Pergamon

Tetrahedron Letters, Vol. 38, No. 39, pp. 6897-6900, 1997
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0040-4039/97 $17.00 + 0.00

PII: S0040-4039(97)01589-X

Preparation and Evaluation of Nitrene Precursors ($PhI=NSO_2Ar$) for the Copper-Catalyzed Aziridination of Olefins

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Abstract: *The preparation of different [*N*-(arenesulfonyl)imino]phenyliodinanes is described, along with an evaluation of their utility as nitrene precursors for the copper-catalyzed aziridination of different olefins. The best results were obtained with* p-NO_2-$C_6H_4SO_2N$=IPh *and* p-MeO-$C_6H_4SO_2N$=IPh, *both of which were found superior to PhI=NTs, which previously has been the reagent of choice for this type of reaction. The corresponding aziridine derivatives were obtained in good to excellent yields (60-99%) using 1.0 equivalent of olefin and 1.5 equivalents of the nitrene precursor.* © 1997 Elsevier Science Ltd.

Introduction

The aziridine unit constitutes a very versatile building-block in organic synthesis and has successfully been used in the synthesis of e.g. alkaloids, amino acids, amino sugars and β-lactams.[1] In addition, aziridines have also found applications as chiral auxiliaries[2] and lately also as chiral ligands in asymmetric catalysis.[3] This calls for efficient methodology for their preparation and very promising reactions for the direct conversion of olefins into aziridines have recently been reported by several research groups.[4] Copper-[4a-d] or manganese-catalyzed[4e-f] nitrenoid transfer to olefins using [*N*-(*p*-toluenesulfonyl)imino]phenyliodinane[5] (PhI=NTs) is to date the most studied one-step approach to aziridines, along with carbenoid addition to imines.[6] The copper-catalyzed aziridination of olefins is advantageous because of the great number of cheap and commercially available starting materials, but so far useful yields and levels of enantioselectivity have been restricted to a small set of styrene derivatives,[4a, c-f] as most other olefins are too unreactive to be useful for the enantioselective versions of the nitrenoid addition. The mechanism of this reaction has been studied in some detail,[4b, 7] and is likely to involve copper-nitrenes as intermediates. The aim of this study was to investigate how changes in the steric and electronic properties of the nitrene source influence the reactivity of the copper-nitrene and if possible improve on the reaction.

In this preliminary communication we report on the preparation of several [*N*-(arenesulfonyl)imino]-phenyliodinanes having different substituents on the arenesulfonyl moiety, together with an evaluation of their utility as reagents for the copper-catalyzed aziridination of olefins.

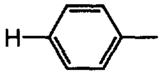
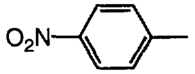
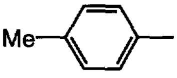
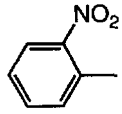
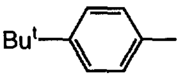
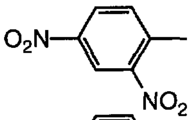
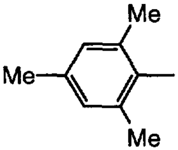
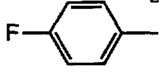
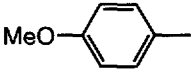
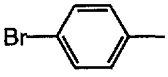
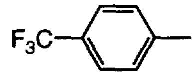
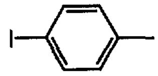
Results and discussion

The [*N*-(arenesulfonyl)imino]phenyliodinanes ($PhI=NSO_2Ar$) were prepared in good to excellent yields (Table 1) using a slight modification of the literature procedure (Scheme 1).[8] We were pleased to find that both the *p*-MeO-$C_6H_4SO_2N$=IPh (**1c**) and *p*-NO_2-$C_6H_4SO_2N$=IPh (**1e**) could be obtained in high yields and pure enough to be used without the need of recrystallization or trituration. For entries 3, 4 and 9, the sulfonamides were obtained.

Scheme 1

$$ArSO_2NH_2 + PhI(OAc)_2 \xrightarrow[0°C\text{-}RT,\ 4\ h]{KOH,\ MeOH} PhI{=}NSO_2Ar$$

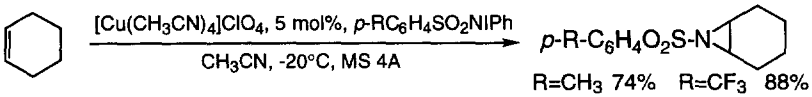
Table 1. Preparation of Nitrene Precursors 1a-i

Entry	Ar	%Yield	Product	Entry	Ar	%Yield	Product
1		78	**1a**	7		97	**1e**
2		83	**1b**	8		94	**1f**
3		0		9		0	
4		0		10		58	**1g**
5		85	**1c**	11		79	**1h**
6		59	**1d**	12		61	**1i**

The initial evaluation of the different nitrene precursors was performed using cyclohexene as substrate. The reactions were carried out in analogy with the method described by Evans (Scheme 2),[4b] employing five equivalents of the olefin and nitrene precursor as the stoichiometrically limiting component, 5 mol% of $[Cu(CH_3CN)_4]ClO_4$ as catalyst and acetonitrile as solvent.

To our surprise, the best results were obtained using *p*-$MeO\text{-}C_6H_4SO_2N{=}IPh$ (**1c**) and *p*-$NO_2\text{-}C_6H_4SO_2N{=}IPh$ (**1e**).[9-11] In comparison to the PhI=NTs (**1b**), both these reagents resulted in a considerable increase of the yield of the aziridines.

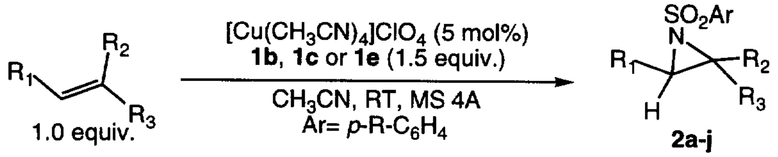
Scheme 2



$R{=}CH_3$	74%	$R{=}CF_3$	88%
R=I	76%	$R{=}NO_2$	92%
R=F	69%	R=OMe	98%

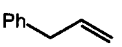
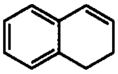
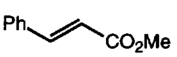
The necessity of using excess olefin in order to obtain good yields of the aziridine is a severe disadvantage, especially when the olefin is considered to be the more valuable reaction component. One of the main goals of this study was to develop a high-yielding procedure using only one equivalent of olefin and a small excess of the aziridination reagent. The results are presented in Table 2.

Scheme 3



2a-j

Table 2. Copper-Catalyzed Aziridination of Olefins

Entry	Substrate	R	Conditions^{a}	Product		
				No.	% Yield^{b}	mp (°C)^{c} or R_f^{d}
1	Styrene	NO_2 (**1e**)	A	**2a**	99	0.73
2	1-Decene	NO_2 (**1e**)	B	**2b**	70	0.75
3		Me (**1b**)	B	**2c**	48	79-80
4		NO_2 (**1e**)	B	**2d**	71^{e}	107-108
5		NO_2 (**1e**)	A	**2e**	97	90-91
6		NO_2 (**1e**)	A	**2f**	89	149-150
7		MeO (**1c**)	A	**2g**	95^{e}	135-136
8		Me (**1b**)	A	**2h**	40	44-45
9		NO_2 (**1e**)	A	**2i**	62	149-150
10		MeO (**1c**)	A	**2j**	60^{e}	0.23

a) Method A: Slow addition (3 h) of 1.5 equiv. of nitrene source; Method B: 1.5 equiv. of nitrene source was added at once. b) Isolated yield after flash chromatography (silica gel) based on the olefin; all compounds are fully characterized by their spectroscopic data (IR, ^{1}H and ^{13}C NMR and mass spectra). c) From EtOAc/Pentane. d) In EtOAc/Pentane: 1/3. e) The reaction was performed at 0°C.

Indeed, the copper-catalyzed alkene aziridination was found to proceed with good to excellent yields using only one equivalent of olefin in a concentration of *ca* 0.4 M. It is important to emphasize that for all olefins studied so far, the aziridination proceeds with better yields when performed using the new nitrene precursors. For instance, the copper-catalyzed aziridination of alkyl-substituted olefins gave even higher yields using *p*-$NO_2C_6H_4SO_2N$=IPh (**1e**) and one equivalent of olefin than was earlier reported in the literature using PhI=NTs (**1b**) and 5 equivalents of these substrates.[4b]

For certain cases it was found that slow addition of the nitrene source had a beneficiary effect. These reactions were carried out by simply adding the solid nitrene precursor portionwise to the reaction mixture over a period of *ca* three hours.[12] Under these conditions, good to excellent yields of the aziridines were obtained from electron-rich as well as from electron-deficient olefins, and again *p*-MeO-$C_6H_4SO_2N$=IPh (**1c**) and *p*-NO_2-$C_6H_4SO_2N$=IPh (**1e**) gave the best results.

In summary, we have developed a set of nitrene precursors for the copper-catalyzed aziridination of olefines, which give good yields of aziridines even when the olefin is used as the stoichiometrically limiting component in the reaction. It should also be noted that another benefit of using *p*-NO_2-$C_6H_4SO_2N$=IPh (**1e**) is that *p*-nitroarylsulfonamides are readily cleaved using thiols by the method described by Fukayama *et al.*[13] We are currently investigating these nitrene precursors for the enantioselective version of the copper-catalyzed aziridination reaction.

Acknowledgments:

Generous financial support from the Swedish Natural Research Council, Astra Arcus and the Tryggers Foundation is gratefully acknowledged.

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7. Li, Z.; Quan, R.W.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1995**, *117*, 5889.

8. The procedures for preparing the new nitrene precursors were slightly modified compared to the procedure described by Yamamoto[5] in that no water was added after the reaction was complete, but the crude products were collected directly by filtration, dried *in vacuo* and used in the aziridination reactions. Furthermore, the solvent volume used for the preparation of **1c** was only half of that employed in the original procedure.

9. For one previous example of the use of p-NO_2-$C_6H_4SO_2N$=IPh for rhodium-catalyzed aziridination of olefins, see Müller, P.; Baud, C.; Jacquier, Y. *Tetrahedron* **1996**, *52*, 1543.

10. Since the nitro and methoxy groups have the opposite electronic properties, one might expect that p-MeO-$C_6H_4SO_2N$=IPh (**1c**) and p-NO_2-$C_6H_4SO_2N$=IPh (**1e**) would show disparate performance in the aziridination reaction. Accordingly kinetic studies,[11] comparing PhI=NTs (**1b**), p-MeO-$C_6H_4SO_2N$=IPh (**1c**) and p-NO_2-$C_6H_4SO_2N$=IPh (**1e**) show that the rate of aziridine formation is significantly faster when **1c** serves as the nitrenoid source, while the use of **1e** results in a considerably slower reaction. The observation that **1c** and **1e** give higher chemical yields than **1b** in all the cases so far observed may be rationalized in terms of differences in the relative kinetics of the two competing reaction pathways from the copper-nitrene complex, i.e. aziridine versus sulfonamide formation.[4b] We speculate that the higher yields obtained with **1c** and **1e** might be due to higher reactivity of **1c** and slower decomposition of **1e**.

11. Södergren, M. J.; Bedekar, A. V.; Alonso, D. A.; Andersson P. G. *unpublished results*.

12. The aziridination of styrene is representative and as follows: Styrene (101 mg, 1.0 mmol) and $[Cu(MeCN)_4]ClO_4$ (16 mg, 0.05 mmol) are dissolved in dry acetonitrile (2.5 mL) containing activated 4A molecular sieves (*ca* 300 mg). **1e** (610 mg, 1.5 mmol) is added portionwise under argon over a period of three hours. The reaction mixture was then stirred overnight, followed by evaporation of the solvent under reduced pressure. The residue was directly subjected to flash chromatography (silica gel, Pentane/EtOAc: 85/15) to afford aziridine **2a** (301 mg, 99%) as a white solid.

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(*Received in UK* 25 *June* 1997; *revised* 24 *July* 1997; *accepted* 1 *August* 1997)