Communication

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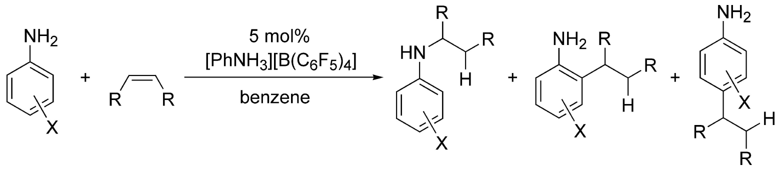

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Proton-Catalyzed Hydroamination and Hydroarylation Reactions of Anilines and Alkenes: A Dramatic Effect of Counteranions on Reaction Efficiency

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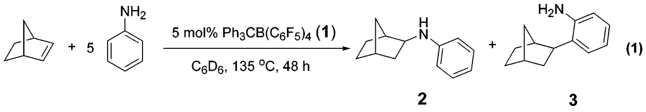
Acid-catalyzed additions of amines to alkenes are generally unsuccessful due to the buffering effect of the amine substrate.[1] Friedel−Crafts alkylations of arylamines are hindered by coordination of the amine to the Lewis acid catalyst.[2] A recent communication by Hartwig et al. reports that several common Brønsted acids catalyze the intramolecular hydroamination of tosyl-protected amino olefins.[3] Beller and co-workers have reported that alkylations of electron-rich anilines with styrene are promoted with $HBF_4 \cdot Et_2O$.[2b,4] Herein we report the first homogeneous[5] acid catalyst that promotes both hydroamination and hydroarylation reactions of anilines and alkenes, including simple cyclic alkenes and dienes. These transformations are air- and moisture-tolerant and can be controlled to favor either N−H or Ar−H addition products based on reaction conditions and aniline substitution pattern. The key to the activity of this system is that the acid counteranion has a dramatic effect on reaction efficiency.

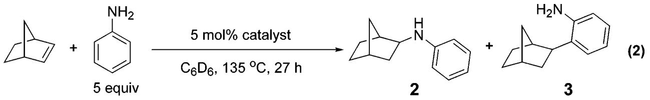
In the course of our studies on metal-catalyzed hydroamination reactions,[6] we found that $Ph_3CB(C_6F_5)_4$ (**1**) catalyzes the reaction of norbornene with aniline. Both hydroamination (**2**) and *ortho*-hydroarylation (**3**) products are formed using 5 mol % of **1** (eq 1).[7]



To determine the role of the trityl cation, the above reaction was run in the presence of several trapping reagents. The addition of radical traps, such as 2,6-di-*tert*-butylphenol and 1,4-cyclohexadiene, did not affect the outcome of the reaction. In contrast, the addition of one catalytic equivalent of NEt_3 completely inhibited both hydroamination and hydroarylation, suggesting that the reaction is acid-catalyzed.

We anticipated that the strongest acid in the reaction solution would be an anilinium salt.[8] Accordingly, $PhNH_3B(C_6F_5)_4 \cdot Et_2O$ (**4**) was synthesized and shown to be as competent as **1**, affording an identical product distribution (Table 1, entry 2). As shown in Table 1, several other anilinium salts and strong acids were screened as catalysts for the addition of aniline to norbornene. It was assumed that the acids in entries 3, 4, and 6 would rapidly react with aniline in the reaction mixture to form the corresponding anilinium salts. As expected, HOTf provided a yield similar to that observed with anilinium triflate. Analogous reactivity was anticipated for $H(Et_2O)_{2.5}B(C_6F_5)_4$ (**5**) and **4**; however, a significant decrease in reactivity was observed for **5**. This discrepancy may be caused by the additional 1.5 equiv of ether associated with **5** and coincides with a lack of reactivity of these catalysts in donor solvents.[9] The trend in reactivity is an increase in catalytic efficiency with decreasing anion coordination ability ($BPh_4^- < OTf^- < NTf_2^- < B(C_6F_5)_4^-$).[10] This suggests that the effective acidity of the anilinium salt in benzene increases with decreasing anion coordination ability and thereby facilitates protonation of the alkene.[11] It has previously been shown that TFA does not catalyze the hydroamination of styrene with aniline. These results are consistent with our observations assuming that trifluoroacetate is a more strongly coordinating anion than OTf^-.[1b]

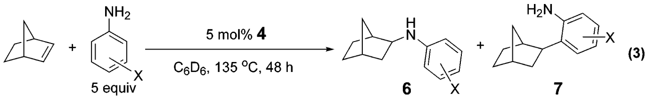
Table 1. Acid Catalysts for the Hydroamination and Hydroarylation of Norbornene



entry	catalyst	% yield[a]	**2**:**3**[a]
1	$Ph_3CB(C_6F_5)_4$ (**1**)	58	1:1
2	$PhNH_3B(C_6F_5)_4 \cdot Et_2O$ (**4**)	60	1:1
3	$H(Et_2O)_{2.5}B(C_6F_5)_4$ (**5**)	33	1:1
4	$HNTf_2$	35	1:1
5	$PhNH_3OTf$	19	1:1
6	HOTf	13	1:1
7	$PhNH_3BPh_4$	0	

[a] Combined yield of **2** and **3**. Yields and product ratios were determined by GC.

Table 2. Effect of Aniline Substitution on Hydroamination and Hydroarylation Product Ratios



entry	X	% yield[a]	**6**:**7**
1	H	84	1:1
2	4-Cl	56 (55[b])	only **6**
3	4-OMe	34	1:2
4	2,6-Me$_2$	50[c]	2:3[d,e]
5	*N*-Me	55[b]	1:4[d]
6	3,5-CF$_3$	80	only **6**

[a] Combined yield of **6** and **7**. [b] With 5 mol % of **3**, 72 h. [c] GC yield. [d] GC ratio of isomers. [e] **7** is the *p*-hydroarylation product.

After determining that **4** was the optimal catalyst for the hydroamination/hydroarylation reaction, a variety of substituted anilines were evaluated to probe steric and electronic effects on product distribution. As shown in Table 2, the addition reaction tolerates substitution on the nitrogen as well as the aromatic ring of the aniline. The *ortho*-addition is favored for the hydroarylation products unless the *ortho*-positions of the aniline substrate are blocked. Electron-withdrawing substituents on the aniline increase the overall yield of the reaction and favor formation of the hydroamination product.[7b] Surprisingly, using aniline as a solvent does not affect the product ratio but decreases the overall yield of the transformation.

Compound **4** also catalyzes the hydroamination and hydroarylation reactions of substituted styrenes (Table 3).[12] Notably, these transformations require lower temperatures and shorter reaction

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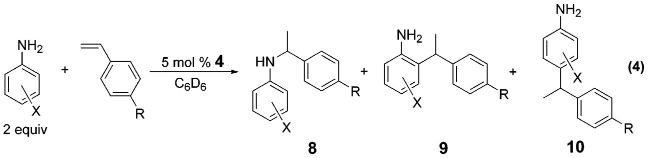
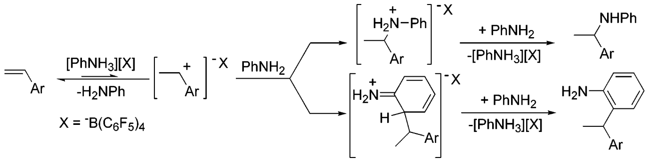
Table 3. Hydroamination and Hydroarylation Reactions of Vinyl Arenes (Unless noted, yields are % yields determined by ^{1}H NMR)



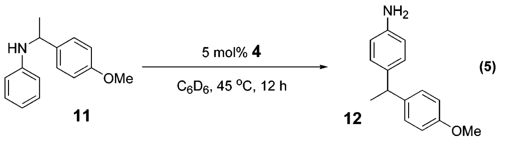
entry	R	X	T (°C)	t (h)	yield	**8**:**9**:**10**
1[a]	OMe	H	45	1	34	87:3:10
2[a]	OMe	H	45	4	83	57:8:35
3	OMe	H	45	8	72[b]	25:10:65
4	OMe	H	75	4	93	4:22:74
5	OMe	4-OMe	45	51	82[b]	90:10:0
6	OMe	4-OMe	75	24	85[b]	20:80:0
7[a]	Cl	4-Cl	105	1	89	50:50:0
8[a]	Cl	4-Cl	105	4	99	25:75:0
9[a]	Cl	3,5-CF_3	45	3	52	100:0:0
10	Cl	3,5-CF_3	45	24	63[b]	100:0:0
11	OMe	3-Cl	25	5	82[b]	40:60:0
12	OMe	3-Cl	45	12	71[b]	0:100:0

[a] Time points from single NMR tube experiments. [b] Combined % yields of isolated products.

Scheme 1. Proposed Mechanism



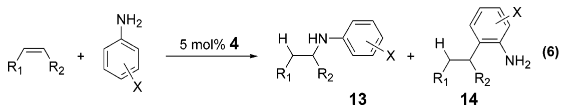
times than the norbornene reactions and are facilitated by electron-donating substituents on the styrene substrate (OMe vs Cl) and electron-withdrawing substituents on the aniline (OMe vs Cl or CF_3). The *para*-substituted hydroarylation products are favored for these styrene substrates unless the *para*-position is blocked. These observations are consistent with the intermediacy of a stabilized carbocation and suggest that these transformations proceed along a reaction pathway similar to that of acid-catalyzed hydration, where either the heteroatom or the aromatic ring can act as the nucleophile (Scheme 1).[13] The difference in the *ortho*−*para* selectivity between norbornene and styrene hydroarylation products may be caused by differences in the stabilities of protonated intermediates.[13]



The most notable trend in Table 3 is that N−H addition dominates at short reaction times, and Ar−H addition is the major product at longer reaction times and higher temperatures (Table 3, entries 1−4). Specifically, the yield of the hydroarylation product increases at the expense of the hydroamination product as the reaction proceeds. A control experiment demonstrated that isolated **11** undergoes a Hofmann−Martius rearrangement[14] in the presence of 5 mol % of **4** to afford **12** (eq 5).[4,12] This observed conversion of hydroamination to hydroarylation products allows for preferential generation of either the kinetic or the thermodynamic product based on reaction time and temperature.

Cyclic alkenes and dienes undergo analogous addition reactions (Table 4). These substrates give primarily hydroarylation products when treated with aniline; however, electron-poor anilines provide hydroamination products. Although these reactions are unoptimized, they illustrate the potential scope of this proton-catalyzed transformation.

Table 4. Hydroamination and Hydroarylation Reactions of Other Unsaturated Substrates



entry	alkene	X	T (°C)	% yield	**13**:**14**
1[a]	cyclopentene	H	135	39	0:1
2[a]	*cis*-cyclooctene	H	135	45[c]	1:3
3[b]	cyclohexadiene	H	105	56	0:1
4[b]	cyclohexadiene	3,5-CF_3	75	20	1:0

[a] Alkene:aniline (1:1), chlorobenzene, 7 days. [b] Alkene:aniline (1:2), benzene, 12 h. [c] NMR yield of **13** and **14**.

In conclusion, $PhNH_3B(C_6F_5)_4$ has been identified as a new catalyst for the hydroamination and hydroarylation of several activated alkenes with anilines. We are currently investigating the details of the mechanism of this transformation and how to further control the selectivity for N−H and Ar−H additions. The control experiment used to identify this catalyst should also serve as a reminder that acid catalysis exists as a possibility in many metal-catalyzed systems and should always be investigated.

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Supporting Information Available: Experimental procedures and characterization data for new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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(9) The reaction can be performed in benzene, toluene, or chlorobenzene. No reaction is observed in CH_2Cl_2, DMF, acetonitrile, THF, or ethanol.
(10) For similar anion effects with transition-metal catalysts, see: (a) Burling, S.; Field, L. D.; Messerle, B. A.; Turner, P. *Organometallics* **2004**, *23*, 1714. (b) Muller, T. E.; Grosche, M.; Herdtweck, E.; Pleier, A. K.; Walter, E.; Yan, Y. K. *Organometallics* **2000**, *19*, 170. (c) Ref 1b.
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