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The Williamson Reaction: A New and Efficient Method for the Alternate Resolution of 2,2′-Bis(bromomethyl)-1,1′-binaphthyl and 1,1′-Binaphthalene-2,2′-diol

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Treatment of 2,2′-bis(bromomethyl)-1,1′-binaphthyl [(*R*,*S*)-**2**] with 1,1′-binaphthalene-2,2′-diol (+)-(*R*)-**1** and cesium or potassium carbonate in refluxing acetone, gave the diastereoisomeric dioxacyclophanes (−)-(*R*,*S*)-**3a** and (+)-(*R*,*R*)-**3b**, both obtained in high yield, and the cyclic tetraether (+)-(*R*,*R*,*R*,*S*)-**4** as isolated side product. Boron tribomide-promoted ether cleavage of **3a** and **3b** gave optically pure (−)-(*S*)-**2** and (+)-(*R*)-**2**, respectively, and the recovered diol (+)-(*R*)-**1**. Alternatively, the same reaction sequence furnished the resolved diols (−)-(*S*)-**1** and (+)-(*R*)-**1** from (*R*,*S*)-**1** and (+)-(*R*)-**2**, as well as optically pure 2,2′-bis(chloromethyl)-1,1′-binaphthyl (+)-(*R*)-**5** from the racemic dibromide (*R*,*S*)-**2** by using boron trichloride for ether cleavage.

Chiral 1,1′-binaphthyl derivatives with C_2-symmetry have been used in a wide range of successful stereodifferentiating reactions.[1] Two main precursors of such compounds are 1,1′-binaphthalene-2,2′-diol (**1**), readily available by resolution,[2] and 2,2′-bis(bromomethyl)-1,1′-binaphthyl (**2**) from which series of chiral auxiliaries such as binaphthylcyclopentadienyl ligands,[3] [NAPHOS(1,1′)],[4] 3,5-dihydro-4*H*-dinaphth[2,1-*c*:1′,2′-*e*]azepine,[5,6] binaphthylic α-amino nitriles,[6] diamines,[7] quaternary ammonium salts,[8] and phosphorus-containing amine ligands[9] have been synthesized. Although enantioselective synthesis of parent derivatives 2,2′-dimethyl-1,1′-binaphthyl[10] and 2,2′-bis(hydroxymethyl)-1,1′-binaphthyl[11] have been reported, only a few methods for resolution of the readily available[12] racemic dibromide (*R*,*S*)-**2** have been examined: optically pure (*R*)-**2** and/or (*S*)-**2** can be obtained by direct crystallization of (*R*,*S*)-**2** as conglomerate,[13] or from resolved 1,1′-binaphthalene-2,2′-dicarboxylic acid,[14] or by our previously proposed procedure involving separation of the diastereoisomeric quaternary ammonium salts resulting from N-alkylation of *l*-ephedrine by (*R*,*S*)-**2**.[12] In the present paper, we report the investigation of the tandem Williamson synthesis/ether cleavage reaction applied to reagents **1** and **2**, which constitutes another route for an efficient resolution of all the enantiomers of both compounds.

Preliminary experiments showed that reaction of (*R*,*S*)-**1** with (*R*,*S*)-**2**, in the presence of K_2CO_3 or Cs_2CO_3 in refluxing acetone, gave a mixture of the cyclic diastereoisomeric diethers (*R**,*S**)-**3a** and (*R**,*R**)-**3b**, which could be separated by crystallization with good yields.[15] The possibility of asymmetric synthesis of **3a**/**3b** by consecutive kinetic resolutions of (*R*,*S*)-**1** then (*R*,*S*)-**2** was also examined, using liquid phase transfer conditions with benzyl quininium chloride as catalyst. However, although the mixed sodium and benzyl quininium disalt of the diol **1** was quantitatively transferred in the organic phase, the enantioselection was poor (*ca.* 5% ee in favor of the (+)-(*R*)-**1** enantiomer). Furthermore, a poor diastereoselection (6−22% de) was also observed in the Williamson cyclization reaction under various experimental conditions.[15] According to these results, resolution of the dibromide **2** using optically pure (+)-(*R*)-**1** as resolving agent was attempted.

When the racemic dibromide (*R*,*S*)-**2**[12] was treated with an equimolar amount of diol (+)-(*R*)-**1**, the cyclic diethers (−)-(*R*,*S*)-**3a** and (+)-(*R*,*R*)-**3b** as well as the cyclic tetraether (+)-(*R*,*R*,*R*,*S*)-**4** present as major side product, were obtained (Scheme 1). The absolute configurations of **3a**, **3b**, and **4** were established or confirmed by the recovery of the dibromides (−)-(*S*)-**2** from **3a**, (+)-(*R*)-**2** from **3b**, and (*R*,*S*)-**2** from **4** after ether cleavage (*vide infra*). The ratio of the two diastereoisomers **3a** and **3b** was determined as *ca.* 1:1 by integration of their distinct $ArCH_2O$ signals in ^1H NMR. Crystallization of the crude

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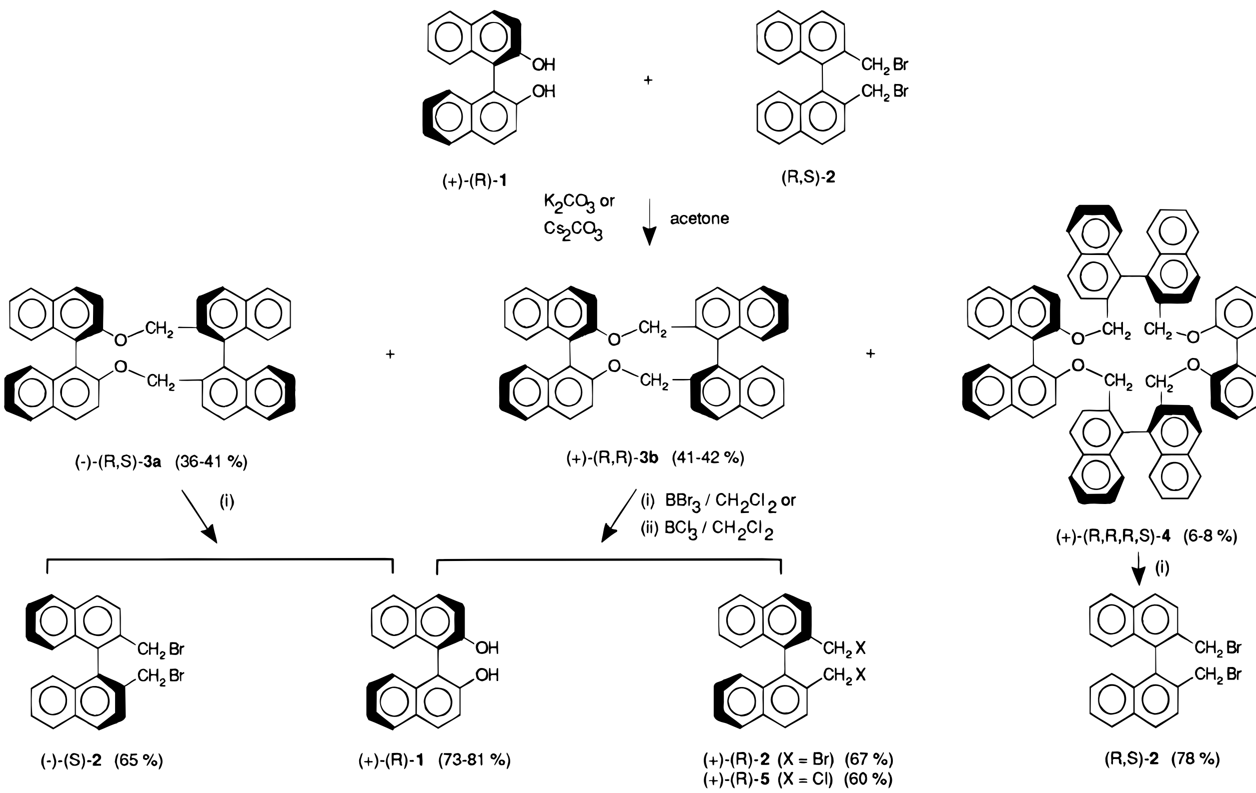
Scheme 1



product from benzene[16] gave analytically pure (−)-(*R*,*S*)-**3a** with 72.2% yield.[17] The other diastereoisomer (+)-(*R*,*R*)-**3b** could not be purified by crystallization and was obtained with 83.6% yield[17] after repeated chromatography of the mother liquor, which allowed its separation from the cyclic tetraether (+)-(*R*,*R*,*R*,*S*)-**4** (6% yield). A duplicate experiment gave 82.2% (−)-(*R*,*S*)-**3a**, 81.7% (+)-(*R*,*R*)-**3b** and 8.1% (+)-(*R*,*R*,*R*,*S*)-**4**. Altogether, the *isolated analytically pure samples* of **3a**, **3b**, and **4** in the two runs represented 84% and 90% overall yield, respectively. The quasiexclusive formation of the cyclic diethers **3a** and **3b** in a 1:1 ratio recorded in the present reaction is a surprise when compared with the recent results of Itoh *et al.*[18] concerning the closely related optical resolution of axially chiral biaryl compounds using a sugar template: typically, in the reaction of 1,1′-binaphthyl-2,2′-dicarbonyl chloride with methyl 4,6-*O*-benzylidene-α-D-glucopyranoside, intramolecular ester cyclization proceeded with excellent diastereoselectivity, furnishing a single (*R*,D) cyclic diester with 70%[17] theoretical yield. Thus, chiral recognition involving biaryl compounds appears to be far lower for intramolecular ether cyclization than for intramolecular ester cyclization.

Treatment of (−)-(*R*,*S*)-**3a** with boron tribromide in dichloromethane gave the recovered diol (+)-(*R*)-**1** with 73% yield after just extraction, and the dibromide (−)-(*S*)-**2** which was easily purified by chromatography. (−)-(*S*)-**2** was obtained optically pure with 65% yield after crystallization from methyl ethyl ketone. The same treatment applied to (+)-(*R*,*R*)-**3b** gave recovered (+)-(*R*)-**1** with 81% yield (crude) and optically pure (+)-(*R*)-**2** with 66.6% yield after crystallization. In the same manner, (+)-(*R*,*R*,*R*,*S*)-**4** gave racemic (*R*,*S*)-**2** with 78% yield. Altogether, the overall yields for the ether cyclization/ether cleavage process were 47−53%[17] for (−)-(*S*)-**2**, 54−57%[17] for (+)-(*R*)-**2**, and 57−60% (crude) for the recovered (+)-(*R*)-**1**. Therefore, as far as resolution of 2,2′-bis (bromomethyl)-1,1′-binaphthyl [(*R*,*S*)-**2**] is concerned, the present method advantageously competes with the previously described procedures, including ours[12] in which the overall yield of resolved (+)-(*R*)-**2** and (−)-(*S*)-**2** was 21%[17] and 29%,[17] respectively.

The same reaction sequence was used for resolution of the diol (*R*,*S*)-**1** which was reacted with a sample of optically pure dibromide (+)-(*R*)-**2**. The resulting diethers (+)-(*S*,*R*)-**3a** (99%)[17] and (+)-(*R*,*R*)-**3b** (99%)[17] were treated with BBr_3 to give optically pure (−)-(*S*)-**1** (64%) and (+)-(*R*)-**1** (70%), respectively, as well as recovered (+)-(*R*)-**2** (70%).

The present resolution method also allowed a two steps synthesis of optically pure 2,2′-bis(chloromethyl)-1,1′-binaphthyl (**5**) from the racemic dibromide (*R*,*S*)-**2**, since the cyclic ether (*R*,*R*)-**3b**, when treated with boron trichloride instead of boron tribromide, gave (+)-(*R*)-**5** with 60% yield. Optically pure (+)-(*R*)-**5** has been recently prepared from (+)-(*R*)-**2** by halogen exchange.[19]

In conclusion, several interesting features appear from the present study: (i) the high yield of cyclic diethers **3a** and **3b** resulting from the Williamson ether synthesis applied to 1,1′-binaphthalene-2,2′-diol **1** and 2,2′-bis-(bromomethyl)-1,1′-binaphthyl **2**. Such cyclic diethers are interesting reagents by themselves as new potential C_2-symmetric chiral auxiliaries;[20] (ii) the availability of

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[16] The compound **3a** has an excellent crystallinity in benzene. Attempts to use toluene or chloroform as crystallization solvent instead of hazardous benzene led to lower yields of crystals.

[17] Theoretical yield (50% of the starting racemic compound).

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both optically pure enantiomers (−)-(*S*)-**2** and (+)-(*R*)-**2** in one step from **3a** or **3b**, with the need of only one enantiomer of the resolving agent (−)-(*S*)-**1** or (+)-(*R*)-**1**; (iii) the recovery of the resolving agent; (iv) the opportunity of alternate resolution of both the diol **1** and the dibromide **2**; (v) the direct availability of both enantiomers of the dichloride **5** from the racemic dibromide **2**. This new method, which has only limited interest concerning the diol **1**, advantageously competes for the number of steps and the overall yield, with the previously described resolution procedures of the dibromide **2**.

Experimental Section

1,1′-Binaphthalene-2,2′-diols (*R*,*S*)-**1** and (+)-(*R*)-**1** were purchased from Aldrich. Racemic 2,2′-bis(bromomethyl)-1,1′-binaphthyl [(*R*,*S*)-**2**] was prepared as previously described.[12] Optical rotations were measured with an accuracy of 0.3%, in a 1 dm thermostated cell. Analytical thin layer chromatography (TLC) and preparative column chromatography were performed on Kieselgel F 254 and on Kieselgel 60 (0.040−0.063 mm) (Merck), respectively, with the following eluent systems: 75% petroleum ether (40−60 °C)−25% ethyl acetate (I), 90% petroleum ether−5% ethyl acetate−5 % toluene (II), 50% petroleum ether−50% toluene (III).

Preparation of the Cyclic Diethers (−)-(*R*,*S*)-3a and (+)-(*R*,*R*)-3b and of the Cyclic Tetraether (+)-(*R*,*R*,*R*,*S*)-4. A mixture of optically pure (+)-(*R*)-**1** {$[\alpha]^{25}_{546}$ = +50.1° (*c* 1; THF)[2b] (0.715 g, 2.5 mmol)}, (*R*,*S*)-**2** (1.100 g, 2.5 mmol), and K_2CO_3 (3.5 g) in acetone (500 mL) was stirred and refluxed under argon for 24 h. After evaporation of acetone *in vacuo*, the residue was solubilized in water (500 mL)/CH_2Cl_2 (500 mL). The decanted organic phase was extracted with two portions of 100 mL of aqueous 10% NaOH, 200 mL of aqueous 2N HCl, and 400 mL of H_2O, dried over $MgSO_4$, filtered, and evaporated *in vacuo*. The crude product was dissolved in CH_2Cl_2 (50 mL), and benzene (50 mL) was added (*caution:* all operations involving benzene were conducted in a well ventilated hood). The resulting solution was heated at 80 °C and concentrated to *ca.* 10 mL. Crystallization occurred during this process. The mixture was left in a refrigerator overnight, and the crystals were filtered, washed with cold benzene, and air-dried to give (−)-(*R*,*S*)-**3a** as white shiny crystals: 0.586 g (83%),[17] mp = 335−345 °C, $[\alpha]^{25}_{546}$ = −209.1° (*c* 0.5; $CHCl_3$). In a second identical run, except that Cs_2CO_3 (8.1 g) was used instead of K_2CO_3, 0.707 g (100%)[17] of crystalline (−)-(*R*,*S*)-**3a** {$[\alpha]^{25}_{546}$ = −210.3° (*c* 0.5; $CHCl_3$)} was obtained as the first crop. A second crystallization of the combined crystals from the two runs led to only a slight increase of the optical rotation (dissolution of the crystals in chloroform was now difficult) of the obtained analytically pure (−)-(*R*,*S*)-**3a**: 1.075 g (76.2%),[17] mp = 345−350 °C (dec at solid state from *ca.* 300 °C). R_f = 0.51 (I), 0.13 (III). ^{1}H NMR ($CDCl_3$) δ 8.1−6.8 (m), 24 H; 5.20 (d, 13.6 Hz) and 4.86 (d, 13.6 Hz), 4 H. ^{1}H NMR (DMSO-d_6) δ 5.58 (d, 12.9 Hz) and 4.60 (d, 13.0 Hz), 4 H. ^{13}C NMR ($CDCl_3$) δ 152.52−118.60; 68.81. ^{13}C NMR (DMSO-d_6) δ 152.12−117.28; 66.89. $[\alpha]^{25}_{578}$ = −199.4°, $[\alpha]^{25}_{546}$ = −226.8°, $[\alpha]^{25}_{436}$ = −339.8°, $[\alpha]^{25}_{365}$ = +491.6° (*c* 0.5; $CHCl_3$). Anal. Calcd for $C_{42}H_{28}O_2$: C, 89.33; H, 5.00; O, 5.67. Found: C, 88.76; H, 5.28; O, 5.02. EI^+ MS *m/z* (relative intensity): 564 (M^+) (100); 279 (60); 266 (86). The combined mother liquors from the first crops of the two runs were evaporated, and the residue was chromatographed on a 3 × 60 cm column of silica gel with eluent (II), to give 0.464 g of chromatographically pure (+)-(*R*,*R*)-**3b** and 0.966 g of a fraction in which **3b** was accompanied by a small proportion of the cyclic tetraether **4** of close R_f. Attempts for further purification of **3b** by crystallization in various solvents failed, as even the pure sample crystallized as an amorphous powder. Flash-chromatography of the less pure fraction on a 2.3 × 68 cm column of silica gel with eluent (III) gave 0.715 g more of analytically pure (+)-(*R*,*R*)-**3b**: total 1.179 g (83.6%),[17] white solid, mp = 185−190 °C. R_f = 0.59 (I), 0.23 (III). ^{1}H NMR ($CDCl_3$) δ 7.9−6.9 (m), 24 H; 5.14 (d, 9.0 Hz) and 4.35 (d, 9.0 Hz), 4 H. ^{13}C NMR ($CDCl_3$) δ 152.27−115.15; 70.65. $[\alpha]^{25}_{578}$ = +707.6°, $[\alpha]^{25}_{546}$ = +842.3°, $[\alpha]^{25}_{436}$ = +1912.2°, $[\alpha]^{25}_{365}$ = +5706.3° (*c* 0.5; $CHCl_3$). Anal. Calcd for $C_{42}H_{28}O_2$: C, 89.33; H, 5.00; O, 5.67. Found: C, 88.61; H, 5.05; O, 5.25. EI^+ MS *m/z* (relative intensity): 564 (M^+) (100); 279 (43); 266 (43), and pure (+)-(*R*,*R*,*R*,*S*)-**4**: 0.173 g (6.1%), white solid, mp = 220−225 °C. R_f = 0.54 (I), 0.16 (III). ^{1}H NMR ($CDCl_3$) δ 8.2−6.3 (m), 48 H; 4.76 (d, 14.0 Hz) and 4.71 (d, 14.0 Hz), 4 H; 4.40 (d, 15.0 Hz) and 4.16 (d, 15.0 Hz), 4 H. ^{13}C NMR ($CDCl_3$) δ 154.95−113.32; 69.74; 67.71. $[\alpha]^{25}_{578}$ = +37.7°, $[\alpha]^{25}_{546}$ = +48.5°, $[\alpha]^{25}_{436}$ = +144.4° (*c* 0.5; $CHCl_3$). Anal. Calcd for $C_{84}H_{56}O_4$: C, 89.33; H, 5.00; O, 5.67. Found: C, 88.49; H, 5.13; O, 5.79. FAB^+ MS (mNBA matrix/CH_2Cl_2) *m/z* (relative intensity): 1128 (M^+) (4.7); 843 (10.3); 564 (13.8); 279 (100).

In a duplicate experiment, reaction of (+)-(*R*)-**1** prepared by resolution,[2e] {$[\alpha]^{25}_{546}$ = +49.5° (*c* 1; THF) (2.964 g, 10.3 mmol)}, (*R*,*S*)-**2** (4.550 g, 10.3 mmol), and Cs_2CO_3 (10.5 g) in refluxing acetone (1 l) for 16 h, followed by the same treatment as above, gave (−)-(*R*,*S*)-**3a** {2.393 g (82.2%)[17] after two crystallizations, $[\alpha]^{25}_{546}$ = −206.2° (*c* 0.5; $CHCl_3$)}, (+)-(*R*,*R*)-**3b** {2.378 g (81.7%),[17] $[\alpha]^{25}_{546}$ = +858.0° (*c* 0.5; $CHCl_3$)}, and (+)-(*R*,*R*,*R*,*S*)-**4** {0.471 g (8.1%), $[\alpha]^{25}_{546}$ = +48.5° (*c* 0.5; $CHCl_3$)}.

In the same manner, racemic (*R*,*S*)-**1** (0.143 g, 0.5 mmol) was reacted with a sample of optically pure (+)-(*R*)-**2** (0.220 g, 0.5 mmol) and Cs_2CO_3 (1.6 g) in refluxing acetone (100 mL) for 15 h. After workup, two consecutive crystallizations from benzene as above yielded (+)-(*S*,*R*)-**3a** {0.139 g (98.9%),[17] $[\alpha]^{25}_{546}$ = +218.7° (*c* 0.5; $CHCl_3$)}. Flash-chromatography of the mother liquor from the first crop on a 1.5 × 41 cm column of silica gel with eluent (III) yielded pure (+)-(*R*,*R*)-**3b** {0.140 g (99.3%),[17] $[\alpha]^{25}_{546}$ = +790.3° (*c* 0.5; $CHCl_3$)}.

Cleavage of the Cyclic Polyethers 3a, 3b, and 4 by BBr_3 or BCl_3. The diether (−)-(*R*,*S*)-**3a** (0.564 g, 1 mmol) obtained from (+)-(*R*)-**1** and (*R*,*S*)-**2** was dissolved in CH_2Cl_2 (50 mL). The solution was cooled to 0 °C, and a solution of BBr_3 (1 M) in CH_2Cl_2 (10 mL) was added by syringe under an argon stream. The resulting solution was stirred under argon atmosphere at 0 °C to room temperature for 1 h and then quenched with aqueous 10% NaOH. The separated organic layer was extracted with aqueous 10% NaOH, washed with water, dried over $MgSO_4$, filtered, and evaporated *in vacuo*. The obtained extract (0.406 g) was chromatographed on a 2.3 × 62 cm column of silica gel with CH_2Cl_2 as eluent, to give 0.324 g (73.6%) of chromatographically pure (−)-(*S*)-**2** [R_f = 0.73 (I), 0.83 (CH_2Cl_2)] and 0.048 g of a fraction presenting a single spot [R_f = 0.43 (I), 0.72 (CH_2Cl_2)] but corresponding to a mixture of several compounds resulting from C-alkylation of binaphthol. The sample of pure dibromide was dissolved in boiling methyl ethyl ketone and the solution concentrated to *ca.* 1.5 mL. Crystallization occurred from the boiling solution. The mixture was left in a refrigerator overnight, and the crystals were filtered, washed with cold methyl ethyl ketone, and air-dried to give 0.240 g (54.5%) optically pure (−)-(*S*)-**2**, pale yellow crystals; mp = 185.3 °C (3 °C/min), $[\alpha]^{23}_{578}$ = −170.2°, $[\alpha]^{23}_{546}$ = −199.8°, $[\alpha]^{23}_{436}$ = −418.3°, $[\alpha]^{23}_{365}$ = −1046.8° (*c* 1; benzene), ≈100% optical purity, lit.[14] mp = 185.5−186.5 °C, $[\alpha]^{23}_{578}$ = −169.4°, $[\alpha]^{23}_{546}$ = −199.8 (*c* 1; benzene), lit.[12] mp = 182−184 °C, $[\alpha]^{23}_{578}$ = −169.8°/+171.1°, $[\alpha]^{23}_{546}$ = −198.6°/+200.2°, $[\alpha]^{23}_{436}$ = −415.2°/+420.3° (*c* 1; benzene). A second crop of crystals was obtained from the mother liquor: yield 0.046 g (10.5%), $[\alpha]^{23}_{546}$ = −200.5° (*c* 1; benzene). The combined initial aqueous 10% NaOH phase (*ca.* 150 mL) was extracted twice with CH_2Cl_2, filtered on glass wool, and acidified with a large excess of concentrated aqueous HCl. The resulting milky solution was extracted twice with CH_2Cl_2, and the combined organic phase was washed with water, dried, filtered, and evaporated. The obtained extract presented a single spot of R_f = 0.33 (I) and was pure by ^{1}H NMR, showing the exclusive extraction of the diol (+)-(*R*)-**1**: yield 0.208 g (72.7%), white/pale yellow crystalline powder, mp (crude) = 210.1 °C (3 °C/min), $[\alpha]^{25}_{578}$ = +36.2°, $[\alpha]^{25}_{546}$ = +49.1°, $[\alpha]^{25}_{436}$ = +220.0°, $[\alpha]^{25}_{365}$ = +1356° (*c* 0.9; THF), ≈100% optical purity, lit.[2b] mp = 207.5−208.5 °C, $[\alpha]^{25}_{578}$ = −37.8°, $[\alpha]^{25}_{546}$ = +50.9°/-51.3°, $[\alpha]^{25}_{436}$ = −228° (*c* 1; THF).

The diether (+)-(*R*,*R*)-**3b** (0.564 g, 1 mmol), obtained from (+)-(*R*)-**1** and (*R*,*S*)-**2**, gave recovered (+)-(*R*)-**1** {yield 0.232 g (81.1%), mp (crude) = 209.2 °C (3 °C/min), $[\alpha]^{25}_{578}$ = +36.2°, $[\alpha]^{25}_{546}$ = +49.3°, $[\alpha]^{25}_{436}$ = +220.0°, $[\alpha]^{25}_{365}$ = +1342° (*c* 1; THF), ≈100% optical purity},[2b] and resolved (+)-(*R*)-**2** {yield 0.349 g (79.3%) after chromatography and 0.293 g (66.6%) after crystallization: first crop, 0.240 g, mp = 185.9 °C (3 °C/min), $[\alpha]^{23}_{578}$ = +170.4°, $[\alpha]^{23}_{546}$ = +199.4°, $[\alpha]^{23}_{436}$ = +417.2°, $[\alpha]^{23}_{365}$ = +1039.2° (*c* 1; benzene), ≈100% optical purity,[12,14] second crop, 0.053 g, mp = 184.4 °C (3 °C / min), $[\alpha]^{23}_{546}$ = +197.8° (*c* 1; benzene)}.

The tetraether (+)-(*R*,*R*,*R*,*S*)-**4** (0.115 g, 0.1 mmol) obtained from (+)-(*R*)-**1** and (*R*,*S*)-**2**, gave pure (*R*,*S*)-**2**: yield 0.070 g (78%) after chromatography, $[\alpha]^{23}_{578, 546, 436, 365}$ = 0 °C (*c* 1; benzene).

In the same manner, the diethers (+)-(*S*,*R*)-**3a** (0.135 g, 0.239 mmol) and (+)-(*R*,*R*)-**3b** (0.138 g, 0.245 mmol) obtained from (*R*,*S*)-**1** and (+)-(*R*)-**2**, respectively, gave resolved (−)-(*S*)-**1** {yield 0.044 g (64.3%), mp (crude) = 208.3 °C (3 °C/min), $[\alpha]^{25}_{546}$ = −48.3° (*c* 1; THF)} and resolved (+)-(*R*)-**1** {yield 0.049 g (70.0%), mp (crude) = 208.6 °C (3 °C/min), $[\alpha]^{25}_{546}$ = +47.5° (*c* 1; THF)}. Crystallization of each of these two samples from benzene gave crystalline compounds (−)-(*S*)-**1** {yield 0.020 g (29.8%), mp = 210.6 °C (3 °C/min), $[\alpha]^{25}_{578}$ = −37.6°, $[\alpha]^{25}_{546}$ = −50.6°, $[\alpha]^{25}_{436}$ = −220.6°, $[\alpha]^{25}_{365}$ = −1348° (*c* 1; THF), ≈100% optical purity[2b]} and (+)-(*R*)-**1** {yield 0.023 g (33.1%), mp = 211.5 °C (3 °C/min), $[\alpha]^{25}_{578}$ = +36.1°, $[\alpha]^{25}_{546}$ = +49.5°, $[\alpha]^{25}_{436}$ = +220.0°, $[\alpha]^{25}_{365}$ = +1349° (*c* 1; THF), ≈100% optical purity}.[2b] Column chromatography of the combined neutral extracts of the two runs gave recovered (+)-(*R*)-**2**: yield 0.149 g (70.0%), mp (crude) = 182.3 °C (3 °C/min), $[\alpha]^{23}_{546}$ = +192.1° (*c* 1; benzene).

The same treatment and workup was applied to the diether (+)-(*R*,*R*)-**3b** (0.564 g, 1 mmol) obtained from (+)-(*R*)-**1** and (*R*,*S*)-**2**, except that BCl_3 (1 M solution in CH_2Cl_2) was used instead of BBr_3. The pure diol (+)-(*R*)-**1** was recovered in the acidic extract, yield 0.184 g (64.3%), $[\alpha]^{25}_{546}$ = +49.6° (*c* 1; THF). Column chromatography as above (SiO_2/CH_2Cl_2) of the crude neutral extract gave 0.080 g of secondary products (a higher proportion than in previous treatments with BBr_3) and 0.212 g (60.4%) of chromatographically pure dichloride (+)-(*R*)-**5**: pale yellow solid, mp (crude) = 172.8 °C (3 °C/min), $[\alpha]^{23}_{578}$ = +151.6°, $[\alpha]^{23}_{546}$ = +177.0°, $[\alpha]^{23}_{436}$ = +358.3° (*c* 1; benzene). Crystallization from a boiling solution of methyl ethyl ketone concentrated to *ca.* 0.5−1 mL gave pale yellow analytically pure crystals of almost unchanged melting point and optical rotation, yield 0.140 g (39.9%). Anal. Calcd for $C_{22}H_{16}Cl_2$: C, 75.22; H, 4.59; Cl, 20.19. Found: C, 74.96; H, 4.57; Cl, 20.58. Mp = 174.0 °C (3 °C/min), $[\alpha]^{23}_{578}$ = +150.7°, $[\alpha]^{23}_{546}$ = +175.1°, $[\alpha]^{23}_{436}$ = +352.8°, $[\alpha]^{23}_{365}$ = +808.3° (*c* 1; benzene), ≈100% optical purity, lit.[20] mp = 174−175 °C, $[\alpha]_D$ = +145° (*c* 1; benzene).

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