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Homogeneously catalyzed, chelate assisted hydrogenolysis of an amine C–N bond

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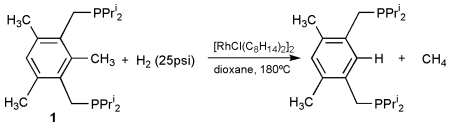
Reaction of $[RhCl(COE)_2]_2$ with an excess of the aromatic aminophosphine 1-(diethylaminomethyl)-3-(di-*tert*-butylphosphinomethyl)-2,4,6-trimethylbenzene (2) in dioxane under mild H_2 pressure results in selective catalytic activation of an unstrained C–N single bond.

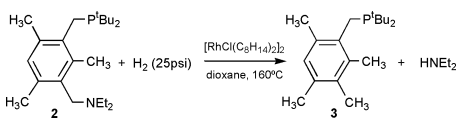
The design of homogeneous processes for selective activation and catalytic functionalization of strong single bonds by transition metal complexes is a highly desirable goal.[1] The catalytic C–N bond activation is of considerable current interest, as it is a key step in hydrodenitrogenation (HDN)—an important part of the hydrotreating process whereby crude oil or coal-derived liquids are upgraded to fuels.[2] Relatively few clear examples of metal-complex promoted C–N cleavage of amines are known, most of them being stoichiometric.[3–6] Catalytic reactions of this type are scarce.[7] We report here a remarkable example of *homogeneous catalytic* hydrogenolysis of an unstrained sp^3 C–N bond. This chelate-assisted rhodium catalyzed process occurs under homogeneous reaction conditions and is highly selective.

We have recently reported that the PCP-based ligand **1** undergoes selective catalytic C–C bond activation by Rh under H_2 pressure at 180 °C (Scheme 1).[8]



Scheme 1

In order to extend the scope of this process to other systems, we tried this reaction with the PCN-based ligand **2**. As we have recently shown, the stoichiometric reaction of **2** with $[RhCl(COE)_2]_2$ (COE = cyclooctene) results in exclusive C–C activation of the Ar–CH_3 bond situated in between the phosphine and amine 'arms'.[9] Surprisingly, when the reaction is performed in a catalytic manner C–N rather than C–C bond activation takes place. Thus, reaction of $[RhCl(COE)_2]_2$ with 10 eq. of **2** under mild H_2 pressure (25 psi) in dioxane at 160 °C for 24 h leads to quantitative formation of the hydrodenitrogenated phosphine **3** and diethylamine (Scheme 2, 10 turnovers based on Rh and 100% yield). The catalysis can be continued by adding more of substrate **2**, demonstrating that the catalyst remains active. The yield was lower when larger quantities of **2** were used. 13 turnovers (93%) were observed when 15 eq. of compound **2** were reacted, and 21 turnovers (47% yield) for 45 eq. of the starting material.



Scheme 2

The product diethylamine was identified and quantified by GC-MS and GC analysis, respectively. It was also detected by ^{1}H-NMR, when the reaction was performed in dioxane-d_8. The phosphine **3** was isolated by evaporation of diethylamine and subsequent extraction of the residue with pentane and was fully characterized by $^{31}P\{^1H\}$, ^{1}H, $^{13}C\{^1H\}$, ^{13}C-DEPT NMR and MS techniques. The structure of **3** was confirmed by comparison with an authentic sample, which was independently prepared by phosphination of bromomethylisodurene.† Formation of **3** is highly selective, no other organic products being catalytically formed (*vide infra*). Control experiments showed that substrate **2** does not undergo catalytic C–N activation under the reaction conditions in the absence of Rh or H_2.

A postulated catalytic cycle is presented in Scheme 3. Initially, selective insertion of Rh(I) into the aryl-CH_3 bond resulting in complex **4** most probably takes place. As reported, the stoichiometric reaction of **2** with $[RhCl(COE)_2]_2$ leads to **4**.[9] Subsequently, **4** reacts with H_2 to yield the hydrido chloride complex **5** and CH_4. Indeed, when the reaction was performed with a small excess of **2** (5–7 eq.), a stoichiometric amount of **5** was detected by NMR spectroscopy. Also, a stoichiometric amount of CH_4 (based on Rh) was regularly observed by GC analysis in the catalytic reaction. Compound **5** and CH_4 were independently obtained by the reaction of **4** with H_2 (25 psi) at 80 °C for 3 d. The products were analyzed by $^{31}P\{^1H\}$, ^{1}H, $^{13}C\{1H\}$, ^{13}C-DEPT NMR‡ and by GC. This reaction may proceed through a Rh(V) intermediate or *via* σ-bond metathesis. Complex **5** is part of the catalytic cycle and can also be used as catalyst under the same reaction conditions.

The exchange of the amine 'arm' of **5** by the phosphine moiety of **2** most probably proceeds *via* intermediates **A** and **B**. Replacement of a pincer-type amino ligand of Ru(II) by a phosphine analog was reported recently.[10] The exchange of the phosphine group in **5** by the amine 'arm' of **2** is impeded, since an amine is, in general, a poorer ligand for low valent late transition metals than a phosphine.[11] At this stage, most probably, C–N bond activation and hydrogenolysis by the unsaturated Rh center takes place, giving the phosphine-coordinated product **C** and diethylamine. Following replacement of **3** by the amine 'arm', **5** is regenerated, this process being assisted by the generation of two stable five-membered chelating rings. The liberated **3** most probably competes with **2**, slowing down the catalytic process as its concentration increases.

An alternative mechanism involving phosphine displacement by the amine group in **B** can be excluded, as we have observed that Ar-CH_3 bond activation occurs immediately even under very mild conditions, when both P and N ligands are coordinated.[12]

In summary, catalytic hydrogenolysis of an unstrained C–N bond has been presented. The phosphinoamine mixed system **3** undergoes selective stoichiometric C–C and catalytic C–N bond activation by Rh. In addition to the general interest in catalytic C–N activation, the reactivity of pincer-type complexes is the focus of much current research.[13]

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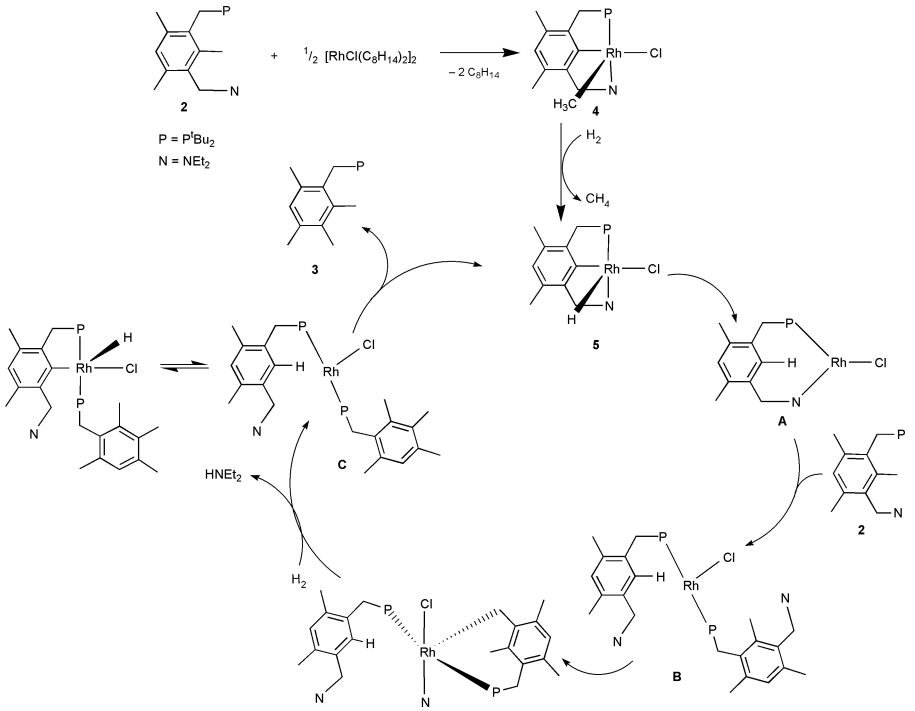

Scheme 3

Notes and references

† *Independent synthesis of 1-(di-tert-butylphosphinomethyl)-2,3,4,6-tetramethylbenzene* (**3**). 1-Bromomethyl-2,3,4,6-tetramethylbenzene was prepared by bromomethylation of isodurene (1,2,3,5-tetramethylbenzene) according to a literature procedure.[14] The resulting bromomethylisodurene (2 g, 8.81 mmol) and di-*tert*-butylphosphine[15] (1.29 g, 8.81 mmol) in acetone (20 ml) were heated under reflux with stirring for 2 h.[16] The mixture was cooled to rt, the white precipitate that formed was filtered off and washed with hexane to remove unreacted starting material. The obtained phosphonium salt was dissolved in water and treated with a 10-fold excess (based on starting bromide) of sodium carbonate. The organic product was extracted with ether (3 × 20 ml). The ether fractions were combined, and the solvent was evaporated, giving the clean phosphine **3** in 86% yield (2.21 g). Selected NMR data for **3**: ^{31}P{^{1}H} NMR ($CDCl_3$): 26.86 (s); δ_H($CDCl_3$): 6.82 (s, 1H, Ar-*H*), 2.91 (d, J_{PH} = 1.9 Hz, 2H, Ar-CH_2-P), 2.49 (s, 3H, Ar-CH_3), 2.47 (s, 3H, Ar-CH_3), 2.13 (s, 3H, Ar-CH_3), 2.03 (s, 3H, Ar-CH_3), 1.10 (d, J_{PH} = 10.3 Hz, 18H, 2 P-C(CH_3)$_3$; δ_H($CDCl_3$): 32.05 (d, J_{PC} = 26.4 Hz, 2 (CH$_3$)$_3$*C*-P), 29.71 (d, J_{PC} = 13.4 Hz, 2 (*C*H$_3$)$_3$C-P), 24.15 (d, J_{PC} = 29.5 Hz, Ar-*C*H$_2$-P), 21.89 (d, J_{PC} = 6.8 Hz, Ar-*C*H$_3$), 20.38 (s, Ar-*C*H$_3$), 18.17 (d, J_{PC} = 10.9 Hz, Ar-*C*H$_3$), 15.87 (s, Ar-*C*H$_3$). (Assignment of ^{13}C {^{1}H} NMR signals was confirmed by ^{13}C DEPT.)

‡ *Spectral data for* **5**. δ_P(benzene-d_6): 95.39 (dd, J_{RhP} = 147.3, J_{HP} = 21.8 Hz); δ_H(benzene-d_6): 6.55 (s, 1H, Ar), 3.84 (br d, J_{HH} = 15.9 Hz, 1H, Ar-CH_2-N), 3.50 (br d, J_{HH} = 15.9 Hz, 1H, Ar-CH_2-N), 3.46 (m, 1H, Ar-CH_2-P), 2.94 (m, 1H, Ar-CH_2-P), 2.68 (m, 1H, CH$_3$-CH_2-N), 2.52 (m, 1H, CH$_3$-CH_2-N), 2.17 (s, 3H, Ar-CH_3), 2.03 (s, 3H, Ar-CH_3), 1.35 (d, J_{PH} = 13.0 Hz, 9H, (CH_3)$_3$C-P), 1.21 (d, J_{PH} = 13.6 Hz, 9H, (CH_3)$_3$C-P), 1.19 (t, J_{HH} = 7.4 Hz, 3H, CH_3-CH$_2$-N), 0.83 (t, J_{HH} = 7.3 Hz, 3H, CH_3-CH$_2$-N), −26.83 (dd, J_{PH} = 23.2, J_{RhH} = 54.7 Hz, 1H, Rh-H); δ_C(benzene-d$_6$): 163.61 (dd, J_{RhC} = 33.8, $J_{PC,cis}$ = 4.8 Hz, C$_{ipso}$, Rh-Ar), 145.81 (s, Ar), 144.47 (dd, J_{PC} = 10.9, J_{RhC} = 3.4 Hz, Ar), 130.79 (dd, J_{PC} = 16.1, J_{RhC} = 1.9 Hz, Ar), 130.03 (s, Ar), 126.65 (s, Ar), 63.39 (s, Ar-*C*H$_2$-N), 54.84 (s, CH$_3$-*C*H$_2$-N), 54.32 (s, CH$_3$-*C*H$_2$-N), 32.28 (dd, J_{PC} = 26.4, J_{RhC} = 3.5 Hz, Ar-*C*H$_2$-P), 29.22 (d, J_{PC} = 3.3 Hz, (CH$_3$)$_3$C-P), 28.77 (d, J_{PC} = 3.2 Hz, (CH$_3$)$_3$C-P), 20.71 (s, CH$_3$-Ar), 19.65 (s, CH$_3$-Ar), 12.38 (s, *C*H$_3$-CH$_2$-N), 11.61 (s, *C*H$_3$-CH$_2$-N). (Assignment of ^{13}C {^{1}H} NMR signals was confirmed by ^{13}C DEPT.)

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