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Resolution and some Properties of (1,1')-Bi(dibenzofuranyl)-2,2'-diol (BIFOL)

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Dedicated to Professor Hans Wynberg with gratitude.

Abstract: The resolution of C_2-symmetric (1,1')-bi(dibenzofuranyl)-2,2'-diol (BIFOL) is reported. Separation *via* recrystallisation of its 1:1 mixture of diastereomeric cyclic phosphoramidates by using (-)-(*S*)-1-phenylethylamine as chiral auxiliary gave both enantiomers in >98% enantiopurity and in good chemical yields. The configuration of BIFOL was determined by X-ray analysis of one of the diastereomeric phosphoramidates. It is shown that the bidibenzofuran skeleton undergoes sulfonation reactions with high regioselectivity. © 1997 Elsevier Science Ltd.

INTRODUCTION

In recent years a wealth of publications on the synthesis and resolution of (1,1')-binaphthalenyl-2,2'-diol (BINOL) have appeared.[1,2,3] The use of C_2-symmetric BINOL as chiral auxiliary[4] in metal-mediated reactions often leads to products in high enantiomeric excess.[5] BINOL is also an important starting material for the synthesis of enantiopure phosphine ligands such as 2,2'-diphenylphosphino-1,1'-binaphthyl, known as BINAP.[6]

The binaphthyl system is by far the most frequently studied chiral auxiliary based on atropisomerism, certainly due to its easy synthesis and high optical stability. A problem of the binaphthyl system could, however, lie in the uncertain regioselectivity of further (electrophilic) functionalization of the ring.[7] Other biaryl-based chiral auxiliaries that have received attention are based on the benzene, benzofuran, benzothiophene, phenanthrene and anthracene substructures.[8] Some years ago we became interested in the use of the bidibenzofuran skeleton for the preparation of chiral auxiliaries. This substructure was expected to allow highly regioselective introduction of further substituents in order to influence its behaviour in enantioselective processes. The recent publication of a patent on the use of a diphosphine with the bidibenzofuran skeleton prompts us to report our early work in this area.[9]

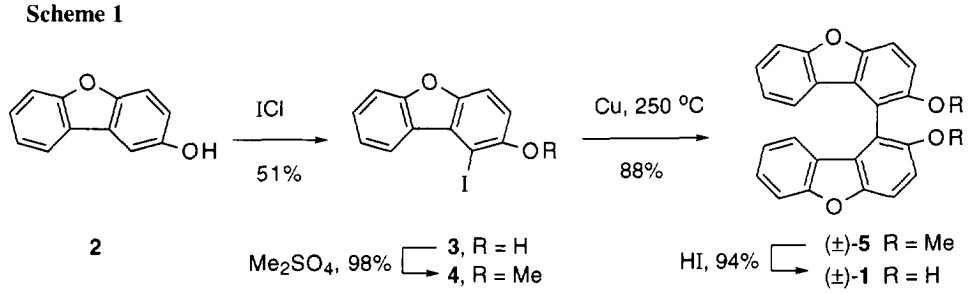
The dibenzofuran unit occurs in metabolites of lower plant lichens. Furthermore, fossil fuels contain dibenzofuran as an important structural moiety, the polychlorinated and brominated dibenzofurans being environmental toxicants.[10] Recently, dibenzofuran has been shown to be a useful building block for organic molecules with special functions. For example, dibenzofuran-based amino acids can function as β-sheet nucleators,[11] and also dibenzofuran-based macrocyclic host molecules have been synthesised.[12] An important synthetic advantage of the dibenzofuran moiety lies in the directing effect of the furan oxygen on further ring functionalization. This oxygen atom activates the *para* positions towards electrophilic substitution. A metal-oxygen chelating effect gives rise to selective metallation at the ortho positions.[13,14]

We here report on the resolution of (1,1')-bi(dibenzofuranyl)-2,2'-diol (**1**), abbreviated as BIFOL, and discuss some of its properties. We feel that enantiopure BIFOL could eventually serve as a useful chiral auxiliary and as a building block for several (phosphorus containing) ligands, taking advantage of the possibilities for selective functionalisation of the dibenzofuran moiety.

RESULTS AND DISCUSSION

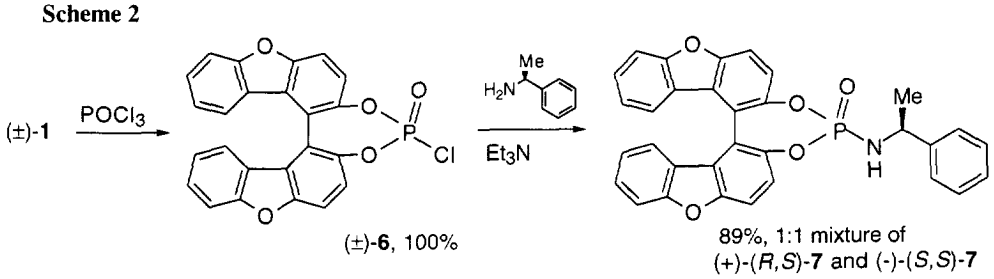
The synthetic pathway to enantiopure **1** is depicted in Scheme 1. We followed the procedure for the synthesis of racemic **1** starting from 2-hydroxydibenzofuran (**2**, available from Aldrich), which was already described by Högberg,[15] more than 20 years ago. The key reaction in this four step procedure is the Ullmann coupling of iodide **4** to the biaryl **5**. After optimisation of this reaction sequence we obtained the racemic diol **1** as a crystalline solid (mp 235-238 °C) in an overall yield of 41% on a 100 gram scale. All attempts to prepare **1** by direct oxidative coupling of **2** similar to the synthesis of BINOL gave unsatisfactory results.

Scheme 1



The resolution of racemic **1** was first attempted by applying the successful enzymatic resolution procedure developed for BINOL by Kazlauskas.[1c] Eleven enzymes were tested to hydrolyse the dipentanoyl derivative of BIFOL,[16] but in all cases only little hydrolysed material was formed. Best results were obtained with the lipase from *Candida cylindrica* in a two phase system of dibutyl ether and water at pH 7.7 (pH-stat). After 4 days 15% of mono-hydrolysed product and 1% of the desired bisphenol **1** was isolated with specific rotations of -31 and -17, respectively.

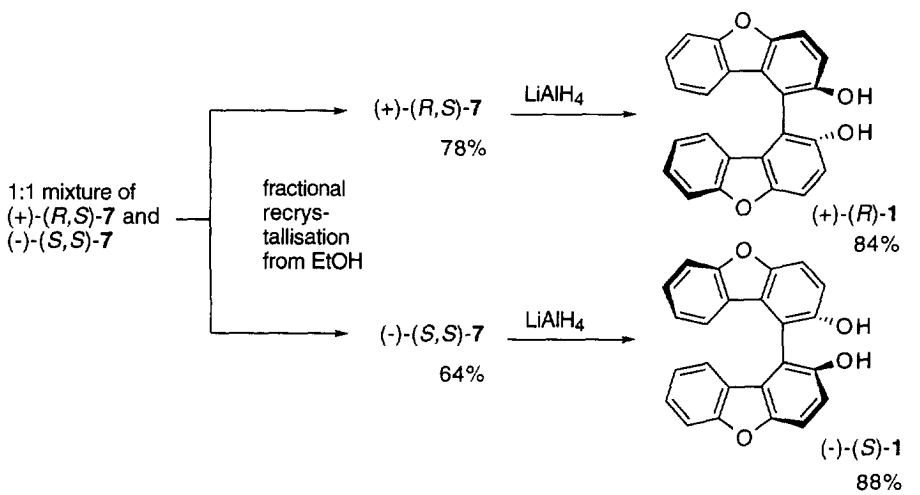
Scheme 2



Better results were obtained by applying the method described by Hu and coworkers for the resolution of BINOL.[1d] This method takes advantage of the difference in solubility of two phosphoramidate diastereomers and enables an efficient resolution *via* recrystallisation. Racemic BIFOL was first converted into phosphoric acid chloride **6**, which was then treated with commercially available (-)-(*S*)-1-phenylethylamine to give a 1:1 mixture (^{31}P NMR: 13.1 and 13.8 ppm) of phosphoramidates **7** in 89% overall yield (see Scheme 2).

The two diastereomers were obtained in >95% diastereomeric purity (observed by ^{1}H and ^{31}P NMR) by recrystallisation from ethanol (see Scheme 3). Seeding of the ethanolic solutions by previously obtained crystals resulted in an efficient three step recrystallisation procedure. The relative configuration of the diastereomers was determined by X-ray analysis of (+)-(*R,S*)-**7** (Figure 1). After reduction with $LiAlH_4$, (+)-(*R*)-**1** and (-)-(*S*)-**1** were obtained as white amorphous solids (mp 74-77 °C) in 84-88% yield with $[\alpha]^{20}_{D}$ values of +35 and -35 (c = 1.0, CH_2Cl_2), respectively. Chiral HPLC analysis showed the enantiomeric purity of the bisphenols to be >98%. The difference in melting point of *ca.* 160 °C between racemic and enantiopure BIFOL is remarkable. For BINOL this difference is less than 10 °C.

Scheme 3



In Figure 1 the axial chirality of the bidibenzofuranyl unit is very clear. The dihedral angle between the two dibenzofuran planes in this structure is 54.5°. Rotation about the central C-C bond is sterically impeded by the hydrogens 8 and 9 (and 8' and 9'). These protons point into the anisotropic field of the other dibenzofuran moiety and this feature accounts for the upfield chemical shift (*ca.* 6.7 ppm) of the H8 and H9 (and H8' and H9') signals in the ^{1}H NMR spectra of all compounds containing the bidibenzofuranyl unit.

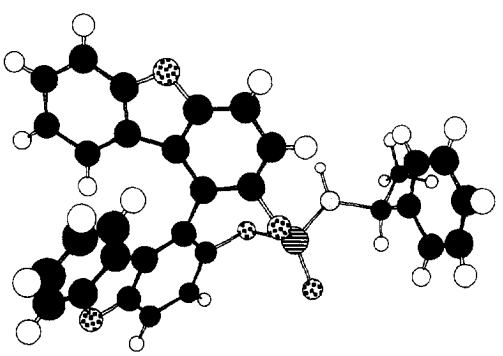
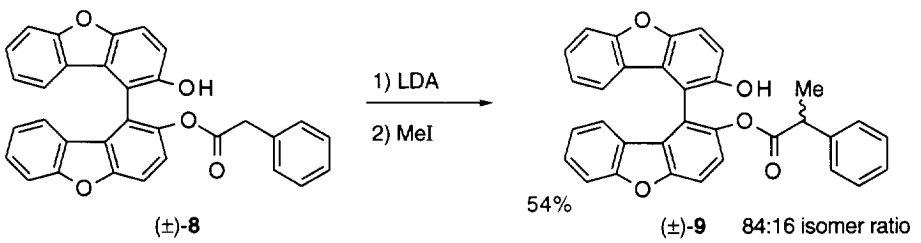


Figure 1. Chem3D™ representation of the crystal structure of (+)-(*R,S*)-**7**.

To assess the usefulness of our novel biaryl system as a chiral auxiliary, we applied the methodology of Fuji and coworkers, who investigated the stereoselectivity of ester alkylation by using BINOL as auxiliary.[4] Racemic **1** was treated with phenylacetyl chloride and base to give the monoester **8** in 84% yield. This monoester was treated with LDA and the resulting enolate reacted with methyl iodide (Scheme 4). The observed isomer ratio of **9** was somewhat higher than that found by Fuji *et al.* using BINOL as the chiral auxiliary (84:16 and 77:23, respectively, observed by ^{1}H NMR). This result clearly indicates that the bidibenzofuranyl system shows similar behaviour as the binaphthyl system.

Scheme 4

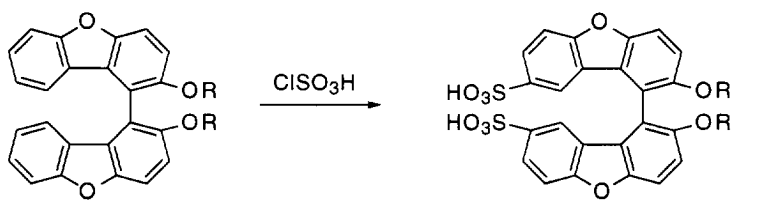


(±)-**8** (±)-**9** 84:16 isomer ratio

To demonstrate the ease and selectivity of electrophilic aromatic substitution of the bidibenzofuranyl unit, both ditriflate ester **10** and dimethyl ether **5** were subjected to sulfonation as shown in Scheme 5. When these compounds were stirred in CH_2Cl_2 for 1 h with 2 equivalents of chlorosulfonic acid at 0 °C the disulfonic acids **11** and **12** were obtained in good to virtually quantitative yields after aqueous work-up. The structural assignment of the products readily followed from the ^{1}H NMR spectra.

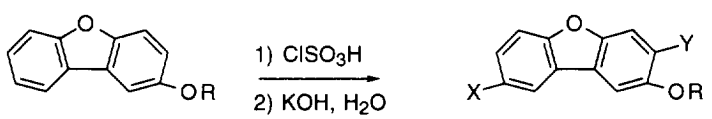
The triflate monomer **13** was also selectively sulfonated at C8 upon treatment with an equimolar amount of chlorosulfonic acid. Interestingly, when the corresponding methoxy monomer **14** was treated likewise, sulfonation occurred at C3 instead of C8. This is in accordance with the position of acylation of 2-methoxydibenzofuran.[17]

Scheme 5



10 R = SO_2CF_3
5 R = Me

11 R = SO_2CF_3
12 R = Me



13 R = SO_2CF_3
14 R = Me

15 R = SO_2CF_3, X = SO_3K, Y = H
16 R = Me, X = H, Y = SO_3K

This difference in behaviour of the monomers **13** and **14** can be explained by examining the electronic effects of the substituents. The methoxy group of **14** increases the electron density in the proximate ring, especially at the positions *ortho* to the methoxy. Carbon 1 is sterically impeded by H9 so that C3 is most favourable for electrophilic attack. On the other hand, the triflate group of **13** apparently deactivates the proximate ring, compared to the distant ring so that substitution occurs at C8, *para* to the furan oxygen.

The difference in sulfonation behaviour between the methoxy monomer **14** and the dimer **5** can be attributed to a steric effect. The torsion angle about the central C-C bond is about 50°. The methoxy groups cannot rotate freely, as in the monomer, but are forced into the direction of C3 and C3'. In this way C3 and C3' are shielded and thus less favourable for substitution. C8 and C8' are not sterically influenced. This sulfonation behaviour is in analogy with the observed trends in sulfonation of 2-methoxy-naphthalene, 2,2'-dimethoxy-1,1'-binaphthalenyl[18], 2-mesyloxynaphthalene and 2,2'-dimesyloxy-1,1'-bi-naphthalenyl.[19] 2-Methoxynaphthalene is also sulfonated *ortho* to the methoxy group, but in this case at the 1-position. The major product from the sulfonation of the dimer 2,2'-dimethoxy-1,1'-binaphthalenyl, however, is the 6,6'-disulfonate. In the case of the mesyloxynaphthalenes sulfonation does not occur in the proximate ring, but at the 5,6 and 8 positions mainly.

The selective sulfonation of the bidibenzofuran system may become advantageous for the synthesis of bidibenzofuran-based, water soluble, bidentate phosphine ligands.[20] Studies along these lines are in progress and will be reported in due course.

Acknowledgements. We gratefully acknowledge financial support from the Research School "Netherlands Institute for Catalysis Research". We thank Dr. B. Kaptein of DSM Research, Geleen, The Netherlands for providing us the opportunity to investigate the enzymatic resolution of BIFOL in the DSM laboratories. R. H. Balk and A. J. C. Berkhout are gratefully acknowledged for their useful synthetic contributions.

EXPERIMENTAL

General information. All reactions were carried out under an inert atmosphere of dry nitrogen and followed by TLC. Glassware was flame dried before use. Standard syringe techniques were applied to transfer dry solvents and reagents. THF was freshly distilled from sodium/benzophenone ketyl under a nitrogen atmosphere. CH_2Cl_2 was distilled from CaH_2 under nitrogen atmosphere and stored over 4 Å molecular sieves. $POCl_3$ and Et_3N were freshly distilled under a nitrogen atmosphere. All other chemicals were used as obtained from Aldrich. Infrared (IR) spectra were obtained from $CHCl_3$ solutions or NaCl plates using a Perkin-Elmer 1310 spectrophotometer and wavelengths (ν) are reported in cm^{-1}. ^1H NMR and ^{13}C NMR (APT) spectra were determined in $CDCl_3$ (unless otherwise indicated) using a Bruker ARX 400 (400 and 100.6 MHz, respectively) spectrometer. Chemical shifts (δ) are given in ppm downfield from tetramethylsilane. ^{31}P NMR spectra were recorded on a Bruker 300 AMX NMR (121.5 MHz) spectrometer. Chemical shifts (δ) are given in ppm downfield from H_3PO_4. Mass spectra and accurate mass measurements were carried out using a VG Micromass ZAB-2HF instrument. Optical rotations were measured with a Perkin-Elmer 241 polarimeter in the indicated solvent at room temperature. Optical purity was checked on a Merck/Hitachi HPLC apparatus equiped with a Chiralpak AS column. Elemental analyses were performed on a Vario EL. Melting points are uncorrected.

Racemic (1,1')-bi(dibenzofuranyl)-2,2'-diol (1). This compound was synthesised according to the known four-step (see Scheme 1) procedure[15] starting from 2-hydroxydibenzofuran (Aldrich). The iodination, *O*-methylation and *O*-demethylation steps were performed exactly according to the literature. The procedure for the Ullmann coupling was slightly modified which considerably improved the yield. The starting material was well powdered and then thoroughly mixed with copper bronze (activated by treatment with I_2 in acetone,

followed by filtration and washing with HCl/acetone 1:1) before the mixture was heated. The most important byproduct, that is the reduction product 2-methoxydibenzofuran, as well as the starting material were removed from the desired product in a Kugelrohr distillation apparatus (bath temperature 100-150 °C, 0.2 mbar). The residue was then recrystallised to pure 2,2'-dimethoxy-(1,1')bidibenzofuranyl. The overall yield of **1** after 4 steps was 41% of white crystals, mp 235-238 °C (lit.[15] 238-240 °C); ^{1}H NMR δ 5.03 (s, 2H, OH), 6.82 (d, J = 7.9 Hz, 2H, H9 and H9'), 6.95 (dt, J = 7.3, 0.9 Hz, 2H, H8 and H8'), 7.29 (d, J = 8.9 Hz, 2H, H3 and H3'), 7.33 (dt, J = 8.5, 1.4 Hz, 2H, H7 and H7'), 7.52 (d, J = 8.3 Hz, 2H, H6 and H6'), 7.69 (d, J = 8.9 Hz, 2H, H4 and H4'); ^{13}C NMR δ 111.4, 111.6, 113.7, 115.8, 121.4, 122.7, 123.4, 123.6, 127.5, 149.9, 150.9, 157.0.

Preparation of a 1:1 mixture of diastereomers of (1,1')-bi(dibenzofuranyl)-2,2'-diyl-*N*-(α-(*S*)-methylbenzyl)phosphoramidate (7). To a stirred suspension of racemic **1** (1.00 g, 2.73 mmol) in 8 mL of dichloromethane was slowly added $POCl_3$ (418 mg, 2.73 mmol). After this mixture was heated to reflux, Et_3N (660 mg, 6.55 mmol) in 2 mL of dichloromethane was added in 30 min. The mixture was refluxed for an additional 1.5 h and then cooled to room temperature. The reaction mixture was washed with water and brine and dried with Na_2SO_4. Removal of the solvent yielded a light yellow crystalline solid (1.22 g, 100%): mp 215-222 °C; ^{1}H NMR δ 6.74 (m, 4H), 7.31 (m, 2H), 7.55 (m, 3H), 7.64 (dd, 1H, J = 8.8, 1.6 Hz), 7.83 (d, 1H, J = 8.8 Hz), 7.84 (dd, 1H, J = 8.8, 0.7 Hz); ^{13}C NMR δ 157.2, 154.1 (d), 153.9 (d), 144.0, 143.9, 143.5, 143.4, 128.9, 124.2, 124.0, 122.8, 122.6, 120.4 (d), 120.0 (d), 119.8 (d), 119.7 (d), 113.9, 113.7, 111.7; ^{31}P NMR δ 12.3. This phosphoric acid chloride **6** was used without further purification.

To a stirred suspension of **6** (1.22 g, 2.73 mmol) in 20 mL of dichloromethane was added at 0 °C in 30 min a mixture of (*S*)-1-phenylethylamine (364 mg, 3.00 mmol) and Et_3N (332 mg, 3.28 mmol) in 5 mL of dichloromethane. The mixture was stirred for 42 h at room temperature. Work-up with 4% aqueous HCl and brine gave after drying with Na_2SO_4 and evaporation of the solvent, the crude product as a light yellow crystalline solid, contaminated with some phosphoric ester. Purification with flash chromatography (silica gel, EtOAc) afforded a 1:1 mixture of phosphoramidates (*R,S*)-**7** and (*S,S*)-**7** (1.29 g, 89%) as a white powder: mp 209-212 °C; $[\alpha]^{20}_D$ +19 (c = 1.0 in CH_2Cl_2); ^{31}P NMR: δ 13.1 and 13.8.

Separation of (*R,S*) and (*S,S*)-7. The 1:1 mixture of diastereomers (1.29 g) was dissolved in 18 mL of boiling absolute ethanol. The solution was seeded with some crystals of (*R,S*)-**7**, obtained from an earlier recrystallisation experiment, and allowed to cool to room temperature very slowly. After 72 h of standing at room temperature, (*R,S*)-**7** was isolated by filtration as colourless crystalline plates (368 mg, 57%): mp 133.5-136.5 °C; $[\alpha]^{20}_D$ +479 (c = 1.0 in CH_2Cl_2); ^{31}P NMR: δ 13.1; ^{1}H NMR δ 1.57 (d, 3H, CH_3, J = 6.8 Hz), 3.73 (t, 1H, NH, J = 10.5 Hz), 4.43 (m, 1H, CH), 6.68 (d, 2H, J = 4.1 Hz), 6.73 (t, 1H, J = 7.6 Hz), 6.79 (d, 1H, J = 7.9 Hz), 7.14 (d, 1H, J = 10.0 Hz), 7.21-7.34 (m, 7H), 7.51-7.60 (m, 4H), 7.77 (d, 1H, J = 8.8 Hz); ^{13}C NMR δ 25.8 (d), 52.2, 111.5 (d), 112.9, 113.4, 119.9 (d), 120.0 (d), 120.3 (d), 120.8 (d), 122.3, 122.4, 122.5, 122.6, 123.0 (d), 123.7, 125.7 (2C), 127.3, 127.8, 128.0, 128.6 (2C), 143.7 (d), 144.2 (d), 144.7 (d), 153.2 (d), 153.6 (d), 157.0 (d); IR (NaCl, cm^{-1}) 3190, 1436, 1410, 1279, 1246, 1196; Anal. Calcd for $C_{32}H_{22}NO_5P$: C, 72.31; H, 4.17; N, 2.64. Found: C, 72.13; H, 4.10; N, 2.62.

Concentration of the filtrate under reduced pressure gave a light yellow solid containing (*R,S*)-**7** and (*S,S*)-**7** in a 3:7 ratio. This mixture was dissolved in 10 mL of boiling ethanol and the solution was seeded with some crystals of (*S,S*)-**7**, obtained from an earlier recrystallisation experiment. The solution was cooled slowly and allowed to stand for 48 h at roomtemperature. (*S,S*)-**7** was obtained as colourless crystalline plates (413 mg, 64%): mp 264-265 °C; $[\alpha]^{20}_D$ -442 (c = 1.0 in CH_2Cl_2); ^{31}P NMR: δ 13.8; ^{1}H NMR δ 1.53 (d, 3H, CH_3, J = 6.8 Hz), 3.54 (t, 1H, NH, J = 10.7 Hz), 4.63 (m, 1H, CH), 6.63-6.74 (m, 5H), 7.21-7.27 (m, 2H), 7.33-7.42 (m, 5H), 7.33 (m, 2H), 7.54 (d, 1H, J = 8.8 Hz), 7.55 (dd, 1H, J = 8.8, 1.3 Hz), 7.72 (d, 1H, J = 8.0 Hz); ^{13}C NMR δ 24.6 (d), 51.9, 111.5 (2C), 112.8, 113.3, 119.8 (d), 120.2 (d), 120.4 (d), 120.8 (d), 122.2, 122.4, 122.5, 122.6, 123.0 (d), 123.6, 123.7, 126.2 (2C), 127.6, 127.8, 127.9, 128.7 (2C), 143.5 (d), 144.2 (d),

144.5-144.6 (3C), 153.2 (d), 153.5, 157.0 (2C); IR (NaCl, cm^{-1}) 3215, 1436, 1410, 1246, 1196; HRMS (FAB+) calcd for $C_{32}H_{23}O_5NP$ $[M+H]^+$ 532.1314, found 532.1291.

The residue was again dissolved in boiling ethanol (3 mL). The solution was seeded with crystals of (*R,S*)-**7** and allowed to cool slowly. After 50 h of standing at room temperature a second crop of (*R,S*)-**7** was obtained (136 mg, 21%).

Crystallographic data of (*R,S*)-**7**: $C_{32}H_{22}NO_5P$, M_r = 531.5, monoclinic, $P2_1$, a = 10.209(1), b = 16.830(4), c = 15.596(2) Å, β = 101.34(1)°, V = 2627.4(8) $Å^3$, Z = 4, D_{calc} = 1.35 gcm^{-3}, λ(MoKα) = 0.71069 Å, μ(MoKα) = 1.42 cm^{-1}, F(000) = 1104. Final R = 0.040 for 4573 observed reflections. Experimental procedure: A crystal with dimensions 0.60 × 0.60 × 0.30 mm approximately was used for data collection on an Enraf-Nonius CAD-4 diffractometer with graphite-monochromated MoKα radiation and ω-2Θ scan. A total of 7837 unique reflections was measured within the range $-13 \leq h \leq 14$, $0 \leq k \leq 23$, $-21 \leq l \leq 0$. Of these, 4573 were above the significance level of 2.5 σ(I). The maximum value of (sin (Θ)/λ was 0.70 $Å^{-1}$. Two reference reflections (-212, 121) were measured hourly and showed no decrease during the 81 h collecting time. In addition 155 Friedel reflections were measured, which were used in establishing the absolute configuration of the structure. Unit-cell parameters were refined by a least-squares fitting procedure using 23 reflections with $40 < 2\Theta < 42°$. Corrections for Lorentz and polarisation effects were applied. The structure was solved by the program CRUNCH.[21] The hydrogen atoms were calculated. Full-matrix least-squares refinement on F, anisotropic for the non-hydrogen atoms and isotropic for the hydrogen atoms, restraining the latter in such a way that the distance to their carrier remained constant at approximately 1.0 Å, converged to R = 0.040, R_w = 0.038, $(\Delta/\sigma)_{max}$ = 0.18, S = 0.361(4). A weighting scheme $w = (6.6 + 0.010*\sigma^2(F_{obs}) + 0.00014/\sigma(F_{obs}))^{-1}$ was used. The secondary isotropic extinction coefficient[22,23] refined to Ext = 0.39(3). The absolute structure parameter[24] refined to Xabs = 0 thus confirming the correct enantiomer. A final difference Fourier map revealed a residual electron density between -0.3 and 0.3 eA^{-3}. Scattering factors were taken from Cromer and Mann.[25] All calculations were performed with XTAL[26], unless stated otherwise. There are two identical molecules in the asymmetric unit. Matching both molecules led to an RMS = 0.44 Å. The largest differences occur in the phenyl moiety (C26-C31).[27]

(*R*)-(1,1')-Bi(dibenzofuranyl)-2,2'-diol (1). To a solution of (*R,S*)-**7** (450 mg, 0.85 mmol) in 4 mL of THF was added $LiAlH_4$ (88 mg, 2.32 mmol) in portions at 0 °C. After being stirred at room temperature for 21 h, the mixture was cooled to 0 °C and 2 mL of 6 N HCl solution was added carefully. After work-up with ether and brine 302 mg of a foamy solid was obtained. Flash chromatography (EtOAc/hexanes 1:1) yielded 262 mg (84%) of (+)-(*R*)-**1** as a white foamy solid. The enantimeric purity of the material was >98% (checked with HPLC): mp 74-77 °C; $[\alpha]^{20}_D$ +35 (c = 1.0 in CH_2Cl_2); ^1H NMR and ^{13}C NMR data were identical with those of racemic **1**.

(*S*)-(1,1')-Bi(dibenzofuranyl)-2,2'-diol (1). (*S,S*)-**7** (400 mg, 0.75 mmol) was reduced the same way to yield 242 mg (88%) of (-)-(*S*)-**1** as a white foamy solid: mp 74-78 °C; $[\alpha]^{20}_D$ -35 (c = 1.0 in CH_2Cl_2). HRMS (FAB+) calcd for $C_{24}H_{15}O_4$ $[M+H]^+$ 367.0970, found 367.0953.

Phenyl-acetic acid 2'-hydroxy-(1,1')bi(dibenzofuranyl)-2-yl ester (8). A mixture of (±)-**1** (100 mg, 0.27 mmol), Et_3N (35 mg, 0.35 mmol) and DMAP (3 mg, 0.024 mmol) in 1 mL of THF was stirred at -5 °C. Phenylacetyl chloride (45.7 mg, 0.29 mmol) in 1 mL of THF is added and the colourless mixture is stirred for 12 min at -5 °C. Work-up with water, brine and diethyl ether yielded a white sticky solid. After flash chromatography (EtOAc/hexanes 1:3) 109 mg of **8** was obtained as a white crystalline solid (84%): mp 198-202 °C; ^1H NMR: δ 3.48 (s, 2H, CH_2), 5.24 (bs, 1H, OH), 6.65 (t, 2H, J = 7.3 Hz), 6.73 (d, 2H, J = 7.2 Hz), 6.89-6.99 (m, 4H), 7.08 (t, 1H, J = 7.4 Hz), 7.16 (d, 1H, J = 8.8 Hz), 7.30 (dt, 1H, J = 8.4, 1.3 Hz), 7.33 (dt, 1H, J = 8.5, 1.3 Hz), 7.39 (d, 1H, J = 8.8 Hz), 7.48-7.54 (m, 3H), 7.78 (d, 1H, J = 8.8 Hz). HRMS (FAB+) calcd for $C_{32}H_{21}O_5$ $[M+H]^+$ 485.1389, found 485.1357.

2-Phenyl-propionic acid 2'-hydroxy-(1,1')-bi(dibenzofuranyl)-2-yl ester (9). To a stirred solution of diisopropylamine (8.5 mg, 0.084 mmol) in 0.5 mL of THF at -20 °C was added a 1.6 M solution of *n*BuLi in hexane (52 mL, 0.083 mmol). After 20 min the reaction temperature was lowered to -78 °C and a mixture of monoester **8** (20 mg, 0.041 mmol) and HMPA (7.2 mL, 0.041 mmol) in 0.5 mL of THF was added. After 30 min methyl iodide (209 mg, 1.48 mmol) was added. After an additional 30 min the reaction mixture was poured in 0.1 M aqueous HCl. Workup with brine and diethyl ether yielded a brown sirup. Flash chromatography (EtOAc/hexanes 1:2) yielded **9** as a 84:16 mixture of diastereomers as a white solid (11 mg, 54%): mp 155-162 °C; ^{1}H NMR: δ 1.3 (m, 3H, CH_3), 3.58 (q, 0.16H, CH), 3.65 (q, 0.84H, CH), 5.25 (bs, 1H, OH), 6.61 (t, 2H, *J* = 7.2 Hz), 6.66 (d, 2H, *J* = 8.2 Hz), 6.85-7.55 (m, 11H), 7.78 (d, 2H, *J* = 8.4 Hz). HRMS (FAB+) calcd for $C_{33}H_{22}O_5$ $[M]^+$ 498.1467, found 498.1420.

2,2'-Bis-(trifluoro-methanesulfonyloxy)-(1,1')-bi(dibenzofuranyl) (10). Racemic diol **1** (2.55 g, 6.96 mmol) was dissolved in 40 mL of 1 M aqueous KOH. To this stirred solution trifluoromethanesulfonic anhydride (1.58 mL, 39.5 mmol) in 40 mL of CCl_4 was added slowly at 0 °C. A white precipitate was formed. After 20 min 20 ml of CH_2Cl_2 was added and the organic layer was separated. The water layer extracted with CH_2Cl_2 and the combined organic fractions washed with brine. Evaporation of the solvents yielded 4.17 g (95%) of **10** as a white solid. Recrystallisation from toluene yielded 3.18 g (72%) of white crystalline plates: mp 169-170 °C; ^{1}H NMR δ 6.64 (d, *J* = 7.9 Hz, 2H, H9 and H9'), 6.90 (t, *J* = 7.6 Hz, 2H, H8 and H8'), 7.38 (dt, *J* = 7.8, 1.2 Hz, 2H, H7 and H7'), 7.59 (d, *J* = 8.3 Hz, 2H, H6 and H6'), 7.65 (d, *J* = 9.0 Hz, 2H, H3 and H3'), 7.88 (d, *J* = 9.0 Hz, 2H, H4 and H4'); ^{13}C NMR δ 111.9, 113.9, 118.3 (q, *J* = 318 Hz CF_3), 120.7, 122.0, 122.5, 123.4, 125.5, 128.8, 142.6, 154.5, 157.4.

2,2'-Bis-(trifluoro-methanesulfonyloxy)-(1,1')-bi(dibenzofuranyl)-8,8'-disulfonic acid (11). To a stirred solution of **10** (106 mg, 0.168 mmol) in 1 mL of CH_2Cl_2 at 0 °C was slowly added chlorosulfonic acid (24 μL, 0.353 mmol) in 1 mL of CH_2Cl_2. After 1 h water was added carefully. The water layer was separated and after evaporation 140 mg of a white solid was obtained (96%): mp 235-238 °C; ^{1}H NMR (CD_3OD) δ 7.17 (d, *J* = 1.6 Hz, 2H, H9 and 9'), 7.71 (d, *J* = 8.7 Hz, 2H), 7.83 (d, *J* = 9.0 Hz, 2H), 7.89 (d, *J* = 8.7 Hz, 2H), 8.09 (d, *J* = 9.0 Hz, 2H); ^{13}C NMR (D_2O) δ 115.3, 117.6, 120.6 (q, *J* = 319 Hz, CF_3), 122.3, 123.0, 124.3, 124.7, 127.0, 129.1, 140.9, 145.1, 157.9, 161.1. HRMS (FAB+) calcd for $C_{26}H_{12}O_{14}F_6S_4Na$ $[M+Na]^+$ 812.8912, found 812.8916.

2,2'-Dimethoxy-(1,1')-bi(dibenzofuranyl)-8,8'-disulfonic acid (12) and sodium salt. To a stirred solution of **5** (48 mg, 0.122 mmol) in 1 mL of CH_2Cl_2 at 0 °C was slowly added chlorosulfonic acid (17 μL, 0.244 mmol) in 1 mL CH_2Cl_2. After 1 h the mixture was evaporated. Flash chromatography (EtOAc/MeOH/H_2O/AcOH 80:10:5:5) yielded 44 mg of a white solid (65%). ^{1}H NMR (CD_3OD) δ 3.76 (s, 3H, Me), 7.42 (d, *J* = 9.0 Hz, 2H), 7.45 (d, *J* = 1.6 Hz, 2H, H9 and 9'), 7.54 (d, *J* = 8.6 Hz, 2H), 7.72 (d, *J* = 9.0 Hz, 2H), 7.84 (dd, *J* = 8.6, 1.7 Hz, 2H). This white solid was treated with 1.6 mL 0.1M aqueuos NaOH. Evaporation of the water yielded 47 mg of a white solid (100%). ^{1}H NMR (D_2O) δ 3.78 (s, 3H, Me), 7.15 (d, *J* = 1.9 Hz, 2H, H9 and H9'), 7.56 (d, *J* = 9.2 Hz, 2H), 7.63 (d, *J* = 8.7 Hz, 2H, H6 and H6'), 7.77 (dd, *J* = 8.7, 1.9 Hz, 2H, H7 and 7'), 7.86 (d, *J* = 9.1 Hz, 2H); ^{13}C NMR (D_2O) δ 59.4, 114.5, 115.2, 115.7, 119.1, 121.5, 125.3, 125.9, 127.5, 139.7, 154.3, 155.3, 160.4. HRMS (FAB+) calcd for $C_{26}H_{17}O_{10}S_2Na_2$ $[M+H]^+$ 599.0059, found 599.0079.

2-(Trifluoro-methanesulfonyloxy)dibenzofuran (13). 2-Hydroxydibenzofuran (395 mg, 1.08 mmol) was dissolved in 3 mL of 1 M aqueous KOH. To this stirred solution trifluoromethanesulfonic anhydride (122 μL, 3.06 mmol) in 3 mL of CCl_4 was added slowly at 0 °C. After 20 min the organic layer was separated, the water layer extracted with CH_2Cl_2 and the combined organic fractions washed with brine. Evaporation of the solvents yielded 654 mg (96%) of **13** as a white solid. ^{1}H NMR δ 7.35 (dd, *J* = 9.0, 2.6 Hz, 1H, H3), 7.39 (dt,

J = 7.9, 0.9 Hz, 1H), 7.53 (dt, J = 7.3, 1.2 Hz, 1H), 7.60 (d, J = 8.9 Hz, 2H), 7.85 (d, J = 2.6 Hz, 1H, H1), 7.95 (d, J = 7.7 Hz, 1H).

2-(Trifluoro-methanesulfonyloxy)dibenzofuran-8-sulfonic acid and its potassium salt (15). To a stirred solution of **13** (100 mg, 0.316 mmol) in 1 mL of CH_2Cl_2 at 0 °C was slowly added chlorosulfonic acid (21 μL, 0.316 mmol) in 1 mL CH_2Cl_2. After stirring for 3 h at room temperature, a white precipitate was isolated (106 mg, 85%). ^{1}H NMR (D_2O) δ 6.55 (d, J = 8.9 Hz, 1H), 6.59 (d, J = 8.6 Hz, 1H), 6.70 (dd, J = 8.8, 2.0 Hz, 1H), 7.13 (d, J = 1.9 Hz, 1H), 7.34 (d, J = 8.4 Hz, 1H), 7.59 (s, 1H). ^{13}C NMR (D_2O) δ 114.2, 114.7, 116.5, 121.4 (q, J = 320 Hz, CF_3), 121.1, 122.5, 124.6, 126.6, 128.4, 140.6, 147.2, 156.8, 159.6. Part of this solid (71 mg, 0.179 mmol) was dissolved in 1.79 mL of 0.1M aqueous KOH. After evaporation a white crystalline solid was obtained (78 mg, 100%). ^{1}H NMR (D_2O) δ 7.44 (dd, J = 9.0, 2.6 Hz, 1H), 7.53 (d, J = 9.0 Hz, 1H), 7.60 (d, J = 8.7 Hz, 1H), 7.92 (s, 1H), 7.93 (dd, J = 6.9, 1.8 Hz, 1H), 8.27 (d, J = 1.6 Hz, 1H). HRMS (FAB+) calcd for $C_{13}H_6O_7F_3S_2K_2$ $[M+K]^+$ 472.8781, found 472.8773.

2-Methoxydibenzofuran-3-sulfonic acid and its potassium salt (16). To a stirred solution of 2-methoxydibenzofuran (366 mg, 1.85 mmol) in 2 mL of CH_2Cl_2 at 0 °C was slowly added chlorosulfonic acid (123 μL, 1.85 mmol) in 5 mL CH_2Cl_2. After stirring for 30 min. at room temperature, a white precipitate was formed. Filtration gave a white solid (503 mg, 98%). ^{1}H NMR (D_2O) δ 4.03 (s, 3H, Me), 7.37 (dt, J = 8.0, 1.0 Hz, 1H), 7.50 (dt, J = 8.3, 1.3 Hz, 1H), 7.57 (d, J = 8.3 Hz, 1H), 7.72 (s, 1H), 8.06 (s, 1H), 8.07 (d, J = 7.2 Hz, 1H); ^{13}C NMR (D_2O) δ 58.9, 105.7, 113.6, 113.7, 123.3, 125.2, 125.3, 129.4, 130.6, 131.9, 150.4, 155.1, 159.1. HRMS (FAB+) calcd for $C_{13}H_{11}O_5S$ $[M+H]^+$ 279.0327, found 279.3025. After addition of 1.81 mL of 1M aqueous KOH and evaporation a white solid was obtained (575 mg, 100%). ^{1}H NMR (D_2O) δ 3.92 (s, 3H, Me), 7.25 (s, 1H), 7.25 (t, J = 7.6 Hz, 1H), 7.33 (d, J = 8.3 Hz, 1H), 7.43 (t, J = 7.6 Hz, 1H), 7.64 (d, J = 8.4 Hz, 1H), 7.66 (s, 1H).

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