December, 1980] © *1980 The Chemical Society of Japan* *Bull. Chem. Soc. Jpn.*, ***53***, *3641—3647 (1980)* 3641

Synthetic Photochemistry. XIX.[1)] The Synthesis of Protoilludanes by Photocycloadditions. Protoillud-7-ene and Several Oxygenated Derivatives

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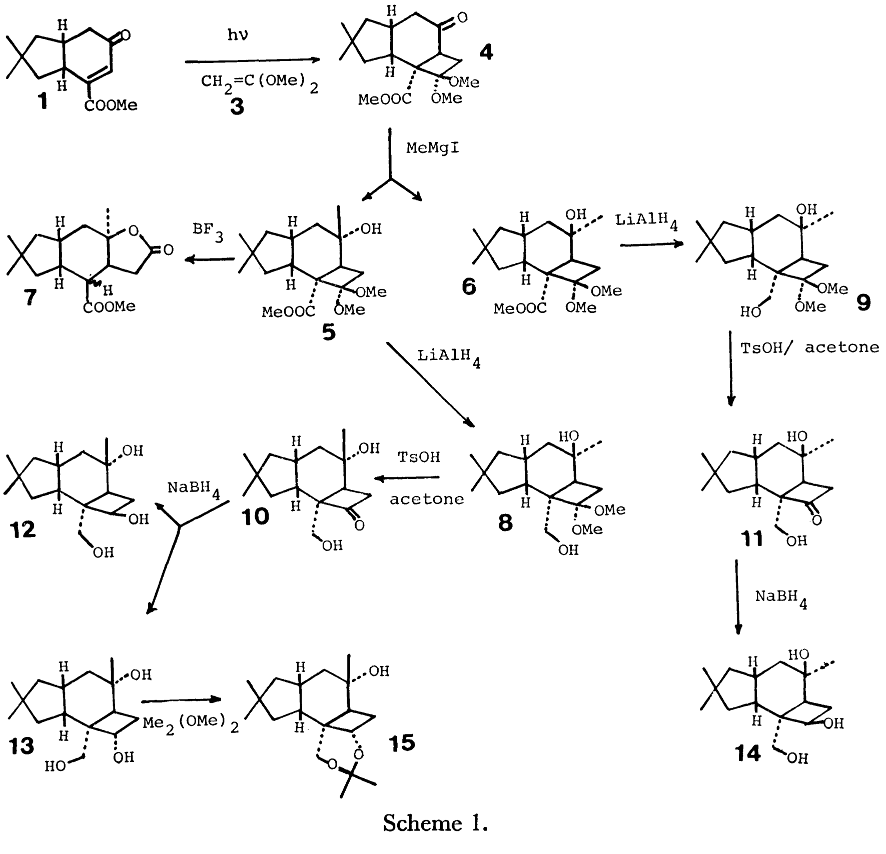
(Received February 27, 1980)

Unlike ethylene, 1,1-dimethoxyethene, an electron-rich olefin, has been photocycloadded to a *cis*-hexahydroindenone to form a norprotoilludane derivative with a correct stereostructure. Methylation and subsequent chemical transformations yielded several oxygenated derivatives, from which the parent hydrocarbon, protoillud-7-ene, was obtained by deoxygenation. Independent evidence for the stereostructures of the synthetic derivatives has been provided by the X-ray crystallographic analysis of a dihydroxy acetal.

In previous papers,[2)] we have described a new approach to obtaining several oxygenated protoilludanes, biogenetic precursors of *gem*-dimethylcyclopentane sesquiterpenoids[3)] from various organisms,[4)] by the application of two-fold photocycloadditions, followed by methylation. However, this approach has a practical limitation; that is, with ethylene (**A**), only the *trans*-isomer (**B**) of the hexahydroindenones, *trans*-2-methoxycarbonyl-8,8-dimethylbicyclo[4.3.0]non-2-en-4-ones, is photochemically reactive, while the stereochemistry of natural protoilludanes possesses the *cis*-relationship. In this paper, we will describe a facile synthesis of the protoilludane derivatives from the *cis*-hexahydroindenones, *cis*-2-methoxycarbonyl-8,8-dimethylbicyclo[4.3.0]non-2-en-4-one (**1**) and 2,8,8-trimethylbicyclo[4.3.0]non-2-en-4-one (**2**), with an electron-rich olefin, 1,1-dimethoxyethene (**3**). According to a preliminary study, 1,1-dichloroethene was also photochemically unreactive to **1**, but vinyl acetate gave a complex product mixture.

Results and Discussion

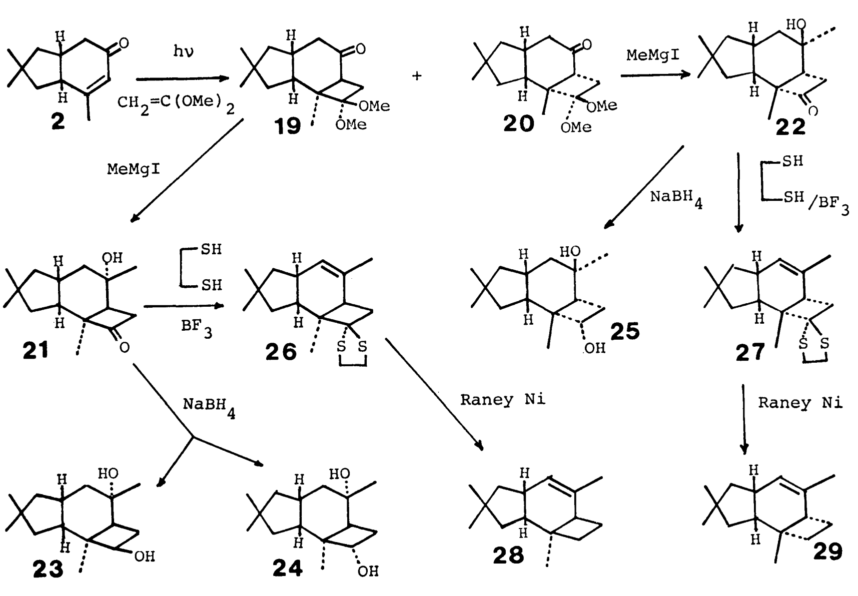
The reaction of **1** with **3** was neat and gave only one adduct, 3,3-dimethoxy-2-methoxycarbonyl-10,10-dimethyltricyclo[6.3.0.0^{2,5}]undecan-6-one (**4**). This stereoselective formation itself may be an indication of the desired *cis-transoid-cis*-structure. With regard to this concept, we have decided to carry out further transformations. Thus, by Grignard methylation, **4** was converted to a pair of epimers, 3,3-dimethoxy-2-methoxycarbonyl-6,10,10-trimethyltricyclo[6.3.0.0^{2,5}]-



Scheme 1.

undecan-6-ols, **5**, the major product, and **6**. Against the attack of the reagent, the methoxycarbonyl group at the quarternary carbon was intact, as in the case of **B**.[3)] Although **5** and **6** could be separated by silica-gel column chromatography, their cyclobutane rings were acid-sensitive; for example, the treatment of **5** with *p*-toluenesulfonic acid (TsOH) caused a ring-cleavage to yield a *seco*-*γ*-lactone, 4-hydroxy-2-methoxycarbonyl-4,8,8-trimethylbicyclo[4.3.0]non-3-ylacetic acid lactone (**7**), which has the same carbon skeleton as the pterosins.[5)] To avoid this, the acetal group was hydrolyzed after an LAH reduction of the methoxycarbonyl group, *via* dihydroxy acetals, 2-hydroxymethyl-3,3-dimethoxy-6,10,10-trimethyltricyclo[6.3.0.$0^{2,5}$]-undecan-6-ols (**8** and **9**), to dihydroxy ketones, 6-hydroxy-2-hydroxymethyl-6,10,10-trimethyltricyclo-[6.3.0.$0^{2,5}$]undecan-3-ones (**10** and **11**). Subsequently, **10** was reduced with sodium borohydride to give isomeric 6-hydroxymethyl-6,10,10-trimethyltricyclo-[6.3.0.$0^{2,5}$]undecan-3,6-diols (**12** and **13**), while **11** yielded only **14**, the isomer of **12** and **13**, on the same treatment. The configuration of the methyl group can be deduced by NMR analysis; *i.e.*, the signals at δ: 1.22 in **6** ascribable to the newly introduced methyl groups have been changed by the reduction of the ester group to 1.12 in **9**, but the 1.12 in **5** has remained unaffected, as appears at 1.12 in **8**. Therefore, from the difference in the chemical shifts, $\Delta\delta_{(5-8)}=0.00$ and $\Delta\delta_{(6-9)}=0.10$, the methyl groups of **5** and **8** may be considered to be *trans* to the substituents carrying oxygen at the quarternary carbon (C-2), while those of **6** and **9** are *cis*. The NMR spectra of **12**, **13**, and **14** also disclosed a stereochemical point: only **13** revealed the methine proton signal (a triplet), which is ascribable to the secondary alcohol on the cyclobutane ring, coupled with the adjacent methylene group, at δ; 4.07 ($J=7$ Hz); on the other hand, **12**, at 4.10 (br. m), and **14**, at 4.03 (br. m), disclosed a further splitting due to a long-range coupling with the C-6 methine proton. Since such long range couplings arise from the *W*-letter-like geometry, the hydroxyl group of the cyclobutanol of **13** must be *cis* to the methine proton at the ring juncture (C-5), but those of **12** and **14** are *trans*. Independently, an attempted formation of the acetals of **12**, **13**, and **14** with 2,2-dimethoxypropane established the correctness of the assumption; only **13** yielded a cyclic acetal 5,5,10,14,14-pentamethyl-4,6-dioxatetracyclo[10.3.0.-$0^{2,7}$.$0^{2,9}$]pentadecane (**15**), at room temperature, while **12** or **14** resulted in the recovery of the respective starting material, plus unidentified products. The stereochemistry shows that the reduction has occurred preferentially from the same side of the oxygen functions in the molecules, which can form the metal-coordinated intermediate.

This strategy on the synthesis can be extended to the parent protoilludene from **2**. To prepare **2**, a primary choice must be a well known procedure,[6)] *i.e.*, the photoaddition of acetylacetone with 4,4-dimethylcyclopentene, followed by the cyclization. However, the photoaddition in this case has been shown to be impractical because of its slow rate. Consequently, **2** was prepared by derivation from **1** as follows: The reaction of **1** with 1,2-ethanediol afforded a 1,3-dioxolane, **16**, which was then reduced by LAH and hydrolyzed by TsOH to give a hydroxy derivative (**17**). An acetate of **17**, *cis*-2-acetoxymethyl-8,8-dimethylbicyclo[4.3.0]-non-2-en-4-one (**18**), was reduced with zinc in acetic acid to form **2**. The photochemical cycloaddition of **2** with **3** produced two photocycloadducts, 3,3-dimethoxy-2,10,10-trimethyltricyclo[6.3.0.$0^{2,5}$]undecan-6-ones (**19** and **20**). Thus, the replacement of the ester group on the quaternary carbon with a methyl group resulted in an inferior stereoselectivity. The Grignard methylation, followed by a mild hydrolysis of **19** and **20**, produced cyclobutanone derivatives, 2,6,10,10-tetramethyl-3-oxotricyclo[6.3.0.$0^{2,5}$]undecan-6-ols (**21** and **22** respectively). By reduction with sodium borohydride, **21** produced an epimeric pair of glycols, 2,6,10,10-tetramethyltricyclo[6.3.0.$0^{2,5}$]undecan-6-ols (**23** and **24**), while **22** produced **25**, the isomer of **23** and **24**, as the



Scheme 2.

sole product. The configurations of their hydroxyl groups were again obtained by means of the NMR spectra: **24** showed a triplet at δ: 4.15 (t, J=8 Hz), but **23** (at 3.68) and **25** (at 3.89) showed multiplets. Therefore, only **24** has a *trans*-relationship to two methine protons on the cyclobutane ring. Both **21** and **22** were converted into 1,3-dithiolanes, **26** and **27**, accompanied by the dehydration of the tertiary alcohol function.7) The Raney nickel desulfurization of these thio-acetals afforded the parent protoillud-7-ene (**28**), *cis-transoid-cis*-2,6,10,10-tetramethyltricyclo[6.3.0.0^{2,5}]undec-6-ene, and epi-protoillud 7-ene (**29**). The identity of **28** with the previous sample was proved by NMR comparison with the reported data.8,9) Consequently, this constitutes an alternative total synthesis of **28** and its related derivatives.

Although the above synthesis of the derivatives with the correct stereochemistry left no doubt as to the working hypothesis, we have also carried out an X-ray crystallographic analysis in order to provide independent evidence. Since every trial of the halogenated derivatives has failed, a halogen-free derivative, **9**, was submitted to the analysis. The single crystal of **9**, monoclinic, belongs to the space group C2/c, and its crystal data showed the following features: a=15.138, b=11.486, c=20.744×10^{-8} cm, β=112.2°, d_x=1.186 g/cm^3, and Z=8. The 1278 non-zero reflections with (F_0) —2.3 σ (F_0) were collected on a Syntex P$\bar{1}$ four-circle diffractometer with graphite-monochromated Mo K_α radiations in the θ-2θ scanning mode. The structure was solved by the direct method.10) After several cycles of block diagonal least-squares refinement with anisotropic thermal parameters for non-hydrogen atoms and with isotropic ones for hydrogen atoms, except for one of the hydroxyl hydrogens, the final R value was 0.05. Figure 1 shows the structure views along the β-axis.

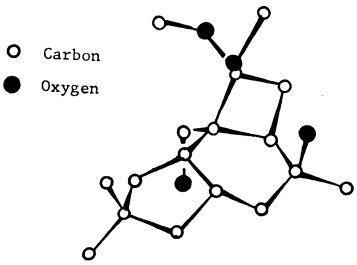


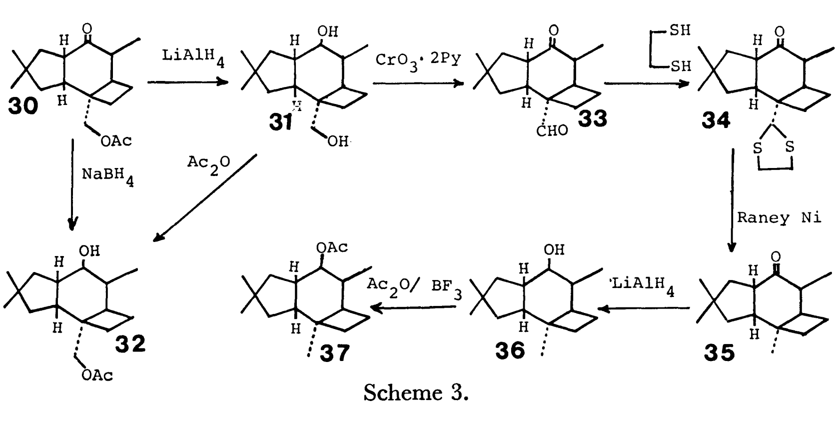
Fig. 1.

Meanwhile, we have carried out some deoxygenation reactions of the previously obtained protoilludanone, 2-acetoxymethyl-6,10,10-trimethyltricyclo[6.3.0.0^{2,5}]undecan-7-one (**30**).3) The LAH reduction of **30** afforded 2-hydroxymethyl-6,10,10-trimethyltricyclo[6.3.0.0^{2,5}]undecan-7-ol (**31**), an oil. The acetylation of **31** occurred at only the primary alcohol group to give a monoacetate (**32**), but a chromium(VI) oxide oxidation in pyridine gave a keto aldehyde, 2-formyl-6,10,10-trimethyltricyclo[6.3.0.0^{2,5}]undecan-7-one (**33**), in a good yield. Upon treatment with 1,2-ethanedithiol and boron trifluoride etherate, **33** formed a mono(ethylenedithioacetal) (**34**). The Raney nickel desulfurization of **34** gave 2,6,10,10-tetramethyltricyclo[6.3.0.0^{2,5}]undecan-7-one (**35**), which corresponds to 8-oxoprotoilludane; it was then converted to a hydroxy derivative, **36**. An acetate (**37**) of **36** could be prepared only under forced conditions, in acetic anhydride with boron trifluoride, showing the sterically hindered environment of the hydroxyl group.

Finally, we would like to make a comment on the biogenesis of the pterosines (*seco*-protoilludanes).11) Sakan *et al.*12) have pointed out that, based on the actual *in vitro* transformation, hypacrone (**C**), a congener *seco*-illudane derivative from brackens, must be a precursor. However, as is shown in the present experiments, oxygenated protoilludanes, like **5** or **6**, caused a retro-aldol cleavage into a pterosane skeleton. Therefore, the oxygenated protoilludanes and their relatives are likely to give these widely distributed aromatic metabolites *in vivo*.

Experimental

The mp's, determined with a Yanagimoto Model apparatus, are uncorrected. The ^{1}H- and ^{13}C-NMR spectra were measured, unless otherwise stated, in $CDCl_3$ by means of an FX 100 Model spectrometer, Nippon Denshi Co. (JEOL), while the chemical shifts expressed are the δ values from the internal standard, Me_4Si. The IR spectra were taken by an A-102 Model spectrometer, Nippon Bunko Kogyo Co. (JASCO), in CCl_4 solutions or KBr disks. The mass spectra were taken by means of an OS Gl Model spectrometer, JEOL, and the high-resolution figures were obtained by visual readings on the photographic plates. The high-pressure liquid chromatography was performed by means of an ALC 440/110 Model Apparatus, Nippon Waters Co. The elemental analyses were performed at The Elemental Analyses Center, The Faculty of Science, Kyushu University.



Scheme 3.

*An Attempted Photoreaction of **1** with 1,1-Dichloroethene.* A mixture of **1** (50 mg) and 1,1-dichloroethene (0.3 cm^3) was externally irradiated by means of a high-pressure mercury lamp for 6 h. The NMR analysis revealed only signals ascribable to the recovered materials.

*Photocycloaddition of **1** with Vinyl Acetate.* A mixture of **1** (30 mg) and vinyl acetate (0.5 cm^3) was externally irradiated for 6 h. The NMR spectral analysis indicated the occurrence of at least three photoadducts. A silica-gel column fractionation showed an extensive decomposition to aldehydic compounds. No further work was carried out.

*Photocycloaddition Reaction of **1** with **3**.* The freshly prepared **3**, from 2-chloro-1,1-dimethoxyethane (8 g) and potassium *t*-butoxide, was mixed with **1** (1.2 g) and then externally irradiated through a Pyrex glass filter by means of a 400 W high-pressure mercury lamp at 15—20 °C for 20 h under a nitrogen atmosphere. After the evaporation of the volatile material, the residue was purified on a silica-gel column; subsequent elution from ethyl acetate–hexane (1 : 9) yielded a colorless oil, **4**, 1.2 g (67%) [Found: C, 65.81%; H, 8.47%. Calcd for $C_{17}H_{26}O_5$: C, 65.78; H, 8.44%. δ: 1.05 (3H, s), 1.10 (3H, s), 1.2—2.9 (11H, m), 3.20 (3H, s), 3.27 (3H, s), and 3.76 (3H, s). δ (C): 31.9, 32.2 (2C), 35.6, 39.1 (2C), 40.1, 42.6, 43.0, 47.8, 49.3, 50.1, 51.8, 65.7, 103.2, 172.4, and 211.3], which was homogeneous in respect to NMR and gas-liquid chromatography.

*The Grignard Methylation of **4**.* To methylmagnesium iodide prepared from methyl iodide (2.3 g) in ether (20 cm^3), an ethereal solution (20 cm^3) of **4** (610 mg) was added, drop by drop, over a 3-h period at 0—5 °C; the mixture was then refluxed for 3 h. The mixture was then hydrolyzed and extracted by ether. The extracts were dried ($MgSO_4$) and chromatographed on a silica-gel column to give a colorless oil (420 mg), which was further fractionated by a pre-packed silica-gel column to give colorless crystals, **5** (mp 95—96 °C (from ethyl acetate–hexane); 300 mg (47%) [Found: C, 65.99; H, 9.21%. Calcd for $C_{18}H_{30}O_5$: C, 66.23; H, 9.26%. δ: 0.99 (3H, s), 1.03 (3H, s), 1.12 (3H, s), 1.4—1.9 (7H, m), 1.90 (1H, br. s), 2.1—2.7 (4H, m), 3.19 (3H, s), 3.35 (3H, s), and 3.71 (3H, s). δ (C): 27.6, 30.4, 30.9, 31.3, 34.6, 36.0, 36.6, 40.3 (2C), 44.1, 48.8, 49.6, 50.6, 51.6, 59.8, 70.1, 102.1, and 174.7]), and a colorless oil, **6** (80 mg (12%)[Found: C, 65.95; H, 9.33%. δ: 0.99 (3H, s), 1.01 (3H, s), 1.22 (3H, s), 1.2—2.7 (12H, m), 2.82 (1H, br. s), 3.30 (3H, s), and 3.69 (3H, s). δ (C): 29.7, 30.9, 31.0, 31.4, 34.2, 36.1, 36.8, 37.2, 41.3, 43.7, 47.5, 49.9, 50.3, 51.4, 61.6, 68.5, 103.7, and 173.7]).

*An Acid-catalyzed Formation of a γ-Lactone (**7**) from **5**.* An anhydrous benzene solution (10 cm^3) of **5** (10 mg) and BF_3 etherate (60 mg) was kept at room temperature for 5 h. After hydrolysis, the mixture was extracted (ether) and chromatographed on silica gel to give **7** (colorless needles, mp 90—91 °C (from hexane), 7 mg [Found: C, 68.08; H, 8.49%. Calcd for $C_{16}H_{24}O_4$: C, 68.54; H, 8.63%. δ: 0.99 (3H, s), 1.09 (3H, s), 1.42 (3H, s), 3.64 (3H, s), and 1.1—3.1 (12H, m). δ (C): 28.5, 30.2, 31.4, 34.4, 35.9, 36.7, 37.3, 37.5, 38.0, 40.7, 45.7, 46.5, 51.8, 85.2, 174.1, and 175.9]).

*Conversion of **5** to a Keto Glycol, **10**.* An anhydrous ether solution (20 cm^3) of **5** (100 mg) was refluxed with LAH (12 mg) for 3 h. Then, a few drops of water were added to the mixture, and the resultant supernatant was collected by decantation. The rest of the solution was acidified and extracted with ether. The combined extract was purified on a silica-gel column to give a colorless oil (68 mg, 75%), **8** [δ: 0.96 (3H, s), 1.04 (3H, s), 1.12 (3H, s), 1.2—2.6 (12H, m), 3.22 (3H, s), 3.23 (3H, m), 3.51 (1H, d, J=11 Hz), and 3.76 (1H, d, J=11 Hz). δ (C): 27.7, 27.9, 29.8, 31.7, 34.8 (2C), 37.7, 38.3, 39.1, 42.8, 49.4, 49.6, 50.0, 54.4, 66.6, 71.7, and 104.2]. Subsequently, an acetone solution (30 cm^3) of **8** (50 mg) and TsOH (2 mg) was stirred at room temperature for 2 h. Subsequent silica-gel chromatography of the mixture, using ethyl acetate–hexane (2 : 3), afforded colorless needles, **10** (mp 152—153.5 °C (from ethyl acetate–hexane), 39 mg (94%) [Found: C, 71.32; H, 9.55%. Calcd for $C_{15}H_{24}O_3$: C, 71.39; H, 9.59%. δ: 0.89 (3H, s), 1.02 (3H, s), 1.24 (3H, s), 1.1—1.9 (9H, m), 2.2—2.6 (2H, m), 3.64 (1H, d, J=10 Hz), and 3.79 (1H, d, J=10 Hz). δ (C): 27.0, 29.3, 29.8, 31.9, 35.5, 35.8, 38.1, 38.6, 42.6, 47.8, 49.8, 65.5, 69.4, 72.2, and 216.2]).

*Conversion of **6** to **11**.* Much as in the above conversion of **5** to **10**, **6** (36 mg) was reduced with LAH to yield **9** (colorless plates, mp 128.5—129.5 °C (from ethyl acetate–hexane), 30 mg (86%) [δ: 0.99 (3H, s), 1.07 (3H, s), 1.12 (3H, s), 1.2—1.8 (8H, m), 2.2—2.8 (4H, m), 3.27 (3H, s), 3.34 (3H, s), and 3.60 (2H, m). δ (C): 29.7, 30.3, 30.5, 31.5, 33.7, 35.4, 35.8, 36.3, 41.9 (2C), 47.3, 49.9, 50.4, 53.9, 67.9, 68.3, and 106.1]). Subsequently, an acetone solution (30 cm^3) of **9** (28 mg) and TsOH (2 mg) was kept at room temperature for 3 h. The mixture was then chromatographed (silica gel) to give colorless needles, **11** (mp 137—138 °C (from ethyl acetate–hexane), 22 mg (91%) [Found: C, 71.27; H, 9.68%. Calcd for $C_{15}H_{24}O_3$: C, 71.39; H, 9.59%. δ: 0.96 (3H, s), 1.04 (3H, s), 1.31 (3H, s), 1.15—2.0 (6H, m), 2.3—2.75 (2H, m), 2.18 (1H, t, J=7 Hz), 3.10 (2H, d, J=7 Hz), 3.61 (1H, d, J=12 Hz), and 3.84 (1H, d, J=12 Hz). δ (C): 29.1, 30.5, 31.5, 33.3, 34.7, 36.6, 37.2, 41.1, 41.7, 45.1, 47.5, 65.9, 69.1, 69.4, and 213.1]).

*The Sodium Borohydride Reduction of **10**: The Formation of Triols (**12** and **13**).* A methanol solution (20 cm^3) of **10** (28 mg) was treated with $NaBH_4$ (5 mg) at 0—5 °C for 3 h. The mixture was then diluted with water, acidified with dil HCl, and extracted with ether. Subsequent silica-gel chromatography of the extracts yielded colorless needles, **13** (mp 95—96 °C (from ethyl acetate), 27 mg (95%) [Found: C, 70.70; H, 10.30%. Calcd for $C_{15}H_{26}O_3$: C, 70.83; H, 10.30%. δ: 1.00 (3H, s), 1.07 (3H, s), 1.15 (3H, s), 1.2—1.95 (8H, m), 2.2—2.7 (3H, m), 3.58 (2H, s), and 4.07 (1H, t, J=7 Hz). δ (C): 27.8, 29.0, 29.7, 30.4, 31.6, 33.3, 35.2, 37.6, 40.2, 40.6, 42.4, 49.4, 68.1, 68.5, and 72.0]), together with a colorless solid, **12** (1.4 mg (5%) [*m/e*, 254 (M$^+$). δ: 0.90 (3H, s), 1.00 (3H, s), 1.12 (3H, s), 1.2—2.9 (14H, m), 3.78 (2H, m), and 4.10 (1H, m). δ (C): 27.2, 29.3, 29.4, 32.2, 32.3, 37.1, 38.2, 39.2, 40.1, 43.0, 48.3, 50.1, 67.1, 72.4, and 92.6]), which was homogeneous with respect to high-pressure liquid chromatography.

*The Reduction of **11** to **14**.* A methanol solution (20 cm^3) of **11** (22 mg) was treated with $NaBH_4$ (5 mg) for 3.5 h. The product mixture was then extracted with ethyl acetate and purifed by silica-gel chromatography to yield colorless needles, **14** (mp 171—172 °C (from ethyl acetate), 21 mg (95%) [Found: 70.64; H, 10.27%. Calcd for $C_{15}H_{26}O_3$: C, 70.83; H, 10.30%. δ: 1.00 (3H, s), 1.05 (3H, s), 1.10 (3H, s), 1.37—2.05 (8H, m), 2.25—2.65 (3H, m), 3.52 (1H, d, J=11 Hz), 3.65 (1H, d, J=11 Hz), and 4.03 (1H, m). δ (C): 29.8, 29.9, 31.1, 31.7, 34.9, 35.0, 37.0, 41.4, 42.3, 42.7, 48.5, 50.8, 67.3, 68.2, and 70.4]).

*Formation of an Acetal (**15**) from **13**.* A mixture of **13** (12 mg) and 2,2-dimethoxypropane (30 cm^3) was kept at room temperature for 20 d. The mixture was then heated in *vacuo* to remove the volatile material. The NMR spectrum [δ: 0.98 (3H, s), 1.06 (3H, s), 1.12 (3H, s), 1.2—2.8 (11H, m), 3.11 (3H, s), 3.22 (3H, s), 3.30 (2H, m), and 3.98 (1H, t, J=8 Hz)] confirmed the formation of **15**. Every attempt to purify the material caused hydrolysis into **13**.

*An Attempted Acetal Formation of **12** or **14**.* Similarly, solutions of 2,2-dimethoxypropane (30 cm^3) of both **12** and **14** (10 mg) were kept at room temperature for 20 d. The residues subsequently obtained by the evaporation of the volatile material were shown by NMR spectrometry to consist of only the recovered **12** and **14**.

*Conversion of **1** to **17**.* A sample of **1** (1.2 g) and TsOH (50 mg) were dissolved in a mixture of anhydrous benzene (150 cm^3) and 1,2-ethanediol (3.1 g), and then the solution was heated for 5 h with an azeotropic removal of water. Subsequently, the mixture was washed with water and extracted by benzene. Silica-gel chromatography of the mixture yielded a colorless oil, **16** (1.5 g (quantitative) [Found: C, 67.47; H, 8.32%. Calcd for $C_{15}H_{22}O_4$: C, 67.64; H, 8.33%. δ: 1.02 (3H, s), 1.06 (3H, s), 1.2—1.4 (2H, m), 1.6—2.0 (4H, m), 2.50 (1H, m), 2.95 (1H, m), 3.71 (3H, s), 4.01 (4H, m), and 6.59 (1H, br. s). δ (C): 30.6, 31.2, 36.0, 36.8, 38.1, 38.8, 45.8, 46.4, 51.6, 64.5, 64.7, 105.5, 135.3, 136.3, and 167.1]). Subsequently, an anhydrous ether solution (50 cm^3) of **16** (1.4 g) was refluxed with LAH (490 mg) for 2 h. After hydrolysis, the mixture was extracted with ether, dried (Na_2SO_4), and evaporated to remove the solvent. The residue was then dissolved in acetone (50 cm^3) and treated with TsOH (10 mg). A colorless oil thus obtained, **17**, was purified (silica gel) to yield 790 mg (75%) [Found: C, 74.42; H, 9.29%. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34%. δ: 1.05 (3H, s), 1.10 (3H, s), 1.2—1.9 (3H, m), 2.3—2.4 (2H, m), 2.6—2.8 (3H, m), 4.22 (2H, br. s), and 6.08 (1H, s). δ (C): 30.6, 31.0, 38.0, 39.0, 39.8, 41.1, 45.8, 46.6, 64.0, 121.5, 166.4, and 200.3].

*Conversion of **17** to **2**.* An acetic anhydride solution (6 cm^3) of **17** (755 mg) was kept at room temperature for 12 h. The residue obtained by removal of the volatile material *in vacuo* was chromatographed on silica gel to give a colorless oil, **18** (790 mg (86%) [Found: 71.26; H, 8.50%. Calcd for $C_{14}H_{20}O_3$: C, 71.16; H, 8.53%. δ: 1.05 (3H, s), 1.12 (3H, s), 1.2—1.8 (3H, m), 2.12 (3H, m), 2.3—2.5 (2H, m), 2.6—2.8 (3H, m), 4.65 (2H, br. s), and 5.95 (1H, s). δ (C): 20.5, 30.5, 30.9, 37.8, 38.8, 39.9, 40.8, 45.6, 46.4, 64.3, 122.9, 159.0, 170.0, and 198.2]). Subsequently, this **18** was dissolved in acetic acid (80 cm^3) and reduced with activated zinc dust (8 g) for 6 h under reflux. The mixture was then filtered, washed with dil NaOH and $NaHCO_3$, and extracted with hexane. By silica-gel chromatography, the extract yielded a colorless oil, **2** (292 mg (50%) [Found: C, 80.69; H, 10.17%. Calcd for $C_{12}H_{18}O$: C, 80.85; H, 10.18%. δ: 1.04 (3H, s), 1.09 (3H, s), 1.2—2.0 (4H, m), 1.91 (3H, d, J=1 Hz), 2.3—2.4 (2H, m), 2.5—2.8 (2H, m), and 5.79 (1H, q, J=1 Hz). δ (C): 23.2, 30.5, 30.9, 37.5, 38.5, 40.5, 43.9, 45.6, 46.6, 125.4, 163.1, and 199.3]).

*The Photochemical Cycloaddition of **2** with **3**: The Formation of Epimeric 1 : 1-Adducts (**19** and **20**).* A benzene solution (100 cm^3) of **2** (680 mg) and **3**, prepared from 2-chloro-1,1-dimethoxyethane (5 g), was irradiated externally by means of a 400-W high-pressure mercury lamp through a Pyrex glass filter for 60 h at 0—5 °C. After the evaporation of the volatile materials, the residue was chromatographed on silica gel to afford an isomeric mixture of photoadducts (**19** and **20**), which was then separated by means of a pre-packed silica-gel column to give two colorless oils, **19** (152 mg (15%) [Found: C, 71.90; H, 9.73%. Calcd for $C_{16}H_{26}O_3$: C, 72.14; H, 9.84%. δ: 1.01 (3H, s), 1.11 (3H, s), 1.28 (3H, s), 1.5—2.0 (4H, m), 2.1—2.9 (7H, m), 3.08 (3H, s), and 3.19 (3H, s). δ (C): 21.8, 31.3, 31.5, 32.3, 35.4, 41.6, 41.7, 42.9, 43.7, 43.9, 47.9, 48.6, 50.1, 54.8, 104.5, and 213.3]) and **20** (48 mg (5%) [Found: C, 71.91; H, 9.80%. δ: 0.94 (3H, s), 1.0—1.9 (5H, m), 1.08 (3H, s), 1.33 (3H, s), 2.0—2.9 (6H, m), 3.18 (3H, s), and 3.20 (3H, s). δ (C): 25.3, 28.0, 29.9, 32.0, 38.5, 40.1, 42.8, 43.0, 43.6, 44.7, 48.6, 48.7, 49.8, 55.1, 104.0, and 216.6]).

*The Grignard Methylation Reaction of **19**: The Formation of **21**.* To an ether solution (15 cm^3) of methylmagnesium iodide (prepared from 500 mg of methyl iodide), an ethereal solution of **19** (82 mg) was added, drop by drop. The mixture was refluxed for 2 h and then extracted with ether. The extract was dissolved in acetone (30 cm^3) containing TsOH (5 mg) and kept at room temperature for 1 h. After the removal of the solvent, the residue was chromatographed on a silica-gel column to yield **21** (81 mg (85%), colorless crystals, mp 62—63.5 °C [Found: C, 75.94; H, 10.27%. Calcd for $C_{15}H_{24}O_2$: C, 76.22; H, 10.24%. δ: 0.96 (3H, s), 1.05 (3H, s), 1.19 (3H, s), 1.1—2.0 (2H, m), 1.28 (3H, s), 2.2—2.7 (8H, m), and 3.0—3.2 (2H, m). δ (C): 22.5, 29.4, 30.6, 31.6, 33.4, 36.4, 37.0, 41.2, 41.7, 42.5, 43.9, 47.8, 63.3, 69.3, and 213.3]).

*The Grignard Methylation of **20** to **22**.* Similarly, **20** (39 mg) was methylated by methylmagnesium iodide and hydrolyzed in acetone with TsOH to give colorless plates, **22** (33 mg (80%), mp 135—136 °C [Found: C, 75.99; H, 10.18%. δ: 0.89 (3H, s), 1.05 (3H, s), 1.11 (3H, s), 1.37 (3H, s), 1.4—1.75 (5H, m), 1.8—2.5 (5H, m), and 3.0—3.1 (2H, m). δ (C): 24.8, 27.2, 28.9, 29.7, 36.4, 38.3, 38.8, 41.6, 42.6, 43.4, 43.5, 48.7, 65.7, 71.9, and 216.7]).

*The Sodium Borohydride Reduction of **21**: The Formation of **23** and **24**.* A methanol solution (20 cm^3) of **21** (18 mg) was treated with $NaBH_4$ (10 mg) for 3 h at 0—5 °C. After the hydrolysis (dil HCl) of the mixture, the product was extracted with ethyl acetate and chromatographed on a silica-gel column to give colorless needles, **23** (mp 116.5—117 °C, 17 mg (93%) [Found: C, 75.37; H, 10.94%. Calcd for $C_{15}H_{26}O_2$: C, 75.58; H, 11.00%. δ: 0.99 (3H, s), 1.04 (3H, s), 1.09 (3H, s), 1.19 (3H, s), 1.2—2.0 (10H, m), 2.05—2.6 (3H, m), and 3.68 (1H, m). δ: (C): 26.4, 28.7, 30.1, 31.1, 31.2, 34.3, 36.5 (2C), 41.6, 42.9, 44.7, 46.5, 48.0, 69.3, and 76.6]), together with an epimer, **24** (colorless needles, mp 106—107 °C, ≈1 mg [Found: m/e, 238 (M$^+$). δ: 0.96 (3H, s), 1.04 (3H, s), 1.05 (3H s), 1.13 (3H, s), 1.1—2.6 (13H, m), and 4.15 (1H, t, J=8 Hz). δ (C): 19.5, 30.1, 31.1, 31.9, 32.1, 33.1, 36.2, 41.5, 42.0, 42.7, 43.2, 45.8, 47.3, 69.3, and 71.8]).

*The Sodium Borohydride Reduction of **22** to **25**.* A methanol solution (20 cm^3) of **22** (15 mg) was treated with $NaBH_4$ (9 mg) for 3 h at 0—5 °C. The mixture was then acidified (dil HCl), extracted (ethyl acetate), and chromatographed (silica gel) to yield colorless needles, **25** (mp 170—171 °C (from hexane–ethyl acetate), 14.4 mg (95%) [Found: C, 75.31; H, 11.13%. δ: 0.95 (3H, s), 1.06 (3H, s), 1.14 (3H, s), 1.22 (3H, s), 1.2—2.4 (13H, m), and 3.89 (1H, m). δ (C): 28.7, 29.6, 30.8, 30.9, 37.3, 38.0, 39.1, 42.7 (3C), 46.4, 46.8, 47.2, 71.6, and 74.0]).

*The Formation of a Dithiolane (**26**) from **21**.*[7] To a glacial acetic acid solution (2 cm^3) of **21** (44 mg) and 1,2-ethanedithiol (75 mg), BF_3 etherate (50 mg) was added, after which the mixture was kept at room temperature for 12 h. The mixture was then diluted with water and extracted with hexane. The extract was chromatographed (silica gel) to give a colorless oil, **26** (30 mg (55%) [δ: 0.99 (3H, s), 1.00 (3H, s), 1.39 (3H, s), 1.60 (3H, s), 1.0—2.0 (5H, m), 2.0—2.4 (3H, m), 2.70 (1H, m), 3.0—3.3 (4H, m), and 5.29 (1H, br. s)]).

*The Thio-acetal Formation of **22** to **27**.*[7] Similarly, a glacial acetic acid solution (2 cm^3) of **22** (15 mg) and 1,2-ethanedithiol (50 mg) was kept at room temperature for 12 h. The mixture was then hydrolyzed (dil HCl), extracted (ethyl acetate), and chromatographed (silica gel) to give colorless oils, **27** (14 mg (93%) [δ: 1.01 (3H, s), 1.03 (3H, s), 1.29 (3H, s), 1.58 (3H, br. s), 1.1—3.1 (8H, m), 3.05—3.3 (4H, m), 3.44 (1H, m), and 5.13 (1H, s)]).

The Raney-nickel Desulfurization of ***26****: The Formation of Protoillud-7-ene (****28****).* An ethanol solution (30 cm^3) of **26** (30 mg) was refluxed with Raney nickel (W-1) (2 g) for 5 h. Then, the catalyst was removed by filtration and washed several times with ethanol. The solvent was evaporated *in vacuo* to leave a colorless oil, which was subsequently chromatographed (silica gel) to give **28** (6.3 mg (30%) [δ (C): 21.3, 24.4, 26.3, 29.7, 30.2, 32.1, 37.5, 38.5, 39.3, 40.8, 41.7, 45.5, 48.2, 125.6, and 132.1]). The ^{1}H-NMR [δ: 0.98 (6H, s), 1.17 (3H, s), 1.59 (3H, br. s), 1.9—2.8 (11H, m), and 5.11 (1H, br. s)] was identical with that of the authentic sample.

The Raney-nickel Desulfurization of ***27****.* Similarly, **27** (19 mg) and Raney nickel (W-1) (1 g) were mixed in ethanol (30 cm^3) and then refluxed for 5 h to give and *epi*-protoillud-7-ene, **29** (3 mg (20%) [Found: *m/e*, 204 (M$^+$). δ: 0.98 (3H, s), 1.01 (3H, s), 1.11 (3H, s), 1.2—2.2 (11H, m), 1.61 (3H, br. s), and 5.42 (1H, br. s). δ (C): 20.7 (2C), 28.5, 28.8, 29.2, 29.8, 38.1, 39.2, 40.5, 42.0, 42.3, 43.5, 48.6, 123.9, and 134.0]).

The LAH Reduction of ***30****.* A sample of **30** (120 mg), prepared by a previously described method,[3] was dissolved in anhydrous ether (120 cm^3) and reduced by LAH (20 mg) at 35 °C. The reaction mixture was then hydrolyzed, extracted with ether, and chromatographed (silica gel) to give **31** (a colorless oil, 110 mg (95%) [Found: M. W., 238.1959. Calcd for $C_{15}H_{26}O_2$: 238.1933. δ: 0.92 (3H, s), 0.97 (3H, d, J=7 Hz), 1.01 (3H, s), 1.2—2.6 (14H, m), 3.49 (1H, br. s), 3.50 (1H, d, J=10 Hz), and 3.64 (1H, d, J=10 Hz). δ (C): 14.8, 17.7, 26.5, 26.9, 29.4, 30.0, 36.6, 37.3, 40.0, 41.7, 43.1, 44.7, 47.9, 69.6, and 77.5]) as the sole product.

The Reduction of ***30*** *with Sodium Borohydride.* A methanol solution (10 cm^3) of **30** (20 mg) was treated with $NaBH_4$ (10 mg) at 0—15 °C for 2 h. The mixture was then acidified by dil HCl and extracted with ether. Subsequent silica-gel chromatography of the extract yielded a colorless oil, **32** (15 mg (74%) [Found: M. W., 280.2040. Calcd for $C_{17}H_{28}O_3$: 280.2038. δ: 0.92 (3H, s), 0.99 (3H, d, J=5 Hz), 1.02 (3H, s), 1.0—2.6 (13H, m), 2.07 (3H, s), 3.51 (1H, br, s), 3.91 (1H, d, J=11.5 Hz), and 4.15 (1H, d, J=11.5 Hz). ν: 3640—3500, 2940, 1735, and 1240 cm^{-1}]).

The Acetylation of ***31****.* A sample of **31** (10 mg) was treated with acetic anhydride (0.5 cm^3) and pyridine (0.3 cm^3) at room temperature for 12 h. The usual work-up of the mixture on a silica-gel column subsequently yielded a colorless oil (10 mg, 85%), which was identical with the authentic **32** obtained by the $NaBH_4$ reduction of **30**.

The Chromium(VI) Oxide Oxidation of ***31****: The Formation of 8,13-Dioxoprotoilludane (****33****).* A dichloromethane solution (5 cm^3) of **31** (10 mg) was treated with the complex prepared from CrO_3 (30 mg) and pyridine (47 mg) at room temperature for 15 min. The supernatant was collected by decantation, and the residue was washed with ether. The combined organic solution was washed with dil NaOH and dil HCl. The extract was then chromatographed (silica gel) to yield a colorless oil, **33** (8.5 mg (86%) [Found: M. W., 234.1698. Calcd for $C_{15}H_{22}O_2$: 234.1620. δ: 0.96 (3H, d, J=7 Hz), 0.98 (3H, s), 1.09 (3H, s), 1.2—2.2 (8H, m), 2.4—3.4 (4H, m), and 9.57 (1H, s). δ (C): 10.4, 16.9, 25.2, 27.8, 29.5, 39.3 (2C), 40.9, 44.5, 44.7, 44.8, 51.2, 51.3, 201.0, and 215.8]).

The Reaction of 1,2-Ethanedithiol with ***33****.* To a benzene solution (10 cm^3) of **33** (50 mg), 1,2-ethanedithiol (400 mg) was added, together with the BF_3 etherate (0.2 cm^3). The mixture was kept at room temperature for 20 min, and then it was diluted with water and extracted by ether. The extracts was chromatographed (silica gel) to give a colorless oil, **34**, (52 mg (75%) [δ: 0.88 (3H, d, J=7 Hz), 0.98 (3H, s), 1.06 (3H, s), 1.2—3.2 (12H, m), 3.26 (4H, s), and 4.85 (1H, s)]).

The Raney-Nickel Desulfurization of ***34*** *to* ***35****.* An ethanol solution (50 cm^3) of **34** (50 mg) was treated with Raney nickel (W-1) (2 g) for 1 h. The mixture was then filtered, the residue was washed, and the extract was purified on a silica-gel column; the colorless oil thus obtained (25 mg, 74%) was **35** [Found: M.W., 220.1799. Calcd for $C_{15}H_{24}O$: 220.1827. δ: 0.88 (3H, d, J=6 Hz), 0.97 (3H, s), 1.08 (3H, s), 1.19 (3H, s), and 1.2—3.2 (12H, m). δ (C): 10.6, 15.9, 27.1, 27.6, 29.7, 30.6, 37.6, 39.4, 40.3, 45.4 (2C), 47.8, 50.3, 50.6, and 218.0].

The LAH Reduction of ***35*** *to* ***36****.* A sample of **35** (10 mg) was dissolved in ether (15 cm^3) and reduced with LAH (5 mg) at room temperature for 3 h. The mixture was then acidified with dil HCl and extracted with ether. The chromatography (silica gel) of the extract afforded a colorless oil, **36** (8.5 mg (84%) [Found: M. W., 222.1994. Calcd for $C_{15}H_{26}O$: 222.1984. δ: 0.93 (3H, s), 0.97 (3H, d, J=7 Hz), 1.01 (3H, s), 1.08 (3H, s), 0.9—2.5 (13H, m), and 3.47 (1H, br. s). δ (C): 14.0, 16.9, 27.1, 28.6, 29.6, 30.8, 32.0, 37.7, 37.8, 42.2, 43.1, 43.5, 44.6, 47.9, and 76.7]).

An Acetylation of ***36*** *under Forced Conditions. The Formation of* ***37****:* A sample of **36** (5 mg) was dissolved in acetic anhydride (0.3 cm^3) and the BF_3 etherate (0.03 cm^3) for 1 h at room temperature. The mixture was then diluted with water and extracted with ether. Subsequent silica-gel chromatography of the extract gave a colorless oil, **37** (3 mg (50%) [Found: *m/e*, 264 (M$^+$). δ: 0.88 (3H, s), 0.91 (3H, d, J=6.5 Hz), 0.96 (3H, s), 1.08 (3H, s), 0.8—2.4 (12H, m), 2.10 (3H, s), and 4.57 (1H, br. s). ν: 2950, 1740, 1240, and 1120 cm^{-1}]).

An attempted acetylation, under ordinary conditions (acetic anhydride with pyridine at room temperature) gave only the recovered starting materials.

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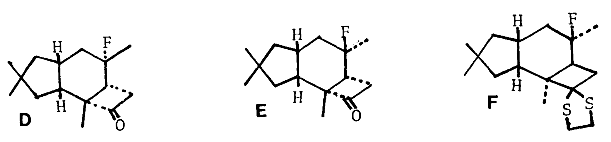
7) From **27**, two fluoro ketones, **D** [δ: 0.90 (3H, s), 1.05 (3H, s), 1.38 (3H, d, J=22 Hz), 1.2—2.2 (8H, m), 2.7—2.9 (2H, m), and 3.15 (1H, m). ν: 2990, 1775 cm^{-1}] and **E** [δ: 0.92 (3H, s), 1.06 (3H, s), 1.2—2.2 (11H, m), 1.25 (3H, s), and 1.29 (3H, d, J=7 Hz). ν: 2990, 1778 cm^{-1}], were obtained as by-products. Similarly, **26** formed a fluoro acetal, **F** [δ: 1.05 (3H, s), 1.12 (3H, d, J=24 Hz), 1.13 (3H, s), 1.19 (3H, s), 0.9—3.1 (11H, m), and 3.13 (4H, br. s)].



Scheme 4.

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