Synthetic Photochemistry. XV. A Total Synthesis of Some Oxygenated Protoilludanes by an Application of Photo-Induced Cycloadditions

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Synthetic Photochemistry. XV.[1] A Total Synthesis of Some Oxygenated Protoilludanes by an Application of Photo-Induced Cycloadditions

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An effective preparation of protoilludanes was developed by use of two-fold photocycloadditions and methylation. Stereochemistry of the photocycloaddition processes was clarified on the basis of chemical transformations as well as the NMR evidence. Taking an advantage of this facile formation of the natural protoilludane ring derivation, some of the biogenetically significant oxygenated derivatives have been totally synthesized.

1. Introduction

Protoilludyl (protoilludanyl) cation[2] has been suggested to be a common biogenetic intermediate from humulene to illudoids, which are typical sesquiterpenoids from ferns,[3] fungi[4] and a marine organism, *Capnella ibmricata*.[5] The stereochemistry of illudol[6] and neoilludol,[7] metabolites of *Clitocybe illudens*, or of a hydrocarbon from *Fomitopsis insularis* (protoillud-6-ene)[8] were shown to possess the correct configuration predicted on this concept. Although illudol[9] and protoillud-7-ene[10] have been already synthesized by Matsumoto, we are interested to synthesizing the oxygenated derivatives in connection with the sequence of *in vivo* oxygenative rearrangements. In this paper, we will show a short-step synthesis of these derivatives.

As shown in Chart 1, a scheme of *retro*-synthesis suggests that the framework of protoilludanes can be prepared by a 5, 6 and 4-membered ring approach, *i.e.*, the photoreaction of 4,4-dimethylcyclopentene (**1**)[11] and a β-diketone, methyl 2,4-diketopentanoate (**2**),[12] must from a single adduct, and must be convertible into a dimethylhydroindenone, which must furnish the desired tricyclic system by another photochemical $(2+2)\pi$ addition with ethylenes. Furthermore, the carbonyl group of the adducts is located in the proper position.

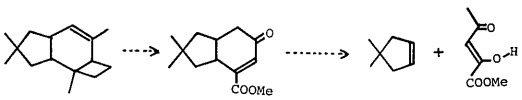

CHART 1

2. Results and Discussions

Thus, when a neat mixture of **1** and **2** was irradiated by means of a 400 W high-pressure mercury lamp at 10°C under nitrogen atmosphere, a formation of single reaction product (**3**) was detected on the thin-layer chromatograms.

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3, a colorless oil, was constantly obtained in more than 80% yields based on the consumed **2**. The NMR [δ[13]: 1.03 (3H, s), 1.10 (3H, s), 1.2–1.5 (2H, m), 1.6–1.8 (4H, m), 2.05 (3H, s), 2.4–2.9 (4H, m), and 3.86 (3H, s)] spectrum of **3** acertained the homogeneity, and the recovered material from the acid-treatment was identical with the starting compound, **3**. Therefore, **3** must be a stable (*trans*-) isomer. In cases of acetylacetone-olefin adducts, the cyclization into α, β-unsaturated ketones was extremely facile,[14] but the present adduct could only be cyclized by azeotropic removal of water from the benzene solution of **3** and *p*-toluenesulfonic acid (TsOH). The products obtained in quantitative yields were *cis*- and *trans*-mixture of hydroindenones (**4** and **5**). Separation of **4**, a colorless oil, and **5**, a colorless oil, was made either on a silica gel column or by use of a high-pressure liquid chromatograph. Since a further acid treatment of **5** caused an isomerization into **4**, and in the NMR spectra, **4** [δ: 1.05 (6H, s), 1.34 (1H, dd, J=13, 6 Hz), 2.09 (1H, dd, J=14, 8 Hz), 2.80 (1H, m), 3.23 (1H, dd, J=17, 7 Hz), 3.84 (3H, s), and 6.66 (1H, d, J=1 Hz)] and **5** [δ: 1.06 (3H, s), 1.11 (3H, s), 1.1–1.4 (2H, m), 1.6–1.8 (2H, m), 2.05–2.3 (2H, m), 2.4–2.8 (2H, m), 3.80 (3H, s), and 6.59 (1H, d, J=3 Hz)], disclosed a clear difference in the magnitude of a long-range coupling constant of the olefinic protons, *i. e.*, J=1 Hz for **4** and J=3 Hz for **5**, the former is *cis*-, and the latter is *trans*-isomer.

In respects of our purpose, the (2+2) π cycloaddition of **4** and ethylene (**6**) should directly give a *nor*-protoilludane, but, **4** was entirely unreactive with **6**, and with some other vinyl derivatives, 1,2-dichloroethylene, trichloroethylene, and allyl acetate. On the other hand, **5** and **6** smoothly produced two 1 : 1-photoadducts (**7**, a colorless oil, and **8**, a colorless oil) in good yields. The stereochemistry of these compounds was deduced from the chemical evidence: With lithium aluminum hydride (LAH), **7** gave **9**, colorless needles, and **8** gave **10**, colorless crystals, in quantitative yields. The NMR spectra of **9** [δ: 1.01 (3H, s), 1.03 (3H, s), 1.1–2.1 (14H, m), 2.60 (1H, m), 3.45 (2H, s), and 3.72 (1H, m)] and **10** [δ: 1.02 (3H, s), 1.06 (3H, s), 0.8–2.3 (15H, m), 3.46 (2H, s), and 3.86 (1H, m)] showed a contrast, an appearance of 1H signal around δ 2.6 for only **9**. This was also the case in the Grignard reaction products; with methylmagnesium iodide, **7** and **8** afforded **11** and **12**, colorless oils, and the NMR spectra of **11** [δ: 1.00 (3H, s), 1.05 (3H, s), 1.07 (3H, s), 1.1–2.6 (13H, m), and 3.68 (3H, s)] and **12** [δ: 1.02 (3H, s), 1.05 (3H, s), 1.09 (3H, s), 1.1–2.6 (12H, m), 2.66 (1H, tm, J=8 Hz), and 3.69 (3H, s)] again disclosed a contrast. Although this contrast might be due to a difference in configuration, determination of the stereochemistry was made on the chemical transformations. Thus, a dehydration of **11** and **12** was at first carried out. By a mild treatment with iodine in benzene, **11** afforded **13**, a colorless oil, in a 98% yield. Its NMR [δ: 1.01 (3H, s), 1.05 (3H, s), 1.56 (3H, br. s), 1.1–2.5 (10H, m), 3.70 (3H, s), and 5.52 (1H, br. s)] acertained the formation of vinyl methyl group. Similarly, **12** gave **14** [δ: 1.04 (6H, s), 1.61 (3H, br. s), 1.1–2.9 (11H, m), 3.70 (3H, s), and 5.52 (1H, br. s)], a colorless oil.

By reduction with LAH, **13** and **14** produced unsaturated alcohols (**15** and **16**), colorless oils, in good yields, which were acetylated into **17** and **18**, colorless oils. The *m*-chloroprbenzoic acid (MCPA)-epoxidation of both **15** and **16** stereospecifically yielded **19**, a colorless oil, and **20**, a colorless oil. **19** and **20** were also characterized as acetates, **21** and **22**, colorless oils. However, the same reaction with **17** (the acetate of **15**) yielded two isomers (**21** and **23**), colorless oils, while **18** (the actate of **16**) solely yielded **22**. The correlation of the minor product (**21**) of the epoxidation of **17** with the product of **15** therefore indicates that the *syn*-direction to the cyclobutane of **16** and **18** is more hindered than that of **15** and **17**. According to a molecular model inspection, the cyclobutane side of *trans-anti-cis* derivatives is more hindered than *trans-syn-cis* derivatives, hence the former series has a correct configuration for natural products syntheses.

This was further confirmed by Lewis acid catalyzed isomerization reaction. When **22** was treated with boron trifluoride etherate in benzene at room temperature for 6 min, a ready rearrangement occurred to give two products (**24** and **25**). **24**, the major product, 53%, was shown to contain fluorine atom and a secondary alcohol group. The NMR [δ: 1.07 (6H, s), 1.29 (3H, s), 1.2-2.0

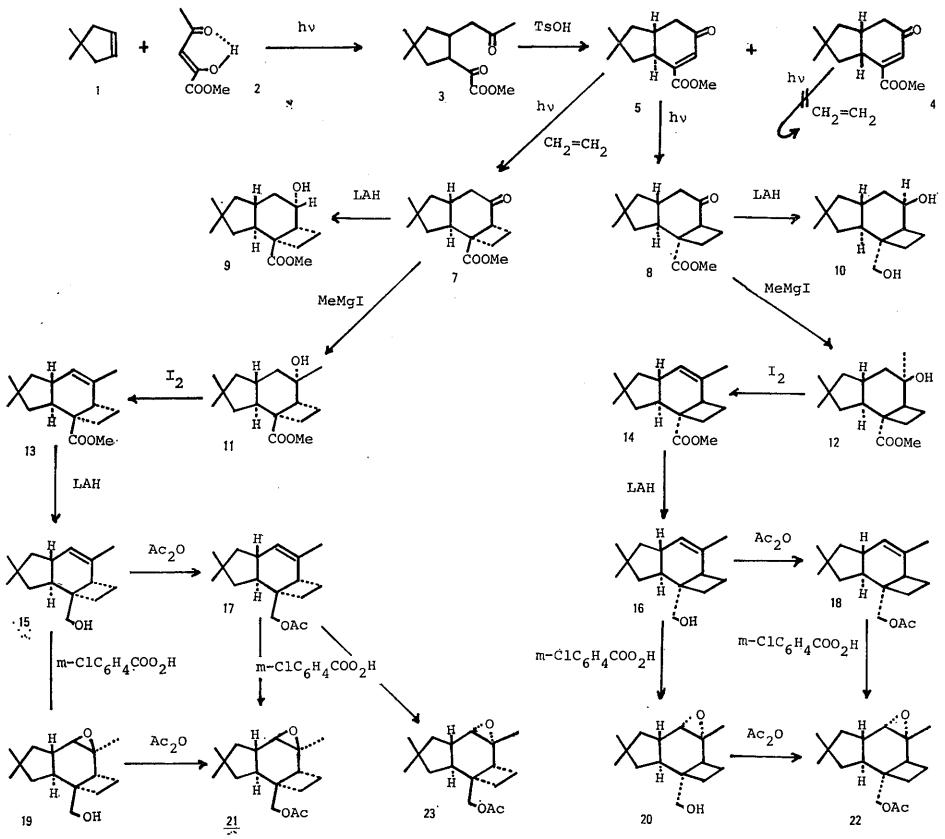

CHART 2

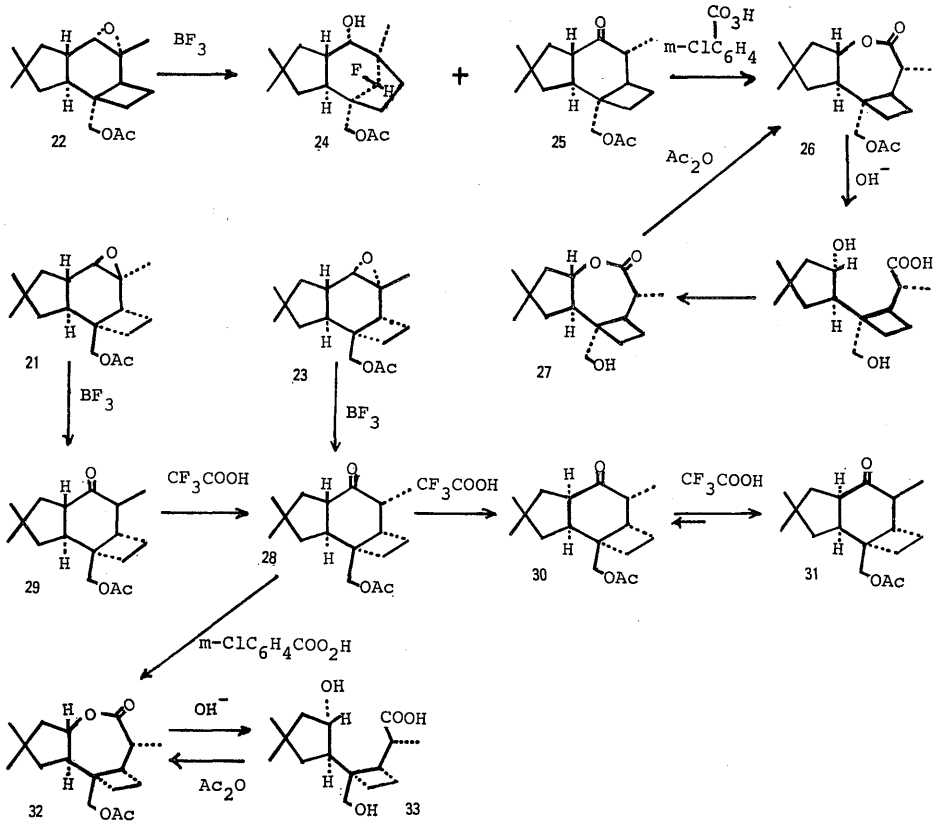

CHART 3

(11H, m), 2.05 (3H, s), 3.36 (1H, m, but changed to d, J=3 Hz by addition of D_2O), 3.86 (1H, d, J=11 Hz), 4.01 (1H, d, J=11 Hz), and 4.44 (1H, d, J=56 Hz)] spectrum and the ^{13}C-NMR [δ: 20.3 (d, J=7 Hz), 21.6 (d, J=2 Hz), 30.0 (d, J=10 Hz), 31.9, 32.3, 36.2, 37.1 (d, J=7.3 Hz), 40.1, 40.6, 43.8, 44.1 (d, J=10 Hz), 45.8 (d, J=15 Hz), 101.2 (d, J=195 Hz)] spectrum clarified the full stereostructure: Since i), no longer doublet methyl signal is present, ii), the carbon bearing the fluorine atom is linked to two carbons bearing no hydrogen, iii), the fluorine atom is spin-coupled with over seven carbon atoms, and iv), a large chemical shift difference is observed for the signals ascribable for the cyclobutane ring, a formation of a bicyclo [3.2.1] octane moiety is indicated. Furthermore, the magnitudes of the $^3J_{C-F}$ with methylene carbons were larger than those with methine carbons, which suggested the orientation of the fluorine atom. The conformation of the hydroxy group must be axial since the coupling constant of the methine proton with the adjacent proton is 3 Hz. These observations all together clarified the stereochemistry of **24** as depicted in Chart 3.

The minor product (**25**), 34%, is a predicted ketoester. The Baeyer-Villiger oxidation of **25** by MCPA yielded a single ε-lactone (**26**), colorless crystals, 76%. The NMR [δ: 1.04 (3H, s), 1.10 (3H, s), 1.16 (3H, d, J=6.5 Hz), 1.4-2.4

(10H, m), 2.06 (3H, s), 3.07 (1H, m), 3.92 (1H, d, J=12 Hz), 4.03 (1H, d, J=12 Hz), and 4.96 (1H, m)] clarified the position of newly introduced oxygen function. Saponification and relactonization of **26** gave an ε-lactone derivative (**27**) which was acetylated into the starting **26**. The other way of lactonization may give a carbon skeleton of fomannosane derivative[15].

Similarly, the Lewis acid-induced isomerizations of **21** and **23** were carried out: A mild boron trifluoride etherate treatment of **21** also produced kinetically controlled products, **28**, 3%, and **29**, 97%, while a similar reaction with **23** produced **30**, 5%, and **28**, 95%. These keto acetates (**28**, **29**, and **30**) were further epimerized into a mixture of stable isomers. Thus, starting either **28**, **29**, or **30**, they have given the same mixture of **30** and **31** in a ratio of 1 : 6, by treatment with trifluoroacetic acid at room temperature. Therefore, the latter two acetates must belong to the natural *cis-anti-cis* series, and they could be designated as protoilludan-8-ones. Interestingly, **28** produced also an ε-lactone (**23**) by Baeyer-Villiger oxidation. Saponification of **32** by alcoholic alkali produced dihydroxyacid (**33**). Acetic anhydride treatment of **33** reproduced the original ε-lactone, **32**.

These findings constitute an establishment of the stereochemistry of photocycloadducts as depicted, and opened a new entry to the natural protoilludane derivatives having various oxygen functions. We are currently undertaking the study on various aspects of chemistry of synthetic protoilludanes and will be reported elsewhere.

3. Experimental Section

Photocycloaddition Reaction of 4,4-*Dimethylclopentene* (**1**) *and Methyl* 2, 4-*Diketopentanoate* (**3**). A neat mixture of **1** (60 cm^3) and **2** (12 g) was placed in a glass cylinder fitted with a 400 W high-pressure mercury lamp with a Pyrex glass filter. The whole apparatus was cooled with ice-water, and irradiated under nitrogen atmosphere. After 20 h, the mixture was distilled *in vacuo* to recover the unreacted olefin and the residue was chromatographed on a silica gel column. A colorless oil thus obtained was **3**, weighed 10 g (81.3%) [Found: C, 64.84; H, 8.41%. M. W., 240.1354. Calcd for $C_{13}H_{20}O_4$: C, 64.98; H, 8.39%. M. W., 240.1362. ν: 1720–1740, 1260, 1100 cm^{-1}], along with the recovered **2** (2.3 g).

Cyclization of **3**: *Formation of* α, β-*Unsaturated Ketoesters* (**4** *and* **5**). An anhydrous benzene solution (20 cm^3) of **3** (2.3 g) and TsOH (20 mg) was refluxed with a Dien-Stark apparatus for 10 h. After removal of the solvent by distillation, the residue was chromatographed on a silica gel column to give a colorless oil, 1.8 g, which was shown to be a mixture of **4** [Found: C, 70.13; H, 8.21%. Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16%. ν: 2960, 1730, 1660 cm^{-1}] and **5** [Found: C, 70.22; H, 8.20%. ν: 2960, 1730, 1667 cm^{-1}], in a variable ratio. The separation of **4** and **5** was achieved by use of a high-pressure liquid chromatograph (Micropolasil with hexane-ethyl acetate).

An Acid-Induced Isomerization of **5** *into* **4**. **5** (40 mg) was dissolved in chloroform containing a small amount of trifluoroacetic acid, and was kept at room temperature for 24 h. The NMR signals of the mixture consisted of solely **4**.

Attempted Photochemical Reaction of **4** *with Ethylene* (**6**). A dichloromethane solution (10 cm^3) of **4** (30 mg) was externally irradiated by a 400 W high-pressure mercury lamp with bubbling of **6** at −70°C for 2 h. Then, the mixture was warmed up to room temperature and heated to remove the solvent. The residue was consisted of solely **4** (290 mg).

Attempted Photoreaction of **4** *with Some Vinyl Derivatives*. The NMR tubings (5 mm in diameter) containing each **4** (*ca.* 40 mg) in *ca.* 0.3 cm^3 of trichlorethylene, dichloroethlene (a commercial sample of *cis/trans*-mixture) or methyl allyacetate were externally irradiated for 6 h. No distinguishable change was observed in every case.

Photocycloaddition Reaction of **5** *with* **6**. A dichlorormethane solution (10 cm^3) of **5** (40 mg) was externally irradiated by a 400 W highpressure mercury lamp with continuous introduction of **6** at −70 to −60°C for 40 min. After removal of the solvent, the residue was separated by use of a high-pressure liquid chromatograph (micropolasil/hexane-ether) to give **8**, a colorless oil [Found: M. W., 250.1572 Calcd for $C_{15}H_{22}O_3$: 250.1569. ν: 2940, 1740, 1705 cm^{-1}], and **7**, a colorless oil [Found: M. W., 250.1577. ν: 2940, 1705 cm^{-1}], in a ratio of 1 : 2.

Preparation of **7** *and* **8** *by Photocyloaddition of* **5** (*a Mixture with* **4**) *and* **6**. A mixture of **4** and **5** (1.8 g) was dissolved in dichloromethane (150 cm^3), and the solution was cooled by ice-water bath (*ca.* 5°C) and externally irradiated by a 400 W high-pressure mercury lamp with continuous introduction of **6** for 1 h. After removal of the solvent, the mixture was chromatographed on a silica gel column. The fractions eluted with benzene-ether (99 : 1) afforded a colorless oil, **8**, 55 mg, as pure form, which was followed by elution of an oily mixture of **7** and **8** 820 mg (2 : 1). Subsequently, a colorless oil, 850 mg, was obtained from the elution of benzene-ether (10 : 1), and identified to be **4**. Rest of the mixture was not further fractionated.

LAH Reduction of **7** *and* **8**. **7** and **8** (as a mixture, 40 mg) was dissolved in anhydrous ether (20 cm^3) and reduced by LAH (10 mg). After 1 h, the mixture was treated with methanol, and extracted by ether. Silica gel column chromatography of the extracts produced **9**, colorless crystals, mp 162–163°C (from methanol), 23.5 mg (65%) [Found: C, 74.77; H, 10.79%. Calcd for $C_{14}H_{24}O_2$: C, 74.95; H, 10.78%. ν: 3550, 2960 cm^{-1}], and **10**, colorless crystals, mp 120–121°C (from methanol), 11 mg (30.5%) [Found: C, 74.86; H, 10.90%. ν: 3550, 2950 cm^{-1}].

LAH Reduction of **8**. **8** (15 mg) dissolved in ether (10 cm^3) was similarly reduced with LAH (10 mg). After an ordinary work up, the sole product isolated was **10**, colorless needles, mp 120–121°C, 11 mg (81%).

The Grignard Methylation Reaction of **7** *and* **8** (*as a Mixture*). Into an ether solution (20 cm^3) of **7** and **8** (298 mg), methylmagnesium iodide (prepared from 800 mg of methyl iodide) in anhydrous ether was added in drop by drop. The mixture was then hydrolyzed by aqueous NH_4Cl, and extracted with ether. A colorless oil obtained after evaporation of the solvent was purified by silica gel chromatography to give **11**, a colorless oil, 95 mg (29.7%) [Found: M. W., 266.1890. Calcd for $C_{16}H_{26}O_3$: 266.1882. ν: 3500, 2950, 1740–1700, 1240 cm^{-1}], and **12**, a colorless oil, 205 mg (64.1%) [Found:

M. W., 266.1861. ν: 3480, 1720, 1240, 1135 cm^{-1}].

Dehydration of **12**: *Formation of* **14**. An anhydrous benzene solution (50 cm^3) of **12** (45 mg) and iodine (*ca.* 3 mg) was refluxed for 10 h. The solution was then treated with aqueous sodium thiosulfate and dried on magnesium sulfate. The mixture obtained by removal of benzene afforded a colorless oil, **14**, 40 mg (95 %) [Found: M. W., 248.1756. Calcd for $C_{16}H_{24}O_2$: 248.1776. ν: 2960, 1720 cm^{-1}].

Dehydration of **11**: *Formation of* **13**. **11** (360 mg) and iodine (5 mg) was dissolved in benzene (80 cm^3) and refluxed for 10 h. Afer thiosulfate treatment, the mixture was purified by silica gel chromatography to give **13**, a colorless oil, 330 mg (98 %) [Found: M. W., 248.1773. ν: 2950, 1730, 1260, 1100 cm^{-1}].

The LAH Reduction of **13**: *Formation of* **15**. **13** (330 mg) dissolved in ether (50 cm^3) was reduced by ether solution of LAH (10 mg) with a gentle reflux for 2 h. Then, the mixture was hydrolyzed by methanol, and extracted with ether. A colorless oil obtained after silica gel chromatography was **15**, 281 mg (96 %) [Found: M. W., 220.1859. Calcd for $C_{15}H_{24}O$: 220.1827. ν: 3550, 2960 cm^{-1}].

The LAH Reduction of **14**: *Formation of* **16**. An anhydrous ether solution (20 cm^3) of **14** (30 mg) was reduced by LAH (5 mg). Then, the mixture was similarly worked up to give a colorless oil, **16**, 25 mg (95 %) [Found: M. W., 220.1858. ν: 3550, 2950 cm^{-1}].

Acetylation of **15** *into* **17**. **15** (20 mg) was acetylated by acetic anhydride (1 cm^3) and pyridine (0.5 cm^3), and a usual work up yielded a colorless oil, **17**, 20 mg (84 %) [Found: M. W., 262.1911. Calcd for $C_{17}H_{26}O_2$: 262.1932. ν: 2930, 1735, 1230, 1035 cm^{-1}].

Acetylation of **16** *into* **18**. Similarly, **16** (40 mg) was acetylated with acetic anhydride (5 cm^3) and pyridine (5 cm^3) to give a colorless oil, **18**, 39 mg (82 %) [Found: M. W., 262.1912. ν: 2940, 1740, 1235, 1040 cm^{-1}].

The Epoxidation of **15** *by MCPA*: *Formation of* **19**. A dichloromethane solution (20 cm^3) of **16** (20 mg) and MCPA (17 mg, 85 %) was kept at room temperature for 2 h. Then, the mixture was treated with sodium sulfite and exteacted by ether. Silica gel column chromatography of the mixture afforded a colorless oil, **19**, 21 mg (98 %) [Found: M. W., 236.1768. Calcd for $C_{15}H_{24}O_2$: 236.1776. ν: 3440, 2930 cm^{-1}].

The Acetylation of **19** *into* **21**. **19** (35 mg) was acetylated similarly to a colorless oil, **21**, 38 mg (92 %) [Found: M. W., 278.1919. Calcd for $C_{17}H_{26}O_3$: 278.1882. ν: 2950, 1740, 1250, 1040 cm^{-1}].

The Epoxidation of **16**: *Formation of* **20**. **16** (30 mg) was dissolved in dichloromethane (20 cm^3) to which, MCPA (24 mg) was added, and kept at room temerature for 2 h. Silica gel chromatography of the mixture yielded a colorless oil, **20**, 39 mg (96 %) [Found: M. W., 236.1776. ν: 3450, 2930 cm^{-1}].

Acetylation of **20** *into* **22**. **20** (30 mg) was acetylated with acetic anhydride (1 cm^3) and pyridine (0.5 cm^3) to give a colorless oil, **22**, 31 mg (88 %) [Found: M. W., 278.1878. ν: 2960, 1740, 1250, 1040 cm^{-1}].

Epoxidation of **17**: *Formation of* **21** *and* **23**. **17** (300 mg) dissolved in dichloromethane (50 cm^3) was epoxidized by MCPA (280 mg) for 4 h. After reduction of the excess reagent with sodium sulfite, the mixture was extracted with ether and chromatographed on silica gel column

to give **21**, 108 mg (34 %), which was identical with the previously obtained sample, and another colorless oil, **23**, 205 mg (64 %) [Found: M. W., 278.1909. ν: 2950, 1740, 1240 cm^{-4}].

Epoxidation of **18**: *Formation of* **22**. **18** (50 mg) dissolved in dichloromethane (25 cm^3) was epoxidized by MCPA (50 mg). Silica gel column chromatography of the mixture yielded a colorless oil, **22**, 52 mg (98 %), which was identical with the previously prepared sample.

BF_3-Catalyzed Isomerization of **22**: *Formation of a Fluoroalcohol* (**24**) *and a Ketone* (**25**). An anhydrous benzene solution (80 cm^3) of **20** (210 mg) was treated with freshly distilled *BF_3*-etherate (0.3 cm^3) at room termperature for a few min. Then the mixture was extracted with ether and aqueous sodium carbonate solution. The organic layer was dried on magnesium sulfate and chromatographed on a silica gel column to give a colorless oil, **25**, 70 mg (33 %) [Found: M. W., 278.1858. Calcd for $C_{17}H_{26}O_3$: 278.1882. δ: 1.06 (6H, s), 1.10 (3H, d, J =7 Hz), 1.1–2.2 (12H, m), 2.04 (3H, s), 3.92 (1H, d, J=11 Hz), and 4.09 (1H, d, J=11 Hz). ν: 2960, 1740, 1710, 1230, 1040 cm^{-1}], and a colorless oil, **24**, 120 mg (53 %) [Found: M. W., 298.1965. Calcd for $C_{17}H_{27}O_3F$: 298.1944. ν: 3620, 2950, 1740, 1240, 1040 cm^{-1}], together with unidentified colorless oil, 11 mg.

Baeyer-Villiger Oxidation of **25**. **25** (15 mg) was dissolved in dichloromethane (20 cm^3) and oxidized with MCPA (30 mg) for 24 h. The mixture was then chromatographed on a silica gel column to give colorless crystals, mp 129–130°C, **26**, 12 mg (76 %) [*m/e*, 294 (M^+). ν: 2960, 1740, 1230, 11230, 1125 cm^{-1}].

A Base-and-Acid Treatment of **26**. **26** (10 mg) was dissolved in methanol (20 cm^3) and saponified with potassium hydroxide. The mixture was then extracted with ether and water. The water layer was then acidified by HCl, and extracted with ether to give a colorless oil, 10 mg (97 %), **27** [*m/e*, 252 (M^+). δ: 1.02 (3H, s), 1.10 (3H, s), 1.13 (3H, d, J=6 Hz), 1.2–2.3 (11H, m), 3.06 (1H, qm, J=6 Hz), 3.50 (1H, d, J=11 Hz), 3.65 (1H, d, J=11 Hz), and 4.96 (1H, m). ν: 3600, 2960, 1725, 1185, 1065 cm^{-1}]. Acetylation of **27** gave the starting **26**, 8 mg.

BF_3-Catalyzed Isomerization of **21**. An anhydrous benzene solution (30 cm^3) of **21** (90 mg) was similarly treated with freshly distilled BF_3-etherate (0.5 cm^3) at room temperature for 10 min. An ordinary work up of the mixture by silica gel chromatography yielded a colorless oil, **28**, 5 mg (5 %) [Found: M. W., 278.1864. δ: 1.08 (3H, d, J=7 Hz), 1.11 (6H, s), 1.2–2.0 (12H, m), 2.07 (3H, s), and 3.99 (2H, s). ν: 2930, 1735, 1700, 1225, 1035 cm^{-1}], and a colorless oil, **29**, 84 mg (93 %) [Found: M. W., 278.1863. δ: 0.88 (3H, d, J=7 Hz), 1.06 (6H, s), 1.2–2.2 (12H, m), 2.12 (3H, s), 4.05 (1H, d, J=12 Hz), and 4.22 (1H, d, J=12 Hz). ν: 2950, 1740, 1715, 1240, 1040 cm^{-1}].

BF_3-Catalyzed Isomerization of **23**. An anhydrous benzene solution (30 cm^3) of **23** (50 mg) was treated with BF_3-etherate (0.4 cm^3) at room temperature. Separation of the product mixture gave a colorless oil, 47 mg (95 %) which was identical with **28**, and another colorless oil, **30**, 1.4 mg (3 %) [Found: M. W., 278.1873. δ: 1.04 (6H, s), 1.08 (3H, d, J=7 Hz), 1.2–2.2 (12H, m), 2.07 (3H, s), and 4.16 (2H, s). ν: 2940, 1740, 1710, 1230, 1040 cm^{-1}].

The Isomerization of **29** *with Trifluoroacetic*

Acid: *Formation of* **30** *and* **31**. **29** (20 mg) was dissolved in CF_3COOD (0.3 cm^3) and kept at room temperature for 7 d. The NMR spectral analysis of the mixture revealed an intermediary occurrence of **28**, but in later stage, the composition of the mixture was shown to be **30** : **31**= 1:6. The new isomer (**31**), 14 mg (70 %) [Found: M. W., 278.1894. δ: 0.90 (3 H, d, J=7 Hz), 0.96 (3H, s), 1.09 (3H, s), 1.1-2.0 (10H, m), 2.09 (3H, s), 3.98 (1H, d, J=12 Hz), and 4.19 (1H, d, J=12 Hz). ν: 2940, 1735, 1710, 1230 cm^{-1}], was isolated after silica gel chromatography.

The Acid-Induced Isomerization of **30**. **30** (15 mg) was dissolved in CF_3COOD (0.3 cm^3) and kept at room temperature for 7 d. The NMR spectrometry indicated the ratio of **30** : **31** as 1 : 6.

Baeyer-Villiger Oxidation of **28**. **28** (50 mg) was dissolved in dichloromethane (25 cm^3) and MCPA (45 mg) was added at room temperature. After 5 h, the mixture was chromatographed on a silica gel column. As a colorless oil, 41 mg (78 %), obtained was **32** [m/e: 294 (M^+). δ: 1.06 (3H, s), 1.10 (3H, d, J=6.5 Hz), 1.16 (3H, s), 2.11 (3H, s), 3.05 (1H, m), 3.95 (1H, d, J=12 Hz), 4.32 (1H, d, J=12 Hz), and 4.98 (1H, m). ν: 2960, 1745, 1240, 1180, 1125 cm^{-1}].

Saponification of **32**. **32** (10 mg) and KOH (30 mg) were dissolved in methanol (10 cm^3) and heated on a steam bath for 30 min. Then, the mixture was diluted with water and extracted by ether. The water layer was acidified by dil HCl, and extracted again with ether. The ether extract was evaporated to dryness to leave a colorless oil, **33**, 8 mg (77 %) [m/e: 252 (M^+). δ: 1.07 (3H, s), 1.11 (3H, d, J=6.5 Hz), 3.14 (1H, m), 3.55 (1H, d, J=12 Hz), 3.72 (1H, d, J=12 Hz), and 5.12 (1H, m). ν: 3500, 2940, 1735, 1240, 1050 cm^{-1}].

Regeneration of **32** *from* **33**. **33** (5 mg) was dissolved in acetic anhydride (0.5 cm^3) and warmed to 80°C for 1 h. Then the mixture was heated to remove the excess reagent and the residue was washed with water and extracted by ethyl acetate. A colorless oil thus obtained was identical with **32** on the basis of an NMR comparison.

References and Note

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