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Cu(I)-catalyzed allylic amination of olefins

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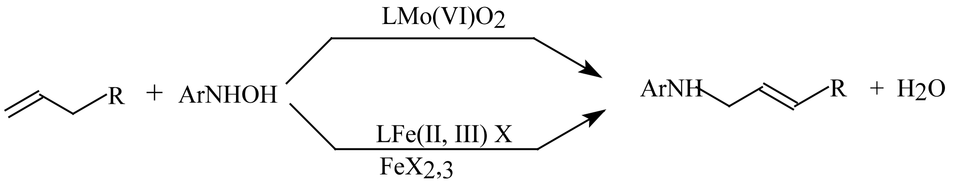
Abstract—The copper(I) complex $[Cu(CH_3CN)_4]PF_6$ catalyzes the allylic amination of alkenes by aryl hydroxylamine in fair to moderate yields. Unsymmetrical alkenes react with high regioselectivity with *N*-functionalization occuring at the less substituted vinylic carbon. Trapping experiments indicate that free PhNO is not an intermediate in these reactions. © 2002 Elsevier Science Ltd. All rights reserved.

1. Introduction

The hunt for new, selective chemical procedures for the direct conversion of petroleum-derived hydrocarbons to functionalized organic compounds is a major thrust of research in both industry and academia. Transition metal-promoted allylic amination of alkenes and alkynes offers an attractive route to functionalized amines via C–N bond formation.[1] While several important processes for the oxidation of hydrocarbons exist,[1] the direct production of organonitrogen compounds from hydrocarbons remains a desirable goal due to the commercial potential of such processes. Contrary to significantly investigated areas of homogeneous metal-catalyzed olefin oxygenation, corresponding metal-promoted nitrogenation reactions are remarkably few and typically add nitrogen to the C–C unsaturation. The stoichiometric formation of allyl amine from an olefin has been reported with Group 16 imido compounds ($R'N{=}X{=}NR'$; $X{=}S$,[2] Se[3]) as aminating agents. This reaction displays moderate regioselectivity for retention of the double bond position, proceeding via an ene reaction followed by [2,3]-sigmatropic rearrangement. Sharpless reported the stoichiometric imido-transfer reactions of molybdooxaziridine complexes $[MoL_n(\eta^2\text{-RNO})]$ with alkenes, producing allyl amines.[4] The ene reactions of azo-,[5] nitroso-[6] and *N*-sulfinylcarbamate[7] derivatives display high regioselectivity with double bond migration, but require additional N–N or N–O reduction steps to produce allyl amines.

We and others have investigated the metal-catalyzed allylic amination of olefins. At the outset, molybdenum[8] and iron[9]-catalyzed aminations of olefins by aryl hydroxylamines were developed. These reactions proceed regioselectively with *N*-functionalization at the less substituted olefinic carbon (Eq. (1)). Subsequently, metal-promoted allylic aminations of olefins using the more readily available nitroarenes as aminating agents, carbon monoxide as reductant, and $Ru_3(CO_{12})$/diimine[10] or $[Cp(*)Fe(CO)_2]_2$[11] as catalysts were discovered (Eq. (2)). These reactions require more strenuous reaction conditions (150–200°C, 25–50 atm), but the iron-catalyzed reactions also display high ene-reaction type regioselectivity.

Just recently, we discovered that photo-assisted, iron-catalyzed allylic aminations using nitroarenes proceed quite smoothly under much milder conditions, allowing the reaction to be carried out in conventional glassware.[12]



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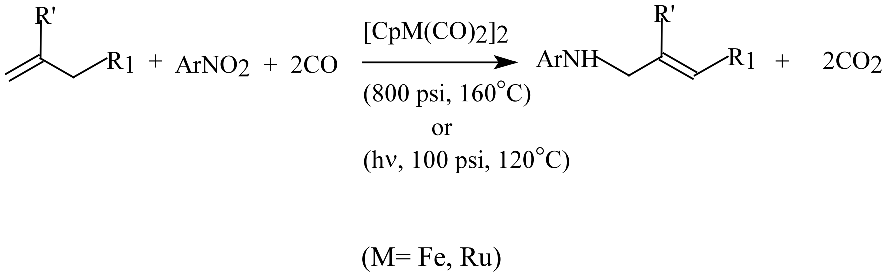


(2)

Seeking new, more efficient metal-catalyzed aminations with hydroxylamines, we were investigating Cu-promoted reactions when a report by Lau and co-workers disclosed allylic aminations with PhNHOH catalyzed by various, mostly Cu(II) salts.[13] A redox-recycle mechanism similar to that of Mo-[8] and FePc[9d]-systems involving the intermediacy of free PhNO was proposed. We describe herein our studies of the copper(I)-catalyzed allylic amination of alkenes using phenyl hydroxylamine as a nitrogen-fragment donor. Trapping experiments indicate that neither *free nitrosobenzene nor phenyl nitrene are intermediates* in these reactions.

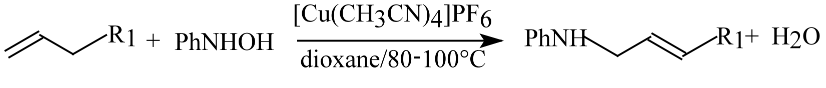
2. Results and discussion

Screening of a series of copper complexes revealed that $[Cu(CH_3CN)_4]PF_6$, (**1**), has the best catalytic properties, with phenyhydroxylamine as aminating agent. Addition of phenyl hydroxylamines to a dioxane solution (80–100°C) with an excess of olefin and 10 mol% **1** produces the corresponding *N*-aryl-*N*-allylamines in fair to moderate yield accompanied by small quantities of azobenzene and azoxybenzene (Eq. (3)).

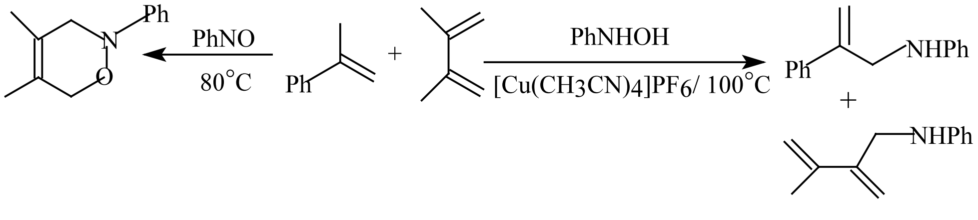
Complex **1** was also employed as a catalyst to survey the scope and selectivity of the amination with a representative set of olefins. The important features of this reaction include: (1) trisubstituted and 1,1-disubstituted alkenes produce the highest yields; (2) unsymmetrical alkenes react to produce the allyl amine derived from double bond transposition, and (3) generally only single isomers are produced. Features 1 and 2 are typical of ene-reactions.[14] Other arylhydroxylamines are also effective as aminating agents, including DNP-NHOH, which provides access to secondary *N*-alkyl-allyl amines upon deprotection/alkylation.[15] The yields, reactivity and chemoselectivity features of this reaction are comparable to the Mo-,[8] Fe-[9] and Cu(II)[13]-catalyzed reactions.

As we mentioned earlier, recent studies indicate that amination of olefins catalyzed by hydrated copper(II)chloride proceeds via free PhNO as the active aminating agent.[13] To probe whether this was also the case for the reactions catalyzed by **1**, we employed the hetero-Diels–Alder reaction of nitrosobenzene, with 2,3-dimethylbutadiene as a trapping test for PhNO.[16] The effective Diels–Alder trapping of PhNO by 2,3-dimethylbutadiene at 100°C in the presence of α-methylstyrene in dioxane (solvent) was first established (Eq. (4)). When the amination reaction of α-methylstyrene by phenyl hydroxylamine catalyzed by **1** (10 mol% **1**) was carried out in the presence of 2,3-dimethylbutadiene (1:2, 100°C, dioxane), allyl amines derived from the alkene (major) and diene (minor) and a *trace* of 3,4-dimethyl-*N*-phenylpyrrole were formed; the Diels–Alder adduct (trapping product from PhNO) was not detected (Eq. (4)). Moreover, in a separate experiment the D–A adduct was shown to be stable under the catalytic conditions employed (DA-adduct, **1** (1:1) and excess AMS, 100°C, 5 h). To test for the possible intermediacy of phenyl nitrene, we heated the dioxane solution of *o*-(hydroxylamino)-biphenyl in the presence of **1**;[17] no carbazole, the product of nitrene C–H insertion, was detected.

These results argue against the intermediacy of free PhNO or phenyl nitrene in the aminations catalyzed by **1**, and suggest that they may proceed via a coordinated organonitrogen species. The differing trapping results from the aminations catalyzed by $CuCl_2{\cdot}2H_2O$ and



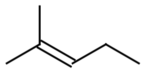
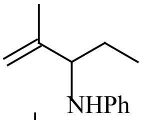
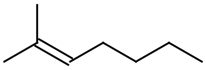
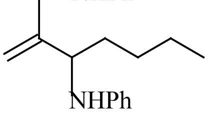
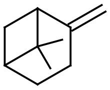
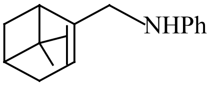
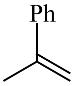
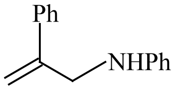
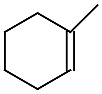
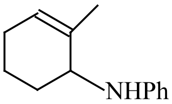
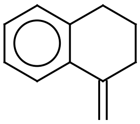
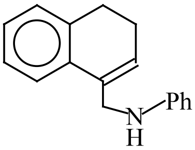
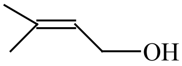
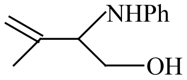
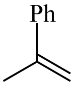
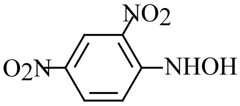
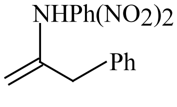
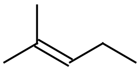
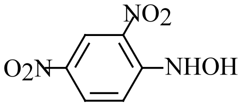
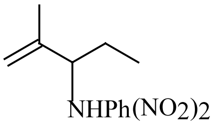
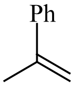
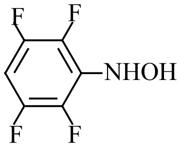
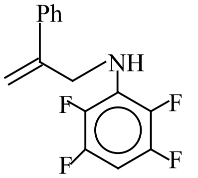
(3)



(4)

$[Cu(CH_3CN)_4]PF_6$ indicate that different intermediates are involved in the two processes. While both systems likely involve Cu(I)/Cu(II) shuttling, the different ligand sets could be responsible for the differing reaction pathways. We and others[9a,d] have established the dramatic influence of the coordinating ligands in the iron-catalyzed aminations. Acetonitrile is a relatively weak donor and likely more loosely bound to copper com-

Table 1. Allylic amination catalyzed by $[Cu(CH_3CN)_4]PF_6$ (**1**)

Run	Substrate	Hydroxylamine	Product	Yield (%)[a]	N-Selectivity (%)[b]
1		PhNHOH		38	72
2		PhNHOH		45	76
3		PhNHOH		15	42
4		PhNHOH		30	52
5		PhNHOH		10	56
6		PhNHOH		60	90
7		PhNHOH		15	51
8				31[c]	96
9				52[c]	98
10				75	98

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[a] GC yield using sensitivity factor versus naphthalene internal standard.

[b] Allyl amine/(allyl amine+*N*-byproducts).

[c] Isolated yield.

pared to chloride ion. Thus, PhNO/PhNHOH could coordinate at the vacant site created by the dissociation of acetonitrile. The resulting complex (of PhNO or azodioxide, ArN(O)N(O)Ar) could react with olefin with transfer of PhNO to generate an allyl hydroxylamine complex. Dissociation of the later and subsequent deoxygenation by Cu(I) would afford allyl amine and Cu(II), which in turn can react with PhNHOH to regenerate the reactive intermediate. The slow deoxygenation step seems to be responsible for the modest yields of allyl amine.

3. Summary

Complex **1** catalyzes the regioselective amination of olefins using phenyl hydroxylamine as an aminating agent. Although further insight into the mechanism of this process is being sought, the absence of free nitrosobenzene and nitrene argue in favor of an 'on the metal' reaction pathway.

4. Experimental

General: The alkene in run 6[18] (Table 1), phenylhydroxylamine,[19] 2,4-dinitrophenylhydroxylamine[20] and 2,3,5,6-tetrafluorophenylhydroxylamine[21] were prepared according to literature methods. Anhydrous 1,4-dioxane (Aldrich), $[Cu(CH_3CN)_4]PF_6$ (Strem), and all other reactants were obtained commercially. GC/MS and MS spectra were obtained at 70 eV (EI). GC analyses utilized a 3′ column packed with 3% OV101.

Catalytic allylic amination of olefins: All reactions were performed under dry argon. The general method for the preparation of compound **4** is as described. The olefin, α-methylstyrene (7 mmol) and **1** (0.15 mmol) were added to 1,4-dioxane (2 mL) and heated to reflux (80–100°C). Phenylhydroxylamine (1.5 mmol) was dissolved in 1,4-dioxane (10 mL) and was slowly added over a period of 5–6 h with a syringe pump. The reaction mixture was then heated for two additional hours. The metal-catalyst was precipitated with hexane and filtered. The resulting solution was concentrated by a rotary evaporator and dried under vacuum. The crude mixture was purified by column chromatography (silica gel) using dichloromethane–petroleum ether (30:70) as the eluent. The components of the mixture were analyzed by GC and GC–MS using naphthalene as the internal standard. Comparison with authentic samples prepared as described in the literature identified the allyl amines.[9] In a separate procedure, compounds **8** and **9** were isolated and identified as described in the literature.[15]

Acknowledgements

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