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Copper-catalyzed allylic amination of olefins with nitrosoarenes

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Abstract—The transition metal catalyzed allylic amination of olefins are studied. A screening of catalysts known for the intermediacy of PhNO in the amination of alkene with phenylhydroxylamine reveals that the hydrated copper salt in conjugation with copper powder as reductant has the best catalytic properties using nitrosobenzene as nitrogen-fragment donor. The catalytic system has been studied for a variety of alkenes. Unsymmetrical alkenes react with high regioselectivity with *N*-functionalization at the less substituted vinylic carbon. © 2003 Elsevier Science Ltd. All rights reserved.

1. Introduction

The method for new, selective, and direct synthesis of organonitrogen compounds from hydrocarbons remains a desirable goal in both industry and academie due to the profit potential. Considerable research has been done with transition metal promoted allylic amination of alkenes and alkynes, which may offer an appealing route to functionalized amines via C-N bond formation.¹ The addition of a N-H bond to an alkene is a noteworthy chemical transformation because it leads to the formation of a C-N bond, and therefore to the functionalization of the hydrocarbon. In contrast to the considerably explored areas of homogeneous metal-catalyzed olefin oxygenation, studied metal-promoted nitrogenation reactions are few. Metal-mediated nitrogenation reactions have received growing attention, as evidenced by recent reports on metal-catalyzed aziridination² and hydroamination³ of olefins, both of which involve addition to double bonds.

The transformation of olefin to allyl amine has been accomplished stoichiometrically with group 16 imido compounds (R'N=X=NR'; $X=S^4$, Se⁵) as aminating agents. This reaction is regioselective for retention of the double bond position as it proceeds via an ene reaction followed by [2,3]-sigmatropic rearrangement. Sharpless has reported the stoichiometric imido-transfer reactions of molybdooxaziridine complexes $[MoL_n(\eta^2-RNO)]$ with alkenes, producing allyl amines.⁶ The ene reactions of azo-,⁷ nitroso-⁸ and *N*-sulfinylcarbamate⁹ derivatives exhibit high regioselectivity with double bond transposition, but require additional N–N or N–O reduction steps to produce allyl amines.

Metal-catalyzed allylic amination of olefins, which produces allyl amines with high regioselectivity, has been investigated by several research groups including our own (Eq. (1)). Initially, molybdenum-¹⁰ and iron¹¹-catalyzed amination of olefins employing arylhydroxylamines was 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 $Ru_3(CO_{12})/diimine^{12}$ or $[Cp(*)Fe(CO)_2]_2^{13}$ as catalysts have been discovered (Eq. (2)). These reactions require demanding reaction conditions (150-200°C, 25-50 atm) and proceed regioselectively with N-functionalization at the less substituted olefinic carbon. Our recent discovery¹⁴ of photo-assisted allylic aminations proceeds smoothly under much milder conditions, allowing the reaction to be carried out expediently. Allylic aminations of olefins using CuCl₂·2H₂O as catalyst and phenylhydroxylamine as aminating agent have been reported recently.^{15,16}



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$$\begin{array}{c} R' \\ R_{1} + ArNO_{2} + 2CO \\ \hline (800 \text{ psi}, 160^{\circ}\text{C}) \\ \text{or} \\ (hv, 100 \text{ psi}, 120^{\circ}\text{C}) \\ (M = Fe, Ru) \end{array}$$

Two-aminating agents for allylic amination have been extensively used. Nitroarene (Eq. (2)) requires rigorous reaction conditions and phenylhydroxylamine (Eq. (1)) is unavailable commercially and must be synthesized. In order to enhance the synthetic utility of metal-catalyzed allylic amination and to explore further the significant advancement in the synthetic utility of allylic amination, new and more stable potential aminating agents such as nitrosoarenes have been studied. Since PhNO is stable, inexpensive, and commercially available, it is

Table 1. Allylic amination catalyzed by $CuCl_2{\cdot}2H_2O$ and Cu-powder



^aG.C. yield using sensitivity factor vs. naphthalene internal standard ^b allyl amine/(allyl amine + GC volatile byproducts)

$$R_1 + PhNO \xrightarrow{CuCl_2.2H_2O/Cu}_{dioxane/100^{\circ}C} PhNH \qquad R_1 + CuO$$
(3)

worthwhile to scrutinize the allylic amination of alkenes using this nitrosoarene as aminating agent, as an alternative to allylic amine synthesis. Although only few nitrosoarenes are commercially available, they can however be synthesized by the oxidation of anilines or the nitrosation of arenes.¹⁷ To the best of our knowledge, exploitation of nitrosoarenes as aminating agents in the catalytic allylic amination of olefins is unexplored. Trapping experiments exhibit that *nitrene is not an intermediate* in these reactions.

2. Results and discussion

Metal catalysts reported for PhNO intermediacy in the catalytic allylic amination with phenylhydroxylamine tested. Thus, we have examined were the MoO₂(dipic)HMPA,¹⁰ Fe-phthalocyanine^{11d} and hydrated CuCl₂·2H₂O¹⁵ as catalysts for the reaction of α -methylstyrene with PhNO. The results suggest that CuCl₂·2H₂O is the best among these catalysts since it produces 33% of the desired product. However, the yield is further improved to 55% by using Cu-powder as reductant. These results reveal that the mixture of CuCl₂·2H₂O and Cu-powder (1:4 molar ratio) 1 has comparable catalytic activity among the tested compounds. Addition of nitrosobenzene to a dioxane solution (100°C) in an excess of olefin and 5-mol% CuCl₂·2H₂O and Cu-powder produces the corresponding N-aryl-N-allylamines in moderate to good yield (Table 1) accompanied by small quantities of azobenzene, and azoxybenzene (Eq. (3)). A control experiment in the absence of catalyst also produces 9% allyl amine, probably due to the disproportionation of allylhydroxylamine generated by the reaction of alkene and PhNO.^{18,19}

Compound 1 was also employed as a catalyst to survey the scope and selectivity of the amination with a representative set of olefins. The yield of the products is comparable to those reported earlier.^{10,11,15} 2-Nitrosotoluene is also effective as an aminating agent (run 9). An attempt to use N,N-diethyl-4-nitrosoaniline, as an aminating agent has been unsuccessful. The essential findings of the reaction include: (a) trisubstituted and 1,1-disubstituted alkenes afford the best yields; (b) unsymmetrical alkenes react with virtually complete regioselectivity to produce the corresponding allyl amine derived from double bond migration; (c) generally single isomers are observed. Features 1 and 2 are typical of ene-type reactions.²⁰ The yields, reactivity, and chemoselectivity features of this reaction are analogous to the Mo-10 and Cu(II)15,16 systems. Electronic variability on alkenes was also accessed with a set of *para*-substituted α -methylstyrene derivatives. Addition of an electron-withdrawing group (run 7) was found to suppress the product yield considerably, while the more electron rich groups produced higher yield of product compared to electron withdrawing groups (run

8). However, the electron-rich alkene gave a lower yield of product compared to the neutral parent compound (run 4). Variable amounts of by-products (azobenzene and azoxybenzene) were detected.

These catalytic reactions exhibit the same ene-type reaction selectivity features as the other catalytic systems,^{10,11d,15} including double bond migration and decreasing olefin reactivity with decreasing degree of substitution. Hence they are likely to be closely related mechanistically. To probe the possible intermediacy of phenyl nitrene, a dioxane solution of o-(hydroxylamino) biphenyl was heated in the presence of 1^{21} and no carbazole, which is a product of nitrene C-H insertion, was detected. The formation of allylhydroxylamine by the reaction of nitrosoarene and alkene has been unequivocally established.^{10,11,15} The reaction mechanism is unclear. Based on the previous studies and our initial trapping experiments, however, the first step in the catalytic cycle appears to be the ene reaction of PhNO with alkene to produce an N-allylhydroxylamine, which could deoxygenate by Cu(I) (Eq. (4)) (generated in situ) to yield N-aryl-N-allylamines. The copper catalyst thus serves as a Cu(II)/Cu(I) redox shuttle. The presence of copper-powder as reductant may shift the equilibrium toward the right (Eq. (4)) to produce Cu⁺, which is required for deoxygenation of allylhydroxylamine.¹⁵ The relative stabilities of Cu⁺ and Cu²⁺ depend on the nature of ligands and the solvent system. The equilibrium can be readily shifted in either direction.22

$$2Cu^{2+} + Cu \quad \checkmark \quad 2Cu^{+} \quad (4)$$

3. Summary

In summary, the advantages of the procedure for the allylic amination of alkenes are (i) nitrosobenzene can now be used as a the nitrogen source, (ii) the catalyst, reductant and PhNO are inexpensive and commercially available, (iii) the reaction is efficient and (iv) the product yield is good.

4. Experimental

4.1. General

Anhydrous 1,4-dioxane, nitrosobenzene, CuCl₂·2H₂O (Aldrich), and Cu-powder (Allied Chemicals) were obtained commercially. GC–MS and MS spectra were obtained at 70 eV (EI). GC analyses utilized a 3' column packed with 3% OV 101.

4.2. Representative procedure

All reactions were performed under dry argon. The olefin (7 mmol), CuCl₂·2H₂O (0.15 mmol) and Cu-pow-

der (0.61 mmol) were added to 1,4-dioxane (2 mL) and heated to reflux (100°C). Nitrosobenzene (0.75 mmol) was dissolved in 1,4-doixane (10 mL) and was slowly added over a period of 6 h through a syringe pump. After 8 h, the resulting dark red mixture was analyzed by GC and GC–MS using naphthalene as the internal standard. Comparisons with authentic samples prepared as described in the literature were used to identify allylamines.^{10,11,13,14}

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References

- (a) Parshall, G. W. Homogeneous Catalysis; Wiley: New York, 1980; pp. 101–119; 129–135; 185–207; (b) Sheldon, R. A.; Kochi, J. K. Metal-Catalyzed Oxidations of Organic Compounds; Academic Press: New York, 1981; pp. 271–279.
- (a) Svastits, E. W.; Dawson, J. H.; Breslow, R.; Gellman, S. H. J. Am. Chem. Soc. 1985, 107, 6427; (b) Mahy, J. P.; Bedi, G.; Battioni, P.; Mansuy, D. New J. Chem. 1989, 13, 645; (c) O'Conner, K. J.; Wey, S.-J.; Burrows, C. J. Tetrahedron Lett. 1992, 33, 1001; (d) Evans, D. A.; Faul, M. M.; Bilodeau, M. T.; Anderson, B. A.; Barnes, D. M. J. Am. Chem. Soc. 1993, 115, 5328; (e) Lowenthal, R. E.; Masamune, S. Tetrahedron Lett. 1991, 32, 7373; (f) Li, Z.; Quan, R. W.; Jacobson, E. N. J. Am. Chem. Soc. 1995, 117, 5889; (g) Atkinson, R. S.; Fawcett, J.; Williams, P. J. Tetrahedron Lett. 1995, 36, 3241; (h) Noda, K.; Hosoya, N.; Irie, R. Synlett 1993, 7, 469; (i) Perez, P. J.; Brrokhart, M.; Tempelton, J. L. Organometallics 1993, 12, 261.
- (a) Gagne, M. G.; Stern, C. L.; Marks, T. J. J. Am. Chem. Soc. 1992, 114, 275; (b) Gagne, M. G.; Marks, T. J. J. Am. Chem. Soc. 1989, 111, 4108; (c) Li, Y.; Marks, T. J. Organometallics 1996, 15, 3770; (d) Giardello, M. A.; Conticello, V. P.; Brard, L.; Gagne, M. R.; Marks, T. J. J. Am. Chem. Soc. 1994, 116, 10241.
- (a) Sharpless, K. B.; Hori, T.; Truesdale, L. K.; Dietrich, C. O. J. Am. Chem. Soc. 1976, 98, 269; (b) Bruncko, M.; Khuong, T.-A. V.; Sharpless, K. B. Angew. Chem., Int. Ed. Engl. 1996, 35, 454.
- 5. Sharpless, K. B.; Hori, T. J. Org. Chem. 1976, 41, 176.
- Liebeskind, L. S.; Sharpless, K. B.; Wilson, R. D.; Ibers, J. A. J. Am. Chem. Soc. 1978, 100, 7061.

- (a) Brimble, M. A.; Heathcock, C. H. J. Org. Chem. 1993, 58, 5261; (b) Brimble, M.; Heathcock, C. H.; Nobin, G. N. Tetrahedron: Asymmetry 1996, 7, 2007; (c) Leblanc, Y.; Zamboni, R.; Berstein, M. A. J. Org. Chem. 1991, 56, 1971.
- (a) Keck, G. E.; Webb, R. R.; Yates, J. B. Tetrahedron 1981, 37, 4007; (b) Ensley, H. E.; Mahadevan, S. Tetrahedron Lett. 1988, 29, 3255; (c) Knight, G. T. J. Chem. Soc., Chem. Commun. 1970, 1016; (d) Banks, R. E.; Haszeldine, R. N.; Miller, P. J. Tetrahedron Lett. 1970, 11, 4417; (e) Seymour, C. A.; Greene, F. D. J. Org. Chem. 1982, 47, 5226.
- Whitesell, J. K.; Yaser, H. K. J. Am. Chem. Soc. 1991, 113, 3526.
- (a) Srivastava, A.; Ma, Y.; Pankayatselvan, R.; Dinges, W.; Nicholas, K. M. J. Chem. Soc., Chem. Commun. 1992, 853; (b) Srivastava, R. S.; Nicholas, K. M. J. Org. Chem. 1994, 59, 5365.
- (a) Srivastava, R. S.; Nicholas, K. M. Tetrahedron Lett.
 1994, 35, 8739; (b) Srivastava, R. S.; Khan, M. A.; Nicholas, K. M. J. Am. Chem. Soc. 1996, 118, 3311; (c) Srivastava, R. S.; Nicholas, K. M. J. Am. Chem. Soc.
 1997, 119, 3302; (d) Johannsen, M.; Jorgenson, K. A. J. Org. Chem. 1994, 59, 214; (e) Johannsen, M.; Jorgenson, K. A. J. Org. Chem. 1995, 60, 5979.
- (a) Cenini, S.; Ragaini, F.; Tollari, S.; Paone, D. J. Am. Chem. Soc. 1996, 118, 11964; (b) Ragaini, F.; Cenini, S.; Tollari, S.; Tummolillo, G.; Beltrami, R. Organometallics 1999, 18, 928.
- (a) Srivastava, R. S.; Nicholas, K. M. J. Chem. Soc., Chem. Commun. 1998, 2705; (b) Kolel-Veetil, M.; Khan, M. A.; Nicholas, K. M. Organometallics 2000, 19, 3754.
- Srivastava, R. S.; Kolel-Veetil, M.; Nicholas, K. M. Tetrahedron Lett. 2002, 43, 931.
- 15. Ho, C.-M.; Lau, T.-C. New J. Chem. 2000, 24, 859.
- Hogan, G. A.; Gallo, A. A.; Nicholas, K. M.; Srivastava, R. S. *Tetrahedron Lett.* **2002**, *43*, 9505–9508.
- 17. (a) Porta, F.; Prati, L. J. Mol. Catal. A 2000, 157, 123;
 (b) Bosch, E.; Kochi, J. K. J. Org. Chem. 1994, 59, 5573.
- 18. Waters, W. A. J. Chem. Soc., Perkin Trans. 1976, 2, 732.
- Yang, C. H.; Lin, Y. C. J. Chin. Chem. Soc. (Taipei) 1987, 34, 19–24.
- For reviews, see: (a) Oppolzer, W.; Snieckus, V. Angew. Chem., Int. Ed. Engl. 1978, 17, 476; (b) Hoffman, H. M. R. Angew. Chem., Int. Ed. Engl. 1969, 8, 556; (c) Snider, B. Acc. Chem. Res. 1980, 13, 426.
- (a) Sundberg, R. J.; Brenner, M.; Suter, S. R.; Das, B. P. *Tetrahedon Lett.* **1970**, *11*, 2715; (b) Sundberg, R. J.; Heintzelmen, R. W. J. Org. Chem. **1974**, *39*, 2546.
- Cotton, F. A.; Wilkinson, G.; Murillo, C. A.; Bochmann, M. *Advances Inorganic Chemistry*, 6th ed.; Wiley: New York, 1999; pp. 855–856.