Novel Azine Reactivity

Novel Azine Reactivity: Facile N–N Bond Cleavage, C–H Activation, and N–N Coupling Mediated by Rh^I**

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Azines ($R_2C{=}N{-}N{=}CR_2$) are very useful compounds. For example, they undergo unusual [1,3] dipolar cycloaddition reactions (the crisscross addition) with dienophiles, which provide a convenient route to five-membered rings.[1] They also participate in [3+2] cycloaddition reactions as an *ene* fragment.[2] Applications of azines include possible nonlinear optical materials[3] and conducting polymers (polyazines).[4] Relevant to dinitrogen fixation, the formation of azines by metal-mediated functionalization of N_2 was demonstrated.[5] Azine derivatives display important biological properties and are of importance for drug development.[6] Complexes of titanium,[7] zirconium,[7c] cobalt,[7c] uranium,[8] and iron[9] are capable of cleaving the N–N bond in azines. In all the reported cases, the azine N–N bond is cleaved symmetrically forming two imide units, $-N{=}CR_2$, coordinated to a metal center. No metal-complex-catalyzed reactions were reported. Herein we report a novel type of azine reactivity, the rhodium-promoted catalytic "nonsymmetrical" N–N bond cleavage accompanied by C–H activation, which leads to an imine and benzonitrile. This is the first metal-promoted nonsymmetric cleavage of the N–N bond in an azine[10] and the first metal-catalyzed N–N activation in an azine.

When a toluene solution of the PCP-pincer rhodium complex **1**[11] was treated with one equivalent of benzalazine at −30 °C, three complexes were formed (Scheme 1). One of them, tentatively identified by NMR spectroscopy as the [(PCP)Rh(benzalazine)] complex **2** (precedents exist for azine complexes[7]), is an intermediate, which converts into

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Supporting information for this article (preparation procedures for complexes **3, 4**, and **6**, and *xyz* coordinates of the computed structures) is available on the WWW under http://www.angewandte.org or from the author.

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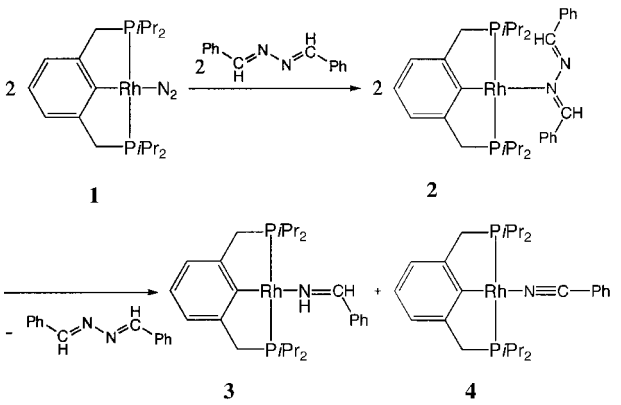
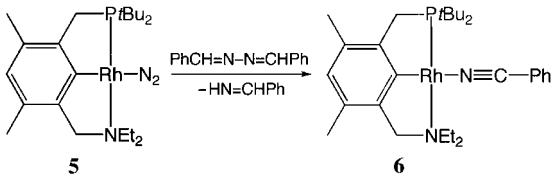


Scheme 1. Reaction of benzalazine with **1**.

the two new complexes **3** and **4** in a 1:1 ratio within an hour at room temperature.

The phenylimine complex **3** and benzonitrile complex **4** were characterized by various NMR spectroscopy techniques (^{31}P, ^{1}H, ^{13}C, and ^{13}C-^{1}H and ^{15}N-^{1}H correlation experiments, Table 1). Formation of the benzonitrile complex **4** was verified by its independent synthesis from complex **1** and PhCN. Complex **3** could not be isolated and was characterized in a mixture with **4**. The exact mode of imine coordination in **3** is uncertain and an η^1-N/η^2-C,N equilibrium of the coordinated imine molecule may exist. Primary imine complexes are known,[12] but to our knowledge, their direct synthesis from azines has not been reported. Within a day at room temperature, the imine complex **3** decomposed to unidentifiable products. Complex **4** was stable at room temperature for days.

The [(PCN)Rh(N_2)] complex **5** exhibits reactivity similar to that of **1**. Upon reaction with benzalazine quantitative formation of the benzonitrile complex **6** (Table 1) was observed together with formation of free imine PhCH=NH (Scheme 2).[13] This imine is unstable and rapidly decomposes



Scheme 2. Reaction of benzalazine with **5**.

(10 min at room temperature), in agreement with literature data.[14] The structure of **6** determined by crystal-structure analysis is presented in Figure 1. Complex **6** is square planar

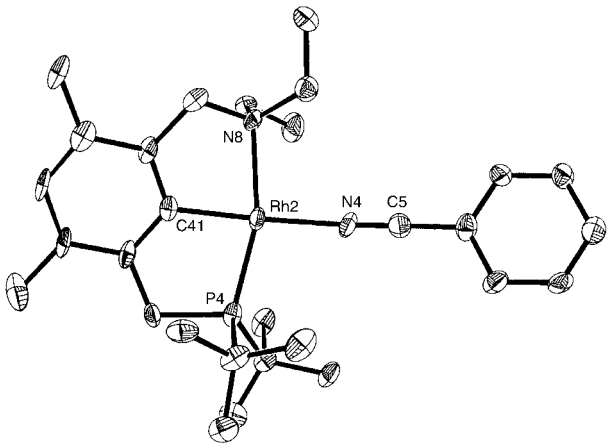


Figure 1. Molecular structure of **6**. Selected bond lengths [Å] and bond angles [°]: Rh2-C41 = 1.986(11), Rh2-N4 = 2.033(9), Rh2-P4 = 2.197(4), Rh2-N8 = 2.196(11), N4-C5 = 1.159(15); N4-Rh2-C41 = 174.2(7), P4-Rh2-N8 = 163.0(3). CCDC-197955 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or deposit@ccdc.cam.ac.uk).

with the PhCN molecule occupying the position *trans* to the aryl ring. Unlike the case of the (PCP)Rh-based system, no azine or imine complex formation was observed, probably reflecting the more sterically congested character of the (PCN)Rh unit in **5**. Formation of the benzonitrile complex **6** was verified by independent synthesis from complex **5** and PhCN.

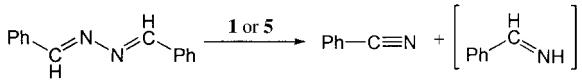
When benzalazine was used in excess (10 equiv) with either complex **1** or **5**, an unprecedented catalytic reaction producing 7 equivalents of benzonitrile took place (Scheme 3). The imine PhCH=NH could not be detected, probably because of its fast decomposition.[14] The same turnover number (TON) was observed upon addition of

Table 1: Selected spectroscopic data for compounds **3, 4**, and **6**. NMR spectra in [D_8]toluene (^{1}H: 400 MHz, ^{13}C: 100 MHz, ^{15}N: 40 MHz, ^{31}P: 162 MHz), δ in ppm, J in Hz.

3: ^{31}P NMR: $\delta = 61.50$ (d, $J_{Rh,P} = 166.0$); ^{1}H NMR: $\delta = 10.25$ (d, $J_{H,H} = 14.7$, 1H, *H*N=CHPh), 7.96 (d, $J_{H,H} = 14.7$, 1H, HN=C*H*Ph); ^{13}C NMR: $\delta = 166.09$ (br s, HN=CHPh); ^{15}N-^{1}H correlation NMR (referenced to liq. NH_3): $\delta = 392.12$ (br s, HN=CHPh, $J_{N,H} = 65.0$); the NMR assignment is verified by ^{1}H-^{1}H COSY, heteronuclear ^{13}C-^{1}H and ^{15}N-^{1}H correlation experiments and ^{13}C DEPT-135

4: ^{31}P NMR: $\delta = 63.85$ (d, $J_{Rh,P} = 162.0$); ^{1}H NMR: $\delta = 7.16$–7.10 (m, 3H, aryl), 7.02–6.92 (m, 2H, aryl), 6.77 (m, 2H, aryl), 6.68 (m, 1H, aryl), 3.10 (vt, $J_{P,H} = 7.2$, 4H, PCH_2-aryl), 2.04 (m, 4H, $(CH_3)_2CHP$), 1.36 (dvt, $J_{P,H} = 15.6$, $J_{H,H} = 7$, 12H, $(CH_3)_2CHP$), 1.19 (dvt, $J_{P,H} = 13.0$, $J_{H,H} = 7$, 12H, $(CH_3)_2CHP$); ^{13}C NMR: $\delta = 180.33$ (dt, $J_{Rh,C} = 36.8$, $J_{P,C} = 12.2$, C_{ipso}), 157.17 (t, $J_{P,C} = 12.8$, PhCNRh), 137.40 (s, aryl), 135.83 (s, aryl), 134.52 (s, aryl), 134.35 (s, aryl), 133.93 (s, aryl), 127.01 (s, aryl), 125.78 (t, $J_{P,C} = 9.6$, aryl), 41.82 (dvt, $J_{P,C} = 21.6$, $J_{Rh,C} = 4.1$, PCH_2-aryl), 31.17 (vt, $J_{P,C} = 17.2$, $(CH_3)_2CHP$), 24.40 (s, $(CH_3)_2CHP$), 19.44 (s, $(CH_3)_2CHP$); IR: $\tilde{\nu} = 2183.8$ cm^{-1} (m, $\nu_{C\equiv N}$)

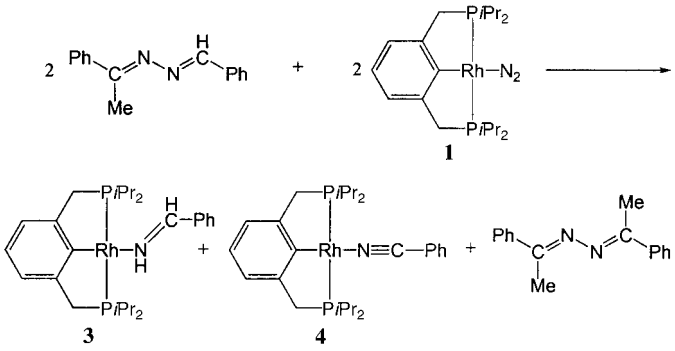
6: ^{31}P NMR: $\delta = 7.51$ (d, $J_{Rh,P} = 231.3$); ^{1}H NMR: $\delta = 7.19$–7.16 (m, 2H, aryl), 6.98–6.93 (m, 3H, aryl), 6.52 (br s, 1H, aryl), 3.90 (s, 2H, aryl-CH_2N), 3.07 (d, $J_{P,H} = 8.2$, 2H, PCH_2-aryl), 2.86 (m, 2H, CH_3CH_2N), 2.76 (m, 2H, CH_3CH_2N), 2.36 (s, 3H, aryl-CH_3), 2.24 (s, 3H, aryl-CH_3), 1.63 (t, $J_{H,H} = 7.2$, 6H, CH_3CH_2N), 1.48 (d, $J_{P,H} = 11.7$, 18H, $(CH_3)_2CHP$); ^{13}C NMR: $\delta = 178.82$ (dd, $J_{Rh,C} = 37.7$, $J_{P,C} = 10.0$, C_{ipso}), 146.55 (dd, $J_{Rh,C} = 19.1$, $J_{P,C} = 6.7$, PhCNRh), 145.86 (s, aryl), 130.81 (s, aryl), 130.55 (s, aryl), 129.57 (s, aryl), 127.95 (s, aryl), 123.81 (s, aryl), 118.99 (s, aryl), 115.12 (s, aryl), 65.12 (s, aryl-CH_2N), 54.48 (s, NCH_2CH_3), 35.76 (dd, $J_{P,C} = 26.1$, $J_{Rh,C} = 5.6$, aryl-CH_2P), 35.19 (dd, $J_{P,C} = 11.7$, $J_{Rh,C} = 1.9$, $(CH_3)_2CP$), 30.42 (d, $J_{P,C} = 5.8$, $(CH_3)_2CP$), 22.18 (s, aryl-CH_3), 20.96 (s, aryl-CH_3), 13.46 (s, NCH_2CH_3)



Scheme 3. Catalytic reaction of **1** or **5** with benzalazine.

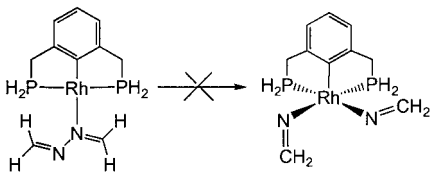
100 equivalents of the azine, which indicates that the catalysis is hampered by the benzonitrile product in both the PCP and PCN cases; PhCN coordinates to the rhodium centers to form the complexes **3** and **6**, and interferes with the azine activation process, which causes low TONs. Optimization of the catalysis is currently being sought in our group. Stoichiometric (not catalytic) C–H and N–N activation in azines are reported,[7] but not the combination of both in one system as in the (PCP)Rh-based one.[15]

Treating complexes **1** or **5** with the ketazine Me(Ph)C=N–N=C(Ph)Me revealed no reactivity even at elevated temperatures. Interestingly, when the nonsymmetrical azine Me(Ph)=N–N=C(Ph)H was reacted with complex **1** in toluene, the same organometallic products as in the benzalazine case, complexes **3** and **4**, were formed in a 1:1 ratio within one hour at room temperature together with an equivalent amount of the ketazine Me(Ph)C=N–N=C(Ph)Me, as observed by NMR spectroscopy and confirmed by GC-MS (Scheme 4).[16]



Scheme 4. Reactivity of **1** towards the nonsymmetrical azine Me(Ph)=N–N=C(Ph)H.

Thus, a symmetric ketazine molecule can be formed from two nonsymmetric aldazine/ketazine molecules. Such a metal-promoted apparent N–N bond cleavage/coupling sequence is unprecedented to our knoweledge. Importantly, only the aldazine "half" gives rise to the imine (and nitrile) complexes. These observations imply involvement of a C–H activation and suggest that a complex reaction mechanism, probably bimolecular, is operative. We believe that the azine splitting observed in the (PCP)Rh- and (PCN)Rh-based systems does not proceed through direct metal insertion into the N–N bond. Further confirmation was obtained from a computational DFT study of the N–N cleavage step (at the mPW1k[17]/LANL2DZ+P//mPW1k/LANL2DZ[18] level of theory[19]). Our model system included a PCP ligand with H-substituted phosphanyl groups and a formaldazine molecule. (No spin-state crossing was considered.) The direct N–N bond cleavage producing the bisimide rhodium complex (Scheme 5) was



Scheme 5. Computational analysis of N–N cleavage in azine in a model system.

found to have a kinetic barrier of 63 kcal mol^{-1} (and to be endergonic by 11.6 kcal mol^{-1}), grossly inconsistent with the experimental observation that the reaction takes place even at −30 °C. The optimized geometry of the bisimide complex exhibits a large deviation from planarity in the chelate core, the two phosphanyl groups acquiring a close to *cis* configuration (P-Rh-P angle is 108°). This is likely to result from the strong *trans* effect of the imide ligands, which destabilizes the complex and causes a high activation barrier as a consequence of the large change in geometry compared to the azine complex. Thus, most probably, direct N–N activation is not operative in our systems—in contrast to the reported examples.[7–9] Computational investigation of the mechanism is currently under way.

In conclusion, we have reported a novel type of azine reactivity, the nonsymmetrical rhodium-mediated N–N bond cleavage, coupled with C–H activation to form a nitrile and an imine. The reaction is catalytic, providing the first example of metal-complex-catalyzed N–N bond cleavage in an azine, although deactivation by the nitrile product takes place. It most probably does not proceed through direct N–N bond cleavage, but through a mechanism involving a C–H activation step. A metal-promoted N–N bond cleavage/N–N coupling sequence was also demonstrated that led to a symmetric ketazine from a mixed aldazine/ketazine molecule. These reactions provide new insight into metal-promoted transformations of azines. The synthetic implications of these findings are being explored.

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Keywords: azines · C–H activation · density functional calculations · N–N activation · pincer ligands

[1] a) "Azomethine Imines": R. Grashey, A. Padwa in *1,3-Dipolar Cycloaddition Chemistry, Vol. 1* (Eds.: D. C. Taylort, A. Weissberger), Wiley, New York, **1984**, p. 733; b) S. Radl, *Aldrichimica Acta* **1997**, *30*, 97.
[2] See, for example: E. E. Schweizer, Z. Cao, A. L. Rheingold, M. Bruch, *J. Org. Chem.* **1993**, *58*, 4339.
[3] H. S. Nalwa, A. Kakatu, A. Mukoh, *J. Appl. Phys.* **1993**, *73*, 4743.
[4] E. C. Kesslen, W. B. Euler, *Chem. Mater.* **1999**, *11*, 336.
[5] Y. Nishibayashi, S. Iwai, M. Hidai, *Science* **1998**, *279*, 540; S. M. Rocklage, R. R. Schrock, *J. Am. Chem. Soc.* **1982**, *104*, 3077.
[6] a) A. I. Kholdair, P. Bertrand, *Tetrahedron* **1998**, *54*, 4859; b) K. Yasumura, K. Miyajima, T. Nagahama, S. Ishikawa, Y. Tohyama, K. Sugiyama. PCT, WO 94/19335.
[7] a) M. Rep, J.-W. F. Kaagman, C. J. Elsevier, P. Sedmera, J. Hiller, U. Thewalt, M. Horacek, K. Mach, *J. Organomet. Chem.* **2000**, *597*, 146; b) A. Ohff, T. Zippel, P. Arndt, A. Spannenberg, R.

Kempe, U. Rosenthal, *Organometallics* **1998**, *17*, 1649; c) T. Zippel, P. Arndt, A. Ohff, A. Spannenberg, R. Kempe, U. Rosenthal, *Organometallics* **1998**, *17*, 4429.
[8] J. L. Kiplinger, D. E. Morris, B. L. Scott, C. J. Burns, *Organometallics* **2002**, *21*, 3073.
[9] A. Zimniak, G. Bakalarski, *J. Mol. Struct.* **2001**, *597*, 211.
[10] Photolytic N–N bond cleavage in benzalazine to form benzonitrile and benzalimine is known: R. W. Binkley, *J. Org. Chem.* **1969**, *34*, 2073.
[11] M. Gandelman, B. Rybtchinski, N. Ashkenazi, R. Gauvin, D. Milstein, *J. Am. Chem. Soc.* **2001**, *123*, 5372.
[12] See, for example: a) W.-Y. Yeh, C.-S. Ting, S.-M. Peng, G.-H. Lee, *Organometallics* **1995**, *14*, 1417; b) D. A. Knight, M. A. Dewey, G. A. Stark, B. K. Bennet, A. M. Arif, J. A. Gladysz, *Organometallics* **1993**, *12*, 4523, and references therein.
[13] PhCH=NH was identified by comparison of its ^{1}H NMR data to the reported ones: D. R. Boyd, P. B. Coulter, R. Hamilton, N. T. Thompson, N. D. Sharma, M. E. Stubbs, *J. Chem. Soc. Perkin Trans. 1* **1985**, 2123.
[14] PhCH=NH was reported to be unstable at room temperature; it decomposes forming oligomers (see ref. [13]).
[15] We detected only traces of benzonitrile upon reaction of benzalazine with $[(i\mathrm{Pr}_3\mathrm{P})_2\mathrm{RhCl}]$ or $[(i\mathrm{Pr}_3\mathrm{P})_2\mathrm{Rh}(\mathrm{N}_2)\mathrm{Cl}]$.
[16] In the absence of **1**, no reaction was observed after several hours at room temperature. Acid- and water-catalyzed disproportionation of the nonsymmetrical azine to the aldazine and ketazine was reported: D. H. Kenny, *J. Chem. Educ.* **1980**, *57*, 462.
[17] B. J. Lynch, P. L. Fast, M. Harris, D. G. Truhlar, *J. Phys. Chem. A* **2000**, *104*, 4811.
[18] P. J. Hay, W. R. Wadt, *J. Chem. Phys.* **1985**, *82*, 299.
[19] See Supporting Information for full details.

