Notes

Stereocontrolled Tandem Radical Cyclization: A New and Facile Route to Syntheses of (±)-α-Biotol and (±)-*β*-Biotol

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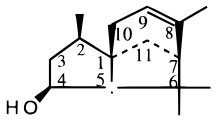
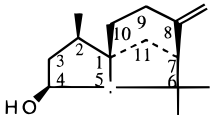
Introduction

α-Biotol (**1**) and *β*-biotol (**2**), isolated from the essential oil of the wood of *Biota orientalis*,[1] are one kind of cedranoid sesquiterpenes containing the tricyclo[5.3.1.$0^{1,5}$]-undecane skeleton and a hydroxyl substituent at the C_4 position. From a synthetic standpoint, the efficiency of constructing a cedrane skeleton and *exo*-4-hydroxyl group is a challenge. Although a number of strategies for the syntheses of α-cedrene and its analogs have been studied[2] and briefly summarized,[3] relatively little attention has been directed to the syntheses of biotols. To date, the total synthesis of biotols has only been reported once[4] while a few partial syntheses[5] have been recorded. The approach by Yates *et al.* included the photosensitized oxadi-*π*-methane rearrangement[4] of bicyclo[2.2.2]octenone and required more than 20 steps.



1

(±)-α-biotol



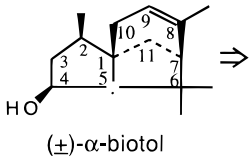
2

(±)-β-biotol

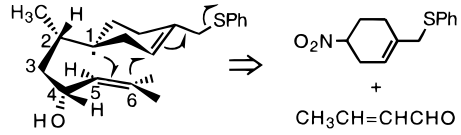
Recently, intramolecular radical cyclizations have received considerable attention and are widely applied to organic synthesis.[6] From our previous studies[3b] on the synthesis of α-cedrene, we have successfully developed a new method involving a tandem radical cyclization[7] through an addition/elimination mechanism to build up a cedrene skeleton. Moreover, the synthetic versatility of the nitro group[8] in Diels−Alder reactions, ionic nitroaldol reactions, and free radical cyclizations, have also been demonstrated. In continuation of our synthetic studies in this series, we describe here new and facile total syntheses of (±)-α-biotol (**1**) and (±)-*β*-biotol (**2**) via a stereocontrolled tandem radical cyclization.

Results and Discussion

Our approach is based on the following hypotheses: (1) A tandem radical cyclization reaction is an efficient method to construct the cedrene skeleton. (2) The 4-hydroxyl group and the 2-methyl substituent in the cedrene molecule could be introduced before the cyclization. (3) The stereochemistry of the radical cyclization must be affected by the 4-hydroxyl substituent, based on the studies of 1,5-stereochemistry controlled by the configuration of the C_4 center of the radical in hex-5-enyl radical cyclizations by Beckwith,[9] Houk,[10] and Rajan-Babu.[11] A directed synthetic design involving these three strategic features is outlined below.



(±)-α-biotol



Scheme 1 presents our synthetic routes to the target molecules. The starting material **3** was readily prepared by a method that we have previously used in the synthesis of α-cedrene. The Michael adduct of compound **3** and crotonaldehyde treated with DBU in acetonitrile at 0 °C gave nitro aldehyde **4** in 66% yield. The Grignard reaction of compound **4** was carried out with isobutenylmagnesium bromide in THF at 0 °C to give a 1:1 mixture of diastereomers **5** and **6** in 60% total yield. Although the pairs of diastereomers **5** and **6** could not be fully separated, the removal of the nitro group would generate the same radical during the cyclization reaction. Therefore, the diastereomers could be used directly without further purification. However, in order to obtain spectroscopic data for each of the four diastereomers of **5** and **6** a pair of diastereomers **4** was separated. Each of the

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(6) For reviews, see: (a) Giese, B. *Radicals in Organic Synthesis: Formation of Carbon-Carbon Bonds*; Pergamon Press: New York, 1986. (b) Ramaiah, M. *Tetrahedron* **1987**, *43*, 3541. (c) Curran, D. P. *Synthesis* **1988**, 417 and 489. (d) Jasperse, C. P.; Curran, D. P.; Fevig, T. L. *Chem. Rev.* **1991**, *91*, 1237.

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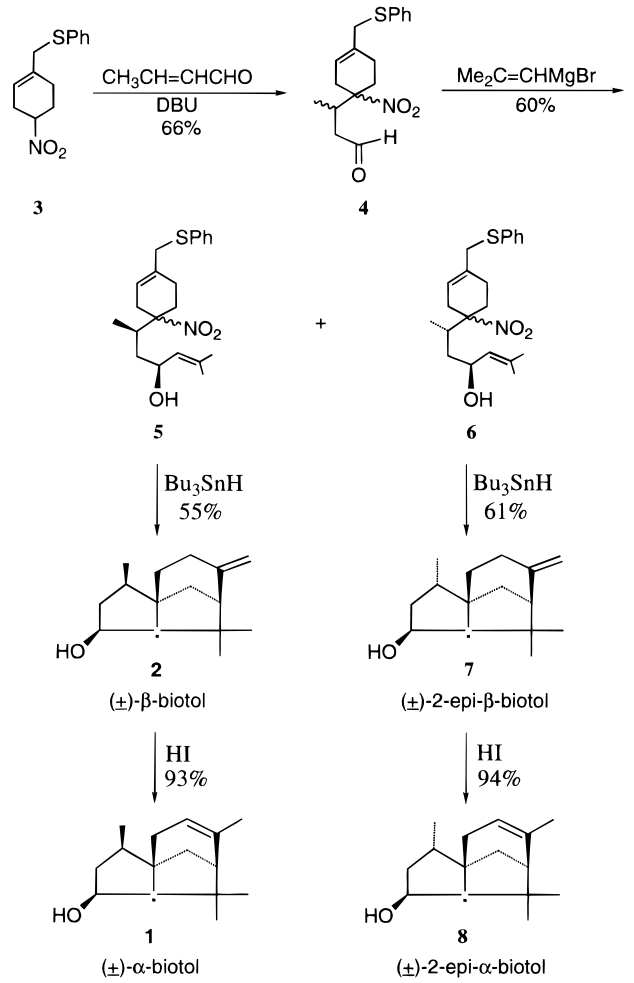
0022-3263/96/1961-2536$12.00/0

Scheme 1



diastereomers **4** was individually reacted with isobutenylmagnesium bromide to give two separable diastereomers of **5** and **6**. Unfortunately, the stereochemistry of the 2-methyl and 4-hydroxyl substituents in these isomers still could not be determined directly from their ^{1}H NMR data. Since the stereochemistry at C_2 and C_4 does not change during the radical cyclization reactions, the relative configurations could be assigned from the products after cyclization.

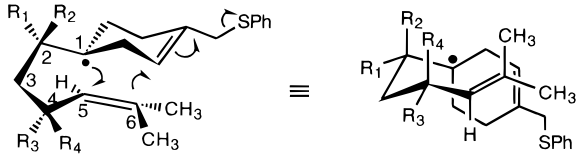
The tandem radical cyclization of a mixture of **5** was effected by treatment with Bu_3SnH in the presence of 20 mol % of azobisisobutyronitrile (AIBN) in refluxing benzene. Surprisingly, only one product (**2**) was isolated in 55% yield. The structure of compound **2** was assigned as (±)-*β*-biotol on the basis of mp, ^{1}H NMR, ^{13}C NMR, IR, and HRMS studies, compared with the reported values by Yates.[4] Moreover, diastereomers **6** were subjected to the same reaction conditions to afford **7** as a single product in 61% yield. The relative stereochemistry of **7** was determined by single-crystal X-ray diffraction[12] of its *p*-nitrobenzoate **10**. The structure of **7** was verified as (±)-2-*epi*-*β*-biotol, an epimer of **2**. From the above observations, the stereochemistry of the 2-methyl and 4-hydroxyl substituents in the cyclization precursor **5** could be deduced as *syn* while the stereochemistry in compound **6** was assigned as *anti*. Finally, the direct isomerization of the *exo* double bond in *β*-biotol **2** and its epimer **7** was effected by treatment with a catalytic amount of HI in benzene at 30 °C to provide (±)-α-biotol (**1**) (93% yield) and (±)-2-*epi*-α-biotol (**8**) (94% yield).

In consideration of the stereochemistry of the ring closure in diastereomers **5** and **6**, our results show that the 4-hydroxyl group assumes a *cis* orientation with the hydrogen at the C_5 position in both cases. Evidently, the 4-hydroxyl substituent plays a more important role in controlling the stereoselectivity of radical cyclizations than the 2-methyl group. To rationalize these observations, we propose that the radical cyclization reactions might proceed through a cyclohexane-like transition state **9**, where the conformation is determined by both steric and stereoelectronic effects of the substituent groups, especially at the C_4 position. This kind of chairlike transition state has been well studied and proposed by Beckwith[9] in studies of the stereochemistry of hex-5-enyl radical cyclizations. The use of transition state models to rationalize the stereochemistry of hex-5-enyl radical cyclizations has been reviewed by RajanBabu.[11b] As pointed out by them, a chairlike conformation for the transition states with substituents in a quasiequatorial orientation, and with the least allylic strain[13] (and the possible stereoelectronic effect) in the local allylic conformation (C_3-C_6), is more favorable.[11b] On the basis of these considerations, we believe that the predominant formation of *β*-biotol (**2**) in the radical cyclization of **5** proceeds through the lower energy transition state **9a**, in which both the 4-hydroxyl and the 2-methyl groups assume equatorial orientations. The former is also in the most favorable allylic conformation for the C_3-C_6 portion of the transition state **9a**. In the case of **6**, unexpectedly, only one predominant stereoisomer of **7** was observed. It appears to be formed through the more favorable transition state **9c** exclusively instead of **9d**. This result shows that the local conformation of the allylic alcohol portion of **9c** is more important in controlling the stereochemistry than the equatorial conformation of the 2-methyl group. To rationalize this observation, we evaluated the results of 1,5-ring closure of the 2- or 4-methylhex-5-enyl radicals in Beckwith's studies.[9c] He found that the k_{cis}/k_{trans} ratio for both cases were 0.56 and 0.21, respectively. He also pointed out that the degree of stereoselectivity should be more pronounced with bulky groups. On the basis of his observations, the different degree of stereoselectivity of 1,5-ring closure with the methyl group at different positions probably could be accounted for by assuming that the 4-substituent more effectively controls stereochemistry than the 2-substituent. However, we doubt that steric factors alone account for the observed selectivity. We believe that the conformational preference of the substituent in a chairlike transition state should be determined by both steric and stereoelectronic effects, in agreement with RajanBabu's observations.[11a]

In conclusion, the target molecules **2** and **1** have been synthesized in three and four steps from the starting material **3** with a total yield of 11% and 10%, respectively. A new and facile route to **2** and **1** through a stereocontrolled tandem radical cyclization has been successfully

(12) Compound **10** crystallizes in the triclinic $P\bar{1}$ space group with a = 7.669(3) Å, b = 13.700(4) Å, c = 18.802(5) Å, V = 1907.0(10) Å^3, and Z = 4. The asymmetric unit contains two independent molecules. The final coordinates were solved by direct methods and refined by full-matrix least-squares methods with R = 5.15%, Rw = 6.33%, and GOF = 1.04 for 487 variables. The atomic coordinates for this work are available, on request, from the Director, Cambridge Crystallographic Data Center, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW, UK. Any request should be accompanied by the full literature citation for this communication.

(13) Hoffmann, R. W. *Chem. Rev.* **1989**, *89*, 1841 and references cited therein.



9a: R_1=CH_3, R_2=H, R_3=OH, R_4=H
9b: R_1=H, R_2=CH_3, R_3=H, R_4=OH
9c: R_1=H, R_2=CH_3, R_3=OH, R_4=H
9d: R_1=CH_3, R_2=H, R_3=H, R_4=OH

demonstrated. Furthermore, the conformation of the hydroxyl substituent at the C_4 position was a more important factor in controlling the stereochemistry of the radical cyclizations than that of the methyl substituent at the C_2 position in this study. The reason is probably that the conformation of the transition state **9** is mainly determined by the local conformation of the allyl alcohol portion of the molecular due to both steric and stereoelectronic effects.

Experimental Section

Melting points were uncorrected. Solvents and reagents were dried prior to use as required. Reactions were monitored by analytical thin-layer chromatography using silica gel 60 F-254, layer thickness 0.2 mm. Column chromatography was performed on silica gel 60 (70−230 mesh). Medium-pressure liquid chromatography was carried out by using Merck Lobar prepacked silica gel columns with elution of gradients of EtOAc and hexane. The starting material **3** was prepared by our previously reported method.[3b]

4-(2′-Formyl-1′-methylethyl)-1-((phenylthio)methyl)-4-nitrocyclohexene (4). To a mixture of 840 mg (3.37 mmol) of the starting material **3** and 514 mg (3.37 mmol) of DBU in 7 mL of acetonitrile at 0 °C was added dropwise 234 mg (3.33 mmol) of crotonaldehyde in 7 mL of acetonitrile within 5 min. After being stirred for another hour at the same temperature, the solution was poured into 30 mL of water and then acidified with 1 N HCl until the pH value reached ∼2. The aqueous layer was extracted with ether. The combined organic layers were rinsed with an additional 50 mL of water, separated, dried over $MgSO_4$, and evaporated *in vacuo*. The crude product was purified by column chromatography (15:1 hexane/EtOAc) to give a pale yellow liquid of 700 mg (2.19 mmol, 66% yield) of the mixture of **2**. Further purification by MPLC was carried out with 20:1 hexane/EtOAc to afford two diastereomers. **4a**: IR (neat) 1720, 1526 cm^{-1}; ^1H NMR δ 0.97 (d, J = 7.2 Hz, 3H), 1.79−1.92 (m, 1H), 2.05−2.38 (m, 4H), 2.40−2.51 (m, 1H), 2.57−2.72 (m, 2H), 2.91 (br d, J = 17.4 Hz, 1H), 3.37 (d, J = 13.8 Hz, 1H), 3.48 (d, J = 13.8 Hz, 1H), 5.36−5.43 (m, 1H), 7.18−7.33 (m, 5H), 9.71 (br s, 1H); ^{13}C NMR δ 15.1 (q), 24.0 (t), 29.4 (t), 29.9 (t), 35.3 (d), 41.3 (t), 45.7 (t), 92.4 (s), 120.9 (d), 126.7 (d), 128.8 (d), 130.8 (d), 133.1 (s), 135.7 (s), 199.9 (d); HRMS m/z 319.1244 (M^+, calcd for $C_{17}H_{21}O_3NS$ 319.1242). **4b**: IR (neat) 1716, 1522 cm^{-1}; ^1H NMR δ 0.97 (d, J = 6.6 Hz, 3H), 1.77−1.89 (m, 1H), 2.12−2.38 (m, 4H), 2.44−2.54 (m, 1H), 2.58−2.71 (m, 2H), 2.92 (br d, J = 16.5 Hz, 1H), 3.37 (d, J = 13.8 Hz, 1H), 3.47 (d, J = 13.8 Hz, 1H), 5.35−5.41 (m, 1H), 7.16−7.32 (m, 5H), 9.72 (br s, 1H); ^{13}C NMR δ 15.1 (q), 24.1 (t), 28.7 (t), 30.7 (t), 35.2 (d), 41.2 (t), 45.9 (t), 92.1 (s), 120.6 (d), 126.7 (d), 128.8 (d), 130.8 (d), 133.2 (s), 135.7 (s), 199.9 (d); HRMS m/z 319.1245 (M^+, calcd for $C_{17}H_{21}O_3NS$ 319.1242). Anal. Calcd for $C_{17}H_{21}O_3NS$: C, 63.92; H, 6.63; N, 4.39; S, 10.04. Found: C, 63.82; H, 6.66; N, 4.62; S, 10.27.

4-(3′-Hydroxy-1′,5′-dimethyl-4′-hexenyl)-1-((phenylthio)-methyl)-4-nitrocyclohexene (5 and 6). A THF solution of isobutenylmagnesium bromide was prepared as follows. Several drops of a THF (2 mL) solution of 1.186 g (8.78 mmol) of 1-bromo-2-methylpropene were added by an addition funnel to 240 mg (9.88 mmol) of activated magnesium in 2 mL of THF, followed by adding a few drops of 1,2-dibromoethane with a syringe. The mixture was warmed by hand until the THF refluxed and the rest of the solution of 1-bromo-2-methylpropene was added dropwise. This solution was kept at reflux by heating for about 45 min. The magnesium almost completely disappeared, and another 4 mL of THF was added. To 397 mg (1.24 mmol) of the mixture of **4a** and **4b** in 12 mL of THF was added 1.2 mL of the Grignard solution at 0 °C. After the mixture was stirred for 2 h, the reaction was monitored and found to be incomplete. After a further addition of 0.6 mL of the Grignard solution was added, the mixture was allowed to stir for 2 more h and then was quenched by adding 15 mL of 1 N HCl. The product was extracted with ether. The combined organic layers were rinsed with water, dried over $MgSO_4$, and evaporated *in vacuo*. The crude product was purified by column chromatography (5:1 hexane/EtOAc) and followed by MPLC (10:1 hexane/EtOAc) to provide two pale yellow liquids of 278 mg (0,74 mmol, 60% yield) of **5** and **6** with a ratio of about 1:1. To obtain the spectroscopic data for each of the four diastereomers of **5** and **6**, each diastereomer of **4** was reacted individually with Grignard reagents by the same method mentioned above to give two separable diastereomers **5** and **6**.

5a: IR (neat) 3400, 1524 cm^{-1}; ^1H NMR δ 0.97 (d, J = 6.6 Hz, 3H), 1.27 (br s, 1H), 1.38−1.48 (m, 2H), 1.69 (s, 3H), 1.74 (s, 3H), 1.84 (ddd, J = 13.5, 11.1, 6.0 Hz, 1H), 1.91−2.03 (m, 1H), 2.03−2.18 (m, 1H), 2.18−2.35 (m, 2H), 2.35−2.45 (m, 1H), 2.84 (br d, J = 18.6 Hz, 1H), 3.36 (d, J = 13.5 Hz, 1H), 3.47 (d, J = 13.5 Hz, 1H), 4.31−4.41 (m, 1H), 4.98−5.05 (m, 1H), 5.38−5.43 (m, 1H), 7.16−7.34 (m, 5H);^{13}C NMR: δ 15.0 (q), 18.2 (q), 24.1 (t), 25.8 (q), 29.0 (t), 38.6 (d), 39.0 (t), 41.4 (t), 67.2 (d), 93.8 (s), 121.3 (d), 126.6 (d), 127.1 (d), 128.8 (d), 130.7 (d), 133.0 (s), 136.0 (s), 137.2 (s); HRMS: m/z 375.1861 (M^+, calcd for $C_{21}H_{29}O_3NS$ 375.1868).

5b: IR (neat) 3368, 1528 cm^{-1}; ^1H NMR δ 0.90 (d, J = 6.6 Hz, 3H), 1.30−1.46 (m, 2H), 1.53−1.62 (m, 1H), 1.70 (s, 3H), 1.76 (s, 3H), 1.83−2.02 (m, 2H), 2.02−2.45 (m, 4H), 2.91 (br d, J = 17.7 Hz, 1H), 3.36 (d, J = 13.5 Hz, 1H), 3.48 (d, J = 13.5 Hz, 1H), 4.34−4.46 (m, 1H), 5.03−5.11 (m, 1H), 5.37−5.44 (m, 1H), 7.16−7.34 (m, 5H);^{13}C NMR δ 14.9 (q), 18.3 (q), 24.1 (t), 25.8 (q), 29.1 (t), 29.2 (t), 38.7 (d), 39.1 (t), 41.3 (t), 67.2 (d), 93.8 (s), 121.3 (d), 126.5 (d), 127.0 (d), 128.8 (d), 130.7 (d), 132.9 (s), 135.9 (s), 137.5 (s); HRMS m/z 375.1866 (M^+, calcd for $C_{21}H_{29}O_3NS$ 375.1868). Anal. Calcd for $C_{21}H_{29}O_3NS$: C, 67.17; H, 7.78; N, 3.73; S, 8.54. Found: C, 67.05; H, 7.85; N, 4.11; S, 8.84.

6a: IR (neat) 3420, 1526 cm^{-1}; ^1H NMR δ 1.00 (d, J = 6.9 Hz, 3H), 1.09 (ddd, J = 13.8, 10.8, 3.0 Hz, 1H), 1.18 (br d, J = 4.2 Hz, 1H), 1.48−1.63 (m, 1H), 1.67 (s, 3H), 1.70 (s, 3H), 1.80−1.93 (m, 1H), 2.05−2.40 (m, 4H), 2.42−2.53 (m, 1H), 2.88 (br d, J = 19.5 Hz, 1H), 3.36 (d, J = 13.5 Hz, 1H), 3.48 (d, J = 13.5 Hz, 1H), 4.29−4.41 (m, 1H), 5.11−5.19 (m, 1H), 5.37−5.45 (m, 1H), 7.16−7.35 (m, 5H);^{13}C NMR δ 14.0 (q), 18.1(q), 24.1 (t), 25.6 (q), 29.0 (t), 29.8 (t), 37.4 (d), 38.9 (t), 41.3 (t), 65.8 (d), 93.5 (s), 121.3 (d), 126.5 (d), 128.0 (d), 128.8 (d), 130.7 (d), 133.0 (s), 135.2 (s), 135.9 (s); HRMS m/z 375.1866 (M^+, calcd for $C_{21}H_{29}O_3NS$ 375.1868).

6b: IR (neat) 3428, 1526 cm^{-1}; ^1H NMR δ 0.97 (d, J = 6.9 Hz, 3H), 1.05 (ddd, J = 14.1, 10.8, 3.3 Hz, 1H), 1.25 (br s, 1H), 1.54−1.66 (m, 1H), 1.67 (s, 3H), 1.71 (s, 3H), 1.82−1.95 (m, 1H), 2.07−2.36 (m, 4H), 2.44−2.54 (m, 1H), 2.96 (br d, J = 19.2 Hz, 1H), 3.36 (d, J = 13.5 Hz, 1H), 3.48 (d, J = 13.5 Hz, 1H), 4.32−4.44 (m, 1H), 5.13−5.20 (m, 1H), 5.36−5.44 (m, 1H), 7.15−7.32 (m, 5H);^{13}C NMR δ 14.0 (q), 18.1(q), 24.1 (t), 25.7 (q), 29.2 (t), 29.8 (t), 37.6 (d), 39.0 (t), 41.3 (t), 66.0 (d), 93.5 (s), 121.3 (d), 126.5 (d), 128.0 (d), 128.8 (d), 130.7 (d), 132.9 (s), 135.3 (s), 136.0 (s); HRMS m/z 375.1874 (M^+, calcd for $C_{21}H_{29}O_3NS$ 375.1868). Anal. Calcd for $C_{21}H_{29}O_3NS$: C, 67.17; H, 7.78; N, 3.73; S, 8.54. Found: C, 66.92; H, 7.87; N, 4.04; S, 8.80.

(±)-*β*-Biotol (2). To a solution of **5a** and **5b** (126 mg, 0.34 mmol) in dry benzene (14 mL) at 80 °C was added by a syringe pump a solution of Bu_3SnH (0.25 mL, 0.9 mmol) and AIBN (30 mg, 0.18 mmol) in dry benzene (33 mL). After the addition was complete (14 h), the reaction mixture was refluxed for another 6 h and then cooled and evaporated *in vacuo*. The crude product was purified by chromatography using hexane and then hexane/EtOAc (2:1) as eluent to remove the byproduct tin compounds. After further purification by MPLC with hexane/EtOAc (50:1) as eluent, a colorless solid **2** (41 mg, 55% yield) was obtained: mp 97−99 °C (recrystalized from acetone, lit.[4b] mp 95−97 °C); IR (CCl_4) 3356 cm^{-1}; ^1H NMR δ 0.92 (d, J = 6.9 Hz, 3H), 1.03 (s, 3H), 1.13 (s, 3H), 1.27 (d, J = 11.4 Hz, 1H), 1.30−1.64 (m, 4H), 1.71 (d, J = 8.1 Hz, 1H), 1.68−1.83 (m, 2H), 2.10 (dt, J = 11.4, 5.4 Hz, 1H), 2.21 (d, J = 4.5 Hz, 1H), 2.31−2.38 (m, 2H),

4.15 (ddd, J = 9.6, 8.7, 5.4 Hz, 1H), 4.52 (br s, 1H), 4.60 (br s, 1H); ^{13}C NMR δ 14.9 (q), 26.1 (q), 26.2 (q), 29.0 (t), 33.7 (t), 39.5 (d), 41.1 (s), 45.5 (t), 46.6 (t), 53.2 (s), 61.1 (d), 65.2 (d), 73.6 (d), 108.1 (t), 151.1 (s); HRMS m/z 220.1828 (M^+, calcd for $C_{15}H_{24}O$ 220.1827).

(±)-α-Biotol (1). Two drops of 57% HI aqueous solution were added to a solution of **2** (72 mg, 0.33 mmol) in benzene (25 mL) at 30 °C, and the mixture was stirred for 24 h. Saturated aqueous $NaHCO_3$ was added, and the mixture was extracted with EtOAc. The combined extracts were dried over $MgSO_4$, and the solvent was evaporated. The residue was purified by liquid chromatogrphy with hexane/EtOAc (20:1) as eluent to give a colorless solid **1** (66.8 mg, 93% yield): mp 73−74 °C (recrystallized from acetone, lit.[4b] mp 68−70 °C); IR (CCl_4) 3384 cm^{-1}; ^{1}H NMR δ 0.94 (d, J = 6.9 Hz, 3H), 1.08 (s, 3H), 1.12 (s, 3H), 1.25 (br s, 1H), 1.46 (d, J = 11.1 Hz, 1H), 1.52−1.69 (m, 3H), 1.67 (d, J = 2.1 Hz, 3H), 1.74−1.93 (m, 2H), 1.77 (d, J = 4.2 Hz, 1H), 2.10 (dt, J = 11.7, 5.4 Hz, 1H), 2.22 (dt, J = 16.8, 2.4 Hz, 1H), 4.10 (ddd, J = 8.7, 7.8, 5.4 Hz, 1H), 5.22 (br s, 1H); ^{13}C NMR δ 15.8 (q), 24.6 (q), 25.7 (q), 27.8 (q), 38.7 (t), 39.5 (d), 40.9 (t), 46.5 (t), 46.6 (t), 52.5 (s), 55.5 (d), 68.8 (d), 73.7 (d), 118.6 (d), 140.4 (s); HRMS m/z 220.1832 (M^+, calcd for $C_{15}H_{24}O$ 220.1827).

(±)-2-*epi*-β-Biotol (7). After a mixture of **6a** and **6b** (87 mg, 0.23 mmol) was subjected to the same procedure as **2**, a colorless solid **7** (31 mg, 61% yield) was obtained: mp 82−83 °C (recrystallized from acetone); IR (CCl_4) 3360 cm^{-1}; ^{1}H NMR δ 0.89 (d, J = 6.9 Hz, 3H), 0.92 (d, J = 11.7 Hz, 1H), 0.97 (s, 3H), 1.03 (s, 3H), 1.24 (br s, 1H), 1.36−1.45 (m, 1H), 1.50−1.66 (m, 1H), 1.68−1.81 (m, 4H), 1.89−2.04 (m, 1H), 2.15 (d, J = 4.8 Hz, 1H), 2.34−2.42 (m, 2H), 4.15 (d, J = 4.2 Hz, 1H), 4.56 (br s, 1H), 4.61 (br s, 1H); ^{13}C NMR δ 13.9 (q), 26.1 (q), 26.2 (q), 30.4 (t), 37.0 (t), 37.2 (t), 38.4 (d), 42.8 (s), 44.0 (t), 55.8 (s), 59.2 (d), 66.5 (d), 72.8 (d), 108.4 (t), 151.1 (s); HRMS m/z 220.1826 (M^+, calcd for $C_{15}H_{24}O$ 220.1827). Anal. Calcd for $C_{15}H_{24}O$: C, 81.76; H, 10.98. Found: C, 81.54; H, 10.93.

(±)-2-*epi*-α-Biotol (8). Treatment of **7** (27.6 mg, 0.13 mmol) with the same procedure as **1** generated a colorless solid **8** (26.0 mg, 94% yield): mp 80−82 °C (recrystallized from acetone); IR (CCl_4) 3348 cm^{-1}; ^{1}H NMR δ 0.91 (d, J = 6.9 Hz, 3H), 0.95 (s, 3H), 1.13 (d, J = 10.5 Hz, 1H), 1.14 (s, 3H), 1.49−1.82 (m, 6H), 1.68 (d, J = 1.5 Hz, 3H), 1.92−2.06 (m, 1H), 2.41 (dt, J = 16.8, 2.1 Hz, 1H), 4.06 (d, J = 4.5 Hz, 1H), 5.26 (br s, 1H); ^{13}C NMR: δ 13.4 (q), 24.7 (q), 25.2 (q), 27.9 (q), 33.5 (t), 37.7 (d), 41.6 (t), 43.6 (t), 48.2 (s), 53.9 (d), 54.6 (s), 70.1 (d), 73.0 (d), 120.0 (d), 140.5 (s); HRMS m/z 220.1823 (M^+, calcd for $C_{15}H_{24}O$ 220.1827). Anal. Calcd for $C_{15}H_{24}O$: C, 81.76; H, 10.98. Found: C, 81.43; H, 10.96.

4-((4′-Nitrobenzoyl)oxy)-2,6,6-trimethyl-8-methylenetricyclo[5.3.1.0^{1,5}]undecane (10). To a solution of **7** (109 mg, 0.5 mmol) in benzene (5 mL) was added pyridine (0.2 mL, 2.5 mmol) and 4-nitrobenzoyl chloride (150 mg, 0.8 mmol). The solution was refluxed for 5 h, and the mixture was diluted with EtOAc. The mixture was filtered and the filtrate was evaporated. The residue was purified by chromatography with 100:1 hexane/EtOAc to give a colorless solid **10** (128 mg, 70% yield). The derivative of (±)-2-*epi*-β-biotol (**7**) was recrystallized from ethyl acetate to provide a crystal for X-ray examination: mp 181−183 °C; IR (KBr) 1698, 1506 cm^{-1}; ^{1}H NMR δ 0.95 (d, J = 6.6 Hz, 3H), 1.01 (d, J = 12.0 Hz, 1H), 1.08 (s, 3H), 1.12 (s, 3H), 1.32−1.43 (m, 1H), 1.66−1.86 (m, 3H), 1.91 (br s, 1H), 1.94−2.09 (m, 2H), 2.23 (d, J = 4.5 Hz, 1H), 2.25−2.45 (m, 2H), 4.56−4.61 (m, 1H), 4.61−4.65 (m, 1H), 5.28 (d, J = 4.8 Hz, 1H), 8.15−8.20 (m, 2H), 8.26−8.31 (m, 2H); ^{13}C NMR: δ 13.7 (q), 25.6 (q), 26.1 (q), 30.2 (t), 36.8 (t), 37.0 (t), 39.4 (d), 40.4 (t), 43.1 (s), 55.9 (s), 58.9 (d), 64.2 (d), 78.7 (d), 108.8 (t), 123.5 (d), 130.6 (d), 136.4 (s), 150.4 (s), 150.5 (s), 164.3 (s); HRMS m/z 369.1936 (M^+, calcd for $C_{22}H_{27}O_4N$ 369.1940).

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