Tetrahedron Vol. 35, pp. 1751 to 1758
Pergamon Press Ltd., 1979. Printed in Great Britain

OPTICALLY ACTIVE α- AND β-NAPHTHALENE DERIVATIVES—IV

SYNTHESIS AND OPTICAL PURITY OF 2-METHYL-3- AND 2,2-DIMETHYL-3- (α- AND β-NAPHTHYL)-BUTANES

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(*Received in UK 30 May 1978*)

Abstract—The (*S*) methyl 3-(α- and β-naphthyl)-butanoates have been related to the optically active title compounds and to 2-(α- and β-naphthyl)-butanoic-, -3-methylbutanoic- and -3,3-dimethylbutanoic acids. The absolute configurations and maximum rotatory powers (this is in fact, all that has been measured, in terms of rotatory power) of the naphthyl hydrocarbons and their related compounds have been established.

In this report we refer to the synthesis and stereochemical correlations of new naphthyl hydrocarbons characterized by the presence of an i-propyl or t-butyl group at the chiral centre bonded to the aromatic nucleus. Starting from optically active methyl 3-(α- and β-naphthyl)-butanoates **1a,b**,[1] the corresponding 2-methyl-3(α- and β-naphthyl)-butanes **4a,b** and 2,2-dimethyl-3-(α- and β-naphthyl)-butanes **5a,b** were prepared by known reactions (Scheme 1).

The methyl esters **1a,b** were converted into the corresponding 2-anions by using the lithium diisopropylamide (LDA) in THF solution and then alkylated by methyliodide in HMPA[2] in very satisfactory yields. The conversion of **2a,b** into **4a,b** was performed by the usual procedure in 70–36% overall yield respectively (Scheme 1). Methyl esters **3a,b**, were obtained from **2a,b** in the same way, and converted into **5a,b** by LAH reduction of the corresponding methane sulphonates (similar reduction of the *p*-toluene-sulphonates) especially in the case of β-naphthyl derivative, resulted in an unsatisfactory yield analogous to the observed reduction of sulphonates of some neopentylic alcohols.[3a] In order to obtain **5b** in the higher yield, a sample of **3b**, by LAH reduction and subsequent oxidation by dicyclohexylcarbodiimide (DCC) in DMSO[3] was converted into **6b** which by Huang-Minlon reaction,[4] afforded **5b** (68% overall yield) (Scheme 1, seq. ii).

A further sequence to prepare **4b** was carried out starting from 2-(β-naphthyl)-propionic acid **7b**, by using a procedure already employed for the determination of the absolute configuration of (+)-2-phenyl-3-methylbutanoic acid[5] (Scheme 1, seq. i).

Some physical data and rotatory powers of the chief intermediates, whose structures were confirmed by NMR and mass spectra, are given in Table 1.

The optically active naphthylbutanes **4a,b**, **5a,b** and 2-(α- and β-naphthyl)-butanes **11a,b** were also prepared starting from the corresponding acids **10a,b**, **12a,b** and **13a,b**.

The racemic **10a** and **12a** were obtained as reported[6] and the acids **10b** and **12b** were prepared in excellent yield by 2-alkylation of methyl β-naphthylacetates[1] and subsequent hydrolysis (Scheme 2). Finally racemic 3,3-dimethyl-2-(α- and β-naphthyl)-butanoic acids **13a,b** were obtained from the olefins **16a,b** via the reactions reported in the Scheme 3 (overall yields 27–48% respectively).

The intermediate olefin **16a** was obtained by the Wittig reaction on (α-naphthyl)-t-butyl ketone,[7] while **16b** was prepared by dehydration of (β-naphthyl)-t-butylmethyl carbinol[7,8] in turn obtained from (β-naphthyl)-methylketone and the Grignard reagent of t-butyl chloride.

The resolution of the acids **10a,b**, **12a,b** and **13a,b** was accomplished by using optically active bases (Experimental) and their conversion into optically active hydrocarbons **4a,b**, **5a,b** and **11a,b** was carried out by a usual procedure in satisfactory overall yields (Scheme 4).

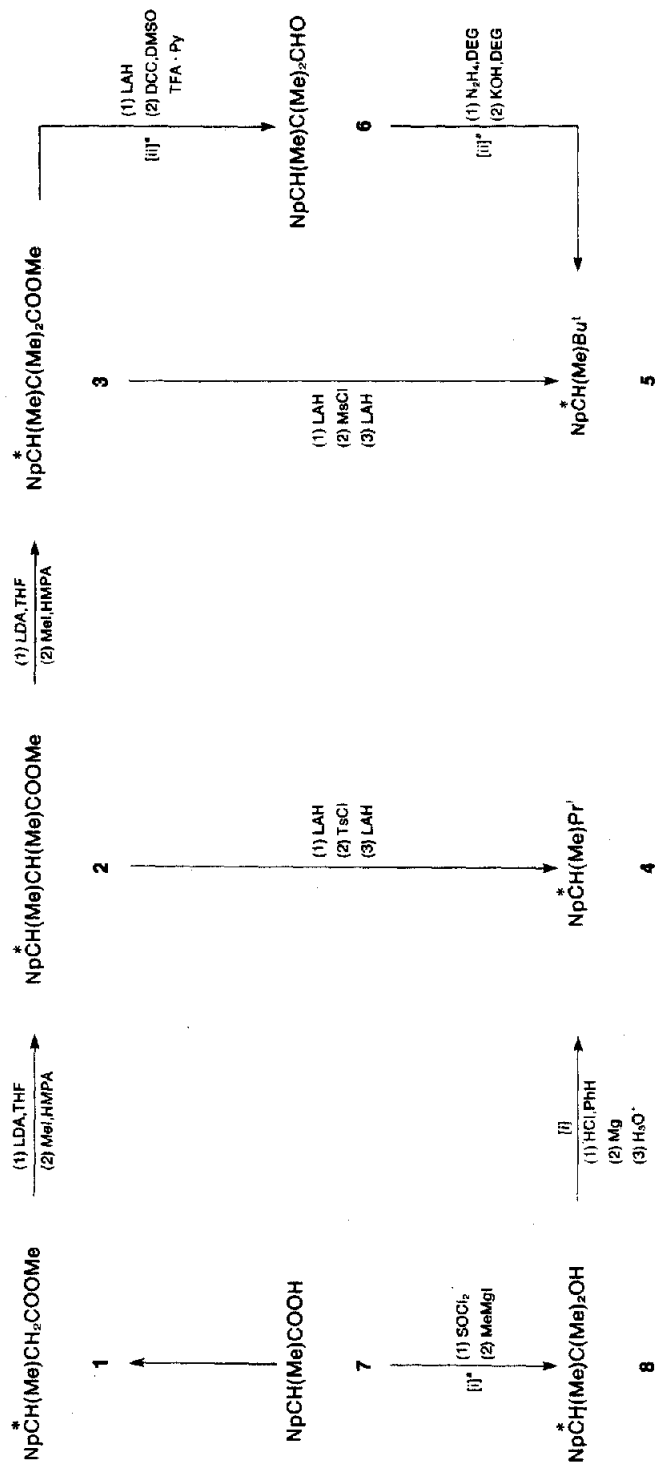
In Table 2 are given some physical properties and the rotatory powers of the compounds reported in the Scheme 4.

DISCUSSION AND CONCLUSIONS

The sequences **1a,b**→**4a,b** and **1a,b** →**5a,b** via **2a,b** and **3a,b** respectively (Scheme 1), were adopted to correlate these new hydrocarbons to known 2-(α- and β-naphthyl)-propionic acids.[1]

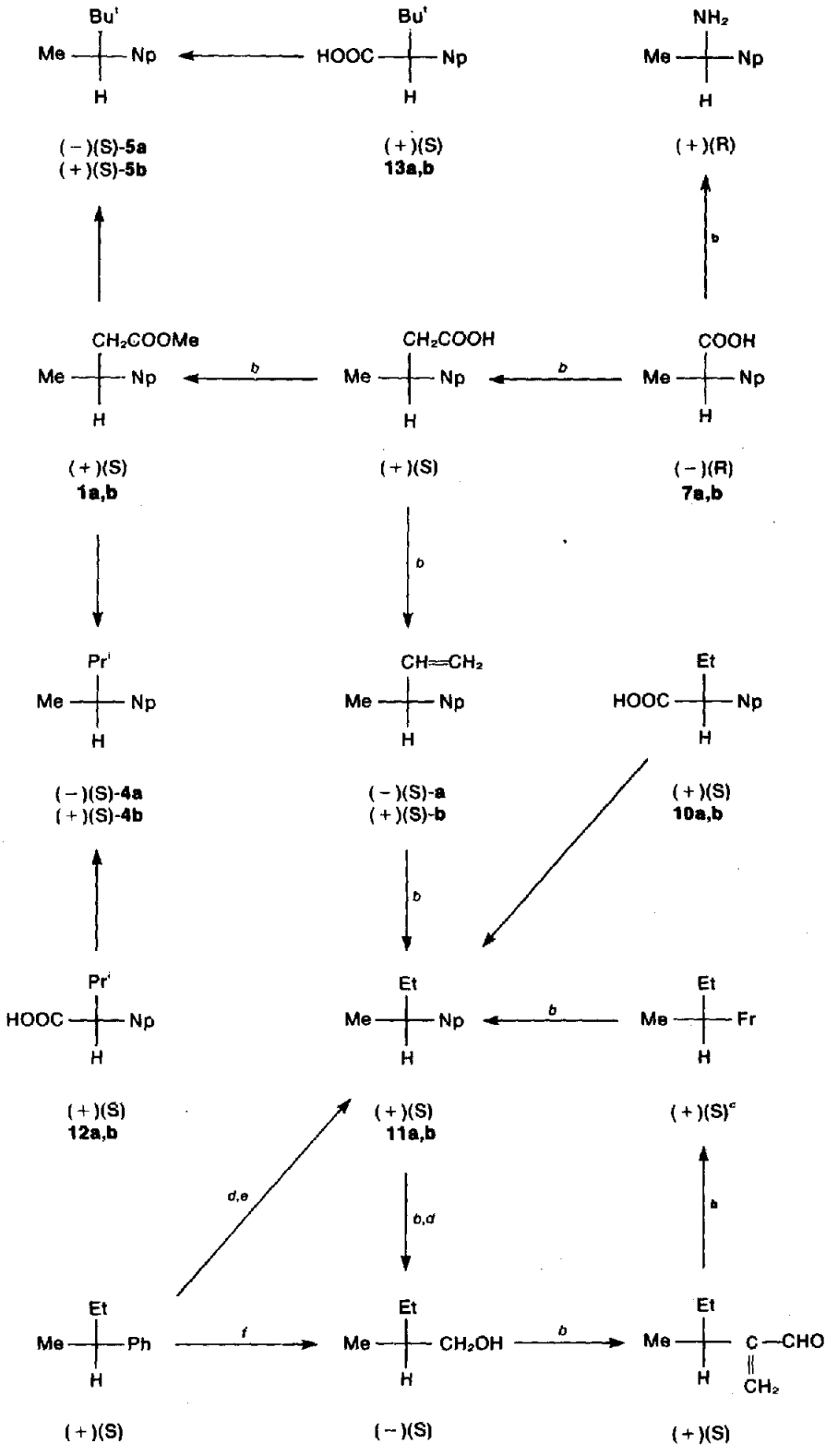
In our opinion the nature of the reactions employed warranted that the chiral centre was not affected; however we have carried out an independent route (Scheme 1, seq. i) whose results confirmed the above reported assumption (Table 1). In the context of the stereodynamic aspects of the conversion of **1a,b** into **2a,b** we noted a relevant asymmetric induction: in fact the diasteromeric esters **2a,b** were recovered in the ratio 1:2.3 as evaluated by NMR and glc analyses.

Moreover the reduction of **2a,b** and **3a,b** into **4a,b** and **5a,b** respectively showed a peculiar behaviour of the sulphonic esters: (1) the reduction of the *p*-toluene sulphonates of 2-methyl-3-(naphthyl)-1-butanols afforded **4a,b** in different yields, higher in the case of the α-naphthyl derivative; (2) the conversion of 2,2-dimethyl-3-(naphthyl)-1-butanols into **5a,b** via the LAH reduction of the corresponding methane sulphonates, while it afforded an appreciable yield (79%) of **5a**, did not appear suitable to obtain **5b** because the hydride fission of the O–S bond was the more important reaction.



Np = α- (a) and β- (b) naphthyl derivatives
*Sequences performed only on β-naphthyl derivatives.

Scheme 1.



Chart[a]

[a]The optical rotations were measured at 589 nm; [b]Ref. 1 and references therein; [c]Fr = 2- and 3-furyl; [d]Only for β-naphthyl derivative; [e]R. Menicagli, O. Piccolo and L. Lardicci, *Chem. Ind. (Milan)* **57**, 499 (1975); [f]G. P. Giacomelli, A. M. Caporusso and L. Lardicci, *J. Chem. Soc. Perkin I*, 1333 (1977).

Table 1. α- and β-naphthyl derivatives of Scheme 1

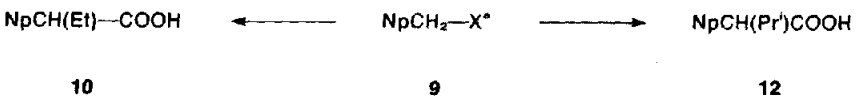
Compound	m.p. °C	b.p. °C (Torr)	$[\alpha]_D^{25}$ (c, solvent)
1a	-	136 (0.07)	-34.56 (3.020, PhH) [a]
4a	-	93 (0.4)	-21.08° (neat) [a,b]
5a	35-50	114 (0.3)	+26.48 (2.776, CCl_4)
1b	-	112 (0.3)	-50.72 (3.760, PhH)
4b	-	97 (0.5)	- 2.69° (neat) [c] + 1.84° (neat) [c,d]
5b	54-64	98 (0.3)	-33.71 (2.032, CCl_4) -33.43 (2.034, CCl_4) [e]

[a] at 365 nm; [b] α_D^{25} (l=1); [c] α_D^{25} (l=0.1); [d] from 7b, $[\alpha]_D^{25}$ -45.54 (0.850, EtOH) sequence [i]; [e] sequence [ii].

Table 2. α- and β-naphthyl derivatives of Scheme 4

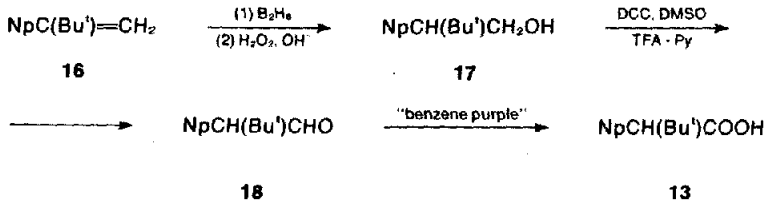
Compound	m.p. °C	b.p. °C (torr)	$[\alpha]_D^{25}$ (c, solvent)
10a	57 - 84	-	-51.37 (2.584, Me_2CO)
11a	-	87 (0.6)	- 8.07 (neat)
12a	-	131 (0.01)	-212.44 (2.363, PhH)
4a	-	93 (0.4)	- 21.99° (neat) [a]
13a	158 - 171	-	+129.78 (2.300, Me_2CO)
5a	-	114 (0.3)	- 24.71 (2.788, CCl_4)
10b	85 - 97	-	+ 38.21 (1.086, EtOH)
11b	-	93 (0.9)	+ 13.60 (neat)
12b	109 - 125	-	- 76.20 (1.148, EtOH)
4b	-	97 (0.5)	- 2.76° (neat) [b]
13b	167 - 177	-	- 10.02 (1.313, PhH)
5b	37 - 50	103 (0.4)	- 11.14 (2.212, CCl_4)

[a] at 365 nm, l=1; [b] l=0.1.

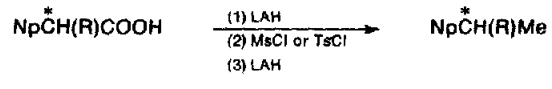


*X = CN for α-naphthyl derivatives and X = COOMe for β-naphthyl ones.

Scheme 2.



Scheme 3.



Scheme 4.

Differences in the reactivity of the sulphonic esters were also observed in the conversion of 3-methyl-2-(β-naphthyl)-1-butanol into **4b** by reduction of its tosylate (30% yield) or mesylate (83% yield) (Scheme 4).

The preparation of 3,3-dimethyl-2-(α- and β-naphthyl)-butanoic acids **13a,b** was accomplished by oxidation of the corresponding aldehydes **18a,b** in turn obtained from 3,3-dimethyl-2-(α- and β-naphthyl)-but-1-enes **16a,b** via the carbinols **17a,b** (Scheme 3). This tedious and almost unsatisfactory sequence was adopted as other synthetic routes failed completely: in fact the chloride (or bromide or methanesulphonate), prepared from 2,2-dimethyl-1-(α-naphthyl)-1-propanol **14a**, as precursor[9,10] of the acid **13a**, did not afford any significant result as well as the 1,4-addition of suitable organometallic system[11] to 2-isopropylidene-α-naphthylacetonitrile.[12] The oxidation of compounds **18a,b** was carried out in fair yield by means of "benzene purple"[13] as other oxidative reagents (e.g. Ag_2O,[14] AgO,[15] etc.) gave worse results owing to the formation of more by products than the former case.

The stereochemical results of the adopted sequences (Scheme 1) showed that the chiral centre of **1a,b** was not affected; therefore it is possible to attribute to **4a,b** and **5a,b** the same absolute configurations of their precursors[1] and consequently the absolute configurations of new optically active acids **10a,b**, **12a,b** and **13a,b** were established (Scheme 4). The relationship between the absolute configuration and the sign of the rotatory power of the main α- and β-naphthyl derivatives prepared is reported in the Chart; moreover in the Table 3 the maximum rotations of the naphthyl hydrocarbons **4a,b**, **5a,b** and of the acids **10a,b**, **12a,b** and **13a,b** are summarized.

The investigation we have carried out in this and in the previous paper was necessary to proceed in our studies of the chiroptical properties of aromatic chromophores; nevertheless our synthetic and stereochemical data can have practical value in the field of biological and pharmacological properties of naphthalene derivatives as well as in the study of asymmetric reactions involving prochiral substrates bearing naphthalene moieties.

EXPERIMENTAL

M.ps and b.ps are uncorrected. Glc analyses [2m × 0.29 cm columns packed with: 8% Carbowax 20 M + 2%KOH on 80–100 mesh Chromosorb W (CW 20 M); 15% Butanediolsuccinate on 90–100 mesh Chromosorb W(BDS); 2.5% Silicone gum rubber on 80–100 mesh AW-DMCS Chromosorb G (SE 301)] were performed on a Perkin–Elmer F 30 or a C.Erba Fractovap mod. instrument with flame ionization detectors and N_2 as carrier gas. Preparative glc's were carried out on a Perkin–Elmer F21 chromatograph, using 2 or 3 m × 0.95 cm columns packed with: 3% Silicone gum rubber on 60–80 mesh Chromosorb G (SE 301), 20% Butanediol succinate on 45–60 mesh Chromosorb A (BDS), 20% Apiezon L on 60–80 mesh Chromosorb G (APZ). NMR spectra were recorded with a Varian T 60 or a Jeol P S100 Spectrometer with TMS as internal standard. Mass spectra were obtained with a Varian Mat CH 7 mass spectrometer (70 eV). Optical rotations were taken with a Perkin–Elmer 142 or with a Schmidt–Haensch polarimeters and refer to pure liquid unless otherwise stated. Microanalyses were carried out in the Micro-

Table 3. Maximum rotations of the main compounds of the Schemes 1 and 3

Compound	$[\alpha]^{25}_{D\ max}$ (solvent)
1a	41.0 (PhH) [a,b]
4a	25.0° (neat) [a,c,d]
5a	31.4 (CCl_4) [d]
11a	25.4 (neat) [b]
10a	161.7 (Me_2CO) [e]
12a	241.5 (PhH) [f]
13a	164.9 (Me_2CO) [g]
1b	57.6 (PhH) [b]
4b	3.05 (neat) [h,i] 2.85 (neat) [h,j]
5b	38.3 (CCl_4) [i] 37.9 (CCl_4) [i,k]
11b	30.2 (neat) [b]
10b	84.8 (EtOH) [l]
12b	84.2 (EtOH) [m]
13b	34.3 (PhH) [n]

[a] at 365 nm; [b] ref.1; [c] α^{25}_D(l=1); [d] evaluated on the optical purity of 1a; [e] evaluated on the optical purity of 11a (Scheme 3); [f] evaluated on the optical purity of 4a (Scheme 3); [g] evaluated on the optical purity of 5a (Scheme 3); [h] α^{25}_D(l=0.1); [i] evaluated on the optical purity of 1b; [j] evaluated on the optical purity of 7b (ref.1) (Scheme 1, sequence [i]); [k] (Scheme 1, sequence [ii]); [l] evaluated on the optical purity of 11b (Scheme 3); [m] evaluated on the optical purity of 4b (Scheme 3); [n] evaluated on the optical purity of 5b (Scheme 3).

analysis Laboratory of the Faculty of Pharmacy of the Pisa University. Solvents and commercial reagents were purified by conventional methods before use.

Methyl 2-methyl-3-(naphthyl)-butanoates **2a,b**. In a typical run, 15.1 g (0.066 mol) of (*R*)-**1a** in 30 ml dry THF was added, at −78°, to a THF soln of LDA, prepared as previously described[2] from 8.2 g (0.081 mol) diisopropylamine and 36 ml of a 20% n-hexane soln of n-BuLi. After 1 hr, 11.4 g (0.080 mol) MeI and 3.7 g dry HMPA were added and the mixture was stirred for 2 hr at −78°, and for 12 hr at room temp., then hydrolyzed with ice and extracted with pentane. The organic phase was washed with 10% HCl, H_2O and dried with Na_2SO_4. The solvent was removed and the residue afforded 14.8 g of **2a** [92%; >99% pure (mixture of diasteroisomers) (SE 301; 170°); b.p. 143°/0.1 Torr; Found: C, 79.18; H, 7.54. Calc. for $C_{16}H_{18}O_2$: C, 79.31; H, 7.49%]. Analogously 16.1 g (0.071 mol) of (*R*)-**1b** afforded 16.8 g of **2b** [98%; 99% pure (mixture of diastereoisomers) (SE 301; 170°); b.p. 150°/0.7–0.8 Torr; mass spectrum *m/e* rel. intensity: 242 (M^+, 13), 155 (100)].

2-Methyl-3-(naphthyl)-1-butanols. To 1.5 g (0.039 mol) of LAH in 50 ml ether was added an ether soln of 4.9 g (0.023 mol) of (*R*)-**2a**. The mixture was refluxed 20 hr and then worked up by standard procedure to give a quantitative yield 4.4 g of the corresponding carbinol (b.p. 124°/0.02 Torr).

In a similar manner 3.5 g (0.014 mol) of (*R*)-**2b** afforded 3.0 g of 2-methyl-3-(β-naphthyl)-1-butanol [91%; b.p. 138°/0.7 Torr].

2-Methyl-3-(naphthyl)-butanes **4a,b**. 4.0 g (0.019 mol) of (*R*)-2-methyl-3-(α-naphthyl)-1-butanol was converted as previously described[1] into the corresponding tosylate which, without any purification, was reduced with 2.4 g (0.064 mol) of LAH in 100 ml ether, at the reflux for 50 hr, to 2.8 g of (*R*)-**4a** [72%; >96% pure (SE 301; 170°)]. A pure sample was obtained by glpc (3 m SE 301; 150°) [Found: C, 90.80; H, 9.21. Calc. for $C_{15}H_{18}$: C, 90.85; H, 9.10; α^{25}_{589} (l = 1) +0.09,°; α^{25}_{365} (l = 1) −21.08°; NMR (100 MHz) δ (CCl_4) 7.89 (1H, m, aromatic), 7.45 (2H, m, aromatic), 7.12 (4H, m, aromatic), 3.22 (1H, m, –CH(Pr^i)–), 1.86 (1H, m, –CH(CH$_3$)$_2$), 1.18 (3H, d, –CH(CH$_3$)Pr^i), 0.82–0.76 (6H, 2d, –CH(CH$_3$)$_2$); mass spectrum *m/e* rel. intensity: 198 (M^+, 20), 155 (100)].

In a similar manner 3.0 g of 2-methyl-3-(β-naphthyl)-1-butanol afforded quantitatively the crude tosylate, which was converted by 1.2 g (0.032 mol) LAH in 200 ml ether-benzene (10:1, V/V) into the corresponding hydrocarbon (*R*)-**4b** [35%; >90% pure (SE 301; 170°)].

A ~100% pure sample was obtained by glpc purification (3 m APZ; 160°) [Found: C, 90.86; H, 9.22; α^{25}_{589} (l = 0.1) −2.69°, $[\alpha]^{25}_{589}$ −30.80 (*c* 4.286, PhH); NMR (100 MHz) δ (neat) 7.49 (3H, m, aromatic), 7.32 (1H, s, aromatic), 7.05 (3H, m, aromatic), 2.32 (1H, m, –CH(Pr^i)–), 1.65 (1H, m, –CH(CH$_3$)$_2$), 1.16 (3H, d, –CH(CH$_3$)Pr^i), 0.85–0.69 (6H, 2d, –CH(CH$_3$)$_2$); mass spectrum *m/e* rel. intensity: 198 (M^+, 21), 155 (100)].

Methyl 2,2-dimethyl-3-(naphthyl)-butanoates **3a,b**. 7.0 g (0.029 mol) of (*R*)-**2a**, under the previously described procedure, was converted, with 2.0 g (0.031 mol) LDA in 30 ml THF and 5.0 g (0.035 mol) MeI in 1.4 g dry HMPA, into 6.4 g of (*R*)-**3a** [86%; 90% pure (SE 301; 185°); b.p.133–4°/0.5 Torr].

In a similar manner 7.9 g (0.033 mol) of (*R*)-**2b** afforded 8.3 g of (*R*)-**3b** [99%; >97% pure (SE 301; 185°); b.p. 133°/0.3 Torr; mass spectrum *m/e* rel. intensity: 256 (M^+, 7), 155 (100)].

2,2-Dimethyl-3-(naphthyl)-1-butanols. 6.4 g (0.026 mol) of (*R*)-**3a** and 8.3 g (0.033 mol) of (*R*)-**3b**, by reduction with 2.1 g (5.3 m.mol) LAH in 100 ml dry ether, afforded respectively (*R*)-2,2-dimethyl-3-(α-naphthyl)-1-butanol [85%; b.p. 150°/0.08 Torr] and the corresponding (*R*)-β-naphthyl derivative [97%, b.p. 140°/0.2–0.25 Torr].

2,2-Dimethyl-3-(naphthyl)-butanes **5a,b**. To a soln of 3.2 g (0.014 mol) of (*R*)-2,2-dimethyl-3-(α-naphthyl)-1-butanol and 2.1 g (0.021 mol) of triethylamine in 71 ml CH_2Cl_2, at 0°, was added 1.8 g (0.016 mol) methanesulphonyl chloride. The mixture was stirred 4 hr at 0°, 15 hr at room temp. and then hydrolyzed with ice and worked up in the usual way. The solvent was removed under reduced pressure (18 Torr) and the crude methanesulphonate, was reduced, with 1.3 g (0.034 mol) LAH in 100 ml dry ether, to 2.3 g of (*R*)-**5a** (79%). A pure sample was obtained by glpc (3 m SE 301; 150°) [Found: C, 90.44; H, 9.48. Calc. for $C_{16}H_{20}$: C, 90.50; H, 9.50%; $[\alpha]^{25}_D$ +26.48 (*c* 2.776, CCl_4); NMR (100 MHz) δ(CCl_4) 8.03 (1H, m, aromatic), 7.54 (2H, m, aromatic), 3.9 (2H, d, CH_2OH), 3.7 (1H, t, –CH(Bu^t)–), 0.8 (3H, d, –CH(CH$_3$)–), 0.88 (9H, s, –C(CH$_3$)$_3$); mass spectrum *m/e* rel. intensity: 212 (M^+, 14.5), 155 (100)].

The crude methansulphonate of (*R*)-2,2-dimethyl - 3-(β-naphthyl) - 1 - butanol, 9.6 g (0.031 mol), obtained in a quantitative yield from the corresponding carbinol, by reacting with 3.2 g (0.084 mol) of LAH in 250 ml ether, afforded ~1.3 g of (*R*)-**5b** and ~6.3 g of the starting alcohol. By glpc (3 m APZ; 150°) pure (*R*)-**5b** was obtained [Found: C, 90.30; H, 9.67; $[\alpha]^{25}_D$ −33.71(*c* 2.032, CCl_4); NMR (100 MHz) δ (CCl_4) 7.55 (3H, m, aromatic), 7.37 (1H, s, aromatic), 7.18 (3H, m, aromatic), 2.64 (1H, q, –CH(Bu^t)–), 1.31 (3H, d, –CH(CH$_3$)–), 0.89 (3H, s, –C(CH$_3$)$_3$); mass spectrum *m/e* rel. intensity: 212 (M^+, 14), 155 (100)].

2,2-Dimethyl-3-(β-naphthyl)-butane **5b** (*seq.ii*). To a benzene soln of 4.5 g (0.020 mol) of (*R*)-2,2-dimethyl-3-(β-naphthyl)-1-butanol, recovered from LAH reduction of the corresponding methanesulphonate, was added 44.0 g (0.563 mol) dry DMSO, 1.6 g (0.020 mol) pyridine, 1.2 g (0.011 mol) TFA and 11.6 g (0.056 mol) DCC in 20 ml benzene. The mixture was stirred for 18 hr at room temp. and then worked up as usual to give 4.4 g crude (*R*)-2,2-dimethyl - 3 - (β-naphthyl) - butanol which were dissolved into 15 ml DEG and 15 ml DMSO and added, at 0°, of 11.9 g (0.238 mol) 85% hydrazine hydrate. After refluxing, 1 hr, the mixture was cooled, treated with 4.0 g KOH dissolved in 10 ml DEG and refluxed again for 1 hr. The water and the excess of hydrazine were removed under reduced pressure (18 Torr) and the soln was heated at 175° for 5 hr. After cooling, the mixture was diluted with water and extracted with pentane. The organic phase was washed with water and dried over Na_2SO_4; after removal of the solvent, the residue, by distillation, afforded 2.8 g of (*R*)-**5b** (68%). A pure sample, obtained by glpc (2 m APZ; 185°) showed $[\alpha]^{25}_D$ −33.43 (*c* 2.034, CCl_4).

2-Methyl-3-(β-naphthyl)-2-butanol **8b**. To an ether soln of 14.0 g (0.070 mol) of (*R*)-**7b** [95% pure (SE 301; 165° on the corresponding methyl ester); $[\alpha]^{25}_D$ −45.54 (EtOH)] was added 28.7 g (0.241 mol) $SOCl_2$ and the mixture was left aside for 12 hr and then refluxed for 8 hr. The crude chloride, in 80 ml dry ether, was slowly added to an ether soln of Grignard reagent prepared from 38.6 g (0.272 mol) MeI and 7.4 g (0.304 g atom) Mg. After one night, the mixture was stirred for 25 hr under reflux temp and then worked up as previously described.[5] The ether was removed to leave 14.2 g of (*R*)-**8b** [95%; 97% pure (SE 301; 180); b.p. 127°/0.35 Torr; $[\alpha]^{25}_{589}$ +11.42 (*c* 2.162, PhH); NMR δ (C_6D_6) 7.9–7.1 (7H, m, aromatic), 2.7 (1H, q, –CH(CH$_3$)–), 1.7 (1H, s, –OH), 1.3 (3H, d, –CH(CH$_3$)–), 1.0 (6H, s, –C(CH$_3$)$_2$)].

2-Methyl-3-(β-naphthyl)-butane **4b** (*seq. i*). 7.0 g (0.033 mol) of (*R*)-**8b**, in 100 ml dry benzene, was converted by HCl (g) in 5 hr in a mixture of two products [b.p. 130°/0.04 Torr; ~1:2 from glc analysis (SE 301; 155°] that was added to 0.72 g (0.030 g atoms) of Mg in ether. After 1 hr under reflux temp, the mixture was hydrolyzed with NH_4Cl aq and processed in the usual way. A sample of (*S*)-**4b** [42% pure (CW 20 M; 180°)], purified by glpc (2 m BDS; 140°) showed α^{25}_{589} (l = 0.1) + 1.84°.

2-(Naphthyl)-butanoicacids **10a,b**. (*R*)(*S*)-**10a** was prepared as previously described[16] from (α-naphthyl)-acetonitrile [85%; m.p. 85–6° (lit.[6a] 86–7°); 96% pure (BDS; 190° on the corresponding methyl ester)]. To a soln of 88.0 g (0.41 mol) of (*R*)(*S*)-**10a** and 118.8 g (0.040 mol) cinchonidine in 132 ml MeOH was added 4000 ml ether; the salt was filtered off and recrystallized from 100 ml MeOH, 1500 ml acetone and 1500 ml water; after hydrolysis, 25.8 g of (*S*)-**10a** [>99% pure (BDS; 190°); $[\alpha]^{25}_D$ + 106.13 (Me_2CO)] was obtained. The mother liquors were combined and afforded 53.5 g of (*R*)-**10a** [>99% pure (BDS; 190°); $[\alpha]^{25}_D$ −51.37 (Me_2CO)]. (*R*)(*S*)-**10b** was obtained from methyl (β-naphthyl)-acetate by the usual procedure[1] [93%; >99% pure (SE 301; 165° on the corresponding methyl ester); m.p. 103° (lit.[16] 91–2°); Found: C, 78.54; H, 6.80. Calc. For $C_{14}H_{14}O_2$: C, 78.48; H, 6.59%]. Equimolecular quantities of the racemic acid **10b** (53.0 g, 0.25 mol) and (*S*)-α-phenylethylamine [29.4 g, α^{20}_D (l = 1) −37.96°] were dissolved in 1015 ml of 95% hot EtOH. The salt, after one recrystallization from 95% EtOH, was hydrolyzed and afforded 15.0 g of (*S*)-**10b** ($[\alpha]^{25}_{589}$ +38.21 (EtOH)). A sample was con-

verted by diazomethane into the corresponding methyl ester [~100% pure (SE 301; 165°); b.p. 124–125°/0.35 Torr; Found: C, 78.80; H, 7.07. Calc. for $C_{15}H_{16}O_2$: C, 78.92; H, 7.06%; $[\alpha]_{589}^{25}$ + 56.91 (*c* 2.372, PhH); NMR δ (neat), 7.9–7.1 (7H, m, aromatic), 3.6 (3H, s, –COOCH$_3$), 3.5 (1H, t, –CH(Et)–), 2.0 (2H, M, –CH$_2$–), 0.9 (3H, t, –CH$_3$)].

2-(*Naphthyl*)-1-*butanols*. 20.0 g (0.093 mol) of (*R*)-**10a** was reduced in 12 hr with 7.0 g (0.184 mol) LAH in 300 ml dry ether under reflux temp to 18.6 g of (*R*) – 2 – (α-naphthyl)-1-butanol [99%; b.p. 128–30°/0.5 Torr; Found: C, 83.70; H, 8.35. Calc. for $C_{14}H_{16}O$: C, 83.95; H, 8.05%: $[\alpha]_D^{25}$ – 5.35 (*c* 2.102, PhH)]. In a similar manner 13.0 g (0.061 mol) of (*S*)-**10b** afforded 11.5 of the corresponding alcohol [95%; b.p. 125–6°/0.3 Torr].

2-(*Naphthyl*)-*butanes* **11a,b**. 10.0 g (0.049 mol) of (*R*)-2-(α-naphthyl)-1-butanol was converted in the usual manner, into 16.5 g of the corresponding tosylate [93%; a sample, recrystallized from MeOH, showed: m.p. 69–72°; Found: S, 9.04. Calc. for $C_{21}H_{22}O_3S$: S, 9.05%; $[\alpha]_D^{25}$ – 9.96 (c 2.484, MeOH)]. 16.0 g (0.045 mol) of the crude tosylate was reduced with 2.7 g (0.071 mol) LAH in 150 ml dry ether. After glpc purification (2 m BDS; 170°) 3.0 g pure (*R*)-**11a** was recovered. 11.0 g (0.055 mol) of (*S*)-2-(β-naphthyl)-1-butanol, following a literature procedure[17] afforded 15.2 g of crude methanesulphonate which, without purification, was reduced with 4.8 g (0.126 mol) LAH in 350 ml dry ether, to 8.2 g of (*S*)-**11b** [82%; >99% pure (SE 301: 155°)].

3-*Methyl*-2-(*naphthyl*)-*butanoic acids* **12a,b**. (*R*)(*S*)-**12a** was prepared from (α-naphthyl)-acetonitrile[16] [71%; 97% pure (SE 301; 160° on the corresponding methyl ester); m.p. 113° (lit.[6a] 113–4°)]. 60.0 g (0.263 mol) of (*R*)(*S*)-**12a** and 32.1 g (0.263 mol) of (*R*)-α-phenylethylamine (α_D^{25} (l = 1) + 36.83°) was dissolved in 660 ml hot EtOH-water (1:1, V/V); the salt, after two crystallizations from EtOH–water, afforded 17.1 g of (*R*)-**12a** ($[\alpha]_D^{25}$ – 212.44 (PhH)). A sample, treated with diazomethane, afforded the corresponding methyl ester [>99% pure (SE 301; 160°); b.p. 120°/0.25 Torr; Found: C, 79.41; H, 7.40. Calc. For $C_{16}H_{18}O_2$: C, 79.31; H, 7.49%; $[\alpha]_D^{25}$ – 208.63 (*c* 3.384, PhH)].

(*R*)(*S*)-**12b** was obtained from methyl (β-naphthyl)-acetate[1] [93%; >99% pure (SE 301; 170° on the corresponding methyl ester); m.p. 132–4°; Found: C, 78.79; 7.17. Calc. for $C_{15}H_{16}O_2$: C, 78.92; H, 7.06%]. From a soln of equimolecular quantities of (*R*)(*S*)-**12b** (58.0 g, 0.25 mol) and (*R*)-α-phenylethylamine [31.3 g, α_D^{25} (l = 1) + 36.83°] in 2200 ml 95% EtOH, was recovered 51.5 g of salt which after two recrystallizations from EtOH, afforded 17.4 g of (*R*)-**12b** ($[\alpha]_{589}^{25}$ – 76.20 (EtOH)). A sample, by diazomethane, was converted into the corresponding methyl ester [~100% pure (SE 301; 180°); m.p. 46–58°; b.p. 124°/0.25–0.3 Torr; Found: C, 79.20; H, 7.40%; $[\alpha]_{589}^{25}$ – 101.76 (*c* 2.162, PhH); mass spectrum *m/e* rel. intensity: 242 (M^+, 100), 200 (71), 183 (59), 168 (57), 141 (90)]. From the mother liquors 18.0 g of (*S*)-**12b**, ($[\alpha]_{589}^{25}$ + 75.75 (EtOH)), was recovered.

3-*Methyl*-2-(*naphthyl*)-1-*butanols*. By reduction with 5.9 g (0.155 mol) LAH in 200 ml dry ether, 15.8 g (0.069 mol) of (*R*)-**12a** afforded quantitatively 14.7 g of (*R*)-3-methyl-2- (α-naphthyl) -1-butanol [b.p. 127–8°/0.01 Torr]. In a similar manner 11.0 g (0.048 mol) of (*R*)-**12b** was converted into 9.9 g of the corresponding alcohol [96%; m.p. 57–61°; b.p. 143°/0.5 Torr; Calc. for $C_{15}H_{18}O$: C, 84.07; H, 8.47. Found: C, 84.29; H, 8.50%; $[\alpha]_{589}^{25}$ – 15.26 (*c* 2.294, PhH)].

2-*Methyl*-3-(*naphthyl*)-*butanes* **4a,b**. Following the usual procedure, 13.4 g (0.063 mol) of (*R*)-3-methyl - 2 - (α-napthyl) - 1 - butanol was converted into the corresponding tosylate which without purification, afforded, via reduction with 5.9 g (0.155 mol) LAH in 160 ml dry ether, 12.4 g of (*R*)-**4a** [99%; >99% pure (SE 301; 150°); α_{589}^{25} (l = 1) + 0.074°; α_{365}^{25} (l = 1) – 21.99°].

Analogously, 9.2 g (0.043 mol) of (*R*)-3-methyl-2-(β-naphthyl)-1-butanol afforded, via LAH reduction of the corresponding tosylate in 350 ml dry ether–benzene (10:1, V/V), 2.6 g of (*R*)-**4b** [30%; >99% pure (SE 301; 165°)].

In another run, the methanesulphonate of (*R*)-3-methyl - 2 - (β-naphthyl) - 1 - butanol was reduced in excellent yield (85%) into the corresponding hydrocarbon.

(R)(S)-3,3-*Dimethyl*-2-(*naphthyl*)-1-*butanols* **17a,b**. A THF soln, 40 ml, of **16a**, 17.0 g(0.081 mol) [≃92%pure, (SE 301; 160°); b.p. 100°/0.5 Torr; NMR δ (neat) 8.2–7.9 (1H, m, aromatic), 7.8–7.0 (6H, m. aromatic), 5.5 (1H, d, =CHH), 4.9 (1H, d, =CHH), 1.1 (9H, s, –C(CH$_3$)$_3$)] prepared in 97% yield by the Wittig reaction on (α-naphthyl)-t-butylketone **15a**,† was reacted with 100 ml of a THF soln of BH_3 (1.15 M). After 24 hr at room temp. the mixture was reacted with 158 ml H_2O, 48 ml 6N NaOH and 24 ml 36% H_2O_2 and worked up as usual. By distillation 16.9 g of **17a** was recovered [92%; b.p. 143°/0.4 Torr; mass spectrum *m/e* rel. intensity: 228 (M^+, 23), 172 (46), 154 (100)].

Analogously 20.6 g (0.097 mol) of **16b**‡ [~99% pure (SE 301; 175°); m.p. 35–7° (lit.[8] 37–38.5°); b.p. 110°/0.75 Torr; NMR δ (CCl_4) 7.8–7.1 (7H, m, aromatic), 5.2 (1H, d, =CHH), 4.9 (1H, d, =CHH), 1.1 (9H, s, –C(CH$_3$)$_3$)] gave 20.1 g of **17b** [90%; 99% pure (SE 301; 190°); m.p. 110–2°; NMR δ (C_6D_6) 7.0–7.1 (7H, m, aromatic), 3.9 (2H, d, CH$_2$OH), 3.7 (1H, t, –CH(Bu^t)-), 0.8 (9H, s, –C(CH$_3$)$_3$), 0.7 (1H, s, OH)].

(R)(S)-3,3-*Dimethyl*-2-(*naphthyl*)-*butanals* **18a,b**. A benzene soln, 110 ml, of 14.0 g (0.062 mol) of (*R*)(*S*)-**17a** was reacted with 143 ml of DMSO, 5.7 ml pyridine, 2.8 ml TFA and 41.5 g (0.201 mol) DCC in 72 ml benzene. The mixture was stirred for 20 hr and then 200 ml diethyl ether, 19.3 g (0.153 mol) oxalic acid dissolved in 180 ml MeOH was added. After 1 hr, 700 ml H_2O was added and the mixture was worked up as described[3] to give 10 g crude **18a** [90% pure (SE 301; 180°); mass spectrum *m/e* rel. intensity: 226 (M^+, 13), 170 (100), 141 (35), 57 (24)]. By adopting the above reaction conditions, starting from 11.7 g (0.051 mol) of **17b**, 11.2 g of **18b** was recovered [97%; 96% pure (SE 301; 180°); b.p. 140°/0.6 Torr; NMR δ (CCl_4) 10.0 (1H, s, CHO), 7.9–7.1 (7H, m, aromatic), 3.3 (1H, d, –CH(Bu^t)–), 1.0 (9H, s, –C(CH$_3$)$_3$); mass spectrum *m/e* rel. intensity: 226 (M^+, 18), 170 (100), 141 (36), 57 (27)].

(R)(S)-3,3-*Dimethyl*-2-(*naphthyl*)-*butanoic acids* **13a,b**. In a typical run, to a benzene soln, 250 ml, of 10.0 g (0.044 mol) of **18a** were added 10.9 g (0.069 mol) $KMnO_4$ and 1.2 g (0.003 mol) dicyclohexyl-18-crown-6 and the mixture was stirred for 80 hr at room temp. The solid products were removed by filtration and washed with 10% NaOH; the aqueous phase was combined with the organic one and the crude acid, 4.3 g, was recovered as usual and it was crystallized from a 6:1 (V/V) mixture of *n*-hexane/diethyl ether to give 2.8 g of **13a** [17%; 98% pure (SE 301; 190° on the corresponding methyl ester); Found: C, 79.20; H, 7.52. Calc. for $C_{16}H_{18}O_2$: C, 79.31; H, 7.49%].

According to the reported procedure, 2.2 g (0.010 mol) of **18b** in 48 hr, afforded 1.3 g of **13b** [55%; 99% pure (SE 301; 200° on the corresponding methyl ester); m.p. 174–9°; Found: C, 79.32; H, 7.61%].

3,3-*Dimethyl*-2-(*naphthyl*)-*butanoic acids* **13a,b**. To a hot soln of 2.8 g (0.012 mol) of (*R*)(*S*)-**13a** in 100 ml of i-propyl ether was added 4.6 g (0.012 mol) brucine dissolved in 30 ml hot MeOH. The mixture was left for 24 hr at room temp. The salt was filtered off and hydrolyzed to give 1.2 g of (*S*)-**13a** ($[\alpha]_{589}^{25}$ + 129.78 (Me_2CO)). A sample, by reacting with diazomethane, yielded the corresponding methyl ester [99% pure (SE 301; 190°); m.p. 90–120°; $[\alpha]_{589}^{25}$ + 167.87 (*c* 1.852, PhH); NMR (100 MHz) δ (CCl_4) 8.23–7.22 (7H, m, aromatic), 4.43 (1H, s, –CH(Bu^t)–), 3.57 (3H, s, –COOCH$_3$), 1.03 (9H, s, –C(CH$_3$)$_3$). From the mother liquors 1.5 g (*R*)-**13a** [97% pure (SE 301; 190° on the corresponding methyl ester); $[\alpha]_{589}^{25}$ – 88.06 (Me_2CO)] was recovered.

Equimolecular quantities of (*R*)(*S*)-**13b** [3.8 (0.016 mol)] and (*S*)-α-phenylethylamine [α_D^{20} (l = 1) – 37.97°] was dissolved in 107 ml boiling 95% EtOH. After 24 hr, 3.0 g of salt was recovered which after hydrolysis, afforded 1.8 g of (*R*)-**13b** ($[\alpha]_{589}^{25}$ – 10.02

†Compound **15a** was obtained by DMSO/Ac_2O oxidation[18] of the corresponding carbinol **14a**, in turn prepared starting from α-naphthyl aldehyde and the Grignard reagent of t-butyl-chloride.

‡The olefin **16b** was obtained by *p*-toluensulphonic acid in refluxing benzene dehydration of the 3,3-dimethyl-2-(β-naphthyl) - 2 - butanol. This last compound was in turn prepared by reacting (β-naphthyl)-methyl ketone with t-butyl magnesium chloride.[8] The compound **16b** was purified from the starting ketone using an SiO_2 (70–230 mesh) column and petroleum ether as eluent.

(PhH)). A sample was converted into the corresponding methyl ester with diazomethane [99% pure (SE 301; 190°); m.p. 107–119°; $[\alpha]_{589}^{25}$ − 14.53 (c 1.900, PhH); NMR (100 MHz) δ (CCl_4) 7.90–7.17 (7H, m, aromatic), 3.60 (3H, s, $-COOCH_3$), 3.52 (1H, S, $-CH(Bu^t)-$), 1.07 (9H, s, $-C(CH_3)_3$)].

3,3-*Dimethyl*-2-(*naphthyl*)-1-*butanols*. 0.8 g (0.003 mol) of (*S*)-**13a** was reduced, in 14 hr, with 0.6 g (0.016 mol) LAH in 120 ml dry ether under reflux, to 0.7 g (*S*)-3,3-dimethyl-2-(α-naphthyl)-1-butanol [93%; m.p. 60–73°].

In a similar manner 1.7 g (0.007 mol) of (*R*)-**13b** yielded 1.5 g of the corresponding carbinol [94%; m.p. 112–118°].

2,2-*Dimethyl*-3-(*naphthyl*)-*butanes* **5a,b**. Following the usual procedure 0.7 g (0.003 mol) of (*S*)-3,3-dimethyl-2-(α-naphthyl)-1-butanol was converted into the corresponding methane sulphonate which without purification, afforded, via reduction with 0.4 g (0.011 mol) LAH in 180 ml dry ether, 0.5 g (*S*)-**5a** [81%; >99% pure (SE 301; 170°)].

Analogously 2.0 g (0.006 mol) crude methanesulphonate, obtained from 1.5 g (0.007 mol) (*R*)-3,3-dimethyl - 2 - (β-naphthyl)-1-butanol, was reduced with 0.8 g (0.021 mol) LAH in 210 ml dry ether–THF soln (6:1, V/V); 1.1 g of (*R*)-**5b** [80%; >99% pure (SE 301; 170°)] were recovered.

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