Catalytic aziridination of electron-deficient olefins with an *N*-chloro-*N*-sodio carbamate and application of this novel method to asymmetric synthesis†

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Received (in Cambridge, UK) 29th July 2008, Accepted 9th September 2008
First published as an Advance Article on the web 29th October 2008
DOI: 10.1039/b812978a

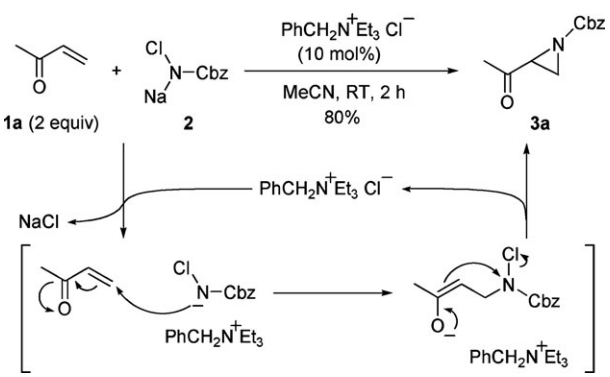
A new method for the aziridination of electron-deficient olefins using an *N*-chloro-*N*-sodio carbamate is described; the reaction was promoted by phase-transfer catalysis (solid–liquid) and afforded aziridines from α,β-unsaturated ketones, esters, sulfones and amides.

Aziridines, which are found in natural products, as well as in biologically active compounds, are important versatile building blocks in synthetic organic reactions.[1] In particular, terminal aziridines are a potential source of two carbon atoms and one nitrogen atom, due to their facile ring-opening with various nucleophiles.[2] Among the various methods available for the synthesis of aziridines,[3] the aziridination of electron-deficient olefins, such as α,β-unsaturated carbonyl compounds,[4] is useful because the products are readily converted into amino acid derivatives by ring-opening reactions.[5] Tardella *et al.*[6] developed an addition–cyclization method that allows the one-step aziridination of electron-deficient olefins[7] using a combination of $NsONHCO_2Et$ and bases. In this reaction, *para*-nitrobenzenesulfonate acts as a good leaving group during cyclization to the corresponding aziridine. Similar representative agents—aminimides[8] and *N*-hydroxy-*N*-pivaloylanilines[9]—have also been used for aziridination *via* the same mechanism. Recently, these two procedures were applied to asymmetric synthesis.[3,10] Although these methods have shown great promise, they both require strong bases for generation of the active nitrogen source, and stoichiometric or large amounts of a chiral source for asymmetric synthesis. Furthermore, the substituents on the substrates or reagents are restricted to aryl groups. Recently, we developed an alternative method for the aziridination of alkyl- or aryl-substituted olefins using *N*-chloro-*N*-sodio-*para*-toluenesulfonamide (chloramine-T, CT).[11] Even though the nitrogen of CT is nucleophilic and the chlorine atom on the nitrogen is an adequate leaving group, CT did not react with electron-deficient olefins.[12] Thus, an alternative *N*-chloro salt, *N*-chloro-*N*-sodio benzyl carbamate (chloramine-Cbz),[13] was chosen to perform the desired aziridination. Since the pK_a value of chloramine-Cbz (pK_a = 15.3) is greater than that of CT (pK_a = 13.5), chloramine-Cbz should attack the β-carbon of electron-deficient olefins. This Communication describes a method for the aziridination of electron-deficient olefins using chloramine-Cbz in the presence of a phase-transfer catalyst (solid–liquid) and the application of this method to asymmetric synthesis.

We began our investigation with a model aziridination reaction between methyl vinyl ketone (**1a**) and chloramine-Cbz (**2**). Because **2** is relatively insoluble in organic solvents, benzyltriethylammonium chloride was employed as a solid–liquid phase-transfer catalyst. As illustrated in Scheme 1, the treatment of 2 equiv. of **1a** with **2** in the presence of 10 mol% of benzyltriethylammonium chloride in acetonitrile at room temperature for 2 h provided the desired aziridine, **3a**, in 80% yield. The pathway of this reaction is very simple; namely, the sodium ion of **2** is exchanged for an ammonium ion, subsequent Michael addition of the soluble nitrogen species to the enone gives the enolate and intramolecular cyclization then affords the desired aziridine.

Various electron-deficient olefins were then subjected to a catalytic aziridination. Methyl acrylate (**1b**) and phenyl vinyl sulfone (**1c**) were efficiently aziridinated (Table 1, entries 1 and 2); unfortunately, the reactions with acrolein, acrylamide and acrylonitrile did not proceed under the conditions described above. Interestingly, olefin **1d**, which has an oxazolidinone auxiliary, was a good substrate for the aziridination reaction. Even though only 1 equiv. of **1d** was employed in the reaction, the aziridination proceeded smoothly and gave high yields. *trans*-Disubstituted olefins with the auxiliaries **1e** and **1f** were also converted to the corresponding aziridines.

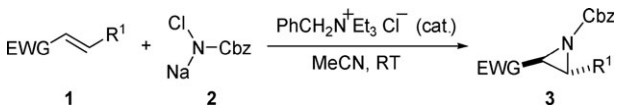
Because the aziridination of olefin **1d**, which has an auxiliary oxazolidinone, was efficient, the asymmetric aziridination



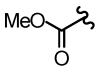
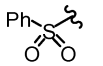
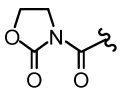
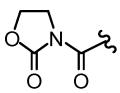
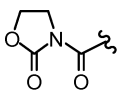
Scheme 1 The aziridination of **1a** with **2**.

Department of Applied Chemistry, Graduate School of Engineering, Osaka University, Yamadaoka 2-1, Suita, Osaka 565-0871, Japan. E-mail: minakata@chem.eng.osaka-u.ac.jp; Fax: +81 6-6879-7402
† Electronic supplementary information (ESI) available: Procedure of synthesis and experimental data for the products. See DOI: 10.1039/b812978a

Table 1 The aziridination of electron-deficient olefins



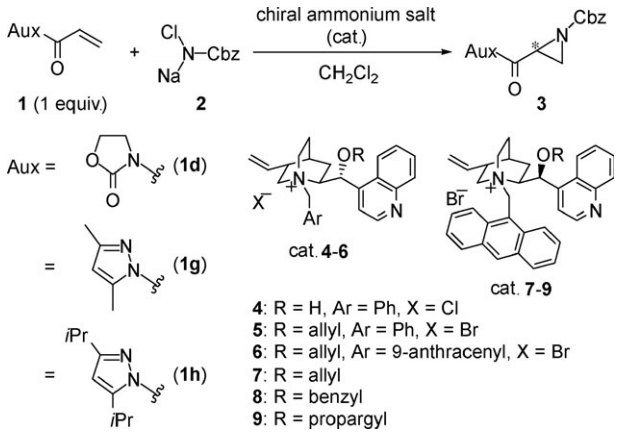
1 2 3

Entry	EWG	R^1	Equiv.[a]	Cat. (mol%)	Time/h	Yield (%)
1		H	2 (**1b**)	20	24	85
2		H	2 (**1c**)	20	4	89
3		H	1 (**1d**)	10	4	93
4		Me	2 (**1e**)	10	24	60
5		CO_2Et	1 (**1f**)	10	24	58

[a] Equiv. of **1**.

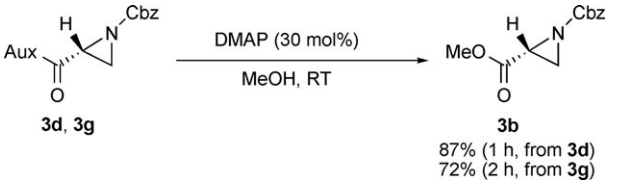
of this type of olefin was investigated using ammonium catalysts derived from cinchonidine and cinchonine. The simplest ammonium salt, **4**, prepared from cinchonidine, was

Table 2 Catalytic asymmetric aziridination



Entry	Olefin	Cat. (mol%)	Temp./°C	Time/h	Yield (%)	ee (%) (config.)
1	**1d**	**4** (10)	0	2	14	6 (*S*)
2	**1d**	**5** (10)	0	2	20	38 (*S*)
3	**1d**	**6** (20)	RT	2	90	61 (*S*)
4	**1d**	**6** (10)	RT	2	98	63 (*S*)
5	**1g**	**6** (10)	RT	6	84	70 (*S*)
6	**1h**	**6** (10)	RT	6	83	71 (*S*)
7	**1g**	**7** (10)	RT	3	76	76 (*R*)
8	**1g**	**8** (10)	RT	3	81	77 (*R*)
9	**1g**	**9** (10)	RT	4	61	74 (*R*)
10	**1g**	**7** (10)	−20	72	44	87 (*R*)
11[a]	**1g**	**7** (10)	−20	72	62	86 (*R*)

[a] **1g**: 2 equiv.



Scheme 2 Removal of the auxiliary, leading to a simple aziridine.

ineffective in the asymmetric aziridination of **1d** (Table 2, entry 1). Etherification of the alcohol moiety in ammonium salt **4** improved the enantioselectivity (Table 2, entry 2). The introduction of a more bulky substituent—an anthracenylmethyl group—on the quinuclidine nitrogen (catalyst **6**) improved the enantioselectivity to 63% ee (Table 2, entries 3 and 4). When olefin **1g**, which has a dimethylpyrazole rather than an oxazolidinone auxiliary, was employed in the reaction, the corresponding aziridine was obtained in 84% yield with 70% ee (Table 2, entry 5). Substitution of the two methyl groups on the pyrazole ring with isopropyl groups did not affect the reaction efficiency (Table 2, entry 6). The effect of the R-substituent of the cinchonine-derived anthracenylmethylated ammonium salt was examined in the aziridination of **1g**; however, enantioselectivities remained unchanged (Table 2, entries 7–9). Eventually, it was determined that the enantioselectivity could be improved to 87% ee by decreasing the reaction temperature (Table 2, entry 10). In addition, the reaction yield was enhanced by using 2 equiv. of olefin (Table 2, entry 11). The absolute configuration of the major chiral aziridines produced by cinchonidine-derived catalysts **4–6** was determined to be the *S*-enantiomer, while those produced by the cinchonine-derived catalysts were predominantly *R*-enantiomers. Other chiral ammonium salts, including Maruoka's catalyst,[14] did not give good results.

The direct asymmetric aziridination of **1b** with **2** under the optimized reaction conditions afforded moderate chemical and optical yields. The resulting chiral aziridines (shown in Table 2) were readily transformed into a simple aziridine that was identical to the product of the reaction between **1b** and **2**. As shown in Scheme 2, removal of the auxiliaries was performed using a DMAP catalyst,[15] yielding the methyl ester-substituted aziridine **3b** with no change in optical purity.

In summary, this Communication describes a simple synthetic method for the catalytic aziridination of electron-deficient olefins with *N*-chloro-*N*-sodio benzyl carbamate. The process was developed based on solid–liquid phase-transfer catalysis. The present system was applied to asymmetric reactions by using chiral ammonium salt catalysts derived from *Cinchona* alkaloids, yielding optically-active aziridines with an enantiomeric purity of up to 87% ee. Current studies aim to further improve the reaction selectivity and to determine the reaction mechanism.

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