Iron-catalysed aziridination reactions promoted by an ionic liquid†

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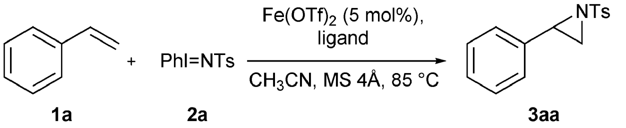
A catalytic system based on iron(II) triflate, quinaldic acid and an ionic liquid allows the aziridination of olefins with equimolar amounts of iminoiodinane providing products in good to moderate yields.

The preparation of aziridines is an important transformation in organic synthesis.[1] Aziridines are encountered in pharmaceutical and natural products that exhibit potent biological activity,[2] and constitute versatile building blocks for a number of nitrogen-containing compounds.[3] Transition metal complex-mediated aziridinations of alkenes using nitrene sources are among the most powerful methods developed until now. A large number of efficient catalytic systems involving manganese,[4] ruthenium,[5] silver,[6] gold,[7] and cobalt[8] have been introduced but most of them suffer from the use of a large excess of olefin to achieve reasonable yields. Although the copper[9] and rhodium[10] complex-mediated aziridination account for the best methods, iron-based catalysts are receiving more and more attention due to their lower cost and toxicity.[11–13]

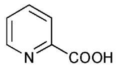
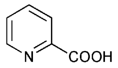
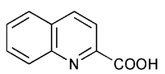
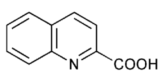
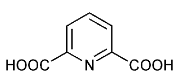
Recently, we reported a method for the conversion of olefins into aziridines[13] using iron(II) triflate[14] in the presence of the preformed iminoiodinanes $PhINSO_2Ar$.[15] Moderate to good yields were obtained using a 7-fold excess of the styrene derivative. Herein we describe a more practical and efficient iron-based catalytic system that allows the conversion of various alkenes into the corresponding aziridines with only one equivalent of olefin.

Initially, we studied the influence of a ligand in the iron catalytic system with styrene (**1a**) as a model substrate. Pyridine type molecules were chosen due to their known affinity to iron.[16] When one equivalent of styrene was submitted to aziridination conditions without any ligand, the yield of *N*-tosylaziridine **3aa** was only 23% (Table 1, entry 1). Under the same conditions, the addition of picolinic acid (**4**) (5 and 15 mol%) increased the yield (to 31% and 40%, respectively; Table 1, entries 2 and 3). The best results were obtained by using 5 and 15 mol% of quinaldic acid (**5**) giving the desired product in 53% and 60%, respectively (Table 1, entries 4 and 5). When more than 15 mol% of **5** were used, problems of solubility were encountered and no significant improvement of the yield could be achieved. In order to increase the number of chelating points between the ligand and iron, pyridine-2,6-dicarboxylic acid (**6**) was tested. However, the addition of 15 mol% of **6** afforded only traces of aziridine **3aa** (Table 1, entry 6).

Table 1 Ligand effects in the iron-catalysed aziridination[a]



1a **2a** **3aa**

Entry	Ligand		(mol%)	Yield (%)
1	—		—	23
2		**4**	5	31
3		**4**	15	40
4		**5**	5	53
5		**5**	15	60
6		**6**	15	Traces

[a] Reaction conditions: **1a** (1.0 equiv.) and **2a** (1.0 equiv.) were used.

For the further optimisation of the system the use of 15 mol% of quinaldic acid (**5**) was retained. Unexpectedly, the addition of 5 mol% of NaCl drastically improved the yield in the formation of aziridine **3aa** to 73% (Table 2, entry 1). The best result (79%) was obtained with 20 mol% of NaCl (Table 2, entry 2). The addition of anhydrous LiCl or KCl afforded *N*-tosylaziridine **3aa** in lower yields of 73% and 61%, respectively (Table 2, entries 3 and 4). Realising that ionic species notably contributed to the nitrene transfer onto alkenes, the replacement of NaCl by a small amount of an ionic liquid was envisaged.[17] Since metal-catalysed aziridination reactions can be sensitive to water, the hydrophobic ethylmethylimidazolium bis[(trifluoromethyl)sulfonyl]amide (emim BTA) (**7**) was chosen.[18] To our delight we found that the addition of 8 mol% of **7** furnished aziridine **3aa** in 89% yield (Table 2, entry 5). The effect of the counter anion BTA was evaluated by using 8 mol% of LiBTA. However, the latter promoted the reaction to a smaller extent (73%, Table 2, entry 6), pointing out the efficiency of ionic liquid **7**.

Next, the iminoiodinane was modified in order to reinforce the electronic and/or chelating properties of the catalytic system. A comparison of the three preformed iminoiodinanes **2a–c** revealed significant reactivity differences (Table 3). Pleasingly, the nitrene transfer to styrene (**1a**) with 5-methyl-2-pyridinesulfonyliminophenyliodinane (**2c**) under

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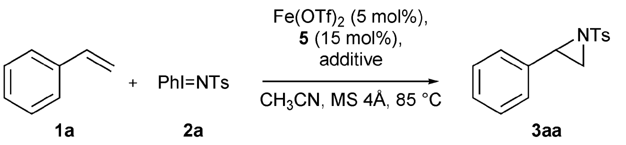
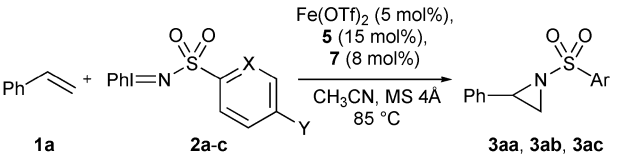
Table 2 Additive effects in the iron-catalysed aziridination[a]



Entry	Additive	(mol%)	Yield (%)
1	NaCl	5	73
2	NaCl	20	79
3	LiCl	20	73
4	KCl	20	61
5	emim BTA (**7**)	8	89
6	LiBTA	8	73

[a] Reaction conditions: **1a** (1.0 equiv.) and **2a** (1.0 equiv.) were used.

Table 3 Variation of iminoiodinane **2**[a]



Entry	**2**	X	Y	Product	Yield (%)
1	**a**	CH	Me	**3aa**	89
2	**b**	CH	NO_2	**3ab**	39
3	**c**	N	Me	**3ac**	>95

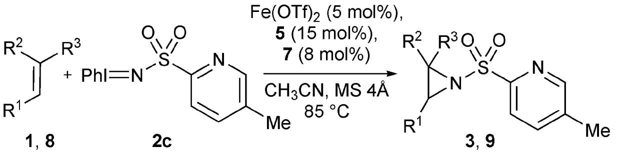
[a] Reaction conditions: **1a** (1.0 equiv.) and **2** (1.0 equiv.) were used.

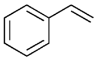
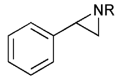
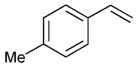
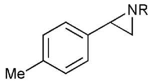
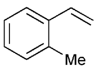
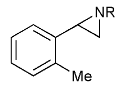
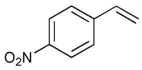
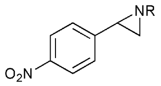
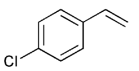
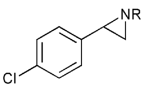
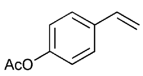
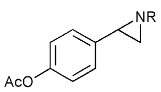
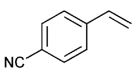
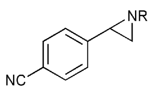
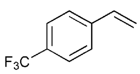
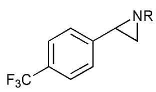
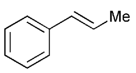
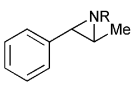
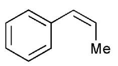
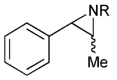
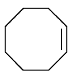
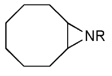
the optimised conditions led to quantitative formation of aziridine **3ac** (Table 3, entry 3). Presumably, coordination effects were responsible for the enhanced reactivity of this iminoiodinane.[19]

Encouraged by these results, the substrate scope of the iron-catalysed aziridination reaction was examined (Table 4). With styrene derivatives **1a–h** it proceeded well giving products with moderate to good yields (entries 2–8). The best results were achieved with *p*-methylstyrene and *p*-nitrostyrene (entries 2 and 4). *p*-Acetoxystyrene, *p*-cyanostyrene and *p*-trifluoromethylstyrene (entries 6–8) gave the corresponding aziridines in reasonable yields (70, 60 and 65%, respectively), while the reaction with *p*-chlorostyrene led to only 36% of aziridine **3ec** (entry 5). No by-products other than traces of sulfonamide were detected (by TLC or NMR). Apparently, the results were irrespective of the electronic effect of the substituents, and thus a clear-cut rationale regarding the reactivity of the styrene derivatives could not be deduced.

Whereas the nitrene transfer onto *trans*-methylstyrene (**1i**) led exclusively to the corresponding *trans*-aziridine **3ic** (50% yield; Table 4, entry 9), the aziridination of *cis*-methylstyrene (**1j**) afforded an inseparable *trans–cis* mixture of **3ic** and **3jc** in a 70 : 30 ratio (55% yield; entry 10). Thus, as in the previously described iron-catalysed aziridination,[13] only the former olefin reacted stereospecifically. This result suggests the presence of radical intermediates during the nitrene transfer process.[20]

Table 4 Substrate scope



Entry	Substrate		Product[a]		Yield (%)
1		**1a**		**3ac**	>95[b]
2		**1b**		**3bc**	>95[b]
3		**1c**		**3cc**	60[c]
4		**1d**		**3dc**	95[b]
5		**1e**		**3ec**	36[c]
6		**1f**		**3fc**	70[c]
7		**1g**		**3gc**	60[b]
8		**1h**		**3hc**	65[b]
9		**1i**		**3ic**	50[c]
10		**1j**		**3ic** (*trans*) **3jc** (*cis*)	55[c]
11		**8**		**9**	57[c]

[a] R = 5-methyl-2-pyridinesulfonyl. [b] Use of 1.0 equiv. of **2c**. [c] Use of 1.2 equiv. of **2c**.

Finally, the reaction was carried out with cyclooctene (**8**) as substrate affording 57% of the corresponding aziridine **9** (entry 11).

In conclusion, we have developed a catalytic system for the aziridination of olefins using ligand-modified $Fe(OTf)_2$ as the catalyst and a preformed iminoiodinane with a pyridine backbone as the nitrene source. Remarkable features are the substrate-to-iminoiodinane ratio of 1 : 1 and the pronounced additive effect.

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