Iron-Catalyzed Allylic Amination

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The transition-metal-catalyzed allylic amination of alkenes is studied. A screening of different transition-metal complexes reveals that iron complexes, especially iron phthalocyanin, have the best catalytic properties, using phenylhydroxylamine as the nitrogen-fragment donor. The iron phthalocyanin-catalyzed reaction has been studied for a variety of alkenes and the best yields are obtained for alkenes substituted with aromatic groups. The scope of this reaction is discussed.

Introduction

The development of simple and general methods for the preparation of functionalized organic compounds from readily available substrates is one of the major challenges in organic synthesis today. The metal-catalyzed regioselective and asymmetric oxygen transfer to a variety of different organic substrates has been developed over the last decade, whereas only very few attempts to transfer organic nitrogen fragments have been pursued. Iron and manganese porphyrins as well as copper salts catalyze the formation of aziridines from alkenes and (*N*-(*p*-toluenesulfonyl)imino)phenyliodinane (PhI=NTs), which is a nitrogen analogue of iodosylbenzene.[1] More recently optically active copper–[2a] and manganese–salen[2b] complexes and copper–(bis)oxazoline complexes[2c] have been shown to behave as good chiral catalysts for the enantioselective aziridination of alkenes, again with PhI=NTs as nitrogen-fragment donor. Attempts to carry out allylic amination of alkenes have been tried using a dioxomolybdenum(VI) complex and with phenylhydroxylamine as the nitrogen-fragment donor.[3] This reaction probably takes place via a molybdeniaoxaziridine intermediate[3] and proceeds with a moderate yield of the allylic amine and a relatively large amount of byproducts such as aniline and azoxybenzene.[3b]

This paper presents a significantly improved metal-catalyzed procedure for the preparation of allylic amines from alkenes and phenylhydroxylamine using mainly iron complexes as the catalyst.

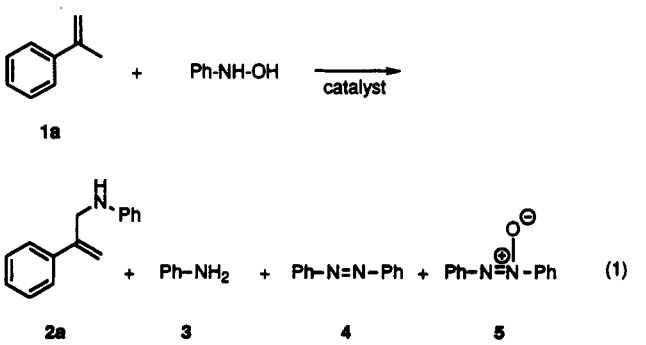
Results and Discussion

A series of transition-metal complexes has been tested as catalyst for allylic amination of alkenes. The results of the reaction between α-methylstyrene (**1a**) (7.5 mmol) and phenylhydroxylamine (1.5 mmol) catalyzed by different transition-metal complexes (0.15 mmol, 2 mol % relative to the alkene) (eq 1) are presented in Table 1 (See Experimental Section for details).

Table 1. Amination of α-Methylstyrene (1a) Using Phenylhydroxylamine as the Nitrogen-Fragment Donor Uncatalyzed and Catalyzed by Different Transition-Metal Complexes

entry	catalyst	yield of 2a[a] (%)	yield of 3[a] (%)	yield of 4[a] (%)	yield of 5[a] (%)
1	none	3	20	1	23
2	$CpTiCl_3$	6	33	1	14
3	$V(O)(acac)_2$[b]	35	30	1	6
4	$(Dipic)MoO_2$[c,h]	14	15	1–2	4
5	$(Sap)MoO_2$[d,h]	27	38	1	2
6	Co(Pc)[e]	10	24	6	8
7	Ni(Pc)[e]	4	42	<1	4
8	Mn(salen)Cl[f]	12	50	–	15
9	$Fe^{II}Cl_2$	52	23	–	1
10	Fe(Pc)[e]	76	22	–	1
11	Fe(tpp)Cl[g]	47	12	–	7

[a] Yield based on charged phenylhydroxylamine and determined by GC/MS with naphthalene as internal standard. A 5-fold excess of alkene and 2 mol % of catalyst, relative to the alkene, were used. [b] acac = acetylacetonato. [c] Dipic = pyridine-2,6-dicarboxylato. [d] Sap = *N*-salicylidene-2-aminophenalato. [e] Pc = Phthalocyanine. [f] salen = 1,2-bis(salicylideneamino)ethane. [g] tpp = *meso*-tetraphenylporphyrin. [h] HMPA is also coordinated to the metal.



(1)

It appears from Table 1 that α-methylstyrene (**1a**) reacts with phenylhydroxylamine even in the absence of a catalyst in an ene-reaction leading to 3% of 2-phenyl-3-(phenylamino)propene (**2a**), but with the major products being **3** and **5** (entry 1). In the presence of either $CpTiCl_3$ or dioxomolybdenum(VI) complexes as the catalysts only a minor increase in the yields of **2a** (entries 2, 4, 5) were found, compared with the uncatalyzed reaction. These complexes again gave a large amount of the byproducts **3** and **5**. The $(Sap)MoO_2$ complex is found to be the best catalyst of the molybdenum complexes studied, but also

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(1) (a) Breslow, R.; Gellman, S. H. *J. Chem. Soc., Chem. Commun.* **1982**, 1400. (b) Breslow, R.; Gellman, S. H. *J. Am. Chem. Soc.* **1983**, *105*, 6728. (c) Svastits, E. W.; Dawson, J. H.; Breslow, R.; Gellman, S. H. *J. Am. Chem. Soc.* **1985**, *107*, 6427. (d) Mansuy, D.; Mahy, J. P.; Dureault, A.; Bedi, G.; Battioni, P. *J. Chem. Soc., Chem. Commun.* **1984**, 1161. (e) Mahy, J. P.; Bedi, G.; Battioni, P.; Mansuy, D. *J. Chem. Soc., Perkin Trans. 2* **1988**, 1517. (f) Mahy, J. P.; Bedi, G.; Battioni, P.; Mansuy, D. *Tetrahedron Lett.* **1988**, *29*, 1927. (g) Mahy, J. P.; Bedi, G.; Battioni, P.; Mansuy, D. *New J. Chem.* **1989**, *13*, 651. (h) O'Conner, K. J.; Wey, S.-J.; Burrows, C. J. *Tetrahedron Lett.* **1992**, *33*, 1001. (i) Evans, D. A.; Faul, M. M.; Bilodeau, M. T. *J. Org. Chem.* **1991**, *56*, 6744.

(2) (a) Li, Z.; Conser, K. R.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1993**, *115*, 5326. (b) Noda, K.; Hosoya, N.; Irie, R.; Ito, Y.; Katsuki, T. *Synlett* **1993**, 469. (c) Evans, D. A.; Faul, M. M.; Bilodeau, M. T.; Anderson, B. A.; Barnes, D. M. *J. Am. Chem. Soc.* **1993**, *115*, 5328.

(3) (a) Liebeskind, L. S.; Sharpless, K. B.; Wilson, R. D.; Ibers, J. A. *J. Am. Chem. Soc.* **1978**, *100*, 7061. (b) Srivastave, A.; Ma, Y.; Pankayatselvan, R.; Dinges, W.; Nicholas, K. M. *J. Chem. Soc., Chem. Commun.* **1992**, 853.

0022-3263/94/1959-0214$04.50/0

here a large amount of the byproducts **3** and **5** are formed. The $V(O)(acac)_2$ complex (entry 3) is the best catalyst of the early transition metal complexes studied. Changing the catalyst to Mn(salen)Cl, Co(Pc), or Ni(Pc) does not alter the reaction course significantly (entries 6–8). However, the iron complexes (entries 9–11) show significantly better catalytic behavior than the other investigated complexes, both in terms of optimizing the yields of **2a**, as well as in minimizing the amount of byproducts formed (entries 9–11). A comparison of the iron-catalyzed amination of α-methylstyrene (**1a**) with the previously reported results of the similar molybdenum-catalyzed ((Dipic)MoO_2 as the catalyst) reaction, where 42% yield of **2a** is obtained,[3b] reveals that especially the Fe(Pc)-catalyzed reaction leads to an improved yield of **2a**.

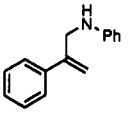
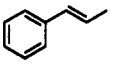
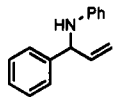
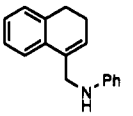
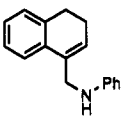
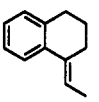
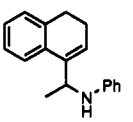
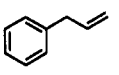
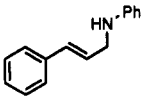
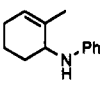
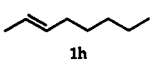
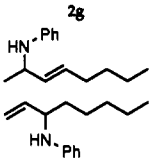
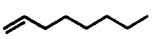
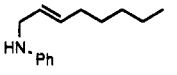
The scope and limitations of the iron-catalyzed allylic amination reaction has been studied, as aromatic and aliphatic alkenes were aminated using phenylhydroxylamine as the nitrogen-fragment donor and Fe(Pc) as the catalyst. The results are presented in Table 2 (see Experimental Section for details).

The results in Table 2 show that aromatic alkenes which allow conjugation of the double bond in the product with the aromatic ring can be aminated to produce the corresponding allylic amine in good yields (entry 1, 3–5). A comparison of the reaction of α-methylstyrene (**1a**) with the reaction of *trans*-β-methylstyrene (**1b**) shows that 2-phenyl-3-(phenylamino)-1-propene (**2a**) is produced in a much higher yield (entry 1) than 3-phenyl-3-(phenylamino)-1-propene (**2b**) (entry 2). This observation can be rationalized through the loss of conjugation in the reaction of *trans*-β-methylstyrene (**1b**). It should also be noted that the iron-catalyzed amination of the *exo*- and *endo*-alkene substrates (**1c–e**) (entries 3–5) leads to products where the phenylamine substituent is found at the *exo*-carbon, **2c–e**. The amination of 1-methylcyclohexene (**1g**) (entry 7) is regioselective as 1-methyl-6-(phenylamino)-cyclohexene (**2g**) is the only observed allylic amine product. 2-Octene (**1h**) can be catalytically aminated to a 1:1 mixture of 2-(phenylamino)-3-octene (**2h**) and 3-(phenylamino)-1-octene (**2h'**) (entry 8), whereas 1-octene (**1i**) only gives a small amount of 1-(phenylamino)-2-octene (**2i**) (entry 9), under the same reaction conditions. *tert*-Butylhydroxylamine has also been tried as a nitrogen-fragment donor in the reaction of α-methylstyrene (**1a**) with $Fe^{II}Pc$ as the catalyst, and in this case about 10% of 2-phenyl-3-(*tert*-butylamino)propene is formed.

According to our knowledge, very few methods for allylic amination are known.[3-7] Bis(*N*-tosyl)sulfodiimide[4,5] and bis(*N*-tosyl)selenodiimide[6] can aminate alkenes in the allylic position in a stoichiometric reaction. It appears after a comparison of the stoichiometric allylic amination of 1-methylcyclohexene (**1g**) with bis(*N*-tosyl)sulfodiimide[4,5] and bis(*N*-tosyl)selenodiimide[6] with the Fe(Pc)-catalyzed amination reaction that the latter method only gives one regioisomer, 1-methyl-6-(phenylamino)cyclohexene (**2g**) whereas both bis(*N*-tosyl)sulfodiimide and bis(*N*-tosyl)selenodiimide give a mixture of products where the *N*-tosyl substituent is attached to either the cyclohexyl ring or to the methyl substituent.[5,6]

(4) Schöenberger, N.; Kresze, G. *Liebigs Ann. Chem.* **1975**, 1725.
(5) Sharpless, K. B.; Hori, T. *J. Org. Chem.* **1976**, *41*, 176.
(6) Sharpless, K. B.; Hori, T.; Truesdale, I. K.; Dietrich, C. O. *J. Am. Chem. Soc.* **1976**, *98*, 269.

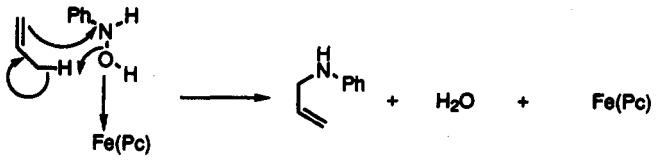
Table 2. Iron–Phthalocyanin-Catalyzed Allylic Amination of Different Alkenes Using Phenylhydroxylamine as the Nitrogen-Fragment Donor

entry	substrate	product	yield %[a]
1	 1a	 2a	76 (60)
2	 1b	 2b	5
3	 1c	 2c	62 (55)
4	 1d	 2d	48 (40)
5	 1e	 2e	45
6	 1f	 2f	30
7	 1g	 2g	22 (16)
8	 1h	 2h, 2h'	18[b] 16[b] (28)[c]
9	 1i	 2i	3

[a] Yields are determined by GC/MS of the crude reaction mixture using naphthalene as internal standard. Isolated yields are tabulated in parentheses. [b] Ratio determined by ^1H NMR. [c] Isolated as a mixture of the two isomers.

The first step in the reaction is tentatively proposed to be a coordination of phenylhydroxylamine to the iron atom of the Fe(Pc) catalyst, as Fe(Pc) becomes dissolved by the addition of phenylhydroxylamine to Fe(Pc) suspended in $CHCl_3$ (Fe(Pc) in nearly insoluble in $CHCl_3$), whereas no solvation of the Fe(Pc) catalyst is observed if only the alkene is added. The latter observation indicates that the alkene does not coordinate to the metal in the catalyst. The solvation of the Fe(Pc) catalyst is evident from ^1H NMR of Fe(Pc) and phenylhydroxylamine in $CDCl_3$ at room temperature as two double doublets appear at 8.900 and 9.359 ppm, respectively, for the aromatic hydrogens of the phthalocyanin ligand. Furthermore, the signals for the phenylhydroxylamine are wiped out, indicating an interaction of this molecule with the metal of the catalyst.

The following mechanism for the allylic amination with phenylhydroxylamine and Fe(Pc) can tentatively be postulated:



The present work shows that some iron complexes catalyze the allylic amination of alkenes using phenylhydroxylamine as the nitrogen-fragment donor. This synthetic method is best for alkenes having the alkene double bond in conjugation with an aromatic group. Amination of *exo*- and *endo*-alkenes both leads to the *endo*-allylic amine isomer. 1-Methylcyclohexene gives exclusively a product where the amine substituent is attached to the cyclohexene ring, whereas 2-octene produces a mixture of 2-(phenylamino)-3-octene and 3-(phenylamino)-1-octene.

Experimental Section

Apparatus. ^{1}H NMR spectra were recorded at 300 MHz using $CDCl_3$ as the solvent and $SiMe_4$ as internal standard. GC/MS was recorded on an OV101 column.

Chemicals. The solvents were purified and dried by standard methods. Compounds **1a,b,f–h** are commercially available and used without further purification. Compounds **1c–e**,[8,9] phenylhydroxylamine,[10] and *tert*-butylhydroxylamine[11] were prepared according to the literature. Silica gel was used for flash-column chromatography.

Amination of α-Methylstyrene (1a) with and without Different Transition-Metal Complexes. α-Methylstyrene (**1a**) (7.5 mmol) was dissolved in 10 mL of toluene. The appropriate catalyst (0.15 mmol) was added and the reaction mixture was heated to 110 °C under nitrogen. To this reaction mixture was added 1.5 mmol of phenylhydroxylamine dissolved in 15 mL of toluene over 5 h. The reaction mixture was stirred further for 10 h at reflux. The transition-metal complex was then precipitated by petroleum ether and the reaction mixture was analyzed by GC/MS with naphthalene as internal standard. The reaction in the absence of a transition-metal catalyst was carried out in a similar way and the total reaction time was 15 h at 110 °C under nitrogen.

Catalytic Amination of 1a–i. The alkene (1) (7.5 mmol) was dissolved in 10 mL of toluene and 0.15 mmol of Fe(Pc) added and the reaction mixture was heated to 110 °C under nitrogen. To this reaction mixture was added 1.5 mmol of phenylhydroxylamine dissolved in 15 mL of toluene over 5 h. The reaction mixture was stirred further for 10 h at reflux. The Fe(Pc) complex was then precipitated by petroleum ether and the solvent evaporated. The reaction mixture was separated by flash-column chromatography using 30% CH_2Cl_2/70% petroleum ether as the eluent. The compounds were identified by ^{1}H NMR and MS. The ^{1}H NMR and MS data are given below. The reaction mixture was also analyzed after initial precipitation of the Fe(Pc) complex followed by GC/MS using naphthalene as internal standard.

2a: δ 3.88 (br s, 1H), 4.16 (br s, 2H), 5.34 (d, J = 1.1 Hz, 1H), 5.49 (d, J = 1.1 Hz, 1H), 6.61–6.78, 7.14–7.49 (m, 10H); MS *m/e* 209 (100), 130 (12), 117 (18), 115 (25), 106 (96), 91 (39), 77 (72).

2b: δ 4.03 (br s, 1H), 4.89–4.97 (br m, 1H), 5.19–5.20, 5.22–5.25, 5.31–5.32 (m, 2H), 5.96–6.12 (m, 1H), 6.57–6.73, 7.11–7.31 (m, 10H); MS *m/e* 209 (36), 182 (17), 117 (100), 115 (47), 104 (12), 91 (35), 77 (46).

2c: δ 2.26–2.38 (m, 2H), 2.79 (t, J = 8.39 Hz, 2H), 3.80 (br s, 1H), 4.10 (br s, 2H), 6.13 (t, J = 4.68 Hz, 1H), 6.62–6.75, 7.15–7.29 (m, 9H); MS *m/e* 235 (100), 143 (76), 142 (31), 141 (31), 128 (61), 115 (22), 106 (24), 93 (36), 91 (20), 84 (27), 77 (29).

2e: δ 1.45 (d, J = 6.60 Hz, 3H), 2.18–2.30 (m, 2H), 2.73 (t, J = 8.38 Hz, 2H), 3.86 (br s, 1H), 4.47–4.57 (q, 1H), 6.15 (t, J = 4.60 Hz, 1H), 6.52–6.71, 7.09–7.36 (m, 9H).

2f: δ 3.87 (br s, 1H), 3.95 (d, J = 5.8 Hz, 2H), 6.30–6.39 (m, 1H), 6.61–6.76, 7.15–7.39 (m, 11H); MS *m/e* 209 (44), 182 (20), 181 (92), 180 (100), 117 (68), 115 (26), 91 (38), 77 (84).

2g: δ 1.51–1.98 (m, 9H), 3.65 (br s, 1H), 3.79 (br s, 1H), 5.59 (br s, 1 H), 6.59–6.70, 7.12–7.21 (m, 5H).

2h′: δ 0.83–0.92 (m, 3H), 1.22–1.66 (m, 9H), 3.60 (br s, 1H), 3.75–3.84 (m, 1H), 5.08–5.24 (m, 2H), 5.65–5.82 (m, 1H), 6.56–6.70, 7.10–7.20 (m, 5H); MS *m/e* 203 (66), 188 (41), 146 (46), 132 (100), 130 (46), 117 (52) 106 (33), 93 (60), 91 (29), 77 (51).

2h: δ 0.82–0.91 (m, 3H), 1.18–1.37 (m, 7H), 1.92–2.06 (m, 2H), 3.56 (br s, 1H), 3.86–3.99 (m, 1H), 5.33–5.44 (m, 1H), 5.54–5.69 (m, 1H), 6.57–6.70, 7.09–7.18 (m, 5H); MS *m/e* 203 (66), 188 (10), 176 (9), 146 (18), 132 (100), 117 (63) 106 (32), 93 (65), 91 (25), 77 (71).

2i: δ 0.88–0.92 (m, 3H), 1.18–1.38 (m, 6H), 1.94–2.06 (m, 2H), 3.58–3.75 (br m, 3H), 5.48–5.76 (m, 2H), 6.56–6.72, 7.11–7.19 (m, 5H); MS *m/e* 203 (21), 174, (57) 160 (43) 146 (74), 132, (100) 130 (45), 117 (32), 106 (18), 104 (29), 93 (68), 91 (25), 77 (79).

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Supplementary Material Available: Copies of ^{1}H NMR spectra of all new compounds (9 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

(7) Hegedus, L. G.; Allen, G. F.; Waterman, E. L. *J. Am. Chem. Soc.* **1976**, *98*, 2674.
(8) Organikum 18. Auf.; VEB Deutscher Verlag der Wissenschaften: Berlin 1990, 499.
(9) Organikum 18. Auf.; VEB Deutscher Verlag der Wissenschaften: Berlin 1990, 465.
(10) Vogel, A. I. *Textbook of Practical Organic Chemistry*, 5th ed.; Longmann Scientific & Technical: New York, 1989, 955.
(11) Calder, A.; Forrester, A. R.; Hepburn, S. P. *Organic Syntheses*; Wiley: New York, 1988; Collect. Vol. VI, p 803.