Experimental Section for:

Regioselective Substitution of Fluorine in F_8BINOL as a Versatile Route to New Ligands with Axial Chirality

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General: Anhydrous THF was obtained by distillation over sodium benzophenone ketyl under nitrogen. 2,2'-dimethoxy-5,5',6,6',7,7',8,8'-octafluoro-1,1'-binaphthyl **2c** and 2,2'-dihydroxy-5,5',6,6',7,7',8,8'-octafluoro-1,1'-binaphthyl **2a** were prepared according to literature procedures.[1] Column chromatography was carried out using 230-400 mesh silica gel. Fresh potassium hydroxide was used in substitution protocols. Catalytic diethylzinc addition and sulfide oxidation experiments were carried out according to literature protocols.[2,3]

2,2'-dibenzyloxy-5,5',6,6',7,7',8,8'-octafluoro-1,1'-binaphthyl (2d)

To a solution of 2,2'-dihydroxy-5,5',6,6',7,7',8,8'-octafluoro-1,1'-binaphthyl **2a** (215.2mg, 0.5mmol) and potassium carbonate (691mg, 5mmol) in THF(15mL) was added benzyl bromide (0.6mL, 5mmol). The mixture was stirred and refluxed for 20hrs. The reaction mixture was diluted with ether and washed with aqueous HCl (5%). The solvent and excess benzyl bromide were removed under reduced pressure. Recrystallization from hexanes / dichloromethane gave **2d** as white solid (224.2mg, 80%). ^{1}H NMR(400MHz, $CDCl_3$): δ8.16(d, J=9.6Hz, 2H), 7.50(d, J=9.6Hz, 2H), 7.23-7.16(m, 6H), 6.98-6.96(m,4H), 5.12(s, 4H). ^{19}F NMR(300MHz, $CDCl_3$): δ-146.72(t, J=17.7Hz), -150.55(dd, J=16.2Hz, 5.1Hz), -158.68(t, J=20.1Hz), -163.22(t, J=20.1Hz).

2,2',7,7'-tetramethoxy-5,5',6,6',8,8'-hexafluoro-1,1'-binaphthyl (3a)

To a solution of 2,2'-dimethoxy-5,5',6,6',7,7',8,8'-octafluoro-1,1'-binaphthyl[1] (91.7mg, 0.2mmol) in anhydrous THF (10mL) was added 81μl (2.0mmol) methanol and 112mg (2.0mmol) KOH. The mixture was stirred and refluxed for 12hrs. The reaction mixture was diluted with ether and washed with aqueous HCl (5%) . The resulting organic extract was dried over $MgSO_4$ and concentrated. Purification of the residue by column chromatography afforded **3a** (91.0mg, 75%) as white solid.

^{1}H NMR(400 MHz, $CDCl_3$): δ8.10(d, J=9.2Hz, 2H), 7.42(d, J=9.2Hz, 2H), 3.91(S, 6H), 3.75(S, 6H). ^{19}F NMR(400MHz, $CDCl_3$): δ -140.93(d, J=16.8Hz), -152.65(dd, J=16.8Hz, 3.2Hz), -158.80(d, J=19.6Hz). ^{13}C NMR(100MHz, $CDCl_3$): δ155.6(s), 147.2(dt, J=249.2Hz, 3.8Hz), 142.4(ddd, J=249.0Hz, 6.1Hz, 4.6Hz), 139.9(ddd, J=250.0Hz, 9.2Hz, 4.5Hz), 135.9(m), 121.6(m), 120.9(m), 117.2(s), 116.0(dd, J=9.9Hz, 4.5Hz), 114.3(s), 62.5(s), 56.9(s). HREI-MS, m/z: Calcd for $C_{24}H_{16}F_6O_4$ 482.0953; found 482.0958.

2,2'-dimethoxy-7,7'-diethoxy-5,5'6,6',8,8'-hexafluoro-1,1'-binaphthyl (3b)

Using the general procedure described above, a total of 78.1mg (71%) of **3b** was obtained as white solid. ^{1}H NMR(400MHz, $CDCl_3$): δ 8.09(d, J=9.2Hz, 2H), 7.38(d, J=9.6Hz, 2H), 4.11(q, J=6.8Hz, 4H), 3.73(S, 6H), 1.29(t, J= 6.8Hz, 6H). ^{19}F NMR(400MHz, $CDCl_3$): δ -139.91(d, J=16.8Hz), -152.68(dd, J=16.8Hz, 2.8Hz), -158.08(d, J=19.6Hz). ^{13}C NMR(100MHz, $CDCl_3$):δ155.6(s), 147.6(dt, J=249.3Hz, 3.8Hz), 142.3(ddd, J=247.0Hz, 6.0Hz, 4.6Hz), 140.2(ddd, J=246.0Hz, 9.2Hz, 4.5Hz), 134.8(m), 121.5(m), 120.9(m), 117.2(s), 116.1(dd, J=9.8Hz, 3.8Hz), 114.2(s), 71.0(s), 56.9(s), 15.5(s). HREI-MS, m/z: Calcd for $C_{26}H_{20}F_6O_4$, 510.1255; found 510.1266.

2,2'-dimethoxy-7,7'-di-*iso*-propoxy-5,5',6,6',8,8'-hexafluoro-1,1'-binaphthyl (3c)

Using the general procedure described above, a total of 87.9mg (80%) of **3c** was obtained as white foam. ^{1}H NMR(400MHz, $CDCl_3$): δ8.08(d, J=9.2Hz, 2H), 7.38(d, J=9.2Hz, 2H), 4.36(sep, J=6.0Hz, 2H), 3.71(s, 6H), 1.23(dd, J=6.0Hz, 3.2Hz, 12H). ^{19}F NMR(400MHz, $CDCl_3$): δ -157.19(d, J=19.6Hz), -152.81(dd, J=16.8Hz, 2.8Hz), -138.60(d, J=16.8Hz). ^{13}C NMR(100MHz, $CDCl_3$): δ 155.6(s), 148.2(dt, J=250.0Hz, 3.8Hz), 142.3(ddd,

J=247.0Hz, 6.0Hz, 4.6Hz), 140.6(ddd, J=245.0Hz, 9.2Hz, 3.8Hz), 133.8(m), 121.5(m), 120.9(m), 117.3(s), 116.2(dd, J=10.6Hz, 3.8Hz), 114.2(s), 77.7(s), 56.8(s), 22.4(s). HREI-MS m/z: Calcd for $C_{28}H_{24}F_6O_4$ 538.1583; found 538.1579.

2,2'-dimethoxy-7,7'-dibenzyloxy- 5,5',6,6',8,8'-hexafluoro-1,1'-binaphthyl (3d)

Using the general procedure described above, a total of 98.6mg (69%) of **3d** was obtained as white foam. ^{1}H NMR(400MHz, $CDCl_3$): δ8.07(d, J=9.2Hz, 2H), 7.37-7.22(m, 12H), 5.06(s, 4H), 3.68(s, 6H). ^{19}F NMR(400MHz, $CDCl_3$): δ -138.78(d, J=16.8Hz), -152.49(dd, J=16.8Hz, 2.8Hz), -157.48(d, J=20.8Hz). ^{13}C NMR(100MHz, $CDCl_3$): δ155.6(s), 147.6(dt, J=250.0Hz, 3.8Hz), 142.3(ddd, J=247.0Hz, 6.8Hz, 4.6Hz), 140.1(ddd, J=246.0Hz, 9.1Hz, 3.8Hz), 136.3(s), 134.4(m), 128.7(d, J=3.1HZ), 128.6(d, J=4.6Hz), 128.5(s), 121.6(m), 120.9(m), 117.2(s), 116.2(dd, J=9.8Hz, 4.6Hz), 114.3(s), 76.5(s), 56.9(s). HREI-MS, m/z: Calcd for $C_{36}H_{24}F_6O_4$, 634.1560; found 634.1579.

2,2'-dibenzyloxy-7,7'-dimethoxy- 5,5',6,6',8,8'-hexafluoro-1,1'-binaphthyl (3e)

To the mixture of 2,2'-dibenzyloxy-5,5',6,6',7,7',8,8'-octafluoro-1,1'-binaphthyl (224.2mg, 0.4mmol) and potassium hydroxide (224mg, 4.0mmol) in THF (20mL) was added methanol (162μl, 4.0mmol). The mixture was stirred and refluxed for 12hrs. The reaction mixture was diluted with ether and washed with aqueous HCl (5%). The resulting organic extract was dried over $MgSO_4$ and concentrated. Purification of the residue by column chromatography afforded pure **3e** as white foam (197.9mg, 70%). ^{1}H NMR(400MHz, $CDCl_3$): δ7.93(d, J=9.2Hz, 2H), 7.24(d, J=9.6Hz, 2H), 7.01-6.96(m, 6H), 6.76(d, J=7.2Hz, 4H), 4.90(s, 4H), 3.74(s, 6H). ^{19}F NMR(300MHz, $CDCl_3$): δ-140.18(d, J=17.3Hz), -152.35(dd, J=16.7Hz, 3.1Hz), -158.30(d, J=21.5Hz).

2,2'-dibenzyloxy-7,7'-diethoxy- 5,5',6,6',8,8'-hexafluoro-1,1'-binaphthyl (3f)

Using the general procedure described for **3e** with 232μl (4.0mmol) ethanol in place of methanol, a total of 208.4mg (79%) of **3f** was obtained. ^{1}H NMR(400MHz, $CDCl_3$): δ8.05(d, J=9.2Hz, 2H), 7.36(d, J=9.2Hz, 2H), 7.16-7.08(m, 6H), 6.88(d, J=7.2Hz, 4H), 5.02(s, 4H), 4.08(q, J=7.2Hz, 4H), 1.27(t, J=7.2Hz, 6H). ^{19}F NMR(400MHz, $CDCl_3$): δ-139.37(d, J=16.8Hz), -152.64(dd, J=16.8Hz, 2.8Hz), -157.73(d, J=20.8Hz).

2,2'-dibenzyloxy-7,7'-di-*iso*-propoxy- 5,5',6,6',8,8'-hexafluoro-1,1'-binaphthyl (3g)

Using the general procedure described for **3e** with 308µl (4.0mmol) *iso*-propanol in place of methanol, a total of 253.0mg (77%) of **3g** was obtained. ^{1}H NMR(400MHz, $CDCl_3$): δ8.05(d, J=9.2Hz, 2H), 7.36(d, J=9.2Hz, 2H), 7.14-7.08(m, 6H), 6.87(d, J=7.2Hz, 4H), 5.01(s, 4H), 4.33(sept, J=6.0Hz, 2H), 1.21(dd, J=6.4Hz, 5.2Hz, 12H). ^{19}F NMR(400MHz, $CDCl_3$): δ-138.15(d, J=16.8Hz), -152.78(dd, J=17.2Hz, 2.8Hz), -156.80(d, J=19.6Hz).

2,2'-dihydroxy-7,7'-dimethoxy- 5,5',6,6',8,8'-hexafluoro-1,1'-binaphthyl (4a)

To a solution of 2,2'-dibenzyloxy-7,7'-dimethoxy-5,5',6,6',8,8'-hexafluoro-1,1'-binaphthyl **3e** (126.5mg, 0.2mmol) was added Pd/C (85.2mg, 10%) under an atmosphere of hydrogen at room temperature. After stirring for 10hrs, the reaction mixture was filtered and concentrated. Purification of the residue by column chromatography afforded pure **4a** (quantitatively) as white foam. ^{1}H NMR(400MHz, $CDCl_3$): δ8.06(d, J=8.8Hz, 2H), 7.30(d, J=9.2Hz, 2H), 5.39(s, 2H), 3.92(s, 6H). ^{19}F NMR(400MHz, $CDCl_3$): δ -142.14(d, J=15.2Hz), -151.24(dd, J=16.8Hz, 2.8Hz), -157.16(d, J=19.6Hz). ^{13}C NMR(100MHz, $CDCl_3$): δ 153.2(s), 146.6(dt, J=248.5Hz, 3.8Hz), 142.7(ddd, J=248.0Hz, 6.0Hz, 4.6Hz), 140.3(ddd, J=248.0Hz, 8.3Hz, 4.6Hz), 136.7(m), 123.5(m), 120.5(m), 118.5(s), 115.9(dd, J=10.6Hz, 3.8Hz), 108.6(s), 62.5(m). HREI-MS: m/z: calcd for $C_{22}H_{12}F_6O_4$ 454.0642; found 454.0640.

2,2'-dihydroxy-7,7'-diethoxy- 5,5',6,6',8,8'-hexafluoro-1,1'-binaphthyl (4b)

Using the general procedure described for **4a** with 132.5mg (0.2mmol) **3f** in place of **3e**, **4b** was obtained quantitatively. ^{1}H NMR(400MHz, $CDCl_3$): δ8.09(d, J=9.2Hz, 2H), 7.32(d, J=9.2Hz, 2H), 5.25(s, 2H), 4.13(q, J=7.2Hz, 4H), 1.30(t, J=7.2Hz, 6H). ^{19}F NMR(400MHz, $CDCl_3$): δ-141.48(d, J=15.6Hz), -151.40(dd, J=16.8Hz, 4.4Hz), -156.52(d, J=19.6Hz). ^{13}C NMR(100MHz, $CDCl_3$): δ153.2(s), 147.0(dt, J=248.5Hz, 3.8Hz), 142.7(ddd, J=247.8Hz, 6.0Hz, 4.6Hz), 140.7(ddd, J=247.4Hz, 9.1Hz, 4.5Hz), 135.7(dt, J=13.7Hz, 2.3Hz), 123.6(t, J=5.4Hz), 120.4(dd, J=3.8Hz), 118.4(s), 116.1(dd, J=10.6Hz, 3.8Hz), 108.4(s), 71.2(d, J=3.0Hz), 15.5(s).

2,2'-dihydroxy-7,7'-di-*iso*propoxy- 5,5',6,6',8,8'-hexafluoro-1,1'-binaphthyl (4c)

Using the general procedure described as **4a** with 138.1mg (0.2mmol) **3g** in place of **3e**, **4c** was obtained quantitatively. ^{1}H NMR(400MHz, $CDCl_3$): δ8.10(d, J=9.2Hz, 2H), 7.32(d, J=8.8Hz, 2H), 5.22(s, 2H), 4.38(sept, J=6.4Hz, 2H), 1.23(dd, J=6.4Hz, 5.2Hz, 12H). ^{19}F NMR(400MHz, $CDCl_3$): δ-140.26(d, J=15.6Hz), -151.48(dd, J=16.8Hz, 2.8Hz), -155.62(d, J=21.2Hz). ^{13}C NMR(100MHz, $CDCl_3$): δ152.9(s), 147.4(d, J=248.5Hz), 142.4(d, J=247.8Hz), 140.8(dd, J=247.0Hz, 11.4Hz), 134.5(t, J=14.5Hz), 123.4(s), 120.1(s), 118.2(s), 116.0(d, J=13.7Hz), 108.1(t, J=31.1Hz), 77.8(s), 22.2(s).

2,2',6,6',7,7'-hexamethoxy- 5,5', 8,8'-tetrafluoro-1,1'-binaphthyl (5)

To a solution of 2,2',7,7'-tetramethoxy-5,5',6,6',8,8'-hexafluoro-1,1'-binaphthyl **3a** (96.5mg, 0.2mmol) in anhydrous THF (8mL) was added 2.0mL (excess) methanol and 240mg (excess) KOH. The mixture was stirred and refluxed for 5 days. The reaction mixture was diluted with ether and washed with aqueous HCl (5%) . The resulting organic extract was dried over $MgSO_4$ and concentrated. Purification of the residue by column chromatography afforded **5** (32.4mg, 32%) as white foam. ^{1}H NMR(400MHz, $CDCl_3$): δ8.05(d, J=9.2Hz, 2H), 7.35(d, J=9.2Hz, 2H), 4.05(s, 6H), 3.85(s, 6H), 3.74(s, 6H). ^{19}F NMR(400MHz, $CDCl_3$): δ-141.47(d, J=18.4Hz), -146.33(d, J=16.8Hz). ^{13}C NMR(100MHz, $CDCl_3$): δ 155.29 (d, J=3.8 Hz), 148.43 (dd, J=3.8, 96.1), 145.96 (dd, J=3.8, 93.8 Hz), 139.87 (dd, J=4.58, 13.7 Hz), 136.27 (dd, J=2.29, 11.44 Hz), 121.22 (d, J=4.6 Hz), 121.10, 117.49, 116.78 (dd, J=4.6, 16.02 Hz), 113.92, 62.21 (d, J=4.6 Hz), 62.16 (d, J= 5.3 Hz), 57.00. HREI-MS m/z: calcd for $C_{26}H_{22}F_4O_6$ 506.1341, found 506.1353.

References

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