The Preparation and Photoreation of Spiro[oxirane-2,6′-tricyclo[3.2.1.$0^{2,7}$]-oct[3]en]-8′-ones. An Intramolecular Cycloaddition of Photochemically Generated Ketene with the Epoxide Ring[1)]

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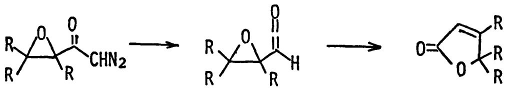
The oxidations of 1,5-dimethyl- and 1,3,5-trimethyl-6-methylenetricyclo[3.2.1.$0^{2,7}$]oct-3-en-8-ones with 3-chloroperbenzoic acid or thallium(III) acetate resulted in the formation of 1′,5′-dimethyl and 1′,3′,5′-trimethylspiro[oxirane-2,6′-tricyclo[3.2.1.$0^{2,7}$]oct[3]en]-8′-ones (**2a** and **2b**). The oxidation occured stereoselectively on the exocyclic double bond from the *exo*-side. The photochemical reactions of **2a** and **2b** resulted in the formation of 4,8-dimethyl- and 4,6,8-trimethyl-3,4-dihydro-1H-2-benzopyran-3-ones, both of which would be derived from an ene-type reaction of the ketene intermediate with the exoxide ring involved in the $[4\pi+2\sigma]$ electronic system. The intermediacy of the ketene was assessed by low-temperature infrared spectroscopy as well as by a trapping experiment, the mechanistic pathways were confirmed by conducting the photoreaction in deuterated methanol.

Recently, the stereoselectivities of the electrophilic reaction of molecules containing a proximal π-bond have been explored.[2)] In connection with these studies and our own previous work,[1,3)] the peroxy-acid oxidation and the thallium(III) acetate-induced oxidation of 1,5-dimethyl- and 1,3,5-trimethyl-6-methylenetricyclo[3.2.1.$0^{2,7}$]oct-3-en-8-ones (**1a** and **1b**) were investigated. The products, 1′,5′-dimethyl and 1′,3′,5′-trimethylspiro[oxirane-2,6′-tricyclo[3.2.1.$0^{2,7}$]oct[3]en]-8′-ones (**2a** and **2b**), have a skeleton of photolabile 3-methyl-4-caren-2-one, which has been shown to photoisomerize to a ketene derivative.[4)] Therefore, **2a** and **2b** were expected to be promising precursors of a ketene possessing another functional group of an epoxide involved in the $[4\pi+2\sigma]$ electronic system.

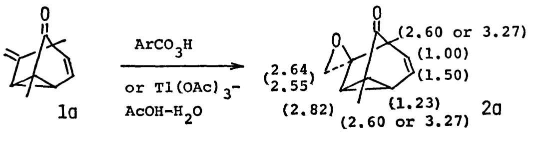
Although the intramolecular cycloaddition of photochemically generated ketenes has been widely known,[5)] little is known about the reaction of such ketenes with an electronic system which involves both π-bonds and a polar or bent σ-bond such as an epoxide ring. Some information on the reaction of an epoxide with a ketene has, however been shown. The epoxide attacks the C=O or C=C bond to afford the acetal or lactone.[6)] The epoxyketene, on the other hand, undergoes a vinylcyclopropane–cyclopentene-type rearrangement, leading to butenolide (Eq. 1)[7)] On understanding some unknown behavior of the epoxide toward a reactive ketene, the photochemical reactions of **2a** and **2b** were investigated.

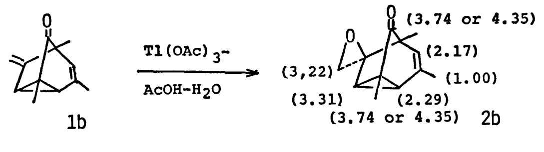


(1)

Results and Discussion

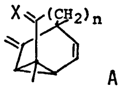
The Epoxidation of 1,5-Dimethyl- and 1,3,5-Trimethyl-6-methylenetricyclo[*3.2.1.$0^{2,7}$*]*oct-3-en-8-ones (**1a** and **1b**).* The treatment of **1a** with 3-chloroperbenzoic acid afforded 1′,5′-dimethylspiro[oxirane-2,6′-tricyclo-[3.2.1.$0^{2,7}$]oct[3]en]-8′-one (**2a**) in a 55% yield, along with the starting meterial, **1a**, in a 29% yield. The structure of **2a** was deduced from its spectral properties. The stereochemistry of the epoxide ring was determined by means of the pseudo-contact NMR spectra obtained by using Eu(fod)$_3$. The relative downfield shifts of δ's are given in parentheses in the structural formula **2a**. The relatively small shifts for the hydrogens of the allylic moiety suggest that the coordination of Eu(fod)$_3$ occurs on the epoxide-oxygen. The large shifts of the two methyl groups and the proton at the 7′-position suggest that the epoxide-oxygen is located *syn* to the carbonyl group. Thus, the stereochemistry of the epoxide was assessed.





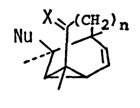
The epoxidation of alkenes with thallium(III) acetate has also been shown.[8)] Thus, the reaction of **1a** with thallium(III) acetate in H_2O–AcOH afforded the epoxide **2a** in a 61% yield. The reaction of the trimethyl analogue **1b** in a similar way also afforded the epoxide **2b** in a 59% yield, along with *ca.* 5% of an unidentified compound, **6**. The orientation of the epoxide-oxygen for **2b** was deduced to be *syn* to the carbonyl group from the pseudo-contact NMR spectra, which were obtained by using Eu(fod)$_3$. The relative downfield shifts of δ's, which are presented in parentheses in the structural formula **2b**, exhibited a trend similar to that of **2a**.

In our previous papers, the solvomercuration-demercuration reaction on the exocyclic double bond of **1a** and its related compounds with the general structure of [**A**] was described as exhibiting a remarkable stereoselectivity to give [**B**].[3)] The stereoselectivity was ex-



A

n=0 or 1

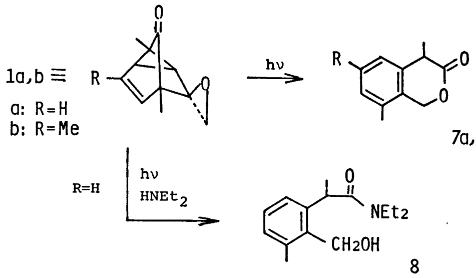


B

X=O or H, OH

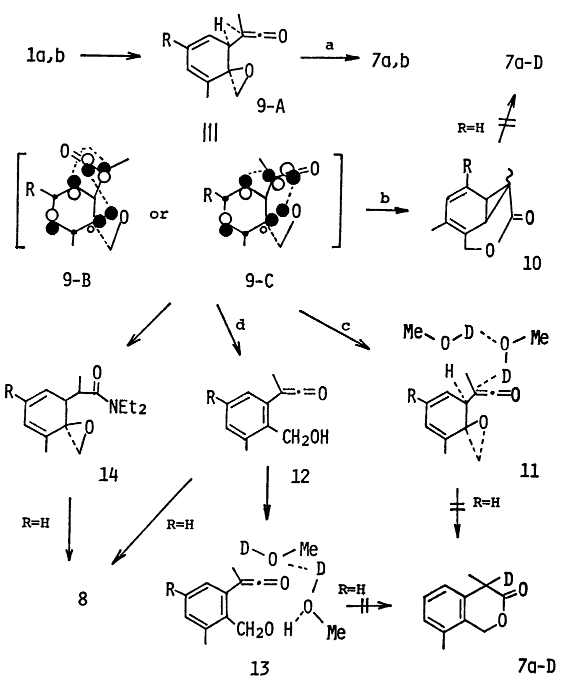
plained by the steric and/or electronic factor of the mercurinium-ion formation and the subsequent incorporation of the nucleophile.[3] In the present reactions, epoxide-oxygen was also stereoselectively incorporated on the exocyclic double bond from the *exo*-side.

*Photochemical Reactions of the Epoxide **2a** and **2b**.* The photoirradiation of **2a** in acetonitrile under a nitrogen atmosphere resulted in the formation of 4,8-dimethyl-3,4-dihydro-1*H*-2-benzopyran-3-one (**7a**) in a 61% yield. Similarly, **2b** afforded 4,6,8-trimethyl-3,4-dihydro-1*H*-2-benzopyran-3-one (**7b**) in a 77% yield. The structures of **7a** and **7b** were deduced from the spectral properties, as well as by comparison with the spectral data of 1,5-dimethyl-3,4-dihydro-1*H*-2-benzopyran-3-one, which had been derived from the oxidation of 1,4-dimethyl-2-indanone.[9] The irradiation of **2a** was also carried out in acetonitrile containing a ten-fold excess of diethylamine, **7a** and the amide **8** were then obtained in 44% and 15% yields respectively.



From the formation of 7a, **7b**, and **8**, the ketene **9** was proposed as the common intermediate. Support for the intermediacy of this ketene was obtained by conducting the irradiation of the film of **2a** at 77 K. During the irradiation, the intensity of the band due to the carbonyl group in the low-temperature IR spectrum slowly decreased. A distinct new band, attributable to the ketene function, appeared at 2120 cm^{-1} after 3 h. On warming to room temperature, the 2120 cm^{-1} band disappeared completely, while there appeared a new band at 1730 cm^{-1} corresponding to **7a**, hence, the intermediacy of the ketene was clarified.

The photoreaction of **2a** in methanol also gave **7a**, while the methanol adduct to the ketene moiety was not obtained. Thus, the pathway for the formation of **7a,b** seems to be the concerted ene-type cyclization represented in the structural formula **9-A** (Scheme 1, Path a). Another possible routes can be envisaged to explain the formation of **7a,b** in acetonitrile or methanol: i) the intramolecular cycloaddition of the ketene moiety with the $[4\pi+2\sigma]$ electronic system to give the norcaradiene intermediate **10** *via* **9-B** or **9-C**, followed by aromatization (Path b),[10] ii) the nucleophilic reaction of the epoxide ring assisted by methanol *via* **11** (Path C), iii) the rearrangement of the ketene **9** to **12** followed by methanol-assisted lactonization to give **7a,b** *via* **13** (Path d).[11] Judging from the forbidded 1,3-hydrogen migration required for the isomerization of **9** to **12**, however, the intermediacy of 12 seems unlikely under neutral conditions.[12] In order to clarify the possibilities of Path b, Path C, or Path d, the photoreaction of **2a** was carried out in 98%-deuterated MeOD. However, the deuterium-incorporated product **7a—D**, which could be expected from Path b, Path c, or Path d, could not be obtained at the early stage of the reaction. The prolonged irradiation, which continued to about 50% of the **2a** has been consumed, caused a deuterium-incorporation at the C-4 position of **7a** (Table 1). Furthermore, the independent irradiation of **7a** in MeOD underwent deuterium exchange at the C-4 position of **7a**. Therefore, the deuterium-incorporation to **7a** seems to result from the subsequent photoreaction of **7a**. This fact suggests that Path b, Path c, or Path d could not be involved in the present photoreaction in methanol or acetonitrile.

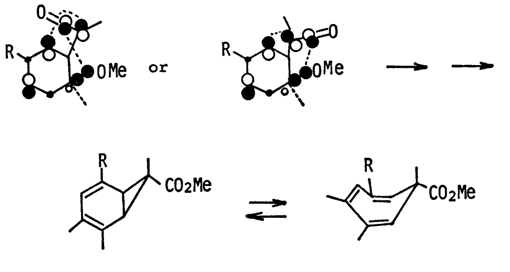


Scheme 1.

Table 1.

Time/h	4	7	14
7a/7a—D	10	2.3	1.0
2a (%)	60	30	16

On the other hand, the formation of the amide **8** in the presence of diethylamine is suggestive of the isomerization of the ketene **9** to the ketene **12**, which undergoes the addition of diethylamine to give **8**, and/or the amine addition to **9** to give **14**, which undergoes aromatization to give **8**, under the basic conditions in the presence of diethylamine.



(2)

In the present photoreaction, the intramolecular cycloaddition of the ketene with the suitably located [$4\pi+2\sigma$] electronic system represented by **9-B** or **9-C** (Path b) is prohibited. The photochemical or thermal reaction of *exo*-6-methoxy-1,5,6-trimethyltricyclo-[3.2.1.0^{2,7}]oct-3-en-8-one has been shown to undergo this type of cycloaddition (Eq. 2).[10] Since compound **10** seems to be very constrained, therefore, this reaction pathway (Path b) is less energetically favored than the ene-type reaction (Path a).

Experimental

The IR spectra were recorded on a Shimadzu IR-400 spectrometer The mass spectral studies were conducted using an Hitachi, RMU-60 spectrometer, All the NMR spectra were recorded on a JEOL PS-100 high-resolution spectrometer, using tetramethylsilane as the internal standard. The shift data were obtained by adding small increments of Eu(fod)$_3$ to the sample and by then nothing the extent to which each peak was shifted. The relative-shift slopes were obtained by dividing each slope by the slope of the least-shifted signal. The VPC analyses and separation were performed on a Shimadzu GC-6A or a Varian Model-920 chromatograph, using a column packed with 5% SE-30 on Chromosorb W. The analyses were performed by the Science and Engineering Research Ladoratory of Waseda University.

Irradiation was carried out using a Rayonet RPR-100 Photoreactor fitted with RPR-300 nm lamps. The solution to be irradiated was placed in a Pyrex tube and was, after deoxygenation with a stream of nitrogen, sealed with a serum cap.

Oxidation of 1,5-Dimethyl-6-methylenetricyclo[3.2.1.0^{2,7}]oct-3-en-8-one (1a) and 3-Chloroperbenzoic Acid. A solution of **1a** (800 mg, 5 mmol) and 3-chloroperbenzoic acid (860 mg, 5 mmol) in dichloromethane (10 cm^3) was stirred at room temperature for 2 h. The 3-chlorobenzaic acid thus precipitated was removed by filtration, and the filtrate was washed with aqueous sodium hydrogencarbonate and dried over sodium sulfate. The subsequent removal of the solvent gave 671 mg of an oil, which was then chromatographed on silica gel, using benzene as the eluent, to give 228 mg (29%) of the starting material **1a** and 443 mg (55%) of the epoxide **2a**: IR (film), 3040, 2974, 2939, 2865, 1742, 993 cm^{-1}; NMR (CCl), δ=0.72 (3H, s), 1.25 (3H, s), 1.64 (1H, d, J=8.0 Hz), 2.02—2.34 (1H, m), 2.64 (1H, d, J=4.0 Hz), 2.68 (1H, d, J=4.0 Hz), 5.42 (1H, dxd, J=8.0, 3.0 Hz), 6,02 (1H, dxd, J=8.0, 5.5 Hz); MS, *m/e* (rel intensity), 176 (M$^+$, 13) 118 (11). Found: C, 74.91; H, 6.68%. Calcd for $C_{11}H_{12}O_2$: C, 74.97; H, 6.86%.

Oxidation of 1a with Thallium(III) Acetate. A solution of **1a** (1.6 g, 10 mmol) and thallium(III) acetate (7.62 g, 20 mmnl) in 60 cm^3 of an acetic acid-water (1/1) mixture was stirred at room temperature overnight and then neutralized with aqueous sodium hydrogencarbonate. To this reaction mixture, was added saturated aqueous sodium chloride, after which the percipitate was removed by filtration. The filtrate was extracted with ether and dried over sodium sulfate. After the removal of the solvent, the residue was distilled to give 1.07 g (61%) of **2a**.

Oxidation of 1,3,5-Trimethyl-6-methylenetricyclo[3.2.1.0.^{2,7}]-oct-3-en-8-one (1b) with Thallium(III) Acetate. The oxidation was carried out as has been described above, using 1.0 g (0.57 mmol) of **1b** and 4.57 g (12 mmol) of thallium(III) acetate. A subsequent workup similar to that described above gave an oil. This oil was separated by TLC on silica gel using chloroform-benzene (1/1) as the eluent. The first band from the TLC plates afforded 640 mg (59%) of **2b**: bp 108—111 °C/798.6 Pa (bath temperature); IR (CCl$_4$), 3040, 2949, 2859, 1737, 992 cm^{-1}; NMR (CCl$_4$), δ=0.80 (3H, s), 1.33 (3H, s), 1.64 (1H, d, J=8.0 Hz), 1.80—2.08 (1H, m), 1.94 (3H, d, J=3.0 Hz), 2.78 (1H, d, J=4.5 Hz), 2.89 (1H, d, J=4.5 Hz), 5.22—5.37 (1H, m). Found: C, 75.82; H, 7.47%. Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42%.

The second band for the TCL plates contained 50 mg (5%) of **6**: IR (CCl$_4$), 3049, 2976, 2941, 2874, 1742, 1689 (shoulder), 1449, 1379 cm^{-1}; NMR (CCl$_4$), δ=1.08 (3H, s), 1.25 (3H, s), 1.09 (3H, s), 2.17—2.43 (3H, m), 2.44 (2H, s), 5.30 (1H, m).

Irradiation of 2a. A solution of **2a** (50 mg, 0.28 mmol) in 10 cm^3 of anhydrous acetonitrile was irradiated at room temperature. The photoreaction, followed by VPC, was completed in 32 h. The photolysate was separated by TLC on silica gel, using benzene as the eluent, to give 41 mg (80%) of **7a**: mp 75—76 °C; IR (KBr), 1730 cm^{-1}; NMR (CCl$_4$), δ=1.60 (3H, d, J=7.0 Hz), 2.36 (3H, s), 3.50 (1H, q, J=7.0 Hz), 5.18 (1H, d, J=14.0 Hz), 5.38 (1H, d, J=14.0 Hz), 7.00—7.36 (3H, m); MS, *m/e* (rel intensity), 176 (M$^+$, 17), 132 (100). Found: C, 74.77; H, 7.11%. Calcd for $C_{11}H_{12}O_2$: C, 74.97; H, 6.88%.

Oxidation of 1,4-Dimethyl-2-indanone with 3-Chloroperbenzoic Acid. A solution of 1,4-dimethyl-2-indanone (480 mg, 3 mmol) and 3-chloroperbenzoic acid (692 mg, 4 mmol) was stirred overnight. To this reaction mixture, we then added 5 cm^3 of saturated aqueous $Na_2S_2O_3$ and water, after with the reaction mixture was extracted with dichloromethane. The evaporation of the dried organic portion and subsequent recrystallization gave 288 mg (55%) of 1,5-dimethyl-3,4-dihydro-1*H*-2-benzopyran-3-one: mp 114—115 °C; IR (CCl$_4$), 1754 cm^{-1}; NMR (CCl$_4$), δ=1.73 (1H, d, J=6.6 Hz), 2.34 (3H, s), 3.62 (1H, d, J=18.6 Hz), 3.87 (1H, d, J=18.6 Hz), 5.55 (1H, q, J=6.6 Hz), 7.20—7.50 (3H, m); MS, *m/e* (rel intensity), 176 (M$^+$, 27), 132 (100). Found: C, 75.36; H, 6.81%. Calcd for $C_{11}H_{12}O_2$: C, 74.94; H, 6.86%.

Irradiation of 2b. A solution of **2b** (64 mg, 0.36 mmol) in 10 cm^3 of anhydrous acetonitrile was irradiated for 19 h. The photolysate was purified by column chromatography on Florisil, using benzene as the eluent, to give 49 mg (77%) of lactone **7b**: mp 117—118 °C; IR (CCl$_4$), 1736 cm^{-1}; NMR (CDCl$_3$), δ=1.77 (3H, d, J=7.5 Hz), 2.53 (3H, s), 2.60 (3H, s), 3.94 (1H, q, J=7.5 Hz), 5.80 (1H, d, J=13.5 Hz, 5.94 (1H, d, J=13.5 Hz), 7.66—7.83 (2H, broad s); MS, *m/e* (rel intensity), 190 (M$^+$, 100), 146 (84). Found: C, 75.44; H, 7.25%. Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42%.

Irradiation of 2a in the Presence of Diethylamine. A solution of **2a** (88 mg, 0.5 mmol) and diethylamine (365 mg, 5 mmol) in 10 cm^3 of anhydrous acetonitrile was irradiated for 3 h in a quartz tube with RPR-300 nm lamps at room temperature. After the evaporation of the solvent, the photolysate was separated by TLC on silica gel, using benzene as the eluent. The first band from the TLC plates gave 39 mg (44%) of **7a**. The second band contained 19 mg (15%) of the amide **8**: mp 121—122 °C; IR (CHCl$_3$), 3300, 1610 cm^{-1}; NMR (CDCl$_3$), δ=0.80—1.30 (6H, broad m), 1.40 (3H, d, J=6.5 Hz), 2.16 (1H, s), 2.41 (3H, s), 2.82—3.80 (4H, broad m), 4.21 (1H, q, J=6.5 Hz), 4.78 (2H, s), 7.00—7.30 (3H, m); MS, *m/e* (rel intensity), 249 (M$^+$, 16), 100 (100). Found: C, 72.53; H, 9.41; N, 5.66%. Calcd for $C_{15}H_{23}O_2N$: C, 72.25; H, 9.30; N, 5.62%.

Trap of the Ketene Intermediate by Low-temperature IR Spectroscopy. A glassy film of **2a** was placed on an infrared cell and irradiated externally with a 450-W medium-pressure mercury lamp through a CaF_2 cell window for infrared spectroscopy at *ca.* 77 K. A distinct new band, attributable to the ketene intermediate, appeared at $2120\ cm^{-1}$ after 3 h. This ketene band gradually disappeared with the rise in the temperature to the ambient temperature, a new band appeared at $1730\ cm^{-1}$ due to the carbonyl group of **7a**.

*Irradiation of **2a** in Methanol*-d_1. Three Pyrex tubes containing 27 mg (0.15 mmol) of **2a** in $0.4\ cm^3$ of MeOD were irradiated for several hours. The irradiation time and the ratio of the photoproducts of **7a—D** to **7a** (as determined by NMR spectroscopy using the signals of the methine proton at δ 3.50 and the methyl protons at δ 1.60), and the recovery yields of **2a** after separation through TLC, are listed in Table 1.

*Irradiation of **7a** in Methanol*-d_1. A solution of **7a** (22 mg, 0.13 mmol) in $1\ cm^3$ of MeOD was irradiated for 8 h. The photolysate was purified by TLC on silica gel, using benzene as the eluent, to give 18 mg (85%) of a mixture of **7a** and **7a—D** in a ratio of 1/1, as determined by means of the NMR spectrum.

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