P[N(*i*-Bu)CH₂CH₂]₃N: A Versatile Ligand for the Pd-Catalyzed Amination of Aryl Chlorides

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SUPPORTING INFORMATION

Experimental Section

General. All reactions were performed under an atmosphere of argon in oven-dried glassware. Toluene was collected from a Grubbs type solvent purification system (Innovative Technologies) and stored over 4 Å molecular sieves. ¹H and ¹³C NMR spectra were recorded at 300 and 75.5 MHz, respectively. Thin-layer chromatography (TLC) was performed using commercially prepared 60 mesh silica gel plates and were visualized with short wavelength UV light (254 nm). Silica gel 60 (9385, 230-400 mesh) was used for column chromatography. Melting points were determined in unsealed capillary tubes and are uncorrected. The yields reported are isolated yields and are the average of two runs. All commercially available reagents were used as received. Although Ligand **1** is commercially available from Aldrich, we prepared it according to our previously reported procedure (Kisanga, P. B.; Verkade, J. G. *Tetrahedron* **2001**, 57, 467). All compounds in Tables 1 - 4 gave satisfactory NMR (¹H and ¹³C) and HRMS data.

Pd₂(dba)₃/1-catalyzed amination of aryl chlorides and chloropyridines with anilines and cyclic secondary amines (Tables 1 - 3). *General Procedure:* An oven-dried Schlenk flask equipped with a magnetic stirring bar was charged with Pd₂(dba)₃ (2 mol

%; 4 mol % for diphenylamine) and NaO-*t*-Bu (1.5 mmol) inside a nitrogen-filled glovebox. The flask was capped with a rubber septum and removed from the glovebox. Ligand **1** (8 mol %; 16 mol % for diphenylamine) was then added by microliter syringe. Aryl halide (1.0 mmol), amine (1.2 mmol) and toluene (5 mL) were then successively added by syringe. The flask was placed in an 80 °C oil bath and the reaction mixture was stirred until the starting material had been completely consumed as judged by TLC. The mixture was cooled to room temperature, adsorbed onto silica gel and then purified by column chromatography using hexanes/EtOAc as the eluent.

Pd(OAc)₂/1-catalyzed amination of aryl chlorides with primary amines and an acyclic secondary amine (Table 4). *General Procedure:* An oven-dried Schlenk flask equipped with a magnetic stirring bar was charged with Pd(OAc)₂ (5 mol %) and NaO-*t*-Bu (1.5 mmol) inside a nitrogen-filled glovebox. The flask was capped with a rubber septum and removed from the glovebox. After ligand **1** (10 mol %) was added by microliter syringe, aryl halide (1.0 mmol), amine (1.5 mmol) and toluene (5 mL) were then added successively by syringe. The flask was placed in an 80 °C oil bath and the reaction mixture was stirred until the starting material had been completely consumed as judged by TLC. The mixture was cooled to room temperature, adsorbed onto silica gel and then purified by column chromatography using hexanes/EtOAc as the eluent.

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Table 1. Amination of Aryl chlorides with Anilines^a

entry	chloride	amine	product	yield (%) ^b
1				88
2				90
3		Ph_2NH		94 ^c
4				87
5				99
6		Ph_2NH		88 ^c
7				87
8				98
9				95
10		Ph_2NH		91 ^c

^a Conditions: 1.0 equiv of aryl chloride, 1.2 equiv of amine, 1.5 equiv of NaO-*t*-Bu, 2.0 mol % of $\text{Pd}_2(\text{dba})_3$, 8.0 mol % ligand 1, 5 mL of toluene, 80 °C. ^b Isolated yields (average of at least two runs). ^c 4.0 mol % of $\text{Pd}_2(\text{dba})_3$ was employed.

Table 2. Amination of Aryl Chlorides with Cyclic Secondary Amines^a

entry	chloride	amine	product	yield (%) ^b
1				90
2				94
3				86
4				95
5				89
6				87

^a Conditions are identical to those used in Table 1. ^b Isolated yields (average of at least two runs).

Table 3. Amination of Chloropyridines^a

entry	chloride	amine	product	yield (%) ^b
1				53
2				89
3				88
4				90
5				87
6				83

^a Conditions are identical to those used in Table 1. ^b Isolated yields (average of at least two runs).

Table 4. Amination of Aryl Chlorides with Primary Amines and an Acyclic Secondary Amine^a

entry	chloride	amine	product	yield (%) ^b
1				90
2				91
3				63
4		<i>n</i> -HexNH ₂		49
5		<i>n</i> -HexNH ₂		43
6		Et ₂ NH		56

^a Conditions: 1.0 equiv of aryl chloride, 1.4 equiv of amine, 1.5 equiv of NaO-*t*-Bu, 5.0 mol % of Pd(OAc)₂, 10.0 mol % ligand 1, 5 mL of toluene, 80 °C. ^b Isolated yields (average of at least two runs).

Table 1, entry 1

Table 1, entry 3

Table 1, entry 5

300 MHz

Table 1, entry 6

7.2639
7.2505
7.2260
7.2224
7.1980
7.0905
7.0783
7.0742
7.0628
7.0494
7.0462
7.0193
7.0124
6.9953
6.9912
6.9713
6.9505
6.9468

— 2.3195

Table 1, entry 8

Table 1, entry 9

Table 2, entry 1

Table 2, entry 2

300 MHz

Table 2, entry 3

300MHz

Table 2, entry 4

7.2700
7.1548
7.1271
6.8935
6.8651

3.9144
3.8990
3.8827

3.1603
3.1440
3.1282

2.3317

1.9502

2.0192

4.0958

4.0510

3.0003

10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
-1.5

(ppm)

able 2, entry 6

300 MHz

Table 3, entry 2

Table 3, entry 3

3.8 MHz

Table 3, entry 4

(ppm)

8.2842
8.1116
8.1035

7.2602
7.1564
7.1503

3.8709
3.8546
3.8392

3.1827
3.1664
3.1509

Table 3, entry 5

Table 4, entry 1

300 MHz

Table 4, entry 2

300 MHz

Table 4, entry 3

7.2700
7.1097
7.0828
7.0559
6.2729
6.2652
6.2477
6.2436
6.2407
6.2212
6.2163
6.1825
6.1752
6.1679

3.7911
3.5494
3.3024
3.2901
3.2771
3.2690
3.2564
3.2437
3.2352
3.2226
3.2104
2.0993
2.0664
2.0570
1.8152
1.8030
1.7896
1.7717
1.7591
1.6948
1.6818
1.6659
1.6541
1.6415
1.4624
1.4510
1.4400
1.4225
1.4123
1.3716
1.3395
1.3297
1.2955
1.2858
1.2670
1.2569
1.2455
1.2174
1.1828
1.1494
1.1425
1.1116
1.1006

(ppm)

300 MHz

Table 4, entry 4

400 MHz

Table 4, entry 5

7.1255
7.1053
7.0852
6.3038
6.2983
6.2834
6.2779
6.2658
6.2628
6.2610
6.2457
6.2425
6.2409
6.1962
6.1917

3.7998
3.6810
3.6623
3.6497
3.6346
3.6190

3.1305
3.1126
3.0948

1.6686
1.6514
1.6329
1.6145
1.5962
1.4596
1.4420
1.4244
1.4040
1.3885
1.3672
1.3585
1.3514
1.3002
0.9567
0.9402
0.9231

0.8457

1.7213

0.8011

2.9883

0.7900

1.7634

1.7478

5.7709

2.6346

Table 4, entry 6

7.4421
7.4356
7.4185
7.4120
7.2635
6.6184
6.6123
6.5944
6.5883

3.4236
3.4000
3.3764
3.3528

1.2068
1.1828
1.1592