Solvent-Controlled Selectivity toward Exclusive C−C or C−H Bond Activation by a Cationic Metal Center

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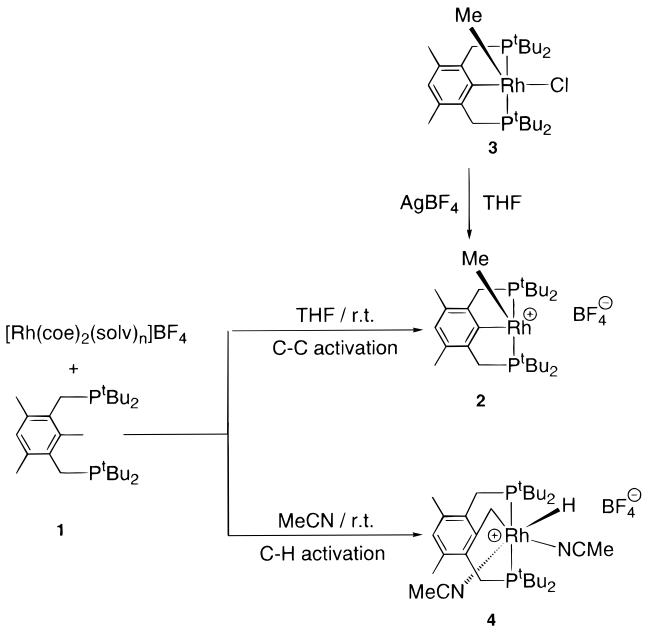
Transition metal insertion into C−C bonds in solution is a topic of much current interest.[1−5] Since C−H bond activation appears to be generally kinetically and thermodynamically more favorable than C−C bond activation,[1,2] special design of systems which can provide thermodynamic and kinetic driving forces for C−C bond activation is required.[1,3] The facile C−C bond oxidative addition of strong unactivated $C_{aryl}-C_{alkyl}$ bonds in pincer PCP (1,3-bis(phosphinomethyl)arene)[1,4] and PCN ((1-phosphinomethyl-3-aminomethyl)arene)[5] systems has been studied in our group, providing insight into this uncommon process. It was found that in the case of *neutral* metal centers and bulky PCP ligands C−C activation was thermodynamically and slightly kinetically more favorable than C−H activation.[4d] Here we report a *cationic* PCP−rhodium system, in which the reaction can be driven toward the *exclusive* activation of a C−C or a C−H bond at room temperature by *solvent choice*. This unique selectivity, together with the reversible interconversion of C−C and C−H activation products by solely varying the reaction solvent, allows the achievement of a remarkable degree of control over metal insertion into strong C−H vs C−C bonds.

Cationic rhodium precursors were obtained by chloride abstraction from $[Rh(coe)_2Cl]_2$ (coe = cyclooctene), according to a known procedure.[6] When $[Rh(coe)_2(solv)_n]BF_4$ was obtained in THF and reacted at room temperature with the phosphine **1**, quantitative formation of the C−C activation product **2** was observed after 1 h (Scheme 1). Complex **2** was characterized spectroscopically[7] and was also independently obtained by the reaction of the known[4d] complex **3** with $AgBF_4$ in THF, confirming the identity of the compound (Scheme 1). Complex **2** gives rise to a doublet centered at 60.16 ppm ($^1J_{RhP}$ = 122.2 Hz) in the $^{31}P\{^1H\}$ NMR spectrum. The Rh-***CH*$_3$** appears as a triplet of doublets at 1.91 ppm ($^3J_{PH}$ = 4.8 Hz, $^2J_{RhH}$ = 3.0 Hz) in the ^1H NMR spectrum and as a doublet of triplets at 3.11 ppm ($^1J_{RhC}$ = 31.7 Hz, $^2J_{PC,cis}$ = 5.0 Hz) in the $^{13}C\{^1H\}$ NMR spectrum, the chemical shifts being characteristic of a methyl group trans to an empty coordination site.[4d] The ipso carbon of the aryl group gives rise to a broad doublet centered at 151.22 ppm ($^1J_{RhC}$ = 29.0 Hz). No signals due to coordinated solvent were observed. The IR spectrum shows no signals assignable to coordinated N_2. ^{19}F NMR detects no coordination of the BF_4 anion. However, stabilization of **2** by weak coordination of the BF_4 anion cannot be completely ruled out. Complex **2** is stable at room temperature for days.

Scheme 1



Interestingly, when $[Rh(coe)_2(solv)_n]BF_4$ was obtained in a CH_3CN/CH_2Cl_2 mixture[8] ($CH_3CN:CH_2Cl_2$ = 1:2) and reacted at room temperature with **1**, exclusive formation of the C−H activation product **4**, which was fully characterized spectroscopically, was observed (Scheme 1).[9] Complex **4** gives rise to a doublet centered at 113.69 ppm ($^1J_{RhP}$ = 136.2 Hz) in the $^{31}P\{^1H\}$ NMR spectrum. The methylene in Rh-***CH*$_2$**-aryl appears as a triplet of doublets at 1.86 ppm ($^3J_{PH}$ = 10.0 Hz, $^2J_{RhH}$ = 2.7 Hz) in the ^1H NMR spectrum and as a broad doublet at 7.21 ppm ($^1J_{RhC}$ = 17.0 Hz) in the $^{13}C\{^1H\}$ NMR spectrum. The ^1H NMR signal of Rh-***H*** appears as a broad doublet at −20.66 ppm ($^2J_{RhH}$ = 4.8 Hz).

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(2) For reviews on hydrocarbon activation, see: (a) Crabtree, R. H. *Chem. Rev.* **1985**, *85*, 245. (b) Arndtsen, B. A.; Bergman, R. G.; Mobley, T. A.; Peterson, T. H. *Acc. Chem. Res.* **1995**, *28*, 154. (c) Shilov, A. E.; Shul'pin, G. B. *Chem. Rev.* **1997** 97, 2879 (d) Stahl, S. S.; Labinger, J. A.; Bercaw, J. E. *Angew. Chem., Int. Ed.* **1998**, *37*, 2180.

(3) For some examples of C−C bond activation in solution, see: (a) Cassar, L.; Eaton, P. E.; Halpern, J. *J. Am. Chem. Soc.* **1970**, *92*, 3515. (b) Periana, R. A.; Bergman, R. G. *J. Am. Chem. Soc.* **1986**, *108*, 7346. (c) Perthuisot, C.; Jones, W. D. *J. Am. Chem. Soc.* **1994**, *116*, 3647. (d) Suggs, J. W.; Jun, C.-H. *J. Am. Chem. Soc.* **1984**, *106*, 3054. (e) Murakami, M.; Amii, H.; Ito, Y. *Nature* **1994**, *370*, 540. (f) Crabtree, R. H.; Dion, R. P.; Gibboni, D. J.; McGrath, D. V.; Holt, E. M. *J. Am. Chem. Soc.* **1986**, *108*, 7222. (g) Bennett, M. A.; Nicholls, J. C.; Rahman, A. K. F.; Redhouse, A. D.; Spencer, J. L.; Willis A. C. *J. Chem. Soc., Chem. Commun.* **1989**, 1328. (h) Suzuki, H.; Takaya, Y.; Takemori, T. *J. Am. Chem. Soc.* **1994**, *116*, 10779. (i) Pulst, S.; Kirchbauer, F. G.; Heller, B.; Baumann, W.; Rosenthal U. *Angew. Chem., Int. Ed.* **1998**, *37*, 1925.

(4) For some examples of C−C bond activation in PCP systems, see: (a) Gozin, M.; Weisman, A.; Ben-David, Y.; Milstein, D. *Nature* **1993**, *364*, 699. (b) Liou, Sh.-Y.; Gozin, M.; Milstein, D. *J. Am. Chem. Soc.* **1995**, *117*, 9774. (c) Liou, Sh.-Y.; Gozin, M.; Milstein, D. *J. Chem. Soc., Chem. Commun.* **1995**, 1965. (d) Rybtchinski, B.; Vigalok, A.; Ben-David, Y.; Milstein, D. *J. Am. Chem. Soc.* **1996**, *118*, 12406. (e) van der Boom, M. E.; Kraatz, H.-B.; Ben-David, Y.; Milstein, D. *Chem. Commun.* **1996**, 2167. (f) Liou, Sh.-Y.; van der Boom, M. E.; Milstein, D. *Chem. Commun.* **1998**, 687. (g) van der Boom, M. E.; Liou, Sh.-Y.; Ben-David, Y.; Gozin, M.; Milstein, D. *J. Am. Chem. Soc.* **1998**, *120*, 13415.

(5) Gandelman, M.; Vigalok, A.; Shimon, L. J. W.; Milstein, D. *Organometallics* **1997**, *16*, 3981.

(6) Schrock, R. R.; Osborn, J. A. *J. Am. Chem. Soc.* **1971**, *93*, 3089.

(7) **Characterization of 2**. $^{31}P\{^1H\}$ NMR (C_6D_6) 60.16 (d, $^1J_{RhP}$ = 122.2 Hz). ^1H NMR 6.57 (s, 1H, Rh-***Ar***), 2.79 (dvt, the left part of the AB quartet, $^2J_{HH}$ = 17.5 Hz, $^3J_{PH}$ = 4.3 Hz, 2H, Ar−C***H***$_2$−P), 2.70 (dvt, the right part of the AB quartet, $^3J_{PH}$ = 3.4 Hz, 2H, Ar−C***H***$_2$−P), 2.10 (s, 6H, 2 Ar−C***H***$_3$), 1.91 (td, $^3J_{PH}$ = 4.8 Hz, $^2J_{RhH}$ = 3.0 Hz, 3H, Rh−C***H***$_3$), 1.27 (vt, $J_{PH,virt}$ = 6.8 Hz, 18H, 2 (C***H***$_3$)$_3$C−P), 1.08 (vt, $J_{PH,virt}$ = 6.3 Hz, 18H, 2 (C***H***$_3$)$_3$C−P). $^{13}C\{^1H\}$ NMR 151.22 (br d, $^1J_{RhC}$ = 29.0 Hz, C_{ipso}), 3.11 (dt, $^1J_{RhC}$ = 31.7 Hz, $^2J_{PC,cis}$ = 5.0 Hz, Rh-***C***H$_3$). Elem. Anal. Found (Calcd) C 52.91 (51.77), H 7.74 (8.05).

(8) Methylene chloride was added to increase the solubility of the reagents, which have limited solubility in acetonitrile.

(9) **Characterization of 4**. $^{31}P\{^1H\}$ NMR (CD_2Cl_2) 113.69 (d, $^1J_{RhP}$ = 136.2 Hz). ^1H NMR 6.50 (s, 1H, Rh-***Ar***), 3.38 (br d, the left part of the AB quartet, $^2J_{HH}$ = 14.8 Hz, 2H, Ar−C***H***$_2$−P), 2.93 (br d, the right part of the AB quartet, 2H, Ar−C***H***$_2$−P), 2.36 (s, 3H, C***H***$_3$CN−Rh), 2.34 (br s, 3H, C***H***$_3$CN−Rh), 2.28 (s, 6H, 2 Ar−C***H***$_3$), 1.86 (td, $^3J_{PH}$ = 10.0 Hz, $^2J_{RhH}$ = 2.7 Hz, Rh−C***H***$_2$−Ar), 1.57 (vt, $J_{PH,virt}$ = 6.0 Hz, 18H, 2 (C***H***$_3$)$_3$C−P), 1.08 (vt, $J_{PH,virt}$ = 6.3 Hz, 18H, 2 (C***H***$_3$)$_3$C−P), −20.66 (unresolved doublet, $^2J_{RhH}$ = 4.8 Hz, Rh-***H***). $^{13}C\{^1H\}$ NMR 7.21 (br d, $^1J_{RhC}$ = 17.0 Hz, Rh-***C***H$_2$−Ar). IR 2314.0 cm^{-1} (m) $\nu_{C\equiv N}$, 2285.3 cm^{-1} (m) $\nu_{C\equiv N}$, 2194.5 cm^{-1} (m) ν_{Rh-H} Elem. Anal. Found (Calcd) C 52.36 (52.55), H 7.75 (7.97).

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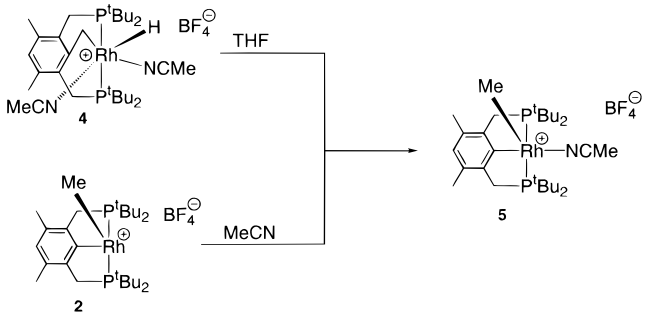
Scheme 2



Coordination of two CH_3CN molecules is evident from the NMR data[9] and further confirmed by IR which shows two bands at 2314.0 cm^{-1} (m) and 2285.3 cm^{-1} (m). Complex **4** is stable at room temperature.

Notably, the C−H activation complex **4**, on dissolving in THF, was quantitatively converted into the C−C activation complex **5**, an analogue of **2**, bearing one molecule of coordinated acetonitrile (Scheme 2). Addition of 10% of THF to a CH_2Cl_2 solution of **4** also resulted in formation of **5**, the process being much slower. Complex **5** was also obtained independently by addition of CH_3CN to a CH_2Cl_2 solution of **2** (Scheme 2). Complex **5** is stable at room temperature and does not coordinate an additional acetonitrile molecule on dissolving in CH_3CN. At room temperature in CH_3CN, **5** is slowly converted into **4**, demonstrating that the C−H activation complex **4** is a *thermodynamic* product, unlike in the case of analogous rhodium and iridium neutral systems.[4d] Complex **5** most probably undergoes slow reductive elimination of the C−C bond, followed by C−H activation, resulting in formation of the thermodynamic product **4**. Importantly, **4** is also the *kinetic* product, since it is the only observed product when the reaction solvent is CH_3CN/CH_2Cl_2. The C−C activation product **5**, which is stable at the reaction conditions, was not observed in the reaction mixture, its rate of formation being much slower than the rate of formation of **4**. Thus, the cationic PCP−rhodium system is very sensitive to the solvent choice, and the reaction can be driven to either C−C or C−H activation simply by replacing one solvent for another. Moreover, the products of C−C and C−H activation, when already formed, can be converted into each other also by a mere exchange of the solvents, providing a remarkable control over reaction selectivity.

Low-temperature follow-up of the reaction of the cationic rhodium complex and ligand **1** in THF revealed the concurrent formation of C−H and C−C activation products in the ratio of 2.3:1. No interconversion of the products was observed up to −30 °C. Taking into consideration that three C−H bonds per one C−C are accessible for activation, $\Delta\Delta G^{\ddagger}_{CH-CC}(243) = 0.537$ kcal/mol. Thus, in THF the C−C activation barrier is slightly lower than that for C−H activation. Gradual heating to room temperature resulted in the clean conversion of the C−H activated product into the C−C activated one, demonstrating that C−C activation in THF is thermodynamically more favorable. The details of the mechanism of C−C bond activation by cationic metal centers are under current investigation.

Our results clearly show that the C−C activation product in THF is both the *thermodynamic and the kinetic* one. Remarkably, the reactivity trend is inverted when an acetonitrile−methylene chloride mixture is used as the reaction medium: the C−H activation complex **4** is both the *kinetic* and the *thermodynamic* product at room temperature (vide supra). We believe that the different coordinating ability and size of the solvent molecule is affecting the kinetic and thermodynamic control. In the case of CH_3CN the reactive intermediate may bear one or two coordinated molecules of the solvent and it is apparently incapable of C−C activation, whereas in the case of THF a less saturated three-coordinate or two-coordinate intermediate can activate the C−C bond.

Addressing the question of the reactive intermediate structure, we carried out an experiment at low concentration of acetonitrile in methylene chloride. Indeed, at concentrations lower than 2% (v/v) formation of the C−C activation product along with the C−H one was observed (e.g., the ratio being C−C:C−H = 1:5 at 1% of CH_3CN and 1:4 at 0.5%). To clarify whether one or two solvent molecules are bound to the metal center in the reactive intermediate, we employed the bulky isopropyl nitrile. The methylene chloride−isopropyl nitrile system showed a remarkable similarity to the acetonitrile−methylene chloride one at various concentrations.[10] Taking into consideration the bulky character of the isopropyl nitrile and the tertiary butyl phosphines, there is a very low probability that two nitrile molecules are bound to the metal center in the transition state. Thus, the C−H activating reactive intermediate seems to be a three-coordinate complex with one solvent molecule bound to the metal center. C−C activation most probably requires a higher degree of unsaturation, and at low concentrations of the nitriles or in THF, a two-coordinate intermediate, capable of both C−H and C−C activation, may be formed. *Thus, it is likely that blocking of a coordination site in the cationic reactive intermediate makes C−C activation kinetically infeasible, while C−H activation can still take place*. While the reason for this is not clear, it may by due to the sterically more demanding C−C activation process in the case of a cationic metal center. Unlike its neutral counterpart, which is almost insensitive to the solvent choice,[4d,11] (probably because of lower tendency to bind solvent molecules) the cationic rhodium center appears to possess a very good selectivity in C−C vs C−H activation, conveniently regulated by the reaction solvent.

In summary, we found that, in C−C and C−H activation by an unsaturated cationic metal center, solvent influence is a major factor, controlling reaction selectivity, most probably due to its ability to coordinate to the metal center, and providing a significant and convenient tool for tuning toward the desired reaction outcome.

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Supporting Information Available: Text describing the general experimental procedures, formation of complexes **2** and **4**, and characterization of complexes **2**−**7** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(10) In the isopropyl nitrile−methylene chloride system the products of C−H activation (complex **6**) and C−C activation (complex **7**) are analogous to those observed using acetonitrile−methylene chloride. For the characterization see Supporting Information.

(11) No significant difference in reactivity as compared to other solvents[4d] was observed when the neutral metal system ($[Rh(coe)_2Cl]_2$ + ligand **1**) was employed in CH_3CN/CH_2Cl_2 as a solvent.