Pergamon

Tetrahedron: Asymmetry, Vol. 8, No. 7, pp. 1101–1109, 1997

Printed in Great Britain
PII: S0957-4166(97)00082-7 0957-4166/97 $17.00 + 0.00

Enantioselective syntheses of (2*S*,4a*S*,8a*R*)-1,1,4a-trimethyldecahydronaphthalen-2-ol [(−)-TMD], (4a*S*,8a*R*)-5,5,8a-trimethyloctahydronaphthalen-2(1*H*)-one, and (−)-Polywood®, through Michael-type reaction of chiral imines

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Abstract: The title compounds **6**, **15**, and **17** have been synthesized in a straightforward way in good yields and high enantiomeric excesses by the chiral imines method, leading to building-blocks **2** and **10**, followed by a few conventional steps. © 1997 Elsevier Science Ltd

The enantioselective Michael addition of chiral imines has proved to be a very efficient method to prepare a variety of building-blocks and many synthetic applications have already been reported.[1]

Synthesis of (−)-TMD 6

Both (−)-TMD **6** and its enantiomer possess important biochemical properties since they specifically inhibit 2,3-oxidosqualene oxide cyclase which plays a crucial role in the cholesterol biosynthesis.[2] These compounds are thus useful cholesterol modulator agents.[3] For this reason several syntheses of TMD have been reported. Racemic **6** was synthesized for the first time in 1958.[4] Since then, both enantiomers have been obtained either by resolution[5] or through hemi-synthesis from the chiral pool.[6] Two total syntheses of (−)-TMD **6** have also been described. The first one involves an enantioselective enzymatic reduction of one of the carbonyl groups of 2,2-dimethylcyclohexane-1,3-dione followed by eight steps to give compound (−)-**6** in 16% yield.[7] The other synthesis relies on a Hajos and Parish-type reaction leading after seven steps (10% yield) to (−)-TMD **6**.[8] We report here a straightforward synthesis of (−)-TMD **6** from the chiral non racemic building-block (+)-**2**, obtained by the chiral imines method from 2-methylcyclohexanone **1** and ethyl vinyl ketone[9] (Scheme 1).

After having tried several reaction conditions, the best result for converting enone **2** to ketone **4** is observed when aniline is used as proton donor to maximize the formation of enolate **3** and when the methylation is performed rapidly at −33°C. If no proton donor is added, the starting enone **2** and the reduced compound **5**[10] are the major products. Besides, if the alkylation takes place at a lower temperature than −33°C, the proportion of compound **5** increases.

The last step of the synthesis involves the reduction of ketone **4** with sodium borohydride, leading to (−)-TMD **6** and its diastereoisomer (95:5). Through recrystallization of the mixture, pure (−)-TMD **6** is obtained.

Synthesis of (−)-ketone 15 and (−)-Polywood® 17

(−)-Ketone **15** has been isolated from Longoza concrète, itself obtained through extraction of the flowers of *Hedychium flavum (Zingiberaceae)*, a plant growing in Madagascar, Nossi-Bé and La Réunion.[11] Polywood® **17** is a synthetic compound. (−)-Enantiomer **15** is strong, woody, amber-like with an earthy note of geosmin type. The (+)-enantiomer is less strong and has a woody-patchouli-like

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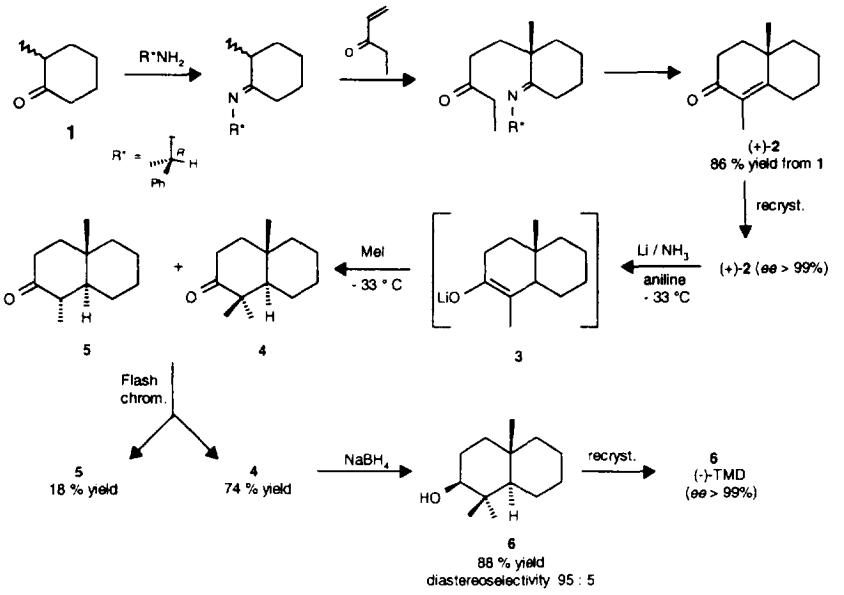


Scheme 1.

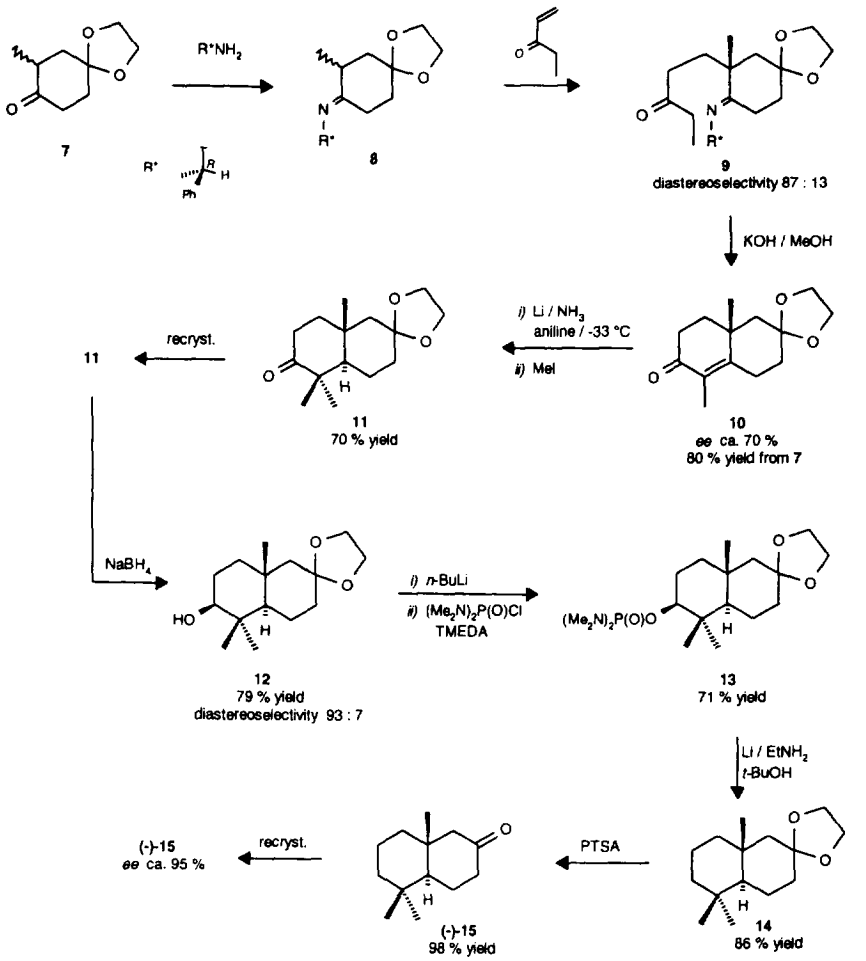
odour. (−)-Polywood® **17** is woody, amber-like while the (+)-enantiomer is stronger, woody, with a powdery ionone-like undertone.[12]

Due to their interesting odours, racemic ketone **15** and racemic Polywood® **17** are of great importance in the perfume industry. (±)-**15**[13] and (±)-**17**[13b,d] have been synthesized from geranyl chloride. (±)-**15** has also been prepared from dihydro-α-ionone,[14] 2,6,6-trimethylcyclohexanone,[15] methyl β-cyclogeranate,[16] or methoxycarbonyldihydroionone.[17] Moreover, (±)-ketone **15** is a key-intermediate leading to other interesting odorous compounds[14c,18] as well as to powerful fungicides.[19]

No enantioselective syntheses of either enantiomer of ketone **15** or Polywood® **17** have been reported. However, by hydrolytic enzymatic kinetic resolution of the chloroacetate equivalent of (±)-Polywood®, a common hydroxy intermediate has been obtained which was oxidized or esterified to lead respectively to (−)-ketone **15** and (−)-Polywood® **17**.[12] Compound (−)-**15** was also recently obtained in nine steps by hemi-synthesis from (*S*)-(+)-carvone with a 4% global yield.[6b]

Our syntheses of (−)-ketone **15** and (−)-Polywood® **17** follow a similar initial path as the one used for the synthesis of (−)-TMD **6**, being achieved with the chiral non racemic mono-protected diketonic building-block **10** (obtained by the usual method from ketone **7**[20] in 80% yield with *ee* 70%) instead of ketonic building-block **2** (Scheme 2).

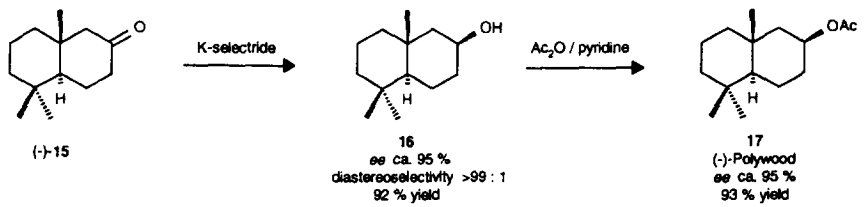
Thus, enone **10** was reduced and methylated under similar conditions as the ones used before, leading to chemically pure ketone **11** in 70% yield. In order to increase its enantiomeric excess, ketone **11** was recrystallized. The transformation of the carbonyl to a methylene group was first tried directly by sodium cyanoborohydride reduction of the corresponding tosylhydrazone. However the tosylhydrazone is difficult to prepare, probably for steric reasons due to the adjacent bulky *gem*-dimethyl group, and the global yield for the two reactions was only 30%. We decided therefore to follow an indirect path by first preparing the corresponding hydroxy compound **12**. This was achieved with sodium borohydride in 79% yield.[21] Ireland's method,[22] *i.e.* reduction of the corresponding *N,N,N′,N′*-tetramethylphosphorodiamidate by lithium in ethylamine, was then used for the conversion of hydroxy compound **12** to the methylene compound **14**. Finally, deprotection of the carbonyl group led to compound (−)-**15** in 98% yield. After recrystallization, the data for compound (−)-**15** (*ee* 95%[23]) are in full agreement with those reported in the literature, specially in what concerns the sign of the specific rotation, thus confirming the absolute configuration of compound (−)-**15** as shown in



Scheme 2.

Scheme 2 as well as that of compound **10**, which is the one predicted according to the rule elaborated previously.[1a]

Synthesis of (−)-Polywood® required then a stereoselective reduction of the carbonyl group of ketone (−)-**15** to give compound **16** bearing an axial hydroxy group (Scheme 3). With K-Selectride® the stereoselectivity is total and compound **16** (*ee* 95%[24]) is obtained in 92% yield.[25] (−)-Polywood® **17** (*ee* 95%[26]) was then obtained by acetylation in 93% yield.



Scheme 3.

Experimental section

General

^1H and ^{13}C NMR spectra were recorded respectively at 300 and 75.5 MHz ($CDCl_3$). Chemical shifts for hydrogen and carbon resonances are reported in ppm (δ) relative to TMS. Thin-layer chromatographies (TLC) were performed with aluminum plates (0.20 mm) precoated with fluorescent silica gel, using EtOAc/hexanes as eluent. Reaction components were then visualized under UV light and dipped in a Dragendorff solution. Silica gel (230–400 mesh) was used for flash chromatography (FC) separations and EtOAc/hexanes (% EtOAc given) was the eluent. Gas chromatography–mass spectrometry (GC–MS) was performed with a Hewlett–Packard 5890 GC apparatus (equipped with a 12 m×0.20 mm dimethylpolysiloxane capillary column) linked to a Model 5971 EIMS, at 140°C for 1 min, then 18°C/min up to 290°C. Uncorrected melting points (mp) were determined with a Fisher–Johns apparatus.

(R)-(+)-1,4a-Dimethyl-4,4a,5,6,7,8-hexahydronaphthalen-2(3H)-one **2**

14.7 g (131 mmol) of 2-methylcyclohexanone **1** and 15.9 g (131 mmol) of (*R*)-(+)-α-methylbenzylamine (*ee*=93.5%) in 70 mL of toluene were heated at reflux temperature under a nitrogen atmosphere in a Dean–Stark water separator for 24 h. After concentration under reduced pressure, 11.0 g (131 mmol) of ethyl vinyl ketone was added and the mixture was stirred at room temperature under nitrogen for 16 h. 100 mL of methanol and 60 mL of 10% acetic acid were then added and the solution was stirred at room temperature for 2 h. After concentration, addition of water and ether extraction, the organic layer was washed with 10% HCl, water and brine, dried over $MgSO_4$ and evaporated. The crude diketone thus obtained was dissolved under nitrogen in 150 mL of methanol; 13 mL of 1 M methanolic KOH was then added and the solution was heated at reflux temperature for 1 h. After neutralization with 0.8 mL of AcOH, the solution was concentrated under reduced pressure and the residue was dissolved in water and extracted with ether. The organic layer was washed with brine, dried over $MgSO_4$ and evaporated. The residue was then distilled (70–75°C/0.02 Torr) to give 20.0 g (86% yield) of compound **2** as a colourless oil containing *ca.* 8% of a regioisomer (GC). Low temperature (−20 to −78°C) successive recrystallizations of this oil in 40 mL, 10 mL and 10 mL of pentane,[27] followed by distillation (70°C/0.02 Torr) yielded 6.4 g of pure compound **2** (*ee*>99%).

2: bp 70°C/0.02 Torr; $[\alpha]_D^{20}$ +199 (*c*3, EtOH); EIMS *m/z* (rel int) 179 (14), 178 (M^+, base), 163 (67), 150 (14), 149 (14), 137 (21), 136 (83), 135 (43), 122 (22), 121 (73), 110 (11), 108 (13), 107 (41), 105 (11), 94 (12), 93 (50), 91 (33), 79 (40), 77 (30), 67 (18), 65 (13), 55 (18), 53 (16); IR (neat) 1670, 1615 cm^{-1}; ^1H NMR 1.21 (s, 3 H), 1.25 to 1.43 (m, 2 H), 1.55 to 1.97 (m, 6 H), 1.75 (d, J=1.5 Hz, 3 H), 2.06 (dddd, J_1=1.5 Hz, J_2=5.2 Hz, J_3=13.4 Hz, J_4=15.1 Hz, 1 H), 2.38 (ddd, J_1=3.7 Hz, J_2=4.8 Hz, J_3=16.9 Hz, 1 H), 2.51 (ddd, J_1=5.5 Hz, J_2=13.6 Hz, J_3=16.9 Hz, 1 H), 2.67 to 2.73 (m, 1 H); ^{13}C NMR 10.89, 21.50, 22.51, 26.90, 27.77, 33.87, 36.25, 37.71, 42.16, 128.4, 163.1, 199.3.

(4aS,8aR)-1,1,4a-Trimethyloctahydronaphthalen-2(1H)-one **4**

0.640 g (9.22 mmol) of lithium was added at −78°C under nitrogen to 25 mL of liquid ammonia. Following the appearance of the blue colour, the mixture was heated up to ammonia reflux (*ca.* −33°C). A 10 mL anhydrous THF solution of 0.17 mL (1.84 mmol) of aniline and 0.41 g (2.30 mmol) of enone **2** was then added dropwise. After 2 h at the same temperature, the lithium excess was destroyed with a few drops of styrene and 1.43 mL (23.0 mmol) of MeI was rapidly added. The mixture was allowed to reach room temperature and after total evaporation of NH_3, 1.0 g of NH_4Cl and 15 mL of water were added. After ether extraction, the crude residue was analyzed by GC–MS, showing a mixture of the reduced compound **5** (2.57 min, 33%) and the alkylated compound **4** (2.87 min, 67%). After FC (5%, then 10%), 75.0 mg (0.42 mmol, 18% yield) of ketone **5** was separated[28] and 330 mg (1.70 mmol, 74% yield) of oily ketone **4** was obtained.

4: EIMS *m/z* (rel int) 195 (15), 194 (M^+, 80), 179 (14), 151 (16), 137 (65), 133 (21), 125 (25), 110 (17), 109 (73), 108 (99), 98 (40), 97 (22), 96 (25), 95 (50), 93 (25), 91 (17), 83 (base), 82 (31), 81

(60), 79 (23), 70 (17), 69 (49), 68 (21), 67 (71), 57 (24), 55 (62), 53 (19); IR (film) 1705 cm^{-1}; ^1H NMR 0.95 to 1.60 (m, 9 H), 1.01 (s, 3 H), 1.06 (s, 3 H), 1.11 (s, 3 H), 1.69 (ddd, J_1=2.9 Hz, J_2=6.2 Hz, J_3=13.2 Hz, 1 H), 1.79 to 1.90 (m, 1 H), 2.31 (ddd, J_1=2.9 Hz, J_2=5.1 Hz, J_3=15.4 Hz, 1 H), 2.71 (ddd, J_1=6.6 Hz, J_2=13.6 Hz, J_3=15.4 Hz, 1 H); ^{13}C NMR 18.32, 21.38, 21.61, 22.64, 25.24, 26.90, 33.97, 35.02, 40.74, 44.09, 47.86, 53.43, 217.1.

(2S,4aS,8aR)-(−)-1,1,4a-Trimethyldecahydronaphthalen-2-ol [(−)-TMD] 6

At 0°C, under nitrogen, 46 mg (1.22 mmol) of $NaBH_4$ in 2 mL of ethanol were slowly added to 235 mg (1.21 mmol) of ketone **4** in 3 mL of ethanol. After 30 min, the solvent was evaporated under reduced pressure and a small amount of water was added. Ether extraction led to a crude mixture which was analyzed by GC–MS, showing compound **6** (3.03 min, 95%) and its diastereoisomer (2.97 min, 5%). Through recrystallization, 0.21 g (1.07 mmol, 88% yield) of (−)-TMD **6** was obtained.

6: mp 87°C (hexane) [Lit.[7a] mp 86.5–87.4°C (*n*-pentane)]; $[\alpha]_D^{20}$ −9 (*c*0.7, EtOH) [Lit.[7a] $[\alpha]_D^{20}$ −11.3 (*c*0.32, MeOH)]; EIMS *m/z* (rel int) 196 (M^+, 19), 163 (40), 139 (47), 138 (32), 137 (35), 135 (11), 121 (10), 109 (40), 107 (10), 97 (16), 96 (19), 95 (33), 93 (11), 83 (base), 82 (44), 81 (37), 79 (13), 71 (14), 69 (40), 68 (10), 67 (34), 57 (31), 55 (39), 53 (13); IR (nujol) 3500 to 3050 cm^{-1}; ^1H NMR 0.76 (s, 3 H), 0.80 to 1.85 (m, 14 H), 0.92 (s, 3 H), 0.97 (s, 3 H), 3.23 (dd, $J_1 \approx 8$ Hz, $J_2 \approx 8$ Hz, 1 H); ^{13}C NMR 15.03, 19.19, 21.59, 21.71, 27.51, 27.62, 27.76, 34.15, 38.79, 40.22, 45.24, 52.70, 79.39.

(R)-(+)-5′,8′a-Dimethyl-3′,4′,8′,8′a-tetrahydrospiro[1,3-dioxolane-2,2′-(1′H)-naphthalen]-6′(7′H)-one 10

A solution of 9.68 g (56.9 mmol) of compound **7**[20] and 7.33 mL (1 eq) of (R)-(+)-α-methylbenzylamine (*ee* 95%) in 65 mL of toluene was heated at refluxing temperature for 16 h in a Dean–Stark apparatus. The solvent was then removed under reduced pressure and 15.5 g of crude imine **8** was obtained.[29] 7.52 mL (75.6 mmol) of ethyl vinyl ketone were then added and the mixture was heated at 50°C for 2 days and then analyzed by GC–MS, showing the unresolved regioisomers of compound **9** (8.42 to 8.61 min), the diastereoisomer of **9** (8.70 min), and compound **9** (8.98 min), the ratio of the last two compounds being 13:87. The mixture was then dissolved in 80 mL of methanol and 40 mL of a 10% aqueous KOH solution was slowly added. After 16 h at 50°C under nitrogen, the mixture was analyzed by GC–MS, showing a regioisomer of **10** (5.08 min, 4%) and compound **10** (5.16 min, 96%). The methanol was then evaporated under reduced pressure and after ether extraction followed by FC (10%+2% Et_3N, then 20%+2% Et_3N), 10.7 g (45.1 mmol, 80% yield from compound **7**) of enone **10** was obtained.

10: mp 45.5–48°C (pentane/Et_2O, 90:10); $[\alpha]_D^{20}$ +76 (*c*1, EtOH); EIMS *m/z* (rel int) 237 (15), 236 (M^+, 94), 221 (37), 207 (10), 193 (18), 180 (11), 164 (12), 163 (12), 149 (10), 139 (14), 135 (13), 121 (13), 108 (25), 107 (19), 105 (11), 100 (23), 99 (53), 93 (18), 91 (29), 87 (17), 86 (base), 79 (21), 77 (21), 55 (16), 53 (10); IR (nujol) 1670, 1610 cm^{-1}; ^1H NMR 1.34 (s, 3 H), 1.55 to 2.00 (m, 6 H), 1.78 (d, *J*=1.5 Hz, 3 H), 2.32 to 2.45 (m, 2 H), 2.53 (ddd, J_1=5.9 Hz, J_2=14.0 Hz, J_3=17.3 Hz, 1 H), 2.74 (ddd, J_1=2.9 Hz, J_2=4.4 Hz, J_3=15.1 Hz, 1 H), 3.88 to 4.05 (m, 4 H); ^{13}C NMR 10.97, 23.57, 25.45, 33.37, 34.46, 36.80, 37.89, 48.36, 63.63, 64.55, 107.7, 128.7, 160.5, 198.7.

(4a′R,8a′R)-(−)-5′,5′,8a′-Trimethylhexahydrospiro[1,3-dioxolane-2,2′-(1′H)-naphthalen]-6′(7′H)-one 11

1.76 g (254 mmol) of Li was added to 410 mL of ammonia at −78°C under nitrogen. After appearance of the blue colour, the temperature of the mixture was raised up to ammonia reflux. A solution of 10.7 g (45.1 mmol) of the crude enone **10** obtained above and 3.28 mL (36.0 mmol) of aniline, in 240 mL of anhydrous THF, was then added dropwise. After 2 h at the ammonia refluxing temperature followed by destruction of the Li in excess with a few drops of styrene, 28.6 mL (459 mmol) of MeI were rapidly added. The mixture was allowed to reach room temperature and after total evaporation of ammonia, NH_4Cl and water were added. Ether extraction yielded a crude mixture

which was analyzed by GC–MS, showing compound **11** (5.19 min, 87%) and the compound resulting from dimethylation of enone **10** (5.36 min, 13%). After FC (5%+2% Et_3N, then 10%+2% Et_3N), 8.0 g (31.7 mmol, 70% yield) of ketone **11** were obtained and recrystallized.

11: mp 98.5°C (hexane/AcOEt 80:20); Found C, 71.4; H 9.64 ($C_{15}H_{24}O_3$ requires C, 71.39; H 9.59); $[\alpha]_D^{20}$ −9 (*c*1, EtOH); EIMS *m/z* (rel int) 252 (M^+, 3), 139 (24), 99 (base), 86 (10); IR (nujol) 1700 cm^{-1}; ^1H NMR 1.03 (s, 3 H), 1.10 (s, 3 H), 1.20 (s, 3 H), 1.30 to 1.75 (m, 8 H), 1.89 (ddd, J_1=2.6 Hz, J_2=5.5 Hz, J_3=12.5 Hz, 1 H), 2.34 (ddd, J_1=2.9 Hz, J_2=5.9 Hz, J_3=16.2 Hz, 1 H), 2.67 (ddd, J_1=6.6 Hz, J_2=12.9 Hz, J_3=16.2 Hz, 1 H), 3.86 to 4.01 (m, 4 H); ^{13}C NMR 18.82, 20.77, 21.30, 25.89, 34.28, 34.69, 35.70, 39.98, 47.31, 50.53, 52.54, 63.44, 64.45, 108.5, 216.5.

(4a'R,6'S,8a'R)-(+)-5',5',8a'-Trimethyloctahydrospiro[1,3-dioxolane-2,2'-(1'H)-naphthalen]-6'-ol ***12***

A solution of 915 mg (24.2 mmol) of $NaBH_4$ in 50 mL of ethanol was slowly added at 0°C under nitrogen to a solution of 6.0 g (23.8 mmol) of ketone **11** in 100 mL of ethanol. After 1 h the mixture was analyzed by GC–MS, showing compound **12** (3.89 min, 93%) and its diastereoisomer (3.99 min, 7%). The solvent was evaporated under reduced pressure and after addition of a small amount of water, ether extraction and FC (30%+2% Et_3N), 4.75 g (18.7 mmol, 79% yield) of alcohol **12** was obtained.

12: mp 51°C (hexane); $[\alpha]_D^{20}$ +13 (*c*0.8, EtOH); EIMS *m/z* (rel int) 254 (M^+, 11), 139 (26), 99 (base); IR (nujol) 3660 to 3180 cm^{-1}; ^1H NMR 0.79 (s, 3 H), 0.84 to 1.75 (m, 11 H), 1.01 (s, 3 H), 1.04 (s, 3 H); 1.87 (ddd, $J_1 \approx 3$ Hz, $J_2 \approx 3$ Hz, J_3=9.6 Hz, 1 H), 3.26 (dd, $J_1 \approx 8$ Hz, $J_2 \approx 8$ Hz, 1 H), 3.80 to 4.00 (m, 4 H); ^{13}C NMR 15.04, 19.69, 19.72, 27.14, 28.02, 34.95, 36.35, 38.49, 39.90, 51.61, 52.27, 63.34, 64.38, 79.04, 108.9.

(4a'R,6'S,8a'R)-(+)-5',5',8'a-Trimethyloctahydrospiro[1,3-dioxolane-2,2'-(1'H)-naphthalen]-6'-yl N,N,N',N'*-tetramethylphosphorodiamidate* ***13***

11.1 mL (27.8 mmol) of *n*-BuLi (2.5 M hexanes) were added dropwise at 0°C under nitrogen to a solution of 4.70 g (18.5 mmol) of alcohol **12** and 20 mL of *N,N,N',N'*-tetramethylethylenediamine, in 70 mL of anhydrous THF. After 5 min at room temperature, 5.51 mL (37.2 mmol) of tetramethylphosphorodiamidic chloride were slowly added, followed after 2 h by the addition of 3 mL of water. Ether extraction and FC (60%+2% Et_3N, then 80%+2% Et_3N) afforded 5.13 g (13.2 mmol, 71% yield) of phosphorodiamidate **13** as white crystals.

13: mp 128–129°C; $[\alpha]_D^{20}$ +7 (*c*1.5, EtOH); EIMS *m/z* (rel int) 388 (M^+, 1), 153 (base), 152 (34), 135 (12), 99 (23); ^1H NMR 0.81 (s, 3 H), 0.85 to 1.90 (m, 11 H), 1.00 (s, 3 H), 1.02 (s, 3 H), 2.59, 2.60, 2.62 and 2.64 (4 s, 12 H), 3.79 to 3.99 (m, 5 H); ^{13}C NMR 15.95, 19.65, 19.72, 25.28, 28.08, 34.59, 36.39, 36.45, 38.37, 38.46, 39.55, 51.41, 52.24, 63.30, 64.35, 83.04, 83.11, 108.8.

(4a'S,8a'R)-5',5',8'a-Trimethyloctahydrospiro[1,3-dioxolane-2,2'-(1'H)-naphthalene] ***14***

1.00 g (144 mmol) of Li was added under nitrogen to 70 mL of ethylamine at 0°C. Following the appearance of the blue colour, a solution of 0.97 g (13.1 mmol) of *t*-BuOH and 5.1 g (1 eq) of phosphorodiamidate **13** in 40 mL of anhydrous THF, was added dropwise. After 1 h at 0°C followed by destruction of Li excess with a few drops of styrene, 30 mL of water were added. Ether extraction and FC (5%+2% Et_3N) afforded 2.69 g (11.3 mmol, 86% yield) of the oily reduced compound **14**.

14: EIMS *m/z* (rel int) 238 (M^+, 17), 139 (26), 99 (base), 86 (10), 55 (10); ^1H NMR 0.75 to 1.95 (m, 13 H), 0.82 (s, 3 H), 0.89 (s, 3 H), 1.04 (s, 3 H), 3.80 to 4.00 (m, 4 H); ^{13}C NMR 18.60, 19.81, 20.18, 21.38, 33.00, 33.94, 35.30, 36.95, 42.44 (2 C), 52.20, 53.65, 63.41, 64.49, 109.4.

(4aS,8aR)-(−)-5,5,8a-Trimethyloctahydronaphthalen-2(1H)-one ***15***

A solution of 2.35 g (9.86 mmol) of acetal **14** and a trace of PTSA in 25 mL of acetone, was stirred at room temperature for 3 h. After evaporation of acetone under reduced pressure and FC (20%), 1.87 g (9.62 mmol, 98% yield) of ketone **15** was obtained and recrystallized.

15: mp 88°C (pentane) [Lit.[12] mp 88–90°C (pentane)]; $[\alpha]_D^{20}$ −84 (*c*1, EtOH) [Lit.[12] $[\alpha]_D^{20}$ −86.1 (*c*1.2, $CHCl_3$)]; EIMS *m/z* (rel int) 195 (13), 194 (M^+, base), 179 (51), 176 (40), 162 (12), 161 (69), 151 (19), 138 (10), 137 (46), 136 (46), 133 (14), 124 (16), 123 (73), 121 (38), 120 (10), 119 (16), 111 (58), 110 (29), 109 (81), 108 (11), 107 (19), 106 (12). 105 (14), 97 (43), 96 (16), 95(84), 93 (19), 91 (19), 83 (30), 82 (31), 81 (41), 79 (23), 77 (15), 69 (49), 68 (17), 67 (44), 56 (12), 55 (36), 53 (18); IR (nujol) 1715 cm^{-1}; ^1H NMR 0.87 (s, 3 H), 0.91 (s, 3 H), 0.98 (s, 3 H), 1.21 to 1.34 (m, 2 H), 1.41 to 1.73 (m, 6 H), 1.97 to 2.08 (m, 2 H), 2.15 (ddd, $J_1 \approx 1$ Hz, $J_2 \approx 1$ Hz, J_3=12.2 Hz, 1 H), 2.29 (dddd, J_1=0.7 Hz, J_2=7.0 Hz, J_3=12.5 Hz, J_4=14.3 Hz, 1 H), 2.44 (dddd, $J_1 \approx 2$ Hz, $J_2 \approx 2$ Hz, $J_3 \approx 5$ Hz, J_4=14.3 Hz, 1 H); ^{13}C NMR 18.83, 19.38, 21.43, 23.10, 33.21, 33.28, 38.43, 41.97, 41.99, 42.32, 52.15, 59.58, 211.7.

(2S,4aS,8aR)-5,5,8a-Trimethyldecahydronaphthalen-2-ol ***16***

5.07 mL (5.07 mmol) of a 1M K-Selectride® solution in THF were added under nitrogen to 0.82 g (4.22 mmol) of ketone **15** in solution in 25 mL of anhydrous THF. After 30 min at room temperature, the mixture was analyzed by GC–MS, showing compound **16** (2.94 min, >99%). 10 mL of water were then added and ether extraction followed by FC (10%, then 30%) afforded 0.76 g (3.87 mmol, 92% yield) of alcohol **16** as a solid.

16: mp 77–78°C; $[\alpha]_D^{20}$ −16.8 (*c*3.1, MeOH); EIMS *m/z* (rel int) 196 (M^+, 7), 164 (10), 163 (base), 137 (18), 135 (17), 123 (15), 121 (13), 111 (11), 109 (18), 107 (17), 95 (29), 94 (11), 93 (21), 91 (14), 83 (18), 82 (17), 81 (39), 79 (22), 69 (33), 68 (14), 67 (34), 57 (13), 55 (36), 53 (12); IR (nujol) 3500 to 3060 cm^{-1}; ^1H NMR 0.80 to 1.75 (m, 13 H), 0.84 (s, 3 H), 0.88 (s, 3 H), 1.16 (s, 3 H), 1.87 to 1.93 (m, 1 H), 4.09 (s, 1 H); ^{13}C NMR 16.89, 18.13, 21.19, 21.34, 32.90, 32.97, 34.13, 35.10, 42.32, 42.35, 51.21, 54.21, 67.81.

(2S,4aS,8aR)-(−)-5,5,8a-Trimethyldecahydronaphthalen-2-yl acetate [(−)-Polywood®] ***17***

0.52 g (2.65 mmol) of alcohol **16** was added under nitrogen to a solution of 0.5 mL of pyridine in 5 mL of acetic anhydride. After 2 days at room temperature the mixture was analyzed by GC–MS, showing compound **17** (3.77 min, >99%). 5 mL of water were then added, followed by extraction (ether/pentane, 30:70) and washing (10% aqueous Na_2CO_3). FC (10%) afforded then 0.59 g (2.47 mmol, 93% yield) of (−)-Polywood® **17**. An analytical sample was obtained by molecular distillation.

17: bp 85°C (bath)/0.5 Torr; $[\alpha]_D^{20}$ −13 (*c*2.1, $CHCl_3$) [Lit.[12] $[\alpha]_D^{20}$ −16.47 (*c*1.42, $CHCl_3$)]; EIMS *m/z* (rel int) 178 (41), 164 (13), 163 (base), 149 (33), 137 (13), 135 (23), 124 (74), 123 (20), 122 (27), 121 (20), 110 (18), 109 (67), 108 (32), 107 (43), 95 (36), 94 (21), 93 (53), 91 (23), 83 (10), 82 (23), 81 (81), 80 (11), 79 (43), 77 (19), 69 (46), 68 (15), 67 (55), 56 (17), 55 (64), 53 (22); IR (neat) 1740 cm^{-1}; ^1H NMR 0.80 to 1.70 (m, 12 H), 0.83 (s, 3 H), 0.88 (s, 3 H), 1.05 (s, 3 H), 1.90 to 1.97 (m, 1 H), 2.04 (s, 3 H), 5.02 (dddd, $J_1 \approx 3$ Hz, $J_2 \approx 3$ Hz, $J_3 \approx 3$ Hz, $J_4 \approx 3$ Hz, 1 H); ^{13}C NMR 17.49, 18.19, 20.64, 21.18, 21.46, 32.03, 32.87, 32.96, 34.06, 41.99, 42.26, 47.64, 53.79, 70.47, 170.5.

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26. Enantiomeric excess based on LISR ^{1}H NMR determinations with Eu(hfc)$_3$.
27. An analogous procedure is described in ref. 1e for the recrystallization of (*R*)-(−)-4,4a,5,6,7,8-hexahydro-4a-methylnaphthalen-2(3*H*)-one.
28. **5**: EIMS *m/z* (rel int) 181 (12), 180 (M$^+$, 74), 165 (15), 152 (15), 147 (15), 137 (15), 125 (88), 124 (31), 123 (77), 109 (27), 108 (25), 97 (15), 95 (50), 93 (21), 84 (20), 83 (48), 82 (18), 81 (56), 79 (21), 69 (base), 68 (21), 67 (64), 57 (23), 55 (64), 53 (22); IR (neat) 1710 cm^{-1}; ^{1}H NMR 0.97 (d, *J*=6.6 Hz, 3 H), 1.05 to 1.18 (m, 4 H), 1.09 (s, 3 H), 1.40 to 1.85 (m, 7 H), 2.20 (ddt, J_1=1.5 Hz, $J_2\approx$7 Hz, $J_3\approx$13 Hz, 1 H), 2.33 (ddd, J_1=2.2 Hz, J_2=4.8 Hz, J_3=14.7 Hz, 1 H), 2.52 (dddd, J_1=1.1 Hz, J_2=6.25 Hz, $J_3\approx$14 Hz, $J_4\approx$14 Hz, 1 H); ^{13}C NMR 11.10, 16.10, 21.10, 25.71, 26.07, 33.64, 38.09, 40.83, 41.73, 45.44, 51.17, 213.2.
29. An analytic sample was obtained by molecular distillation under reduced pressure. **8**: bp 90°C (bath)/0.02 Torr; EIMS *m/z* (rel int) 273 (M$^+$, 7), 187 (12), 126 (20), 115 (11), 106 (10), 105 (base), 104 (11), 103 (11), 82 (11), 79 (17), 77 (18); 1H NMR (C_6D_6), 50:50 mixture of two diastereoisomers 1.11 to 2.09 (m, 5H), 1.23+1.25 (two d, *J*=6.6 Hz, 3H), 1.36+1.38 (two d, *J*=6.6 Hz, 3H), 2.54 to 2.74 (m, 2H), 3.43 to 3.57 (m, 4H), 4.58 (two q, *J*=6.6 Hz), 7.04 to 7.48 (m, 5H); ^{13}C NMR (C_6D_6), 50:50 mixture of two diastereoisomers 17.68, 25.85, 26.04+26.83, 35.47+36.20, 39.45+40.65, 44.79+44.91, 59.06, 65.00+65.04, 108.7, 126.5 to 129.3, 147.9+148.1, 171.0+171.2.

(Received in UK 4 February 1997)