A New Enantiospecific Synthesis of α-Santalanes via Homofragmentation of 1,4-Diol Monosulfonate Esters

Petrus M. F. M. Bastiaansen, Joannes B. P. A. Wijnberg,* and Aede de Groot*

Laboratory of Organic Chemistry, Agricultural University, Dreijenplein 8, 6703 HB Wageningen, The Netherlands

Received February 26, 1996[⊗]

The homofragmentation of 1,4-diol monosulfonate esters was applied as a key step in the synthesis of α-santalanes. The enantiospecific synthesis of (+)-α-santalan-12-one (**1d**) was achieved via the tricyclic dione **2** as an intermediate that could be obtained from (*R*)-(−)-carvone. A 1,2-carbonyl transposition in dione **2** followed by functional group transformations afforded the tricyclic 1,4-diol monomesylate **3**, which could be homofragmented in 76% yield to the tricyclic aldehyde **4**. From this compound the synthesis of several α-santalanes can be achieved; the synthesis of **1d** was accomplished in 11 steps from **2** in 8% overall yield.

Introduction

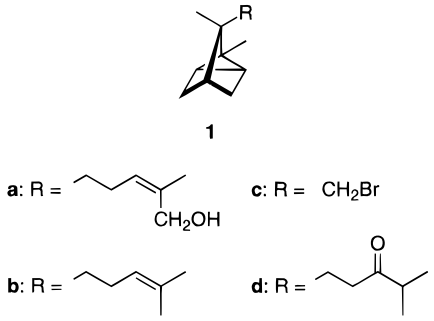
Our detailed studies on the chemical consequences of long-range orbital interactions in the stereochemically rigid *trans*-perhydronaphthalene- and norbornane-1,4-diol monosulfonate esters have shown that the chief pathways by which these compounds react upon treatment with strong base in nonpolar solvents are rearrangement, *β*-elimination, and homofragmentation.[1]

The synthetic utility of the rearrangement and elimination reaction of *trans*-perhydronaphthalene-1,4-diol monosulfonate esters has been demonstrated in the total syntheses of guaiane[2] and alloaromadendrane sesquiterpenes.[3] We now report on the applicability of the homofragmentation reaction of these 1,4-diol monosulfonate esters in the synthesis of α-santalane sesquiterpenes having the tricyclenic ring system **1** as a common structural feature (Chart 1).

α-Santalanes belong to the characteristic components of East Indian sandalwood oil[4,5] and lavender oil,[6] two important essential oils in perfumery. From the α-santalanes that are of sensory importance, (+)-(*Z*)-α-santalol (**1a**) and (+)-α-santalene (**1b**) have received the most synthetic attention.[7] As far as we know, all enantiospecific syntheses of **1a**, **1b**, and other α-santalanes started with (−)-*π*-bromotricyclene (**1c**), which can be prepared from (+)-camphor in a four-step reaction sequence.[8]

In our synthetic approach to the α-santalane ring skeleton, the recently described tricyclic dione **2**,[9] easily prepared from (*R*)-(−)-carvone,[10] was used as the starting material (Scheme 1). A 1,2-transposition of the C(11) carbonyl to C(12) was needed to convert **2** into the mesylate **3**.[11] The key step in our approach, the transformation of mesylate **3** to aldehyde **4**, involved a base-induced homofragmentation reaction in which the C(2)−C(6) bond formation occurs with simultaneous breaking of the C(6)−C(12) bond.[1a−c] With aldehyde **4** in hand, further elaboration to α-santalanes is demonstrated by the enantiospecific synthesis of (+)-α-santalan-12-one (**1d**), recently isolated from *Severinia buxifolia*.[12]

Chart 1



Results and Discussion

Our starting material, the tricyclic dione **2**, was obtained in ca. 30% overall yield from (*R*)-(−)-carvone following the procedure recently described in the literature[9b] (Scheme 2). In order to achieve an oxygen function at C(12), α-hydroxylation of the silyl enol ether **6** seemed to be the easiest route.[13] As depicted in Scheme 2, **6** was postulated as an intermediate in the TMSI-promoted cyclobutane ring opening of **5** and was thought

[⊗] Abstract published in *Advance ACS Abstracts,* July 1, 1996.

(1) (a) Orrū, R. V. A.; Wijnberg, J. B. P. A.; Jenniskens, L. H. D.; de Groot, A. *J. Org. Chem.* **1993**, *58*, 1199. (b) Orrū, R. V. A.; Wijnberg, J. B. P. A.; Bouwman, C. T.; de Groot, A. *J. Org. Chem.* **1994**, *59*, 374. (c) Bastiaansen, P. M. F. M.; Wijnberg, J. B. P. A.; de Groot, A. *J. Org. Chem.* **1995**, *60*, 4240. (d) Orrū, R. V. A.; Wijnberg, J. B. P. A.; de Groot, A. *J. Org. Chem.* **1995**, *60*, 4233.

(2) Wijnberg, J. B. P. A.; Jenniskens, L. H. D.; Brunekreef, G. A.; de Groot, A. *J. Org. Chem.* **1990**, *55*, 941.

(3) Jenniskens, L. H. D.; Wijnberg, J. B. P. A.; de Groot, A. *J. Org. Chem.* **1991**, *56*, 6585.

(4) Demole, E.; Demole, C.; Enggist, P. *Helv. Chim. Acta* **1976**, *59*, 737.

(5) Brunke, E.-J.; Schmaus, G. *Dragoco Rep.* **1995**, *42*, 197 and 245 and references cited therein.

(6) Kaiser, R.; Lamparsky, D. *Helv. Chim. Acta* **1983**, *66*, 1835.

(7) For some representative examples, see: (a) Ho, T.-L. *Enantioselective Synthesis: Natural Products from Chiral Terpenes*; Wiley Interscience: New York, 1992; pp 231−234. (b) Schlosser, M.; Zhong, G. *Tetrahedron Lett.* **1993**, *34*, 5441.

(8) Corey, E. J.; Chow, S. W.; Scherrer, R. A. *J. Am. Chem. Soc.* **1957**, *79*, 5773.

(9) (a) Zhang, W.; Dowd, P. *Tetrahedron Lett.* **1994**, *29*, 5161. (b) Dowd, P.; Zhang, W.; Geib, S. J. *Tetrahedron* **1995**, *51*, 3435. We are indepted to Professor P. Dowd for sending us the experimental procedure for the synthesis of dione **2** prior to publication.

(10) Another approach to (α)-santalanes, in which (*R*)-(−)-carvone was used as the starting material, led to complete racemization: Hodgson, G. L.; MacSweeney, D. F.; Money, T. *J. Chem. Soc., Perkin Trans. 1* **1973**, 2113.

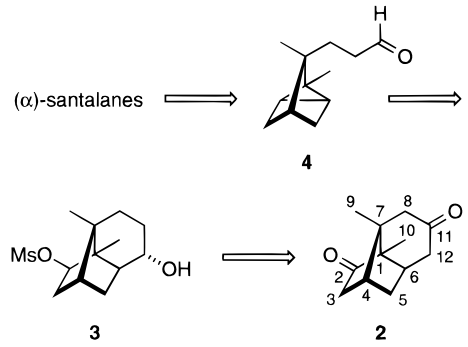
(11) The numbering system as given in structure **2** is based on the system adopted for camphor and will be followed throughout the text of this paper.

(12) Wu, T.-S.; Niwa, M.; Furukawa, H. *Phytochemistry* **1984**, *23*, 595.

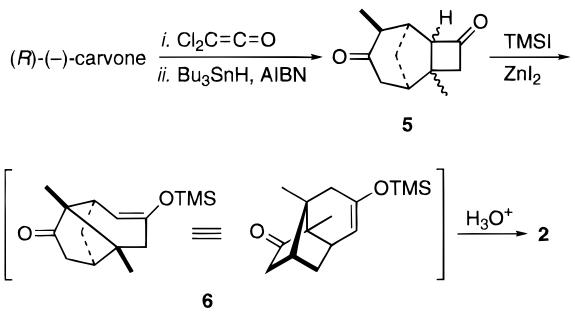
(13) For example, see: Hassner, A.; Reuss, R. H.; Pinnick, H. W. *J. Org. Chem.* **1975**, *40*, 3427.

S0022-3263(96)00389-1 CCC: $12.00 © 1996 American Chemical Society

Scheme 1



Scheme 2

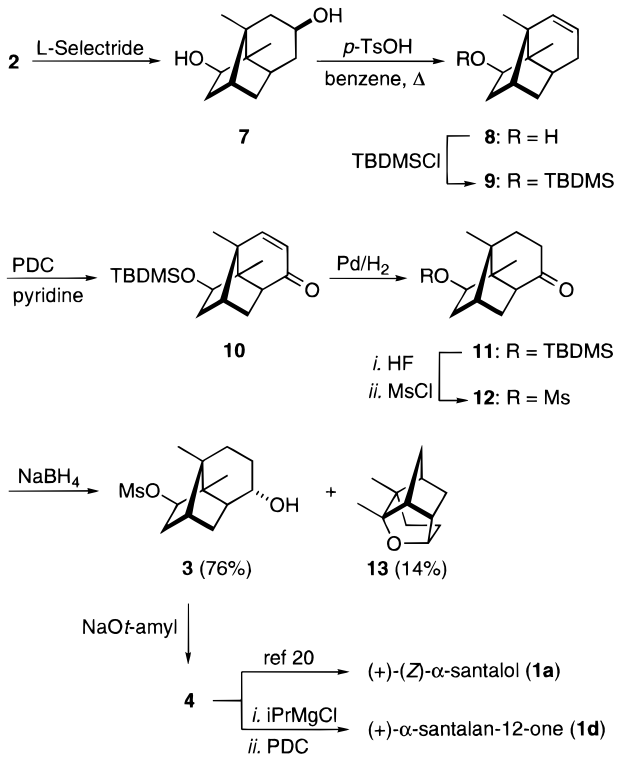


to give the dione **2** only upon hydrolytic workup. With this in mind, we tried to modify the reaction conditions for cyclobutane ring opening in such a way that isolation of silyl enol ether **6** could be achieved. However, all our attempts failed and led only to the dione **2**. We also have tried to prepare **6** from dione **2** under kinetically as well as thermodynamically controlled conditions, but in all cases a strong preference for the formation of the silyl enol ether with the double bond in the C(8)−C(11) position was observed. These disappointing results forced us to develop an alternative route for introduction of an oxygen function at C(12).

From the enolization experiments with dione **2**, it appeared that the double bond in the C(8)−C(11) position is energetically more favorable than in the C(11)−C(12) position. It was therefore expected that elimination of an axial hydroxyl group at C(11) would result in the selective formation of the C(8)−C(11) double bond. Via allylic oxidation, the planned 1,2-transposition of the carbonyl function (C(11) → C(12)) then can be achieved.

The introduction of an axial hydroxyl group at the C(11) position of dione **2** was accomplished with L-Selectride (Aldrich) giving the diol **7** as the sole product in 77% yield. The ^{1}H NMR spectrum of **7** shows a double double double doublet with J = 2.9, 4.7, 7.8, and 7.8 Hz at δ 4.16, which is consistent with an axial hydroxyl group at C(11). The exo orientation of the hydroxyl group at C(2) in **7** was concluded from comparison with camphor, which was stereoselectively reduced to isoborneol upon treatment with L-Selectride.[14] Because the hydroxyl group at C(2) and the hydrogen atoms at C(3) in **7** are not properly aligned for an anti elimination, it was expected that selective elimination of the axial hydroxyl group at C(11) would be possible. For that purpose, diol **7** was treated with a catalytic amount of *p*-TsOH in refluxing toluene. After a reaction time of 11 h, the yield of olefin **8** was 66% on the basis of recovered **7** (Scheme 3). Products resulting from an acid-catalyzed Wagner−

Scheme 3



Meerwein rearrangement, often observed with camphor-like systems,[15] were not isolated. The C(8)−C(11) position of the double bond in **8** follows from its COSY and ^{1}H−^{13}C heteronuclear shift correlation spectrum. After protection of the hydroxyl group at C(2) as its TBDMS ether (**8** → **9**), allylic oxidation with excess PDC in refluxing pyridine[16] afforded the enone **10** in ca. 50% overall yield from **8**. The appearance of a one-proton doublet with J = 9.7 Hz at δ 6.52 in the ^{1}H NMR spectrum of **10** is consistent with the C(8)═C(11)−C(12)═O unit. Catalytic reduction of the double bond in **10** produced the saturated ketone **11** in 87% yield.

At this stage, the straightforward conversion of **11** into (+)-α-santalen-12-one (**1d**) was investigated. It was hoped that addition of isopropylmagnesium chloride (iPrMgCl) to the C(12) carbonyl of **11**, followed by conversion of the TBDMS ether group at C(2) into a mesylate group, would give a product that should homofragmentate to **1d** upon heating with sodium *tert*-amylate in benzene.[1] However, treatment of **11** with iPrMgCl or its cerium analog[17] did not give any addition product; only starting material was recovered. Probably due to steric hindrance, nucleophilic addition to the carbonyl group of **11** was hampered, and instead, enolization had taken place.

Confronted with this negative result, we returned to our original strategy via the mesylate **3** (see Scheme 1). Thus, cleavage of the TBDMS ether bond in **11** with aqueous HF in MeCN at 55 °C and subsequent treatment of the intermediate keto alcohol with MsCl in the presence of DMAP afforded the mesylated ketone **12** in 85% yield. The reduction of the carbonyl function of **12** was accomplished with $NaBH_4$ in EtOH at room temperature and gave, along with the desired mesylate **3**

(14) Brown, H. C.; Krishnamurthy, S. *J. Am. Chem. Soc.* **1972**, *94*, 7159.

(15) Berson, J. A. In *Molecular Rearrangements*; de Mayo, P., Ed.; Interscience Publishers: New York, 1963; Part 1, Chapter 3.

(16) Parish, E. J.; Wei, T.-Y. *Synth. Commun.* **1987**, *17*, 1227.

(17) Molander, G. A. *Chem. Rev.* **1992**, *92*, 29 and references cited therein.

(76%), a small amount (14%) of the cyclic ether **13**. The ^{1}H NMR spectrum of **3** shows a double double doublet with J = 3.4, 3.4, and 6.9 Hz at δ 3.90 indicating an axial hydroxyl group at C(12). The formation of the cyclic ether **13** can be explained by a Wagner−Meerwein rearrangement followed by direct trapping of the positive charge at C(1) by the hydroxyl function at C(12).

The key step in our synthetic plan to α-santalanes, the homofragmentation reaction of **3** into aldehyde **4**, was investigated next. From our previous work on the chemical consequences of long-range orbital interactions,[1c] it is known that the yield of aldehydes obtained via homofragmenation is considerably lowered by aldol condensation reactions. In order to suppress these yield-lowering reactions as much as possible, a dilute solution of **3** (0.01 M in benzene) was treated with 2 equiv of sodium *tert*-amylate at reflux temperature for 1 min. In this way, the aldehyde **4**, better known as tricycloekasantalal, was obtained in 76% yield.[18] Our synthetic **4** was spectroscopically identical to the natural product isolated from sandalwood oil[19] and can be used to prepare (+)-(*Z*)-α-santalol (**1a**) as previously reported.[20]

The synthesis of (+)-α-santalan-12-one (**1d**) was completed by treatment of **4** with iPrMgCl in ether followed by oxidation of the adduct with PDC in CH_2Cl_2, affording **1d** in 73% yield. The spectroscopic data of our synthetic **1d** were identical with those reported in the literature.[6,12] The synthesis of **1d** requires 11 steps from dione **2** and proceeds in ca. 8% overall yield.[21]

In an attempt to develop a more direct approach to **1d**, the mesylate **3** was treated with excess iPrMgCl in refluxing benzene. It was hoped that iPrMgCl would act first as a base to achieve homofragmentation to **4** and then as a trapping reagent of the resulting aldehyde function. With such a procedure aldol condensation reactions could also be avoided. However, the reaction of **3** with iPrMgCl only led to the selective formation of the cyclic ether **13**. Apparently, the electron-donating ability of the alkoxide group with $MgCl^+$ as counterion, produced after deprotonation of **3** by iPrMgCl, is not strong enough for the induction of homofragmentation, and consequently, only rearrangement and cyclic ether formation take place.[1b]

Summarizing these results, we may state that our "carvone" route to α-santalanes represents a nice illustration of the applicability of the homofragmentation reaction in natural product synthesis and presents an attractive alternative for the commonly applied "camphor" route. Like camphor, carvone is an excellent chirogen on account of its commercial availability in both optical isomers and thus allows the enantiospecific synthesis of both enantiomeric forms of the α-santalanes.

Experimental Section[22]

Materials. All reagents were purchased from Aldrich or Janssen and were used without further purification, unless otherwise stated. The dione **2** was prepared as previously described.[9b]

(−)-(3*R*,7*R*)-5,6-Dimethyltricyclo[4.4.0.0^{5,9}]decane-3,7-diol (7). To a stirred solution of 2.03 g (10.57 mmol) of **2** in 100 mL of dry THF was slowly added drowise 29.0 mL of L-Selectride (1 M in THF) at 0 °C. The solution was stirred at 0 °C for 30 min and at rt for 1 h, and then 150 mL of 75% aqueous EtOH was carefully added at 0 °C. After being stirred at rt for 2 h, the reaction mixture was treated with 75 mL of 4 M aqueous NaOH and 225 mL of 30% H_2O_2 at 0 °C. The reaction mixture was stirred at rt for another 16 h and then concentrated under reduced pressure. The remaining residue was mixed with 100 mL of water and extracted with three 100 mL portions of ether. The combined organic layers were dried and evaporated. Purification by flash chromatography (2:1 petroleum ether (bp 40−60 °C)/EtOAc) yielded 1.60 g (77%) of **7**: $[\alpha]_D$ −42.8° (*c* 0.71); ^{1}H NMR (400 MHz) δ 0.93 (s, 3 H), 1.00 (s, 3 H), 1.16 (dd, J = 8.5, 12.8 Hz, 1 H), 1.35−1.90 (m, 9 H), 2.03 (m, 1 H), 2.16 (ddd, J = 3.6, 7.6, 14.5 Hz, 1 H), 3.59 (dd, J = 4.5, 7.9 Hz, 1 H), 4.16 (dddd, J = 2.9, 4.7, 7.8, 7.8 Hz, 1 H); ^{13}C NMR (50 MHz) δ 9.83 (q), 20.33 (q), 34.42 (t), 36.82 (t), 39.73 (d), 41.25 (t), 41.85 (t), 44.52 (d), 45.30 (s), 48.00 (s), 63.77 (d), 78.63 (d); MS *m*/*z* (relative intensity) 196 (M^+, <1), 152 (31), 135 (12), 134 (100), 119 (25), 107 (12), 106 (14), 93 (11), 91 (9); HRMS calcd for $C_{12}H_{20}O_2$ (M^+) 196.1463, found 196.1459. Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.41; H, 10.42.

(−)-(7*R*)-5,6-Dimethyl-7-hydroxytricyclo[4.4.0.0^{5,9}]dec-3-ene (8). To a solution of 1.06 g (5.46 mmol) of diol **7** in 400 mL of toluene was added 0.075 g of *p*-TsOH. The reaction mixture was refluxed under Dean−Stark conditions for 11 h. During this reflux period, two additional 0.075 g portions of *p*-TsOH (one after 5 h, the other after 7 h) were added to the reaction mixture. The solution was allowed to come to rt and washed successively with two 100 mL portions of saturated aqueous $NaHCO_3$ and one 100 mL portion of brine. After drying and evaporation, the remaining residue was flash chromatographed (20:1 to 2:1 petroleum ether (bp 40−60 °C)/EtOAc) to give 0.517 g (54%) of **8**: $[\alpha]_D$ −108.8° (*c* 0.49); ^{1}H NMR (400 MHz) δ 0.90 (s, 3 H), 1.04 (s, 3 H), 1.18 (dd, J = 8.2, 12.3 Hz, 1 H), 1.32−1.44 (m, 2 H), 1.64 (br s, OH), 1.66−1.86 (m, 2 H), 1.87 dd, (J = 7.9, 12.6 Hz, 1 H), 2.04 (t, J = 4.4 Hz, 1 H), 2.26 (m, 1 H), 3.60 (dd, J = 4.8, 7.2 Hz, 1 H), 5.38 (ddd, J = 1.6, 1.6, 9.5 Hz, 1 H), 5.50 (dddd, J = 1.6, 1.6, 4.2, 9.5 Hz, 1 H); ^{13}C NMR (100 MHz) δ 9.42 (q), 17.69 (q), 33.42 (t), 35.81 (t), 39.51 (d), 41.14 (t), 48.05 (s), 48.60 (s), 48.86 (d), 79.12 (d), 124.08 (d), 136.34 (d); MS *m*/*z* (relative intensity) 178 (M^+, 79), 163 (30), 160 (67), 145 (70), 119 (100), 109 (86), 107 (71), 106 (66), 91 (85), 79 (43); HRMS calcd for $C_{12}H_{18}O$ (M^+) 178.1358, found 178.1356. Anal. Calcd for $C_{12}H_{18}O$: C, 80.85; H, 10.18. Found: C, 81.14; H, 10.39. Further elution afforded 0.198 g (19%) of unreacted **7**.

(−)-(7*R*)-5,6-Dimethyl-7-[[(1,1-dimethylethyl)dimethylsilyl]oxy]tricyclo[4.4.0.0^{5,9}]dec-3-ene (9). To a solution of 0.485 g (2.76 mmol) of **8** in 10 mL of DMF were added 0.335 g (4.92 mmol) of imidazole and 0.488 g (3.24 mmol) of TBDMSCl. The reaction mixture was stirred at rt for 22 h and at 60 °C for 3 h. Then an additional 0.488 g portion of TBDMSCl was added, and stirring was continued at 70 °C for 7 h. The reaction mixture was allowed to come to rt, and 0.25 mL of MeOH was added. After being stirred for 10 min, the mixture was poured into 150 mL of water and extracted with five 75 mL portions of ether. The combined organic layers were washed with 100 mL of brine, dried, and evaporated. Purification by flash chromatography (50:1 petroleum ether (bp 40−60 °C)/ether) gave 0.738 g (92%) of **9** as a clear oil: $[\alpha]_D$ −107.1° (*c* 1.00); ^{1}H NMR (200 MHz) δ 0.01 (s, 6 H), 0.80 (s, 3 H), 0.88 (s, 9 H), 0.99 (s, 3 H), 1.11 (dd, J = 8.1, 12.2 Hz, 1 H), 1.23−1.41 (m, 2 H), 1.55−1.80 (m, 3 H), 1.97 (t, J = 4.2 Hz, 1 H), 2.23 (m, 1 H), 3.47 (dd, J = 4.4, 7.2 Hz, 1 H), 5.35 (ddd, J = 1.6, 1.6, 9.5 Hz, 1 H), 5.46 (dddd, J = 1.6, 1.6, 4.2, 9.5 Hz, 1 H); ^{13}C NMR (50 MHz) δ −5.14 (q), −4.61 (q), 9.66 (q), 17.05 (q), 17.93 (s), 25.78 (3q), 33.20 (t), 35.51 (t), 39.21 (d), 42.42 (t), 47.91 (s), 48.28 (s), 48.60 (d), 78.47 (d), 123.41 (d), 136.18 (d); MS *m*/*z* (relative intensity) 292 (M^+, 6), 237

(18) Under standard conditions (0.1 M mesylate in benzene, 5 equiv of sodium *tert*-amylate),[1c] the yield of aldehyde **4** dropped to ca. 50%.

(19) Kretschmar, H. C.; Barneis, Z. J.; Erman, W. F. *Tetrahedron Lett.* **1970**, 37.

(20) (a) Lewis, R. G.; Gustafson, D. H.; Erman, W. F. *Tetrahedron Lett.* **1967**, 401. (b) Corey, E. J.; Yamamoto, H. *J. Am. Chem. Soc.* **1970**, *92*, 226.

(21) Except for the homofragmentation reaction (**3** → **4**), no attempts have been made to improve the yields.

(22) For a general description of the experimental procedures employed in this research, see: Kesselmans, R. P. W.; Wijnberg, J. B. P. A.; Minnaard, A. J.; Walinga, R. E.; de Groot, A. *J. Org. Chem.* **1991**, *56*, 7237. NMR spectra were recorded at 200 and 400 MHz (^{1}H), and at 50 and 100 MHz (^{13}C) in $CDCl_3$. Optical rotations were measured in $CHCl_3$ solutions.

(5), 236 (20), 235 (100), 161 (12), 159 (13), 119 (10), 105 (7), 75 (61), 73 (10); HRMS calcd for $C_{18}H_{32}OSi$ (M^+) 292.2222, found 292.2221.

(−)-(7*R*)-5,6-Dimethyl-7-[[(1,1-dimethylethyl)dimethylsilyl]oxy]tricyclo[4.4.0.0^{5,9}]dec-3-en-2-one (10). To a stirred solution of 0.703 g (2.42 mmol) of **9** and 2.75 g of 4 Å molecular sieves in 120 mL of dry pyridine was added 12.0 g of PDC. The reaction mixture was refluxed for 6 h and, after being cooled on an ice bath, diluted with 1 L of ether. The organic layer was stirred at rt for 2 h, filtered through Celite, and evaporated. The remaining residue was flash chromatographed (50:1 petroleum ether (bp 40−60 °C)/ether) to yield 0.391 g (53%) of **10**: $[\alpha]_D$ −128.8° (*c* 0.49); ^{1}H NMR (200 MHz) δ 0.00 (s, 3 H), 0.01 (s, 3 H), 0.85 (s, 3 H), 0.86 (s, 9 H), 1.22 (s, 3 H), 1.41−1.68 (m, 3 H), 1.87 (m, 1 H), 1.98−2.12 (m, 3 H), 3.43 (dd, *J* = 4.4, 7.4 Hz, 1 H), 5.87 (dd, *J* = 1.8, 9.7 Hz, 1 H), 6.52 (d, *J* = 9.7 Hz, 1 H); ^{13}C NMR (50 MHz) δ −5.14 (q), −4.63 (q), 9.72 (q), 16.89 (q), 17.89 (s), 25.74 (3q), 32.88 (t), 43.04 (d), 43.30 (t), 51.97 (s), 55.86 (d), 60.36 (s), 77.08 (d), 126.57 (d), 155.78 (d), 203.75 (s); MS *m*/*z* (relative intensity) 306 (M^+, 5), 250 (20), 249 (100), 231 (8), 181 (13), 157 (12), 75 (33), 73 (10); HRMS calcd for $C_{18}H_{30}O_2Si$ (M^+) 306.2015, found 306.2017.

(−)-(7*R*)-5,6-Dimethyl-7-[[(1,1-dimethylethyl)dimethylsilyl]oxy]tricyclo[4.4.0.0^{5,9}]decan-2-one (11). A mixture of 0.361 g (1.19 mmol) of **10** and 0.160 g of 10% Pd/C in 60 mL of EtOH was hydrogenated in a Parr hydrogenator under 23 psi of H_2 for 90 min. The reaction mixture was filtered through Celite and evaporated. Purification by flash chromatography (50:1 petroleum ether (bp 40−60 °C)/EtOAc) gave 0.314 g (87%) of **11**: $[\alpha]_D$ −63.1° (*c* 0.32); ^{1}H NMR (200 MHz) δ −0.06 (s, 3 H), −0.05 (s, 3 H), 0.79 (s, 9 H), 0.81 (s, 3 H), 0.99 (s, 3 H), 1.24 (br dd, *J* = 8.5, 13.4 Hz, 1 H), 1.52−2.20 (m, 8 H), 2.44 (m, 1 H), 3.44 (dd, *J* = 4.4, 7.4 Hz, 1 H); ^{13}C NMR (50 MHz) δ −5.21 (q), −4.72 (q), 10.40 (q), 17.81 (s), 19.66 (q), 25.67 (3q), 30.46 (t), 31.61 (t), 33.88 (t), 43.83 (t), 46.10 (d), 47.13 (s), 53.01 (s), 56.79 (d), 77.96 (d), 214.88 (s); MS *m*/*z* (relative intensity) 308 (M^+, 3.5), 253 (6), 252 (32), 251 (100), 159 (17), 157 (48), 107 (13), 75 (36), 73 (7); HRMS calcd for $C_{18}H_{32}O_2Si$ (M^+) 308.2172, found 308.2166.

(−)-(7*R*)-5,6-Dimethyl-7-[(methylsulfonyl)oxy]tricyclo[4.4.0.0^{5,9}]decan-2-one (12). To a solution of 0.280 g (0.91 mmol) of **11** in 20 mL of MeCN was added 10 drops of 40% aqueous HF. The reaction mixture was stirred at 55 °C for 5 h, poured into 50 mL of saturated aqueous $NaHCO_3$, and then extracted with four 25 mL portions of EtOAc. The combined organic layers were washed with 50 mL of brine, dried, and evaporated. The remaining residue was dissolved in 10 mL of $CHCl_3$, and 0.48 g (3.92 mmol) of DMAP and 0.414 g (3.61 mmol) of MsCl were successively added in small portions at 0 °C. The reaction mixture was stirred at rt for 30 h, concentrated under reduced pressure, and taken up in 80 mL of ether. The solution was washed successively with 20 mL of 10% aqueous H_2SO_4, 20 mL of saturated aqueous $NaHCO_3$, and 20 mL of brine. The organic layer was dried and evaporated, and the remaining oil was purified by flash chromatography (3:1 petroleum ether (bp 40−60 °C)/EtOAc) to afford 0.209 g (85%) of **12**: $[\alpha]_D$ −43.6° (*c* 1.60); ^{1}H NMR (200 MHz) δ 0.92 (s, 3 H), 1.00 (s, 3 H), 1.35 (dd, *J* = 8.4, 13.7 Hz, 1 H), 1.55−1.84 (m, 2 H), 1.90−2.27 (m, 6 H), 2.50 (m, 1 H), 2.94 (s, 3 H), 4.40 (dd, *J* = 3.9, 8.0 Hz, 1 H); ^{13}C NMR (50 MHz) δ 10.28 (q), 19.48 (q), 29.68 (t), 31.04 (t), 33.63 (t), 38.26 (q), 41.02 (t), 46.07 (d), 47.58 (s), 52.75 (s), 55.93 (d), 86.57 (d), 212.76 (s); MS *m*/*z* (relative intensity) 272 (M^+, 21), 150 (100), 122 (74), 94 (37), 86 (23), 84 (36), 49 (27); HRMS calcd for $C_{13}H_{20}O_4S$ (M^+) 272.1082, found 272.1082. Anal. Calcd for $C_{13}H_{20}O_4S$: C, 57.33; H, 7.40. Found: C, 57.07; H, 7.52.

(+)-(2*S*,7*R*)-5,6-Dimethyltricyclo[4.4.0.0^{5,9}]decan-2,7-diol 7-Methanesulfonate (3). To a stirred solution of 0.198 g (0.73 mmol) of **12** in 20 mL of EtOH was added 0.180 g (4.74 mmol) of $NaBH_4$. The reaction mixture was stirred at rt for 90 min, quenched with saturated aqueous NH_4Cl at 0 °C, and, after addition of 50 mL of water, extracted with five 25 mL portions of ether. The combined organic layers were washed with 25 mL of brine, dried, and evaporated. The remaining residue was flash chromatographed (3:1 petroleum ether (bp 40−60 °C)/EtOAc) to give 0.017 g (14%) of 2,7-dimethyl-3-oxatetracyclo[6.2.1.0^{2,7}.0^{4,10}]decane (**13**): $[\alpha]_D$ +8.23° (*c* 0.51); ^{1}H NMR (200 MHz) δ 0.83 (s, 3 H), 1.10−1.30 (m, 2 H), 1.24 (s, 3 H), 1.40−2.10 (m, 8 H), 2.53 (m, 1 H), 4.32 (dd, *J* = 5.4, 7.6 Hz, 1 H); ^{13}C NMR (50 MHz) δ 18.41 (q), 24.32 (q), 27.50 (t), 29.69 (t), 32.65 (t), 35.57 (t), 39.85 (d), 41.31 (s), 49.29 (d), 54.49 (d), 76.20 (d), 88.21 (s); MS *m*/*z* (relative intensity) 178 (M^+, 40), 135 (24), 121 (29), 120 (100), 108 (43), 107 (29), 105 (21), 93 (58), 91 (55), 79 (30); HRMS calcd for $C_{12}H_{18}O$ (M^+) 178.1358, found 178.1354. Further elution provided 0.151 g (76%) of **3**: $[\alpha]_D$ −49.6° (*c* 1.16); ^{1}H NMR (400 MHz) δ 0.98 (s, 3 H), 1.18 (dd, *J* = 8.6, 13.4 Hz, 1 H), 1.28 (s, 3 H), 1.34 (dddd, *J* = 2.5, 3.4, 5.2, 13.4 Hz, 1 H), 1.45−1.72 (m, 5 H), 1.86 (t, *J* = 4.5 Hz, 1 H), 1.91 (dd, *J* = 8.6, 13.4 Hz, 1 H), 1.95−2.07 (m, 2 H), 3.00 (s, 3 H), 3.90 (ddd, *J* = 3.4, 3.4, 6.9 Hz, 1 H), 4.44 (dd, *J* = 4.5, 8.0 Hz, 1 H); ^{13}C NMR (50 MHz) δ 11.02 (q), 20.40 (q), 26.36 (t), 28.61 (t), 32.46 (t), 38.24 (q), 40.82 (t), 44.05 (d), 46.24 (s), 46.51 (d), 48.98 (s), 72.72 (d), 88.48 (d); MS *m*/*z* (relative intensity) 274 (M^+, <0.1), 152 (100), 120 (17), 108 (54), 97 (75), 95 (40), 94 (64), 93 (18), 85 (56), 83 (83); HRMS calcd for $C_{13}H_{22}O_4S$ (M^+) 274.1239, found 274.1235.

(+)-Tricycloekasantalal (4). A solution of 0.067 g (0.244 mmol) of **3** in 25 mL of dry benzene was degassed and refluxed under an Ar atmosphere. To the refluxing solution was added at once, via syringe, 0.32 mL of sodium *tert*-amylate (1.56 M in toluene).[23] The reaction mixture was refluxed for 1 min, quenched with precooled saturated aqueous NH_4Cl, and then quickly cooled to 0 °C. The mixture was vigorously stirred at rt for 20 min, followed by extraction with five 10 mL portions of ether. The combined organic layers were dried and evaporated. Purification by flash chromatography (100:1 pentane/ether) afforded 0.033 g (76%) of **4**: $[\alpha]_D$ +15.2° (*c* 1.52); ^{13}C NMR (100 MHz) δ 10.95 (q), 17.71 (q), 19.81 (d, *J* = 175.8 Hz), 20.07 (d, *J* = 172.2 Hz), 26.73 (t), 27.70 (s), 31.33 (t), 31.83 (t), 38.58 (d), 40.31 (t), 46.08 (s), 203.39 (s); MS *m*/*z* (relative intensity) 178 (M^+, 16), 121 (48), 120 (32), 119 (33), 111 (24), 105 (21), 93 (100), 92 (24), 91 (36); HRMS calcd for $C_{12}H_{18}O$ (M^+) 178.1358, found 178.1355. The ^{1}H NMR data of **4** were identical with those reported in the literature.[19,20a]

(+)-α-Santalan-12-one (1d). To a solution of 0.016 g (0.087 mmol) of **4** in 2 mL of ether was added 0.3 mL of iPrMgCl (1.5 M in ether) at 0 °C. The reaction mixture was stirred at 0 °C for 5 min and then at rt for 30 min. The reaction mixture was quenched with an excess of saturated aqueous NH_4Cl at 0 °C. After being stirred at rt for 15 min and diluted with 25 mL of ether, the two phase-mixture was separated, and the organic layer was washed with 10 mL of brine, dried, and evaporated. The remaining residue was dissolved in 3 mL of CH_2Cl_2 and, after addition of 0.071 g of PDC, stirred at rt for 16 h. The suspension was then diluted with 50 mL of ether, and stirring was continued at rt for an additional 1 h. After filtration through Celite, the filtrate was concentrated under reduced pressure. Purification by flash chromatography (25:1 pentane/ether) gave 0.014 g (73%) of **1d**: $[\alpha]_D$ +17.5° (*c* 0.48) (lit.[6] $[\alpha]_D$ +17.8°) (lit.[12] $[\alpha]_D$ +3.7°); ^{13}C NMR (100 MHz) δ 10.98 (q), 17.70 (q), 18.76 (2q), 19.86 (d, *J* ≈ 160 Hz), 19.99 (d, *J* ≈ 160 Hz), 27.74 (s), 28.70 (t), 31.35 (t), 31.86 (t), 36.40 (t), 38.59 (d), 41.25 (d), 45.88 (s), 215.84 (s). The ^{1}H NMR and mass spectral data for **1d** were identical with those reported in the literature.[6,12]

Acknowledgment. We thank A. van Veldhuizen for recording NMR spectra and Dr. M. A. Posthumus, H. Jongejan, and R. van Dijk for mass spectral data and elemental analyses.

Supporting Information Available: ^{1}H NMR spectra for compounds **3**, **9**−**11**, and **13** (5 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO9603892

(23) Conia, M. J.-M. *Bull. Soc. Chim.* **1950**, *17*, 537.