A General and Mild Ullmann-Type Synthesis of Diaryl Ethers

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Supporting Information

General Considerations

All reactions were carried out in 35 mL Schlenk tubes under a pure and dry nitrogen atmosphere. Acetonitrile was distilled under nitrogen from P_4O_{10} and stored on 3 Å activated molecular sieves[1] under a nitrogen atmosphere. DMF was distilled under vacuum from $MgSO_4$ and stored protected from light on 4 Å activated molecular sieves under a nitrogen atmosphere. All solid materials were stored in the presence of P_4O_{10} in a benchtop desiccator under vacuum at room temperature and weighed in the air. K_3PO_4 (Fluka), K_2CO_3 (Aldrich) and Cs_2CO_3 (Aldrich) were ground to a fine powder. Copper (I) iodide and copper (I) bromide were purified according to literature procedures.[2] The former was stored protected from light. Copper (I) oxide and copper (II) oxide (both Aldrich) were used without further purification. Salicylaldoxime and dimethylglyoxime were purchased from commercial sources. The former was recrystallized in petroleum ether prior to use. All aryl halides and phenols were purchased from commercial sources (Aldrich, Acros, Avocado, Fluka, Lancaster). If solids, they were recrystallized in an appropriate solvent.[3] If liquids, they were distilled under vacuum and stored under an atmosphere of nitrogen. Special care was taken with liquid aryl iodides: the samples were regularly distilled over copper powder to remove iodine and stored protected from light. All phenols were also stored protected from light. Molecular sieves were activated and stored under vacuum at 100 °C in the presence of P_4O_{10}.

Isolated yields refer to compounds estimated to be 95 % pure or higher as determined by GC and ^{1}H NMR. Flash column chromatography was performed with SDS 60 A C.C silica gel (35-70 μm or 70-200 μm). Thin layer chromatography was carried out using Merck silica gel 60 F_{254} plates. All products were characterized by ^{1}H NMR, ^{13}C NMR and GC/MS. New compounds and previously partially characterized compounds were further characterized by IR and elemental analysis. IR spectra were recorded on a Nicolet 210 FT-IR instrument (neat, thin film for liquid products and KBr pellet or in dichloromethane solution for solid products). Elemental analysis was performed by the CNRS Service Central d'Analyse, Vernaison, France. ^{1}H NMR and ^{13}C {^{1}H} NMR spectra were recorded at room temperature on a Bruker AC 200 MHz or a Bruker Avance 250 MHz

instrument with chemical shifts reported in ppm relative to the residual deuterated solvent peak. ^{19}F {^{1}H} NMR spectra were recorded at room temperature on a Bruker Avance 250 MHz instrument with chemical shifts reported in ppm relative to $CFCl_3$. The peak patterns are indicated as s, singlet; d, doublet; t, triplet; q, quadruplet; dd, doublet of doublets; m, multiplet. Gas chromatographic analysis were performed on a Delsi Nermag DI-200 instrument with a FID detector, a Delsi Nermag Enica 31 integrator and a SGE BPX5 25 m x 0.53 mm semi-capillary apolar column (Stationary phase: 5 % phenylpolysil-phenylenesiloxane film, 1 µm). Gas chromatography - mass spectra (GC/MS) were recorded on an Agilent Technologies 6890 N instrument with an Agilent 5973 N mass detector (EI) and a HP5-MS 30 m x 0.25 mm capillary apolar column (Stationary phase: 5 % diphenyldimethylpolysiloxane film, 0.25 µm). FAB+ mass spectra were recorded on a JEOL JMS-DX300 spectrometer (3 Kev, xenon) in a *m*-nitrobenzylalcohol matrix. Melting points were determined using a Büchi B-540 apparatus and are uncorrected.

General procedure for the O-arylation of phenols (2 mmol scale)

After standard cycles of evacuation and back-filling with dry and pure nitrogen, an oven-dried Schlenk tube equipped with a magnetic stirring bar was charged with Cu_2O (0.1 mmol), the ligand (0.4 mmol), Cs_2CO_3 (4.0 mmol), activated and powdered 3 Å molecular sieves (600 mg), the phenol coupling partner (2.0 mmol), if a solid, and the aryl halide (3.0 mmol), if a solid. The tube was evacuated, back-filled with nitrogen and capped with a rubber septum. If liquids, the phenol and the aryl halide were added under a stream of nitrogen by syringe at room temperature, followed by anhydrous and degassed acetonitrile or DMF (1.2 mL). The septum was removed, the tube sealed under a positive pressure of nitrogen and stirred in an oil bath (preheated to 82 °C or 110 °C), for the required time period. The reaction mixture was allowed to cool to room temperature, diluted with dichloromethane and filtered through a plug of celite®, the filter cake being further washed with dichloromethane (~ 20 mL). The filtrate was concentrated *in vacuo* to yield the crude product, that was purified by silica gel chromatography with an eluent of hexanes and dichloromethane.

General procedure for reactivity comparisons of phenols or aryl halides (0.5 mmol scale)

After standard cycles of evacuation and back-filling with dry and pure nitrogen, a 35 mL oven-dried Schlenk tube equipped with a magnetic stirring bar (12 × 4.5 mm) was charged with Cu_2O (25 µmol), the ligand (0.1 mmol), Cs_2CO_3 (1.0 mmol), activated and powdered 3 Å molecular sieves (150 mg), the phenol coupling partner (0.5 mmol), if a solid, and the aryl halide (0.75 mmol), if a solid. The tube was evacuated, back-filled with nitrogen and capped with a rubber septum. If liquids, the phenol and the aryl halide were added under a stream of nitrogen by syringe at room temperature, followed by anhydrous and degassed acetonitrile or DMF (300 µL). The septum was removed, the tube sealed under a positive pressure of nitrogen and stirred in an oil bath (preheated to 82 °C or 110 °C), for the required time period. The reaction mixture was allowed to cool to room temperature and was diluted with dichloromethane (5 mL). 65 µL of 1,3-dimethoxybenzene (internal standard) were added. A small sample of the reaction mixture was taken and filtered through a plug of celite®, the filter cake being further washed with dichloromethane. The filtrate was washed three times with water and analyzed by gas chromatography. The GC yields were determined by obtaining the correction factors using authentic samples of the expected products.

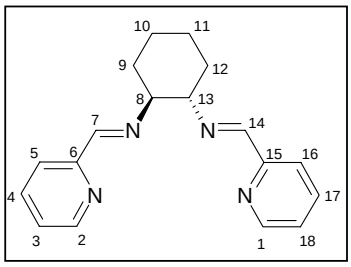
Experimental procedures and characterization data

Synthesis of *trans*-1,2-bis(2'-pyridylidenamino)-cyclohexane (Chxn-Py-Al, **1**)

Experimental procedure

To a solution of 2-pyridylaldehyde (6.66 mL, 70.0 mmol) in absolute ethanol (50 mL) were successively added anhydrous magnesium sulphate (12.65 g, 105.1 mmol) and rac-*trans*-1,2-diaminocyclohexane (4.2 mL, 35.0 mmol). The mixture was stirred for 20 hours at room temperature, heated at reflux for 2.5 hours and filtered through a frit while still hot. The solid was discarded and the filtrate was concentrated *in vacuo*. The residue was recrystallized in ethanol to provide 8.2 g (80 % yield) of the desired product as pale yellow crystals. Only the 1S, 2S stereoisomer is known in literature.[4]

Identification



Mp: 140-141 °C (EtOH).
^{1}H NMR (250 MHz, $CDCl_3$): δ 8.54 (ddd, 2H, $^3J_{HH}$ = 4.9 Hz, $^4J_{HH}$ = 1.7 Hz, $^5J_{HH}$ = 1.0 Hz, $H_{1,2}$), 8.30 (s, 2H, $H_{7,14}$), 7.87 (ddd, 2H, $^3J_{HH}$ = 7.9 Hz, $^4J_{HH}$ = 1.5 Hz, $^5J_{HH}$ = 1.0 Hz, $H_{5,16}$), 7.63 (dddd, 2H, $^3J_{HH}$ = 7.9 Hz, $^3J_{HH}$ = 7.5 Hz, $^4J_{HH}$ = 1.7 Hz, $^5J_{HH}$ = 0.6 Hz, $H_{4,17}$), 7.22 (ddd, 2H, $^3J_{HH}$ = 7.5 Hz, $^3J_{HH}$ = 4.9 Hz, $^4J_{HH}$ = 1.5 Hz, $H_{3,18}$), 3.50 (m, 2H, $H_{8,13}$), 1.83 (m, 6H), 1.40-1.55 (m, 2H).
^{13}C NMR {^{1}H} (50 MHz, $CDCl_3$): δ 161.42 ($C_{7,14}$), 154.61 ($C_{6,15}$), 149.21 ($C_{1,2}$), 136.39 ($C_{4,17}$), 124.43 ($C_{3,18}$), 121.29 ($C_{5,16}$), 73.53 ($C_{8,13}$), 32.70 ($C_{9,12}$), 24.33 ($C_{10,11}$).
FAB+ (NBA matrix) **:** M/Z 293 (100 %, M+1), 107 (52 %), 92 (38 %), 119 (25 %), 294 (23 %, M+2), 204 (22 %), 79 (21 %), 187 (20 %), 585 (1 %, 2M+1).
IR (KBr) : ν (cm^{-1}) = 3273, 3071, 3055, 3050, 2941, 2934, 2925, 2865, 2857, 2850, 1644, 1586, 1566, 1467, 1449, 1433, 1372, 1338, 991, 934, 867, 839, 771, 743.

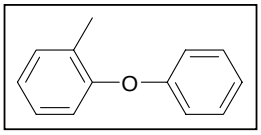
Copper-Catalyzed Synthesis of Diaryl Ethers

1) 2-methyl-diphenylether[5]

Experimental procedure (Table 5, entry 5)

Following the general procedure (82 °C, 40 hours), *o*-cresol (206 µL, 2.0 mmol) was coupled with iodobenzene (336 µL, 3.0 mmol) using cesium carbonate (1.303 g, 4.0 mmol), Cu_2O (14.4 mg, 0.1 mmol), Chxn-Py-Al (117 mg, 0.4 mmol), activated and powdered 3 Å molecular sieves (600 mg), and acetonitrile (1.2 mL). The crude oily residue was purified by flash chromatography on silica gel (eluent: hexanes) to provide 343 mg (93 % yield) of the desired product as a colorless oil, which can be crystallized in a few hours if left at 0 °C (colorless crystals, Lit.[5]: Mp = 21.5-22 °C).

Identification



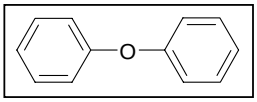
^{1}H NMR (200 MHz, $CDCl_3$): δ 7.19-7.35 (m, 3H), 7.00-7.18 (m, 3H), 6.87-6.94 (m, 3H), 2.25 (s, 3H, CH_3).
^{13}C NMR {^{1}H} (50 MHz, $CDCl_3$): δ 158.08 (Cq), 154.60 (Cq), 131.60 (CH), 130.14 (Cq), 129.81 (2 CH), 127.30 (CH), 124.15 (CH), 122.48 (CH), 119.94 (CH), 117.44 (2 CH), 16.35 (CH_3).
GC/MS (EI): rt = 15.25 min, M/Z = 184.
R_f: 0.36 (eluent: hexanes).

2) Diphenylether

Experimental procedure (Table 5, entry 6)

Following the general procedure (82 °C, 24 hours), phenol (188 mg, 2.0 mmol) was coupled with iodobenzene (336 µL, 3.0 mmol) using cesium carbonate (1.303 g, 4.0 mmol), Cu_2O (14.4 mg, 0.1 mmol), salicylaldoxime (55 mg, 0.4 mmol), activated and powdered 3 Å molecular sieves (600 mg), and acetonitrile (1.2 mL). The crude oily residue was purified by flash chromatography on silica gel (eluent: hexanes) to provide 344 mg (quantitative yield) of the desired product as a colorless oil, which can be crystallized in a few hours if left at -5 °C (colorless crystals).

Identification



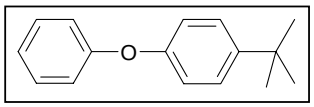
Mp: 26 °C (Lit.[6]: 26.85 °C).
^{1}H NMR (200 MHz, $CDCl_3$): δ 7.37-7.47 (m, 4H), 7.10-7.23 (m, 6H).
^{13}C NMR {^{1}H} (50 MHz, $CDCl_3$): δ 157.38 (2 Cq), 129.88 (4 CH), 123.35 (2 CH), 119.02 (4 CH).
GC/MS (EI): rt = 14.43 min, M/Z = 170.
R_f: 0.33 (eluent: hexanes).

3) 4-*t*-butyl-diphenylether

Experimental procedure (Table 5, entry 7)

Following the general procedure (82 °C, 25 hours), 4-*t*-butylphenol (300 mg, 2.0 mmol) was coupled with iodobenzene (336 µL, 3.0 mmol) using cesium carbonate (1.303 g, 4.0 mmol), Cu_2O (14.4 mg, 0.1 mmol), Chxn-Py-Al (117 mg, 0.4 mmol), activated and powdered 3 Å molecular sieves (600 mg), and acetonitrile (1.2 mL). The crude oily residue was purified by flash chromatography on silica gel (eluent: hexanes) to provide 430 mg (95 % yield) of the desired product as a colorless oil, which can be crystallized in a few hours if left at -5 °C (colorless crystals).

Identification



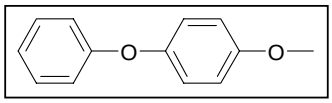
Mp: 52 °C (Lit.[7]: 53-54 °C).
^{1}H NMR (200 MHz, DMSO-d_6): δ 7.33-7.41 (m, 4H), 7.06-7.14 (m, 1H), 6.91-6.99 (m, 4H), 1.27 (s, 9H, Me).
^{13}C NMR {^{1}H} (50 MHz, DMSO-d_6): δ 156.94 (Cq), 154.09 (Cq), 145.73 (Cq), 129.88 (2 CH), 126.61 (2 CH), 123.05 (CH), 118.21 (4 CH), 33.96 (Cq), 31.18 (3 CH_3).
GC/MS (EI): rt = 18.50 min, M/Z = 226.
R_f: 0.36 (eluent: hexanes).

4) 4-methoxy-diphenylether[8]

Experimental procedure (Table 5, entry 8)

Following the general procedure (82 °C, 28 hours), 4-hydroxyanisole (248 mg, 2.0 mmol) was coupled with iodobenzene (336 µL, 3.0 mmol) using cesium carbonate (1.303 g, 4.0 mmol), Cu_2O (14.4 mg, 0.1 mmol), Chxn-Py-Al (117 mg, 0.4 mmol), activated and powdered 3 Å molecular sieves (600 mg), and acetonitrile (1.2 mL). The crude orange oil was purified by flash chromatography on silica gel (eluent: hexanes / dichloromethane 100/0 to 95/5) to provide 380 mg (95 % yield) of the desired product as a colorless oil.

Identification



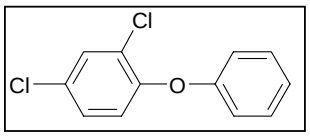
^{1}H NMR (200 MHz, $CDCl_3$): δ 7.30-7.39 (m, 2H), 6.89-7.09 (m, 7H), 3.84 (s, 3H).
^{13}C NMR {^{1}H} (50 MHz, $CDCl_3$): δ 158.60 (Cq), 155.97 (Cq), 150.18 (Cq), 129.69 (2 CH), 122.49 (CH), 120.91 (2 CH), 117.64 (2 CH), 114.92 (2 CH), 55.67 (CH_3).
GC/MS (EI): rt = 17.67 min, M/Z = 200.
R_f: 0.25 (eluent: hexanes / dichloromethane 80/20).

5) 2,4-dichloro-diphenylether[9]

Experimental procedure (Table 5, entry 9)

Following the general procedure (82 °C, 40 hours), 2,4-dichlorophenol (326 mg, 2.0 mmol) was coupled with iodobenzene (336 µL, 3.0 mmol) using cesium carbonate (1.303 g, 4.0 mmol), Cu_2O (14.4 mg, 0.1 mmol), salicylaldoxime (55 mg, 0.4 mmol), activated and powdered 3 Å molecular sieves (600 mg), and acetonitrile (1.2 mL). The crude product was purified by flash chromatography on silica gel (eluent: hexanes) to provide 191 mg (40 % yield) of the desired product as a colorless oil.

Identification



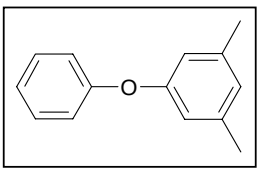
^{1}H NMR (200 MHz, $CDCl_3$): δ 7.50 (dd, 1H, $^4J_{HH}$ = 2.3 Hz, $^5J_{HH}$ = 0.6 Hz, H_4), 7.34-7.42 (m, 2H), 7.15-7.19 (m, 2H), 6.90-7.02 (m, 3H).
^{13}C NMR {^{1}H} (50 MHz, $CDCl_3$): δ 156.66 (Cq), 151.49 (Cq), 130.52 (CH), 129.96 (2 CH), 129.16 (Cq), 128.08 (CH), 126.65 (Cq), 123.78 (CH), 121.39 (CH), 118.07 (2 CH).
GC/MS (EI): rt = 18.51 min, M/Z = 238, 240 and 242.
R_f: 0.40 (eluent: hexanes).

6) 3,5-dimethyl-diphenylether

Experimental procedure (Table 5, entry 11)

Following the general procedure (82 °C, 29 hours), 3,5-dimethylphenol (244 mg, 2.0 mmol) was coupled with iodobenzene (336 µL, 3.0 mmol) using cesium carbonate (1.303 g, 4.0 mmol), Cu_2O (14.4 mg, 0.1 mmol), Chxn-Py-Al (117 mg, 0.4 mmol), activated and powdered 3 Å molecular sieves (600 mg), and acetonitrile (1.2 mL). The crude brown oil was purified by flash chromatography on silica gel (eluent: hexanes) to provide 381 mg (96 % yield) of the desired product as a colorless oil.

Identification



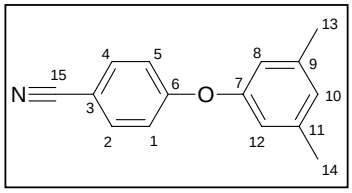
^{1}H NMR (200 MHz, $CDCl_3$): δ^{10} 7.28-7.42 (m, 2H), 7.12-7.17 (m, 1H), 7.03-7.14 (m, 2H), 6.79 (m, 1H), 6.69 (m, 2H), 2.33 (s, 6H, CH_3).
^{13}C NMR {^{1}H} (50 MHz, $CDCl_3$): δ^{10} 157.50 (Cq), 157.22 (Cq), 139.61 (2 Cq), 129.70 (2 CH), 125.04 (CH), 123.02 (CH), 118.89 (2 CH), 116.67 (2 CH), 21.35 (2 CH_3).
GC/MS (EI): rt = 16.87 min, M/Z = 198.
R_f: 0.19 (eluent: hexanes).

7) 3',5'-dimethyl-4-cyano-diphenylether[11]

Experimental procedure (Table 5, entry 12)

Following the general procedure (82 °C, 24 hours), 3,5-dimethylphenol (244 mg, 2.0 mmol) was coupled with 4-iodobenzonitrile (595 mg, 2.6 mmol) using cesium carbonate (1.303 g, 4.0 mmol), Cu_2O (14.4 mg, 0.1 mmol), Chxn-Py-Al (117 mg, 0.4 mmol), activated and powdered 3 Å molecular sieves (600 mg), and acetonitrile (1.6 mL). The crude product was dried for 2 hours at 100 °C and then purified by flash chromatography on silica gel (eluent: gradient hexanes / dichloromethane 100/0 to 50/50) to provide 415 mg (93 % yield) of the desired product as an orange oil.

Identification



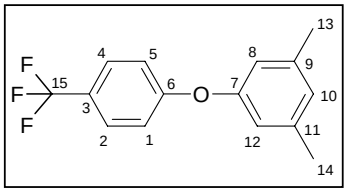
Mp: 58 °C.
^{1}H NMR (200 MHz, $CDCl_3$): δ 7.53-7.60 (m, 2H), 6.95-7.00 (m, 2H), 6.86 (m, 1H), 6.68 (m, 2H), 2.32 (s, 6H, CH_3).
^{13}C NMR {^{1}H} (50 MHz, $CDCl_3$): δ 161.90 (C_6), 154.76 (C_7), 140.17 ($C_{9,11}$), 134.07 ($C_{2,4}$), 126.86 (C_{10}), 118.92 (C_{15}), 118.03 (2 CH), 117.88 (2 CH), 105.55 (C_3), 21.28 ($C_{13,14}$).
GC/MS (EI): rt = 20.54 min, M/Z = 223.
IR (KBr) : ν (cm^{-1}) = 3058, 3017, 2958, 2230 (CN), 1603, 1587, 1504, 1298, 1239 (C-O), 1166, 1134, 1024, 950, 859, 838.
R_f: 0.32 (eluent: hexanes / dichloromethane 50/50).

8) 3',5'-dimethyl-4-trifluoromethyl-diphenylether

Experimental procedure (Table 5, entry 13)

Following the general procedure (82 °C, 24 hours), 3,5-dimethylphenol (244 mg, 2.0 mmol) was coupled with 1-iodo-4-trifluoromethyl-benzene (294 µL, 2.6 mmol) using cesium carbonate (1.303 g, 4.0 mmol), Cu_2O (14.4 mg, 0.1 mmol), Chxn-Py-Al (117 mg, 0.4 mmol), activated and powdered 3 Å molecular sieves (600 mg), and acetonitrile (1.2 mL). The crude product was purified by flash chromatography on silica gel (eluent: hexanes) to provide 506 mg (95 % yield) of the desired product as an orange oil.

Identification



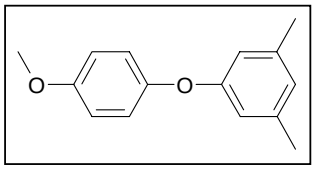
^{1}H NMR (200 MHz, $CDCl_3$): δ 7.59 (m, 2H, $H_{2,4}$), 7.06 (m, 2H, $H_{1,5}$), 6.87 (m, 1H, H_{10}), 6.71 (m, 2H, $H_{8,12}$), 2.35 (s, 6H, $H_{13,14}$).
^{13}C NMR {^{1}H} (50 MHz, $CDCl_3$): δ 160.78 (C_6), 155.65 (C_7), 140.01 ($C_{9,11}$), 127.04 (q, $^3J_{CF}$ = 3.8 Hz, $C_{2,4}$), 126.25 (C_{10}), 124.59 (q, $^2J_{CF}$ = 32.7 Hz, C_3), 118.92 (q, $^1J_{CF}$ = 271.1 Hz, C_{15}), 117.78 ($C_{8,12}$), 117.63 ($C_{1,5}$), 21.26 ($C_{13,14}$).
^{19}F NMR {^{1}H} (235 MHz, $CDCl_3$): δ -62.11 (s).
Elemental analysis: Calculated for $C_{15}H_{13}F_3O$: C, 67.66; H, 4.92; F, 21.41. Found: C, 67.37; H, 5.03; F, 21.80.
GC/MS (EI): rt = 16.71 min, M/Z = 266.
IR (CH_2Cl_2) : ν (cm^{-1}) = 3053, 2985, 1615, 1591, 1513, 1326 (CF_3), 1237 (C-O), 1169 (CF_3), 1123, 1066, 840.
R_f: 0.68 (eluent: hexanes).

9) 3',5'-dimethyl-4-methoxy-diphenylether

Experimental procedure (Table 5, entry 14)

Following the general procedure (82 °C, 48 hours), 3,5-dimethylphenol (244 mg, 2.0 mmol) was coupled with 4-iodoanisole (655 mg, 2.8 mmol) using cesium carbonate (1.303 g, 4.0 mmol), Cu_2O (14.4 mg, 0.1 mmol), Chxn-Py-Al (117 mg, 0.4 mmol), activated and powdered 3 Å molecular sieves (600 mg), and acetonitrile (1.12 mL). The crude product was dried for 2 hours at 100 °C and then purified by flash chromatography on silica gel (eluent: hexanes) to provide 420 mg (92 % yield) of the desired product as a colorless solid which can be recrystallized in petroleum ether.

Identification



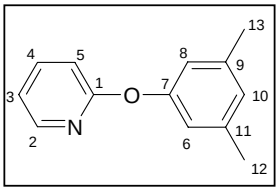
Mp: 67 °C (petroleum ether) (Lit.[12]: 67 °C).
^{1}H NMR (200 MHz, $CDCl_3$): δ 6.99-7.06 (m, 2H), 6.88-6.99 (m, 2H), 6.74 (m, 1H), 6.64 (m, 2H), 3.85 (s, 3H, MeO), 2.32 (s, 6H, Me).
^{13}C NMR {^{1}H} (50 MHz, $CDCl_3$): δ 158.52 (Cq), 155.76 (Cq), 150.26 (Cq), 139.45 (2 Cq), 124.22 (CH), 120.84 (2 CH), 115.31 (2 CH), 114.77 (2 CH), 55.59 (CH_3), 21.35 (2 CH_3).
GC/MS (EI): rt = 19.77 min, M/Z = 228.
R_f: 0.61 (eluent: hexanes).

10) 2-(3,5-dimethyl-phenoxy)-pyridine

Experimental procedure (Table 5, entry 15)

Following the general procedure (110 °C, 24 hours), 3,5-dimethylphenol (244 mg, 2.0 mmol) was coupled with 2-bromopyridine (292 µL, 3.0 mmol) using cesium carbonate (1.303 g, 4.0 mmol), Cu_2O (14.4 mg, 0.1 mmol), Chxn-Py-Al (117 mg, 0.4 mmol), activated and powdered 3 Å molecular sieves (600 mg), and acetonitrile (1.2 mL). The crude oily residue was dried for 2 hours at 100 °C and then purified by flash chromatography on silica gel (eluent: gradient hexanes / dichloromethane 100/0 to 85/15) to provide 371 mg (93 % yield) of the desired product as a yellow oil. This compound is not kown in literature.

Identification



^{1}H NMR (250 MHz, $CDCl_3$): δ 8.21 (ddd, 1H, $^3J_{HH}$ = 5.0 Hz, $^4J_{HH}$ = 2.0 Hz, $^5J_{HH}$ = 0.7 Hz, H_2), 7.66 (ddd, 1H, $^3J_{HH}$ = 8.2 Hz, $^3J_{HH}$ = 7.2 Hz, $^4J_{HH}$ = 2.0 Hz, H_4), 6.97 (ddd, 1H, $^3J_{HH}$ = 7.2 Hz, $^3J_{HH}$ = 5.0 Hz, $^4J_{HH}$ = 0.9 Hz, H_3), 6.88 (ddd, 1H, $^3J_{HH}$ = 8.2 Hz, $^4J_{HH}$ = 0.9 Hz, $^5J_{HH}$ = 0.7 Hz, H_5), 6.84 (m, 1H, H_{10}), 6.76 (m, 2H, $H_{6,8}$), 2.32 (s, 6H, $H_{12,13}$).
^{13}C NMR {^{1}H} (50 MHz, $CDCl_3$): δ 164.02 (C_1), 154.15 (C_7), 147.87 (C_2), 139.47 ($C_{9,11}$), 139.27 (C_4), 126.53 (C_{10}), 118.80 ($C_{6,8}$), 118.22 (C_5), 111.47 (C_3), 21.34 ($C_{12,13}$).
Elemental analysis: Calculated for $C_{13}H_{13}NO$: C, 78.21; H, 6.69; N, 7.04. Found: C, 78.36; H, 6.58; N, 7.03.
GC/MS (EI): rt = 17.65 min, M/Z = 199.
IR (KBr) : ν (cm^{-1}) = 3057, 3051, 3013, 2918, 2856, 1616, 1583, 1572, 1467, 1429, 1296, 1246 (C-O), 1138, 856, 779.
R_f: 0.22 (eluent: hexanes / dichloromethane 75/25).

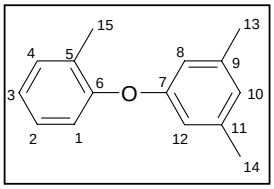
11) 2,3',5'-trimethyl-diphenylether

Experimental procedure (Table 5, entry 16)

Following the general procedure (82 °C, 118 hours), 3,5-dimethylphenol (244 mg, 2.0 mmol) was coupled with 2-iodotoluene (383 µL, 3.0 mmol) using cesium carbonate (1.303 g, 4.0 mmol), Cu_2O (14.4 mg,

0.1 mmol), Chxn-Py-Al (117 mg, 0.4 mmol), activated and powdered 3 Å molecular sieves (600 mg), and acetonitrile (1.2 mL). The crude oily residue was purified by flash chromatography on silica gel (eluent: hexanes) to provide 399 mg (94 % yield) of the desired product as an orange oil.

Identification



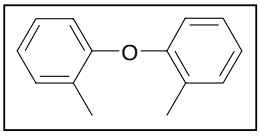
^{1}H NMR (200 MHz, $CDCl_3$): δ^{13} 7.08-7.33 (m, 3H), 6.95-6.99 (m, 1H), 6.76 (m, 1H), 6.61 (m, 2H, $H_{8,12}$), 2.33 (s, 6H, $H_{13,14}$), 2.32 (s, 3H, H_{15}).
^{13}C NMR {^{1}H} (50 MHz, $CDCl_3$): δ^{13} 157.94 (Cq), 154.69 (Cq), 139.55 ($C_{9,11}$), 131.41 (CH), 130.02 (C_5), 127.14 (CH), 124.22 (CH), 123.83 (CH), 119.81 (CH), 115.11 ($C_{8,12}$), 21.42 ($C_{13,14}$), 16.30 (C_{15}).
GC/MS (EI): rt = 17.46 min, M/Z = 212.
R_f: 0.26 (eluent: hexanes).

12) 2,2'-dimethyl-diphenylether[14]

Experimental procedure (Table 5, entry 17)

Following the general procedure (110 °C, 35 hours), *o*-cresol (206 µL, 2.0 mmol) was coupled with 2-iodotoluene (383 µL, 3.0 mmol) using cesium carbonate (1.303 g, 4.0 mmol), Cu_2O (14.4 mg, 0.1 mmol), Chxn-Py-Al (117 mg, 0.4 mmol), activated and powdered 3 Å molecular sieves (600 mg), and DMF (1.2 mL). The crude oily residue was purified by flash chromatography on silica gel (eluent: hexanes) to provide 389 mg (98 % yield) of the desired product as a colorless oil.

Identification



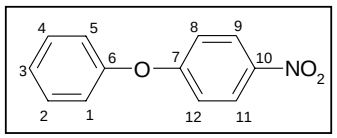
^{1}H NMR (200 MHz, $CDCl_3$): δ 7.32 (m, 2H), 7.04-7.25 (m, 4H), 6.81 (m, 2H), 2.38 (s, 6H, CH_3).
^{13}C NMR {^{1}H} (50 MHz, $CDCl_3$): δ 155.35 (Cq), 131.39 (CH), 128.90 (Cq), 127.09 (CH), 123.11 (CH), 117.74 (CH), 16.25 (CH_3).
GC/MS (EI): rt = 16.10 min, M/Z = 198.
R_f: 0.40 (eluent: hexanes).

13) 4-nitro-diphenylether

Experimental procedure (Table 5, entry 18)

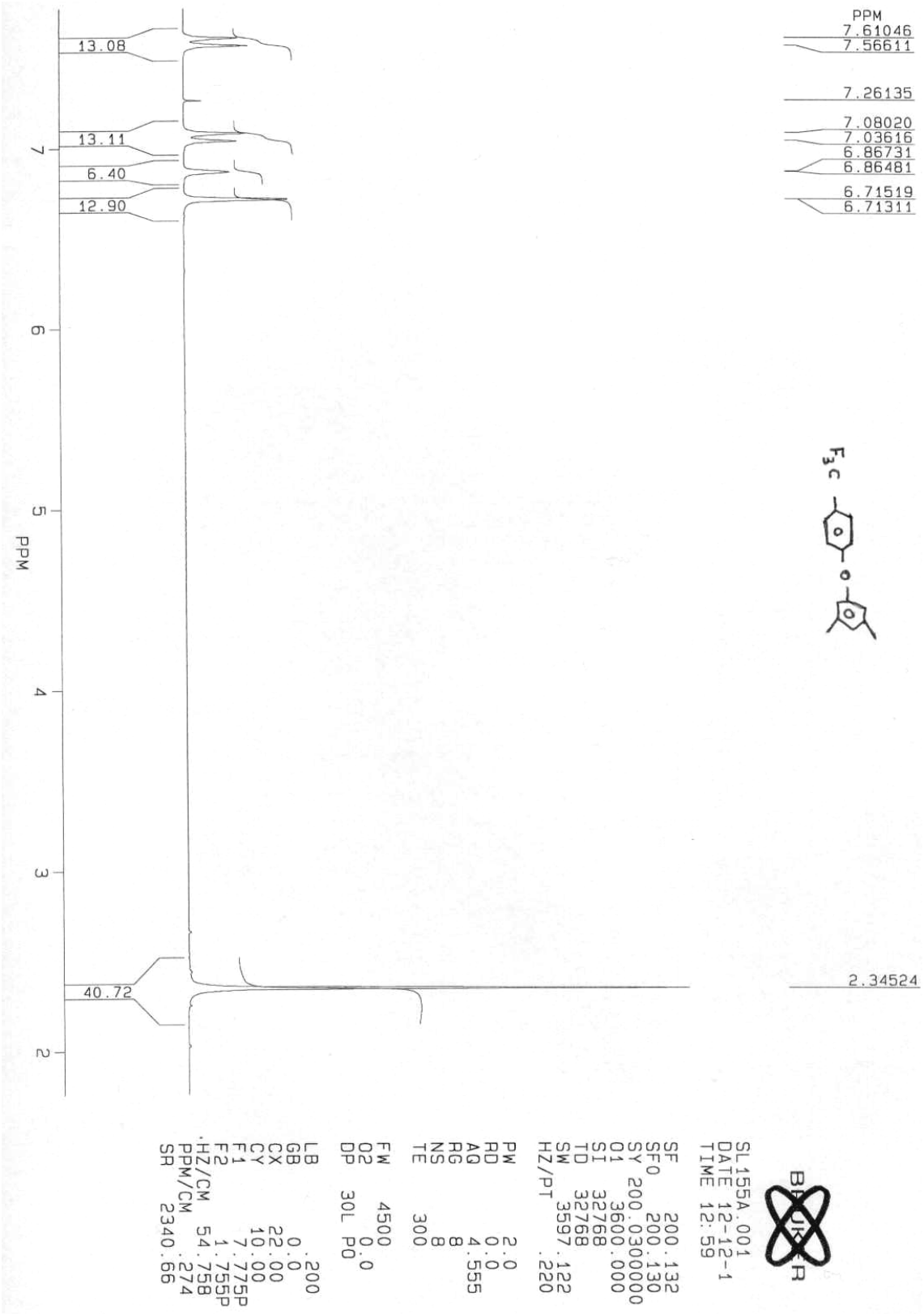
Following the general procedure (82 °C, 24 hours), phenol (188 mg, 2.0 mmol) was coupled with 4-iodonitrobenzene (747 mg, 3.0 mmol) using cesium carbonate (1.303 g, 4.0 mmol), Cu_2O (14.4 mg, 0.1 mmol), Chxn-Py-Al (117 mg, 0.4 mmol), activated and powdered 3 Å molecular sieves (600 mg), and acetonitrile (1.2 mL). The crude product was purified by flash chromatography on silica gel (eluent: hexanes) to provide 400 mg (93 % yield) of the desired product as a light yellow solid, which can be recrystallized in petroleum ether / diethylether.

Identification



Mp: 60 °C (petroleum ether / diethylether) (Lit.[15]: 60 °C, MeOH).
^{1}H NMR (200 MHz, $CDCl_3$): δ 8.15-8.21 (m, 2H, $H_{9,11}$), 7.40-7.48 (m, 2H, $H_{2,4}$), 7.21-7.30 (m, 1H, H_3), 7.07-7.13 (m, 2H, $H_{1,5}$), 6.98-7.05 (m, 2H, $H_{8,12}$).
^{13}C NMR {^{1}H} (50 MHz, $CDCl_3$): δ 163.38 (C_7), 154.72 (C_6), 142.64 (C_{10}), 130.34 ($C_{2,4}$), 125.94 ($C_{9,11}$), 125.44 (C_3), 120.55 ($C_{1,5}$), 117.10 ($C_{8,12}$).
GC/MS (EI): rt = 19.99 min, M/Z = 215.
R_f: 0.37 (eluent: hexanes).

^{1}H NMR spectrum of 3',5'-dimethyl-4-trifluoromethyldiphenylether (Table 5, Entry 13). (200 MHz, $CDCl_3$):



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