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Enantiopure *vic*-amino alcohols and *vic*-diamines from (1*R*,2*S*)-1,2-dihydroxy-1,2-dihydronaphthalene

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Abstract—(1*S*,2*S*)-2-Hydroxy-1-amino-1,2,3,4-tetrahydronaphthalene, (1*R*,2*R*)-1-hydroxy-2-amino-1,2,3,4-tetrahydronaphthalene, (1*S*,2*R*)-1,2-diamino-1,2,3,4-tetrahydronaphthalene, (2*R*,3*S*)-2-hydroxy-3-amino-1,2,3,4-tetrahydronaphthalene and (2*S*,3*S*)-2,3-diammino-1,2,3,4-tetrahydronaphthalene have been synthesized from (1*R*,2*S*)-1,2-dihydroxy-1,2-dihydronaphthalene. The latter was obtained, using a protocol reported in a previous paper, from naphthalene using an *Escherichia coli* recombinant strain containing the naphthalene dioxygenase gene cloned from *Pseudomonas fluorescens N3*.

1. Introduction

The preparation of enantiopure compounds is an extremely important task and many efforts have been devoted to the development of new asymmetric synthetic methods; nevertheless, the development of a generally useful chiral building block is still a significant target. In this context, chiral *vic*-amino alcohols[1] and chiral *vic*-diamines[2] have been recognized as generally useful and versatile chiral auxiliaries for the preparation of enantiopure compounds. To this end, we report herein the synthesis of (1*S*,2*S*)-2-hydroxy-1-amino-1,2,3,4-tetrahydronaphthalene **4**, (1*R*,2*R*)-1-hydroxy-2-amino-1,2,3,4-tetrahydronaphthalene **8**, (1*S*,2*R*)-1,2-diammino-1,2,3,4-tetrahydronaphthalene **13**, (2*R*,3*S*)-3-hydroxy-2-amino-1,2,3,4-tetrahydronaphthalene **20** and (2*S*,3*S*)-2,3-diammino-1,2,3,4-tetrahydronaphthalene **21**, from (1*R*,2*S*)-1,2-dihydroxy-1,2-dihydronaphthalene,[3] previously obtained in our laboratory by bioconversion of naphthalene and now also a commercially available compound.[4]

2. Results and discussion

The synthetic precursors for the enantiopure *vic*-amino alcohols and *vic*-diamines listed above are (1*R*,2*S*)-1,2-dihydroxy-1,2,3,4-tetrahydronaphthalene **1** (Scheme 1) and (2*R*,3*R*)-2,3-dihydroxy-1,2,3,4-tetrahydronaphthalene **2** (Scheme 3). Both of these compounds were easily obtained from (1*R*,2*S*)-1,2-dihydroxy-1,2-dihydronaphthalene: the former, in almost quantitative yields, by catalytic hydrogenation in the presence of palladium on charcoal; the latter in three steps, with a 75% total yields.[3] Enantiopure *trans*-amino alcohols **4** and **8** and *cis*-diamine **13** were obtained from (1*R*,2*S*)-1,2-dihydroxy-1,2,3,4-tetrahydronaphthalene, as illustrated in Schemes 1 and 2.

(1*S*,2*S*)-2-Hydroxy-1-amino-1,2,3,4-tetrahydronaphthalene **4** was obtained in 80% yield by catalytic hydrogenation of the (1*S*,2*S*)-2-hydroxy-1-azido derivative **3** (Scheme 1). The latter was synthesized using two different protocols: (a) by direct treatment of **1** with diphenylphosphoryl azide in the presence of triphenylphosphine and diethyldiazadicarboxylate;[5] (b) via the carbonate **5**, obtained in 95% yields from the diol **1**, and subsequent reaction with sodium azide in dimethylformamide. The first, single step, procedure is more straightforward: however, the experimental conditions, in particular the reaction time, must be carefully controlled to obtain reasonable yields (maximum 40% with about 50% recovery of starting diol) and thus avoid loss of material. The second procedure requires two steps, but neither chromatographic purification of the product nor of the intermediate are required and, in addition, the total yield is better (81%). The reaction of the carbonate **5** with sodium azide proceeded in almost quantitative yields and afforded as a unique stereoiso-

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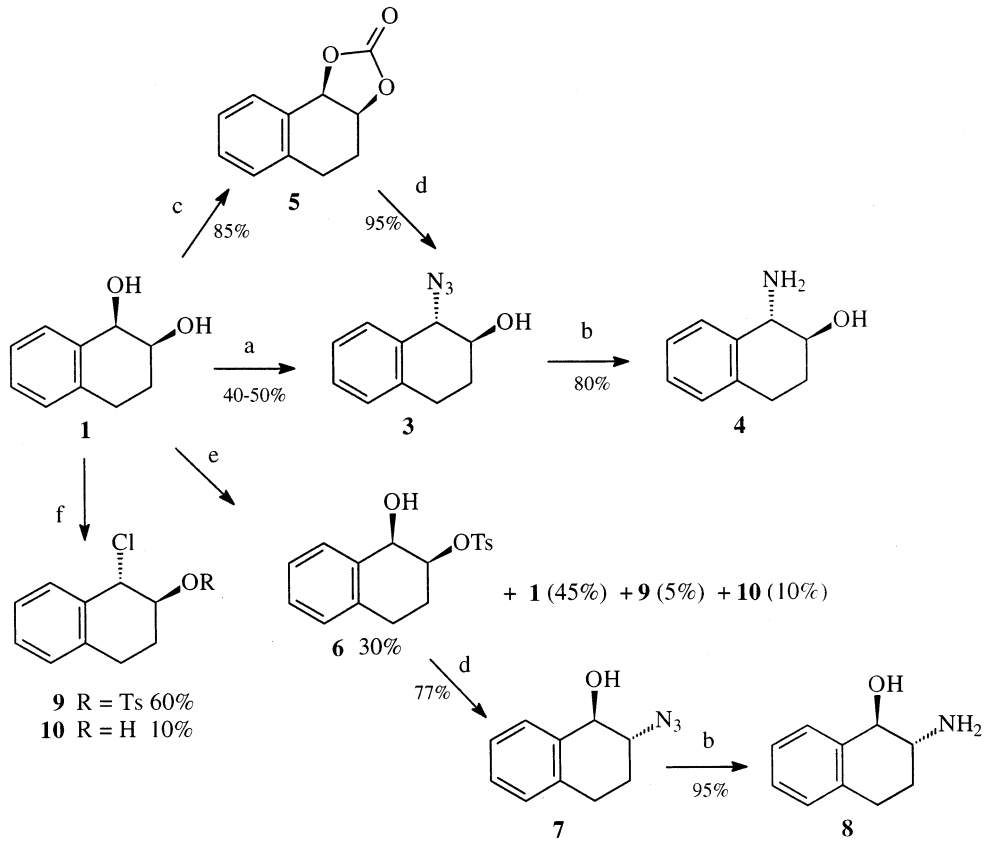
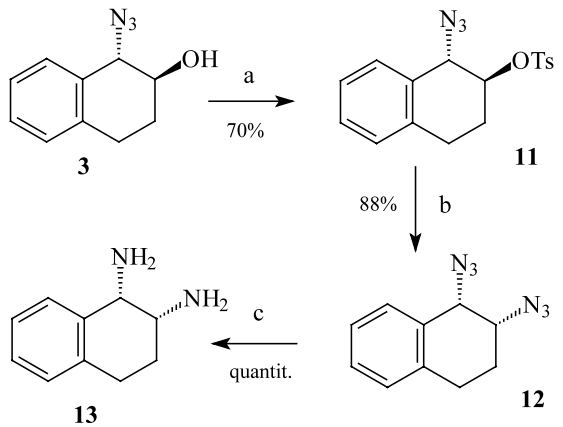


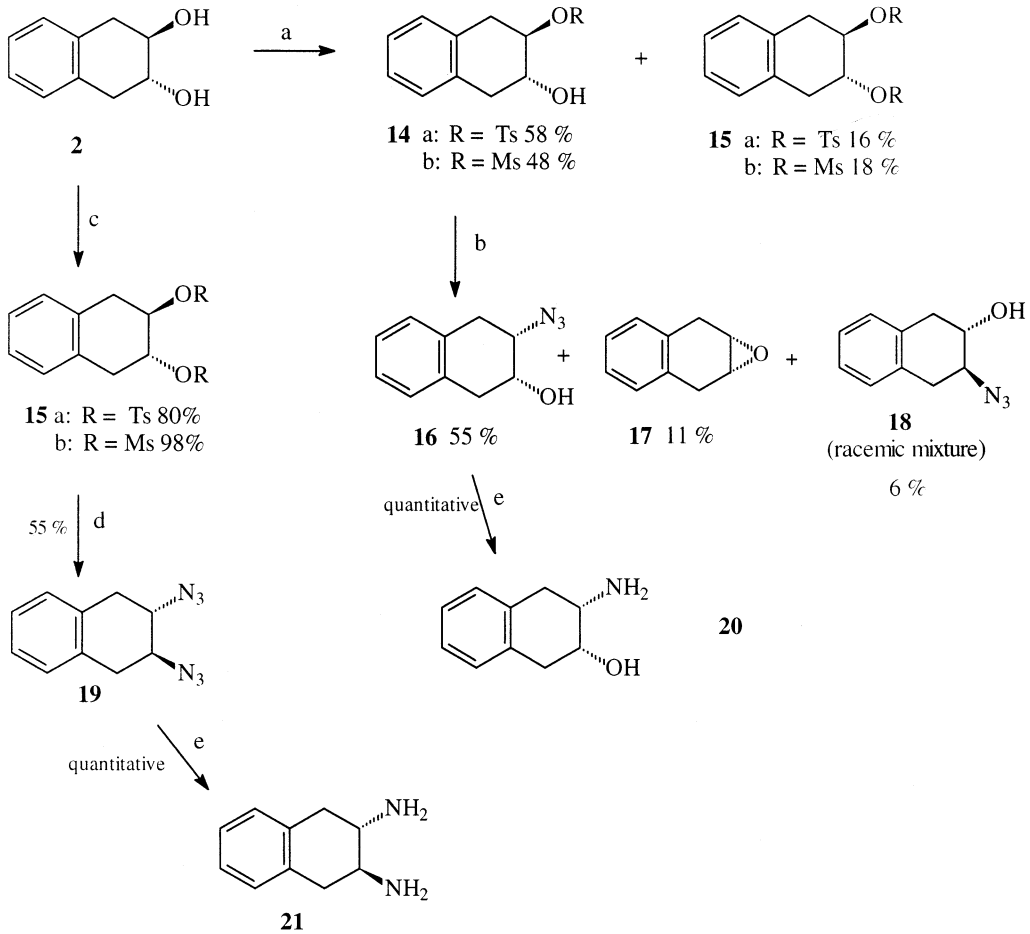
Scheme 1. (a) Ph_3P, diethylazodicarboxylate, diphenylphosphoryl azide; (b) H_2, Pd/C, MeOH; (c) triphosgene, Py, CH_2Cl_2; (d) NaN_3, DMF, 110°C; (e) TsCl (1, 2 equiv.), Py; (f) TsCl (4 equiv.), Py.



Scheme 2. (a) TsCl, Py; (b) NaN_3, DMF, 110°C; (c) H_2, Pd/C, MeOH.

mer the *trans*-azido alcohol **3**, whose stereochemistry was inferred from the predictable stereochemical outcome of the substitution reaction (which involves only the C(1) stereogenic centre) and verified by comparison of the H_1–H_2 NMR coupling constants for both the azido alcohol **3** ($J_{1,2}=6.9$ Hz,) and the amino alcohol **4** ($J_{1,2}=8.0$ Hz) with respect to the values reported for *cis*-(1*R*,2*S*)-2-hydroxy-1-azido-1,2,3,4-tetrahydronaphthalene ($J_{1,2}=3.8$ Hz) and *cis*-(1*R*,2*S*)-2-hydroxy-1-amino-1,2,3,4-tetrahydronaphthalene[6] ($J_{1,2}=4.7$ Hz).

The two protocols reported above exclusively afford the *trans*-amino alcohol **4**: the corresponding *cis*-(1*R*,2*S*)-2-hydroxy-1-amino-1,2,3,4-tetrahydronaphthalene has been obtained by treatment of the diol **1** with triflic acid in acetonitrile, followed by water, as already reported in the literature.[6] (1*R*,2*R*)-1-Hydroxy-2-amino-1,2,3,4-tetrahydronaphthalene **8**, was obtained in three steps, by treatment of **1** with tosyl chloride followed by reaction with sodium azide or tetrabutylammonium azide, and finally catalytic reduction of the resulting azide. In the first step, the regioselective tosylation of the C(2) hydroxyl group, the conditions of the reaction must be carefully controlled to obtain reasonable yields of the 2-tosyl derivative **6** (30%, with 45% recovery of starting diol, easily separated and recycled) and to minimize the (1*S*,2*S*)-1-chloro-2-hydroxy-1,2,3,4-tetrahydronaphthalene **10** and (1*S*,2*S*)-1-chloro-2-tosyl-1,2,3,4-tetrahydronaphthalene **9** side products. The latter was the main product when an excess (4 equiv.) of tosyl chloride was used. The reaction of **6** with sodium azide (the only reaction in the synthetic scheme which involves a stereogenic centre, the C(2)) produced a single stereoisomer, to which structure **7** was assigned on the basis of the expected stereochemical course of the substitution reaction and the H_1–H_2 NMR coupling constant ($J_{1,2}=6.9$ Hz).



Scheme 3. (a) TsCl (1.2 equiv.), Py; (b) NaN_3, DMF, 110°C; (c) TsCl (2.2 equiv.), Py; (d) $(Bu)_4N^+N_3^-$, toluene, 60°C; (e) H_2, Pd/C, MeOH.

(1*S*,2*R*)-1,2-Diamino-1,2,3,4-tetrahydronaphthalene **13** (Scheme 2) was obtained from (1*S*,2*S*)-2-hydroxy-1-azido-1,2,3,4-tetrahydronaphthalene **3** in three steps and 62% total yield: treatment with tosyl chloride in pyridine, substitution with sodium azide using the protocol reported above and eventually catalytic hydrogenation in the presence of palladium on charcoal. The *cis*-1,2-configuration in compound **12**, the only stereoisomer obtained from **11**, was in agreement with the observed H_1–H_2 NMR coupling constant ($J_{1,2}$=2.3 Hz).

(2*R*,3*S*)-2-Hydroxy-3-amino-1,2,3,4-tetrahydronaphthalene **20** and (2*S*,3*S*)-diammino-1,2,3,4-tetrahydronaphthalene **21** were synthesized from (2*R*,3*R*)-2,3-dihydroxy-1,2,3,4-tetrahydronaphthalene **2**, already successfully used as a chiral auxiliary[7] (Scheme 3). Reaction of **2** with 2.2 equiv. of tosyl chloride in dry pyridine afforded the ditosylate **15a** in 80% yields (path c), accompanied by a small amount of **14a** (5%). Both **14a** and **15a** were obtained in 58 and 16% yields, respectively by reaction of **2** with 1.2 molar equiv. of tosyl chloride (path a). The same protocols, using mesyl chloride, were applied to the synthesis of the dimesylate **15b** and of the monomesylate **14b**. Treatment of **15a** or **15b** with sodium azide in dimethylformamide, followed by reduction in the presence of palladium on charcoal afforded the diamine **21** (characterized via the corresponding bis-hydrochloride), respectively in 16 and 27% total yield from the diol **2**.

The crucial step of this synthetic sequence is the conversion of the tosylate/mesylate **15** to the corresponding diazide **19** as the yields are significantly lowered by the competitive elimination reaction, made easier by the formation of an aromatic compound such as naphthalene. To improve this step, several options were considered concerning the solvent used (toluene, toluene–water under phase transfer catalysis, dimethylformamide), the temperature (from 50 to 120°C), the nucleophile (sodium azide, tetralkylammonium azide both free[8] or supported on a basic resin[9]). An improvement from 20 to 55% yield was achieved with dimesylate **15b**, using tetrabutyl ammonium azide in toluene at 60°C, taking the overall yield to 54%. Under the conditions used for phase transfer catalysis, the diazide **19** was obtained in 15% yields, accompanied by (2*R*,3*S*)-2-mesyloxy-3-azido-1,2,3,4-tetrahydronaphthalene and naphthalene.

The enantiomeric purity of the diamine **21** was determined by ^{1}H NMR analysis of the corresponding Mosher's[10] mono-amide ((+)-α-methoxy-α-trifluoromethylphenylacetic amide) and diamide.[11] The conversion of the monotosylate **14a**/monomesylate **14b** to the azido alcohol **16** was accompanied by two side-products: the *meso*-epoxide **17** and the racemic *trans*-azido alcohol **18**, which formed in variable amounts depending on the experimental conditions. Minimisation of side reactions was achieved by treatment of the monomesylate **14b** with sodium azide in dimethylformamide at 110°C which afforded the *cis*-azido alcohol **16** in 55% yields, accompanied by 11% of *meso*-epoxide **17**[12] and 6% of racemic *trans*-azido alcohol **18**. The *cis*-(2*S*,3*R*)-configuration assigned to the azido alcohol **16** ($J_{1,2}=2.3$) is in agreement with a S_N2 displacement of the leaving group at C(2) of the mono-tosylate/mesylate **14a/b**. The formation of the racemic *trans*-azido alcohol **18** is in agreement with the presence of the *meso*-epoxide **17**, quite reactive towards sodium azide.

Hydrogenation of **16** in the presence of palladium on charcoal quantitatively afforded (2*R*,3*S*)-2-hydroxy-3-amino-1,2,3,4-tetrahydronaphthalene **20**. Direct introduction of the azido group, under Mitsunobu conditions, by treatment of **2** with diphenylphosphoryl azide in the presence of triphenylphosphine and diethyldiazadicarboxylate,[5] as reported for the amino alcohol **4**, was unsuccessful and afforded the *meso*-epoxide **6**[12] as the main product.

3. Conclusion

In conclusion, the described protocols, coupled with the ability of the naphthalene dioxygenase from *P. fluorescens* to produce enantiopure *cis*-1,2-diols, allows efficient and convenient access to compounds **4**, **8**, **13**, **20**, and **21**, starting from an easily available, low-cost material. Ongoing research focuses on the application of the synthesized enantiopure compounds in asymmetric synthesis and as ligands to metal centres in biologically active complexes.

4. Experimental

Reagent grade tetrahydrofuran was refluxed over $LiAlH_4$ and distilled. Reagent grade dichloromethane was heated under reflux over P_2O_5 and distilled. Reagent grade dimethylformamide was distilled at reduced pressure under nitrogen and kept over 4 Å molecular sieves. Reagent grade acetonitrile was heated under reflux over CaH_2 and distilled. Proton and carbon nuclear magnetic resonance (^{1}H and ^{13}C NMR) spectra were recorded at 200 and 300 MHz on Brucker spectrometers. Mass spectra were recorded with a VG7070 E9 spectrometer. Melting points were obtained by using a Buchi 535 apparatus. Optical rotation measurements were obtained with a Perkin–Elmer 241 Polarimeter and the elemental analyses for the new compounds were determined on a Perkin–Elmer 240 Analyser. Flash-column chromatography was performed on silica gel Merck Kieselgel 60 (230–400 mesh). Thin-layer chromatography was performed on silica gel plates (60 F254, Merck): zones were detected visually by ultraviolet irradiation (254 nm) or by spraying with methanol:H_2SO_4 9:1, followed by heating at 100°C. All reactions were performed in a dry nitrogen atmosphere, using glassware dried by flaming in a stream of dry nitrogen.

4.1. (1*S*,2*S*)-2-Hydroxy-1-azido-1,2,3,4-tetrahydronaphthalene 3

4.1.1. One-step synthesis. (1*R*,2*S*)-1,2-Dihydroxy-1,2,3,4-tetrahydronaphthalene (1.0 g, 6.10 mmol) was added at 0°C to a magnetically stirred solution of triphenylphosphine (1.6 g, 6.10 mmol) and diethylazodicarboxylate (1.062 g, 6.10 mmol), in dry tetrahydrofuran (17 mL). After stirring the mixture for 10 min, diphenylphosphoryl azide (1.678 g, 6.10 mmol) was added dropwise over 10 min and stirring was continued for about 30 h. The reaction was monitored by thin layer chromatography (silica gel, eluting with *n*-hexane:ethyl acetate 8:2). The solvent was removed under reduced pressure and the crude material (4.972 g) was purified by column chromatography (silica gel, eluting with petroleum–ether:ethyl acetate 9:1; 8:2; 7:3; 1:1) to give (1*S*,2*S*)-2-hydroxy-1-azido-1,2,3,4-tetrahydronaphthalene **3** (0.46 g, 2.43 mmol, 40%), accompanied by unreacted starting diol (0.55 g, 55%). Compound **3**: Colorless oil, $[\alpha]_D=-18.6$ ($c=0.89$, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 1.91 (dddd, 1H, $J=13.7$, 8.6, 6.9, 6.0 Hz, H-3), 2.12 (dddd, 1H, $J=13.7$, 10.3, 6.9, 6.9 Hz, H-3′), 2.85 (m, 1H, H-4), 2.95 (m, 1H, H-4′), 4.01 (ddd, 1H, $J=10.3$, 8.6, 6.9 Hz, H-2), 4.45 (d, 1H, $J=6.9$ Hz, H-1), 7.12 (d, 1H, $J=7.5$ Hz, H-5 or H-8), 7.2 (dd, 1H, $J=7.5$, 7.5 Hz, H-6 or H-7), 7.21 (dd, 1H, $J=7.5$, 7.5 Hz, H-7 or H-6), 7.5 (d, 1H, $J=7.5$ Hz, H-8 or H-5); ^{13}C NMR ($CDCl_3$): 26.5 (t), 28.5 (t), 66.6 (d), 71.1 (d), 126.6 (d), 128.1 (d), 128.7 (d), 128.8 (d), 132.4 (s), 136.14 (s); MS (EI) m/z: 189 (M^+), 171 (M^+-H_2O), 161 (M^+-N_2).

4.1.2. Two step synthesis via carbonate 5. Triphosgene (0.2 g, 0.67 mmol) in dry DCM (1 mL) was added dropwise to a stirred solution of (1*R*,2*S*)-1,2-dihydroxy-1,2,3,4-tetrahydronaphthalene **1** (0.1 g, 0.60 mmol) in dry pyridine (0.5 mmol). The reaction was monitored by thin layer chromatography (silica gel, eluting with petroleum ether:ethyl acetate 6:4). After about 0.5 h, the solution was diluted with water and the two phases were separated. The aqueous phase was extracted with DCM (3×2 mL). The combined organic phases were dried (Na_2SO_4), and the solvent was removed under reduced pressure to afford pure carbonate **5** (0.095 g, 0.5 mmol, 85%). Compound **5**: Colorless crystals, mp=96–98°C (ethyl acetate–petroleum ether); $[\alpha]_D=+206.4$ ($c=1.0$, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 1.96 (dddd, 1H, $J=14.0$, 10.0, 4.0, 4.0 Hz, H-3), 2.28 (dddd, 1H, $J=14.0$, 4.0, 4.0, 4.0 Hz, H-3′), 2.68 (ddd, 1H, $J=15.0$, 4.0, 4.0 Hz, H-4), 2.94 (ddd, 1H, $J=15.0$, 10.0, 4.0 Hz H-4′), 5.18 (ddd, 1H, $J=7.5$, 4.0, 4.0 Hz, H-2), 5.68 (d, 1H, $J=6.5$ Hz, H-1), 7.10 (d, 1H, $J=7.5$ Hz, H-5 or H-8), 7.33 (m, 3H, H-8 or H-5, H-6, H-7);

^{13}C NMR ($CDCl_3$): 23.7 (t), 27.0 (t), 75.3 (d), 75.6 (d), 127.3 (d), 128.6 (d), 129.7 (d), 130.7 (d), 129.3 (s), 138.1 (2C) (s); MS (EI) m/z: 190 (M^+), 146 (M^+-CO_2).

Sodium azide (0.43 g, 6.6 mmol) was added to a solution of the carbonate **5** (0.85 g, 4.4 mmol) in dry DMF (20 mL). The resulting suspension was heated at 120°C in a pre-heated oil bath and the reaction was monitored by thin layer chromatography (silica gel, eluting with petroleum ether:ethyl acetate 7:3). After ca.10 h, the reaction mixture was cooled, diluted with water (20 mL) and extracted with ethyl acetate (3×20 mL). The combined organic extracts were dried (Na_2SO_4) and the solvent removed under reduced pressure. The crude material was flash-chromatographed (silica gel, eluting with petroleum ether:ethyl acetate 7:3) to afford the azido alcohol **3** (0.80 g, 95%).

4.2. (1*S*,2*S*)-2-Hydroxy-1-amino-1,2,3,4-tetrahydronaphthalene 4

A solution of (1*S*,2*S*)-2-hydroxy-1-azido-1,2,3,4-tetrahydronaphthalene **3** (0.64 g, 3.3 mmol) in methanol (100 mL) was hydrogenated for 3 h in the presence of 10% palladium on charcoal (0.26 g). The suspension was filtered on a Celite pad and the solvent removed under reduced pressure. The crude material was purified by column chromatography (silica gel, eluting with chlorofom:methanol 95:5; chloroform:methanol:di-*iso*-propylamine 95:5:5) and afforded pure (1*S*,2*S*)-2-hydroxy-1-amino-1,2,3,4-tetrahydronaphthalene **4** (0.435 g, 2.66 mmol, 80%). Compound **4**: Colorless crystals; mp = 111–113°C (ethyl acetate–petroleum ether); $[\alpha]_D = -85.4$ ($c = 0.634$, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 1.81 (dddd, 1H, $J = 18.0$, 4.0, 8.0, 4.0 Hz, H-3), 2.19 (dddd, 1H, $J = 18.0$, 10.0, 8.0, 4.0 Hz, H-3′), 2.91 (m, 2H, H-4, H-4′), 3.56 (ddd, 1H, $J = 10.0$, 8.0, 4.0 Hz, H-2), 3.65 (d, 1H, $J = 8.0$ Hz, H-1), 7.0–7.5 (m, 4H aromatic hydrogens); ^{13}C NMR ($CDCl_3$): 27.8 (t), 29.3 (t), 57.7 (d), 73.4 (d), 126.3 (d), 126.6 (d), 126.8 (d), 128.5 (d), 135.8 (s), 139.3 (s); MS (EI) m/z: 163 (M^+), 146 (M^+-NH_3), 128 ($M^+-NH_3-H_2O$). Calcd for $C_{10}H_{13}NO$: C, 73.62; H, 7.98; N, 8.59. Found: C, 73.98; H, 7.90; N, 8.31%.

4.3. (1*R*,2*S*)-2-*p*-Toluenesulphonyloxy-1-hydroxy-1,2,3,4-tetrahydronaphthalene 6

Tosyl chloride (0.813 g, 4.28 mmol) in dry pyridine (2 mL) was added dropwise over 1 h, at 0°C under stirring, to a solution of diol **1** (0.5 g, 3.4 mmol) in dry pyridine (5 mL). The reaction was monitored by TLC (Silica gel, eluting with *n*-hexane:ethyl acetate 6:4). After stirring the reaction mixture for 3.5 h, ice-water was added and the mixture extracted with ethyl acetate (3×7 mL). The combined organic extracts were washed with a 0.3N HCl till acid pH and then with a saturated NaCl solution till neutral pH. The organic phase was dried (Na_2SO_4) and the solvent removed under reduced pressure. The crude material (0.632 g) was chromatographed (silica gel, eluting with *n*-hexane:ethyl acetate, 6:4) and afforded the mono-tosylate **6** (0.29 g, 0.91 mmol, 30%), accompanied by 1-chloro-2-tosyl derivative **9** (0.055 g, 0.3 mmol, 10%) and by 1-chloro-2-hydroxy derivative **10** (0225 g, 1.37 mmol, 45%). Compound **6**: Colorless oil, $[\alpha]_D = -30.5$ ($c = 1.98$, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 1.88 (dddd, 1H, $J = 12.5$, 6.3, 6.3, 3.8 Hz, H-3), 2.35 (dddd, 1H, $J = 12.5$, 8.8, 6.3, 6.3 Hz, H-3′), 2.45 (s, 3H, Me), 2.75 (ddd, 1H, $J = 17.5$, 6.3, 6.3 Hz, H-4), 2.97 (ddd, 1H, $J = 17.5$, 6.3, 6.3 Hz, H-4′), 4.78 (d, 1H, $J = 3.8$ Hz, H-1), 4.88 (ddd, 1H, $J = 8.8$, 3.8, 3.8 Hz, H-2), 7.05 (dd, 1H, $J = 7.0$, 1.5 Hz, H-5 or H-8), 7.20 (ddd, 2H, $J = 7.0$, 7.0, 1.5 Hz, H-6, H-7), 7.33 (dd, 1H, $J = 7.0$, 1.5 Hz, H-8 or H-5), 7.34 (d, 2H, $J = 8.0$ Hz, H-3″, H-5″), 7.84 (d, 2H, $J = 8.0$ Hz, H-2″, H-6″); ^{13}C NMR ($CDCl_3$): 21.5 (q), 23.8 (t), 26.2 (t), 68.6 (d), 80.9 (d), 126.4 (d), 127.7 (2C, d), 128.3 (2C, d), 129.2 (d), 129.8 (2C, d), 133.8 (s), 135.1 (2C, s), 144.9 (s); MS (EI) m/z: 146 (M^+–PTSH), 128 (M^+–PTSH–H_2O). Calcd for $C_{17}H_{18}O_4S$: C, 64.15; H, 5.66. Found: C, 64.35; H, 6.01%.

4.4. (1*S*,2*S*)-1-Chloro-2-*p*-toluenesulphonyloxy-1,2,3,4-tetrahydronaphthalene 9

Colorless crystals, mp = 113–115°C (ethyl acetate–petroleum ether); $[\alpha]_D = -4.0$ ($c = 1.98$, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 1.99 (dddd, 1H, $J = 14.0$, 6.0, 4.0, 4.0 Hz, H-3), 2.42 (dddd, 1H, $J = 14.0$, 10.0, 6.0, 2.0 Hz, H-3′), 2.45 (s, 3H, CH_3), 2.80 (ddd, 1H, $J = 16.0$, 6.0, 4.0 Hz, H-4), 2.87 (ddd, 1H, $J = 16.0$, 10.0, 6.0 Hz, H-4′), 5.06 (ddd, 1H, $J = 7.0$, 4.0, 2.0 Hz, H-2), 5.07 (d, 1H, $J = 7.0$ Hz, H-1), 7.10 (dd, 1H, $J = 7.1$, 1.8 Hz, H-5 or H-8), 7.20 (ddd, 2H, $J = 7.1$, 7.1, 1.8 Hz, H-6, H-7), 7.25 (dd, 2H, $J = 7.1$, 1.8 Hz, H-8 or H-5), 7.32 (d, 2H, $J = 8.0$ Hz, H-3″, H-5″), 7.80 (d, 2H, $J = 8.0$ Hz, H-2″, H-6″); ^{13}C NMR ($CDCl_3$): 21.6 (q), 23.3 (t), 23.8 (t), 55.8 (d), 79.9 (d), 126.7 (d), 127.8 (2C, d), 128.7 (2C, d), 128.8 (2C, d), 130.8 (d), 132.3 (s), 134.0 (s), 135.2 (s), 145.1 (s); MS (EI) m/z: 336–338 (M^++1), 301 (M^+–Cl). Calcd for $C_{17}H_{17}ClO_3S$: C, 60.71; H, 5.06. Found: C, 60.75; H, 5.2%.

4.5. (1*S*,2*S*)-1-Chloro-2-hydroxy-1,2,3,4-tetrahydronaphthalene 10

Colorless oil; $[\alpha]_D = -39$ ($c = 0.7$, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 1.99 (dddd, 1H, $J = 14.0$, 6.0, 4.0, 4.0 Hz, H-3), 2.21 (dddd, 1H, $J = 14.0$, 10.0, 6.0, 2.0 Hz, H-3′), 2.95 (m, 2H, H-4, H-4′), 4.15 (ddd, 1H, $J = 7.0$, 4.0, 2.0 Hz, H-2), 5.02 (d, 1H, $J = 7.0$ Hz, H-1), 7.1 (m, 1H, aromatic hydrogen), 7.25 (m, 1H, aromatic hydrogen), 7.36 (m, 1H, aromatic hydrogen), 7.57 (m, 1H, aromatic hydrogen); ^{13}C NMR ($CDCl_3$): δ 26.2 (t), 27.6 (t), 64.3 (d), 69.1 (d), 126.4 (d), 128.1 (d), 128.5 (d), 130.2 (d), 133.9 (s), 135.5 (s); MS (EI) m/z: 184–182 (M^+), 164 (M^+-H_2O), 146 (M^+–Cl). Calcd for $C_{10}H_{11}ClO$: C, 65.93; H, 6.04. Found: C, 66.03; H, 6.05%.

4.6. (1*R*,2*R*)-1-Hydroxy-2-azido-1,2,3,4-tetrahydronaphthalene 7

Sodium azide (0.43 g, 6.6 mmol) was added to a solution of the mono-tosylate **6** (1.05 g, 3.3 mmol) in dry DMF (20 mL). The resulting suspension was heated at 120°C in a pre-heated oil bath for 2 h, diluted with

water (20 mL) and extracted with *n*-pentane (3×20 mL). The crude material (0.53 g) was purified by flash-chromatography (silica gel, eluting with petroleum ether:ethyl acetate 7:3) to afford the azido alcohol **7** (0.470 g, 2.5 mmol, 77%), accompanied by a small amount of α-tetralone (0.05 g, 0.37 mmol, 11%). Compound **7**: Colorless crystals; mp = 84–85°C (DCM-di-*iso*-propyl ether); $[\alpha]_D = +40.8$ ($c = 0.7$, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 1.91 (dddd, 1H, $J = 10.2$, 6.2, 5.2, 3.4 Hz, H-3), 2.21 (dddd, 1H, $J = 10.2$, 10.2, 6.2, 5.2 Hz, H-3′), 2.93 (m, 2H, H-4, H-4′), 3.72 (ddd, 1H, $J = 10.2$, 6.9, 3.4 Hz, H-2), 4.64 (d, 1H, $J = 6.9$ Hz, H-1), 7.10 (m, 1H, aromatic hydrogen), 7.25 (2H, aromatic hydrogens), 7.52 (m, 1H, aromatic hydrogen); ^{13}C NMR ($CDCl_3$): 25.5 (t), 27.2 (t), 64.3 (d), 72.4 (d), 126.7 (d), 127.6 (d), 127.9 (d), 128.4 (d), 137.2 (s), 139.5 (s); MS (EI) m/z: 189 (M^+), 143 ($M^+-N_2-H_2O$), 129 ($M^+-N_3-H_2O$). Calcd for $C_{10}H_{11}N_3O$: C, 63.49; H, 5.82; N, 22.22. Found C, 63.3; H, 5.67; N, 22.18%.

4.7. (1*R*,2*R*)-1-Hydroxy-2-amino-1,2,3,4-tetrahydronaphthalene 8

A solution of (1*R*,2*R*)-1-hydroxy-2-azido-1,2,3,4-tetrahydronaphthalene **7** (0.42 g, 2.2 mmol) in methanol (60 mL) was hydrogenated for 4 h in the presence of 10% palladium on charcoal (0.17 g). The suspension was filtered on a Celite pad and the solvent removed under reduced pressure to give the pure amino alcohol **8** (0.340 g, 2.1 mmol, 95%). Compound **8**: colorless crystals; mp = 112–113°C (ethyl acetate–petroleum ether); $[\alpha]_D = +75.36$ ($c = 0.276$, MeOH); ^1H NMR (CD_3OD): δ 1.7 (m, 1H, H-3), 2.03 (m, 1H, H-3′), 2.4 (m, 3H, H-2, H-4, H-4′), 4.33 (d, 1H, $J = 8.8$ Hz, H-1), 7.0–7.2 (3H, m, aromatic hydrogens), 7.5 (1H, m, aromatic hydrogen); ^{13}C NMR (CD_3OD): 28.7 (t), 29.5 (t), 55.3 (d), 75.8 (d), 127.1 (d), 129.2 (d), 128.5 (d), 129.3 (d), 137.2 (s), 139.5 (s); MS (EI) m/z: 163 (M^+), 145 (M^+-H_2O). Calcd for $C_{10}H_{13}NO$: C, 73.62; H, 7.98; N, 8.59. Found: C, 73.98; H, 7.90; N, 8.65%.

4.8. (1*S*,2*S*)-2-*p*-Toluenesulphonyloxy-1-azido-1,2,3,4-tetrahydronaphthalene 11

Tosyl chloride (0.425 g, 2.23 mmol) was added at 0°C to a magnetically stirred solution of (1*S*,2*S*)-2-hydroxy-1-azido-1,2,3,4-tetrahydronaphthalene **3** (0.215 g, 1.14 mmol) in dry pyridine (1.1 mL). The reaction was monitored by TLC (silica gel, eluting with petroleum ether:ethyl acetate 8:2). After about 18 h, the reaction mixture was diluted with ice-water and extracted with ethyl acetate (3×7 mL). The combined organic extracts were washed with 5% aqueous HCl till acidified and then with saturated NaCl solution till neutral. The organic phase was dried (Na_2SO_4) and the solvent removed under reduced pressure. The crude material was purified by flash-chromatography (silica gel, eluting with petroleum ether:ethyl acetate 9:1) to afford pure (1*R*,2*S*)-2-tosyl-1-azido-1,2,3,4-tetrahydronaphthalene **11** (0.274 g, 0.8 mmol, 70%). Compound **11**: Colorless crystals, mp = 92–94°C (ethyl acetate–petroleum ether); $[\alpha]_D = +18.1$ ($c = 1.19$, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 2.25 (dddd, 1H, $J = 14.0$, 7.0, 7.0, 7.0 Hz, H-3), 2.22 (dddd, 1H, $J = 14.0$, 8.5, 7.0, 3.5 Hz, H-3′), 2.45 (s, 3H), 2.82 (ddd, 1H, $J = 17.5$, 7.0, 7.0 Hz, H-4), 2.92 (ddd, 1H, $J = 17.5$, 8.5, 7.0 Hz, H-4′), 4.48 (d, 1H, $J = 6.3$ Hz, H-1), 4.75 (ddd, 1H, $J = 7.0$, 6.3, 3.5 Hz, H-2), 7.12 (dd, 1H, $J = 8.0$, 3.5 Hz, H-5 or H-8), 7.2–7.25 (m, 3H, H-8 or H-5, H-6, H-7), 7.35 (d, 2H, $J = 8.0$ Hz, H-3″, H-5″), 7.82 (d, 2H, $J = 8.0$ Hz, H-2″, H-6″); ^{13}C NMR ($CDCl_3$): δ 21.6 (q), 24.9 (t), 25.4 (t), 62.0 (d), 79.2 (d), 126.6 (d, 2C), 127.8 (d, 2C), 128.6 (d), 128.9 (d), 129.2 (d), 129.9 (d), 130.4 (s), 133.7 (s), 135.6 (s), 145.0 (s); MS (EI) m/z: 315 (M^+-N_2), 301 (M^+-N_3), 171 (M^+–TsOH), 155 (CH_3SO_2), 143 (171-N_2), 129 (171-N_3).

4.9. (1*S*,2*R*)–1,2-Diazido-1,2,3,4-tetrahydronaphthalene 12

Sodium azide (0.178 g, 2.74 mmol) was added to a solution of the ditosylate **11** (0.229 g, 0.667 mmol) in dry DMF (6 mL). The resulting suspension was heated at 120°C (using a pre-heated oil bath) and the reaction was monitored by thin-layer chromatography (silica gel, eluting with petroleum ether:ethyl acetate 95:5). After 8 h, the cooled reaction mixture was diluted with water (2 mL) and extracted with *n*-pentane (3×6 mL). The combined organic phases were dried (Na_2SO_4) and the solvent removed under reduced pressure to give, after purification on a small column of silica gel (eluting with *n*-pentane) pure (1*S*,2*R*)-1,2-diazido-1,2,3,4-tetrahydronaphthalene **12** (0.126 g, 0.59 mmol, 88%). Compound **12**: Colorless oil; $[\alpha]_D = +122.1$ ($c = 1.5$, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 2.18 (m, 2H, H-3, H-3′), 2.88 (ddd, 1H, $J = 16.1$, 10.4, 5.8 Hz, H-4), 3.09 (ddd, 1H, $J = 16.1$, 4.0, 5.8 Hz, H-4′), 3.8 (ddd, 1H, $J = 10.4$, 4.6, 2.3 Hz, H-2), 4.65 (d, 1H, $J = 2.3$ Hz, H-1), 7.1–7.4 (4H, aromatic hydrogens); ^{13}C NMR ($CDCl_3$): δ 22.8 (t), 27.4 (t), 59.7 (d), 62.6 (d), 126.6 (d), 129.1 (d), 129.3 (d), 129.6 (d), 131.7 (s), 135.4 (s); MS (EI) m/z: 186 (M^+-N_2), 157 (M^+-N-NH_3), 130 (M^+-2N_3).

4.10. (1*S*,2*R*)-1,2-Diamino-1,2,3,4-tetrahydronaphthalene 13

A solution of (1*S*,2*R*)-1,2-diazido-1,2,3,4-tetrahydronaphthalene **12** (0.149 g, 0.69 mmol) in methanol (20 mL) was hydrogenated for 4 h in the presence of 10% palladium on charcoal (0.17 g). The suspension was filtered on a Celite pad and the solvent removed under reduced pressure to give the pure diamine **13** in quantitative yield. Compound **13**: Colorless crystals, mp = 170–172°C (di-*iso*-propyl ether, *iso*-propyl alcohol); $[\alpha]_D = +33.47$ ($c = 0.49$, $CHCl_3$); ^1H NMR (PyD_5): δ 1.82 (m, 1H, H-3), 2.05 (m, 1H, H-3′), 2.85 (ddd, 1H, $J = 15.5$, 10.5, 5.3 Hz, H-4), 2.96 (ddd, 1H, 15.5, 7.0, 3.5 Hz, H-4′), 3.2 (ddd, 1H, 10.5, 3.5, 1.7 Hz, H-2), 4.05 (d, 1H, $J = 3.5$ Hz, H-1), 7.2 (4H, aromatic hydrogens); ^{13}C NMR (PyD_5): δ 27.1 (t), 28.5 (t), 51.6 (d), 54.1 (d), 126.5 (d), 127.3 (d), 129.3 (d), 1330.5 (d), 136.4 (s), 141.3 (s); MS (EI) m/z: 145 (M^+-NH_3), 119 (M^+-2NH_3). Calcd for $C_{10}H_{14}N_2$: C, 74.07; H, 8.64; N, 17.28. Found: C, 74.14; H, 8.90; N, 17.28%.

4.11. (2*R*,3*R*)-2-*p*-Toluenesulphonyloxy-3-hydroxy-1,2,3,4-tetrahydronaphthalene 14a

Tosyl chloride (0.152 g, 0.80 mmol) was added, at 0°C in 4 portions over 4 h to a stirred solution of diol **2** (0.096 g, 0.58 mmol) in dry pyridine (1.5 mL). The reaction was monitored by TLC (silica gel, eluting with *n*-hexane:ethyl acetate 7:3). After stirring for a further 2 h, the reaction mixture was diluted with ice-water and extracted with ethyl acetate (3×7 mL). The combined organic extracts were washed with 0.3N aqaueous HCl till acid pH and then with saturated NaCl solution till neutral pH. The organic phase was dried (Na_2SO_4) and the solvent removed under reduced pressure. The crude material was flash-chromatographed (silica gel, eluting with *n*-hexane:ethyl acetate 7:3) and afforded the mono-tosylate **14a** (0.108 g, 0.34 mmol, 58%), the ditosylate **15a** (0.044 g, 0.093 mmol, 16%) and unreacted diol **2** (0.016 g, 0.098 mmol, 17%). Compound **14a**: Colorless crystals, mp: 107–108°C; (ethyl acetate/*n*-hexane) $[\alpha]_D=-90.5°$ ($c=1.2$; $CHCl_3$); ^1H NMR ($CDCl_3$): δ 2.3 (1H, disappears with D_2O), 2.5 (s, 3H), 2.8 (dd, 1H, $J=16.3$, 8.4 Hz, H-4 or H-1), 3.0 (dd, 1H, $J=16.3$, 8.4 Hz, H-1 or H-4), 3.5 (dd, 1H, $J=16.3$, 6.1 Hz, H-1′ or H-4′), 3.51 (dd, 1H, $J=16.3$, 6.1 Hz, H-4′ or H-1′), 4.1 (ddd, 1H, $J=8.4$, 8.4, 6.1 Hz, H-3), 4.8 (ddd, 1H, 8.4, 8.4, 6.1 Hz, H-2), 7.05–7.15 (m, 4H, aromatic hydrogens), 7.6–7.7 (4H, aromatic hydrogens); ^{13}C NMR ($CDCl_3$): 21.67 (q), 33.98 (t), 35.60 (t), 68.70 (d), 82.20 (d), 126.51 (d), 126.72 (d), 2×127.88 (d), 128.58 (d), 128.81 (d), 129.97 (d), 2×131.96 (s), 132.78 (8s), 145.08 (s); MS (EI) *m*/*z*: 300 (M^+-H_2O), 172 (TsOH), 146 (M^+–TsOH), 128 (naphthalene). Calcd for $C_{17}H_{18}O_4S$: C, 64.15; H, 5.66. Found: C, 64.41; H, 5.63%.

4.12. (2*R*,3*R*)-2,3-Di-*p*-toluenesulphonyloxy-1,2,3,4-tetrahydronaphthalene 15a

Tosyl chloride (0.258 g, 1.35 mmol) was added, at 0°C to a stirred solution of diol **2** (0.096 g, 0.58 mmol) in dry pyridine (1.5 mL). The reaction was performed as described above and afforded the ditosylate **14a** in 80% yield, accompanied by a small amount of mono-tosylate **14a**. Compound **15a**: Colorless crystals; mp: 126.5–127.5°C (ethyl acetate/*n*-hexane); $[\alpha]_D=-42.5$ ($c=1.1$; $CHCl_3$); ^1H NMR ($CDCl_3$): δ 2.50 (s, 2×3H, 2×CH_3), 2.85 (ddd, 2H, $J=16.0$, 6.0 e 1.6 Hz, H-1, H-4), 3.30 (dd, 2H, $J=16.0$ e 4.5 Hz, H-1′, H-4′), 4.85 (m, 2H, H-2, H-3), 7.05–7.15 (4H, aromatic hydrogens), 7.50–7.55 (8H, aromatic hydrogens); ^{13}C NMR ($CDCl_3$): 2×21.7 (q), 2×32.1 (t), 2×75.5 (d), 2×126.8 (d), 2×128.8 (d), 2×130.8 (s), 2×133.3 (s), 2×145.1 (s); MS (EI) *m*/*z*: 300 (M^+–TsOH), 172 (TsOH), 128 (M^+–2TsOH). Calcd for $C_{24}H_{24}O_6S_2$: C, 61.00; H, 5.08. Found: C, 61.17; H, 5.08%.

4.13. (2*R*,3*R*)-2-Methanesulphonyloxy-3-hydroxy-1,2,3,4-tetrahydronaphthalene 14b

A solution of mesyl chloride (0.166 g, 1.46 mmol) in dry DCM (2 mL) was added dropwise to a solution of the diol **2** (0.190 g, 1.16 mmol) in DCM (3 mL) and dry pyridine (0.9 mL) over 3 h. The reaction was monitored by TLC (silica gel, eluting with *n*-hexane:ethyl acetate 7:3). After stirring the mixture for a further 1 h, ice-water was added and the resulting mixture extracted with ethyl acetate (3×7 mL). The combined organic extracts were washed with a 0.3N aqueous HCl until acidic and then with saturated NaCl solution till neutral pH was reached. The organic phase was dried (Na_2SO_4) and the solvent removed under reduced pressure. The crude material was flash-chromatographed (silica gel, eluting with *n*-hexane:ethyl acetate 1:1) and afforded the mono-mesylate **14b** (0.135 g, 0.56 mmol, 48%), the dimesylate **15b** (0.067 g, 0.21 mmol, 18%) and unreacted diol **2** (0.038 g, 0.23 mmol, 20%). Compound **14b**: Colorless crystals, mp, 103–104°C (ethyl acetate, *n*-hexane); $[\alpha]_D=-98.8$ ($c=0.7$, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 2.70 (1H, disappears with D_2O), 2.90 (dd, 1H, $J=16.4$, 9.0 Hz, H-4 or H-1), 3.05 (dd, 1H, $J=16.4$, 9.0 Hz, H-1 or H-4), 3.10 (s, 3H, CH_3), 3.25 (dd, 1H, $J=16.4$, 6.0 Hz, H-4′ or H-1′), 3.40 (dd, 1H, $J=16.4$, 6.0 Hz, H-1′ or H-4′), 4.15 (ddd, 1H, $J=9.0$, 9.0, 6.0 Hz, H-3), 4.85 (ddd, 1H, $J=9.0$, 9.0, 6.0 Hz, H-2), 7.05–7.15 (4H, aromatic hydrogens); ^{13}C NMR ($CDCl_3$): 34.7 (t), 36.2 (t), 38.5 (q), 68.8 (d), 82.2 (d), 126.6 (d), 126.8 (d), 128.6 (d), 128.8 (d), 132.0 (s), 132.8 (s); MS (EI), *m*/*z*: 242 (M^+), 224 (M^+-H_2O), 146 (M^+–MsOH). Calcd for $C_{11}H_{14}O_4S$: C, 54.54; H, 5.78. Found: C, 54.87; H, 5.83%

4.14. (2*R*,3*R*)-2,3-bis(methanesulphonyloxy)-1,2,3,4-tetrahydronaphthalene 15b

Mesyl chloride (0.556 g, 4.9 mmol) was added at 0°C to a solution of the diol **2** (0.200 g, 1.22 mmol) in dry pyridine (6 mL). The reaction was monitored by TLC (silica gel, eluting with *n*-hexane:ethyl acetate 7:3). After 1 h, the reaction mixture was diluted with ice-water (10 mL) and extracted with ethyl acetate (3×7 mL). The combined organic extracts were washed with 0.3N HCl till acid pH, then with saturated NaCl solution till neutral pH. The organic phase was dried (Na_2SO_4) and the solvent removed under reduced pressure to give dimesylate **15b** (0.380 g, 1.19 mmol, 98%). The product was purified by crystallization from ethyl acetate–*n*-hexane. Compound **15b**: Colorless crystals; mp: 111–112°C (ethyl acetate, *n*-hexane); $[\alpha]_D=-76.6$ ($c=0.38$; $CHCl_3$); ^1H NMR ($CDCl_3$): δ 3.10 (s, 2×3H, 2×CH_3), 3.15 (ddd, 2H, $J=16.0$, 6.0, 1.6 Hz, H-1, H-4), 3.45 (dd, 2H, $J=16.0$, 4.5 Hz, H-1′, H-4′), 5.05 (m, 2H, H-2, H-3), 7.05–7.15 (4H, aromatic hydrogens); ^{13}C NMR ($CDCl_3$): 2×33.97 (t), 2×38.66 (q), 2×76.89 (d), 2×127.09 (d), 2×128.70 (d), 2×131.18 (s); MS (EI), *m*/*z*: 321 (M^+–MsOH), 128. Calcd for $C_{12}H_{16}O_6S_2$: C, 45.00; H, 5.00. Found: C, 45.22; H, 4.95%.

4.15. Synthesis of (2*S*,3*S*)-2,3-diazido-1,2,3,4-tetrahydronaphthalene 19

With NaN_3 in DMF/H_2O: Sodium azide (0.132 g, 2.04 mmol) and urea (0.05 g) were added to a solution of dimesylate **15b** (0.220 g, 0.68 mmol) in DMF (4 mL) and water (0.2 mL). The resulting solution was heated at 110–120°C and the reaction was monitored by TLC

(silica gel, eluting with *n*-hexane:ethyl acetate 8:2). After 3 h the solution was diluted with water (10 mL) and extracted with *n*-pentane (3×15 mL) The combined organic extracts were washed with water (5 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure. The crude material was flash-chromatographed (silica gel, eluting with *n*-pentane) and afforded 0.036 g (25%) of the diazide **19**. Compound **19**: Colorless oil; $[\alpha]_D = +52.5$ ($c = 0.28$; $CHCl_3$); ^1H NMR ($CDCl_3$): δ 2.90 (ddd, 2H, $J = 16.5, 6.8, 2.2$ Hz, H-1, H-4), 3.30 (dd, 2H, $J = 16.5, 4.1$ Hz, H-1′, H-4′), 3.75 (m, 2H, H-2, H-3), 7.05–7.15 (4H, aromatic hydrogens); ^{13}C NMR ($CDCl_3$): 2×33.62 (t), 2×61.25 (d), 2×126.79 (d), 2×128.64 (d), 2×133.3 (s); MS (EI), *m*/*z*: 215 (M^++1), 187 (M^+−N2).

The same protocol, applied to the ditosylate **15a** afforded **19** in 20% yield.

With NaN_3 in DMF: Sodium azide (0.596 g, 9.17 mmol) was added to a solution of the dimesylate **15b** (0.734 g, 2.29 mmol) in dry DMF (10 mL). The resulting suspension was heated at 120°C (using a pre-heated oil bath) for 2 h, diluted with water (20 mL) and extracted with *n*-pentane (3×20 mL). The crude material was chromatographed (silica gel, eluting with *n*-hexane; ethyl acetate 8:2) and afforded **19** (0.134 g, 0.63 mmol, 28%) and naphthalene.

With NaN_3 under phase-transfer catalysis: A 3 M aqueous solution of sodium azide (2.4 mL, 7.2 mmol) and tetra *n*-hexylammonium bromide (0.02 g) were added to a solution of the dimesylate **15b** (0.18 g, 0.57 mmol) in toluene (3 mL). The resulting biphasic system was warmed at 70–80°C. The reaction was monitored by TLC (silica gel, eluting with *n*-hexane:ethyl acetate 8:2). The two phases were separated and the aqueous phase was extracted with ethyl acetate (3×15 mL). The combined organic phases were washed with a saturated solution of NaCl (5 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure. The crude material was chromatographed (silica gel, eluting with *n*-hexane:ethyl acetate 7:3) and afforded **19** (0.02 g, 0.09 mmol, 15%), 2-mesyloxy-3-azido-1,2,3,4-tetrahydronaphthalene (0.027 g, 0.10 mmol, 18%), and naphthalene.

4.16. (2*R*,3*S*)-2-Mesyloxy-3-azido-1,2,3,4-tetrahydronaphthalene

Colorless crystals, mp: 104–105°C (ethyl acetate/*n*-hexane); $[\alpha]_D = +11.2$ ($c = 0.65$; $CHCl_3$); ^1H NMR ($CDCl_3$): δ 3.10 (s, 3H, CH_3), 3.12–3.15 (3H, m, H-1, H-4, H-4′), 3.35 (dd, 1H, $J = 16.0, 6.0$ Hz, H-1′), 4.15 (m, 1H, H-3), 5.20 (m, 1H, H-2), 7.05–7.15 (4H, aromatic hydrogens); ^{13}C NMR ($CDCl_3$): 31.31 (t), 33.16 (t), 38.80 (q), 58.59 (d), 77.51 (d), 2×126.93 (d), 128.94 (d), 129.09 (d), 131.22 (s), 131.01 (s); MS (FAB^+), *m*/*z*: 268 (M^++1), 240 (M^+-N_2), 144 (M^+-N_2_MsOH). Calcd for $C_{11}H_{13}N_3O_3S$: C, 49.44; H, 4.87. Found: C, 49.19; H, 4.80%

With tetrabutyl ammonium azide: A solution of tetrabutyl ammonium azide[6] (2.1 g, 7.4 mmol) in toluene (20 mL) was distilled under azeotropic removal of water and the volume reduced to approximately one third. The solution was cooled to room temperature for the addition of the dimesylate **15b** (0.190 g, 0.60 mmol), and then warmed at 60–65°C for about 8 h. The solution was diluted with water (5 mL) and extracted with ethyl acetate (3×10 mL). The combined organic extracts were dried (Na_2SO_4) and the solvent removed under reduced pressure. The crude material (0.322 g) was chromatographed (silica gel, eluting with *n*-hexane:ethyl acetate 66:1) and afforded the diazide **19** (0.070 g, 0.33 mmol, 55%).

4.17. (2*R*,3*S*)-2-Hydroxy-3-azido-1,2,3,4-tetrahydronaphthalene 16

With NaN_3 in DMF: Sodium azide (0.190 g, 2.90 mmol) was added to a solution of the mono-mesylate **14b** (0.350 g, 1.47 mmol) in dry DMF (10 mL). The resulting suspension was heated at 120°C in a pre-heated oil bath for 3 h, diluted with water (20 mL) and extracted with *n*-pentane (3×20 mL). The crude material (0.220 g) was purified by flash-chromatography (silica gel, eluting with *n*-hexane:ethyl acetate 8:2) and afforded the *cis*-azido alcohol **16** (0.153 g, 0.81 mmol, 55%), the *meso*-epoxide **12** (0.024 g, 0.16 mmol, 11%) and the racemic *trans*-azido alcohol **18** (0.017 g, 0.088 mmol, 6%).

Compound **16**: Colorless crystals, mp: 53–54°C (ethyl acetate, *n*-hexane); $[\alpha]_D = +46.4$ ($c = 0.42$ $CHCl_3$); ^1H NMR ($CDCl_3$): δ 3.00 (1H, dd, $J = 15.0, 6.5$ Hz, H-1), 3.05 (1H, dd, $J = 15.0, 4.5$ Hz, H-1′), 3.24 (1H, dd, $J = 15.0, 5.5$ Hz, H-4), 3.33 (1H, dd, $J = 15.0, 4.5$ Hz, H-4′), 3.90 (1H, disappears with D_2O), 3.95 (ddd, 1H, $J = 6.5, 4.5, 2.5$ Hz, H-3), 4.23 (ddd, 1H, $J = 5.5, 4.5, 2.5$ Hz, H-2) 7.05–7.15 (4H, aromatic hydrogens); ^{13}C NMR ($CDCl_3$): 31.03 (t), 34.90 (t), 61.11 (d), 68.17 (d), 126.39 (d), 126.55 (d), 128.86 (d), 129.36 (d), 131.98 (s), 132.62 (s); MS (EI), *m*/*z*: 189 (M^+), 171 (M^+-H_2O), 143 ($M^+-H_2O-N_2$), 129 ($M^+-H_2O-N_3$). Calcd for $C_{10}H_{11}N_3O$: C, 63.49; H, 5.82. Found: C, 63.54; H, 5.85%.

Compound **18**: Colorless solid, mp: 69–70°C (ethyl acetate/*n*-hexane); ^1H NMR ($CDCl_3$): δ 2.3 (s, 1H, disappears with D_2O), 2.85 (dd, 1H, $J = 17.0, 9.4$ Hz, H-4), 2.90 (dd, 1H, $J = 17.0, 9.4$ Hz, H-1), 3.21 (dd, 1H, $J = 17.0, 5.0$ Hz, H-1′), 3.23 (dd, 1H, $J = 17.0, 5.0$ Hz, H-4′), 3.70 (ddd, 1H, $J = 9.4, 9.4, 5.0$ Hz, H-3), 3.92 (ddd, 1H, $J = 9.4, 9.4, 5.0$ Hz, H-2), 7.05–7.15 (4H, aromatic hydrogens); ^{13}C NMR ($CDCl_3$): 33.61 (t), 36.48 (t), 63.69 (d), 70.48 (d), 126.47 (d), 126.65 (d), 128.65 (d), 128.84 (d); MS (EI) *m*/*z*: 189 (M^+), 171 (M^+-H_2O), 161 (M^+-N_2).

With polymeric quaternary ammonium azide: Amberlite IR-400 was washed with 20% sodium azide solution, then with water, methanol, and chloroform. The poly-

mer was dried at room temperature in vacuum. The mono-mesylate **14b** (0.150 g, 0.63 mmol) was added to the polymer (2.967 g) in dry acetonitrile (4.5 mL). The reaction mixture was heated at 50–60°C for 4 h. The polymer was removed by filtration and the filtrate was concentrated under reduced pressure. The crude material was purified by flash-chromatography (silica gel, eluting with *n*-hexane:ethyl acetate 8:2) to afford *cis*-azido alcohol **16** (36%), the epoxide **17** (20%), *trans*-azido alcohol **18** (10%).

4.18. (2*R*,3*S*)-2-Hydroxy-3-amino-1,2,3,4-tetrahydronaphthalene 20

A solution of 2-hydroxy-3-azido-1,2,3,4-tetrahydronaphthalene **16** (0.120 g, 0.63 mmol) in methanol (10 mL) was hydrogenated for 3 h in the presence of 10% palladium on charcoal (0.50 g). The suspension was filtered on a Celite pad and the solvent removed under reduced pressure to give pure 2-hydroxy-3-amino-1,2,3,4-tetrahydronaphthalene **20** in quantitative yield as colorless crystals (ethyl acetate/*n*-hexane), mp; 118.5–119°C; $[\alpha]_D = 10.1$ ($c = 0.74$; MeOH); ^{1}H NMR ($C_6D_5N+D_2O$): δ 3.03–3.3 (4H, H-1, H-1′, H-4, H-4′), 3.40 (m, 1H, H-3), 4.50 (m, 1H, H-2), 7.05–7.15 (4H, aromatic hydrogens); ^{13}C NMR (C_5D_5N): 31.38 (d), 35.40 (t), 36.38 (t), 69.42 (d), 2×126.19 (d), 128.46 (d), 129.69 (d), 134.94 (s), 135.63 (s); MS (EI), m/z: 163 (M^+), 145 (M^+-H_2O). Calcd for $C_{10}H_{13}NO$: C, 73.62; H, 7.98. Found: C, 73.50; H, 7.94%.

4.19. (2*S*,3*S*)-2,3-Diamino-1,2,3,4-tetrahydronaphthalene 21

A solution of 2,3-diazido-1,2,3,4-tetrahydronaphthalene **19** (0.195 g, 0.9 mmol) in methanol (10 mL) was hydrogenated for 8 h in the presence of 10% palladium on charcoal (0.150 g). The suspension was filtered on a Celite pad and the solvent removed under reduced pressure to give pure (2*S*,3*S*)-2,3-diamino-1,2,3,4-tetrahydronaphthalene **21** in quantitative yield (0.147 g, 0.9 mmol) which was converted to the corresponding dihydrochloride. Compound **21**: Colorless solid; mp = 180°C (ethyl acetate–di-*iso*-propyl ether); $[\alpha]_D = +53.4$ ($c = 7.53$ mg/mL; MeOH); ^{1}H NMR (C_5D_5N): δ 2.70 (2H, m, H-1, H-4), 2.90 (2H, H-1′, H-4′), 3.20 (2H, H-2, H-3), 3.30 (disappears with D_2O), 7.05–7.15 (4H, aromatic hydrogens); ^{13}C NMR (C_5D_5N): δ 2×35.44 (t), 2×62.27 (d), 2×127.47 (d), 2×130.80 (d), 2×132.55 (s); MS (EI) m/z: 162 (M^+), 145 (M^+-NH_3). Calcd for $C_{10}H_{14}N_2$: C, 74.07; H, 8.64; N, 17.28. Found: C, 74.18; H, 8.94; N, 17.38%.

Dihydrochloride 21: Colorless solid; mp >250°C (Chloroform, methanol), $[\alpha]_D = +18.3$ ($c = 0.3$; MeOH); ^{1}H NMR (CD_3OD): δ 3.05 (ddd, 2H, $J = 17.5$, 6.0, 1.5 Hz, H-1, H-4), 3.35 (dd, 2H, $J = 17.5$, 4.5 Hz, H-1′, H-4′), 3.90 (m, 2H, H-2, H-3), 7.20–7.30 (4H, aromatic hydrogens); ^{13}C NMR (CD_3OD): 2×31.43 (t), 2×49.35 (d), 2×128.37 (d), 2×130.06 (d), 2×131.91 (s); MS (EI) m/z: 162 (M^+-2 HCl), 145 ($M^+-2HCl-NH_3$).

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