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Computational Chemistry

Hydroamination of Alkynes with Ammonia: Unforeseen Role of the Gold(I) Catalyst**

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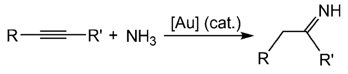
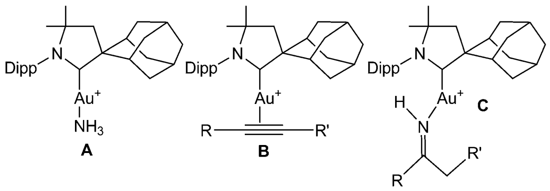
The formation of nitrogen–carbon bonds represents a highly valuable synthetic method to prepare products ranging from chemical feedstocks to pharmaceutical materials. It is therefore not surprising that such reactions have been the focus of catalysis research.[1] The use of ammonia as a reactant is highly desired as the addition of NH_3 to C–C multiple bonds represents a highly attractive process for C–N bond formation, and complete atom economy is achieved.[2] Nevertheless, atom-efficient processes for combining NH_3 with simple organic molecules are rather scarce.[3] It is known that transition-metal complexes can make N–H bonds reactive for additional functionalization, however in most cases when metals react with ammonia (there are some exceptions)[4] the supposedly inert Werner complex is formed. Hence, functionalization of NH_3 was difficult to obtain until the groups of Hartwig[5] and Buchwald[6] described the palladium-catalyzed coupling of ammonia with aryl halides.

Hydroamination is the addition reaction of the N–H bond of an amine moiety to an unsaturated carbon–carbon double bond. Earlier, several metal complexes involving palladium,[7] rhodium,[8] ruthenium,[9] and platinum[10] centers were found to be active catalysts for this process, and gold has been recently identified as an efficient hydroamination catalyst.[11–13]

Bertrand and co-workers recently reported a seminal work describing the hydroamination of a variety of unactivated alkynes and allenes[14] catalyzed by gold complexes prepared with a cyclic (alkyl)(amino)carbene (CAAC; Scheme 1).[15] The authors also carried out mechanistic investigations, in which several gold complexes formed in the presence of ammonia and 3-hexyne were detected. The precursor complex reacted with ammonia to form the cationic complex **A**, and with 3-hexyne to form complex **B** (Scheme 2). The addition of NH_3 to complex **B** instantaneously forms complex **A**. However, **A** in the excess of the alkyne substrate is transformed directly to the gold imine complex **C**. One of the reasonable interpretations of these data suggests that during the reaction NH_3 does not add to the coordinated alkyne through an outer-sphere mechanism, but the reaction proceeds through insertion of the alkyne into the Au–N bond.



Scheme 1. Catalytic hydroamination of alkynes with ammonia.



Scheme 2. Experimentally detected intermediates in solution. Dipp = 2,6-diisopropylphenyl.

Herein we present the results of the theoretical investigation[16] of the reaction pathway that shows the particular role of the gold catalyst and NH_3 in the reaction mechanism. We have recently performed a detailed analysis of the possible mechanistic pathways for the gold-catalyzed hydroamination of conjugated dienes and olefines with $CbzNH_2$ (benzyl carbamate).[17] The most favorable reaction mechanism involves 1) coordination of the unsaturated substrate to the metal center, 2) nucleophilic attack of the amine moiety on the C–C double bond, and 3) the key step of the reaction, that is, the proton transfer from the NH_2 to the unsaturated carbon atom, which is always facilitated by a proton-transfer agent.

The relative stabilities of the actual complexes identified by Bertrand et al. were initially analyzed.[18] The calculations showed that in solution, the Werner complex **1** that is formed with NH_3 is the most stable one, compared to the alkyne complex **2**; the calculations are in agreement with experiments (Figure 1). These results show the remarkable difference between NH_3 and other N nucleophiles, such as $CbzNH_2$: the formation of $[R_3PAu(NH_2Cbz)]^+$ was much less favorable from PR_3AuOTf than that of the π complex with the diene substrate.[17] Here, we carried out bond dissociation energy (BDE) calculations for NH_3 and $CbzNH_2$ on a series of $[AuL]^+$ species and showed that NH_3 forms more stable complexes with Au^I than with $CbzNH_2$, independently of the ligand.[19]

The possible pathways for the nucleophilic addition of NH_3 are the outer- (*anti*) and inner-sphere (*syn*) mechanisms.

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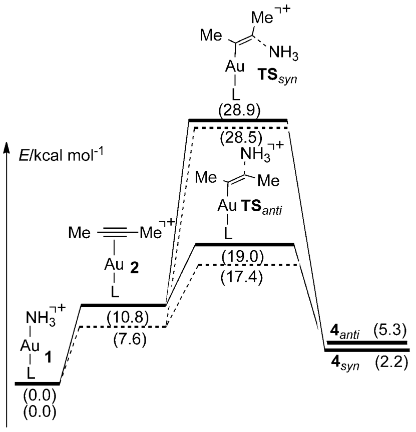


Figure 1. Energy profile in toluene for the outer- and inner-sphere nucleophilic attacks. Solid line: relative energy values with the model system; Dashed line: relative energy values with the real catalyst. L = ligand (model or real CAAC).

In the *syn* pathway, ammonia attacks from the side adjacent to the metal, as suggested by Bertrand and co-workers given the proposal by Tanaka et al.[20] on the hydroamination of alkynes with aniline. In contrast, for the *anti* pathway the nucleophile comes from the other side of the alkyne.

The transition states for both possible nucleophilic attacks (**TS**$_{syn}$ and **TS**$_{anti}$) and the corresponding products (**4**$_{syn}$ and **4**$_{anti}$) have been located on the potential energy surface (Figure 1) and the structures are shown in Figure 2. We have to mention that transition states corresponding to the insertion of the alkyne into the N–H bond of NH_3 were not possible to obtain. Regarding the energy barriers, **TS**$_{anti}$ lies 19.0 kcal mol^{-1} above the most stable complex, **1**, whereas the barrier for the *syn* attack is 28.9 kcal mol^{-1}. This shows that the outer-sphere nucleophilic attack is strongly favored (by 9.9 kcal mol^{-1})[21] compared to the attack the side with the metal (Figure 1). As the preference for the inner- versus outer-sphere depends on the corresponding barriers for the nucleophilic attack, **2** is the most favorable starting point for the catalytic cycle despite the relative stabilities of the species **1** and **2** in solution. The energy difference between **1** and **2** is 10.8 kcal mol^{-1}, and the tricoordinated complex **3** (see the Supporting Information) was found as a minimum with the model system, which lies only 12.6 kcal mol^{-1} above **1**, thus showing the facile interconversion between **1** and **2**. On the basis of these results, complex **1** is the resting state of the catalyst, whereas species **2** is directly involved in the catalytic cycle, an interpretation that is also in agreement with experiments.[14]

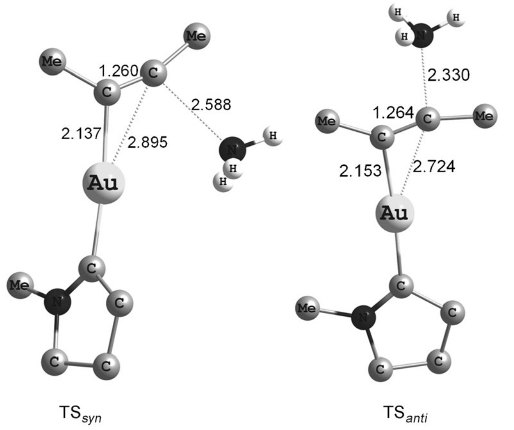


Figure 2. Optimized transition-state structures for the inner- and outer-sphere nucleophilic attacks.

The most intriguing step of hydroamination is the proton transfer from the nitrogen to the other carbon atom which leads to product formation. As the final product is the corresponding imine, two proton transfers have to take place. The direct proton transfer from the NH_3 group (first proton transfer) to the carbon atom is an unfavorable pathway involving a stressed four-membered (CCNH) ring transition state (**TS**$_{P1'}$, see the Supporting Information) with a barrier of 47.4 kcal mol^{-1} (consistent with our previous results with gold phosphines).[17] It is already well known from the literature that a counter anion[22] or a Lewis base[23] (which can also be the reacting nucleophile) can play the role of a proton-transfer agent, thus remarkably lowering energy barriers. In previously studied gold-catalyzed hydroamination reactions, we showed such a role for triflate anions[17a,b] and carbamate.[17b] Since in the present case, the corresponding $[B(C_6F_5)_4]^-$ anion is too bulky to act as a proton-transfer agent, the best candidates are the ammonia molecules, which are present in excess in the reaction mixture.[14]

The transition state for the nucleophile-assisted proton transfer from the NH_3 group to the unsaturated carbon atom (**TS**$_{P1}$) is shown in Figure 3. In **TS**$_{P1}$ an NH_4^+ is formed, thus acting as a proton shuttle which can transfer the proton either to the carbon or nitrogen atom. The energy barrier for the first NH_3-assisted proton transfer is quite low (5.5 kcal mol^{-1}), thus representing a feasible reaction step (Figure 4). In the product (**5**) of the proton-transfer reaction the N atom is planar and sp^2 hybridized ($\theta_{HNCH} = 178.6°$), whereas the C–C bond has single bond character (d(C-C) = 1.435 Å); that is, a protonated imine moiety is formed after the first proton transfer.

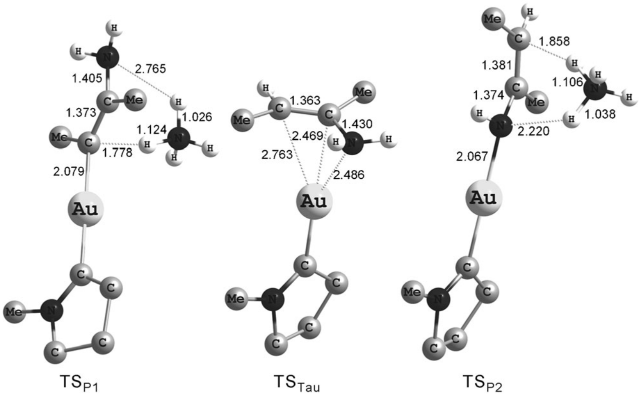


Figure 3. Optimized geometries for the transition states involved in the proton-transfer steps.

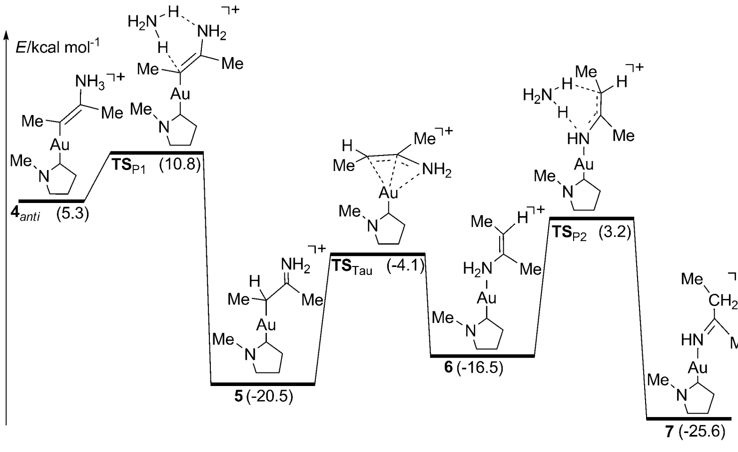


Figure 4. Energy profile in toluene for the proton-transfer steps.

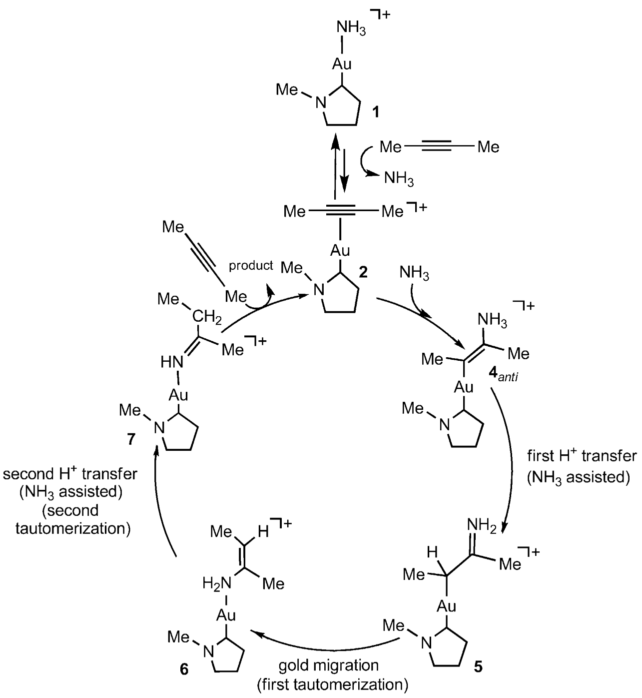
To obtain the imine product, a proton has to migrate from the NH_2 group to the carbon atom connected to the metal center, thus breaking the Au–C bond and releasing the final product of the reaction. It was found that not only the direct proton transfer ($\mathbf{TS}_{P2'}$, 54.4 kcal mol^{-1}), but also the nucleophile-assisted (NH_3) proton transfer ($\mathbf{TS}_{P2''}$, 46.4 kcal mol^{-1}) represent unfeasible reaction pathways (see the Supporting Information). This at first surprising result can be explained by the fact, that the proton shuttle is not strong enough of an acid to break the Au–C bond when protonating the carbon atom. Comparison of bond distances show that in the latter case the transition state does not involve NH_4^+ (as it was found for the first proton transfer), but in $\mathbf{TS}_{P2''}$ the transferred proton lies between the protonating nitrogen and carbon atoms (d(N-H) = 1.341 Å and d(C-H) = 1.404 Å in $\mathbf{TS}_{P2''}$), thus accounting for the high barrier.

An alternative mechanism is proposed here, wherein a particular tautomerization involving the migration of the cationic gold moiety from the carbon to nitrogen atom takes place instead of a proton migration. This step leads to the intermediate **6**, which involves the formation of a C=C bond (d(C-C) = 1.337 Å) and an sp^3-nitrogen center (θ_{HNCH} = 116.4°) connected to the metal center (enamine tautomer). The process takes place through $\mathbf{TS}_{Tau}$ (Figure 3 and Figure 4) with a barrier of 16.4 kcal mol^{-1}. As the formation of the enamine tautomer involves rupturing the gold–carbon bond, a subsequent ammonia-assisted proton transfer can take place, similar to the first proton transfer, to form the final imine product. The transition-state $\mathbf{TS}_{P2}$ resembles $\mathbf{TS}_{P1}$, that is, an NH_4^+ is present in the transition state from which proton transfer to the carbon atom leads to the imine intermediate **7**, which lies 9.1 kcal mol^{-1} below **6**; proton transfer to the NH group leads to the corresponding enamine intermediate **6**. This transfer is in accord with the experimental results where the analogous complex **C** was detected in solution.[14]

The energy profile for the most favorable pathway of the proton-transfer steps is shown in Figure 4. We can see that the global barrier corresponds to the second proton transfer, $\mathbf{TS}_{P2}$ (23.7 kcal mol^{-1}), which is higher than that of the nucleophilic attack (19.0 kcal mol^{-1}), thus the proton transfer represents the global barrier for the whole mechanism. It is consistent with the fact that the reaction takes place in the presence of excess ammonia, which serves not only as nucleophile, but as proton-transfer agent in the reaction.

On the basis of the theoretical analysis, we propose the catalytic cycle for the hydroamination of alkynes with NH_3 catalyzed by an CAAC/gold complex[14] as shown in Scheme 3.

Analysis of the relative stabilities of the model complexes analogous to the experimentally identified ones (**A**–**C**), showed that the most stable species in solution is the Werner complex **1**, which is consistent with experimental data. These calculations also demonstrated a remarkable difference between NH_3 and other N nucleophiles such as benzyl carbamate, which we studied earlier; benzyl carbamate does not tend to coordinate to the metal center. However, as the results also showed that formation of the alkyne complex **2** from **1** is not very energetically demanding (**2** lies 10.8 kcal mol^{-1} above **1** in energy) and the energy barrier is reasonably low (9.9 kcal mol^{-1}) for the outer-sphere attack compared to that of the inner-sphere attack; the alkyne complex **2** is the more favored one to be involved in the catalytic cycle. In contrast, **1** represents the resting state of the catalyst. We also showed that the proton-transfer steps, which are required for the formation of the imine product, take place with the assistance of the nucleophile which serves as a proton-transfer agent and is present in excess in the reaction mixture. Probably the most intriguing point of the reaction mechanism is the one in which the gold moiety migrates from the carbon to nitrogen atom, thus giving rise to an unforeseen tautomerization. This tautomerization is a



Scheme 3. Catalytic cycle proposed for the reaction.

necessary step,[24] as a simultaneous second proton transfer and rupture of the gold–carbon bond is energetically too demanding.

BDE calculations confirmed that ammonia behaves differently from the typically used nucleophiles, thus forming strong complexes with the gold center. However, Bertrand's CAAC ligand does not render the formation of the alkyne complex energetically unfeasible, thus facilitating the reaction to take place. We also showed the peculiar role of Au^I to be an optimal system for the tautomerization processes in both the activation of nucleophile-assisted proton-transfer steps and the gold migration from the carbon to nitrogen atom, thus giving rise to product formation. These factors can largely contribute to the development of gold-catalyzed hydroamination reactions with ammonia.

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[1] Some reviews: a) R. R. Schmidt, *Acc. Chem. Res.* **1986**, *19*, 250–259; b) T. E. Müller, M. Beller, *Chem. Rev.* **1998**, *98*, 675–703; c) A. Deiters, S. F. Martin, *Chem. Rev.* **2004**, *104*, 2199–2238; d) S. Hong, T. J. Marks, *Acc. Chem. Res.* **2004**, *37*, 673–686; e) N. T. Patil, Y. Yamamoto, *Chem. Rev.* **2008**, *108*, 3395–3442; f) T. E. Müller, K. C. Hultzsch, M. Yus, F. Foubelo, M. Tada, *Chem. Rev.* **2008**, *108*, 3795–3892.

[2] Some reviews: a) F. Pohlki, S. Doye, *Chem. Soc. Rev.* **2003**, *32*, 104–114; b) P. W. Roesky, T. E. Müller, *Angew. Chem.* **2003**, *115*, 2812–2814; *Angew. Chem. Int. Ed.* **2003**, *42*, 2708–2710; c) F. Alonso, I. P. Beletskaya, M. Yus, *Chem. Rev.* **2004**, *104*, 3079–3159; d) M. Beller, J. Seayad, A. Tillack, H. Jiao, *Angew. Chem.* **2004**, *116*, 3448–3479; *Angew. Chem. Int. Ed.* **2004**, *43*, 3368–3398; e) K. C. Hultzsch, *Adv. Synth. Catal.* **2005**, *347*, 367–391; f) R. Severin, S. Doye, *Chem. Soc. Rev.* **2007**, *36*, 1407–1420.

[3] Some reviews on catalytic reactions with ammonia: a) J. I. van der Vlugt, *Chem. Soc. Rev.* **2010**, *39*, 2302–2322; b) Y. Aubin, C. Fischmeister, C. M. Thomas, J.-L. Renaud, *Chem. Soc. Rev.* **2010**, *39*, 4130–4145; c) J. L. Klinkenberg, F. H. Hartwig, *Angew. Chem.* **2011**, *123*, 88–98; *Angew. Chem. Int. Ed.* **2011**, *50*, 86–95.

[4] a) E. G. Bryan, B. F. G. Johnson, K. Lewis, *J. Chem. Soc. Dalton Trans.* **1977**, 1328–1330; b) G. L. Hillhouse, J. E. Bercaw, *J. Am. Chem. Soc.* **1984**, *106*, 5472–5478; c) A. L. Casalnuovo, J. C. Calabrese, D. Milstein, *Inorg. Chem.* **1987**, *26*, 971–973; d) M. M. B. Holl, P. T. Wolczanski, G. D. Van Duyne, *J. Am. Chem. Soc.* **1990**, *112*, 7989–7994; e) J. Zhao, A. S. Goldman, J. F. Hartwig, *Science* **2005**, *307*, 1080–1082; f) Y. Nakajima, H. Kameo, H. Suzuki, *Angew. Chem.* **2006**, *118*, 964–966; *Angew. Chem. Int. Ed.* **2006**, *45*, 950–952; g) A. L. Kenward, W. E. Piers, *Angew. Chem.* **2008**, *120*, 38–42; *Angew. Chem. Int. Ed.* **2008**, *47*, 38–41; h) J. M. Lynam, *Angew. Chem.* **2008**, *120*, 843–845; *Angew. Chem. Int. Ed.* **2008**, *47*, 831–833.

[5] Q. Shen, J. F. Hartwig, *J. Am. Chem. Soc.* **2006**, *128*, 10028–10029.

[6] D. S. Surry, S. L. Buchwald, *J. Am. Chem. Soc.* **2007**, *129*, 10354–10355.

[7] See for instance: a) M. Kawatsura, J. F. Hartwig, *J. Am. Chem. Soc.* **2000**, *122*, 9546–9547; b) S. S. Stahl, *Angew. Chem.* **2004**, *116*, 3480–3501; *Angew. Chem. Int. Ed.* **2004**, *43*, 3400–3420; c) P. H. Phua, S. P. Mathew, A. J. P. White, J. G. de Vries, D. G. Blackmond, K. K. Hii, *Chem. Eur. J.* **2007**, *13*, 4602–4613.

[8] See for instance: a) M. Ahmed, A. M. Seayad, R. Jackstell, M. Beller, *Angew. Chem.* **2003**, *115*, 5773–5777; *Angew. Chem. Int. Ed.* **2003**, *42*, 5615–5619; b) M. Utsunomiya, R. Kuwano, M. Kawatsura, J. F. Hartwig, *J. Am. Chem. Soc.* **2003**, *125*, 5608–5609; c) L. D. Field, B. A. Messerle, K. Q. Voung, P. Turner, *Organometallics* **2005**, *24*, 4241–4250.

[9] See for instance: a) Y. Oe, T. Ohta, Y. Ito, *Chem. Commun.* **2004**, 1620–1621; b) M. Utsunomiya, J. F. Hartwig, *J. Am. Chem. Soc.* **2004**, *126*, 2702–2703.

[10] See for instance: a) H. Qian, X. Han, R. A. Widenhoefer, *J. Am. Chem. Soc.* **2004**, *126*, 9536–9537; b) K. L. Toups, R. A. Widenhoefer, *Chem. Commun.* **2010**, *46*, 1712–1714.

[11] Reviews on gold catalysis: a) E. Jiménez-Núñez, A. M. Echavarren, *Chem. Commun.* **2007**, 333–346; b) A. S. K. Hashmi, *Chem. Rev.* **2007**, *107*, 3180–3211; c) N. Marion, S. P. Nolan, *Angew. Chem.* **2007**, *119*, 2806–2809; *Angew. Chem. Int. Ed.* **2007**, *46*, 2750–2752; d) R. A. Widenhoefer, *Chem. Eur. J.* **2008**, *14*, 5382–5391; e) Z. Li, C. Brouwer, C. He, *Chem. Rev.* **2008**, *108*, 3239–3265; f) A. Arcadi, *Chem. Rev.* **2008**, *108*, 3266–3325; g) E. Jiménez-Núñez, A. M. Echavarren, *Chem. Rev.* **2008**, *108*, 3326–3350; h) D. J. Gorin, B. D. Sherry, F. D. Toste, *Chem. Rev.* **2008**, *108*, 3351–3378; i) H. C. Shen, *Tetrahedron* **2008**, *64*, 3885–3903; j) N. Marion, S. P. Nolan, *Chem. Soc. Rev.* **2008**, *37*, 1776–1782; k) A. S. K. Hashmi, M. Rudolph, *Chem. Soc. Rev.* **2008**, *37*, 1766–1775; l) R. Skouta, C. L. Li, *Tetrahedron* **2008**, *64*, 4917–4938; m) N. Bongers, N. Krause, *Angew. Chem.* **2008**, *120*, 2208–2211; *Angew. Chem. Int. Ed.* **2008**, *47*, 2178–2181; n) A. Fürstner, *Chem. Soc. Rev.* **2009**, *38*, 3208–3221; o) C. Nevado, *Chimia* **2010**, *64*, 247–251; p) A. S. K. Hashmi, *Angew. Chem.* **2010**, *122*, 5360–5369; *Angew. Chem. Int. Ed.* **2010**, *49*, 5232–5241.

[12] Selected examples for gold-catalyzed hydroamination: a) J. Zhang, C.-G. Yang, C. He, *J. Am. Chem. Soc.* **2006**, *128*, 1798–1799; b) Z. B. Zhang, C. F. Bender, R. A. Widenhoefer, *J. Am. Chem. Soc.* **2007**, *129*, 14148–14149; c) L. Leseurre, P. Y. Toullec, J. P. Genet, V. Michelet, *Org. Lett.* **2007**, *9*, 4049–4052; d) X. Giner, C. Nájera, *Org. Lett.* **2008**, *10*, 2919–2922; e) T. Enomoto, S. Obika, Y. Yasui, Y. Takemoto, *Synlett* **2008**, 1647–1650; f) X. Zhang, A. Corma, *Dalton Trans.* **2008**, 397–403; g) M. C. P. Yeh, H. F. Pai, Z. J. Lin, B. R. Lee, *Tetrahedron* **2009**, *65*, 4789–4794; h) N. Nishina, Y. Yamamoto, *Tetrahedron* **2009**, *65*, 1799–1808; i) A. M. Manzo, A. D. Perboni, G. Broggini, M. Rigamonti, *Tetrahedron Lett.* **2009**, *50*, 4696–4699; j) X. Zeng, R. Kinjo, B. Donnadieu, G. Bertrand, *Angew. Chem.* **2010**, *122*, 954–957; *Angew. Chem. Int. Ed.* **2010**, *49*, 942–945; k) N. T. Patil, R. D. Kavthe, V. S. Raut, V. S. Shinde, S. Balasubramanian, *J. Org. Chem.* **2010**, *75*, 1277–1280; l) A. S. K. Hashmi, M. Buhrle, *Aldrichimica Acta* **2010**, *43*, 27–33; m) H. Li, S. D. Lee, R. A. Widenhoefer, *J. Org. Chem.* **2011**, *76*, 316–320.

[13] Z. J. Wang, D. Benítez, E. Tkatchouk, W. A. Goddard III, F. D. Toste, *J. Am. Chem. Soc.* **2010**, *132*, 13064–13071.

[14] V. Lavallo, G. D. Frey, B. Donnadieu, M. Soleilhavoup, G. Bertrand, *Angew. Chem.* **2008**, *120*, 5302–5306; *Angew. Chem. Int. Ed.* **2008**, *47*, 5224–5228.

[15] a) V. Lavallo, Y. Canac, C. Präsang, B. Donnadieu, G. Bertrand, *Angew. Chem.* **2005**, *117*, 5851–5855; *Angew. Chem. Int. Ed.* **2005**, *44*, 5705–5709; b) V. Lavallo, Y. Canac, A. DeHope, B. Donnadieu, G. Bertrand, *Angew. Chem.* **2005**, *117*, 7402–7405; *Angew. Chem. Int. Ed.* **2005**, *44*, 7236–7239; c) R. Jazzar, R. D. Dewhurst, J. B. Bourg, B. Donnadieu, Y. Canac, G. Bertrand, *Angew. Chem.* **2007**, *119*, 2957–2960; *Angew. Chem. Int. Ed.* **2007**, *46*, 2899–2902.

[16] The investigations were carried out at the following computational level: The model system was: NH_3, 3-butyne, and [(1-

methyl-pyrrolidine-2-ylidene)Au]$^+$ as gold catalyst. However, in some cases calculations with the real CAAC ligand were carried to check the reliability of the model system. Geometry optimizations were carried out at B3LYP/SDD-6-31G* level of theory and single-point calculations on the optimized structures were carried out at M06/SDD-6-311++G(d,p) level of theory using the SMD model for the solvent (details are provided in the Supporting Information).

[17] a) G. Kovács, G. Ujaque; A. Lledós, *J. Am. Chem. Soc.* **2008**, *130*, 853 – 864; b) G. Kovács, A. Lledós, G. Ujaque, *Organometallics* **2010**, *29*, 5919 – 5926.

[18] For the experimentally detected complexes we carried out calculations with the real catalyst, thus showing the reliability of our model ligand (see details in the Supporting Information).

[19] The BDE values were found to be 6.7–21.9 kcal mol^{-1} higher for NH_3 with respect to $CbzNH_2$ (details are provided in the Supporting Information).

[20] E. Mizushima, T. Hayashi, M. Tanaka, *Org. Lett.* **2003**, *5*, 3349 – 3352.

[21] The difference between the energy barriers for the inner- and outer-sphere attack was found to be 11.1 kcal mol^{-1} with the real CAAC catalyst, thus showing that the preference for the outer-sphere attack is not related to the model we used (see the Supporting Information).

[22] a) L. N. Appelhans, D. Zuccaccia, A. Kovacevic, A. R. Chianese, J. R. Miecznikowski, A. Macchioni, E. Clot, O. Eisenstein, R. H. Crabtree, *J. Am. Chem. Soc.* **2005**, *127*, 16299 – 16311; b) D. L. Davies, S. M. A. Donald, S. A. Macgregor, *J. Am. Chem. Soc.* **2005**, *127*, 13754 – 13755; c) D. García-Cuadrado, A. A. C. Braga, F. Maseras, A. M. Echavarren, *J. Am. Chem. Soc.* **2006**, *128*, 1066 – 1067; d) M. G. Basallote, M. Besora, C. E. Castillo, M. J. Fernández-Trujillo, A. Lledós, F. Maseras, M. A. Máñez, *J. Am. Chem. Soc.* **2007**, *129*, 6608 – 6618; e) E. Clot, *Eur. J. Inorg. Chem.* **2009**, *16*, 2319 – 2328.

[23] a) D. Balcells, G. Ujaque, I. Fernandez, N. Khiar, F. Maseras, *J. Org. Chem.* **2006**, *71*, 6388 – 6396; b) F. Q. Shi, X. Li, Y. Xia, L. Zhang, Z.-X. Yu, *J. Am. Chem. Soc.* **2007**, *129*, 15503 – 15512; c) D. Balcells, G. Ujaque, I. Fernandez, N. Khiar, F. Maseras, *Adv. Synth. Catal.* **2007**, *349*, 2103 – 2110; d) L. Simón, J. M. Goodman, *Org. Biomol. Chem.* **2009**, *7*, 483 – 487.

[24] Our calculations also showed that tautomerization in the free enamine has high energy barriers, thus confirming the important role of gold in this step (details are in the Supporting Information.).