Synthesis, Characterization and Catalytic Activity of *N*-Heterocyclic Carbene (NHC) Palladacycle Complexes

Mihai S. Viciu, Roy A. Kelly, III, Edwin D. Stevens, Frederic Naud, Martin Studer and Steven P. Nolan*

Department of Chemistry, University of New Orleans, New Orleans, Louisiana 70148
Solvias AG, WRO-1055.6.16, Klybeckstrasse 191, Basel, Switzerland CH-4002

Email: snolan@uno.edu

Supporting Information

- **General Considerations**: All aryl halides and ketones used were distilled over $MgSO_4$ (Aldrich). Dioxane and toluene (Aldrich) were dried and distilled over sodium benzophenone ketyl. NaO^tBu (Aldrich) was sublimed prior to storage in a MBraun glovebox. Palladacycle dimmer precursors were synthesized as reported in the literature.[1] Flash chromatography was performed on silica gel 60 (320-400 mesh) with hexanes/ethyl acetate or hexanes/THF.
- The imidazolium salt: IPrHCl (IPrHCl =1,3Bis-(2,6-diisopropylphenyl)imidazolium chloride) and corresponding carbene were prepared according to reported procedures[2].
- ^1H and ^{13}C NMR spectra were recorded on Varian-300 or Varian-400 MHz spectrometer at room temperature. Deuterated solvents were purchased from Cambridge Isotope Laboratories, Inc. and dried prior to use.
- Elemental analysis was performed at Desert Analysis, Tucson, AZ.
- Anaerobic reactions were performed in oven dried, screw cap vials with magnetic stirring, under argon atmosphere. All reported yields are isolated yields and are the average of two runs.

Syntheses of 1 : The IPr carbene (372 mg, 0.95 mmol) and palladacycle dimer (300 mg, 0.45 mmol) were mixed together in a Schlenk tube inside a dry-box. Dry THF (4 ml) was added by a cannula and stirred at room temperature for 2 hours. The mixture was filtered, THF was removed in vacuum and 40 ml of anhydrous hexane was added to precipitate the product. The product was filtered in air and washed with hexane. Yield 412mg, 63%.

^{1}H-NMR(400MHz ,CD_2Cl_2): 7.502(t, *J*= 8 Hz, 1H), 7.390 (d, *J*= 7.6Hz, 1H), 7.290 (d, *J*= 7.6 Hz, 1H), 7.186 (t ,*J*= 7.6 Hz, 1H), 7.136-7.076 (m 3H), 7.018 (t, *J*= 6.8 Hz, 1H), 6.950 (d, *J*= 8 Hz, 1H), 6.923-6.801 (m 6H), 6.740-6.718 (dd 1H), 3.799 (heptet, 1H), 3.695 (heptet, 1H), 2.88 (s 3H), 2.624 (heptet, 1H), 2.158 (heptet, 1H), 2.047 (s 3H), 1.69 (d, *J*= 7.6 Hz, 2H), 1.42 (d, *J*= 6.4 Hz, 2H), 1.27 (d, *J*= 6.4 Hz, 2H), 1.13 (d, *J*= 6.8 Hz, 2H), 0.98 (d, *J*= 6.4 Hz, 2H), 0.83 (d, *J*= 6.4 Hz, 2H), 0.71 (d, *J*= 6.8 Hz, 2H), 0.46 (d, *J*= 6.4 Hz, 2H).

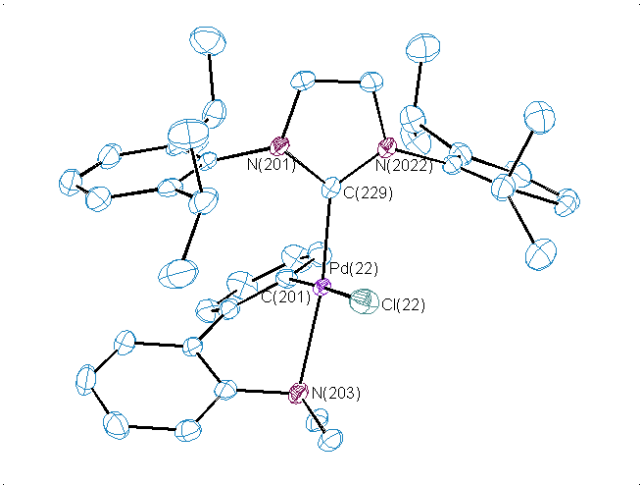
^{13}C-NMR(125MHz $CDCl_3$) 172.68, 152.88, 148.5, 147.34, 147.06, 144.32, 144.22, 142.59, 141.55, 136.82, 136.4, 136.22, 129.9, 129.85, 129.33, 126.98, 126.91, 125.55, 124.76, 124.63, 124.21, 123.62, 123.32, 122.94, 116.46, 115.53, 51.18, 31.75, 29.32, 28.89, 28.58, 28.46, 27.68, 26.89, 25.8, 25.69, 24.65, 24.3, 22.89, 21.91.

Elemental analysis:

Anal. Calcd: C, 67.76, H, 6.93, N, 5.78.

Found: C, 67.46; H, 6.92; N, 5.82.

Pd-IPr (**1**)



Syntheses of 2: The IMes carbene (344 mg, 1.13 mmol) and the palladacycle dimer (409.2 mg, 0.57mmol) were mixed together in a Schlenk tube inside a dry-box. Dry THF (2 ml) was added by a cannula and the resulting suspension was stirred at room temperature for 2 hours. The mixture was filtered, THF was removed in vacuum and 40 ml of anhydrous hexane was added to precipitate the product. The product was filtered in air and washed with hexane. Yield 244mg, 67%.

^{1}H-NMR(400MHz CD_2Cl_2): 7.168-7.095 (m, 3H); 7.017-6.87 (m, 8H); 6.8-6.76 (m, 1H); 6.48 (d, *J*= 22 Hz, 2H); 2.922 (s, 3H) ; 2.63 (s, 3H); 2.415 (s,3H); 2.2 (s,3H); 2.15 (s, 3H); 1.385 (s,3H).

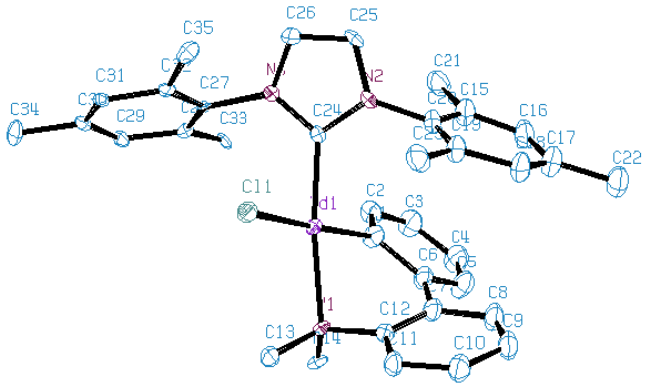
^{13}C-NMR (125MHz CD_2Cl_2) 175.1; 148.7; 147.3; 147.1; 142.6; 140.9; 135.8; 135.5; 129.0; 128.3; 128.1; 126.9; 126.0; 125.5; 125.4; 124.2; 123.9; 123.2; 123.0; 122.6; 122.3; 121.9; 121.3; 121.0; 116.4; 114.9; 50.8; 33.7; 28.3; 28.1; 27.8.

Elemental analysis:

Anal. Calcd.: C, 65.42, H, 5.97, N, 6.54.

Found: C, 65.70; H, 6.10; N, 6.60.

Pd-IMes ( ) :



Anaerobic Amination Reactions Procedure: Under argon, 7.1mg (1 mol%) of **1**, 100 mg of NaO^{t}Bu and 3 ml of dry dioxane were loaded into oven-dried vials capped with a septum seal. Then 1 mmole aryl halide and 1.1 mmole amine were added through the septum using a syringe. When one or both substrates were solids they were loaded first inside the dry-box followed by the catalyst, base and solvent. The reactions were run at indicated temperatures. All reactions were monitored by GC. After consumption of reactants or no further conversion, the reactions were stopped by quenching in aqueous NH_4Cl solution and extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4, mixed with silica gel and evaporated. The product/silica gel mixture was placed at the top of a flash chromatography column and eluted.

4-(4-Methoxyphenyl)morpholine[3] The general procedure afforded 177mg (92%) of the title compound.

4-(4-Tolyl)morpholine[4] The general procedure afforded 173mg (98%) of the title compound.

4-(4-Tolyl)morpholine[3] The general procedure afforded 141.6mg (80%) of the title compound.

4-(4-Methoxyphenyl)morpholine[2] The general procedure afforded 183mg (95%) of the title compound.

N-(3-Pyridyl)morpholine[5] The general procedure afforded 144mg (88%) of the title compound.

N-(2-Pyridyl)morpholine[4] The general procedure afforded 154mg (94%) of the title compound.

N-(2-Methoxyphenyl)morpholine[6] The general procedure afforded 174mg (90%) of the title compound.

N-(2-Methylphenyl)morpholine[7] The general procedure afforded 156mg (88%) of the title compound.

N-(4-Cyanophenyl)morpholine[8] The general procedure afforded 156mg (83%) of the title compound.

N-[4-(trifluoromethyl)phenyl]morpholine[9] The general procedure afforded 194mg (84%) of the title compound.

N-phenyl-morpholine[10] The general procedure afforded 145mg (89%) of the title compound.

N-Methyl-p-methoxydiphenylamine[7] The general procedure in argon afforded 204.5mg (96%) of the title compound.

N-Methyl-p-methyldiphenylamine[11] The general procedure in argon afforded 177 mg (90%) of the title compound.

N,N-Dibutyl-4-methylbenzenamine[10] The general procedure afforded 190.5mg (87%) of the title compound.

N-(4-Methylphenyl)piperidine[7] The general procedure afforded 174mg (99%) of the title compound.

3-Anilinopyridine[12] The general procedure afforded 156mg (92%) of the title compound

2-Anilinopyridine[13] The general procedure afforded 139mg (82%) of the title compound.

(4-Methoxyphenyl)phenylamine[14] The general procedure in argon afforded 149mg (75%) of the title compound.

(4-Methylphenyl)phenylamine[7] The general procedure in argon afforded 176mg (96%) of the title compound.

N-Cyclohexyl-p-toluidine[15] The general procedure in argon afforded 166mg (88%) of the title compound.

N-Hexyl-4-methylaniline[10] The general procedure in argon afforded 130mg (68%) of the title compound.

4-Benzoyldiphenylamine[16] The general procedure in argon afforded 267mg (98%) of the title compound in.

α-Ketone Arylation Reaction Procedure: The vials with magnetic stirrers were loaded inside the dry box with 3 ml dry dioxane, 100 mg NaO^{t}Bu and 7.1mg (1 mol%) **1** . Ketone (1.0 mmole) and aryl halide (1.0 mmole) were added outside of dry box, through the septum of the reaction vial using a syringe. When one or both substrates were solids they were added to the reaction vial inside the drybox. The reactions were run at indicated temperatures. All reactions were monitored by GC. After consumption of reactants or no further conversion, the reactions were stopped by quenching in aqueous NH_4Cl solution and extracted in diethyl ether. The organic layer was dried over Na_2SO_4, mixed with silica gel and evaporated. The product/silica gel mixture was placed at the top of a flash chromatography column and eluted using ethyl acetate/hexane mixtures.

2-Phenylpropiophenone[17] The general procedure afforded 199mg (89%) of the title compound.

2-Phenylpropiophenone[16] The general procedure afforded 175mg (78%) of the title compound.

1-phenyl-2-(3-pyridinyl)- 1-propanone[16] The general procedure afforded 201mg (90%) of the title compound.

2-(p-tolyl)-cyclohexanone[18] The general procedure afforded 163.5mg (87%) of the title compound.

References:

(1) (a) Beletskaya, I. P.; Cheprakov, A. V. *Chem. Rev.,* **2000**, *100*, 3009-3066. (b) Schnyder, A.; Indolese, A.F.; Studer, M.; Blaser, H-U. *Angew. Chem. Int. Ed.*, **2002**, *41*, 3668-3671.

(2)For synthesis of carbenes see: (a) Arduengo III, A. J.; Calabrese, J. C.; Davidson, F.; Rasika Dias, H. V.; Goerlich, J. R.; Krafczyk, R.; Marshall, W. J.; Tamm, M.; Schmutzler, R. *Helv. Chim. Acta* **1999**, *82*, 2348-2364. and references cited (b) Trnka, T.M.; Grubbs,R.H. *Acc. Chem. Res.* **2001**, 34, 18-29. and references cited. (c) Huang, J.; Nolan, S.P. *J. Am. Chem. Soc.*, **1999**, *120*, 9889-9890.

(3) Old, D.W.; Wolfe, J.P.; Buchwald, S.L. *J. Am. Chem. Soc.*, **1998**, *120*, 9722-9723.

(4) Tsuji, Y.; Huh, K. T.; Ohsugi, Y.; Watanabe, Y. *J. Org. Chem.* **1985**, *50*, 1365-1370.

(5) Wagaw, S.; Buchwald, S.L. *J. Org. Chem*, **1996**, *61*, 7240-7241.

(6) Ali, M.H.; Buchwald, S.L. *J. Org. Chem.*, **2001**, *66*, 2560-2565.

(7) Barluenga, J.; Aznar, F.; Fernandez, M. *Chem. Eur. J.* **1997**, *3*, 1629-1637.

(8) Wolfe, J. P.; Buchwald, S. L. *J. Am. Chem. Soc.* **1997**, *119*, 6054-6058.

(9) Kamikawa, K.; Sugimoto, S.; Uemura, M. *J. Org. Chem.,* **1998**, 63, 8407-8410.
(10) Desmarets, C.; Schneider, R.; Fort, Y. *Tetrahedron Lett*., **2000**, *41*, 2875-2879.
(11) Wolfe, J. P.; Buchwald, S L. *J. Org. Chem.* **1996**, *61*, 1133-1136.
(12) Schleimann, W., Bueghe, A. *Pharmazie*, **1980**, *35*, 203-204.
(13) Katritzky, A.R.; Huang, T-B.; Voronkov, M.V. *J. Org. Chem.,* **2001**, *66*, 1043-1045.
(14) Louie, J.; Driver, M.S.; Hamann, B.C.; Hartwig, J.F. *J. Org. Chem.,***1997**, *62*, 1268-1273.
(15) Bowman, W.R.; Stephenson, P.T.; Terrett, N.K.; Young, A.R. *Tetrahedron*, **1995**, *51*, 7959-7980.
(16) Datta, I.; Das, T.K.; Ghosh, S. *Tetrahedron*, **1990**, 46, 6821-6830.
(17) Kawatsura, M.; Hartwig, J.F. *J. Am. Chem. Soc.*, **1999**, *121*, 1473-1478.
(18) Nakamura, S.; Kaneeda, M.; Ishihara, K.; Yamamoto, H. *J. Am. Chem. Soc.*, **2000**, 122, 8120-8130.