Synthetic Photochemistry. XLVIII.
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Type 5–8–5-Membered Tricyclic Ring System

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Synthetic Photochemistry. XLVIII.1) Stereocontrolled Generation of the Ophiobolane Type 5-8-5-Membered Tricyclic Ring System

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Starting from the chromium (II) chloride-mediated condensation of (3S, 8R)-9-benzyloxy-l-iriden-7-al and (3S)-7-chloro-1,8-iridadiene, ophiobolane type skeleton, was constructed.

Introduction

Ophiobolins2) are the first members of sesterterpenoid family and they have the characteristic 5-8-5-membered tricyclic carbon framework. After the discovery, similar tricyclic systems3) have been found as the physiologically active compounds from various organisms. Particularly interesting was that their stereochemistries are mutually different depending on the natural sources, and therefore, their biogenetic modes of cyclization might be different. Since then, the total synthesis of these natural products has attracted a considerable interest.4) To our knowledge, however, either total synthesis of natural products, or construction of their exact carbon skeletons has remained unsuccessful until our synthesis of optically active cycloaraneosene,5) metabolite of Sordaria araneosa Cain.6) Herein, we wish to report the synthesis of the ring system, that should be designated as methyl 10,15-diepi-16-hydroxyophiobola-2,7,18-trien-25-oate.7)

Results and Discussions

First of all, the stereochemistries of natural 5-8-5-membered tricyclic terpenoids differ depending on the origins of compounds. On the stereochemical relation of C-6 hydrogen and C-11 methyl group, the most of such diterpenoids possess anti-relationship, but most of sesterterpenoids possess the syn-relationship. In cases of the sesterterpenoids, stereochemistries of the Cs-side chain on the C-ring between ophiobolanes from microorganisms and ceroplastanes from insects were different. We have already shown that these stereochemically different ring systems can be constructed via reductive condensations of appropriate combinations of two optically active iridoid synthons and subsequent stereochemically controlled Cope rearrange-
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ment; the original trans-relationship between the C-14 hydrogen and C-11 methyl is retained during the Cope rearrangement. On the other hand, if one needs an inverted cis-Cope thermolysate, the Cope rearrangement should be performed under "the lactol regulated" conditions as shown in our recent total synthesis of dictymal and ceroplastol II.

Although the most of the ophiobolane natural products were highly oxygenated, following fundamental features should be considered: i) the configurations of C-6 and C-14 indicate the starting iridoids must be a combination of two of (3R)-derivatives, ii) the stereochemistry of C-15 relative to C-14 is opposite to the normal hydroboration products of 1,8-iridadiene derivatives, and it must be inverted in the subsequent steps of the synthesis, and iii) the functionalized A ring must be generated by functionalization of the tetrasubstituted double bond after the Cope rearrangement, since it is indispensable for the rearrangement. With these in mind, we have investigated a construction of basic stereostructure, which is seen in ophiobolin F, from the adduct (1) prepared previously by the condensation of (38)-1,8-iridadienal and (38, 8R)-9-benzyloxy-7-chloro-1-iridene.

Cope Rearrangement. Since the isopropyl side chain should have a functional group for further transformation, 1 was converted to a trimethylsilyl (TMS) ether (2) and further oxidized with m-chloroperbenzoic acid (MCPBA) to an epoxy derivative (3) together with two by-products (4 and 5). Subsequent treatment of 3 with aluminum isopropoxide formed an allyl alcohol (6) and a by-product (7). Since the protection of the allylic hydroxyl groups as TMS ethers is necessary to form the Cope thermolysates, 6 was converted to the TMS ether (8) and heated at 200°C for 17 h to yield a single thermolysate (9). A mild hydrolysis of the TMS-enol ether function of 9 furnished two products (10 and 11); the former, 10, was kinetically-controlled product, since it isomerized to 11 by passing through an alumina column. On the basis of the Dreiding's Stereomolecular Model inspections, kinetical product, 10, might be the correct precursor to ophiobolanes, but, simply due to an availability of the sample, the further
Transformations were performed by starting from 11 as a model study for the construction of ophiobolane-type skeleton.

**Ring Closure.** Treatment of 11 with methanesulfonyl (mesyl) chloride formed a mesylate (12), in good yield, and was treated with chromium (II) chloride to give an epimeric mixture of condensates (13 and 14), both of which gave the same dehydro ketone (15) by Swern's oxidation. Interestingly, the lithium aluminum hydride (LAH) reduction of 15 exclusively gave 14. Thus, although the stereochemistry was different in respect to that of C-10 of natural products, the carbocyclic framework was prepared, and in view of their highly oxygenated character, the stereochemistry should be adjusted in later desired occasions.

**Transformation of Tricyclic Derivatives.** A usual acid treatment of dehydro ketone, 15, despite being $\beta, r$-unsaturated ketone, did not give an $\alpha, \beta$-unsaturated ketone (16). However, it could be isomerized to 16 by treatment with potassium fluoride supported on Florisil. The diisobutylaluminum hydride (DIBAH) reduction of 14 gave an allyl alcohol (17) in 96% together
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with a small amount, 2%, of 1,4-reduction product (18). After acetylation to 19, it was reduced under Birch reduction conditions to a mixture of double bond isomers (20 and 21), and a hydrolyzed alcohol (22), which were separated with high-pressure liquid chromatography (HPLC). However, the predominant product of this reduction was 22, and in order to obtain 20 or 21 in better yields, the Birch reduction was carried out in tetrahydropyranyl (THP) ether (23) derived from 17; the combined yield of 20 and 21 were nearly quantitative.

Homologation. The mixture of 20 and 21, obtained from Birch reduction of 23, was then converted to aldehydes (24 and 25) by Swern’s oxidation. Thus, the C₅-homologation of 24 should complete the carbon framework of the sesterterpenoid. The dianion species of 2-methyl-2-butenolic acid was condensed with 24 to form a secondary alcohol (26). Natural ophiobolins are highly oxygenated, and there are many derivatives, of which stereostructures were deviated from the original form; e.g., only the compounds supposed to possess the original stereostructure are ophiobolin C and F, and A/B-ring juncture, the cis-form was lost by introduction of C=C bond in ophiobolin D, and C-14 hydrogen was displaced by oxygen functions on ophiobolins

(Scheme 4)
A and B. Therefore, the most desirable transformation from 26 would be an inversion of B/C-juncture to the trans-form. And the related study on this point is currently undergoing.

Conclusion. Beside our recent achievement of synthesizing the tricyclic higher terpenoids, i.e., cycloaraneosene (which also constitutes a formal total synthesis of hydroxycycloaraneosene), ceroplastol II, and albolic acid, as well as dictymal, a B-seco-derivative of epoxydictymene, we now added here a construction of basic skeleton of the ophiobolan system. Although we employed the thermodynamically stable aldehyde, 11, for ring closure to the tricyclic system to result in the formation of cis-B/C juncture, there might be no reason to assume that the same reaction with epimeric 10 should not be applicable, and in views of our current findings on the related works, we are confident to get a totally synthesized ophiobolins in near future.

Experimental

Elemental analyses were performed by Miss S. Hirashima, of This Institute. The NMR spectra were measured in CDCl₃ with an FX 100 Model spectrometer, JEOL, and the chemical shift were expressed in δ values. The mass spectra were measured with a OISG-2 spectrometer, JEOL. IR spectra were measured with a Jasco IR-A 102 Model spectrometer as KBr disks, inserted liquid films, or in CHCl₃ solutions. The optical rotations were measured with a Union Model PM-101 apparatus. The solvents were carefully dehydrated and distilled immediately before the use under N₂ atmosphere; therefore, they were anhydrous unless otherwise stated.

Preparation of 1 by Condensation of Two Iridoid Synthons. For details see the previous paper.²¹

Formation of TMS-Ether (2) from 1. A pyridine solution (100 cm³) of 1 (10.28 g) was treated with TMSCl (2.5 cm³) to give 2 [a colorless oil, 12.58 g; 100%. Found: C, 77.42; H, 9.81%. C₂₈H₄₆O₂Si: C, 77.19; H, 9.93%. δ₁H NMR δ=0.06 (9H, s), 1.02 (3H, d, J=7 Hz), 1.17 (3H, s), 1.59 (3H, br s), 1.66 (3H, br s), 2.60 (1H, br m), 2.88 (1H, br m), 3.12 (1H, t, J=8.5 Hz), 3.18 (1H, br m), 3.45 (1H, dd, J=8.5, 3.5 Hz), 4.33 (1H, d, J=11.5 Hz), 4.37 (1H, s), 4.49 (1H, d, J=11.5 Hz), 4.6–4.8 (4H, m), and 7.27 (5H, br s). ¹³C NMR δ=0.6 (3C, q), 15.2 (q), 18.1 (2C, q), 23.4 (t), 24.1 (q), 28.0 (t), 35.6 (t), 35.9 (d), 37.6 (t), 50.9 (s), 51.7 (d), 53.6 (d), 72.3 (t), 73.3 (t), 74.3 (d), 107.4 (t), 112.7 (t), 127.2 (d), 127.5 (2C, d), 128.2 (2C, d), 136.7 (s), 137.4 (s), 139.1 (s), 146.5 (s), and 159.7 (s). IR ν: 2950, 2875, 1642, 1452, 1370, 1248, 1095, 1063, 1030, 883, 742, 727, and 693 cm⁻¹].

Epoxidation of 2 to 3, 4, and 5. To a CH₂Cl₂ solution (300 cm³) of 2 (11.57 g) added were NaHCO₃ (2.1 g; 10 mol eq) and MCPBA (2.2 g; 0.5 mol eq) at 0–5°C and kept in the dark for 15 h. The mixture was then diluted with aq NaHCO₃, extracted with ether, and chromatographed on a silica-gel column, and the recovered 2 was repeatedly oxidized. After repetition with five times, 3 [a colorless oil, 10.18 g; 85%. m/z, 482 (M⁺)]. ¹H NMR δ=0.04 (9H, s), 1.01
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(3H, d, \(J=7\) Hz), 1.18 (3H, s), 1.21 (3H, s), 1.64 (3H, br s), 2.51 (0.4H, s), 2.70 (1.6H, s), 2.84 (1H, br m), 3.10 (1H, t, \(J=8.5\) Hz), 3.43 (1H, dd, \(J=8, 3.5\) Hz), 4.29 (1H, s), 4.36 (1H, d, \(J=12\) Hz), 4.48 (1H, d, \(J=12\) Hz), 4.87 (1.6H, m), 4.92 (0.2H, m), 5.13 (0.2H, m), and 7.27 (5H, br s). IR \(\nu\) : 2970, 1647, 1458, 1372, 1098, 1035, 901, 879, 839, 745, 732, and 697 cm\(^{-1}\) was obtained together with variable amounts of 4 [a colorless oil. \(m/z, 347\) (M\(^+\)-135). \(^1\)H NMR \(\delta=0.14\) (9H, s), 1.01 (3H, d, \(J=7\) Hz), 1.20 (3H, s), 1.34 (3H, s), 1.62 (3H, br s), 3.10 (1H, t, \(J=8.5\) Hz), 3.21 (1H, s), 3.38 (1H, s), 3.97 (1H, dd, \(J=8.5, 3\) Hz), 4.39 (1H, d, \(J=12\) Hz), 4.59 (1H, d, \(J=12\) Hz), 4.75 (2H, m), 4.84 (1H, m), 4.96 (1H, m), and 7.29 (5H, br s). Formation of Allyl Alcohol (6) from 3 by Treatment with Al(O-i-Pr)\(_3\). A toluene solution (280 cm\(^3\)) of 3 (0.2 g) and Al(O-i-Pr)\(_3\) (50 fold excess) was refluxed until no starting material was detected on the tlc. The mixture was then extracted with ether, and dried on \(\text{K}_2\text{CO}_3\). Silica-gel column chromatography of the organic material afforded 6 [a colorless oil, 7.44 g; 73%. Found: C, 74.64; H, 9.60%. Calcd for C\(_{30}\)H\(_{46}\)O\(_3\)Si: C, 74.47; H, 9.74%. [\(\alpha\)]\(_D\)\(^{18}\) = \(-97.9^\circ\) (c 2.06, CHCl\(_3\)). \(^1\)H NMR \(\delta=0.06\) (9H, s), 1.01 (3H, d, \(J=7\) Hz), 1.18 (3H, s), 1.65 (3H, br s), 2.60 (1H, br m), 2.86 (1H, br m), 3.11 (1H, t, \(J=8.5\) Hz), 3.20 (1H, br m), 3.44 (1H, dd, \(J=8.5, 3\) Hz), 4.07 (2H, br d, \(J=2.5\) Hz), 4.32 (1H, d, \(J=12\) Hz), 4.36 (1H, s), 4.48 (1H, d, \(J=12\) Hz), 4.73 (1H, br d, \(J=2.5\) Hz), 4.82 (1H, br d, \(J=2.5\) Hz), 4.92 (1H, br s), 5.16 (1H, m), and 7.27 (5H, br s). \(^{13}\)C NMR \(\delta=0.5\) (3C, q), 11.0 (q), 15.1 (q), 18.0 (q), 23.3 (t), 24.2 (q), 28.5 (t), 35.3 (t), 35.7 (d), 37.4 (t), 50.5 (d), 50.8 (t), 51.5 (d), 63.6 (t), 72.3 (t), 73.2 (t), 74.2 (d), 107.5 (t), 111.5 (t), 127.2 (d), 127.5 (2C, d), 128.2 (2C, d), 136.3 (s), 137.5 (s), 139.0 (s), 150.2 (s), and 160.6 (s). IR \(\nu\) : 3350, 2950, 2875, 1647, 1500, 1455, 1370, 1250, 1098, 1064, 1032, 900, 875, 839, 747, and 695 cm\(^{-1}\) and 7 [a colorless oil, 1.08 g; 11%. Found: C, 74.33; H, 9.98%. Calcd for C\(_{30}\)H\(_{48}\)O\(_3\)Si: C, 74.07; H, 10.19%. \(^1\)H NMR \(\delta=0.05\) (9H, s), 0.75 (3H, d, \(J=7\) Hz), 1.01 (3H, d, \(J=7\) Hz), 1.13 (3H, s), 1.65 (3H, br s), 2.64 (1H, br m), 2.84 (1H, br m), 3.11 (1H, dd, \(J=9, 8\) Hz), 3.3–3.7 (3H, m), 4.32 (1H, d, \(J=12\) Hz), 4.44 (1H, s), 4.48 (1H, d, \(J=12\) Hz), 4.73 (1H, d, \(J=2.5\) Hz), 4.82 (1H, d, \(J=2.5\) Hz), and 7.27 (5H, br s). \(^{13}\)C NMR \(\delta=0.5\) (3C, q), 11.0 (q), 15.1 (q), 18.0 (q), 22.8 (t), 23.3 (t), 23.8 (q), 35.1 (t), 35.6 (d), 37.4 (t), 44.4 (d), 51.0 (s), 51.4 (d), 67.5 (t), 72.2 (t), 73.1 (t), 74.2 (d), 105.7 (t), 127.1 (d), 127.1 (2C, d), 128.1 (2C, d), 136.4 (s), 137.3 (s), 139.0 (s), and 160.4 (s). IR \(\nu\) : 3350, 2960, 2875, 1645, 1545, 1370, 1250, 1095, 1063, 1030, 880, 840, 745, 730, and 695 cm\(^{-1}\)].

Cope Rearrangement of 6 to 9. A pyridine solution (50 cm\(^3\)) of 6 (7.44 g) was treated with TMSCl (1.5 cm\(^3\)) to give 8 [a colorless oil, 8.62 g; 100%. [\(\alpha\)]\(_D\)\(^{24}\) = \(-98.7^\circ\) (c 2.48, CHCl\(_3\)). Found: C, 71.34; H, 9.75%. Calcd for C\(_{33}\)H\(_{54}\)O\(_3\)Si\(_2\): C, 71.42; H, 9.81%. \(^1\)H NMR \(\delta=0.06\) (9H, s), 0.12 (9H, s), 1.02 (3H, d, \(J=3\) Hz), 1.18 (3H, s), 1.65 (3H, br s), 2.60 (1H, br m), 2.88 (1H, br m), 3.11 (1H, t, \(J=8\) Hz), 3.16 (1H, br m), 3.45 (1H, dd, \(J=8, 3.5\) Hz), 4.03 (2H, br s), 4.32
(1H, d, J=12 Hz), 4.36 (1H, s), 4.48 (1H, d, J=12 Hz), 4.74 (1H, m), 4.82 (1H, m), 4.88 (1H, m), 5.16 (1H, m), and 7.26 (5H, br s). 13C NMR δ=0.4 (3C, q), 0.6 (3C, q), 15.1 (q), 18.0 (q), 23.3 (t), 24.1 (q), 28.9 (t), 35.3 (t), 35.8 (t), 37.5 (t), 49.9 (d), 50.8 (t), 51.5 (d), 63.1 (t), 72.3 (t), 73.2 (t), 74.2 (d), 107.6 (t), 110.7 (t), 127.2 (d), 127.5 (2C, d), 128.1 (2C, d), 136.5 (s), 137.5 (s), 139.1 (s), 149.6 (s), and 160.0 (s). IR ν: 2950, 2875, 1647, 1500, 1455, 1370, 1250, 1093, 1065, 1032, 875, 838, 745, and 695 cm⁻¹, which was then dissolved in toluene (150 cm³) and heated in an autoclave at 200°C for 17 h. Toluene was removed by evaporation to leave essentially pure 9 [a colorless oil, 8.62 g; 100%. 1H NMR δ=0.12 (9H, s), 0.15 (9H, s), 1.00 (3H, s), 1.02 (3H, d, J=7 Hz), 1.64 (3H, br s), 2.80 (1H, br m), 3.19 (1H, t, J=9 Hz), 3.36 (1H, br m), 3.45 (1H, dd, J=9, 4 Hz), 3.97 (2H, br s), 4.41 (1H, d, J=12 Hz), 4.47 (1H, d, J=12 Hz), 4.67 (1H, br s), 5.01 (1H, m), 6.01 (1H, d, J=2.5 Hz), and 7.27 (5H, br s)].

**KF-Catalyzed Hydrolysis of 9 to 10 and 11.** A tetrahydrofuran (THF) solution (60 cm³) of 9 (2.4 g) was treated with KF-SiO₂ (1: 2, 15 fold excess) at room temperature for 2 d under N₂ atmosphere. The mixture was then filtered on a Florisil column and chromatographed on a silica-gel column to give 10 [a colorless oil, 1.05 g; 56%]. m/z, 301 (M⁺-109). 1H NMR δ=0.94 (3H, d, J=7 Hz), 0.95 (3H, s), 1.67 (3H, br s), 2.50 (1H, tm, J=6 Hz), 3.27 (1H, dd, J=9, 5.5 Hz), 3.35 (1H, br m), 3.42 (1H, dd, J=9, 4 Hz), 3.93 (2H, br s), 4.41 (1H, d, J=12 Hz), 4.47 (1H, d, J=12 Hz), 4.69 (1H, br s), 4.97 (1H, m), 7.26 (5H, br s), and 9.65 (1H, d, J=6 Hz). 13C NMR δ=15.1 (q), 16.6 (q), 24.2 (q), 28.6 (t), 29.1 (t), 35.6 (d), 36.9 (t), 38.6 (2C, t), 45.4 (d), 47.5 (s), 53.5 (d), 62.0 (d), 63.8 (t), 73.0 (t), 74.6 (t), 108.8 (t), 127.5 (3C, d), 128.2 (2C, d), 133.3 (s), 138.1 (s), 138.4 (s), 151.4 (s), and 205.9 (d). IR ν: 3445, 2935, 2875, 1713, 1095, 1453, 1378, 1111, 1095, 1068, 900, 835, 697, and 677 cm⁻¹ and 11 [a colorless oil, 520 mg; 28%. m/z, 392 (M⁺-18)].

**Alumina-Catalyzed Isomerization of 10 to 11.** The 10 (304 mg) was passed through an Al₂O₃ (neutral, Activity I; 5 g) column by hexane-ether (20:1) to give essentially pure 11 (284 mg; 93%).

**Mesylate (12) of 11.** To a benzene solution (1.5 cm³) of 11 (30 mg) and collidine (0.15 cm³) MsCl (30 mg) was added and kept at room temperature for 1 h. The mixture was then diluted with water, extracted with ether, chromatographed on a silica-gel column to give 12 [a colorless oil, 33 mg; 92%. Found: C, 68.58; H, 8.24%. Calcd for C₂₈H₄₀O₇S: C, 68.82; H, 8.25%]. 1H NMR δ=0.87 (3H, d, J=7 Hz), 1.13 (3H, s), 1.68 (3H, br s), 2.61 (1H, qdd, J=7, 6.2, 2.5 Hz).
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5.3 Hz), 2.98 (3H, s), 3.25 (1H, dd, \(J=9\), 5.3 Hz), 3.31 (1H, dd, \(J=9\), 6.2 Hz), 3.40 (1H, br m), 4.41 (2H, br s), 4.53 (2H, br s), 4.86 (1H, br s), 5.13 (1H, m), 7.28 (5H, br s), and 9.66 (1H, br d, \(J=4\) Hz). \(^{13}\)C NMR: \(\delta=14.8\) (q), 15.0 (q), 27.6 (q), 27.6 (t), 28.5 (t), 31.4 (t), 36.5 (t), 37.3 (d), 37.8 (q), 38.1 (t), 40.9 (d), 49.9 (s), 53.3 (d), 65.6 (d), 70.6 (t), 72.6 (t), 73.9 (t), 114.7 (t), 127.2 (3C, d), 127.9 (2C, d), 132.5 (s), 138.2 (s), 138.6 (s), 143.9 (s), and 205.2 (d).

**CrCl\(_2\)-Mediated Cyclization of 12 to 13 and 14.** A THF suspension of 12 (300 mg) was treated with CrCl\(_2\) (prepared from CrCb, 2 g, and LAH, 260 mg). Silica-gel column chromatography of the mixture afforded 13 [68 mg; 28%]. m/z, 394 (M\(^+\)). \(^{1}\)H NMR: \(\delta=0.73\) (3H, s), 1.00 (3H, d, \(J=7\) Hz), 1.60 (3H, br s), 3.07 (1H, br m), 3.23 (1H, dd, \(J=9\), 6.5 Hz), 3.51 (1H, dd, \(J=9\), 5 Hz), 3.94 (1H, br m), 4.46 (2H, br s), 4.90 (1H, m), 4.94 (1H, br s), and 7.28 (5H, br s). IR \(\nu\): 3465, 2950, 2870, 1640, 1498, 1453, 1375, 1099, 1073, 1027, 889, 732, and 698 cm\(^{-1}\) ] and 14 [67 mg; 28%]. \(^{1}\)H NMR: \(\delta=0.78\) (3H, s), 1.00 (3H, d, \(J=7\) Hz), 1.60 (3H, br s), 2.83 (1H, dd, \(J=13.5\), 3.5 Hz), 3.26 (1H, dd, \(J=9\), 7 Hz), 3.50 (1H, dd, \(J=9\), 5 Hz), 4.47 (2H, br s), 4.83 (1H, m), 4.90 (1H, m), and 7.29 (5H, br s).]

**Swern's Oxidation of 13 and 14 to 15.** A 1:1-mixture of 13 and 14 (111 mg) was dissolved in CH\(_2\)Cl\(_2\) (2 cm\(^3\)) and treated with (COCI\(_2\))\(_2\) (35 mg), dimethyl sulfoxide (DMSO, 70 mg), and Et\(_3\)N (0.4 cm\(^3\)) to give 15 [a colorless crystals, mp 75-76.5 °C, 104 mg; 94%. \([\alpha]\)\(^{21}\)_D = +139.0° (c 1.65, CHCl\(_3\)). Found: m/z, 392.2711 (M\(^+\)). Calcd for C\(_{27}\)H\(_{36}\)O\(_2\): 392.2713. \(^{1}\)H NMR: \(\delta=0.89\) (3H, d, \(J=7\) Hz), 0.94 (3H, s), 1.56 (3H, br s), 2.79 (1H, dm, \(J=6\) Hz), 3.04 (1H, d, \(J=12\) Hz), 3.10 (1H, dd, \(J=9\), 7 Hz), 3.16 (1H, d, \(J=12\) Hz), 3.39 (1H, br m), 3.40 (1H, dd, \(J=9\), 4.3 Hz), 4.42 (2H, br s), 4.94 (1H, br s), 4.97 (1H, m), and 7.25 (5H, br s). IR \(\nu\): 2970, 2930, 2870, 1700, 1642, 1498, 1458, 1378, 1261, 1197, 1100, 1070, 1028, 890, 730, and 697 cm\(^{-1}\)].

**LAH-Reduction of 15 to 13.** A THF solution (2 cm\(^3\)) of 15 (38 mg) was reduced with LAH to solely give 13 (36 mg; 96%).

**KF-on-Florisil Treatment of 15 to 16.** An MeOH solution (2 cm\(^3\)) of 15 (48 mg) was treated with KF (170 mg) and Florisil (330 mg) at room temperature for 2 d. The mixture was then filtered and the residue obtained by evaporation of the solvent was chromatographed on a silica-gel column to give 16 [a colorless oil, 48 mg; 100%. Found: m/z, 392.2718 (M\(^+\)). Calcd for C\(_{27}\)H\(_{36}\)O\(_2\): 392.2713. \([\alpha]\)\(^{21}\)_D = 305.2° (c 1.32, CHCl\(_3\)). \(^{1}\)H NMR: \(\delta=0.91\) (3H, d, \(J=7\) Hz), 0.94 (3H, s), 1.62 (3H, br s), 1.90 (3H, br s), 2.67 (1H, br m), 3.02 (1H, dm, \(J=3.5\) Hz), 3.15 (1H, dd, \(J=9\), 8 Hz), 3.53 (1H, dd, \(J=9\), 4 Hz), 4.18 (1H, br m), 4.44 (1H, d, \(J=12\) Hz), 4.50 (1H, d, \(J=12\) Hz), 5.97 (1H, m), and 7.28 (5H, br s). IR \(\nu\): 2930, 2875, 1730, 1672, 1613, 1499, 1378, 1100, 732, and 698 cm\(^{-1}\)].

**DIBAH-Reduction of 16 to 17 and 18.** A toluene solution (1.5 cm\(^3\)) of 16 (30 mg) was treated with DIBAH (17 mg) at-65 °C for 30 min. The mixture was then extracted with ether, 

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dried on K$_2$CO$_3$, and chromatographed on a silica-gel column to give 17 [a colorless oil, 29 mg; 96%. Found: m/z, 394.2870 (M$^+$). Calcd for C$_{27}$H$_{38}$O$_2$: 394.2870. $^1$H NMR: δ=0.87 (3H, s), 0.89 (3H, d, J=7 Hz), 1.62 (6H, br s), 3.62 (1H, dd, J=9, 4 Hz), 3.50 (1H, br m), 3.54 (1H, dd, J=9, 8 Hz), 4.44 (1H, d, J=12 Hz), 4.54 (1H, d, J=12 Hz), 4.77 (1H, dm, J=8 Hz), 5.47 (1H, dm, J=8 Hz), and 7.29 (5H, br s). IR $\nu$: 3440, 2950, 2870, 1660, 1499, 1453, 1378, 1090, 1071, 1028, 1011, 732, and 698 cm$^{-1}$] and 18 [colorless needles, mp 109.5–111 °C, 0.7 mg; 2%. Found: C, 82.34; H, 9.64%. Calcd for C$_{27}$H$_{38}$O$_2$: C, 82.18; H, 9.71%. $^1$H NMR: 0=0.84 (3H, s), 0.87 (3H, d, J=7 Hz), 1.58 (3H, br s), 2.65 (1H, d, J=5.3 Hz), 2.75 (1H, dqq, J=7.5, 4.5 Hz), 3.04 (1H, br m), 3.13 (1H, dd, J=9, 7.5 Hz), 3.40 (1H, dd, J=9, 4.5 Hz), 4.42 (2H, br s), and 7.26 (5H, br s). $^{13}$C NMR: δ=14.0 (q), 14.6 (q), 16.7 (q), 27.1 (q), 28.9 (t), 29.1 (t), 36.0 (d), 36.5 (t), 36.7 (t), 39.6 (d), 41.8 (t), 47.3 (s), 49.6 (d), 51.7 (d), 53.1 (t), 64.0 (d), 73.0 (t), 74.6 (t), 127.5 (3C, d), 128.2 (2C, d), 133.0 (s), 137.1 (s), 138.6 (s), and 218.0 (s). IR $\nu$: 2960, 2870, 1735, 1685, 1499, 1455, 1370, 1245, 1212, 1095, 958, 732, and 695 cm$^{-1}$].

**Acetylation of 17 to 19.** A CH$_2$Cl$_2$ solution (4 cm$^3$) of 17 (360 mg) was treated with N,N-dimethylaminopyridine (100 mg), Et$_3$N (0.5 cm$^3$), and Ac$_2$O (1 cm$^3$) at room temperature for 1 h. The mixture was then chromatographed on silica-gel column to give an acetate, 19 [a colorless oil, 373 mg; 94%. m/z, 376 (M$^+$)]. $^1$H NMR: δ=0.94 (3H, s), 1.02 (3H, d, J=5.3 Hz), 1.62 (6H, br s), 1.94 (3H, d, J=7 Hz), 3.54 (1H, dd, J=9, 5 Hz), 3.58 (1H, br m), 4.45 (2H, br s), 5.42 (1H, dm of quint, J=8, 1.5 Hz), 5.91 (1H, ddm, J=8, 2 Hz), and 7.27 (5H, br s). IR $\nu$: 2960, 2870, 1735, 1662, 1499, 1455, 1370, 1245, 1212, 1095, 958, 732, and 698 cm$^{-1}$].

**Birch Reduction of 19 to 20, 21, and 22.** To liq NH$_3$ (25 cm$^3$) containing 19 (50 mg), Li (45 mg) was added. An ordinary workup of the mixture gave 20 [a colorless oil, 12%]. Found: m/z, 288 (M$^+$). $^1$H NMR: δ=0.88 (3H, br s), 1.02 (3H, br d, J=7 Hz), 1.61 (6H, br s), 3.41 (1H, ddm, J=11.5, 7 Hz), 3.67 (1H, ddm, J=11.5, 4 Hz), and 5.40 (1H, tm, J=8 Hz)] [21 [a colorless oil, 4 mg; 12%. $^1$H NMR δ=0.79 (3H, s), 0.83 (3H, d, J=7 Hz), 1.02 (3H, dm, J=6 Hz), 1.61 (3H, s), 3.38 (1H, dd, J=11.5, 7 Hz), 3.42 (1H, br m), 3.66 (1H, ddm, J=11.5, 3 Hz), 4.96 (1H, ddd, J=12.5, 5.5, 2.5 Hz), and 5.34 (1H, ddd, J=12.5, 3, 2 Hz)], and 22 [a colorless oil, 26 mg; 74%. Found: m/z, 304.2402 (M$^+$). Calcd for C$_{20}$H$_{32}$O$_2$: 304.2401. $^1$H NMR δ=0.89 (3H, d, J=7 Hz), 0.90 (3H, s), 1.63 (6H, br s), 3.41 (1H, dd, J=12, 4 Hz), 3.70 (1H, dd, J=12, 8 Hz), 4.83 (1H, dm, J=8 Hz), and 5.49 (1H, dm, J=8 Hz). IR $\nu$: 3350, 2950, 2875, 1447, 1375, 1033, 1012, 860, and 802 cm$^{-1}$].

**THP Ether (23) of 17.** An anhydrous CH$_2$Cl$_2$ solution of 19 (325 mg) was refluxed with dihydroxypropyran (0.15 cm$^3$) and PPTS (6 mg) for 3 h. Then, aq NaHCO$_3$ was added and extracted with ether. Silica-gel column chromatography of the extract gave 23 [a colorless oil, 395 mg; 100%. Found: m/z, 478.3482 (M$^+$). Calcd for C$_{32}$H$_{46}$O$_3$: 478.3445. $^1$H NMR δ=0.86 (3H, s), 1.00 (3H, d, J=7 Hz), 1.61 (6H, br s), 3.2–4.0 (5H, m), 4.3–4.9 (4H, m), 5.57 (1H, br d, J=8 Hz, 1.5 Hz), 5.91 (1H, ddm, J=8 Hz), and 7.27 (5H, br s). IR $\nu$: 2960, 2870, 1735, 1662, 1499, 1455, 1370, 1245, 1212, 1095, 958, 732, and 698 cm$^{-1}$].
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Hz), and 7.28 (5H, br s) for isomer-a; δ = 0.90 (3H, s), 1.03 (3H, d, J=7 Hz), 1.61 (6H, br s), 3.2–4.0 (5H, m), 4.3–4.9 (4H, m), 5.33 (1H, br d, J=8 Hz), and 7.28 (5H, br s) for isomer-b (a: b = 3: 2). IR ν: 2949, 2875, 1660, 1475, 1379, 1200, 1135, 1110, 1075, 1020, 1001, 865, 810, 731, and 695 cm⁻¹.

Birch Reduction of 23 to and 21. Anhydrous EtNH₂ (25 cm³) was trapped in a cold vessel, to which an anhydrous THF solution of 23 (37 mg) containing EtOH (0.05 cm³) was introduced and reduced with Li metal. Ordinary workup of the mixture afforded 20 and 21 in a quantitative amount.

Swern’s Oxidation of 20 and 21 (a mixture) to 24. A CH₂Cl₂ solution (2.5 cm³) of 20 and 21 (40 mg) and (COCl)₂ (30 mg) was treated with DMSO (60 mg) and Et₃N (55 mg) to give 24 [a colorless oil, 17 mg; 42%. Found: m/z, 286.2271 (M⁺). Calcd for C₂₀H₃₀O: 286.2295. ¹H NMR δ = 0.86 (3H, s), 1.21 (3H, d, J=7 Hz), 1.61 (6H, br s), 5.42 (1H, m), and 9.54 (1H, d, J=3 Hz). IR ν: 2950, 2925, 2875, 1727, 1455, 1377, 1260, 1095, 1075, 1020, and 800 cm⁻¹] and 25 [a colorless oil, 16 mg; 41%. ¹H NMR δ = 0.81 (3H, s), 0.82 (3H, d, J=7 Hz), 1.22 (3H, d, J=7 Hz), 1.61 (3H, br s), 4.9–5.4 (2H, m), and 9.73 (1H, d, J=3 Hz)].

Homologation of 24 to 26. A THF solution (10 cm³) of (i-Pr)₂NH (0.5 cm³) added was BuLi (2.2 cm³, 1.5M) at −78°C under an N₂ atmosphere. After stirred for 30 min, a THF solution (2 cm³) of tiglic acid (190 mg) was introduced gradually. While cooling at −78°C, a THF solution (1.5 cm³) of 24 (30 mg) was added drop by drop. After 30 min, N,N-dimethylformamide (DMF, 4 cm³) was introduced and stirred for another 30 min, and kept room temperature for 15 h, and finally heated to 75°C for 2.5 h. The mixture was then diluted with aq NaHCO₃, extracted with ether, and dried on K₂CO₃. The organic layer was evaporated, dissolved in ether, and treated with ethereal CH₂N₂. Silicagel column chromatography of the mixture afforded 26 [a colorless oil, 5 mg; 12%. Found: m/z, 400.2977. Calcd for C₂₆H₄₀O₃: 400.2975. ¹H NMR δ = 0.88 (3H, s), 0.94 (3H, d, J=7 Hz), 1.62 (6H, br s), 1.87 (3H, d, J=1 Hz), 3.72 (3H, s), 3.6–3.9 (1H, m), 5.45 (1H, m), and 6.79 (1H, tm, J=8 Hz). IR ν: 3460, 2870, 1715, 1647, 1452, 1473, 1377, 1281, 1247, 1125, 1099, and 742 cm⁻¹].

References


7) The numbering has been adopted after S. Nozoe. et al. See ref. 2a.


13) To obtain natural stereochemistry, both of these should be (3R)-iridane derivatives. We, however, did not care about absolute configurations for the preliminary studies.