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Divergent Pathways in the Reaction of Fischer Carbenes and Palladium

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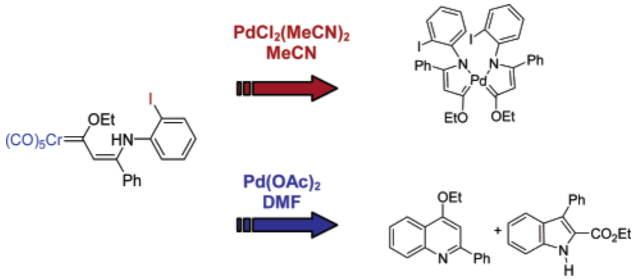
ABSTRACT



The Pd-catalyzed reaction of *β*-arylaminochromium(0) carbene complexes produces by transmetalation the first isolated and X-ray structurally characterized bis-Pd(II) carbene complex, as well as other alternative reaction pathways, such as the oxidative addition–transmetalation sequence, not seen before in this chemistry.

Transmetalation is one of the key processes in most of the catalytic and stoichiometric reactions useful in organic and organometallic synthesis.[1] Strikingly, the possibility of effecting reactions of group 6 metal carbene complexes[2] under mild conditions by transmetalation (either catalytic or stoichiometric) was neglected before we reported the Pd-catalyzed self-dimerization of alkoxychromium and tungsten(0) carbenes a few years ago.[3] Interest in these processes has progressively increased after this initial report, although their full potential for organic synthesis as well as their reaction mechanisms remain mainly unexplored.[4] The proposed catalytic cycle for these transmetalation reactions[3] suggested the participation of mono- and bis-palladacarbene intermediates **1** and **2** in the Pd-induced self-dimerization of Fischer metal carbenes (Scheme 1). Espinet[5] reported the isolation and characterization of palladium carbene complexes **3** having the carbene ligand stabilized by an amino group during the transmetalation of aminotungsten(0) carbene complexes, followed by reaction with PMe$_3$. Previously, Barluenga[6] had reported the isolation of Cu(I) carbene complex **4** by reaction of alkoxychromium(0) carbenes and [Cu(MeCN)$_4$][PF$_6$]. It should be remarked that while complex **3** did not evolve to self-dimerization products, complex **4** produces these final products efficiently. We report here for the first time the isolation and X-ray and spectroscopic characterization of bis-palladacarbenes of type **2** from a Pd-transmetalation reaction of chromium(0) Fischer carbenes by different Pd reagents.

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(1) Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Mill Valley, CA, 1987.

(2) Selected reviews in the chemistry of Fischer metal carbene complexes: (a)Wulff, W. D. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon: Oxford, 1995; Vol. 12, p 470. (b) Harvey, D. F.; Sigano, D. M. *Chem. Rev.* **1996**, *96*, 271. (c) Hegedus, L. S. *Tetrahedron* **1997**, *53*, 4105. (d) Sierra, M. A. *Chem. Rev.* **2000**, *100*, 3591. (e) de Meijere, A.; Schirmer, H.; Duetsch, M. *Angew. Chem., Int. Ed.* **2000**, *39*, 3964. (f) Barluenga, J.; Flórez, J.; Fañanás, F. J. *J. Organomet. Chem.* **2001**, *624*, 5. (g) Barluenga, J.; Santamaría, J.; Tomás, M. *Chem. Rev.* **2004**, *104*, 2259.

(3) Sierra, M. A.; Mancheño, M. J.; del Amo, J. C.; Gómez-Gallego, M. *J. Am. Chem. Soc.* **2001**, *123*, 851.

(4) For a revision, see: Gómez-Gallego, M.; Mancheño, M. J.;. Sierra, M. A. *Acc. Chem. Res.* **2005**, *38*, 44.

(5) Albéniz, A. C.; Espinet, P.; Manrique, R.; Pérez-Mateo, A. *Angew. Chem., Int. Ed.* **2002**, *41*, 2363.

(6) Barluenga, J.; López, L. A.; Löbet, O.; Tomás, M.; García-Granda, S.; Álvarez-Rúa, C.; Borge, J. *Angew. Chem., Int. Ed.* **2001**, *40*, 3392.

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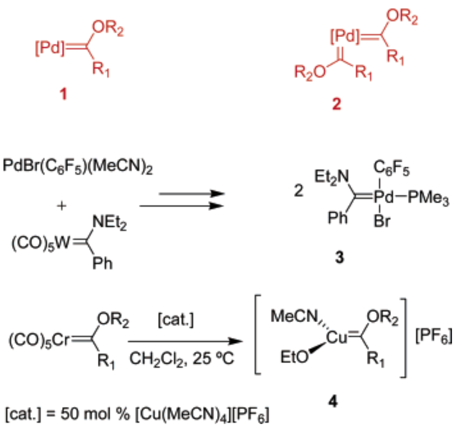
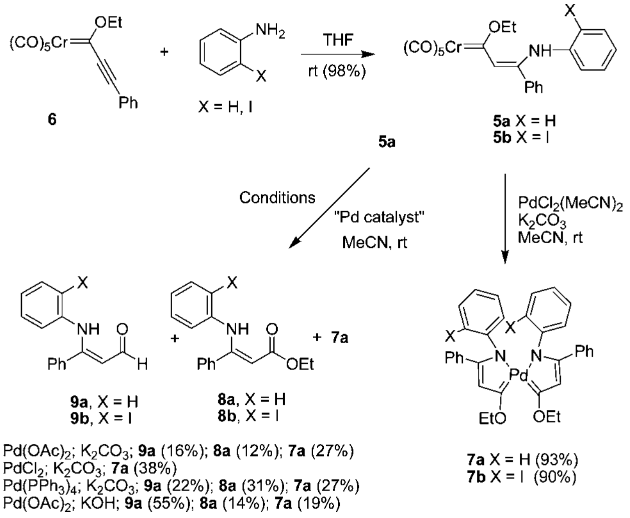
Scheme 1



Scheme 2



Complexes **5**[7] were prepared in nearly quantitative yields by reaction of complex **6** and aniline and *o*-iodoaniline, respectively, in THF at rt. Reaction of compound **5a** with a slight excess (1:0.6 ratio) of PdCl$_2$(MeCN)$_2$ in MeCN as solvent in the presence of K$_2$CO$_3$ led to the quantitative formation of a Pd complex identified as bis-palladacarbene **7a** on the basis of spectroscopic grounds.[8] Analytically pure compound **7a** was isolated in 93% yield. Other Pd reagents such as Pd(OAc)$_2$, PdCl$_2$, or Pd(PPh$_3$)$_4$ also led to complex **7a** (27%, 38%, and 27% yields respectively). For reaction with Pd(OAc)$_2$ and Pd(PPh$_3$)$_4$, ester **8a** and aldehyde **9a** were isolated as side products (Scheme 2). Other bases such as KOH gave poorer yields of the Pd complex (19%) and increased amounts of aldehyde **9a** (55%) (Scheme 2). Other solvents such as DMF led mainly to aldehyde **9a**.

Similarly, reaction of complex **5b** with PdCl$_2$(MeCN)$_2$ in MeCN as solvent in the presence of K$_2$CO$_3$ led to bis-palladacarbene **7b** in high yield (Scheme 2). Crystals adequate for X-ray diffraction analysis were grown from DCM/pentane, allowing the unambiguous assignment of the *cis*-bis-palladacarbene structure **7b** for this compound and therefore the analogous for **7a** by extension. HRMS determined the molecular mass of **7b** and **7a** and confirmed the absence of hydrogens attached to the nitrogen (Figure 1).

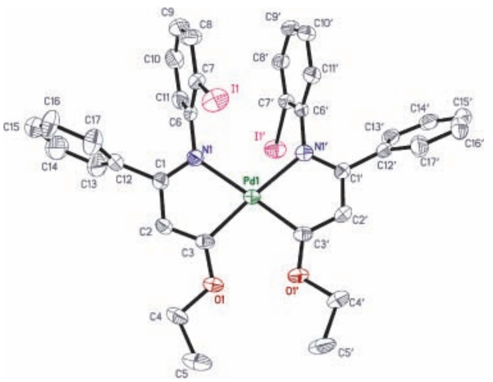


Figure 1. ORTEP drawing of bis-palladacarbene **7b**. The geometry around the Pd1 is almost square planar. Selected bond lengths (Å) and angles (deg): Pd1−N1, 2.164(4); Pd1−N1′, 2.145(4); Pd1−C3, 1.994(4); Pd1−C3′, 1.984(4); C3−O1, 1.339(5); O1−C4, 1.444(5); C3′−O1′, 1.334(5); O1′−C4′, 1.452(5); N1−Pd1−C3, 79.2(2); C3−Pd1−C3′, 98.3(2); C3′−Pd1−N1′, 79.1(2); N1′−Pd1−N1, 103.8(1).

It should be pointed out that complex **5b** has two potentially reactive sites toward Pd reagents. Thus, conditions to effect the oxidative addition/transmetalation sequence were pursued next. The reaction of complex **5b** and a catalytic amount (30%) of Pd(OAc)$_2$ was carried out in the presence of an excess of K$_2$CO$_3$ at room temperature and using DMF as the solvent.[9] Two products were isolated from this reaction: quinoline **10** (49% isolated yield) and indole **11** (38% isolated yield) (Scheme 3). The structure of compound **10** was assigned using a combination of mono- and bidimensional NMR experiments and by comparison with the reported data for 4-methoxy-2-phenylquinoline.[10] An analogous study was carried out to establish the structure of indole **11** whose ^{1}H NMR data were identical to those previously reported.[11]

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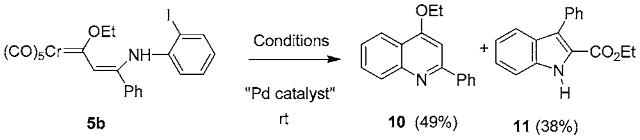
(7) The procedure for the synthesis of of carbene complex **5b** is representative: A solution of 313 mg (1.43 mmol) of *o*-iodoaniline and 500 mg (1.43 mmol) of carbene complex **6** in THF was stirred for 36 h at room temperature to yield 800 mg (98%) of complex **5b** as an orange-red solid. ^{1}H NMR (CDCl$_3$, 300 MHz): $\delta = 1.76$ (t, $J = 7.0$ Hz, 3H), 5.10 (q, $J = 7.0$ Hz, 2H), 6.46 (d, $J = 6.0$ Hz, 1H), 6.75 (m, 2H), 6.95 (m, 1H), 7.27−7.38 (m, 5H), 7.83 (d, $J = 6.0$ Hz, 1H), 10.01 (bs, 1H). ^{13}C NMR (CDCl$_3$, 125 MHz): $\delta = 16.3$, 75.5, 93.1, 123.0, 126.0, 126.8, 128.5, 128.7, 129.0, 130.3, 134.9, 139.3, 140.6, 145.3, 218.0, 224.1, 306.1. IR (CCl$_4$): ν 3463, 2050, 1969, 1924, 1899, 1569, 1541 cm^{-1}. Anal. Calcd for $C_{22}H_{16}CrINO_6$: C, 46.42; H, 2.83; Cr, 9.13; I, 22.29; N, 2.46. Found: C, 46.30; H, 2.86.

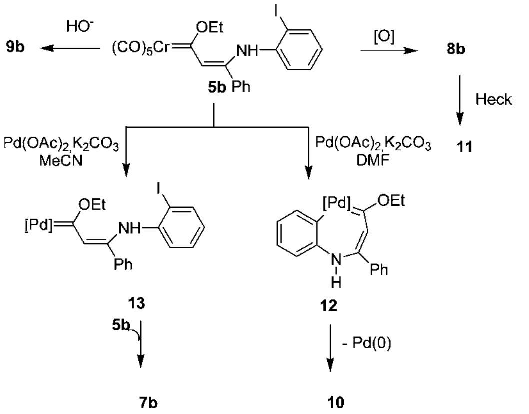
(8) The synthesis of complex **7a** is representative: A solution of of 25 mg (0.06 mmol) of carbene complex **5a**, 88 mg (0.03 mmol) of PdCl$_2$-(MeCN)$_2$, and 39 mg (0.28 mmol) of K$_2$CO$_3$ in 1 mL of MeCN was stirred under an argon atmosphere at room temperature for 2 h. Then, the solvent was eliminated in vacuo, and the residue obtained was disaggregated in AcOEt and filtered over a short pad of Celite. The organic layers were washed with brine and dried over magnesium sulfate. The solvent was removed in vacuo, and 17 mg (93%) of **7a** was obtained. ^{1}H NMR (CDCl$_3$, 200 MHz): $\delta = 1.50$ (t, $J = 7.1$ Hz, 6H), 4.05 (q, $J = 7.1$ Hz, 4H), 5.45 (s, 2H), 6.31−6.36 (m, 4H), 6.53−6.57 (m, 6H), 6.92−6.95 (m, 4H), 7.05−7.09 (m, 6H). ^{13}C NMR (CDCl$_3$, 50 MHz): $\delta = 14.6$, 65.1, 109.7, 123.2, 124.3, 127.4, 127.7, 127.9, 128.0, 137.3, 148.1, 182.1, 208.5. IR (KBr): ν = 3028, 1479, 1454, 1437, 1198 cm^{-1}. HRMS (FAB): calcd for $C_{34}H_{33}N_2O_2{}^{104}Pd$ 605.1582, found 605.1566.

Scheme 3



$Pd(OAc)_2$ (30%); K_2CO_3; DMF, **10** (49%); **11** (38%)
$Pd(PPh_3)_4$ (1:0.6 ratio); DMF; **10** (40%); **11** (48%); **8b** (6%)
$Pd(PPh_3)_4$ (1:0.6 ratio); K_2CO_3; DMF; **11** (42%); **8b** (20%)

Scheme 4



The choice of the solvent and catalyst was essential to achieve the formation of compounds **10** and **11**. Thus, reaction of complex **5b** and a catalytic amount of $Pd(OAc)_2$ (10%) using MeCN instead of DMF as the solvent formed complex **7b** (8% yield), together with aldehyde **9b** (27%) and ester **8b** (38%). Analogous results were obtained by increasing the amount of catalyst up to 30%. The yield of complex **7b** increased (21%) with aldehyde **9b** (14%) being obtained as the accompanying product.

The results obtained above may be rationalized on the basis of two different reaction pathways. The reaction in DMF should involve the initial oxidative addition of the Pd catalyst into the C−I bond of complex **5b** followed by an intramolecular transmetalation to produce cyclic Pd carbene **12**, which would form the quinoline **10** by reductive elimination. Alternatively, in MeCN transmetalation may occur into the carbene carbon to yield Pd carbene **13** which experiences a second transmetalation to yield the stable bis-Pd carbene **7b**.

Within this scenario, indole **11** may be formed from ester **8b** (the oxidation product of complex **5b** or of the monopalladacarbene intermediate) through a Heck process,[12] while aldehyde **9b** is a side product of the basic hydrolysis of complex **5b** (Scheme 4).[13]

These results may be due to the existence of two competitive processes, transmetalation versus oxidative addition. Oxidative addition is preferred for Pd(0) catalysts in DMF and transmetalation generally governs the reactivity of complexes **5** in MeCN solution. This is also supported by the reaction of complexes **5** with $Pd(PPh_3)_4$/DMF (1:0.6 ratio) which leads to quinoline **10** and indole **11**. With this catalyst, complex **7b** was not observed when the reaction was carried out in the same conditions in the presence of base either in DMF or MeCN.

Finally, we addressed the role of complexes **7** as intermediates in the self-dimerization of carbene complexes. All attempts to convert this type of Pd-complexes into the carbene dimers were fruitless. Thermal decomposition (THF refluxed), oxidation including UV−vis light/air, cerium(VI) ammonium nitrate (CAN), iodine, and bases (Et_3N) were unable to effect this transformation for **7b**. Unreacted starting complex or decomposition to complex reaction mixtures were the result of these experiments. Treatment with PMe_3, conditions that generated monomeric complexes **3**, were also used resulting again in the recovery of unaltered compound **7b**. Otherwise, reaction with strong acids (10% H_2SO_4) yielded benzoyl ethyl acetate for complex **7a**.

In conclusion, here is described the very first bis-palladacarbene complexes obtained by a transmetalation reaction from an alkoxychromium carbene complex, as well as alternative reaction pathways not seen before in this chemistry. The synthesis of new late transition metal bis-carbene complexes and the study of the participation of these species in the catalytic transmetalation of group 6 carbene complexes are being pursued in these laboratories.

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Supporting Information Available: Full experimental and characterization data for all of the compounds prepared in this work and data for the X-ray characterization of compound **7b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(9) A solution of 250 mg (0.44 mmol) of carbene complex **5b**, 30 mg (0.044 mmol) of $Pd(OAc)_2$, and 304 mg (2.2 mmol) of K_2CO_3 in 10 mL of DMF was stirred for 12 h. After extraction and solvent elimination, the residue obtained was dissolved in 50 mL of (1:1) hexane/AcOEt, exposed to sunlight for 8 h, and then filtered over a short pad of Celite. The products obtained were separated by flash column chromatography on silica gel to give 54 mg (49%) of quinoline **10** and 44 mg (38%) of indole **11**. **Quinoline 10.** ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 1.55$ (t, $J = 7.0$ Hz, 3H), 4.30 (q, $J = 7.0$ Hz, 2H), 7.09 (s, 1H), 7.39−7.69 (m, 5H), 8.01−8.19 (m, 4H). ^{13}C NMR ($CDCl_3$, 50 MHz): $\delta = 14.6$, 64.1, 98.6, 120.5, 121.7, 125.3, 127.6, 128.7, 129.1, 129.2, 130.0, 140.4, 149.2, 158.8, 162.2. IR ($CHCl_3$): $\nu = 1652$, 1593, 1558, 1506, 1215 cm^{-1}. ESI-MS: [$C_{17}H_{15}NO + H^+$] 250. MS-EI *m/z*: 249 (100), 234 (33), 221 (72), 220 (66), 193 (36), 165 (28). Anal. Calcd for $C_{17}H_{15}NO$: C, 81.90; H, 6.06; N, 5.62. Found: C, 82.12; H, 6.27.

(10) (a) Kuo, S.-C.; Lee, J.-P.; Juang, H.-Z.; Lin, Y.-T.; Wu, T.-S.; Chang, J.-J.; Lednicer, D.; Paull, K. D.; Lin, C. M.; Hamel, E.; Lee, K.-H. *J. Med. Chem.* **1993**, *36*, 1146. (b) Varma, S. R.; Kumar, D. *Tetrahedron Lett.* **1998**, *39*, 9113.

(11) Penoni, A. A.; Nicholas, K. M. *Chem. Commun.* **2002**, 484.

(12) Hegedus, L. S. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1113.

(13) (a) Bernasconi, C. F.; Flores, F. X.; Sun, W. *J. Am. Chem. Soc.* **1995**, *117*, 4875. (b) Aumann, R.; Hinterding, P.; Krüger, C.; Goddard, R. *J. Organomet. Chem.* **1993**, *459*, 145.