2,2′-Disubstituted F_{12}binaphthyl derivatives: stannanes, boranes, and (*R*)-F_{12}BINOL†

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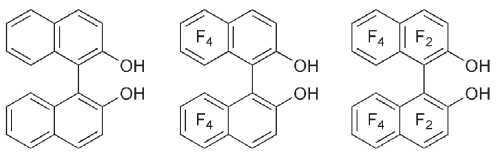
2,2′-Distannyl derivatives of dodecafluorobinaphthalene are converted to a novel D_2 symmetric borane dimer, which can be oxidized to (±)-F_{12}BINOL; resolution using (*S*)-acetoxypropanoyl chloride affords enantiopure material.

The axially asymmetric 1,1′-binaphthyl framework is one of the most effective and common chiral auxiliaries in chemistry. Donor functionalized, chiral chelating ligands such as 1,1′-bi-2-naphthol (BINOL)[1] and 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl (BINAP)[2] are powerful catalyst modifiers for a myriad of asymmetric transformations. When Lewis acid (LA) functions are installed into the 2,2′ positions, effective chiral Lewis acids result.[3]



Modifications to the basic 1,1′-binaphthyl framework generally involve various substitution patterns around the naphthyl rings.[1a] While this inevitably perturbs the electronic environment to a degree, it is mainly the steric effect of substitution that influences the ligand's behavior in catalytic applications. In some cases, however, increases in activities and enantioselectivities of LA catalysts derived from partially halogenated or fluoroalkylated BINOLs have been attributed directly to the electronic perturbation by these electronegative groups.[4] Yudin and co-workers introduced the most substantial electronic modification with the synthesis, resolution[5] and applications[6] of F_8BINOL, in which the back aryl rings (the 5,5′, 6,6′, 7,7′, and 8,8′ positions) are fluorinated. While sterically very similar to the unfluorinated BINOL, partial fluorination results in a more acidic BINOL which imparts greater Lewis acidity to its metal complexes. We now report the synthesis and resolution of 2,2′-dihydroxy-3,3′,4,4′,5,5′,6,6′,7,7′,8,8′-dodecafluoro-1,1′-binaphthyl (F_{12}BINOL, **1**) *via* selective manipulation of the 2,2′ positions of a novel F_{12}binaphthyl scaffold.

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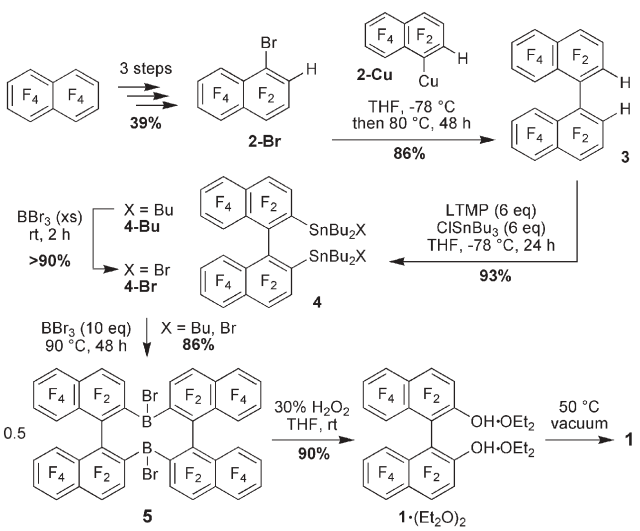
† Electronic supplementary information (ESI) available: synthetic procedures and X-ray data for **1**·$(Et_2O)_2$, **3**, **5** and (R_{ax},*S*,*S*)-**6** as CIF files. See DOI: 10.1039/b605716k

Our interest in perfluoraryl boranes,[7] coupled with the proven track record of the 1,1′-binaphthyl scaffold as a chiral auxiliary, led us to explore routes to 2,2′ functionalized F_{12}binaphthyl derivatives for various applications in catalysis. The starting point for entry into this family of binaphthyl compounds is the known 1-bromo-3,4,5,6,7,8-hexafluoronaphthalene[8] **2-Br** shown in Scheme 1. Modification of literature methods[9] led to improved yields of this compound (39%) in multigram quantities over three steps from commercially available octafluoronaphthalene. Copper mediated coupling of this substrate with its *in situ* generated arylcopper coupling partner **2-Cu** gave the F_{12}binaphthyl derivative **3** in 86% yield.‡

Two strategies for functionalization of the 2,2′ positions of **3** were considered: 1) electrophilic halogenation to give 2,2′ dihalides as precursors for metallation reactions, and 2) direct deprotonation with strong bases. Unfortunately, all attempts at selective halogenation reactions were unsuccessful. Halogenating reagents such as Br_2/Fe, NBS/CCl_4, NBS/BF_3·H_2O,[10] and $I(py)_2BF_4$/TfOH[11] resulted in either no reaction and/or partial decomposition at room temperature. Unselective bromination occurred at elevated temperatures with Br_2/Fe and with stronger brominating agents (20% $AlBr_3$/Br_2/SO_3/H_2SO_4).[12] Since the hydrogen atoms of the 2,2′ positions of **3** were expected to be substantially acidic due to the inductive electron-withdrawing effects of the fluorine atoms, attention was turned to deprotonative approaches. Use of alkyllithium reagents led to rapid reduction of the fluoroaryl substrate and non-regioselective loss of LiF. Selective functionalization of



Scheme 1

the 2,2′ positions of **3** was achieved by deprotonation using the poorly reducing, non-nucleophilic base lithium 2,2,6,6-tetramethylpiperidide (LTMP) at low temperature and in the presence of a quenching electrophile. Attempts to deprotonate **3** with LTMP in the absence of electrophile also led to complex mixtures; thus, it is necessary to use electrophiles that are compatible with LTMP at −78 °C.[13] Tributyltin chloride is one such electrophile, and the 2,2′-distannane **4-Bu** is available in high yield using this procedure. Preliminary work has shown that chlorosilanes and -phosphines are also suitable electrophiles for this chemistry; unfortunately, a compatible boron-based electrophile was not identified.

Compound **4-Bu**, however, can be used to install boron in the 2,2′ positions. Treatment with an excess of BBr_3 at high temperatures led to dark solutions from which large, yellow crystals deposited over the course of several hours. Although the ^{11}B (δ_B 49.2 ppm)[14] and ^{19}F NMR spectroscopic signatures of this compound were consistent with the C_2-symmetric structure of the anticipated 2,2′-*bis*-dibromoboryl derivative, its low solubility was not. X-Ray structural analysis of yellow block crystals grown by cooling a toluene solution to −30 °C revealed the compound to be the striking D_2 symmetric homochiral bromoborane dimer **5** shown in Fig. 1.‡ At room temperature, this reaction leads to the ditin derivative **4-Br**; boron–tin transmetallation requires higher temperature and no other intermediates are observed. Similar condensations have been observed in other perfluoroaryl *bis*-dibromoboryl systems.[15] In **5**, the boron centers are planar with an angle of 79.0° between the trigonal planes, suggesting that the two will behave as non-cooperating Lewis acid centers. Nonetheless, **5** is a promising asymmetric LA and preliminary experiments suggest that it can be converted to its more hydrolytically stable *bis*-C_6F_5 derivative by treatment with $[Cu(C_6F_5)]_4$.[14]

As a borane, however, **5** can of course be oxidized to the corresponding phenol, in this case F_{12}BINOL **1**. As seen in Scheme 1, treatment of a THF solution of **5** with 30% H_2O_2 furnishes, after work-up and purification, the *bis*-diethyl ether adduct **1**·$(Et_2O)_2$ which was characterized by X-ray crystallography (Fig. 2). The gross molecular and extended structural features of **1**·$(Et_2O)_2$ are analogous to those in the recently reported crystal structure of BINOL·$(Et_2O)_2$.[16] However, slightly shorter O···$O_{solvent}$ distances [O(1)–O(1S), 2.686(2); and O(2)–O(2S), 2.691(2) Å] in **1**·$(Et_2O)_2$ compared to an average O···$O_{solvent}$ distance of 2.74 Å in BINOL·$(Et_2O)_2$ are perhaps indicative of more strongly bound Et_2O molecules to the presumably more acidic fluorobinaphthol **1**. Solvent free **1** can be obtained simply by heating at 50 °C under a dynamic vacuum to effect removal of the coordinated Et_2O.

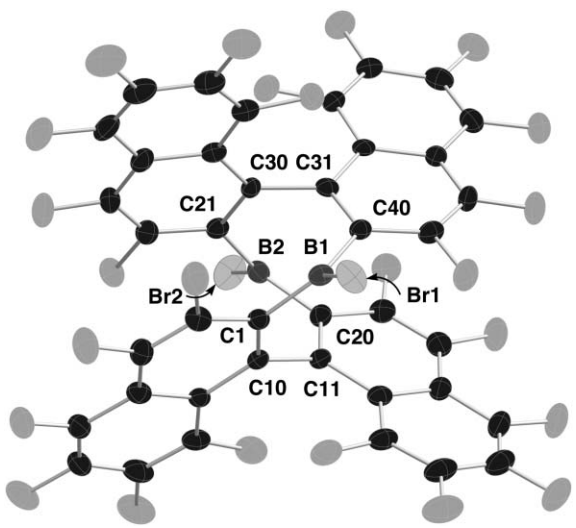


Fig. 1 Thermal ellipsoid diagram of the molecular structure of **5** (*R*,*R* enantiomer shown); the two toluene molecules of solvation are omitted for clarity. Selected bond distances (Å): B(1)–C(1), 1.551(9); B(1)–C(40), 1.574(9); B(1)–Br(1), 1.902(7). Selected bond angles (°): C(1)–B(1)–C(40), 123.0(5); C(1)–B(1)–Br(1), 118.3(5); C(40)–B(1)–Br(1), 118.8(5). Selected dihedral angle (°): C(1)–C(10)–C(11)–C(20), 96.7(7).

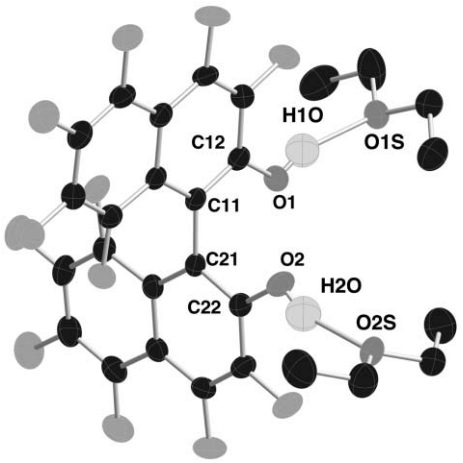
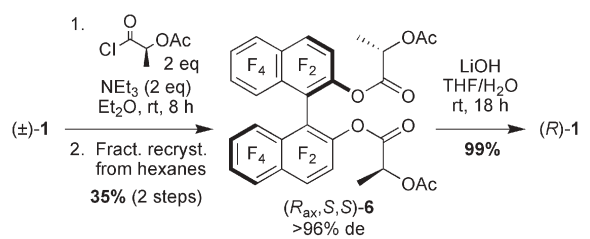


Fig. 2 Thermal ellipsoid diagram of the molecular structure of racemic **1**·$(Et_2O)_2$ (*S* enantiomer shown). Selected bond and non-bonded distances (Å): O(1)–C(12), 1.344(2); O(2)–C(22), 1.341(2); O(1)–O(1S), 2.686(2); O(2)–O(2S), 2.691(2). Selected bond angles (°): O(1)–H(1O)···O(1S), 157.9; O(2)–H(2O)···O(2S), 155.7. Selected dihedral angle (°): C(12)–C(11)–C(21)–C(22), 80.5(2).

Acylation of **1** with (*S*)-acetoxypropanoyl chloride[17] followed by fractional crystallization gave the diester (R_{ax},*S*,*S*)-**6** in > 96% de as measured by ^1H and ^{19}F NMR spectroscopy (Scheme 2). The molecular structure of (R_{ax},*S*,*S*)-**6** was determined crystallographically;‡ due to the low scattering power of the light atoms in the structure, the absolute configuration of the compound could not be assigned based on the X-ray data alone, but the stereochemistries of C(2) and C(7) were known from the precursor compound. Saponification with LiOH in THF/H_2O[17b] gave (*R*)-**1** without any degradation in optical purity, as evidenced by conversion of (*R*)-**1** into its methyl ether (*R*)-**7** which was > 98% ee as determined by chiral HPLC analysis.

In summary, we have demonstrated the synthesis of a family of 2,2′-disubstituted F_{12}binaphthyl derivatives including the



Scheme 2

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perfluorobinaphthol (*R*)-**1**. The key synthetic step involves the deprotonation of the parent F_{12}binaphthyl **3** with the strong base LTMP in the presence of a tin electrophile to form the distannane **4-Bu**. The introduction of (*R*)-**1** for asymmetric catalysis applications where high Lewis or Brønsted acidity is desired[18] is a significant new tool that we are currently exploring. Extension of the methodology to the synthesis of other F_{12}binaphthyl derivatives, for example diphosphines, is also promising.

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Notes and references

‡ Crystal data for **1**·$(Et_2O)_2$: $C_{28}H_{22}F_{12}O_4$, M = 650.46, T = 193 K, space group $P2_1/n$ (No. 14), monoclinic, a = 10.9881(9), b = 20.1333(16), c = 12.9050(10) Å, β = 103.3641(14)°, V = 2777.6(4) Å^3, Z = 4, D_c = 1.555 g cm^{-3}, μ(Mo-K$_\alpha$) = 0.156 mm^{-1}, 21180 reflections measured, 5687 unique (R_{int} = 0.0448) which were used in all calculations. The final $R(F)$ was 0.0880.

Crystal data for **3**: $C_{20}H_2F_{12}$, M = 470.22, T = 173(2) K, space group *Pbca*, orthorhombic, a = 13.1128(2), b = 23.9042(5), c = 10.1940(2) Å, V = 3295.3(1) Å^3, Z = 8, D_c = 1.955 g cm^{-3}, μ(Mo-K$_\alpha$) = 0.213 mm^{-1}, 8107 reflections measured, 4604 unique (R_{int} = 0.0407) which were used in all calculations. The final $R(F)$ was 0.0649.

Crystal data for **5**: $C_{54}H_{16}B_2Br_2F_{24}$, M = 1302.11, T = 173(2) K, space group *C2/c*, monoclinic, a = 35.880(6), b = 12.916(9), c = 25.835(10) Å, β = 126.545(16)°, V = 9619(8) Å^3, Z = 8, D_c = 1.798 g cm^{-3}, μ(Mo-K$_\alpha$) = 1.820 mm^{-1}, 26643 reflections measured, 5869 unique (R_{int} = 0.0772) which were used in all calculations. The final $R(F)$ was 0.1143.

Crystal data for **6**: $C_{30}H_{14}F_{12}O_8$, M = 730.41, T = 193(2) K, space group $P2_1$, monoclinic, a = 10.1781(12), b = 12.7075(15), c = 11.4937(14) Å, β = 99.4442(17)°, V = 1466.4(3) Å^3, Z = 2, D_c = 1.654 g cm^{-3}, μ(Mo-K$_\alpha$) = 0.168 mm^{-1}, 11649 reflections measured, 5994 unique (R_{int} = 0.0316) which were used in all calculations. The final $R(F)$ was 0.0378.

CCDC 299722–299725. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b605716k

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