Improvements in Cross Coupling Reactions of Hypervalent Siloxane Derivatives

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SUPPORTING INFORMATION

General. All ^{1}H and ^{13}C NMR spectra were recorded on a 400 MHz instrument in $CDCl_3$ unless otherwise indicated. Gas chromatography data was obtained on a Hewlett Packard 5890A equipped with a 25m methyl silicon capillary column. Mass spectral data was obtained on a VG-7070E. GCMS was performed on a Shimadzu QP5000MS coupled with a GC17A gas chromatograph.Dimethyl formamide (DMF) was distilled from molecular sieves. Glassware used in the reactions was dried overnight in an oven at 120 ^{o}C. All reactions were performed under an atmosphere of argon unless noted otherwise.

Phenyltrimethoxysilane, tri-*ortho*-tolyl-phosphine (P(*o*-tol)$_3$), tris(dibenzylideneacetonedipalladium (0) (Pd_2dba_3), all aryl bromides, and all aryl chlorides were purchased from Aldrich and used as received. Palladium (II) acetate ($Pd(OAc)_2$) was purchased from Acros. 2-(Dicyclohexylphosphino)biphenyl (Figure, **1**) was purchased from Strem Chemical Company and recrystallized from absolute ethanol (EtOH) prior to use. Tri(*tert*-butyl)phosphine (P(*t*-Bu)$_3$) was purchased from Acros and stored under argon. Tetrabutylammonium fluoride (TBAF) was used as a 1.0 M solution in THF and is commercially available from Acros and Aldrich. Triphenylphosphine (PPh_3) was purchased from Aldrich and recrystallized from pentane prior to use. Phenyltris(trifluoroethoxy)silane was prepared according to the literature procedure.[1] All compounds were determined to be > 95% pure by GC and ^{1}H NMR unless otherwise noted.

Preparation of Phenyltris(trifluoroethoxy)silane.

The siloxane was prepared according to previously published procedures.[1,2] The physical and spectroscopic properties were identical to previously reported values.[1,2]

Cross Coupling Reactions of Aryl Bromides.

4-Acetylbiphenyl (Table 1, entry 1).

To a solution of 0.201 g (1.01 mmol) of 4-bromoacetophenone, 0.024 g (0.107 mmol) of $Pd(OAc)_2$, and 0.055 g (0.210 mmol) of PPh_3 in 10 mL of DMF was added 0.419 g (2.11 mmol) of phenyltrimethoxysilane. Then 2.10 mL (2.10 mmol) of TBAF was added to the reaction mixture via syringe. The reaction mixture was degassed to remove oxygen via one freeze-pump-thaw cycle. The resulting orange solution was heated at 90 ^oC and after 5 h the reaction had turned black. The reaction was heated for a total of 24 h at 90 ^oC. The resulting black suspension was quenched by the addition of 50 mL of water; the aqueous layer was extracted with 4X50 mL of Et_2O and the combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. Purification of the residue by flash chromatography (30 mm, 14 cm, 0-10% Et_2O/pentane) gave 171 mg (86%) of 4-acetylbiphenyl. TLC R_f = 0.41 (25% Et_2O/pentane). The spectroscopic properties were identical to previously reported values.[2,3]

4-Acetylbiphenyl (Table 1, entry 2).

Substitution of P(*o*-tol)$_3$ for PPh_3 gave 157 mg (78%) of 4-acetylbiphenyl.

4-Methylbiphenyl (Table 1, entry 3).

Following the method described for the preparation of 4-acetylbiphenyl (Table 1, entry 1), the cross coupling of 4-bromotoluene with phenyltrimethoxysilane gave 162 mg (82%) of 4-methylbiphenyl TLC R_f = 0.44 (pentane) and 10 mg (10%) of 4,4'-dimethylbiphenyl. The spectroscopic properties were identical to previously reported values.[2,3]

4-Methylbiphenyl (Table 1, entry 4).

Substitution of P(*o*-tol)$_3$ for PPh_3 gave 156 mg (78%) of 4-methylbiphenyl and 3 mg (3%) of 4,4'-dimethylbiphenyl.

4-Methoxybiphenyl (Table 1, entry 5).

Following the method described for the preparation of 4-acetylbiphenyl (Table 1, entry 1), the cross coupling of 4-bromoanisole with phenyltrimethoxysilane gave 153 mg (74%) of 4-methoxybiphenyl. TLC R_f = 0.30 (pentane). The spectroscopic properties were identical to previously reported values.[2,3]

4-Methoxybiphenyl (Table 1, entry 6).

Substitution of P(*o*-tol)$_3$ for PPh$_3$ gave 137 mg (70%) of 4-methoxybiphenyl.

2,6-Dimethylbiphenyl (Table 2, entry 15).

Following the method described for the preparation of 4-acetylbiphenyl (Table 1, entry 1), the cross coupling of 2-bromo-*m*-xylene with phenyltrimethoxysilane gave 825 mg (85%) of 2,6-dimethylbiphenyl as a clear oil. Also obtained in the mixture were 20 mg (2%) of starting material, 2-bromo-*m*-xylene, and 29 mg of biphenyl. The final product was 95% pure by GC analysis, and the two impurities were unable to be removed from the major product by column chromatography or distillation. The impurities were identified by comparison of GC retention times of authenic samples. TLC R_f = 0.43 (pentane); IR (CCl_4) 3062 (w), 3022 (w), 2962 (w), 2924 (w), 1558 (vs), 1541 (vs), 1463 (m), 1443 (w), 1251 (m), 1216 (m), 1111 (m), 1072 (m), 1072 (m), 1009 (s), 973 (m), 829 (s), 808 (m); ^{1}H NMR ($CDCl_3$) δ 2.03 (s, 3H), 7.07-7.18 (m, 5H), 7.31-7.35 (m, 1H), 7.40-7.44 (m, 2H); ^{13}C NMR ($CDCl_3$) 20.8, 126.6, 127.0, 127.3, 128.4, 129.0, 136.1, 141.1, 141.9; GCMS 183 ((M+1), 13), 182 ((M^+), 88), 181 (30), 168 (15), 167 (100), 166 (30), 165 (56), 152 (22), 83 (25).

2-Phenylpyridine (Table 3, entry 1).

Following the method described for the preparation of 4-acetylbiphenyl (Table 1, entry 1), the cross coupling of 2-bromopyridine with phenyltrimethoxysilane gave 152 mg (76%) of 2-phenylpyridine. TLC R_f = 0.20 (10% Et_2O/pentane); IR (CCl_4) 3089 (m), 3067 (s), 3037 (m), 3010 (m), 2976 (w), 2967 (w), 2928 (w), 1587 (vs), 1565 (vs), 1534 (s), 1468 (vs), 1469 (vs), 1540 (vs), 1446 (vs), 1425 (vs), 1294 (m), 1253 (m), 1217 (m), 1182 (m), 1151 (s), 1095 (w), 1074 (s), 1021 (s), 988 (s), 919 (w), 834 (s); ^{1}H NMR ($CDCl_3$) δ 7.21-7.24 (m, 1H), 7.39-7.49 (m, 3H), 7.71-7.77 (m, 2H), 7.98 (d, J=7.3, 2H), 8.69 (d, J=4.6, 1H); ^{13}C NMR ($CDCl_3$) δ 120.6, 122.1, 127.0, 128.7, 129.0, 136.8, 139.2, 149.5, 157.4; LRMS 156 ((M+1), 14), 155 ((M^+), 100), 154 (65), 79 (15), 50 (12); HRMS (EI) calcd for $C_{11}H_9N$ 155.0735 (M^+), found 155.0731. The IR and ^{1}H NMR are identical to the spectral data reported in reference 4. The ^{13}C NMR data is identical to data reported in reference 5. Additional ^{1}H NMR data is reported in reference 6, and mass spectral data is reported in reference 7.

3-Phenylpyridine (Table 3, entry 3).

Following the method described for the preparation of 4-acetylbiphenyl (Table 1, entry 1), the cross coupling of 3-bromopyridine with phenyltrimethoxysilane gave 123 mg (62%) of 3-phenylpyridine. TLC R_f = 0.04 (10% Et_2O/pentane); IR (CCl_4) 3089 (w), 3067

(w), 3053 (w), 3035 (w), 2957 (w), 2921 (w), 1547 (vs), 1474 (m), 1446 (w), 1408 (m), 1253 (s), 1217 (s), 1110 (m), 1075 (m), 1006 (s), 979 (s); ^{1}H NMR ($CDCl_3$) δ 7.34-7.49 (m, 4H), 7.57 (m, 2H), 7.87 (d, J=7.9, 1H), 8.58 (d, J=4.4, 1H), 8.84 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 123.6, 127.1, 128.1, 129.1, 134.5, 136.7, 137.8, 148.2, 148.3; LRMS 156 ((M+1), 11), 155 ((M^+), 100), 154 (31); HRMS (EI) calcd for $C_{11}H_9N$ 155.0735 (M^+), found 155.0731. The IR is identical to the spectral data reported in reference 8. The ^{1}H NMR and mass spectral data are identical to data reported in reference 9. The ^{13}C NMR is identical to the data in reference 10. Additional ^{1}H NMR data as well as elemental analysis data is reported in reference 11.

3-Phenylpyridine (Table 3, entry 4).

Substitution of phenyltris(trifluoroethoxy)silane for phenyltrimethoxysilane gave 124 mg (62%) of the heterocoupled adduct, 3-phenylpyridine, and approximately 7 mg (3%) of the starting material was recovered.

2-Thienylbenzene (Table 4, entry 1).

Following the method described for the preparation of 4-acetylbiphenyl (Table 1, entry 1), the cross coupling of 2-bromothiophene with phenyltrimethoxysilane gave 175 mg of a mixture of the heterocoupled adduct, 2-thienylbenzene (132 mg (64%), along with 32 mg (30%) of the homocoupled adduct, 2,2'-bithiophene as a colorless oil. A small amount biphenyl was also contained in the final product (7%), which could not be separated by column chromatography. Analysis of the mixture by GC gave the percentages of products present. The impurities were identified by comparison of GC retention times of authenic samples. Attempts to separate the homocoupled adduct from the heterocoupled adduct by column chromatography were unsuccessful. TLC R_f = 0.48 (pentane); IR (CCl_4) 3077 (m), 3066 (m), 3030 (w), 1602 (s), 1521 (s), 1490 (vs), 1448 (s), 1417 (w), 1383 (w), 1257 (s), 1210 (s), 1159 (m), 1110 (m), 1073 (m), 1032 (m), 1009 (m), 986 (m), 956 (m), 905 (w), 852 (vs), 838 (s); ^{1}H NMR ($CDCl_3$) δ 7.07 (dd, j=5.0, 3.6, 1H), 7.25-7.39 (m, 5H), 7.58-7.62 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 123.1, 124.8, 126.0, 127.4, 128.0, 128.9, 134.5, 144.5; GCMS 162 ((M + 2), 5), 161, ((M + 1), 12), 160 ((M^+), 100), 134 (5), 128 (11), 116 (10), 115 (33), 102 (5), 89 (6), 80 (6), 63 (6), 51 (9), 50 (7). The IR, ^{1}H, ^{13}C, and MS data are identical to data reported in reference 12. Additional IR data is reported in reference 13. UV data is reported in reference 12.

3-Thienylbenzene (Table 4, entry 2).

Following the method described for the preparation of 4-acetylbiphenyl (Table 1, entry 1), the cross coupling of 3-bromothiophene with phenyltrimethoxysilane gave 143 mg

(70%) of the desired heterocoupled adduct, 3-thienylbenzene as white flakes. Approximately 6 mg (6%) of the homocoupled adduct, 3,3'-bithiophene present in the product. A trace of biphenyl (2%) was also present in the final product. Attempts to separate the homocoupled adduct and biphenyl from the heterocoupled adduct by column chromatography were unsuccessful. Analysis of the mixture by GC gave the percentages of products present. The impurities were identified by comparison of GC retention times of authenic samples. TLC R_f = 0.50 (pentane); mp 90-92.5 ^oC (91.5-92 ^oC)[15]; IR (CCl_4) 3116 (w), 3087 (w), 3066 (w), 3036 (w), 1600 (m), 1578 (w), 1527 (w), 1507 (m), 1489 (m), 1265 (m), 1196 (s), 1113 (vs), 1071 (s), 1016 (m), 985 (w), 969 (w), 862 (w), 851 (w); ^1H NMR ($CDCl_3$) δ 7.26-7.44 (cm, 6H), 7.58 (d, J=7.4, 2H); ^{13}C NMR ($CDCl_3$) δ 120.3, 126.2, 126.4, 126.5, 127.1, 128.8, 135..9, 142.4; GCMS 162 ((M + 2), 8), 161 ((M + 1), 20), 160 ((M^+), 100), 159 (16), 128 (20), 116 (20), 115 (54). The ^1H and ^{13}C NMR are identical to spectral data reported in reference 15. MS data is reported in reference 14. HRMS and elemental analysis results is reported in reference 15.

Cross Coupling Reactions of Aryl Chlorides.

4-Acetylbiphenyl (Table 1, entry 7) .

To a solution of 0.202 g (1.31 mmol) of 4-chloroacetophenone, 0.030 g (0.134 mmol) of $Pd(OAc)_2$, and 0.071 g (0.271 mmol) of PPh_3 in 10 mL of DMF was added 0.514 g (2.53 mmol) of phenyltrimethoxysilane. Then 2.60 mL (2.60 mmol) of TBAF was added to the reaction mixture via syringe. The reaction mixture was degassed to remove oxygen via one freeze-pump-thaw cycle. After heating at 80 ^oC for 2.6 h, the color of the solution changed from orange to brown. The reaction was heated for 45 h at 80 ^oC. The resulting suspension was quenched by the addition of 50 mL of water; the aqueous layer was then extracted with 4X50 mL of Et_2O and the combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. Purification of the residue by flash chromatography (30 mm, 14 cm, 0-50% Et_2O/pentane) gave 74 mg (29%) of 4-acetylbiphenyl, and 144 mg (71%) of recovered starting material, 4-chloroacetophenone.

4-Acetylbiphenyl (Table 1, entry 8).

Substitution of P(*o*-tol)$_3$ for PPh_3 gave 78 mg (30%) of 4-acetylbiphenyl, and 141 mg (70%) of recovered starting material, 4-chloroacetophenone.

4-Acetylbiphenyl (Table 5, entry 1) .

To a solution of 0.200 g (1.29 mmol) of 4-chloroacetophenone, 0.058 g (0.063 mmol) of Pd_2dba_3, 0.069 g (0.197 mmol) of 2-(dicyclohexylphosphino)biphenyl **1**, and 0.523 g (2.64 mmol) of phenyltrimethoxysilane in 10 mL of DMF was added 2.60 mL (2.60

mmol) of TBAF was added to the reaction mixture via syringe. The reaction mixture was degassed to remove oxygen via one freeze-pump-thaw cycle. The reaction was heated for 27 h at 87 ^{o}C. The resulting suspension was quenched by the addition of 50 mL of water; the aqueous layer was then extracted with 4X50 mL of Et_2O and the combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. Purification of the residue by flash chromatography (30 mm, 14 cm, 0-10% Et_2O/pentane) gave 119 mg (47%) of 4-acetylbiphenyl.

4-Methylbiphenyl (Table 5, entry 2) .

Following the method described for the preparation of 4-acetylbiphenyl (Table 5, entry 1), the cross coupling of 4-chlorotoluene with phenyltrimethoxysilane gave 170 mg (63%) of the desired heterocoupled adduct, 4-methylbiphenyl.

4-Methoxybiphenyl (Table 5, entry 3).

Following the method described for the preparation of 4-acetylbiphenyl (Table 5, entry 1), the cross coupling of 4-chloroanisole with phenyltrimethoxysilane gave 168 mg (71%) of the desired heterocoupled adduct, 4-methoxybiphenyl.

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