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Regioselective Allylic Amination Catalyzed by Iron Salts

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Abstract: Alkenes react with phenylhydroxylamine in the presence of Fe(II) and Fe(III) salts to produce N-phenyl-N-allyl amines in moderate to good yields. Unsymmetrical substrates react with high regioselectivity giving the products of double bond transposition.

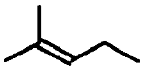
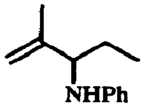
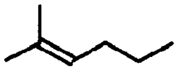
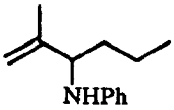
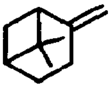
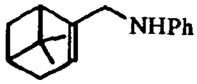
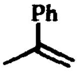
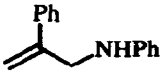
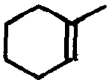
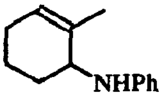
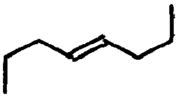
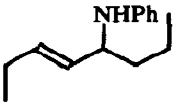
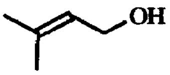
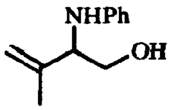
The development of selective methodologies for direct hydrocarbon functionalization represents one of the great challenges in synthetic chemistry. Simple methods for the introduction of nitrogen-based functional groups are rare with *stoichiometric* allylic amination by S[1]- and Se[2]-imido derivatives and metal-catalyzed aziridination of olefins[3] being the most important. We recently reported the regioselective Mo-*catalyzed* allylic amination of alkenes with phenylhydroxylamine as the aminating agent.[4] Mechanistic studies have revealed that these reactions takes place via a molybdenum-oxaziridine (MoONR) intermediates and that the -NR transfer occurs "off" the metal through free nitrosobenzene.[5] Jorgensen and coworkers[6] recently described similar allylic aminations using iron(II) phthalocyanine as the catalyst. Both the Mo- and the Fe-catalyzed processes are accompanied by variable quantities of byproducts from hydroxylamine decomposition- aniline, azobenzene and azoxybenzene. In the course of attempting to improve the selectivity of the Mo-catalyzed reactions by the use of Lewis acid co-catalysts, we have discovered that independent catalysis by Fe(II) and Fe(III) salts suppresses the formation of N-byproducts while retaining the distinctive ene-like regioselectivity observed for the Mo-catalyzed reactions.[7] Moreover, various trapping experiments demonstrate that *free PhNO is not an intermediate* in these reactions.

Slow addition of phenylhydroxylamine (1.5 mM in dioxane) to a heated (70-100°C) dioxane solution containing an excess of olefin and 10 mole % $FeCl_{2,3}{\cdot}nH_2O$ or $Fe(ClO_4)_{2,3}{\cdot}nH_2O$ produces after 8 hr the corresponding N-phenyl-N-allylamines in fair to good yield accompanied by small to moderate quantities of aniline and traces of azo- and azoxybenzene (eq. 1, Table 1).[8]

(1)

Important features of these iron-catalyzed reactions include: (1) trisubstituted and 1,1-disubstituted alkenes give the best yields; (2) unsymmetrical alkenes react with virtually complete (>95%) regioselectivity to produce the corresponding allyl amine derived from double bond transposition; (3) generally no other olefin-derived products are observed[9]; and (4) high yields based on olefin can be achieved using excess hydroxylamine (run 2). Features 1 and 2 are typical of ene-type reactions.[10]

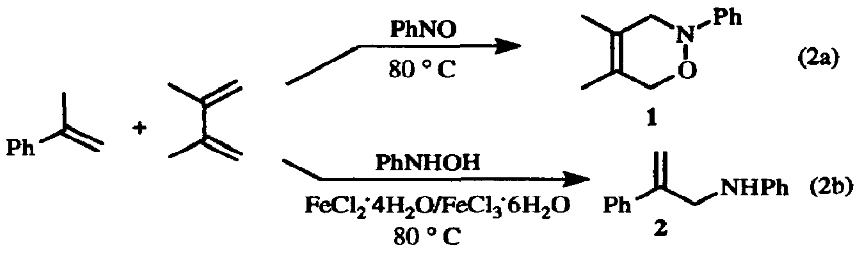
Table. Allylic Amination Catalyzed by Iron Salts

Run	Substrate	Catalyst	Product	Yield (%)[a]	N-chemo-selectivity (%)[b]
1		A + B (9:1)[c]		61(48)	90
2		" + "		72[d]	>90[e]
3		C + D (9:1)[c]		23	67
4		A + B (9:1)		50	93
5		A + B (9:1)		43(29)	82
6		A + B (9:1)		34(22)	92
7		A		26	76
8		B		29	90
9		$FeCl_2$		25	71
10		$FeCl_3$		28	62
11		C + D (9:1)		41	80
12		A + B (9:1)		22	40
13		A + B (9:1)		13	42
14		A + B (9:1)		12	48
15		A + B (9:1)		11	40

[a] GC yield, naphthalene standard (isolated yield after chromatography); [b] allyl amine/(allyl amine + aniline + azobenzene + azoxybenzene); [c] A=$FeCl_2 \cdot 4H_2O$, B=$FeCl_3 \cdot 6H_2O$, C=$Fe(ClO_4)_2 \cdot 6H_2O$, D=$Fe(ClO_4)_3 \cdot 6H_2O$; [d] 2.5:1 PhNHOH/olefin ratio used; [e] olefin chemoselectivity by GC

Catalyst oxidation and hydration state and counterion have a modest and variable effect on yield and selectivity, e.g. a) both Fe(II) and Fe(III) salts catalyze the reaction with similar efficiency (c.f. runs 7/8, 9/10); b) anhydrous and hydrated iron chlorides are comparable as catalysts (c.f. runs 7/9, 8/10); but c) in some cases a combination of Fe(II)/Fe(III) (9:1) gives slightly improved results (e.g. run 6 vs. 7-10); and d) the relative benefits of $FeCl_{2,3}\cdot nH_2O$ vs. $Fe(ClO_4)_{2,3}\cdot nH_2O$ as catalysts are substrate dependent (c.f. runs 1/3, 6/11).

Although the reaction mechanism is uncertain at present, our initial mechanistic experiments indicate that the active aminating species is not free nitrosobenzene as in the case of the Mo-catalyzed reactions.[5] The hetero-Diels-Alder reaction of PhNO with 2,3-dimethylbutadiene[11] (DMB) was selected as the trapping reaction. First the effective Diels-Alder trapping of PhNO by DMB at 80°C (dioxane) in the presence of α-methylstyrene was established (eq. 2a). When the iron-catalyzed reaction of phenylhydroxylamine with α-methylstyrene was carried out in the presence of DMB (1:1, 80°C, dioxane), however, 2-phenyl-3-(phenylamino)-1-propene (**2**, 24%), the product of allylic amination, was formed exclusively[12]; i.e the PhNO adduct **1** was not detected (eq.2b). A control experiment established that the prospective adduct **1** is stable under the amination conditions.



These results clearly demonstrate that *free* nitrosobenzene is not produced in the iron-catalyzed reactions. Although the identity of the true aminating agent in these reactions remains to be determined, this finding is consistent with the involvement of an Fe-coordinated species. The similar efficacy of both Fe(II) and Fe(III) salts suggests the intervention of a common catalyst for both reactions and/or a redox shuttling process involving both oxidation states. The ready ability of hydroxylamines to undergo oxidation or reduction is consistent with either of these possibilities.[13]

The present results illustrate the iron-catalyzed allylic amination of alkenes by phenylhydroxylamine with a high degree of regiocontrol. This selectivity complements and improves upon that generally observed in stoichiometric aminations by $(TolN)_2X$ (X=S, Se),[1,2] which typically prefer preservation of the double bond position but with variable selectivity. Further, the catalysts used in the present system are commercially available and inexpensive. Studies are underway to extend the scope of these reactions, to elucidate their mechanism(s), and to develop enantioselective variants.

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References and Notes

1. Sharpless, K.B.; Hori, T. J. *Org. Chem.*, **1976**, *41*, 176; Kresze, G.; Braxmeier, H.; Munsterer, H. *Org. Syn.* **1987**, *65*, 159.
2. Sharpless, K.B.; Hori, T.; Truesdale, L.K.; Dietrich, C.O. *J. Am. Chem. Soc.* **1976**, *98*, 269.
3. 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*, 651; (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. *J. Org. Chem.* **1991**, *56*, 6744; (e) Perez, P.J.; Brookhart, M.; Templeton, J.L. *Organometallics*, **1993**, *12*, 261.
4. Srivastava, A.; Ma, Y.; Pankayatselvan, R.; Dinges, W.; Nicholas, K.M. *J. Chem. Soc. Chem. Commun.* **1992**, 853.
5. Srivastava, R.S.; Nicholas, K.M. *J. Org. Chem.* (in press).
6. Johannsen, M.; Jorgensen, K.A. *J. Org. Chem.* **1994**, *59*, 214.
7. Ref. 6 cites one example of amination of α-methylstyrene with PhNHOH (toluene solvent) catalyzed by $FeCl_2$ in fair yield and modest N-chemoselectivity.
8. Reaction aliquots were analyzed by GC (OV 101) and GC/MS; products were identified by comparison of their retention times and mass spectra with authentic samples and by NMR and high resolution MS in the case of new compounds.
9. Catalysis of α-methyl styrene amination by anhydrous $FeCl_2$ produces a substantial quantity of a byproduct identified by NMR and MS as 2,4-diphenyl-4-methyl-pent-2-ene.
10. Ene-reaction reviews: Oppolzer, W.; Snieckus, V. *Angew. Chem. Int. Ed. Eng.* **1978**, *17*, 476; Hoffmann, H.M.R. *Angew. Chem. Int. Ed. Eng.* **1969**, *8*, 556; Snider, B. *Accts. Chem. Res.* **1980**, *13*, 426.
11. Taylor, E.C.; Tseng, C.-P.; Rampal, J.B. *J. Org. Chem.* **1982**, *47*, 552.
12. A trace (<5%) of the allylic amination product of DMB was also detected by GC/MS.
13. Review: Sandler, S.R.; Karo, W. *Organic Functional Group Preparations*, vol.III, **1989**, p. 377 and references cited therein.

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