Intermolecular Hydroamination of 1,3-Dienes Catalyzed by Bis(phosphine)carbodicarbene−Rhodium Complexes

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Ⓢ *Supporting Information*

ABSTRACT: A carbodicarbene (CDC)-based pincer ligand scaffold is reported, along with its application to site-selective Rh(I)-catalyzed intermolecular hydroamination of 1,3-dienes with aryl and alkyl amines. To the best of our knowledge, this is the first example of the use of a well-defined CDC complex as an efficient catalyst. Transformations proceed in the presence of 1.0−5.0 mol % Rh complex at 35−120 °C; allylic amines are obtained in up to 97% yield and with >98:2 site selectivity.

Carbon-based donors represent an important class of ligands for transition metals that promote multiple reaction types.[1] A significant objective in developing catalytic reactions is the design and synthesis of new classes of ligands. Accordingly, the development of new classes of carbon-based ligands for use in transition-metal catalysis is an important goal in chemical synthesis. Carbodicarbenes (CDCs),[2,3] also referred to as bent allenes, are a family of compounds that contain a divalent carbon(0) center, captodatively stabilized by two carbene donors. These ligands can effectively bind to transition metals, and their σ- and π-electron-donating properties have been established both experimentally[4] and by theoretical calculations[5] to be stronger than those of N-heterocyclic carbenes (NHCs). Surprisingly, only monodentate CDC complexes have been characterized to date (Au (**1**),[4d,6] Ru (**2**),[7] Fe,[8] Rh,[4a−c,9] Pd[9]); in addition, there is an absence of reports demonstrating the ability of CDCs to act as effective ligands for transition-metal catalysis. Furthermore, metal complexes supported by tridentate CDC-based ligands have not been prepared, despite the utility of pincer scaffolds in promoting a number of important reactions.[10] In light of these limitations, we initiated a program for the study of a new class of tridentate bis(phosphine)carbodicarbenes and examined their ability to yield catalysis and effect a number of useful transformations.
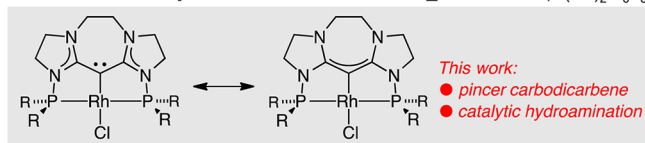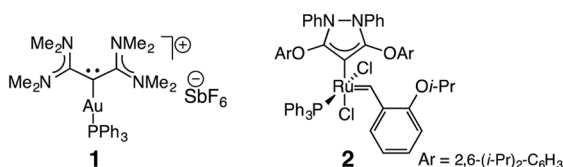
Scheme 1. Synthesis and X-ray Structure of (CDC)-Rh(I) Complexes 6−8[a]
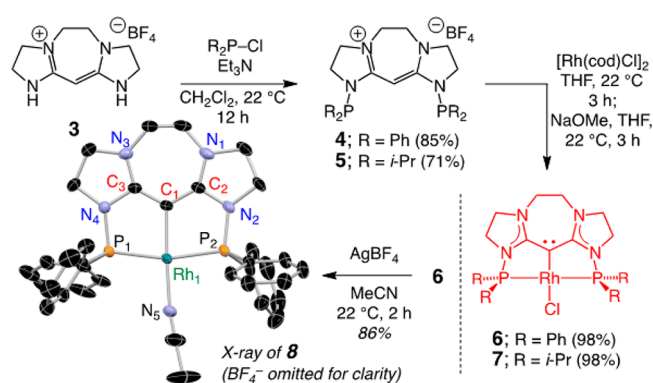
[a]See SI for experimental details; all reactions were performed under N₂ atm. Selected bond lengths for **8** (Å): Rh_1-C_1, 2.043; Rh_1-N_5, 2.027; Rh_1-P_1, 2.240; Rh_1-P_2, 2.230; C_1-C_2, 1.398; C_1-C_3, 1.387; C_2-N_1, 1.352; C_2-N_2, 1.374; C_3-N_3, 1.359; C_3-N_4, 1.379.

Herein we report the synthesis, structure, and catalytic activity of easily prepared tridentate bis(phosphine)(CDC)-Rh(I) complexes that effect formation of allylic amines via selective *intermolecular* hydroamination of 1,3-dienes with aryl and alkyl amines. General catalytic procedures for the synthesis of functionalized unsaturated N-containing molecules by the direct addition of amines to C−C π-bonds offer desirable, atom-economical transformations for chemical synthesis.[11] Transition-metal-catalyzed *intermolecular* addition of amines to dienes to selectively afford allylic amines has been studied;[12,13] however, poor control of site selectivity and the lack of a general catalytic system capable of both aryl and alkyl amine additions limit the field.[14] Catalytic protocols have focused on the use of aryl and alkyl amines in order to obtain high site selectivity.[12] The (CDC)-Rh(I)-promoted hydro-aminations described herein proceed with low catalyst loadings (1−5 mol %) and are tolerant of both alkyl and aryl amines; levels of site selectivity and efficiency are similar to those obtained with previous intermolecular metal-catalyzed meth-ods. Notably, the identity of the phosphine substituents (aryl vs alkyl) plays an important role in determining the catalyst activity.

We initiated our studies by the synthesis of the required 1,4-diazepenium salts. As shown in Scheme 1, phosphination of

heterocyclic base **3** with Ph$_2$PCl (or *i*-Pr$_2$PCl) in the presence of Et$_3$N affords 1,4-diazepenium salts **4** and **5** in 85% and 71% yield, respectively. Both salts are bench stable and purified by silica gel column chromatography. The tetrafluoroborate salts **4** and **5** may then undergo cyclometalation by treatment with a suspension of [Rh(cod)Cl]$_2$ in THF at 22 °C, followed by deprotonation of the corresponding cationic Rh(III)-H with NaOMe in THF at 22 °C, to afford square-planar (CDC)-Rh(I) complexes **6** and **7** as orange/yellow solids, each in 98% yield.[15] The ^{13}C NMR signal of the CDC carbon(0) appears as a doublet of triplets in the ^{13}C{^{1}H} NMR spectrum: 72.98 ppm for **6** ($^1J_{Rh}$ = 36.0 Hz, ^1J_P = 11.7 Hz) and 73.74 ppm for **7** ($^1J_{Rh}$ = 36.3 Hz, ^1J_P = 10.4 Hz). These values are consistent with those previously reported by Bertrand and Fürstner,[4,6] with the upfield shift indicating the electron-rich nature of the divalent carbon(0). To elucidate some of the structural features of (CDC)-Rh complexes (Scheme 1), we obtained the X-ray crystal structure of acetonitrile complex **8**.[16] As indicated by the ORTEP diagram, the Rh$_1$–C$_1$ bond length is 2.043 Å. Bond lengths of the CDC ligand indicate a CDC structure with average C$_3$–C$_1$ bond lengths of 1.395 Å, in comparison to the shorter N$_2$–C$_2$ carbene in NHCs (average 1.365 Å). The Rh$_1$–N$_5$ bond length of 2.029 Å indicates the strong trans influence of the CDC carbon.[17]

To gain insight into the electronic nature of the ligand, we treated **4** with 1 equiv of HBF$_4$·OEt$_2$ in CD$_2$Cl$_2$ at 22 °C (eq 1), which generated dication **9**. The symmetrical ^{1}H NMR
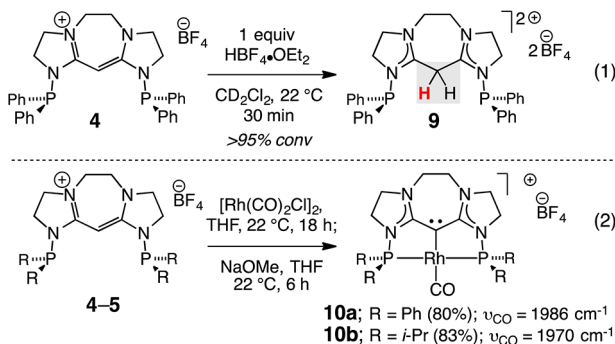
confirms protonation at the central carbon, in accord with previously described systems.[4d,5e] This demonstrates the presence of significant electron density at the central carbon of cation **4** and supports its reactivity as a CDC. The electron-donating properties of the CDCs derived from **4** and **5** were further evaluated through the carbonyl stretching frequencies of **10a,b** (eq 2). The cationic Rh(I) complexes exhibit infrared ν_{CO} values (**10a**, 1986 cm^{-1}; **10b**, 1970 cm^{-1}) lower than those observed for analogous cationic Rh(I) pincer complexes.[18]

With Rh(I) complexes in hand, we began to investigate whether **6** and **7** are effective catalysts for hydroamination. As the data in Table 1 illustrate, the ability of Rh(I) complexes **6** and **7** to catalyze the hydroamination of phenyl-1,3-butadiene with aniline requires an additive; <2% conversion is observed (entries 1 and 2). In contrast, as shown in entries 3 and 4, when 5 mol % (CDC)-Rh and 5 mol % AgBF$_4$ are used (80 °C, C$_6$H$_5$Cl), the reactions proceed to deliver allylic amine **11** (>98% Markovnikov site selectivity) in 66% and 65% isolated yield, respectively. Less-coordinating ions (PF$_6$, SbF$_6$, and OTf) are less efficient (31–59% yield; entries 5–7). Gratifyingly, the hydroamination can be effected with 1 mol % **6** to deliver **11** (63% conversion) in slightly diminished yield (59%). Catalytic

**Table 1. Evaluation of (CDC)-Rh(I) Complexes in Hydroamination**[a]

entry	complex; mol %	additive; mol %	conv (%)[b]	yield (%)[c]
1	**6**; 5	–	<2	nd
2	**7**; 5	–	<2	nd
3	**6**; 5	AgBF; 5	75	66
4	**7**; 5	AgBF; 5	73	65
5	**6**; 5	AgPF$_6$; 5	70	59
6	**6**; 5	AgSbFe; 5	40	31
7	**6**; 5	AgOTf; 5	60	51
8	**6**; 1	AgBF; 1	63	59
9	**8**; 5	–	72	67
10	–	HBF$_4$·OEt$_2$; 5	<2	nd
11	–	AgBF; 5	<2	nd

[a]See SI for experimental details; all reactions performed under N$_2$ atm; >98% site selectivity in all cases. [b]Values determined by analysis of 400 or 600 MHz ^{1}H NMR spectra of unpurified mixtures with DMF as an internal standard. [c]Yields of purified products are an average of two runs; nd = not determined.

hydroamination with 5 mol % Rh(I)-NCMe complex **8** (entry 9) affords **11** with 72% conversion, similar to that achieved with catalysts generated *in situ* with silver(I) salts, suggesting that a cationic Rh(I) complex is the active catalyst. Control reactions with HBF$_4$·OEt$_2$ and AgBF$_4$ (entries 10 and 11) exclude an acid- or silver(I)-catalyzed process.

Next, we examined the influence of changing the identity of the amine on the activity of (CDC)-Rh(I)-catalyzed hydroamination. As the representative examples in Table 2

Table 2. (CDC)-Rh-Catalyzed Hydroaminations of Phenyl-1,3-butadiene with Aryl and Secondary Alkyl Amines[a]
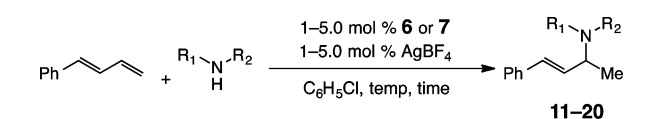
| entry	amine; product	complex; mol %	temp (°C)	time (h)	conv (%)[b]	yield (%)[c]
1	C$_6$H$_5$NH$_2$; **11**	**6**; 1	60	24	88	71
2	*p*-CF$_3$C$_6$H$_4$NHa; **12**	**7**; 2	60	24	96	91
3	*p*-MeOC$_6$H$_4$NH$_2$; **13**	**7**; 3	60	48	68	64
4	*o*-BrC$_6$H$_4$NH$_2$; **14**	**6**; 3	50	48	86	85
5	*o*-MeC$_6$H$_4$-NH$_2$; **15**	**7**; 5	60	48	89	80
6	morpholine; **16**	**7**; 3	80	48	92	89
7	pyrrolidine; **17**	**6**; 5	80	48	80	75[d]
8	Bn$_2$NH; **18**	**7**; 2	80	48	58	56
9	Bn(Me)NH; **19**	**7**; 5	80	48	74	72
10	*n*-Pr$_2$NH; **20**	**7**; 5	80	48	14[e]	6

[a–c]See Table 1. [d]With 20 mol % NH$_4$BF$_4$ additive; 11% without NH$_4$BF$_4$. [e]12% conv at 100 °C.

demonstrate, Rh complexes **6** and **7** catalyzed hydroamination of phenyl 1,3-butadiene with various aryl and alkyl amines to generate allylic amines with >98% γ-selectivity. Entries 2 and 3 of Table 2 illustrate that allylic aryl amines with electron-withdrawing (**12**) and electron-donating (**13**) groups can be accessed with high site selectivity; the reaction of *p*-CF$_3$-substituted aniline proves to be slightly more efficient. Sterically

hindered *o*-bromoaniline and *o*-toluidine (entries 4 and 5) require 3−5 mol % of **6** and **7** to generate allylic amines **14** and **15** with complete site selectivity in 85% and 80% yield, respectively. As shown in entries 6 and 7, cyclic alkyl amines morpholine and pyrrolidine are tolerated and react to furnish allylic amines **16** (89% yield) and **17** (75% yield); however, pyrrolidine requires the use of 20 mol % NH_4BF_4 additive. Moreover, secondary alkyl amines bearing benzyl (entries 8 and 9) and *n*-propyl (entry 10) groups can participate in Rh-catalyzed site-selective hydroamination, albeit with varying efficiency. Two points regarding Table 2 merit mention. First, the optimal complex (**6** vs **7**) and reaction conditions in each case vary depending on the amine structure.[19] Second, in general, (CDC)-Rh-catalyzed hydroaminations with alkyl amines require higher temperatures (80 °C) to proceed compared to aryl amines (50−60 °C).

To further evaluate the catalytic properties of (CDC)-Rh(I), we investigated the reaction with respect to the electronics of the aryl diene component. A notable aspect of these studies is the observed increased reactivity of complex **6** with electronically disparate dienes. As illustrated in Scheme 2, Rh-catalyzed

Scheme 2. Site-Selective Rh(I)-Catalyzed Hydroaminations of Electronically Different Aryl Dienes
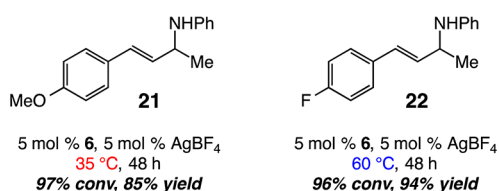
addition of aniline to *p*-MeO-substituted diene occurs at significantly lower temperature compared to that of *p*-F-substituted diene (35 vs 60 °C) to afford **21** and **22**, respectively, each in >85% yield.

Rhodium-catalyzed diene hydroaminations promoted by pincer CDC complexes display significant synthetic scope. As the representative examples in Table 3 indicate, Rh complexes **6** and **7** promote the hydroamination of alkyl diene substrates to deliver allylic amine products bearing di- or trisubstituted olefins (up to >98% *γ*-selectivity). Under optimal reaction conditions (5 mol % **6** at 60 °C), cyclohexylbutadiene is efficiently converted to **23** in 89% yield (entry 1). It is worthy of note that *n*-alkyl-derived substrates undergo efficient catalytic hydroamination to generate allylic amines but as mixtures of constitutional isomers; **24** (5 mol % **6**, 70 °C; entry 2) is generated in 70% yield as an inseparable 3:2 mixture of *γ*:*α* addition products. This underscores a current limitation of Rh complexes **6** and **7** toward site-selective hydroamination of sterically unbiased 1,3-dienes. As illustrated in entries 3, 7, and 8, trisubstituted 1,3-dienes undergo site-selective (>98%) Rh-catalyzed hydroamination (5 mol % **6** or **7**, 65−80 °C, 48 h) to deliver the corresponding allylic amines in good yield: **25** (97%), **29** (77%), and **30** (69%). The Rh-catalyzed protocol is also effective for the generation of cyclic allylic amines, as demonstrated by the formation of **28** (entry 6) in 96% yield. It should be noted that a number of functional groups are compatible under the relatively mild reaction conditions, including alkenes (entry 3), esters (entry 4), alcohols (entry 5), and *N*-tosyl amines (entry 8).

The four representative examples in Scheme 3 further underline the generality and synthetic utility of this (CDC)-

Table 3. (CDC)-Rh(I)-Catalyzed Hydroaminations of Dienes with Aniline[a]

[a]See SI for experimental details; all reactions performed under N_2 atm with 2 equiv of diene; up to >98% site selectivity. [b]Yields of purified products are an average of two runs. [c]3:2 mixture of *γ*:*α* addition. [d]4 equiv of diene was used.

Scheme 3. (CDC)-Rh-Catalyzed Hydroaminations of 1,3-Dienes with Secondary Alkyl Amines[a]
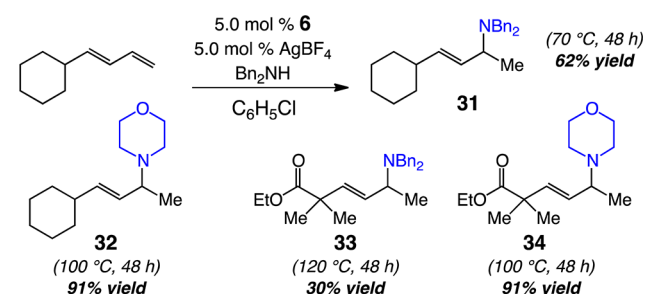
[a]See Table 3.

Rh(I) hydroamination protocol. As noted (*vide supra*), catalytic hydroamination with aliphatic amines generally requires higher temperatures (70−120 °C) than that with aryl amines. Site-selective formation of aliphatic allylic amines **31** (62%) and **32** (91%) from dibenzyl amine and morpholine proceeds efficiently in the presence of 5 mol % **6** (70 and 100 °C). Incorporation of ester functionality is also tolerated, as catalytic hydroamination (5 mol % (CDC)-Rh **6** and 5 mol % $AgBF_4$) delivers **33** (120 °C, 48 h) and **34** (100 °C, 48 h) in modest to excellent yields (30% and 91%, respectively).

In conclusion, we have developed a tridentate carbodicarbene ligand scaffold that enables efficient Rh-catalyzed site-selective intermolecular hydroamination of 1,3-dienes compatible with both alkyl and aryl amines. The reactions described represent the first examples of a CDC−transition metal complex functioning as an effective catalyst. Further investigations into the mechanistic details of (CDC)-Rh(I)-catalyzed hydro-

aminations, in addition to the development of new CDC ligands and their application to other catalytic methods, are in progress.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental procedures and spectral and analytical data for all products. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

■ REFERENCES

(1) Díez-González, S.; Marion, N.; Nolan, S. P. *Chem. Rev.* **2009**, *109*, 3612−3676.

(2) Frenking, G.; Tonner, R. Carbodicarbenes. In *Contemporary Carbene Chemistry*; Moss, R. A., Doyle, M. P., Eds.; John Wiley & Sons, Inc.: Hoboken, NJ, 2013; Chapter 8, p 216.

(3) (a) Kaufhold, O.; Hahn, F. E. *Angew. Chem., Int. Ed.* **2008**, *47*, 4057−4061. (b) Melaimi, M.; Soleilhavoup, M.; Bertrand, G. *Angew. Chem., Int. Ed.* **2010**, *49*, 8810−8849.

(4) (a) Dyker, C. A.; Lavallo, V.; Donnadieu, B.; Bertrand, G. *Angew. Chem., Int. Ed.* **2008**, *47*, 3206−3209. (b) Lavallo, V.; Dyker, C. A.; Donnadieu, B.; Bertrand, G. *Angew. Chem., Int. Ed.* **2008**, *47*, 5411−5414. (c) Melaimi, M.; Parameswaran, P.; Donnadieu, B.; Frenking, G.; Bertrand, G. *Angew. Chem., Int. Ed.* **2009**, *48*, 4792−4795. (d) Alcarazo, M.; Lehmann, C. W.; Anoop, A.; Thiel, W.; Fürstner, A. *Nat. Chem.* **2009**, *1*, 295−301.

(5) (a) Tonner, R.; Frenking, G. *Angew. Chem., Int. Ed.* **2007**, *46*, 8695−8698. (b) Tonner, R.; Frenking, G. *Chem.—Eur. J.* **2008**, *14*, 3260−3272. (c) Tonner, R.; Frenking, G. *Chem.—Eur. J.* **2008**, *14*, 3273−3289. (d) Tonner, R.; Heydenrych, G.; Frenking, G. *ChemPhysChem* **2008**, *9*, 1474−1481. (e) Fernández, I.; Dyker, C. A.; DeHope, A.; Donnadieu, B.; Frenking, G.; Bertrand, G. *J. Am. Chem. Soc.* **2009**, *131*, 11875−11881. (f) Klein, S.; Tonner, R.; Frenking, G. *Chem.—Eur. J.* **2010**, *16*, 10160−10170.

(6) Fürstner, A.; Alcarazo, M.; Goddard, R.; Lehmann, C. W. *Angew. Chem., Int. Ed.* **2008**, *47*, 3210−3214.

(7) DeHope, A.; Donnadieu, B.; Bertrand, G. *J. Organomet. Chem.* **2011**, *696*, 2899−2903.

(8) Pranckevicius, C.; Stephan, D. W. *Organometallics* **2013**, *32*, 2693−2697.

(9) Chen, W.-C.; Hsu, Y.-C.; Lee, C.-Y.; Yap, G. P. A.; Ong, T.-G. *Organometallics* **2013**, *32*, 2435−2442.

(10) (a) *The Chemistry of Pincer Compounds*; Morales-Morales, D., Jensen, C., Eds.; Elsevier: Amsterdam, 2007. (b) *Organometallic Pincer Chemistry*; van Koten, G., Milstein, D., Eds.; Topics in Organometallic Chemistry 40; Springer: Berlin, 2013. (c) Albrecht, M.; van Koten, G. *Angew. Chem., Int. Ed.* **2001**, *40*, 3750−3781. (d) Selander, N.; J Szabó,

K. *Chem. Rev.* **2011**, *111*, 2048−2076. (e) Choi, J.; MacArthur, A. H. R.; Brookhart, M.; Goldman, A. S. *Chem. Rev.* **2011**, *111*, 1761−1779.

(11) (a) Müller, T. E.; Beller, M. *Chem. Rev.* **1998**, *98*, 675−704. (b) Roesky, P. W.; Müller, T. E. *Angew. Chem., Int. Ed.* **2003**, *42*, 2708−2710. (c) Hong, S.; Marks, T. J. *Acc. Chem. Res.* **2004**, *37*, 673−686. (d) Müller, T. E.; Hultzsch, K. C.; Yus, M.; Foubelo, F.; Tada, M. *Chem. Rev.* **2008**, *108*, 3795−3892.

(12) For Pd-catalyzed examples, see: (a) Löber, O.; Kawatsura, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2001**, *123*, 4366−4367. (b) Minami, T.; Okamoto, H.; Ikeda, S.; Tanaka, R.; Ozawa, F.; Yoshifuji, M. *Angew. Chem., Int. Ed.* **2001**, *40*, 4501−4503. (c) Johns, A. M.; Utsunomiya, M.; Incarvito, C. D.; Hartwig, J. F. *J. Am. Chem. Soc.* **2006**, *128*, 1828−1839. (d) Kuchenbeiser, G.; Shaffer, A. R.; Zingales, N. C.; Beck, J. F.; Schmidt, J. A. R. *J. Organomet. Chem.* **2011**, *696*, 179−187. For a Ni-catalyzed example, see: (e) Pawlas, J.; Nakao, Y.; Kawatsura, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2002**, *124*, 3669−3679. For a Ru-catalyzed example, see: (f) Yi, C. S.; Yun, S. Y. *Org. Lett.* **2005**, *7*, 2181−2183. For Ca- and Sr-catalyzed examples, see: (g) Brinkmann, C.; Barrett, A. G. M.; Hill, M. S.; Procopiou, P. A. *J. Am. Chem. Soc.* **2012**, *134*, 2193−2207. For a Ti-catalyzed example, see: (h) Preuß, T.; Saak, W.; Doye, S. *Chem.—Eur. J.* **2013**, *19*, 3833−3837.

(13) For related catalytic intermolecular hydroamidations of 1,3-dienes, see: (a) Brouwer, C.; He, C. *Angew. Chem., Int. Ed.* **2006**, *45*, 1744−1747. (b) Giner, X.; Nájera, C. *Org. Lett.* **2008**, *10*, 2919−2922. (c) Qin, H.; Yamagiwa, N.; Matsunaga, S.; Shibasaki, M. *J. Am. Chem. Soc.* **2006**, *128*, 1611−1614. (d) Giner, X.; Nájera, C.; Kovács, G.; Lledós, A.; Ujaque, G. *Adv. Synth. Catal.* **2011**, *353*, 3451−3466. (e) Banerjee, D.; Junge, K.; Beller, M. A. *Angew. Chem., Int. Ed.* **2014**, *53*, 1630−1635.

(14) For examples of catalytic intramolecular hydroamination and hydroamidation of 1,3-dienes, see: (a) Hong, S.; Marks, T. J. *J. Am. Chem. Soc.* **2002**, *124*, 7886−7887. (b) Hong, S.; Kawaoka, A. M.; Marks, T. J. *J. Am. Chem. Soc.* **2003**, *125*, 15878−15892. (c) Shapiro, N. D.; Rauniyar, V.; Hamilton, G. L.; Wu, J.; Toste, F. D. *Nature* **2011**, *470*, 245−249. (d) Kanno, O.; Kuriyama, W.; Wang, Z. J.; Toste, F. D. *Angew. Chem., Int. Ed.* **2011**, *50*, 9919−9922. (e) Deschamp, J.; Collin, J.; Hannedouche, J.; Schulz, E. *Eur. J. Org. Chem.* **2011**, 3329−3338. (f) Pierson, J. M.; Ingalls, E. L.; Vo, R. D.; Michael, F. E. *Angew. Chem., Int. Ed.* **2013**, *52*, 13311−13313.

(15) Attempts to deprotonate **4** and **5** and isolate the free CDC were unsuccessful.

(16) Complexes **6** and **7** crystallize as plates, and X-ray-quality crystals could not be obtained at the present time.

(17) For a cationic PNP-Rh(I)-NCMe complex, see: (a) Hahn, C.; Sieler, J.; Taube, R. *Polyhedron* **1998**, *17*, 1183−1193. (b) Hermann, D.; Gandelman, M.; Rozenberg, H.; Shimon, L. J.; Milstein, D. *Organometallics* **2002**, *21*, 812−818. For a POP-Rh(I)-NCMe complex, see: (c) Julian, L. D.; Hartwig, J. F. *J. Am. Chem. Soc.* **2010**, *132*, 13813−13822.

(18) (a) Feller, M.; Ben-Ari, E.; Gupta, T.; Shimon, L. J. W.; Leitus, G.; Diskin-Posner, Y.; Weiner, L.; Milstein, D. *Inorg. Chem.* **2007**, *46*, 10479−10490. (b) Feller, M.; Diskin-Posner, Y.; Shimon, L. J. W.; Ben-Ari, E.; Milstein, D. *Organometallics* **2012**, *31*, 4083−4101. (c) See ref 17c..

(19) Please see Supporting Information.