reaction mixture was washed with 150 ml of 5% sodium carbonate solution, and three 25-ml portions of saturated brine solution and dried. Evaporation of solvent afforded a brown residue which was dissolved in benzene and decolorized with charcoal. Evaporation of benzene and recrystallization of the residual oil from benzene–petroleum ether afforded 124 mg (19%) of 2-bromo-5-hydroxy-1,2-*endo*-dimethyl-*cis*-bicyclo-[3.3.0]- octan-6-one (**31**) as colorless crystals: m.p. 136·0–137·5°; IR (CH_2Cl_2) 2·93 (OH), 5·72 μ (C=O); NMR τ 7·0–7·1 (broad, O$\underline{H}$), 7·8–8·4 (superimposed multiplets, methylene protons), 8·28 (s, 3, $C\underline{H}_3C(Br)$), 8·82 (s, 3, $C\underline{H}_3C$—).

Anal Calcd for $C_{10}H_{15}O_2Br$: C, 48·60; H, 6·07. Found: C, 48·55; H, 6·05%.

An NMR spectrum of the mother liquors from the above recrystallization indicated the presence of only the bromide **31**.

Reaction of 3,8-*cyclocamphor* (**7**) *with hydrogen bromide. Preparation of* 2-*bromo*-1,5-*dimethyl*-cis-*bicyclo*-[3.3.0]*octan*-6-*one* (**17**)

The procedure of Corey[12] was employed for treatment of 200 mg of 3,8-cyclocamphor[12] with hydrogen bromide. After work-up there was isolated 300 mg of crude bromide. Recrystallization of the crude product from petroleum ether afforded 47 mg of 2-bromo-1,5-dimethyl-*cis*-bicyclo[3.3.0]octan-6-one (**17**) as needles: m.p. 119–120° (Lit[12] m.p. 121·5–122·5°); IR (CCl_4) 1740 cm^{-1} (Lit[12] IR 1740 cm^{-1}); NMR ($CDCl_3$) τ 6·16 [apparent t, 1, J = 6·5 ± 0·5 Hz, (Br–C$\underline{H}$—)], 7·6–8·6 (overlapping multiplets, methylene protons), 8·88 (s, 3, $C\underline{H}_3$—), 8·97 (s, 3, $C\underline{H}_3$—).

Anal Calcd for $C_{10}H_{15}BrO$: C, 51·95; H, 6·54; Br, 34·60. Found: C, 51·95; H, 6·50; Br, 34·56%.

Preparation of seqcis (**32**) *and* seqtrans (**33**) 4-*carbomethoxymethyl*-2,4-*dimethylcyclohexanone*

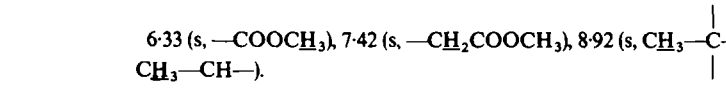
A solution of 3·007 g (0·015 mole) of the crude product from irradiation of 4-acetoxyisopiperitenone in methanol, above, in 70 ml of 2M potassium hydroxide in water–methanol (1:9) solution was stored at 26–27° for a period of 16 hr. The bulk of the methanol was removed under reduced pressure. The resulting residue was diluted with 25 ml of water and extracted with 125 ml of ether.

The organic layer was washed with four 25-ml portions of water and dried. Evaporation of ether afforded 400 mg (16% yield based on starting 4-acetoxyisopiperitenone) of the ketoalcohol **30** of 93% purity as analyzed on column 1 at 145° and 60 ml/min helium flow. Purification by GLPC afforded pure **30**, m.p. 192–194°. The IR spectrum of this material was identical with that of ketone **30** isolated by hydrolysis of pure ketoacetate **28**, above.

The water layer was cooled to 0–5° and was acidified with 7·5 ml of conc hydrochloric acid. The precipitated acid product was extracted with two 75-ml portions of ether and the combined ethereal layer

was washed with four 25-ml portions of water and dried. Evaporation of ether afforded 2·133 g of crude acid. A 1·018 g sample of the crude acid was dissolved in 50 ml of ether and treated with 100 ml of 2–3% diazomethane solution. The mixture was stored at 0–5° for 60 min and the excess diazomethane was destroyed by addition of 10 ml of 1N hydrochloric acid solution. The ethereal layer was washed with water, 10 ml of sat sodium bicarbonate and water and was dried. Evaporation of ether afforded 951 mg of crude ester. Distillation of the crude ketoester afforded 580 mg (45% yield based on 4-acetoxyisopiperitenone) of liquid, b.p. 128–134° (1·25 mm), consisting of the two epimeric ketoesters **32** and **33** in a ratio of approximately 1:1. The two ketones were partially resolved on column 2 at 175° and 65 ml/min helium flow. Although the isomers underwent partial epimerization during collection by preparative GLPC on the same column, above, satisfactory analytical data was obtained on the enriched mixture of each.

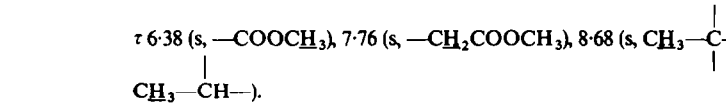
The isomer of shorter retention time (29·3 min) tentatively assigned the structure **32**, displayed the following spectral properties: IR (CCl_4) 5·74 μ (ester C=O), 5·83 μ (cyclohexanone C=O); NMR ($CDCl_3$)



6·33 (s, —COOC$\underline{H}_3$), 7·42 (s, —C$\underline{H}_2$COOCH$_3$), 8·92 (s, C$\underline{H}_3$—C(CH$_3$)—CH$_2$—COOCH$_3$), 9·02 (d, J = 6·5 Hz, C$\underline{H}_3$—CH—).

Anal Calcd for $C_{11}H_{18}O_3$: C, 66·64; H, 9·15. Found: C, 66·35; H, 9·21.

The isomer of longer retention time (34·7 min), tentatively assigned the structure **33**, displayed the following spectral properties: IR (CCl_4) 5·74 μ (ester C=O); 5·83 μ (cyclohexanone C=O); NMR ($CDCl_3$)



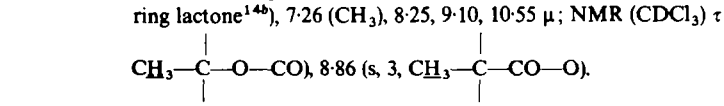
τ 6·38 (s, —COOC$\underline{H}_3$), 7·76 (s, —C$\underline{H}_2$COOCH$_3$), 8·68 (s, C$\underline{H}_3$—C(CH$_3$)—CH$_2$—COOCH$_3$), 9·02 (d, J = 6·5 Hz, C$\underline{H}_3$—CH—).

Anal Calcd for $C_{11}H_{18}O_3$: C, 66·64; H, 9·15. Found: C, 66·63; H, 9·25%.

Diels–Alder condensation of isoprene and methacrylic acid. Preparation of 1,4-*dimethylcyclohexene*-4-*carboxylic acid* (**20a**), 1,5-*dimethyl*-6-*oxa*-7-*oxobicyclo*[3.2.1]*octane* (**18**), *and* 1,4-*dimethyl*-2-*oxa*-3-*oxobicyclo*[2.2.2]*octane* (**19**)

A variation of the procedure of Nazarov[15] was employed for the condensation of isoprene and methacrylic acid. A mixture of 20·0 g (0·29 mole) of isoprene and 37·9 g (0·44 mole) of methacrylic acid was heated at 200–210° under a back pressure of 1350 psi of nitrogen for 16 hr in a 500 ml glass lined autoclave. The cooled reaction mixture was extracted with 500 ml of ether. The ether soluble portion was extracted with three 100-ml portions of 10% sodium hydroxide solution and the layers were partitioned.

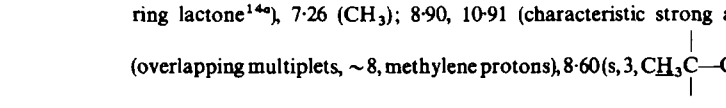
The neutral ethereal layer was washed with four 100-ml portions of water and dried. Evaporation of ether under reduced pressure afforded 16·62 g of residual liquid. A 1·275 g portion of the residue was distilled from a modified Hickman still to afford 1·057 g of distillate b.p. 130–134° (4·0–4·25 mm) consisting of lactone **18** (49%; 17% yield; rel ret time, 12·0 min) and lactone **19** (51%; 17% yield; rel ret time, 16·3 min) as analyzed by GLPC on column 2 at 175° and 60 ml/min helium flow. The remaining 15·35 g of the neutral fraction was distilled from an 18 in. spinning band column to afford 0·489 g of forerun, b.p. 126–138°, 5·267 g (13%) of lactone **18**, b.p. 76–82° (2·50 mm), m.p. 49–52°, 1·184 g of a mixture of **18** and **19**, b.p. 82–93° (2·50 mm), and 3·599 g (8·5%) of lactone **19**, b.p. 93° (2·50 mm), m.p. 48–50°. The residue from the distillation was recrystallized from petroleum ether (b.p. 30–60°) to afford an additional 116 mg of lactone **19** as colorless prisms (total isolated yield of **19** = 9%): m.p. 46–48°; IR (CCl_4) 5·72 μ (C=O, 6-membered ring lactone[14b]), 7·26 (CH_3), 8·25, 9·10, 10·55 μ; NMR ($CDCl_3$) τ 8·29 (s, 8, methylene protons), 8·66 (s, 3,



C$\underline{H}_3$—C(CH$_3$)—O—CO), 8·86 (s, 3, C$\underline{H}_3$—C(CH$_3$)—CO—O).

Anal Calcd for $C_9H_{14}O_2$: C, 70·10; H, 9·15. Found: C, 70·07; H, 9·11%.

A 520 mg sample of the lactone **18**, b.p. 76–82 (2·50 mm), was recrystallized from petroleum ether (b.p. 30–60°) to afford 118 mg of pure lactone **18** as colorless plates: m.p. 49–50°; IR (CCl_4) 5·65 μ (C=O, 5-membered ring lactone[14a]), 7·26 (CH_3); 8·90, 10·91 (characteristic strong absorptions); NMR ($CDCl_3$) τ 8·0–8·7



(overlapping multiplets, ~8, methylene protons), 8·60 (s, 3, C$\underline{H}_3$C(CH$_3$)—O—CO), 8·82 (s, ~3, C$\underline{H}_3$—C(CH$_3$)—CO—O).

Anal Calcd for $C_9H_{14}O_2$: C, 70·10; H, 9·15. Found: C, 70·22; H, 9·07%.

The sodium hydroxide soluble layer from the extraction above was cooled to 0–5° and acidified with

70 ml of conc hydrochloric acid. The precipitated oil was extracted with two 400-ml portions of ether, the combined ethereal layer was washed with four 100-ml portions of water and dried. Evaporation of ether under reduced pressure afforded 21·37 g of a viscous liquid. Short-path distillation of the liquid afforded 8·71 g (19%) of acid product, primarily *1,4-dimethylcyclohexene-4-carboxylic acid* (**20a**), as a colorless liquid: b.p. 103–106° (1·50 mm). The above acid was shown to consist of 88% **20a** and 6% **21a** by GLPC analysis of the corresponding ester derivative, prepared below. Recrystallization of a 575 mg sample of the acid afforded 181 mg of **20a** as colorless crystals: m.p. 66·5–68·0° (Lit[15b] m.p. 62–63°]; IR (coconitrile mull) 3–4 μ (broad, carboxyl OH), 5·9 (C=O); NMR ($CDCl_3$) τ 4·70 (m, 1, CH_3—C=C<u>H</u>—), 7·50 (broad d, J = 15 Hz, 1, allyl H), 7·8–8·6 (overlapping multiplets, methylene <u>H</u>), 8·36 (m, C<u>H</u>$_3$C=CH—), 8·88 (s, 3, C<u>H</u>$_3$C(—)—COOH).

Anal Calcd for $C_9H_{14}O_2$: C, 70·10; H, 9·15. Found: C, 70·40; H, 9·04%.

A 500 mg sample of the acid **20a**, b.p. 103–106° (1·5 mm), was dissolved in 50 ml of ether and treated with 50 ml of a 2–3% solution of diazomethane in ether. The reaction mixture was stored at 0–5° for 35 min. Excess diazomethane was destroyed by dropwise addition of 2·5 ml of 10% hydrochloric acid. The water layer was decanted and the ethereal layer was washed with two 10 ml portions of water, 5 ml of saturated sodium bicarbonate, three 10 ml portions of water and dried. Evaporation of the ethereal layer and short-path distillation of the residual liquid afforded 455 mg (77%) of colorless liquid, b.p. 110° (6·5 mm) consisting of methyl 1,4-dimethylcyclohexene-4-carboxylate (**20b**) (88%) and 1,5-dimethylcyclohexene-4-carboxylate (**21b**) (6%) as analyzed on a 150 ft capillary column coated with polyphenylether-OS138 at a flow rate of 60 ml/min and programmed temperature from 8°–100°.* The 88% pure ester **20b** showed the following spectral properties: IR(neat) 5·75 μ (C=O stretching) 8·0–8·7 (C=O bending), 9·0; NMR ($CDCl_3$) τ 4·74 (m, 1, —C=C<u>H</u>—), 6·41 (s, 3, —COOC<u>H</u>$_3$), 7·51 (broad d, J = 15 Hz. 1, equatorial allyl methylene proton), 8–8·7 (overlapping multiplets, methylene protons), 8·41 (m, 3, C<u>H</u>$_3$—C=C—), 8·85 (s, 3, C<u>H</u>$_3$—C(—)—COOCH$_3$).

Anal Calcd for $C_{10}H_{16}O_2$: C, 71·58; H, 9·72. Found: C, 71·39; H, 9·59%.

Preparation of 1,4-*dimethyl*-2-*oxa*-3-*oxobicyclo*[2.2.2]*octane* (**19**) *from* 1,4-*dimethylcyclohexene*-4-*carboxylic acid* (**20a**)

To a solution of 506 mg (0·003 mole) of the acid **20a**, b.p. 103–106° (1·5 mm), above, in 15 ml of 1,2-dichloroethane was added 4 ml of freshly distilled boron trifluoride etherate and this mixture was heated at reflux under a nitrogen atmosphere for a period of 90 min. The mixture was cooled to 26–27° and was poured cautiously into 10 ml of water. The product was extracted with 90 ml of ether and the ethereal layer was washed with 3–5 ml portions of saturated sodium bicarbonate, three 10 ml portions of water, and dried. Evaporation of ether under reduced pressure and distillation of the residual solid afforded 292 mg (58%) of liquid, b.p. 128° (4·75 mm), consisting of lactone **18** (6%) and lactone **19** (94%) as analyzed by GLPC on column 1 at 150° and 60 ml/min helium flow. Recrystallization of the solidified distillate from petroleum ether provided colorless camphoraceous prisms, m.p. 46–47·5°. The m.p. of a mixture of the above lactone and a sample of the lactone **19**, m.p. 46–48°, prepared from the condensation of isoprene and methacrylic acid, above, showed no depression: m.p. 46–48°.

Diels–Alder condensation of isoprene and methyl methacrylate. Preparation of the mixture of acids **20a** *and* **21a**

The procedure of Nazarov *et al.*[15] was followed for the condensation of isoprene and methyl methacrylate. A mixture of 20·0 g (0·294 mole) of isoprene and 44·1 g (0·441 mole) of methyl methacrylate was heated

* The authors are indebted to Dr. L. R. Chapman and Mr. D. E. Stitzel for the capillary chromatographic analysis.

at 200–210° in a glass-lined autoclave under a back pressure of 1350 psi nitrogen for a period of 16 hr. Distillation of the crude reaction product, isolated by ether extraction, afforded 16·67 g (34%) of a mixture of **20a** and **21a**, b.p. 67–70° (4·25–4·50 mm) [Lit[15a] b.p. 92–94° (12 mm)]. Analysis of the ester mixture by GLPC on column 2 at 110° and 60 ml/min helium flow indicated the presence of ~50% ester **20b** and 30% ester **21b**. A solution of 16·339 g of the above ester mixture in 500 ml of 10% aqueous methanolic potassium hydroxide solution was refluxed under a nitrogen atmosphere for a period of 2 hr. The bulk of the methanol was removed under reduced pressure and the residual semi-solid was dissolved in 200 ml of water and washed with 500 ml of ether. The ethereal layer was extracted with three 100-ml portions of water and the cooled water layer (0–5°) was acidified by dropwise addition of 25 ml of conc hydrochloric acid. The precipitated oil was extracted with two 350-ml portions of ether and the ethereal layer was washed with two 50-ml portions of water and dried. Evaporation of ether under reduced pressure afforded 13·754 g (92%) of the crude mixture of acids **20a** and **21a** as an oil: IR 3–4 μ (carboxyl OH), 5·9 (C=O). The crude acid was used for the Arndt–Eistert homologation step without further purification.

Arndt–Eistert homologation of acid mixture **20a** *and* **21a**. *Preparation of 5-carbomethoxymethyl-1,5-dimethylcyclohexene* (**6**) *and of 4-carbomethoxymethyl-1,4-dimethylcyclohexene* (**22**)

To a stirred solution of 6·000 g (0·111 mole) of sodium methoxide in 400 ml of absolute methanol was added dropwise under a nitrogen atmosphere 13·754 g (0·082 mole) of the crude mixture of acids **20a** and **21a**, above, in 400 ml of absolute methanol over a 60 min period. This mixture was stirred at 26–27° for 90 min and the bulk of the methanol was removed under reduced pressure. Final traces of methanol were removed under high vacuum (16 hr) to yield 15·9 g of the sodium salts of **20a** and **21a**: IR (coconitrile mull) absence of carboxyl OH and C=O), presence of bonds at 6·45 and 7·06 μ. The sodium salts were suspended in 700 ml of petroleum ether; 2 ml of pyridine was added; and 22·60 g (0·178 mole) of oxalyl chloride was added dropwise under a nitrogen atmosphere over a 45 min period. The mixture was stirred at 26–27° for 1 hr 45 min, filtered and the petroleum ether and oxalyl chloride were removed under reduced pressure. A solution of the crude acid chloride, IR 5·56 μ, in 350 ml of anhydrous ether was added dropwise under a nitrogen atmosphere to a solution of ~28 g of diazomethane in 1000 ml of ether (0–5°) over a 90 min period and this mixture was stored at 0–5° for 16 hr. The excess diazomethane and ether were removed under reduced pressure to afford 12·9 g of diazoketone, IR (neat) 3·22 μ ($COCHN_2$), 4·73 (C—N), 6·15 (C=O). To a solution of the crude diazoketone in 500 ml of absolute methanol maintained at 41–56° was added 12·0 g of silver oxide suspended in 100 ml of methanol over a 60 min period. The mixture was heated at reflux for 2 hr, cooled to 26–27°, filtered and the methanol removed under reduced pressure. The residue was dissolved in 500 ml of ether and the ethereal layer was washed with 50 ml of water, 25 ml of 10% hydrochloric acid, two 100-ml portions of water, 20 ml of saturated sodium bicarbonate, two 100-ml portions of water and dried. Evaporation of solvent and fractional distillation afforded 0·3983 g of forerun, b.p. 42–49° (4·5 mm), 5·66 g (38%) of a mixture of the esters **6** (34%) and **22** (66%), b.p. 49–50° (4·5 mm) and ~3·5 g of residual material. The two esters were separated and collected by preparative GLPC on column 2 at 100° and 60 ml/min helium flow.

The GLPC relative retention time (64·0 min) and the IR and NMR spectra of the ester **6**, collected by GLPC from this run, were identical in all major respects with that produced from the irradiation of isopiperitenone, above.

The ester **22** was collected as a colorless liquid: relative retention time 72 min; IR 5·74 μ (ester C=O); NMR ($CDCl_3$) τ 4·76 (m, 1, $CH_3C(=)CH$—), 6·43 (s, 3, —$COOCH_3$), 7·80 (s, 2, —CH_2COO—), 7·9–8·8 (overlapping multiplets, methylene protons), 8·38 (broad s, $CH_3C(=)CH$—), 9·01 (s, 3, CH_3—$C(-CH_2COO$—$)$—).

Anal Calcd for $C_{11}H_{18}O_2$: C, 72·49; H, 9·96. Found: C, 71·96; H, 9·75%.

The GLPC retention time and the IR and NMR spectrum of the above ester **22** and the ester **22** prepared from the pure acid **20a**, below, were identical in all major respects.

Arndt–Eistert homologation of acid **20a**. *Preparation of 4-carbomethoxymethyl-1,4-dimethylcyclohexene* (**22**)

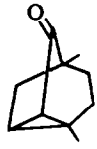
The procedure was essentially the same as that employed above for the mixed acids. From 2·00 g of the acid **20a**, b.p. 103–106° (1·5 mm) and 2·00 g of sodium methoxide there was isolated 2·39 g of crude sodium salt. Treatment of the salt with 3·30 g of oxalyl chloride afforded 2·25 g of crude acid chloride.

Treatment of the acid chloride with 200 ml of a 2–3% solution of ethereal diazomethane gave 1·800 g of crude diazoketone. The diazoketone on treatment with 1·503 g of silver oxide in 10 ml of methanol for a period of 2·5 hr afforded 1·633 g of crude ester **22**. Short-path distillation afforded 896 mg (38%) of liquid, b.p. 125–139° (5·75 mm) consisting of three peaks as analyzed by GLPC on column 2 at 125° and 60 ml/min helium flow. The three peaks were collected by preparative GLPC on column 2 above.

The substance of the first peak (11%) rel ret time, 9·3 min, was isolated as a colorless liquid. The IR spectrum indicated a mixture of a four-membered ring ketone [IR (CCl_4) 5·64 μ] and an ester (5·75 μ).

The second peak consisted of pure ester **22** (70%), the rel ret time (11·3 min) and the NMR and IR spectra of which were identical with the ester **22** prepared above.

The third peak, rel ret time 12·0 min, was isolated as a colorless liquid and displayed the following spectral characteristics consistent with the structure 2,5-dimethyltricyclo[3.2.1.$0^{2,7}$]octan-8-one (**55**): IR (CCl_4) 5·78 μ (~1736 cm^{-1}) (C=O conj to cyclopropane ring [compare to 1735 cm^{-1} for tricyclo-[3.2.1.$0^{2,7}$]- octan-8-one;[28] NMR ($CDCl_3$) τ 8·0–8·6 (overlapping multiplets), 9·94 and 9·12 (singlets, 3 each, $C\underline{H}_3$—). No further characterization of the cyclopropyl ketone **55** was made.



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Irradiation of isopiperitenone in the presence of an internal standard

A. *In cyclohexane.* A solution of 0·3098 g (2·06 × 10^{-3} mole) isopiperitenone and 0·3086 g tetradecane (internal standard) in 50 ml cyclohexane was irradiated with a 3500 Å light source through Pyrex. GLPC analysis on an SE-30 column at 120°C provided the results shown in Table 1.

TABLE 1

Time (min)	Tricyclic ketone* Moles × 10^3
0	0
15	0·075
45	0·227
75	0·40
105	0·58
135	0·64
165	0·82
195	0·89
225	1·03
225	1·07
285	1·11
315	1·18 (58%)

* Relative areas were calculated by triangulation and by the product of the retention times (relative to air) and the peak heights.

A plot of these data revealed a nearly straight line over about 65% reaction. From the slope of this curve the initial rate of appearance of tricyclic ketone was determined to be 0·92 × 10^{-7} moles/sec.

B. *In methanol.* A solution of 0·3082 g (2·06 × 10^{-3} mole) of isopiperitenone and 0·3089 g of tetradecane in 50 ml methanol was irradiated as above with the results as given in Table 2.

TABLE 2

Time (min)	Moles × 10^{-3} Tricyclic ketone
0	–
15	0·09
45	0·25
75	0·39
105	0·57
135	0·63
165	0·69
195	0·71

A plot of these data revealed a straight line over about 65% reaction. The rate of appearance of tricyclic ketone was observed to be 0·88 × 10^{-7} moles/sec.

While these data are qualitative, they do show that the initial rates of formation of tricyclic ketone **5** in the two solvents are very nearly equal.

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