A Formal Total Synthesis of Racemic Sesquiterpenoid Sativene

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Several key reactions involving intramolecular cyclization, Grignard reaction, and ionic hydrogenation have been employed in a formal synthesis of sativene. The synthesis affords 3-isopropyl-6-methyltricyclo-[4.4.0.0^{2,8}]decan-7-one, **12**, McMurry's penultimate precursor to sativene, in 28% overall yield in eight steps starting with the commercially available racemic Wieland−Miescher ketone.

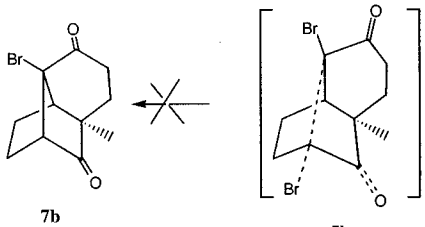
The tricyclic sesquiterpene sativene, first isolated from *Helminthosporium sativum*, has been of synthetic interest for nearly three decades.[1] We have previously reported several dehydrohalogenations[2] of α-bromoketones and recently used this method to make a convenient entry into the ring system of sativene.[3] In this work, we describe an eight-step synthesis of compound **12**, from the commercially available racemic Wieland−Miescher ketone, in an overall yield of 28%. Furthermore, we report a new synthesis of dibromide **5**. In our previously reported synthesis of **5**,[3] direct bromination of dione **2**, using either Br_2 in $CHCl_3$ or $CuBr_2$ in $CHCl_3$/EtOAc, involved a laborious separation of the two isomeric dibromides, **5** and **6**, with moderate yields. Our new method, i.e., treatment of a 3:1 mixture of bis-silyl enol ethers[4] **3** and **4** with NBS, affords dibromides **5** and **6** in 58% and 10% yield, respectively, from dione **2** (Scheme 1).

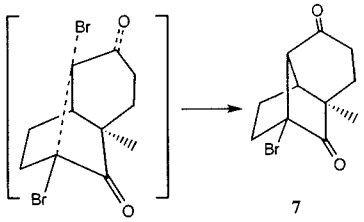
Results and Discussion

Racemic Wieland−Miescher ketone **1** was catalytically hydrogenated in 95% ethanol with 5% Pd/C to afford dione **2**[3,5] in 89% yield. Treatment of dione **2** with 3 equiv of LDA and trimethyl silyl chloride gave a quantitative yield of a mixture of silyl enol ethers **3** and **4** in a 3:1 ratio. Bromination of the crude mixture of **3** and **4** with NBS in THF afforded dibromide **5** (58% yield) as a mixture of diastereomers and dibromide **6** (10% yield) as a single isomer. Dehydrohalogenation of **5** with DBU in THF gave the tricyclic ketone **7** (88%) as the only product.[3] The structure of ketone **7** was proven by a single-crystal X-ray structure determination.

It is noteworthy that the transformation of compound **5** to **7** is only possible for a *cis*-fused geometry in the ring system of dione **2**. Further evidence for the *cis*-fused geometry is established from the X-ray structures of compounds **5** and **6**.[3] The transition states **5a** and **5b** derived from **5** might shed some light on the regioselective dehydrohalogenation of compound **5** with DBU. This reaction led to exclusive formation of compound **7** without a trace of **7b** (GC/MS, ^{1}H NMR). In **5a**, the transition state leading to **7**, the pentacoordinate carbon appears to be coplanar with the plane of the adjacent carbonyl p-orbitals. From the molecular orbital point of view, this transition state is stabilized due to the interaction between the developing electron density of the apparently parallel pentacoordinate carbon and the LUMO of the adjacent carbonyl p-orbitals.[6] In **5b** on the other hand, the developing pentacoordinate carbon appears to be nearly perpendicular to the plane of the p-orbitals of the adjacent carbonyl group; hence no particular stabilization energy is gained in the transition state. Therefore, the more favorable transition state in **5a**, as indicated above, explains why compound **7** should be formed more readily.

Furthermore, calculation of the heat of formation for compounds **7** ($\Delta H = -69.83$ kcal/mol) and **7b** ($\Delta H = -68.69$ kcal/mol), using PC Model version 6, concurs with the experimental result and indicates a stabilization energy of ∼1 kcal/mol in favor of **7**.





While examining a variety of methods aimed at introducing the isopropyl group at carbonyl C-3 in **7**, we were finally successful with isopropenylmagnesium bromide[7] (derived from 2-bromopropene and Mg in THF), which led to formation of the desired 3° alcohol, 8-bromo-3-isopropenyl-6-methyl-3-oxy-6-tricyclo[4.4.0.0^{2,8}]decan-7-one, **8**, in 88% yield (Scheme 2). The identity of this product was revealed by its ^{1}H and ^{13}C NMR spectra as well as the GC/MS analysis. In the ^{1}H NMR spectrum of **8**, the protons of the isopropenyl methyl group show as a singlet at 1.8 ppm, and the methyl group at the ring junction appears as a singlet at 1.0 ppm. The olefinic protons show as a broad singlet at 4.98 ppm. The INEPT spectrum of **8** gave positive signals for the five CH_2's in the molecule, at 113.4, 38.4, 35.6, 32.9, and 23.9 ppm, and negative (inverted) signals for the CH_3's and CH's, appearing at 57.8, 50.9, 19.2, and 17.4 ppm, respectively. The GC/MS spectrum data for **8** indicated loss of OH and a molecular ion with ($M^+ - OH$) 283/285.

On the basis of the stereochemistry of the isopropyl group resulting from hydrogenation of compound **9** and

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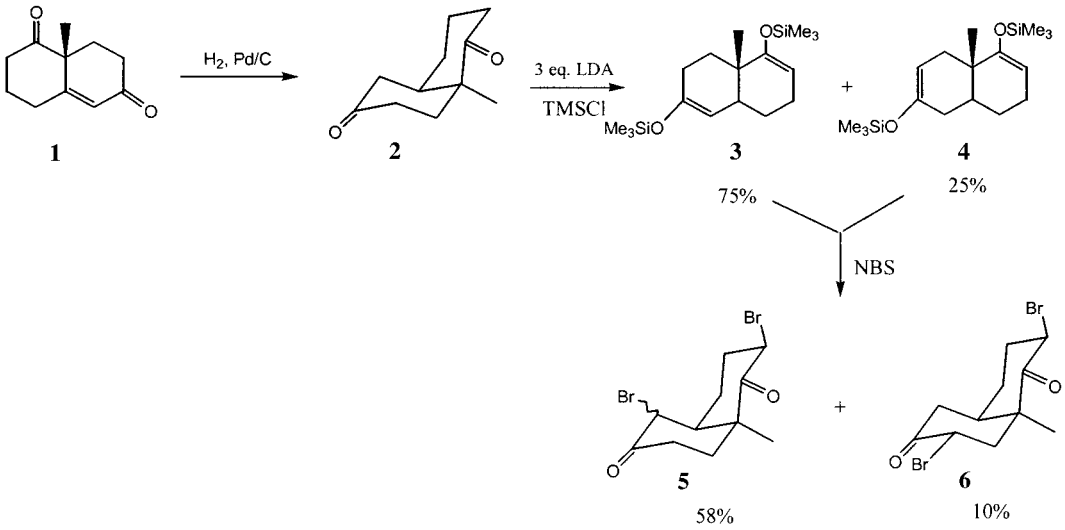
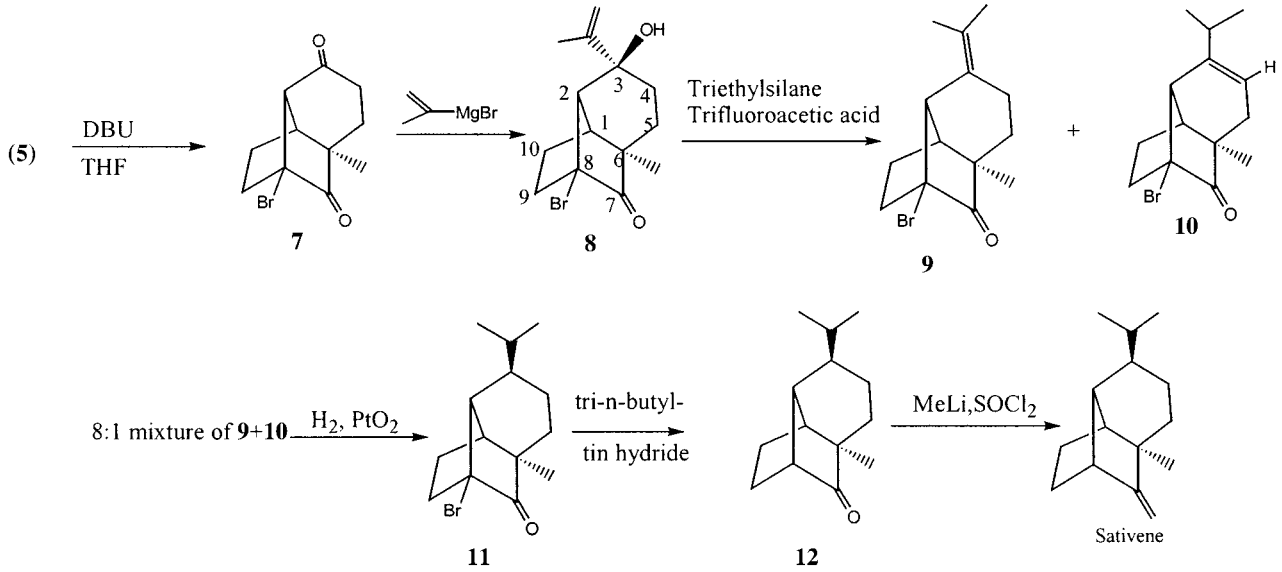
Scheme 1



Scheme 2



observations made by Snowden[8] in a similar system, we predict that the Grignard reagent approached the carbonyl group at C-3 from the α-face,[8] leading to an endo-isopropenyl group as shown in **8**. The fact that we observed only a single compound from the Grignard reaction further supports this argument. In any event, the stereochemistry of **8** with respect to the remaining part of the synthesis is irrelevant.

Alcohol **8** was subjected to ionic hydrogenation[9] in the presence of triethylsilane and trifluoroacetic acid. This reaction afforded a mixture of 8-bromo-3-isopropylidene-6-methyltricyclo[4.4.0.0^{2,8}]decan-7-one, **9**, and 8-bromo-3-isopropyl-6-methyltricyclo[4.4.0.0^{2,8}]dec-3-ene-7-one, **10**, in a ratio of 8:1. The mixture crystallized upon standing, and the next hydrogenation step was performed on the crude mixture (Scheme 2). Catalytic hydrogenation[8] of the 8:1 mixture of **9** and **10** in the presence of PtO_2 afforded 8-bromo-3-isopropyl-6-methyltricyclo[4.4.0.0^{2,8}]decan-7-one, **11**, in 77% yield with an exo-isopropyl group. The ^{1}H NMR spectrum of **11** revealed a diastereotopic relationship of the isopropyl methyl groups at 0.94 and 0.80 ppm with coupling constants of 6.6 Hz. The structure of **11,** including the stereochemistry of the isopropyl group, was firmly established by a single X-ray structure determination (Figure 1).

Our initial approach to introduction of the isopropyl group was to explore the Wittig reaction of tricyclic bromoketone **7** with isopropyltriphenylphosphorane, expecting **9** as the product. This approach, using a variety of reaction conditions however, proved unsuccessful.

Next, attempts to add the Grignard reagent, isopropylmagnesium bromide, to the carbonyl group at C-3 led only to a 1:1 mixture of reduced product **13** and unreacted starting material **7**, with no addition to the carbonyl site that would have given rise to **14** (Scheme 3). This result is consistent with the previously observed reductions of sterically hindered ketones.[10] For this reason, we tried a variation of the Grignard reagent using an organocerium reagent[11] designed to alkylate sterically hindered enolizable ketones. This reaction also failed, and starting material was recovered quantitatively.

On the other hand, catalytic hydrogenation of **8** in the presence of 5% Pd/C in 95% ethanol for 2 h gave rise to compound **14** in quantitative yield. In the ^{1}H NMR spectrum of compound **14**, it is interesting to note that the isopropyl methyl groups are in fact diastereotopic and show as two sets of doublets of doublets at 0.94 and 0.89 ppm, both with coupling constants of 6.7 Hz. The GC/MS data further established the identity of compound **14** and indicated the molecular ion with *m*/*z* 300/302. Dehydration

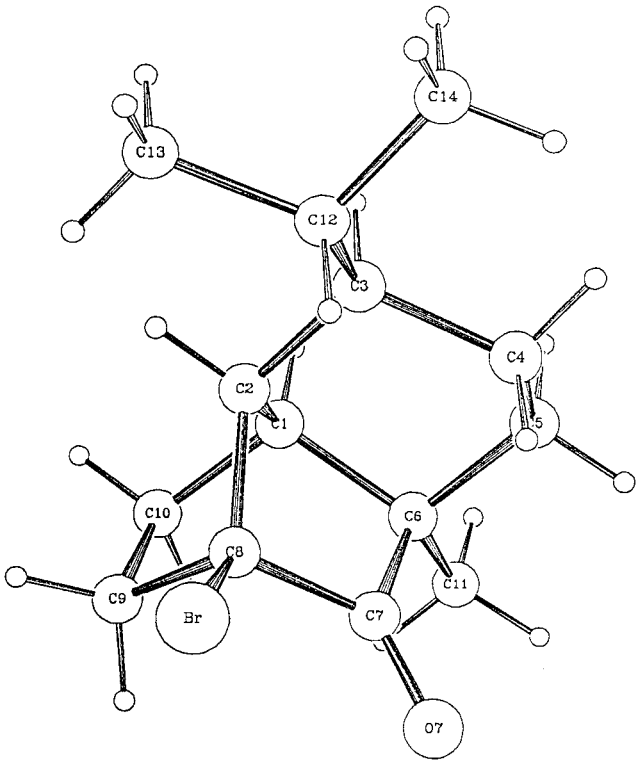


Figure 1. X-ray structure of compound **11**.

of the tertiary alcohol **14** by the use of concentrated HBr (48%) afforded a mixture of **9** and **10** (87% yield) in a ratio of 1:5, as evidenced from ^{1}H NMR, ^{13}C NMR, and GC/MS spectra analyses. The ^{1}H NMR spectrum of **10** strongly suggested the presence of a newly formed double bond, with an olefinic proton at 5.2 ppm appearing as a broad singlet. The diastereotopic methyl protons of the isopropyl group in **10** show as two sets of doublets of doublets at 0.97 and 0.95 ppm, both with coupling constants of 6.7 Hz. Catalytic hydrogenation of this mixture in the presence of PtO_2 afforded a mixture of diastereomers of **11** (Scheme 3).

As described above, ionic hydrogenation[9] of alcohol **8** gave a 8:1 mixture of **9** and **10**, leading upon hydrogenation to a 77% yield of **11**. Reductive debromination of **11** in the presence of tri-*n*-butyl tin hydride[12] afforded the desired 3-isopropyl-6-methyltricyclo[4.4.0.0^{2,8}]decan-7-one, **12**, in 93% yield. The final conversion of ketone **12** to sativene, as mentioned earlier, has already been accomplished by McMurry[5] by the use of methyllithium followed by dehydration of the alcohol in thionyl chloride and pyridine.

Conclusion. We have described an efficient synthetic approach to sativene. The key intramolecular cyclization reaction of dibromide **5** is employed for the construction of the sativene skeleton in one step (e.g., **7**), and **7** was fashioned from Wieland−Miescher ketone in four steps (45%). Elaboration of **7** led to **12**, the penultimate precursor of sativene, in another four steps (63%). Presently, we are engaged in application of this synthetic protocol to related natural products such as longifolene.

Experimental Section

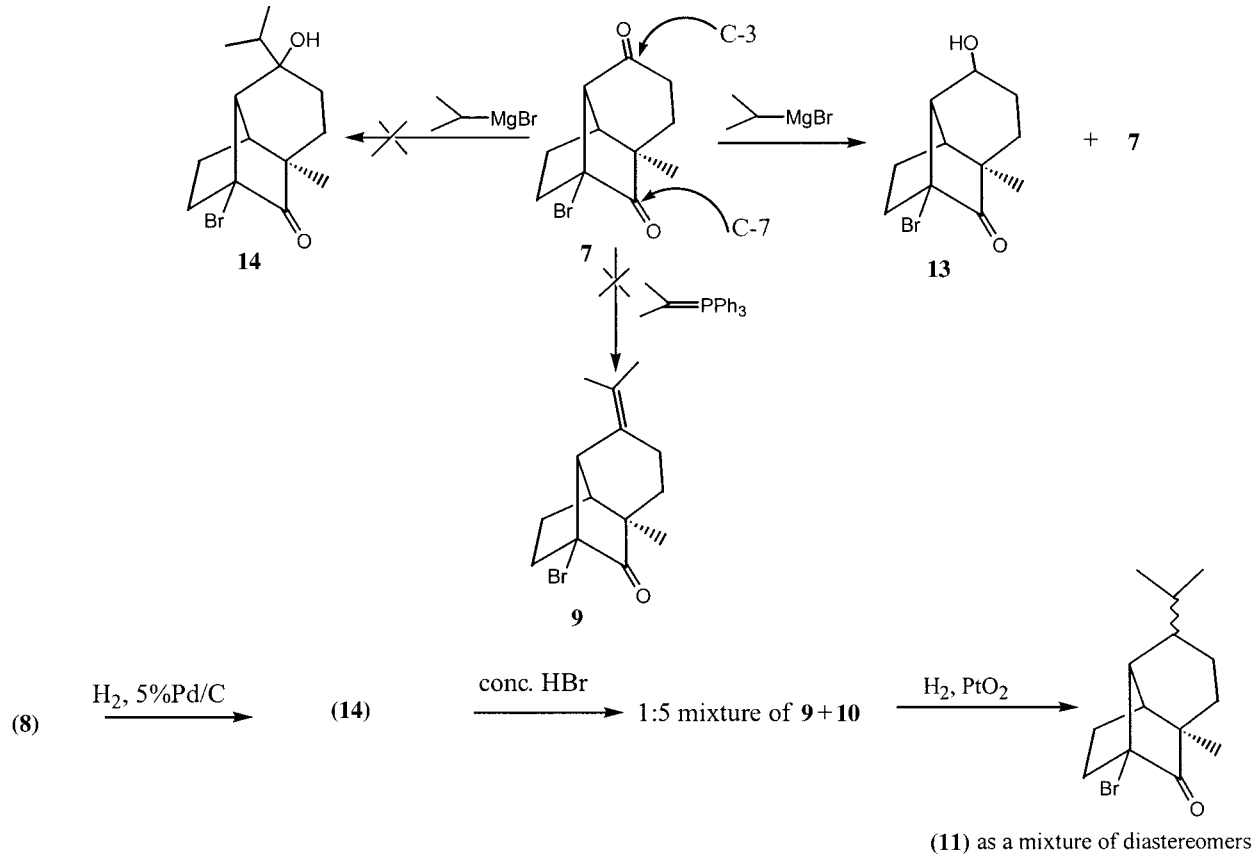
General Experimental Procedures. All air-moisture sensitive reactions were performed under a positive pressure of N_2. All solvents and reagents were distilled, dried, and/or recrystallized prior to use according to standard laboratory procedures. Melting points are uncorrected. Proton and carbon NMR spectra including INEPT were measured in $CDCl_3$ with a Bruker 400 MHz spectrometer. Analytical thin-layer chromatography (TLC) was conducted on DC-Alufolien Kieselgel 60 F_{254} from EM Separations. Column chromatography was performed using Si gel 7024-1 for flash chromatography from Baker. Radial chromatography was performed using a Chromatotron from Harrison Research Co. and Merck TLC grade 7749 Si gel from Aldrich. Mass spectra were obtained with a Hewlett-Packard 5989A GC mass spectrometer (EI) and HP 1100 LC/MSD. X-ray structures were determined with an Enraf-Nonius CAD4 diffractometer (graphite-monochromated Cu Kα radiation). Structures were solved by a multiple solution procedure and refined by full matrix least squares. In the final refinement, the non-hydrogen atoms were refined anisotropically. The hydrogen atoms were included in the structure factor calculations, but their parameters were not refined. The final discrepancy indices were $R = 0.05$ and $R_w = 0.06$.

***cis*-1-Methylbicyclo[4.4.0]decan-2,8-dione (2).** To a solution of racemic Wieland−Miescher ketone (5.93 g, 33.3 mmol) in 95% ethanol (80 mL) was added palladium on carbon (0.5 g, 5%). The reaction mixture was degassed, flushed under hydrogen, and stirred under a hydrogen atmosphere for 3−4 h. The completion of the reaction was observed by the disappearance of the UV active starting material by TLC analysis. The resulting black suspension was filtered by gravity, and the solvent was concentrated in vacuo to give quantitative yield of the crude oily dione **2** (6.0 g), which crystallized upon standing. Purification by chromatography (15% ethyl acetate in hexane) gave **2** (5.4 g, 89%) as white crystals: mp 65−66 °C (lit.[3] mp 67−68 °C). Dione **2** can also be recrystallized from 5:1 hexane/ether: ^{1}H NMR δ 2.52 (m, 6H), 2.10 (m, 4H), 1.50 (m, 3H), 1.35 (s, 3H).

***cis*-2,8-Bis[(trimethylsilyl)oxy-1-methylbicyclo[4.4.0]-deca-2,7-diene (3) and *cis*-2,8-Bis[(trimethylsilyl)oxy-1-methylbicyclo[4.4.0]deca-2,8-diene (4).** To a solution of LDA prepared from diisopropylamine (2.52 mL, 18 mmol) and *n*-butyllithium (7.2 mL, 18 mmol) in THF (60 mL) at −78 °C was slowly added dione **2** (1.08 g, 6 mmol) dissolved in 60 mL of dry THF under N_2. This mixture was stirred at −78 °C for 45 min, and then trimethyl silyl chloride (2.4 mL, 19 mmol) was added. The mixture was subsequently warmed to room temperature during 1 h and quenched with 1−2 mL of water. The THF was evaporated under reduced pressure, and diethyl ether (100 mL) was added. Subsequent workup was performed rapidly: the organic layer was extracted with ice cold saturated aqueous $NaHCO_3$ (25 mL) and brine (15 mL). The organic layer was separated and dried over $MgSO_4$, filtered, and concentrated in vacuo to afford a crude oil (2.35 g, 120%), which without purification was carried on to the next step. Examination of ^{1}H NMR and ^{13}C NMR spectra, particularly in the olefinic region (for ^{1}H δ between 4 and 5, and ^{13}C δ 145−160), showed evidence of two isomeric enol ethers, in a ratio of 75% and 25% for **3** and **4**. ^{1}H NMR for mixture of **3** and **4**: olefinic region δ 4.68 (m, 1H), 4.63 (t, 2H), 4.57 (m, 1H). ^{13}C NMR of mixture of **3** and **4**: olefinic region δ 158, 155, 151, 148, 108, 102, 101.7, 100.8.

***cis*-3,7-Dibromo-1-methylbicyclo[4.4.0]decan-2,8-dione (5) and *cis*-3,9-(dieq)Dibromo-1-methylbicyclo[4.4.0]-decan-2,8-dione (6).** Recrystallized NBS (from $CHCl_3$; 2.34 g, 13 mmol) was added as solid to a solution of the crude mixture of the bis-silyl enol ethers **3** and **4** (2.35 g) dissolved in THF (100 mL), and the reaction mixture was stirred at room temperature under N_2 for 1 h. Solvent (THF) was evaporated, diethyl ether (100 mL) was added, and the mixture was extracted with ice cold saturated $NaHCO_3$ (25 mL) and brine (15 mL). The combined aqueous layers were washed with additional ether (30 mL). The organic layers were combined, dried over $MgSO_4$, filtered, and concentrated in vacuo to afford a crude mixture of dibromides **5** and **6** (2.80 g). Purification by chromatography (20% ethyl acetate in hexane) gave **5** (1.13 g, 58%, based on the dione **2**) as an oily mixture of diastereomers, and **6** (0.2 g, 10%) with an mp (dec) 182−183 °C. The oily **5** was dissolved in a minimum amount of ether and placed in a refrigerator to afford crystals of **5** as a mixture of diastereomers: mp (dec) 122−126 °C; ^{1}H NMR of **5** as a

Scheme 3



mixture of diastereomers, δ 5.02 (dd, 1H, J = 12.6, 7 Hz), 4.87 (dd, 1H), 4.4 (d, 1H, J = 12 Hz), 2.7−2.3 (m, H), 2.0 (ddd), 1.56 (s, 3H, methyl), 1.38 (s, 3H, methyl); ^{13}C NMR 203.5, 202.4, 200.9, 199.3, 58.8, 57.9, 55.2, 54.4, 53.4, 52.9, 52.3, 52.2, 38.1, 37.7, 37.1, 35.7, 34.1, 32.3, 27.3, 27.1, 25.4, 20.5; IR (KBr) 2960, 2927, 1744, 1728, 1462, 1325, 1104 cm^{-1}; GC/MS *m/z* 338 (M^+) 259 (M − Br), 217, 55 (100%).

The second compound was eluted from the column (20% ethyl acetate in hexane) and concentrated in vacuo to afford **6** as white crystals: mp (dec) 182−183 °C; ^{1}H NMR δ 5.1 (dd, 1H, J = 12.7, 6.9 Hz), 4.97 (dd, 1H, J = 13.1, 6.3 Hz), 3.13 (dd, 1H, J = 13.5, 6.3 Hz), 2.67 (m, 1H), 2.4 (m, 6H), 1.85 (t, 1H, J = 13.3 Hz), 1.41 (s, 3H); ^{13}C NMR 203.7, 200.4, 53.1, 52.5, 52.3, 47.2, 46.5, 42.4, 35.1, 27.3, 25.5; IR (KBr) 2982, 2952, 1724, 717, 676 cm^{-1}; GC/MS using positive electrospray ionization gave ion masses 360, 361, 362 for $[M + Na]^+$ and 698.8 for $[2M + Na]^+$.

8-Bromo-6-methyltricyclo[4.4.0.0^{2,8}]decane-3,7-dione (7). To a room temperature solution of dibromide **5** (4.67 g, 13.82 mmol) in dry THF (300 mL) under N_2 was added DBU (6.62 g, 43.5 mmol). The mixture was then stirred at 65 °C for 16 h. The reaction was quenched with ice−water, and the solvent was evaporated. To the dark residue were added CH_2Cl_2 (300 mL) and diethyl ether (35 mL). The dark mixture became yellowish when it was neutralized with 1 M HCl. The organic layer was washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo to give **7** (3.90 g) as crystals. The dark crude product, which had clean proton and carbon NMR spectra, was purified using silica gel with 15% ethyl acetate in hexane to afford white crystals of **7** (3.15 g, 88%). Compound **7** was recrystallized from ethyl acetate/hexane: mp 116−117 °C; ^{1}H NMR δ 3.04 (s, 1H), 2.54 (d, 1H, J = 2.1 Hz), 2.46 (dd, 1H, J = 17.6, 6.37 Hz), 2.23 (m, 2H), 2.02 (m, 4H), 1.78 (dd, 1H, J = 13.1, 6.3 Hz), 1.24 (s, 3H); ^{13}C NMR 210.3, 206.2, 68.3, 66.2, 49.9, 49.1, 36.4, 35.8, 34.7, 24.4, 16.8; IR (KBr) 2963, 2932, 1766, 1712 cm^{-1}; GC/MS *m/z* 256/258 (M^+, 20%), 177 (M − Br, 31%), 133 (100%).

8-Bromo-3-isopropenyl-6-methyl-3-oxy-6-tricyclo-[4.4.0.0^{2,8}]decan-7-one (8). Isopropenylmagnesium bromide, prepared from Mg turnings (0.19 g, 8 mmol) and isopropenyl bromide (0.71 mL, 8 mmol) in dry THF (8 mL), was added dropwise to a cooled (−78 °C) solution of ketone **7** (0.5 g, 1 mmol) in dry THF (20 mL) under N_2. The solution was stirred at −50 °C for 4 h, allowed to warm to room temperature, and quenched by dropwise addition of saturated aqueous NH_4Cl. The mixture was extracted with ether (2 × 20 mL), and the combined ether layers were washed with brine (40 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo to give the alcohol **8** (0.63 g, 100%). The crude alcohol was chromatographed using radial chromatography with 10% ethyl acetate in hexane, to afford **8** (0.51 g, 88%) as white crystals. Recrystallization from CH_2Cl_2/hexane gave **8** as white crystals: mp 87.5−88 °C; ^{1}H NMR δ 4.98 (s, 2H), 2.68 (s, 1H), 2.5 (br s, 1H), 2.4 (m, 2H), 2.0 (d, 1H, J = 4 Hz), 1.8 (s, 3H methyl), 1.5 (m, 6H), 1.0 (s, 3H methyl); ^{13}C NMR 213.6, 146.6, 113.4, 75.1, 69.5, 57.8, 50.9, 46.7, 38.4, 35.6, 32.9, 23.9, 19.2, 17.4; IR (KBr) 3558, 3483, 2954, 2919, 1753, 1655, 1637, 1475, 1458, 1448, 1367, 1173, 1079, 1061, 999, 926, 804 cm^{-1}; GC/MS *m/z* 283/285 (M^+ at 300 not seen, loss of OH), 255/257, 219 (M − Br), 173, 145, 131, 119, 105 (100%).

8-Bromo-3-isopropylidene-6-methyltricyclo[4.4.0.0^{2,8}]-decan-7-one (9) and 8-Bromo-3-isopropyl-6-methyltricyclo-[4.4.0.0^{2,8}]dec-3-ene-7-one (10). To a solution of alcohol **8** (0.37 g, 1.233 mmol) dissolved in CH_2Cl_2 (12 mL) were added triethylsilane (0.37 mL, 2.3 mmol) and trifluoroacetic acid (0.925 mL, 12 mmol). The reaction mixture was stirred for 24 h at room temperature, then CH_2Cl_2 (30 mL) and ether (10 mL) were added. The mixture was neutralized with saturated aqueous $NaHCO_3$, and the organic layer was separated and dried over $MgSO_4$, filtered, and concentrated in vacuo to give a quantitative yield (0.35 g) of an oily mixture of alkenes **9** and **10** in a ratio of 8:1. The crude mixture of alkenes crystallized upon standing, and without further purification was carried on to the hydrogenation step. Further purification of the crude solid was accomplished with radial chromatography using 5% ethyl acetate in hexane to give **9**: mp 89−91 °C; ^{1}H NMR δ 3.3 (s, 1H), 2.5 (dd, 1H, J = 18, 5 Hz), 2.1−1.78 (m, 7H), 1.7 (s, 3H, methyl), 1.6 (s, 3H, methyl), 1.3 (m, 1H),

1.0 (s, 3H, methyl); ^{13}C NMR 215, 128.9, 125.5, 72.1, 56.2, 50.9, 48.4, 37.5, 36.7, 24.6, 24.4, 21.4, 20.9, 18.3; IR (neat) 2966, 2931, 1754, 1672, 1472, 1449, 1372, cm^{-1}; GC/MS *m*/*z* 282/284 (M+), 267, 239, 203 (M-Br), 175, 161, 145, 133, 119, 105, 91(100%). Data for **10**: ^{1}H NMR δ 5.2 (br t, 1H, J = 4 Hz), 2.6 (d, 1H, J = 2 Hz), 2.3−1.8 (m, 8H), 1.1 (s, 3H, methyl), 0.97 (d, 3H, J = 6.7 Hz), 0.95 (d, 3H, J = 6.8 Hz); ^{13}C NMR 213.5, 144.9, 118.2, 75.6, 54.4, 50.1, 46.0, 40.5, 36.6, 34.1, 23.6, 23.1, 20.9, 18.7; GC/MS *m*/*z* 282/284 (M+), 267, 239, 203 (M − Br), 161 (100%), 145, 133, 119, 105, 91.

The ratio of **9** to **10** was determined by integration values of ^{1}H NMR of the methyl groups at δ 1.7 and 1.6 in compound **9** vs 0.97 and 0.95 in compound **10**.

8-Bromo-3-isopropyl-6-methyltricyclo[4.4.0.0^{2,8}]decan-7-one (11). The crude 8:1 solid mixture of **9** and **10** (0.35 g, 1.23 mmol) in a stirred mixture (20 mL) of 3:1 acetic acid and ethyl acetate was hydrogenated over PtO_2 (0.2 g) in a flask equipped with an H_2 filled balloon.[8] After 1.5 h, the cloudy dark mixture formed visible black particles and became much clearer. The solution was filtered and concentrated in vacuo to give an oil. The oil was dissolved in ether (50 mL) and washed with saturated aqueous $NaHCO_3$ and brine, then dried over $MgSO_4$, filtered, and concentrated in vacuo to give **11** (0.33 g, 94%). The crude **11** was purified by radial chromatography, using 5% ethyl acetate in hexane, and concentrated in vacuo to afford crystalline **11** (0.27 g, 77%): mp 71−73 °C; ^{1}H NMR δ 2.6 (s, 1H), 2.1 (m, 2H), 1.7 (m, 7H), 1.4 (m, 2H), 1.0 (s, 3H, methyl), 0.94 (d, 3H, methyl, J = 6.6 Hz), 0.80 (d, 3H, methyl, J = 6.6 Hz); ^{13}C NMR 214.5, 69.0, 52.8, 50.5, 49.9, 45.7, 38.8, 37.7, 30.2, 25.9, 23.8, 22.4, 22.2, 18.1; IR (neat) 2966, 2937, 2872, 2849, 1754, 1472, 1449, 1384, 1367, 1149, 1043, 967, 885, 808, 791, cm^{-1}; GC/MS *m*/*z* 284/286 (M+), 213, 205, 188, 177, 161, 145, 133, 121, 105, 91, 79.

X-ray crystallographic data unambiguously established the structure of **11** including the stereochemistry of the isopropyl group.

3-Isopropyl-6-methyltricyclo[4.4.0.0^{2,8}]decan-7-one (12). To compound **11** (0.119 g, 0.42 mmol) dissolved in benzene (3 mL) was added tri-*n*-butyl tin hydride (0.45 mL, 1.67 mmol), and the resulting mixture was refluxed for 24 h. The reaction mixture was then concentrated in vacuo to remove benzene. Ether was added (40 mL), followed by saturated aqueous NaF (10 mL). The organic layer was washed with brine, then dried over $MgSO_4$, filtered, and concentrated in vacuo to give 0.61 g of a crude mixture. This was chromatographed using radial chromatography with 5% ethyl acetate in hexane. The first, UV active, band collected was presumably Bu_3SnBr (0.38 g). Further elution afforded a second, non-UV active, fraction which produced **12** (0.0798 g, 93%) as a clear oil. Spectral analysis of compound **12** fits well with McMurry's spectra:[5] ^{1}H NMR δ 2.4 (d, 1H, J = 4 Hz), 2.1 (s, 1H), 1.8 (s, 1H), 1.7−1.3 (m, 7H), 1.1 (ddd, 1H), 0.91 (s, 3H, methyl), 0.85 (d, 3H, methyl, J = 6.6 Hz), 0.80 (d, 3H, methyl, J = 6.6 Hz); ^{13}C NMR 224.4, 51.9, 50.9, 50.5, 49.4, 43.3, 37.0, 33.2, 27.2, 26.0, 22.5, 21.7, 21.4, 17.5; IR (neat) 2954, 2931, 2872, 1737, 1472, 1461, 1449, 1367, 1055, 1026, 750, cm^{-1}; GC/MS *m*/*z* 207 (M + 1), 206 (M+), 191, 188, 173, 163, 145, 135, 107, 93, 81, 79.

Synthesis of a Mixture of 9 and 10. To alcohol **8** (0.18 g, 0.6 mmol) at room temperature was added HBr (18 mL, 48%). After 1.5 h, ether (5 mL) was added and the mixture was stirred for 21 h, then diluted with ice water (50 mL). The aqueous layer was extracted with ether (2 × 40 mL), and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo to give a mixture of **9** and **10** (0.14 g, 87% yield) in a 1:5 ratio, respectively. Data for **9**: ^{1}H NMR δ 3.3 (s, 1H), 2.5 (dd, 1H, J = 18, 5 Hz), 2.1−1.78 (m, 7H), 1.7 (s, 3H, methyl), 1.6 (s, 3H, methyl), 1.3 (m, 1H), 1.0 (s, 3H, methyl); ^{13}C NMR 215, 128.9, 125.5, 72.1, 56.2, 50.9, 48.4, 37.5, 36.7, 24.6, 24.4, 21.4, 20.9, 18.3; IR (neat) 2966, 2931, 1754, 1672, 1472, 1449, 1372, cm^{-1}; GC/MS *m*/*z* 282/284 (M+), 267, 239, 203 (M − Br), 175, 161, 145, 133, 119, 105, 91(100%). Data for **10**: ^{1}H NMR δ 5.2 (br t, 1H, J = 4 Hz), 2.6 (d, 1H, J = 2 Hz), 2.3−1.8 (m, 8H), 1.1 (s, 3H, methyl), 0.97 (d, 3H, J = 6.7 Hz), 0.95 (d, 3H, J = 6.8 Hz); ^{13}C NMR 213.5, 144.9, 118.2, 75.6, 54.4, 50.1, 46.0, 40.5, 36.6, 34.1, 23.6, 23.1, 20.9, 18.7; GC/MS *m*/*z* 282/284 (M+), 267, 239, 203 (M − Br), 161 (100%), 145, 133, 119, 105, 91.

The ratios of **9** to **10** were determined by integration values of ^{1}H NMR of the methyl groups at δ 1.7 and 1.6 in compound **9** vs 0.97 and 0.95 in compound **10**.

8-Bromo-3-isopropyl-6-methyl-3-oxy-6-tricyclo[4.4.0.0^{2,8}]-decan-7-one (14). To crude alcohol **8** (0.55 g, 1.83 mmol) dissolved in ethanol (15 mL, 95%) under an H_2 atmosphere at room temperature was added 0.19 g of 5% Pd/C. Hydrogenation took about 2 h to complete. After the reaction mixture was filtered, solvent was removed and the crude oily residue (0.5 g, 90% yield) was chromatographed, using 15% ethyl acetate in hexane, to afford pure **14** (0.4 g, 73%) as a colorless oil: ^{1}H NMR δ 2.5 (s, 1H), 2.1 (m, 2H), 2.0 (m, 1H), 1.9−1.4 (m, 6 H), 1.3 (m, 2H), 1.0 (s, 3H methyl), 0.94 (d, 3H methyl, J = 6.7 Hz), 0.89 (d, 3H methyl, J = 6.7 Hz); ^{13}C NMR 213.9, 74.3, 69.7, 58.7, 50.8, 45.6, 37.9, 34.6, 32.7, 32.4, 23.8, 17.2, 16.8, 16.4; IR (neat) 3571, 2965, 2877, 1757, 1472, 1378, 1279, 1181, 987, 806; GC/MS *m*/*z* 302 (M+), 257/259 (100%), 241, 221, 211, 199, 177, 175, 150, 131, 121, 107, 91, 79, 55, 43.

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Supporting Information Available: Copies of ^{1}H and ^{13}C NMR and IR spectra of all new compounds and X-ray crystallographic data for compounds **7** and **11**. This material is available free of charge via the Internet at http://pubs.acs.org.

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