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Novel Acyclic Diaminocarbene Ligands with Increased Steric Demand and Their Application in Gold Catalysis

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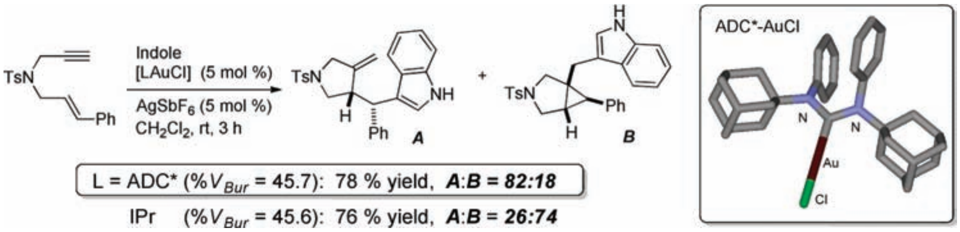
ABSTRACT



Sterically demanding and conformationally stable *N,N′*-ditertiaryalkyl-*N,N′*-diphenyl acyclic diaminocarbenes (ADCs) were developed. Bulky ADC−Au catalysts not only showed competitive reactivities in hydroamination and enyne cyclization but also demonstrated unique ligand properties different from bulky N-heterocyclic carbene (NHC) counterparts.

N-Heterocyclic carbenes (NHCs) are useful ligands for various catalytic transformations, which is often attributed to their σ-donating capacity as well as tunable steric profile.[1] Recently, acyclic diaminocarbenes (ADCs) have emerged as interesting ligands, as they show unique electronic and steric parameters.[2] Without geometric constraint, ADCs feature a broader variation of the N−C$_{carbene}$−N angle as well as free rotation about the C$_{carbene}$−N bonds.[2a] Previous reports indicate that ADCs are more electron donating than NHCs.[2o,p] Additionally, one might expect that ADCs' typically wider N−C$_{carbene}$−N angle can increase steric encumbrance at the metal coordination sphere. Nevertheless, the development of ADCs has lagged behind that of NHCs. ADCs tend to be less stable than NHCs, as they dimerize easily and are more vulnerable to moisture and oxygen.[2r,3] Control of rotational freedom in differentially substituted ADCs could be an issue, e.g., to design chiral ADC ligands. Steric bulk is essential to protect carbene carbons from

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(1) (a) Díez-González, S.; Marion, N.; Nolan, S. P. *Chem. Rev.* **2009**, *109*, 3612–3676. (b) Hahn, F. E.; Jahnke, M. C. *Angew. Chem., Int. Ed.* **2008**, *47*, 3122–3172. (c) Glorius, F. *Top. Organomet. Chem.* **2007**, *21*, 1–20. (d) *N-heterocyclic Carbenes in Synthesis*; Nolan, S. P., Ed.; Wiley-VCH: Weinheim, 2006.

(2) (a) Vignolle, J.; Cattoën, X.; Bourissou, D. *Chem. Rev.* **2009**, *109*, 3333–3384. (b) Slaughter, L. M. *Comments Inorg. Chem.* **2008**, *29*, 46–72. (c) Snead, D. R.; Inagaki, S.; Abboud, K. A.; Hong, S. *Organometallics* **2010**, *29*, 1729–1739. (d) Snead, D. R.; Ghiviriga, I.; Abboud, K. A.; Hong, S. *Org. Lett.* **2009**, *11*, 3274–3277. (e) Hirsch-Weil, D.; Snead, D. R.; Inagaki, S.; Seo, H.; Abboud, K. A.; Hong, S. *Chem. Commun.* **2009**, 2475–2477. (f) Kremzow, D.; Seidel, G.; Lehmann, C. W.; Fürstner, A. *Chem.—Eur. J.* **2005**, *11*, 1833–1853. (g) Bartolomé, C.; García-Cuadrado, D.; Ramiro, Z.; Espinet, P. *Inorg. Chem.* ASAP, DOI: 10.1021/ic101059c. (h) Bartolomé, C.; García-Cuadrado, D.; Ramiro, Z.; Espinet, P. *Organometallics* **2010**, *29*, 3589–3592. (i) Bartolomé, C.; Ramiro, Z.; García-Cuadrado, D.; Pérez-Galán, P.; Raducan, M.; Bour, C.; Echavarren, A. M.; Espinet, P. *Organometallics* **2010**, *29*, 951–956. (j) Bartolomé, C.; Ramiro, Z.; Pérez-Galán, P.; Bour, C.; Raducan, M.; Echavarren, A. M.; Espinet, P. *Inorg. Chem.* **2008**, *47*, 11391–11397. (k) Wanniarachchi, Y. A.; Subramanium, S. S.; Slaughter, L. M. *J. Organomet. Chem.* **2009**, *694*, 3297–3305. (l) Wanniarachchi, Y. A.; Slaughter, L. M. *Organometallics* **2008**, *27*, 1055–1062. (m) Wanniarachchi, Y. A.; Kogiso, Y.; Slaughter, L. M. *Organometallics* **2008**, *27*, 21–24. (n) Moncada, A. I.; Manne, S.; Tanski, J. M.; Slaughter, L. M. *Organometallics* **2006**, *25*, 491–505. (o) Frey, G. D.; Herdtweck, E.; Herrmann, W. A. *J. Organomet. Chem.* **2006**, *691*, 2465–2478. (p) Denk, K.; Sirsch, P.; Herrmann, W. A. *J. Organomet. Chem.* **2002**, *649*, 219–224. (q) Alder, R. W.; Blake, M. E.; Bufali, S.; Butts, C. P.; Orpen, A. G.; Schütz, J.; Williams, S. J. *J. Chem. Soc., Perkin Trans. 1* **2001**, 1586–1593. (r) Alder, R. W.; Allen, P. R.; Murray, M.; Orpen, A. G. *Angew. Chem., Int. Ed.* **1996**, *35*, 1121–1123.

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dimerization as well as moisture or oxygen,[3] and popular NHC ligands such as IMes or IPr are typically equipped with a high level of steric encumbrance. However, to the best of our knowledge, there are no such ADCs displaying a similar level of steric demands.[2−4] We envisioned that introduction of bulky alkyl substituents to *N*,*N*′-diaryl ADCs[5] could result in increasing the steric demands as well as limiting conformations (Figure 1). Herein we report synthesis of novel bulky ADC ligands and their application in gold catalysis.

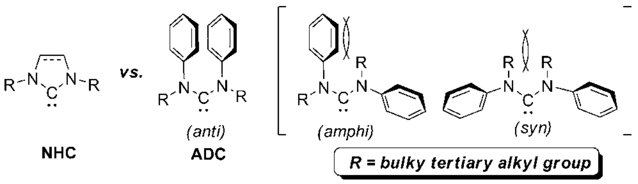
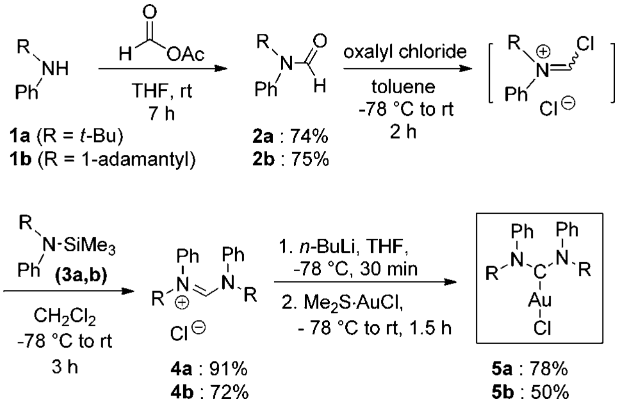


Figure 1. Sterically demanding, conformationally stable *N*,*N*′-dialkyl-*N*,*N*′-diaryl acyclic diaminocarbenes.

N,*N*′-Diaryl ADCs were first developed by Bielawski and co-workers, and the formamidinium ADC precursors were nicely prepared by the double S_N2 alkylation of *N*,*N*′-diarylformamidine with 2 equiv of alkyl halide.[5c] However, the S_N2 alkylation strategy is not applicable to the synthesis of *N*,*N*′-diaryl ADCs bearing tertiary alkyl groups. We were pleased to find that reactions of silylated amines with chloroiminiums afforded the desired hindered formamidiniums (**4a**,**b**) in high yield (Scheme 1). TMS-Cl (chlorotrimethylsilane) elimination protocol for the synthesis of formamidiniums, which was originally developed by Schroth,[6] provides a distinct advantage over the common procedure using free amines. TMS-Cl is the only byproduct and can be easily removed by evaporation or washing with hydrocarbon solvents, whereas HCl generated from the conventional procedure can complicate the product isolation from other byproducts such as amine−HCl salts.[2q] Two novel ADC−gold complexes (**5a**,**b**) were then prepared by deprotonation of formamidiniums (**4a**,**b**) with $LiN(SiMe_3)_2$ followed by metalation using $Me_2S{\cdot}AuCl$.

Scheme 1. Synthesis of ADC−Gold Complexes (**5a**, **5b**)



The X-ray structure of **5a** and **5b** shows "anti" conformation where both phenyl rings are located away from the gold metal (Figure 2). The two phenyl rings in **5a** and **5b** adopt a face-to-face, parallel-displaced stacking arrangement, implying possible $\pi-\pi$ interactions.[7] It is also interesting to note that both phenyl rings are twisted out of the $N-C_{carbene}-N$ plane, shown by relatively large $C_{phenyl}-N-C_{carbene}-N$ dihedral angles (−24.3(3)°, −47.8(3)° for **5a** and −41.0(2)° for **5b**). These geometries might be preferred to accommodate bulky tertiary alkyl substituents but could result in weakening π-overlap between nitrogens

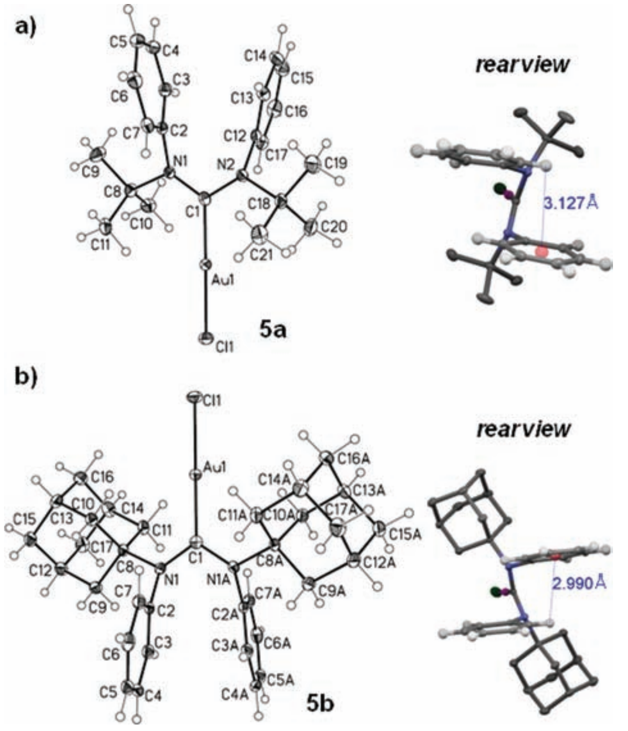


Figure 2. (a) X-ray structure of **5a**. (b) X-ray structure of **5b**. Ellipsoids are drawn at the 50% probability level.

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(3) Alder, R. W.; Blake, M. E.; Chaker, L.; Harvey, J. N.; Paolini, F.; Schütz, J. *Angew. Chem., Int. Ed.* **2004**, *43*, 5896–5911.

(4) Hashmi, A. S. K.; Hengst, T.; Lothschütz, C.; Rominger, F. *Adv. Synth. Catal.* **2010**, *352*, 1315–1337.

(5) (a) Collins, M. S.; Rosen, E. L.; Lynch, V. M.; Bielawski, C. W. *Organometallics* **2010**, *29*, 3047–3053. (b) Rosen, E. L.; Sung, D. H.; Chen, Z.; Lynch, V. M.; Bielawski, C. W. *Organometallics* **2010**, *29*, 250–256. (c) Rosen, E. L.; Sanderson, M. D.; Saravanakumar, S.; Bielawski, C. W. *Organometallics* **2007**, *26*, 5774–5777.

(6) (a) Cattoën, X.; Miqueu, K.; Gornitzka, H.; Bourissou, D.; Bertrand, G. *J. Am. Chem. Soc.* **2005**, *127*, 3292–3293. (b) Sheludvakav, V. D.; Belvakova, Z. L.; Shevchenko, V. M.; Chernvshev, E. A. *Russ. Chem. Bull. (Engl. Transl.)* **1997**, *46*, 997−1002; *Izv. Akad. Nauk. SSSR, Ser. Khim.* **1997**, 1035−1040. (c) Schroth, W.; Jahn, U.; Ströhl, D. *Chem. Ber.* **1994**, *127*, 2013–2022. (d) Jahn, U.; Schroth, W. *Tetrahedron Lett.* **1993**, *34*, 5863–5866.

(7) Meyer, E. A.; Castellano, R. W.; Diederich, F. *Angew. Chem., Int. Ed.* **2003**, *42*, 1210–1250.

and the carbene carbon. The buried volume (% V_{Bur})[8,9] of **5a** (44.3%) is larger than that of similarly substituted NHC−Au complex **5f** (39.3%), possibly owing to the larger N−C$_{\mathrm{carbene}}$−N angle of **5a** (115.0(2)°) than that of **5f** (107.8(2)°) (Figure 3). Importantly, the bulkier adamantyl substituent further increases % V_{Bur} of **5b** to 45.7%, which constitutes one of the highest among the reported ADC ligands[4] and is comparable to that of bulky NHCs such as IPr (45.6%).

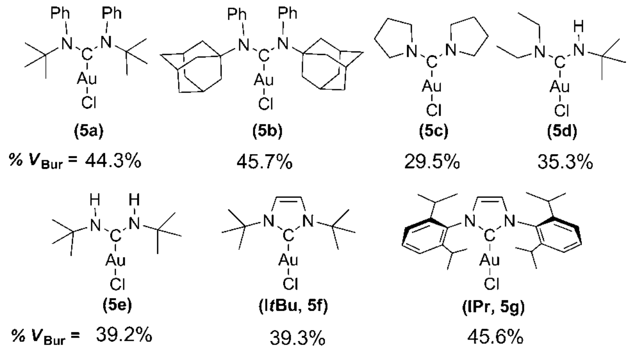
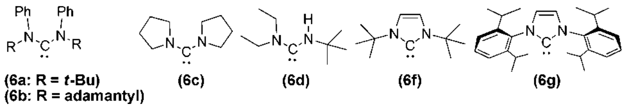


Figure 3. % V_{Bur} of ADC and NHC ligands in Au complexes (calculated using X-ray crystallographic data).

Electron-donating capacities of the new ADCs were estimated by density functional theory (DFT) calculations (Table 1). The energies of the carbene lone pair orbital (E_σ) were computed, after an initial geometry optimization, using the B3LYP,[10] TPSSTPSS,[11] M06,[12] and M06L[13] functional and the 6-31G** basis set[14] on carbenes **6a−d** and **6f,g.** These calculations were run using GAUSSIAN 09.[15] The ADCs (**6a−d**) have higher E_σ values than the NHCs (**6f**,**g**), suggesting that they are better σ-donors. The same trends were observed across the carbenes for all four functionals.

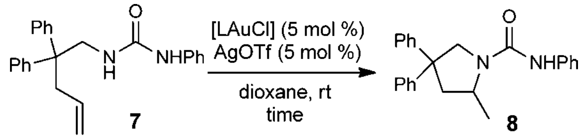
Table 1. Energies of Carbene Lone Pair Orbitals, E_σ [eV]

	6a	**6b**	**6c**	**6d**	**6f**	**6g**
B3LYP	-4.59	-4.57	-4.42	-4.86	-5.25	-5.61
TPSS	-3.74	-3.71	-3.53	-3.95	-4.34	-4.69
M06	-4.95	-4.94	-4.73	-5.20	-5.59	-6.06
M06L	-3.91	-3.88	-3.66	-4.13	-4.52	-4.99



Phosphines and NHC ligands play a crucial role in Au-catalyzed reactions where very different reactivities as well as selectivities were often observed depending on ligands.[16] Thus, we decided to evaluate new ADC−gold complexes **5a** and **5b** in representative Au-catalyzed reactions to gain insights into their properties. First, Au(I)-catalyzed intramolecular hydroamination was investigated (Table 2).[17] The reaction proceeded smoothly at room temperature when catalyzed by ADC−Au catalyst **5a** (entry 1). The bulkier adamantyl catalyst **5b** gave better conversion after 24 h (entry 2 vs entry 1), whereas less bulky ADC catalysts **5c** and **5d**

Table 2. Au(I)-Catalyzed Hydroamination of Alkenyl Urea[a]



entry	catalyst	% V_{Bur}	time (h)	% convn[b]
1	*t*Bu$_2$Ph$_2$ADC−AuCl (**5a**)	44.3	24	82
2	**Adm$_2$Ph$_2$ADC−AuCl (5b)**	**45.7**	**24**	**87**[c]
3	Pyrr$_2$ADC−AuCl (**5c**)	29.5	24	<2
4	Et$_2$*t*BuHADC−AuCl (**5d**)	36.0	24	<2
5	*t*Bu$_2$H$_2$ADC−AuCl (**5e**)	39.2	24	3
6	I*t*Bu−AuCl (**5f**)	39.3	24	3
7	**IPr−AuCl (5g)**	**45.6**	**16**	**>98**

[a] 0.033 M concd [LAuCl] and AgOTf in dioxane were stirred for 30 min before addition of **7**. [b] Determined by ^{1}H NMR. [c] >98% conversion observed after 48 h.

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(8) For detailed calculations, see the Supporting Information.

(9) For explanation of % V_{Bur} (a measure of the space occupied by the ligand in the metal coordination sphere), see: Poater, A.; Cosenza, B.; Correa, A.; Giudice, S.; Ragone, F.; Scarano, V.; Cavallo, L. *Eur. J. Inorg. Chem.* **2009**, 1759–1766.

(10) (a) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648–5652. (b) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785–789. (c) Vosko, S. H.; Wilk, L.; Nusair, M. *Can. J. Phys.* **1980**, *58*, 1200–1211. (d) Stephens, P. J.; Devlin, F. J.; Chabalowski, C. F.; Frisch, M. J. *J. Chem. Phys.* **1994**, *98*, 11623–11627.

(11) Tao, J.; Perdew, J. P.; Staroverov, V. N.; Scuseria, G. E. *Phys. Rev. Lett.* **2003**, *91*, 146401.

(12) Zhao, Y.; Truhlar, D. G. *Theor. Chem. Acc.* **2008**, *120*, 215–241.

(13) Zhao, Y.; Truhlar, D. G. *J. Chem. Phys.* **2006**, *125*, 194101.

(14) (a) Ditchfield, R.; Hehre, W. J.; Pople, J. A. *J. Chem. Phys.* **1971**, *54*, 724–728. (b) Hehre, W. J.; Ditchfield, R.; Pople, J. A. *J. Chem. Phys.* **1972**, *56*, 2257–2261. (c) Hariharan, P. C.; Pople, J. A. *Theor. Chem. Acc.* **1973**, *28*, 213–222. (d) Hariharan, P. C.; Pople, J. A. *Mol. Phys.* **1974**, *27*, 209–214. (e) Francl, M. M.; Pietro, W. J.; Hehre, W. J.; Binkley, J. S.; Gordon, M. S.; DeFrees, D. J.; Pople, J. A. *J. Chem. Phys.* **1982**, *77*, 3654–3665.

(15) Frisch, M. J. *Gaussian 09*, Revision A.02; Gaussian, Inc.: Wallingford, CT, USA, 2009. See Supporting Information for a full list of the authors.

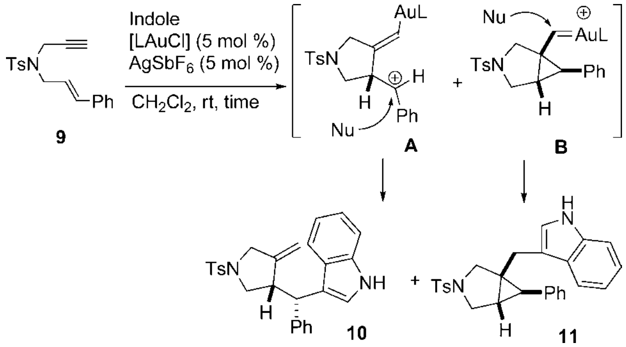
(16) (a) Gorin, D. J.; Sherry, B. D.; Toste, F. D. *Chem. Rev.* **2008**, *108*, 3351–3378. (b) Jiménez-Núñez, E.; Echavarren, A. M. *Chem. Rev.* **2008**, *108*, 3326–3350. (c) Li, Z.; Brouwer, C.; He, C. *Chem. Rev.* **2008**, *108*, 3239–3265. (d) Marion, N.; Nolan, S. P. *Chem. Soc. Rev.* **2008**, *37*, 1776–1782. (e) Alcarazo, M.; Stork, T.; Anoop, A.; Thiel, W.; Fürstner, A. *Angew. Chem., Int. Ed.* **2010**, *49*, 2542–2546. (f) Benitez, D.; Tkatchouk, E.; Gonzalez, A. Z.; Goddard, W. A., III; Toste, F. D. *Org. Lett.* **2009**, *11*, 4798–4801.

(17) (a) Li, H.; Widenhoefer, R. A. *Org. Lett.* **2009**, *11*, 2671–2674. (b) Bender, C. F.; Widenhoefer, R. A. *Chem. Commun.* **2008**, 2741–2743. (c) Zhang, Z.; Bender, C. F.; Widenhoefer, R. A. *J. Am. Chem. Soc.* **2007**, *129*, 14148–14149. (d) Zhang, Z.; Bender, C. F.; Widenhoefer, R. A. *Org. Lett.* **2007**, *9*, 2887–2889. (e) Zhang, Z.; Liu, C.; Kinder, R. E.; Han, X.; Qian, H.; Widenhoefer, R. A. *J. Am. Chem. Soc.* **2006**, *128*, 9066–9073. (f) Bender, C. F.; Widenhoefer, R. A. *Org. Lett.* **2006**, *8*, 5303–5305. (g) Bender, C. F.; Widenhoefer, R. A. *Chem. Commun.* **2006**, 4143–4144. (h) Han, X.; Widenhoefer, R. A. *Angew. Chem., Int. Ed.* **2006**, *45*, 1747–1749.

did not show noticeable product formation after 24 h (entries 3 and 4). There seems to be a good correlation between the steric bulk of the carbene ligands (% V_{Bur}) and the hydroamination rate, although steric parameters alone cannot fully explain the reactivity difference between **5b** and **5g**. Although sterics are known to be important for an aminoauration step,[18a] the rate of protodeauration could also be affected by the ligand electronics.[18b] It is also interesting to note that the recently reported *N*,*N*′-disubstituted ADC−gold complex (**5e**)[4] was not very effective in hydroamination at room temperature, even though **5e** also has two *t*-Bu groups facing toward the Au metal center (entry 5).

In Au(I)-catalyzed indole addition to 1,6-enyne, the product ratio is known to vary greatly depending on the ligand electronic and steric properties.[19] Previous reports showed that sterically bulky phosphite−Au complexes yielded **10** as the major product, whereas sterically bulky NHC−Au complexes yielded mainly **11**.[19] New bulky diaryl ADC−Au complexes (**5a**,**b**) gave good yields (76−78%), showing reactivity similar to the IPr−Au catalyst (Table 3).

Table 3. Indole Addition to 1,6-Enyne Catalyzed by Au(I)[a]



entry	catalyst	time (h)	% yield[b]	10/11[c]
1	*t*Bu$_2$Ph$_2$ADC−AuCl (**5a**)	3	76	51/49
2	**Adm$_2$Ph$_2$ADC−AuCl (5b)**	**3**	**78**	**82/18**
3	Pyrr$_2$ADC−AuCl (**5c**)	5	0	-
4	Et$_2$*t*BuHADC−AuCl (**5d**)	3	45	46/54
5	*t*Bu$_2$H$_2$ADC−AuCl (**5e**)	3	22	46/54
6	I*t*Bu−AuCl (**5f**)	3	67	43/57
7	**IPr−AuCl (5g)**	**3**	**75**	**26/74**

[a] 0.075 M concd [LAuCl] and AgSbF$_6$ in CH$_2$Cl$_2$ were stirred for 15 min before addition of **9** and indole. [b] Isolated yield of the mixture of **10** and **11**. Average of 2 runs. [c] Determined by ^{1}H NMR. Average of 2 runs.

Note that bulky diaryl ADC−Au catalyst **5b** prefers the alkene product **10** (entry 2), whereas similarly bulky NHC−Au catalyst **5g** favors the cyclopropane product **11** (entry 7). The dramatic reversal of product distribution exhibited by similarly encumbered catalysts **5b** and **5g** seems to suggest that new bulky diaryl ADCs might have very unique properties compared to other carbene ligands. It is possible that such ADCs could be more π-accepting than the NHC counterparts, resulting from the larger $C_{\mathrm{phenyl}}-N-C_{\mathrm{carbene}}-N$ dihedral angle,[20] even though ADCs are generally better σ-donors than NHCs. This selectivity reversal could be rationalized by the more π-accepting nature of bulky diaryl ADCs rendering the carbenoid intermediate (**B**) less favorable. However, more detailed studies on electronic properties of these bulky ADC ligands must be done before drawing any generalized conclusion.

To summarize, sterically demanding and conformationally stable *N*,*N*′-dialkyl-*N*,*N*′-diaryl ADCs featuring tertiary alkyl substituents were developed. The formamidinium precursors were efficiently prepared via a TMS-Cl elimination route, and X-ray structures of Au complexes confirmed that the new diaryl ADCs show steric demands comparable to IPr. The ADC−Au catalysts not only showed competitive reactivities in hydroamination and enyne cyclization but also demonstrated unique ligand properties different from bulky NHC counterparts or other acyclic carbenes. Further studies on electronic properties of these new ADC ligands and research on other metal complexes are currently in progress.

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Supporting Information Available: Detailed synthetic procedures and characterization of **1a**,**b**−**5a**,**b**,**c**, coordinates of optimized structures of **6a**−**d** and **6f**,**g**, and X-ray crystallographic data for **5a**−**5c**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(18) (a) LaLonde, R. L.; Brenzovich, W. E., Jr.; Benitez, D.; Tkatchouk, E.; Kelley, K.; Goddard, W. A., III; Toste, F. D. *Chem. Sci.* **2010**, *1*, 226–233. (b) Roth, K. E.; Blum, S. A. *Organometallics* **2010**, *29*, 1712–1716.

(19) (a) Amijs, C. H. M.; López-Carrillo, V.; Raducan, M.; Pérez-Galán, P.; Ferrer, C.; Echavarren, A. M. *J. Org. Chem.* **2008**, *73*, 7721–7730. (b) Amijs, C. H. M.; Ferrer, C.; Echavarren, A. M. *Chem. Commun.* **2007**, 698–700.

(20) In *N*,*N*,*N*′-trisubstituted ADCs, all atoms of the $N-C_{\mathrm{carbene}}-N$ unit have a flat, planar geometry. See ref 4.