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Readily available nitrene precursors increase the scope of Evans' asymmetric aziridination of olefins

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Abstract: The performance of the copper-catalyzed asymmetric aziridination of olefins is highly dependent on the properties of the nitrene precursor. Our preliminary results show significant improvements of both enantioselectivity and chemical yields when [*N*-(4-nitrobenzenesulfonyl)imino]phenyliodinane **1b** (*p*-$NO_2C_6H_4SO_2N$=IPh) is employed instead of the commonly used *p*-tolyl analog **1a** (PhI=NTs). This paper reports the comparison of some nitrene precursors for the copper-catalyzed asymmetric aziridination of olefins, utilizing the olefin as the limiting component and 1.5 equivalents of the nitrene precursor. The aziridine derivatives of several olefins were obtained in moderate to excellent yields and with enantioselectivity up to 95% ee. © 1997 Elsevier Science Ltd

Aziridines are important building blocks for the preparation of compounds containing nitrogen functionality, and also occur as subunits in many natural products.[1] Furthermore, chiral aziridines have been employed as efficient chiral auxiliaries[1] and ligands for asymmetric catalysis.[2] Therefore, general methodology for the one-step formation of nonracemic aziridines from olefins would be very useful. In the last few years, Evans[3] and Jacobsen[4] have reported promising results in the asymmetric aziridination of olefins using copper catalysts with chiral dinitrogen ligands. Routes to aziridines starting from imines have also been reported.[5] The addition to olefins is attractive because of the wide range of easily accessible and cheap starting materials. However, one disadvantage of the copper-catalyzed system is that the presence of a chiral ligand drastically deteriorates the catalyst performance, so that only a limited number of olefins give the aziridines in good yields.

We have recently reported that the yields of aziridines can be improved by the use of nitrene precursors with different electronic properties.[6,7] In this paper we report on the evaluation of these reagents in the asymmetric version of the reaction. The aziridination of styrene was first investigated, and the most promising results are shown in Table 1. The catalytic system chosen for the study was the one described by Evans,[3c] employing copper(I) triflate [$CuOTf\cdot(C_6H_6)_{1/2}$] in the presence of a chiral *bis*-oxazoline.[8] Excellent yields were obtained even when only one equivalent of olefin and a slight excess of the nitrene precursor were used. In addition, the enantioselectivity was considerably improved with the use of *p*-nitro and *p*-methoxybenzene derivatives (**1b** and **1c**, respectively) instead of the *p*-tolyl analog **1a** (*cf.* entries 1–3, Table 1).

A series of olefins was then investigated,[9] comparing the efficiency of the nitrene precursors **1a–c** (Table 1). Interestingly, the two least reactive olefins (*trans*-stilbene and methyl cinnamate) both gave the highest yields with the use of **1c** (*cf.* entries 18–20 and 24–26, respectively, Table 1), although **1b** was superior for all the other substrates in the study.

In summary, we have demonstrated that the nature of the nitrene precursor has a strong influence on the yield as well as on the enantioselectivity of the copper-catalyzed asymmetric aziridination of olefins. Furthermore, in all the cases studied, it was found that the results with either of the nitrene precursors **1b** (*p*-$NO_2C_6H_4SO_2N$=IPh) or **1c** (*p*-$MeOC_6H_4SO_2N$=IPh) were superior to those obtained with **1a** (PhI=NTs). Our results suggest that the choice of nitrene source could be a crucial

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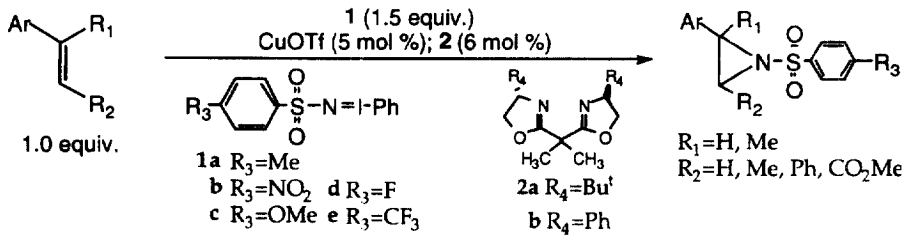
Table 1. Asymmetric aziridination with different nitrene precursors



entry	olefin	reagent	ligand	solvent	time (h)	temp.(°C)	% yield[a]	% ee[b]	product[c, d]
1		1a	2a	benzene	12	0	77	52	
2		1b	"	"	"	"	**94**	66	
3	Ph	1c	"	"	"	"	86	**78**	
4		1d	"	"	"	"	91	50	
5		1e	"	"	"	"	89	43	(*R*)-3a-e
6		1a	2a	MeCN	48	-25	44	62	
7	Me	1b	"	"	"	"	**83**	**80**	
8	Ph	1c	"	"	"	"	54	69	(2*S*,3*S*)-4a-c
9	Me	1a	2a	MeCN	48	-25	27	33	
10		1b	"	"	"	"	**36**	35	
11	Ph	1c	"	"	"	"	26	**45**	5a-c[e]
12		1a	2a	toluene	12	0	48	31	
13	*p*-Tol	1b	"	"	"	"	**78**	**58**	
14		1c	"	"	"	"	46	57	(*R*)-6a-c
15		1a	2a	benzene	48	23	12	31	
16		1b	"	"	"	"	18	35	
17	Ph	1c	"	"	"	5	**27**	**44**	
18[f]	Ph	1a	"	"	"	23	8	32	
19[f]		1b	"	"	"	"	12	33	7a-c[e]
20[f]		1c	"	"	"	"	**57**	**47**	
21		1a	2b	benzene	48	23	42	91	
22		1b	"	"	"	"	31	**95**	
23	CO_2Me	1c	"	"	"	"	**43**	90	
24[f]	Ph	1a	"	"	"	23	17	**89**	
25[f]		1b	"	"	"	"	30	83	(2*R*,3*S*)-8a-c
26[f]		1c	"	"	"	5	**97**	87	
27		1a	2a	benzene	12	0	45	53	
28	β-napht	1b	"	"	"	"	**93**	**55**	
29		1c	"	"	"	"	71	44	β-napht (*R*)-9a-c

[a] Isolated yield after column chromatography, based on the olefin, except for entries 18-26, where the values are based on the nitrene precursor. [b] Determined by HPLC analysis (WHELK-O column) of the crude reaction mixture. For entries 16-26 by the use of ^{1}H NMR spectroscopy after titration with Eu(hfc)$_3$. [c] All compounds gave satisfactory spectroscopic data. [d] Absolute configuration of the new compounds are tentatively assigned. [e] Absolute configuration not determined. [f] Reaction carried out in the presence of five equivalents of olefin, using the nitrene precursor as the limiting component.

tool in optimizing the conditions for a specific substrate. An additional advantage of using precursor **1b** (*p*-$NO_2C_6H_4SO_2N$=IPh) is that nitrobenzenesulfonamides, in contrast to toluenesulfonamides, are readily cleaved under mild conditions to give the free amines.[10]

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9. The aziridination of *trans*-β-methylstyrene represents a typical procedure, as follows: a solution of **2a** (49 mg, 0.17 mmol) in dry MeCN (3 mL) was added via syringe to a Schlenck-type flask containing $CuOTf\cdot(C_6H_6)_{1/2}$ (35 mg, 0.14 mmol) under Ar. The resulting solution was stirred at room temperature for 30 min. and then cooled to −25°C before it was transferred to a flask containing a precooled slurry (−25°C) of the olefin (0.34 g, 2.9 mmol), activated 4 Å molecular sieves (*ca* 2.5 g), nitrene source **1b** (1.7 g, 4.3 mmol) and acetonitrile (2 mL). The catalyst transfer was completed with another portion of solvent to make a final olefin concentration of *ca* 0.4 M. The reaction mixture was stirred at −25°C for two days, before it was diluted with EtOAc (5 mL) and filtered through a plug (3×2 cm) of silica gel. The silica was washed with additional EtOAc (2×5 mL) and the combined filtrates were concentrated at reduced pressure. The enantiomeric excess was determined on a sample from the residue to be 80% *ee* [WHELK-O, hexane/*i*-PrOH 99:1, 0.7 mL/min., t_R 31.7 (major); 33.1 min.]. Flash chromatography (silica gel, pentane/EtOAc: 75:25; R_f 0.56) afforded then aziridine **4b** (0.75 g, 83%) as a thick, colorless oil, that crystallized upon standing. **(2*S*,3*S*)-*N*-*p*-nitrobenzenesulfonyl-3-methyl-2-phenylaziridine**: $[\alpha]_D^{24}$ +60.4 (c=1.08, $CDCl_3$); IR (neat): 3105, 1351, 1164, cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ref. $CHCl_3$: 7.26 ppm) δ 8.29 (app. d, 2H, J=8.9 Hz); 8.11 (app. d, 2H, J=8.9 Hz); 7.30–7.22 (m, 3H); 7.17–7.10 (m, 2H); 3.87 (d, 1H, J=4.4 Hz); 3.06 (qd, 1H, J=6.0, 4.4 Hz); 1.88 (d, 3H, J=6.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$ ref. $CDCl_3$: 77.0 ppm): δ 150.1, 146.2, 134.5, 128.6, 128.5, 128.3, 126.1, 124.1, 50.2, 50.1, 14.5.
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