followed by vacuum distillation of the crude enone gave 0.84 g (68% overall yield) of pure 2,6-dimethyl-2-cyclohexen-1-one (**12**), bp 72–74 °C (13 mm). The IR, NMR, and mass spectral properties of **12** are in agreement for those reported in ref 33.

2,6,6-Trimethyl-2-cyclohexen-1-one (10) from the Alkylation of 12. The alkylation of **12** was patterned after the procedure given in ref 34. A solution containing 4.5 mL (32.0 mmol) of diisopropylamine, 0.18 mL of HMPA, and 50 mL of dry THF was cooled to −20 °C (dry ice/acetone) and treated with 19.5 mL (31.0 mmol) of 1.6 M *n*-butyllithium. The resulting solution was cooled to -78 °C and treated with 3.65 g (29.0 mmol) of neat **12**, and stirring was continued for 20 min. At this point, 5.6 mL (89.0 mmol) of methyl iodide was slowly added (ca. 5 min), and the resulting mixture stirred for 1 h at -78 °C. The mixture was then warmed to room temperature, the THF was removed in vacuo, and then the residue was partitioned between 100 mL of diethyl ether and 100 mL of water. The layers were separated, and the aqueous layer was extracted with diethyl ether (2 × 30 mL). The combined etheral layers were dried and filtered, and the solvent was removed in vacuo to give crude **10**. Vacuum distillation afforded 3.41 g (85%) of pure 2,6,6-trimethyl-2-cyclohexen-1-one (**10**), bp 63–67 °C (12 mm) [lit.[35] bp 60–65 °C (10 mm)]. The spectral properties (IR, NMR, MS) are in accord with those reported in ref 35 and are identical with those of **10** prepared from the enol silyl ether **9** (see above).

2,6,6-Trimethyl-1-(trimethylsiloxy)-1,3-cyclohexadiene (13). Compund **13** was prepared by the method cited above for the preparation of **9**. Thus, from 37.0 mmol of diisopropylamine, 30 mL of DME, 37.0 mmol of *n*-butyllithium, 30.8 mmol of **10** in 10 mL of DME, and 77.0 mmol of Me_3SiCl was obtained, after vacuum distillation, 4.66 g (72%) of pure 2,6,6-trimethyl-1-(trimethylsiloxy)-1,3-cyclohexadiene (**13**): bp 77–79 °C (5 mm); IR (neat) 3035, 1670 (sh), 1658 cm^{-1}; ^1H NMR (CCl_4) δ 0.18 (s, 9 H), 0.87 (s, 6 H), 1.52 (s, 3 H), 1.83–2.10 (m, 2 H), 5.00–5.76 (m, 2 H); MS, *m/z* (relative intensity) 210 (M^+, 100), 195 (58), 179 (5), metastables (m*) 181.1, 164.3. Anal. Calcd for $C_{12}H_{22}OSi$: C, 68.50; H, 10.54. Found: C, 68.54; H, 10.51.

2-Acetoxy-2,6,6-trimethyl-3-cyclohexen-1-one (15). Compound **15** was prepared by the method outlined above for the preparation of **5**. Thus, from 10.0 mmol of **13**, 30 mL of dry hexane, 10.0 mmol of MCPBA, 75 mL of methylene chloride, and 60 mmol of triethylammonium fluoride was obtained crude hydroxy ketone **14**. Compound **14** was then acetylated with 21.0 mmol of acetic anhydride, 15.0 mmol of triethylamine, and 0.4 mmol of DMAP to give, after vacuum distillation, 1.08 g (55% from **13**) of pure 2-acetoxy-2,6,6-trimethyl-3-cyclohexen-1-one (**15**): bp 70 °C (5 mm, molecular distillation); IR (neat) 3040, 1725, 1715 cm^{-1}; ^1H NMR (CCl_4) δ 1.03 (s, 3 H), 1.07 (s, 3 H), 1.30 (s, 3 H), 2.38–2.84 (m, 2 H), 5.29–6.12 (complex m, 2 H); MS, *m/z* (relative intensity) 196 (M^+, 8), 153 (33), 126 (47), 98 (14), 93 (15), 84 (59), 71 (15), 69 (17), 55 (11), 43 (100), 41 (25). Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 67.34; H, 8.18.

Hydroxy Lactone 16. The hydroxy lactone **16** was prepared by the method cited in ref 23. A solution containing 0.85 mL (6 mmol) of diisopropylamine in 50 mL of dry diethyl ether was cooled to -20 °C (dry ice/acetone) and treated with stirring with 3.5 mL (5.5 mmol) of 1.55 M *n*-butyllithium. After 20 min of stirring, the solution was cooled to -78 °C (dry ice/acetone), and 0.98 g (5.0 mmol) of **15** was added. After 10 min, the reaction mixture was quenched with a solution containing 10 mL of glacial acetic acid in 40 mL of water. The mixture was transferred to a separatory funnel and extracted with chloroform (3 × 30 mL). The combined organic extracts were extracted with saturated $NaHCO_3$ (5 × 30 mL), dried, and filtered, and the solvent was removed from the filtrate in vacuo to afford a residue that was crystallized from diethyl ether/hexane to give 0.61 g (62%) of pure hydroxy lactone **16**: mp 145.5–147 °C (lit.[12] mp 140–142 °C); IR (Nujol) 3440, 1765, 1745 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.05 (s, 6 H), 1.52 (s, 3 H), 2.07–2.20 (m, 3 H), 2.39 (d, 1 H, J = 18 Hz), 2.90 (d, 1 H, J = 18 Hz), 2.68 (br s, 2 H); ^{13}C NMR ($CDCl_3$) 174.84, 130.27, 126.93, 87.90, 80.87, 40.82, 39.15, 36.53, 25.27, 22.53, 20.61 ppm; MS, *m/z* (relative intensity) 196 (M^+, 64), 171 (12), 114 (20), 113 (99), 112 (24), 87 (43), 86 (31), 85 (100), metastables (m*) 120.5, 65.5, 64.5, 44.1, 36.6. Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 67.10; H, 8.17. The spectral properties of **16** were identical with those of authentic **16** prepared by the method of Demole and Enggist.[12]

Actinidiolide (3). The dehydration of **16** was carried out according to the procedure given in ref 12. Thus, 0.3 mmol of **16**, 0.8 mmol of thionyl chloride (freshly distilled), and 1 mL of dry pyridine gave, after silica gel chromatography, an 80% yield of pure actinidiolide (**3**), mp 37–38.5 °C (lit.[18] mp 38–39 °C). The IR and NMR properties of **3** agree with those reported in ref 12 and 18: MS, *m/z* (relative intensity) 178 (M^+, 40) 163 (70), 150 (52), 135 (100), 111 (22), 107 (24), metastables (m*) 126.4, 121.5.

Acknowledgment. We thank the Research council of the University of Idaho and acknowledge the donors of the Petroleum Research Fund, administered by the American Chemical Society, for the support of this work.

Registry No. **1**, 19432-07-6; **2**, 15356-74-8; **3**, 35035-19-9; **5**, 16797-54-9; **9**, 83999-44-4; **9** (bromo ketone), 2816-63-9; **10**, 20013-73-4; **11**, 63547-53-5; **11** (bromo ketone), 55234-03-2; **12**, 40790-56-5; **13**, 83999-45-5; **14**, 83999-46-6; **15**, 83999-47-7; **16**, 83999-48-8; 2,6-dimethylcyclohexanone, 2816-57-1; 2,2,6-trimethylcyclohexanone, 2408-37-9; chlorotrimethylsilane, 75-77-4.

(33) Trost, B. M.; Salzmann, T. N.; Hiroi, K. *J. Am. Chem. Soc.* **1976**, *98*, 4887.
(34) Stork, G.; Danheiser, R. L. *J. Org. Chem.* **1973**, *38*, 1775.
(35) Oppolzer, W.; Sarkar, T.; Mahalanabis, K. K. *Helv. Chim. Acta* **1976**, *59*, 2012.

Metal-Catalyzed Organic Photoreactions. Bond-Cleavage Selectivity and Synthetic Application of the Iron(III) Chloride Catalyzed Photooxidation of Cyclic Olefins[1]

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Photooxidation of olefins in pyridine in the presence of iron(III) chloride produced either α-chloro ketones (type A), *gem*-dichloro ketones (type B), or α,ω-dichloro ketones (type C), depending upon the substitution pattern of the substrate olefin. The synthetic utility of the type B reaction was demonstrated by the synthesis of some natural products. The synthesis of optically active solanone from D-*p*-menthene confirmed the D configuration of the natural product.

We reported in our previous paper that iron(III) chloride exhibited a characteristic effect on the photooxidation of olefins in pyridine and induced production of either α-chloro ketone or dichloro ketone as the final product,

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Scheme I

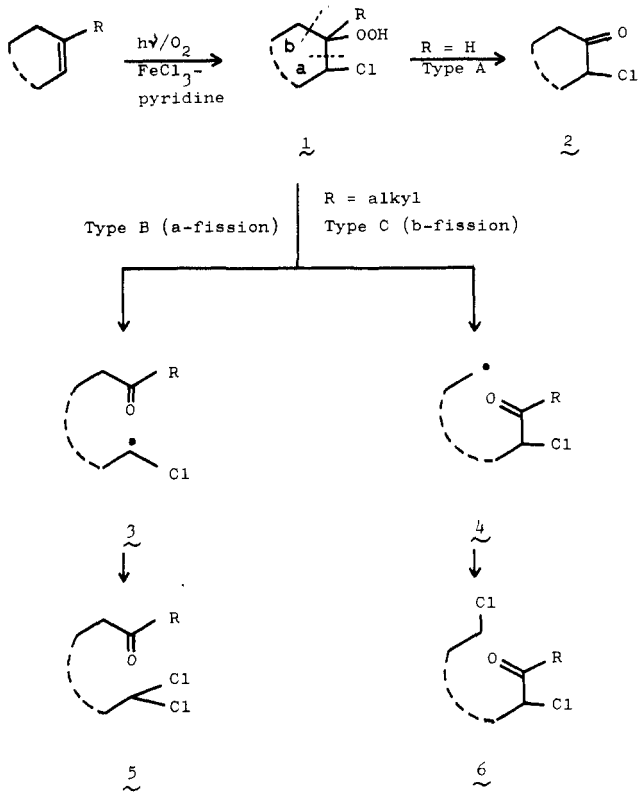
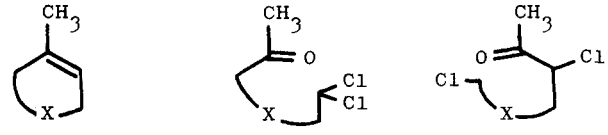


Table I. Photooxidation of 1-Alkylcycloalkenes



starting olefin	X	product yield, % 8	9
7a	CH_2	45	8
7b	$(CH_2)_2$	47	7
7c	CH_2-$CH(i\text{-}Pr)$[a]	26	12
7d	$(CH_2)_3$	6	0
7e	$(CH_2)_5$	35	33

[a] D-(+)-*p*-Menthene. Compound 10 was the main product (43%).

depending upon the substitution pattern of the substrate olefin.[2] As typical examples, cyclohexene gave 2-chlorocyclohexanone, while 1-methylcyclohexene (**7b**) gave a *gem*-dichloro ketone **8b** as a major product (47%), accompanied by a small amount of an α-chloro ketone **9b** (7%). We have called the reaction producing the α-chloro ketones type A and the reaction producing the dichloro ketones type B. It has been assumed, and in some cases confirmed, that a β-chloro hydroperoxide, **1**, is the primary product of the photooxidation.[2] The hydroperoxide from a mono- or disubstituted olefin is secondary (R = H) and undergoes dehydration to produce the α-chloro ketone **2** (Scheme I), while the hydroperoxide from tri- or tetrasubstituted olefin is tertiary (R = alkyl) and undergoes C–C bond cleavage either at the a or b position to produce the dichloro ketone **5** or **6**, respectively, after trapping another chlorine atom. We thought that the bond cleavage at the a position would be more facile than the alternative bond cleavage at the b position because the bond cleavage at the a position produces a radical **3** in which the radical center is stabilized by the neighboring chlorine atom. However, it was found, as shown in Table I, that the trend is not necessarily valid for some compounds, indicating that the chlorine atom is not effective in inducing the selectivity for the bond cleavage. In view of the fact that the bond cleavage at the b position occurred considerably, at least in some cases, we would like now to amend the classification as shown in Scheme I: a type A reaction involves no C–C bond cleavage as in case of cyclohexene to produce 2-chlorocyclohexanone; a type B reaction involves bond cleavage at the double bond (a fission) to produce a *gem*-dichloro ketone **5**; type C reaction involves bond cleavage at the position adjacent to the double bond (b fission) to produce an α,ω-dichloro ketone **6**.

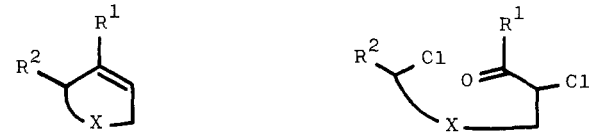
Although both the selectivity in the direction of the bond cleavage and the yield are not always satisfactory with some monosubstituted cyclic olefins (Table I), they were found to be improved remarkably by introducing an extra alkyl group to an appropriate position of the cycloalkenes. As shown in Tables II and III, the introduction of an alkyl group (R^2) to the C-2 position of the cycloalkene promoted the type B reaction, producing **12**, while the introduction of the alkyl group to the C-ω position promoted the type C reaction, producing **14**. The selectivity is quite high, and

Table II. Photooxidation of 1,2-Dialkylcycloalkenes

starting olefin[d]	X	R^2	yield of **12**, %
11a	$(CH_2)_2$	CH_3	86
11b	$CH(CH_3)CH_2$[a]	C_2H_5	18,[b] 11[c]
11c	$(CH_2)_3$	CH_3	65
11d	$(CH_2)_5$	CH_3	60

[a] 1-Ethyl-2,4-dimethylcyclohexene. [b] 4-Methyl-7,7-dichlorononan-2-one. [c] 6-Methyl-8,8-dichlorononan-3-one. [d] $R^1 = CH_3$ throughout.

Table III. Photooxidation of 1,ω-Dialkylcycloalkenes



starting olefin[b]	X	R^1	yield of **14**, %
13a	$(CH_2)_2$	CH_3	64
13b	$(CH_2)_2$	C_2H_5	64
13c	CH_2-$CH(CH_3)$[a]	C_2H_5	31
13d	$(CH_2)_3$	CH_3	77
13e	$(CH_2)_4$	C_2H_5	72
13f	$(CH_2)_5$	CH_3	65

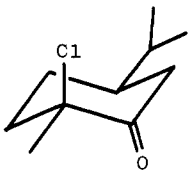
[a] 1-Ethyl-*cis*-4,6-dimethylcyclohexene. Compound 15 was the main product (33%). [b] $R^2 = CH_3$ in all cases.

(1) Preliminary report: T. Sato, K. Maemoto, and A. Kohda, *J. Chem. Soc., Chem. Commun.*, 951, 1116 (1981).
(2) A. Kohda, K. Ueda, and T. Sato, *J. Org. Chem.*, **46**, 509 (1981).

none of the products from the alternative type of the reaction were identified. It is evident that the alkyl group is more effective than the chlorine atom in directing the bond cleavage in the hydroperoxide intermediate.

Both the type B and type C reactions have potential as synthetic methods because they afford a compound carrying an alkyl ketone or α-chloro ketone function on one end and a *gem*-dichloro or monochloro function on the other end of the chain. A further merit is that we can prepare a wide variety of compounds by selecting the ring size and alkyl substituents of the starting cycloalkenes. As a demonstration for the preparative utility of the type B reaction, we describe the syntheses of brevicomin, muscone, and D-solanone.

Brevicomin, an attractant pheromone produced by the western pine beetle, *Dendroctonus brevicomis*, has been shown to be *exo*-7-ethyl-5-methyl-6,8-dioxabicyclo[3.2.1]-octane (**16a**).[3] Among several synthetic methods for this



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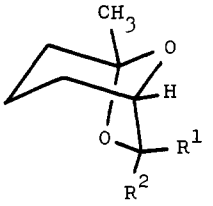
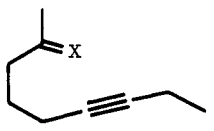


16

a: $R^1 = C_2H_5$, $R^2 = H$

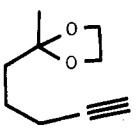
b: $R^1 = H$, $R^1 = C_2H_5$



17

a: X = O

b: X = 

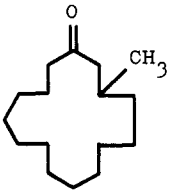


18

pheromone, the routes reported by Kociensky[4] and Coke[5] utilize an acetylenic compound **17a** or **17b** as the key intermediate, and these methods are characteristic in that they accomplish the stereoselective syntheses of *exo*- and *endo*-brevicomin. We expected that the *gem*-dichloro ketone **8b**, which is the type B reaction product from 1-methylcyclohexene in 47% yield, might be a suitable starting material for the synthesis of the intermediate **17b**.

The dichloro ketone **8b**, after the protection of the carbonyl group with ethylene glycol, was treated with sodium amide in liquid ammonia to produce an ethynyl compound **18**. Ethylation of **18** with butyllithium and ethyl iodide afforded product whose spectroscopic data were identical with those reported for **17b**. The stereoselective synthesis of *exo*- or *endo*-brevicomin from **17b** has been accomplished by Kociensky in 42% and 77% overall yields, respectively. The present four-step synthesis of **17b** from 1-methylcyclohexene (overall yield of 38%) may be contrasted with the five-step synthesis by Kociensky from 3-methyl-4-(ethoxycarbonyl)-2-cyclohexen-1-one (Hagemann's ester), involving the thermal fragmentation of its epoxy ketone tosylhydrazone (overall yield of 53%), or the three-step synthesis of **17a** by Coke from cyclohexane-1,3-dione, involving a fragmentation by methyllithium (overall yield of 12%).

As described above, the acyclic acetylenic ketones could be obtained by the ring cleavage of cyclic α,β-enone or 1,3-diketone systems, as well as by the present photooxidation of cycloalkenes. However, the cycloalkenes are much more accessible than the cyclic compounds having any other functionality, particularly with larger ring system. As a demonstration for this point, we chose muscone (**19**) as our next target molecule. Among many methods



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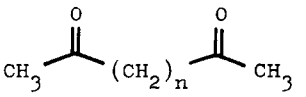
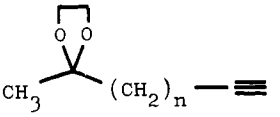


20

a: n = 12

b: n = 10

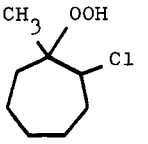
of muscone synthesis, the one based on the intramolecular aldol condensation of 2,15-hexadecanedione (**20a**) became promising, owing to the exploitation by Tsuji and his group of an organoaluminum compound as the condensing reagent.[6] It was expected that the desired skeleton of the diketone could be obtained from a *gem*-dichloro ketone, a type B reaction product, via dehydrochlorination and oxidative dimerization of the resulted ethynyl compound. In order to reach the final C-16 diketone, we started first from 1-methylcycloheptene (**7d**) as a C-8 olefin. Although the type B reaction product **8d**, after the protection of the carbonyl group, was successfully dehydrochlorinated to produce a C-8 ethynyl ketal, **21a**, the oxidation step **7d** →



21

a: n = 4

b: n = 3



22

8d was complicated, unlike the case of the six-membered analogue, and the yield of **8d** was only 6%. When the intermediate hydroperoxide **22** was isolated and then decomposed with iron(II) sulfate and iron(III) chloride in acidic ethanol, the yield was improved up to 29%, but the method is still far from satisfactory. In view of the observation that the photooxidation proceeded more cleanly with disubstituted cycloalkenes, we expected that the desired ketal **21a** could be obtained more satisfactorily by utilizing 1,2-dimethylcyclohexene (**11a**) as a starting C-8 olefin for the present synthetic purpose. The *gem*-dichloro ketone **12a**, which was obtained in 86% yield from **11a**, was ketalized with ethylene glycol and treated with lithium diisopropylamide to produce **21a** in 89% yield. This reagent induced the dehydrochlorination exclusively at the

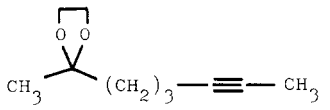
(3) R. M. Silverstein, R. G. Brownlee, T. E. Bellas, D. L. Wood, and L. E. Browne, *Science*, **159**, 889 (1968).

(4) P. J. Kociensky and R. W. Ostrow, *J. Org. Chem.* **41**, 398 (1976).

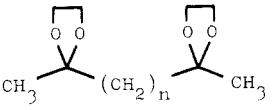
(5) J. L. Coke, H. J. Williams, and S. Natarajan, *J. Org. Chem.*, **42**, 2380 (1977).

(6) J. Tsuji, M. Kaito, and T. Takahashi, *Bull. Chem. Soc. Jpn*, **51**, 547 (1978).

terminal position, while sodium amide in liquid ammonia gave a 1.3:1 mixture of terminal and internal acetylenic compounds **21a** and **23**. The copper(I) chloride catalyzed



23



24

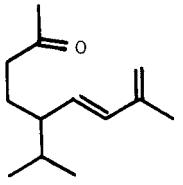
a: n = 12

b: n = 10

oxidative dimerization of **21a** with molecular oxygen gave the dimer in 72% yield. The catalytic hydrogenation of the dimer over platinum oxide, followed by the deprotection of the ethylene ketal group, gave the desired 2,15-hexadecanedione (**20a**) in an overall yield of 37% from 1,2-dimethylcyclohexene. The IR and NMR data coincided completely with those reported.[6] In the same way, the C-14 diketone **20b** was prepared from 1-methylcyclohexene (**7b**) in an overall yield of 11% (not optimized).

Another merit of the type B photooxidation is that we have a wide selection of substituted cycloalkenes having the desired stereochemistry for the synthesis of an optically active compound. We now describe the synthesis of D-solanone from D-*p*-menthene by utilizing the present reaction.

Solanone (**25**) is a member of the tobacco terpenoids and represents a unique structural feature in that it apparently violates the isoprene rule. Its structure was elucidated and confirmed by the synthesis of the racemate by Johnson and Nicholson in 1965.[7] However, the stereochemistry of solanone remains controversial: the same authors assigned the L-configuration by comparing the optical rotation of the tetrahydro derivative **26** of the product of natural



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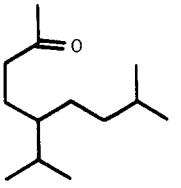

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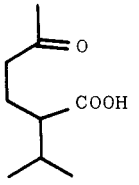

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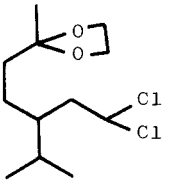

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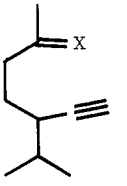
origin with that of the compound synthesized from D-*p*-menthene, while Fukuzumi and his co-workers[8] assigned the D configuration in view of the optical rotations of the carboxylic acids **27** of natural and synthetic origin. An attempt to synthesize optically active solanone was carried out by Johnson and Nicholson,[7] but the reaction was complicated, and no optical activity was determined. A number of solanone-related constituents have been isolated from tobacco since then, and the D configuration has been tentatively assigned to all of them,[9] in compliance with the assignment made by Fukuzumi and his co-workers. We thought that a *gem*-dichloro ketone, **8c**, which is a product of the type B photooxidation from D-*p*-menthene (**7c**), might be a suitable starting material for the synthesis of D-solanone. As revealed in the Table I, however, the photooxidation of D-*p*-methene afforded the desired *gem*-dichloro ketone **8c** only in 26% yield and produced an α,ω-dichloro ketone **9c** and an α-chloro ketone **10** in 12% and 43% yields, respectively. The formation of **10**, which is the major product of the present reaction, is quite unusual for a monosubstituted cycloalkene and will be interpreted later in terms of the steric effect of the isopropyl group. In spite of the low yield and poor selectivity of the desired compound, we still thought that the present route would be more convenient than any of the alternatives, and we embarked on a synthetic approach to D-solanone by utilizing **8c** as a pivotal intermediate.

The crude product obtained by the photooxidation of D-*p*-menthene in the presence of iron(III) chloride and lithium chloride in a solvent mixture of pyridine and benzene (3:2) was distilled to separate a mixture of **8c** and **9c** from **10**. The mixture of **8c** and **9c** was treated with ethylene glycol in refluxing benzene in the presence of a catalytic amount of *p*-toluenesulfonic acid to produce a ketal, **28**. Unexpectedly, no product from **9c** was identified in the product. The treatment of **28** with lithium diisopropylamide in tetrahydrofuran afforded an ethynyl ketal, **29b**, in 79% yield. When the dehydrochlorination was



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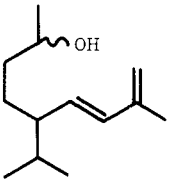
a: X = O

b: X =



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carried out with sodium amide in liquid ammonia, the product did not show the optical activity, probably due to the abstraction of the proton on the chiral center. The ethylene glycol moiety was deprotected by treating **29b** under acidic conditions, and the resulting ketone **29a** was first reacted with catecholborane and then with 2-bromopropene in the presence of tetrakis(triphenylphosphine)palladium(0) and sodium ethoxide in a refluxing solvent of benzene and ethanol.[10] The product obtained in 55% yield was **30**, in which the geometry of the double bond was shown to be exclusively trans by NMR analysis. Although the configuration of the hydroxyl group was not determined, the IR spectrum of **30** completely coincided with that of solanol which had been isolated from tobacco.[11] Jones oxidation of the alcohol **30** yielded optically active solanone (**25**) in 61% yield. The IR, NMR, and mass spectra completely coincided with those of the natural product.[11] In view of the optical rotation of this

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(8) T. Fukuzumi, H. Kaneko, and H. Takahara, *Agric. Biol. Chem.*, **31**, 607 (1967).
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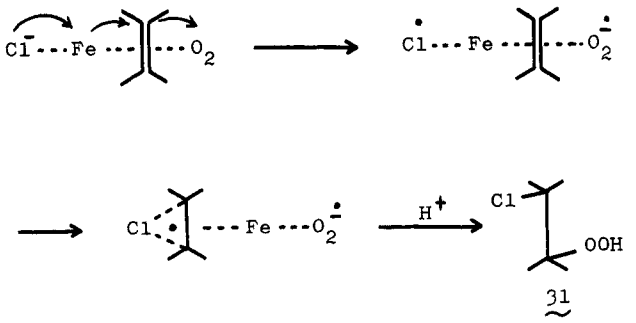
(11) We are grateful to Dr. H. Kaneko, The Japan Tobacco and Salt Public Corp., for the data on natural products.

Scheme II



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product, $[\alpha]^{18.5}_D$ +10.4°, which is comparable to that of the natural product, $[\alpha]^{23}_D$ +13.6°,[7] we could determine definitely that the natural solanone has the D configuration.

We now discuss the unusual formation of the α-chloro ketone **10** from *p*-menthene. The present photooxidation has been postulated as involving a photoinduced interligand electron transfer from the chlorine ligand to molecular oxygen through the metal ion and olefin molecule as shown in the Scheme II, which we called long-range electron transfer.[3] Once the chlorine ligand is furnished with radical character through the electron transfer, it adds to the olefin, and successive coupling of the resulting radical with an oxygen anion radical followed by protonation completes the reaction to give the β-chloro hydroperoxide **31**. The addition of the chlorine radical to the olefin would precede the addition of oxygen anion radical due to the more electrophilic character of the former species. With an ordinary system such as 1-methylcyclohexene, the reaction proceeds in the Markovnikov way, thus producing a tertiary hydroperoxide, **32**, rather than a secondary hydroperoxide, **33**. The tertiary hydroperoxide **32** undergoes a C–C bond cleavage as shown in the Scheme I. However, with a system such as *p*-menthene, in which the bulky isopropyl group restricts the conformation of the ring, there arises a steric factor. There are two ways of chlorine attack as shown in Scheme III; one is from the bottom of the ring (case I), and the other is from the top (case II). In case I, the succeeding attack of the oxygen anion radical to the tertiary carbon in a *trans*-diaxial way would compel the ring system to take an unfavorable twisted boat form, **34**, thus favoring oxygen attack of the secondary carbon to produce a secondary hydroperoxide, **35**, which is an electronically unfavorable product in the absence of the steric effect. The scheme involving such a *trans*-diaxial opening of the bridged intermediate in the radical addition has been well documented.[12] The dehydration of **35** produces the observed α-chloro ketone **10**. In case II, both electronic and steric effects favor the oxygen attack in normal way to produce a tertiary hydroperoxide and afford C–C bond cleavage products. The observation that the carbonyl band of **10** appears at 1720 cm^{-1} indicates the noncoplanarity of the carbonyl group with the C–Cl bond, thus establishing the stereochemistry of **10** as having an axial chlorine atom, which is required from the proposed reaction

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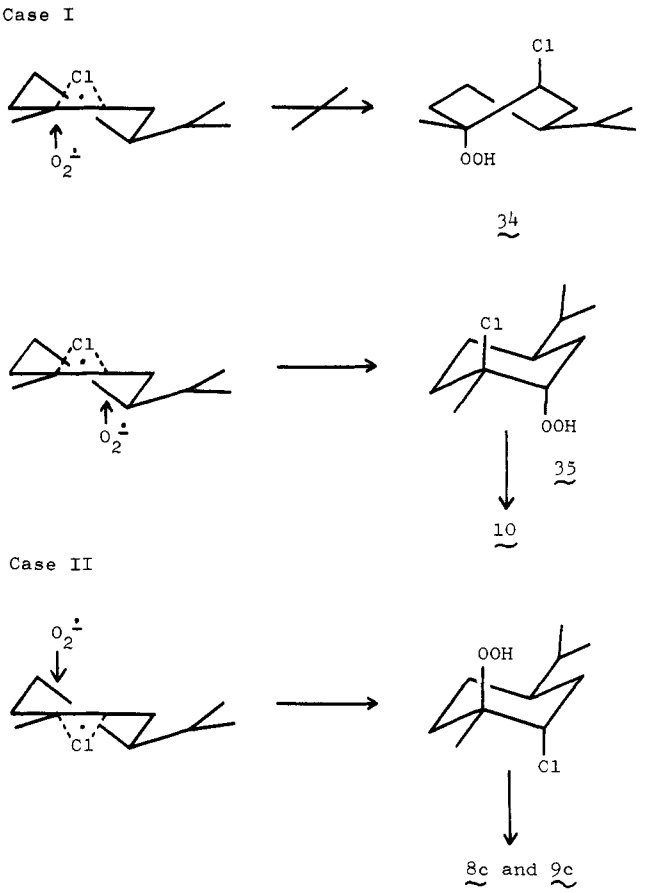
Scheme III



scheme. In view of the product ratio of (**8c** + **9c**)/**10** of about 1, both ways of chlorine attack seem to occur comparably.

The abnormality was also observed with 1-ethyl-*cis*-4,6-dimethylcyclohexene (**13c**), which produced an unusual α-chloro ketone **15** in 33% yield, as well as the normal C–C bond cleavage product **14c** in 31% yield (Table III). Evidently two *cis*-methyl groups exert the same steric effect as one isopropyl group on the reaction pattern. However, the photooxidation of **13a** or **13b** gave the bond-cleavage product **14a** or **14b** as a sole product, both in 63% yield, indicating that only one methyl group is not sufficient to develop the abnormality.

Experimental Section

General Procedures. The instrumentation was the same as has been described previously.[13] Preparative GLC analyses were carried out on a 2.5 m × 6 mm stainless steel column packed with silicone SE-30 or Carbowax 20M on silanized Chromosorb W. Preparative TLC was carried out on a silica gel plate by using benzene or $CHCl_3$ as a developing solvent. Unless otherwise state, all the spectroscopic data were determined on the sample collected on preparative GLC or TLC, a CCl_4 solution being used for the IR and NMR spectral determinations.

Materials. The materials described below were synthesized from the corresponding cycloalkanones by the successive Grignard reaction and dehydration according to the reported method for the preparation of **7b** from cyclohexanone:[14] 1-methylcyclopentene (**7a**),[15] 1-methylcyclohexene (**7b**),[14] 1-methylcycloheptene (**7d**),[16] 1-methylcyclododecene (**7e**),[17] 1,2-dimethylcyclohexene (**11a**),[18]

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and 1,2-dimethylcycloheptene (**11c**).[19] D-(+)-Menthene (**7c**) was prepared from D-limonene according to the reported method;[20] $[\alpha]^{27}_D$ +95.3° (lit.[20] $[\alpha]^{25}_D$ +100°).

1-Ethyl-2,4-dimethylcyclohexene (11b). *cis*-3,5-Dimethylcyclohexanone was silylated and ethylated according to the reported method.[21] A solution of the resulting 2-ethyl-3,5-dimethylcyclohexanone (2.2 g, 14.9 mmol) in ether (3.2 mL) was added to a solution of $LiAlH_4$ (0.27 g, 7.9 mmol) in ether (50 mL) at 0 °C under N_2. The solution was stirred at room temperature for 1 h and then refluxed for 2 h. A mixture of methanol (1.2 mL) and ether (1.2 mL) and then a saturated NH_4Cl solution were added, and the solution was extracted with ether. The extract was dried (Na_2SO_4), and the solvent was removed by evaporation. The remaining oil (1.6 g) was heated at 130–140 °C for 3 h in the presence of a catalytic amount of sulfuric acid and distilled to give a mixture (0.9 g) of **11b** and 3-ethyl-4,6-dimethylcyclohexene (**36**). Each component was isolated by preparative GLC. For **11b**: IR ν_{max} 2940, 2900, 2860, 1450, 1373, 1246, and 858 cm^{-1}; NMR δ 0.8–1.1 (6 H, m), 1.59 (3 H, s), 1.3–1.8 (3 H, m), 1.3–2.4 (6 H, m). For **36**: IR ν_{max} 2955, 2930, 2880, 1460, 1382, 1258, 865 cm^{-1}; NMR δ 0.8–1.1 (9 H, m), 1.1–2.5 (7 H, m), 5.60 (2 H, br s).

1-Ethyl-*cis*-4,6-dimethylcyclohexene (13c). A crude oil (1.0 g) obtained from the $LiAlH_4$ reduction of 2-ethyl-3,5-dimethylcyclohexanone as described above was dissolved in hexamethylphosphortriamide (HMPA, 4.2 mL), and the solution was heated slowly so that all the material distilled.[22] Some amount of pentane was added to the distillate, and the mixture was washed with NaCl solution and dried over $CaCl_2$. The solvent was removed by evaporation to afford a mixture (0.56 g) of **13c** and **36**. Each component was isolated by preparative GLC. For **13c**: IR ν_{max} 2950, 2900, 2875, 2835, 1455, 1378, 1288, 1250, 860 cm^{-1}; NMR δ 0.8–1.1 (9 H, m), 1.3–2.4 (8 H, m), 5.17–5.43 (1 H, b).

1,2-Dimethylcyclododecene (11d) and 1,12-Dimethylcyclododecene (13f). A crude alcohol, obtained by the reaction of 2-methylcyclododecanone[23] with methylmagnesium iodide, was refluxed in a mixture of an equal volume of ethanol and 20% H_2SO_4 for 4 h. Water was addied, and the mixture was extracted with CCl_4. The solvent was removed, and the remaining oil was fractionally distilled. The fraction of boiling point 149–154 °C (24 mmHg) was mainly **13f**, accompanied by a small amount of **11d** (~5%). A pure sample of **11d** was isolated by preparative GLC. For **11d**: IR ν_{max} 2940, 2860, 1470, 1445, 1373, 780 cm^{-1}; NMR δ 1.1–1.7 (16 H, m), 1.60 (6 H, s), 2.05 (4 H, distorted t). For **13f** (a mixture of equal amounts of cis and trans isomers): IR ν_{max} 2920, 2850, 1467, 1443, 1380, 783 cm^{-1}; NMR δ 0.90 (d, J = 8 Hz) and 0.93 (d, J = 8 Hz) (3 H, for cis and trans), 1.1–1.7 (16 H, m), 2.05–2.4 (3 H, m), 4.8–5.05 (m) and 5.25–5.4 (m) (1 H, for cis and trans).

1,6-Dimethylcyclohexene (13a). To a solution of 2-methylcyclohexanone tosylhydrazone (1.4 g, 5 mmol) in *N,N,N',N'*-tetramethylethylenediamine (TMEDA, 10 mL) was added a hexane solution of BuLi (1.53 M, 13 mL, 20 mmol) at −55 °C with stirring under N_2 during a period of 10 min.[24] The solution was stirred for 4 h at room temperature and then cooled to 0 °C. Dimethyl sulfate (2 mL, 21 mmol) was added at 0 °C and the mixture stirred for 90 min at room temperature. The solution was acidified with dilute HCl, and some amount of pentane was added. The organic layer was successively washed with water, saturated $CuSO_4$, and saturated NaCl and dried over Na_2SO_4. Distillation gave an oil of **13a** (172 mg), containing a small amount (~5%) of 3-methylcyclohexene; bp 90–107 °C (20 mmHg). For **13a**: NMR δ 1.00 (3 H, d, J = 7 Hz), 1.60 (3 H, br s), 1.2–2.3 (7 H, m), 5.30 (1 H, br).

1-Ethyl-6-methylcyclohexene (13b) and 1-Ethyl-8-methylcyclooctene (13e). These olefins were prepared from the corresponding 2-methylcycloalkanone tosylhydrazone in the same way as described above. Ethyl bromide was used as an alkylating reagent. For **13b**: IR (neat) ν_{max} 2960, 2860, 1456, 1375 cm^{-1}; NMR δ 0.72–2.37 (15 H, m), 5.33 (1 H, br). For **13e**: IR ν_{max} 2900, 2670, 1655, 1450, 1377, 1253, 900, 853 cm^{-1}; NMR δ 0.88–2.30 (18 H, m), 2.6–3.0 (1 H, m), 5.32 (1 H, br t, J = 9 Hz).

Photooxidation. The irradiation was carried out on a solution of olefin (10 mL, 0.025 M) in Pyrex test tubes for 30–140 min while oxygen gas was bubbled through. A medium-pressure mercury vapor lamp [Ushio UM 452 (450 W)] was used as a light source. The irradiated solution was conventionally worked up in the following way. The solvent was removed in vacuo, and the reaction products were extracted with CCl_4 or CH_2Cl_2 from the residue. The extract was passed through a short column of Florisil, and the solvent was removed in vacuo. The material that remained after the evaporation of the solvent was practically pure and was directly analyzed by the GLC or NMR technique. 1,1,2,2-Tetrachloroethane was used as an internal reference for the NMR analysis. In cases where the isolation of the chloro hydroperoxides was desired, the pyridine solution after the irradiation was neutralized with 4 M HCl and shaken with $CHCl_3$ or CH_2Cl_2. The extract was dried (Na_2SO_4), and the solvent was removed in vacuo. Spectroscopic data of the products are as follows. For **8a**: IR ν_{max} 2900, 2840, 1715, 1547, 1356, 1140 cm^{-1}; NMR δ 1.6–2.3 (4 H, m), 2.05 (3 H, s), 2.40 (2 H, t, J = 6 Hz), 5.70 (1 H, t, J = 6 Hz). For **9a**: NMR δ 1.7–2.2 (4 H, m), 2.25 (3 H, s), 3.48 (2 H, t, J = 6 Hz), 4.05 (1 H, dd, J = 8, 5 Hz). For **8b** and **9b** the data were reported previously.[2] For **8c**: IR (neat) ν_{max} 2960, 2880, 1710, 1477, 1366, 1165, 750 cm^{-1}; NMR δ 0.88 (3 H, d, J = 7 Hz), 0.90 (3 H, d, J = 7 Hz), 1.2–2.2 (6 H, m), 2.06 (3 H, s), 2.36 (2 H, t, J = 7 Hz), 5.73 (1 H, t, J = 7 Hz). For **9c**: IR (neat) ν_{max} 2960, 2875, 1715, 1466, 1360, 1165, 740 cm^{-1}; NMR δ 0.8–1.1 (6 H, m), 1.3–2.1 (6 H, m), 2.25 (3 H, s), 3.47 (2 H, t, J = 6 Hz), 4.11 (1 H, t, J = 7 Hz). For **10**: MS, m/e (relative intensity) 188 (M, with isotope peak of chlorine at M + 2, 35), 152 (M − HCl), 145 (base peak), 125, 109, 97, 81, 69, 55, 43; IR (neat) ν_{max} 2960, 2930, 2875, 1720, 1680, 1450, 1380, 1373 cm^{-1}; NMR δ 0.92 (6 H, d, J = 6 Hz), 1.52 (3 H, s), 1.23–2.42 (7 H, m), 2.63 (1 H, t, J = 13 Hz); mol wt calcd for $C_{10}H_{17}ClO$ 188.0967; Found 188.0962. For **8d**: NMR δ 1.15–2.60 (10 H, m), 2.12 (3 H, s), 5.83 (1 H, t, J = 6 Hz). For **8e**: IR (neat) ν_{max} 2917, 2851, 1710, 1467, 1442, 1357, 1166, 739 cm^{-1}; NMR δ 1.22–2.0 (16 H, m), 2.05 (3 H, s), 2.1–2.5 (4 H, m), 5.73 (1 H, t, J = 6 Hz). For **9e**: IR (neat) ν_{max} 2926, 2851, 1718, 1470, 706 cm^{-1}; NMR δ 1.2–2.1 (18 H, m), 2.24 (3 H, s), 3.56 (2 H, t, J = 6 Hz), 4.12 (1 H, dd, J = 6.5 and 6 Hz). Data for **12a** were reported previously.[2] For **12b** (R^1 = CH_3, R^2 = C_2H_5): IR ν_{max} 2960, 2930, 1718, 1620, 1460, 1370, 1350, 1268, 1235 cm^{-1}; NMR δ 0.95 (3 H, d, J = 6 Hz), 1.17 (3 H, t, J = 6 Hz), 1.3–1.7 (3 H, m), 1.9–2.4 (6 H, m), 2.03 (3 H, s). For **12b** (R^1 = C_2H_5, R^2 = CH_3): IR ν_{max} 2960, 2930, 1720, 1620, 1460, 1380, 1350, 1265, 1235 cm^{-1}; NMR δ 0.8–1.2 (6 H, m), 1.4–2.0 (3 H, m), 2.0–2.6 (6 H, m), 2.18 (3 H, s). For **12c**: IR ν_{max} 2940, 1710, 1580, 1438 cm^{-1}; NMR δ 1.2–2.0 (6 H, m), 2.06 (3 H, s), 2.10 (3 H, s), 2.25–2.5 (4 H, m). For **12d**: IR ν_{max} 2930, 2860, 1715, 1465, 1370 cm^{-1}; NMR δ 1.1–1.9 (16 H, m), 2.08 (3 H, s), 2.18 (3 H, s), 2.2–2.5 (4 H, m). For **14a**: IR ν_{max} 2930, 1720, 1360, 1236 cm^{-1}; NMR δ 1.45 (3 H, d, J = 6 Hz), 1.2–2.0 (m), 2.16 (3 H, s), 3.7–4.3 (2 H, m). For **14b**: MS, m/e (relative intensity) 210 (M, with isotope peaks of chlorine at M + 2, 68, and M + 4, 14), 175, 146, 106 (base peak), 81, 57; IR (neat) ν_{max} 2940, 1713, 1458, 1382 cm^{-1}; NMR δ 1.09 (3 H, t, J = 6 Hz), 1.50 (3 H, d, J = 6 Hz), 1.4–2.2 (6 H, m), 2.63 (2 H, qd, J = 7, 3 Hz), 3.92 (1 H, sextet, J = 6 Hz), 4.09 (1 H, dd, J = 6.5, 5.5 Hz). Anal. Calcd for $C_9H_{16}Cl_2O$: C, 51.20; H, 7.64. Found: C, 51.76; H, 7.43. For **14c**: IR ν_{max} 2975, 2940, 1720, 1460, 1380 cm^{-1}; NMR δ 0.95 (3 H, d, J = 5 Hz), 1.09 (3 H, t, J = 7 Hz), 1.53 (3 H, d, J = 6 Hz), 1.4–2.3 (m), 2.5–3.0 (2 H, m), 3.9–4.5 (2 H, m). For **14d**: NMR δ 1.2–2.0 (8 H, m), 1.54 (3 H, d, J = 6 Hz), 2.21 (3 H, s), 4.1–4.5 (2 H, m). For **14e**: IR (neat) ν_{max} 2930, 2860, 1710, 1456, 1410, 1380, 1355, 1108 cm^{-1}; NMR δ 1.04 (3 H, t, J = 7 Hz), 1.2–2.0 (10 H, m), 1.45 (3 H, d, J = 7 Hz), 2.60 (2 H, q, J = 7 Hz), 3.8–4.2 (2 H, m). For **14f**: IR ν_{max} 2930, 2860, 1728, 1472, 1362, 1240 cm^{-1}; NMR 1.2–2.1 (18 H, m), 1.47 (3 H, d, J = 6 Hz), 2.24 (3 H, s), 3.8–4.3 (2 H, m). For **15**: IR ν_{max} 2950, 2870, 1715, 1456, 1375, 1240 cm^{-1}; NMR δ 0.8–1.2 (9 H, m), 1.5–2.4 (7 H, m), 2.6–2.9 (1 H, m).

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7,7-Dichloro-2-heptanone Ethylene Ketal. The dichloro ketone **8b** was ketalized with ethylene glycol in benzene in the presence of *p*-toluenesulfonic acid: 97% yield; bp 81–89 °C (0.4 mmHg); IR (neat) ν_{max} 1380, 1225, 1065 cm^{-1}; NMR δ 1.22 (3 H, s), 1.3–1.8 (6 H, m), 2.05–2.35 (2 H, m), 3.83 (4 H, s), 5.70 (1 H, t, J = 6 Hz).

6-Heptyn-2-one Ethylene Ketal (18). To a suspension of $NaNH_2$, prepared from 523 mg (22.7 mmol) of sodium and 50 mL of liquid NH_3, was added the dichloro ketal prepared above (1.02 g, 4.5 mmol), and the mixture was stirred at −33 °C for 5 h. After evaporation of the ammonia, NH_3(aq) (20%, 50 mL) was added, and the mixture was shaken with CH_2Cl_2. After the mixture was dried over Na_2SO_4, evaporation of the solvent gave 908 mg (97%) of **18** in an almost pure state. Distillation gave a pure sample: bp 40–45 °C (0.5 mmHg); IR (neat) ν_{max} 3280, 2115, 1380, 1063 cm^{-1}; NMR δ 1.23 (3 H, s), 1.5–1.7 (4 H, m), 1.77 (1 H, t, J = 2 Hz), 2.05–2.25 [2 H, d (J = 2 Hz) of t (J = 7 Hz)], 3.86 (4 H, s). Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 70.07; H, 9.54.

6-Nonyn-2-one Ethylene Ketal (17b). A solution of *n*-BuLi in hexane (5.59 mmol) was added to a solution of **18** (717 mg, 4.66 mmol) in THF (40 mL) with stirring at −78 °C. Ethyl iodide (872 mg, 5.59 mmol) was then added and stirred for 2 h at −78 °C. The mixture was warmed to room temperature and stirred overnight. The solvent was removed in vacuo, and the residue was neutralized with 4 M HCl(aq). The mixture was shaken with CH_2Cl_2. After the mixture was dried over Na_2SO_4, evaporation of the solvent gave crude **17b**, which was distilled to afford 700 mg (82%) of **17b** in a pure state. The sample showed the identical spectroscopic data with those reported.[4]

7,7-Dichloro-2-octanone Ethylene Ketal. The ketone **8d** (1.56 g) was ketalized with ethylene glycol (40 g) in benzene (148 mL) in the presence of *p*-toluenesulfonic acid (476 mg). Distillation gave 1.84 g (97%) of the ketal: bp 104–110 °C (1.7 mmHg); IR (neat) ν_{max} 2950, 2880, 1447, 1380, 1210, 1062, 950, 853 cm^{-1}; NMR (CCl_4) δ 1.1–2.4 (8 H, m), 1.22 (3 H, s), 2.10 (3 H, s), 3.78 (4 H, s).

7-Octyn-2-one Ethylene Ketal (21a). To a solution of LDA, prepared from diisopropylamine (2.26 g) in THF (20 mL) and *n*-BuLi in *n*-hexane (1.56 N, 12.8 mL), was added the dichloro ketal obtained above (0.24 g) at 0 °C under N_2. The mixture was stirred for 8 h at 0 °C and treated with crushed ice. The solution was neutralized with HCl(aq) and extracted with ether. After being dried over Na_2SO_4, the solvent was removed in vacuo to give **21a**: 0.14 g (89%); bp 68–78 °C (1.5 mmHg); IR (neat) ν_{max} 3290, 2950, 2870, 2120, 1378, 1220, 1060 cm^{-1}; NMR δ 1.24 (3 H, s), 1.4–1.6 (6 H, m), 1.83 (1 H, t, J = 2 Hz), 2.0–2.3 (2 H, m), 3.83 (4 H, s).

2,15-Hexadecanedione Ethylene Ketal (24a). Oxygen gas was bubbled through a solution of **21a** (195 mg) and CuCl (57 mg) in a mixture of pyridine (5 ml) and TMEDA (94 mg) at 40 °C for 3 h.[25] The mixture was diluted with a double volume of water, neutralized with HCl(aq), and extracted with CH_2Cl_2. The extract was dried over Na_2SO_4, and the solvent was removed in vacuo. The residue was passed through a Florisil column to afford 135 mg of an oil. The oil, without being further purified, was hydrogenated over PtO_2 (4.6 mg) in methanol (1 mL) under atmospheric pressure.[26] After the calculated amount of hydrogen gas had been absorbed, the solid was filtered off with diatomaceous earth. Upon evaporation of the solvent, almost pure solid ketal **24a** (128 mg, 66% from **21a**) was obtained. The NMR spectrum was the same as that reported.[6]

2,15-Hexadecanedione (20a). The ethylene ketal group was deprotected in the same way as reported;[6] mp 82–83 °C (lit[6]. mp 83.5–84.5 °C). NMR and IR data were identical with those reported.[6]

The C-14 diketone **20b** was prepared from 7,7-dichloro-2-heptanone (**8b**) by the same methods as described above except for the dehydrochlorination step, where sodium amide in dry Me_2SO was used instead of LDA.

Physical data of the intermediates are as follows.

7,7-Dichloro-2-heptanone ethylene ketal: bp 61–72 °C (1.5 mmHg); IR (neat) ν_{max} 2930, 2860, 1375, 1210, 1055, 845 cm^{-1}; NMR (CCl_4) δ 1.18 (3 H, s), 1.2–2.5 (8 H, m), 3.76 (4 H, s), 5.66 (1 H, t, J = 6.0 Hz).

6-Heptyn-2-one ethylene ketal (21b): bp 79–92 °C (13 mmHg); IR (neat) ν_{max} 3280, 2950, 2870, 2110, 1378, 1220, 1060 cm^{-1}; NMR δ 1.23 (3 H, s), 1.5–1.9 (5 H, m), 2.05–2.25 (2 H, m), 3.81 (4 H, s).

6,8-Tetradecadiyne-2,13-dione ethylene ketal: IR (neat) ν_{max} 2950, 2880, 2260, 2170, 1460, 1380, 1265, 1228, 1135, 1106, 1064, 952 cm^{-1}; NMR δ 1.23 (6 H, s), 1.4–1.8 (8 H, m), 2.2–2.35 (4 H, br t), 3.85 (8 H, s).

2,13-Tetradecanedione ethylene ketal (24b): IR ν_{max} 2980, 2935, 2880, 2860, 1472, 1380, 1260, 1228, 1060, 952 cm^{-1}; NMR δ 1.20 (6 H, s), 1.0–1.7 (20 H, m), 3.78 (8 H, s).

2,13-Tetradecanedione (20b): mp 74–75 °C (lit. mp 76–77 °C,[27] 72.5–74.5 °C[28]); IR and NMR data were identical with those reported.[29]

Photooxidation of D-*p*-Menthene. A solution of D-*p*-menthene (69 mg, 0.5 mmol), $FeCl_3 \cdot 6H_2O$ (135 mg, 0.5 mmol), and LiCl (64 mg, 1.5 mmol) in a solvent mixture of pyridine (6 mL) and benzene (4 mL) was irradiated with a medium-pressure mercury lamp [Ushio UM 452 (450 W)] in a Pyrex test tube for 30 min while oxygen gas was bubbled through. The solvent was removed under reduced pressure, and the resulting residue was extracted with CCl_4. The solution was passed through a short column of Florisil, and the solvent was removed. The residual colorless oil was a mixture of **8c**, **9c**, and **10**, and the yield of each component was determined from NMR analysis by comparing the signals at δ 5.73 of **8c**, δ 4.11 of **9c**, and δ 2.63 of **10** with that of 1,1,2,2-tetrachloroethane used as an internal standard.

For a larger scale preparation, a solution 80 times as large as that shown above (using 5.25 g of *p*-menthene) was passed with oxygen gas through a spiral tube which fitted around the mercury lamp (Sen 1000-J, 1 kW) during a period of 5 h. The solution was worked up in the same way as described above, and the crude oil was distilled under reduced pressure into two parts. The fraction boiling at 40–65 °C (0.25 mmHg) was mainly **10**, and the fraction boiling at 75–80 °C (0.25 mmHg) was mainly a mixture of **8c** and **9c**. Further fractionation of **8c** and **9c** was not achieved by distillation. The mixture of **8c** and **9c** was used directly for the next step.

7,7-Dichloro-5-isopropyl-2-heptanone Ethylene Ketal (28). A mixture of **8c** and **9c** (1.57 g, containing 60% of **8c**) was heated with ethylene glycol (10.9 g) in the presence of *p*-toluenesulfonic acid (120 mg) in benzene (50 mL) with a conventional Dean–Stark apparatus for 8 h. The benzene solution was washed with $NaHCO_3$(aq) and then with water and dried over Na_2SO_4. After the solvent was removed by evaporation, the residual oil was distilled with a Kugelrohr apparatus, and a fraction (1.50 g) boiling at 150–180 °C (3 mmHg) was collected. GLC analysis showed that the purity of **28** was ~95%: IR (neat) ν_{max} 2950, 2875, 1475, 1387, 1256, 1235, 1047, 855, 740 cm^{-1}; NMR δ 0.86 (3 H, d, J = 7 Hz), 0.88 (3 H, d, J = 7 Hz), 1.20 (3 H, s), 1.3–2.3 (8 H, m), 3.84 (4 H, s), 5.73 (1 H, dd, J = 6, 7 Hz).

5-Isopropyl-6-heptyn-2-one Ethylene Ketal (29b). To a solution of diisobutylamine (1.97 g, 19.5 mmol) in THF (20 mL) was added 12.6 mL (1.55 M, 19.5 mmol) of *n*-BuLi in hexane at 0 °C during a period of 1 h under a nitrogen atmosphere. After the solution was stirred for 20 min, a solution of **28** (898 mg, 3.34 mmol) in THF (2 mL) was added dropwise and stirred at 0 °C for 8 h. The resulting solution was added to crushed ice and neutralized with 4 M HCl, and the mixture was shaken with ether. The extract was dried over Na_2SO_4, and the solvent was evaporated to give an oil, which was purified by distillation in a Kugelrohr apparatus. A fraction (708 mg) boiling at 130–160 °C (3 mmHg) was shown to contain ~95% of **29b** by a GLC analysis: IR (neat) ν_{max} 3280, 2960, 2870, 2110, 1460, 1377, 1253, 1222, 1053 cm^{-1}; NMR δ 0.95 (3 H, d, J = 7 Hz), 0.97 (3 H, d, J = 7 Hz), 1.22 (3 H, s), 1.3–2.3 (7 H, m), 3.84 (4 H, s).

5-Isopropyl-6-heptyn-2-one (29a). The acetylenic ketal **29b** (708 mg, 2.58 mmol) was dissolved in acetone (100 mL) containing 1 M H_2SO_4 (10 mL), and the solution was stirred at room temperature for 6 h. Half of the solvent was removed in vacuo, and

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the residue was neutralized with saturated $NaHCO_3$(aq). The mixture was shaken with CH_2Cl_2, and after the mixture was dried over Na_2SO_4, the solvent was evaporated. The remaining oil was distilled in a Kugelrohr apparatus to afford **29a** (277 mg, 61%) in an almost pure state: bp 150–155 °C (17 mmHg); IR (neat) ν_{max} 3270, 2955, 2870, 2110, 1710, 1366, 1165 cm^{-1}; NMR δ 1.0 (6 H, d, J = 8.7 Hz), 1.1–2.8 (7 H, m), 2.09 (3 H, s).

Solanol (30). A mixture of the ethynyl ketone **29a** (277 mg, 1.57 mmol) and catecholborane (456 mg, 3.61 mmol) was stirred at 70 °C for 2 h under N_2, and benzene (2 mL) and 2 M EtONa in EtOH (1.4 mL, 2.83 mmol) were added. This solution was added to a mixture obtained by stirring $Pd(PPh_3)_4$ (36 mg, 0.0314 mmol) and 2-bromopropene (172 mg, 1.42 mmol) in benzene (3.1 mL). The mixture was refluxed for 2 h, and a solution of 3 M NaOH (0.08 mL) and 30% H_2O_2 (0.08 mL) was added and the mixture stirred at room temperature for 1 h. An equal volume of water was added, and the mixture was extracted with pentane. The solution was passed through a Florisil column, and the solvent was removed by evaporation. The residual material was purified by distillation with a Kugelrohr apparatus to afford solanol: 201 mg; bp 180–190 ° (3 mmHg). The IR spectrum completely coincided with that of the natural product:[11] IR (neat) ν_{max} 3330, 3070, 2950, 2860, 1607, 1455, 1370, 1120, 967, 880 cm^{-1}; NMR, δ 0.8–1.1 (6 H, m), 1.1–2.2 (6 H, m), 1.09 (3 H, d, J = 7 Hz), 1.79 (3 H, s), 3.14 (1 H, br s), 3.43–3.77 (1 H, m), 4.77 (2 H, s), 5.27 and 5.96 (2 H, AB q, J = 16 Hz, upper field signals further split into doublet with J = 9 Hz).

D-**Solanone (25).** To a solution of **30** (147 mg, 0.75 mmol) in acetone (10 mL) was added Jones reagent (0.125 mL, 1 mmol) at 0 °C. The mixture was stirred for 3 h at 0–5 °C, and the solution was concentrated to half its volume by evaporation in vacuo. The solution was neutralized with a saturated solution of $NaHCO_3$ and extracted with CH_2Cl_2. The extract was dried over Na_2SO_4, and the solvent was removed to afford solanone (82 mg) in an almost pure state. Further purification was performed by preparative HPLC; $[\alpha]^{18.5}_D$ +10.4° (c 0.011 g/mL, CCl_4). The IR, NMR, and mass spectra coincided with those of the natural product.[11]

Registry No. **7a**, 693-89-0; **7b**, 591-49-1; **7c**, 1195-31-9; **7d**, 1453-25-4; **7e**, 23070-53-3; **8a**, 74067-03-1; **8b**, 66241-43-8; **8b** ethylene ketal, 74066-95-8; **8c**, 84098-59-9; **8d**, 74067-00-8; **8d** ethylene ketal, 81504-99-6; **8e**, 81505-00-2; **9a**, 84098-60-2; **9b**, 66241-44-9; **9c**, 81522-17-0; **9e**, 81505-01-3; **10**, 84129-72-6; **11a**, 1674-10-8; **11b**, 81505-02-4; **11c**, 20053-89-8; **11d**, 36616-90-7; **12a**, 66241-45-0; **12b** (R^1 = CH_3; R^2 = C_2H_5), 81505-04-6; **12b** (R^1 = C_2H_5; R^2 = CH_3), 84098-61-3; **12c**, 81505-03-5; **12d**, 81505-05-7; **13a**, 1759-64-4; **13b**, 72018-30-5; **13c**, 81505-09-1; **13d**, 81505-07-9; **13e**, 84098-62-4; *cis*-**13f**, 84098-63-5; *trans*-**13f**, 84098-64-6; **14a**, 81505-10-4; **14b**, 84098-65-7; **14c**, 81505-13-7; **14d**, 81505-11-5; **14e**, 84098-66-8; **14f**, 81505-12-6; **17b**, 24403-63-2; **18**, 74066-96-9; **20a**, 18650-13-0; **20b**, 7029-11-0; **21a**, 19985-86-5; **24a**, 66432-75-5; **24b**, 74066-99-2; **25**, 1937-54-8; **28**, 84098-67-9; **29a**, 21889-84-9; **29b**, 84098-68-0; **30**, 40525-38-0; **36**, 84098-69-1; $FeCl_3$, 7705-08-0; *cis*-3,5-dimethylcyclohexanone, 27922-05-0; 2-ethyl-3,5-dimethylcyclohexanone, 84098-70-4; 2-methylcyclododecanone, 16837-94-8; 2-methylcyclohexanone tosylhydrazone, 52826-41-2; 2-methylcyclooctanone tosylhydrazone, 84098-71-5; 6,8-tetradecadiyne-2,13-dione ethylene ketal, 74066-98-1; 2-bromopropene, 557-93-7.

Synthesis of Protected 2-Amino-8-oxo-9,10-epoxydecanoic Acid from 2-Aminosuberic Acid Derivatives[1]

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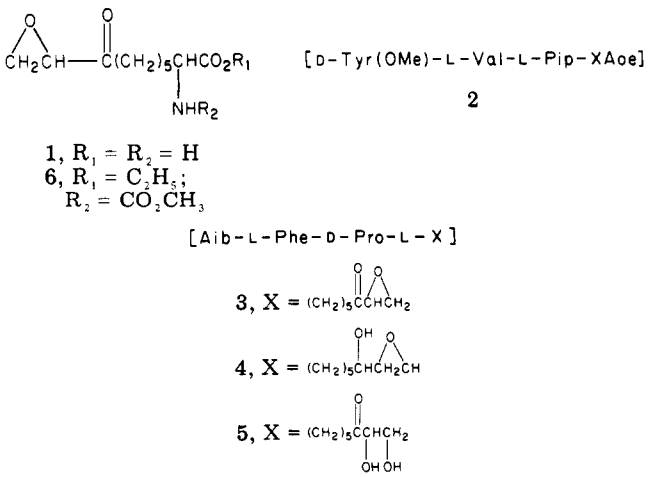
A method is reported for synthesizing derivatives of 2-amino-8-oxo-9,10-epoxydecanoic acid (Aoe) from 2-aminosuberic acid (Asu) derivatives under conditions that do not disrupt peptide bonds. The epoxy ketone amino acid Aoe is found in three biologically active cyclic peptides. Ethyl 2-(acetylamino)suberate was converted to ethyl 2-DL-(acetylamino)-8-oxo-(*RS*)-9,10-epoxydecanoate in 45–50% yield by sequential reactions with phosphorus pentachloride followed by reaction with tetravinyltin and benzylchlorobis(triphenylphosphine)palladium(II) to give the vinyl ketone in 70% yield. Epoxidation of enone with *tert*-butyl hydroperoxide using triton B as catalyst gave the *N*-acetyl ethyl ester of Aoe in 70% yield. Methods for preparing protected 2-aminosuberic acid derivatives from glycine ester benzal imine are also described.

Introduction

The amino acid 2-amino-8-oxo-9,10-epoxydecanoic acid (Aoe, **1**, Chart I),[2] has been found in three natural products, the phytotoxins Cy1-2 (**2**)[3a] and HC-toxin[3b] and chlamydocin (**3**), a cytostatic cyclic tetrapeptide.[4] In the latter case Aoe seems to be essential for biological activity because both the reduced ketone analogue dihydrochlamydocin (**4**) and the diol derivative of chlamydocin **5** are essentially inactive,[5] suggesting an important role, possibly as an alkylating agent, for the epoxy ketone functional group. Closse and Huguenin synthesized the Aoe derivative **6** via a seven-step route in order to confirm

Chart I



(1) Abstracted in part from the Ph.D. Dissertation of Jasbir Singh, University of Wisconsin–Madison, 1982.

(2) Abbreviations: Aoe, 2-amino-8-oxo-9,10-epoxydecanoic acid; Asu, 2-aminosuberic acid (2-amino-1,6-octanedioic acid); LDA, lithium diisopropylamine; Bzl, benzyl; Aib, α-aminoisobutyric acid; Pip, pipicolic acid.

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