N-bromosuccinimide/cerium ammonium nitrate: an efficient reagent for stereo-controlled deamination of ketoaziridines

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An efficient and novel method for the deamination of trans-1-alkyl (H or benzoyl)-2-aroyl aziridines in a completely stereo-controlled reaction in the presence of N-bromosuccinimide/cerium (IV) ammonium nitrate is described. In comparison with the previous reported work, this reaction reveals a substituent-reactivity relationship and important role for the substituent on C1 and C2 in determining whether deamination or oxidation reaction takes place.

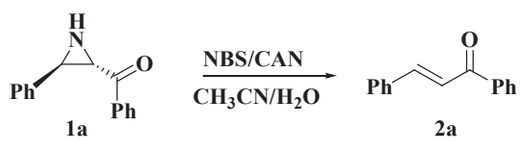
Keywords: ketoaziridine, deamination, stereo-controlled, N-bromosuccinimide, cerium ammonium nitrate

Aziridines are an important class of saturated heterocycles which are often used as synthetic intermediates.[1,2] The strained three-membered ring of aziridine reacts with a variety of nucleophilic or electrophilic reagents affording valuable products which are important in synthetic or mechanistic studies.[3,4]

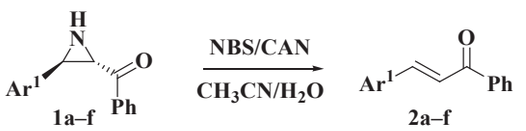
Aziridines have been classified as 'activated' or 'non-activated' according to whether or not nucleophilic ring-opening reactions proceed in the absence of a positive charge on the nitrogen. The presence of electron-withdrawing substituents activates the ring, which then reacts easily with nucleophiles to form ring-opened products. Efforts, have been devoted to the development of the reactions of activated' aziridines with different reagents over the past decade, leading to a variety of the products[5,6] In contrast to activated aziridines, non-activated aziridines are relatively inert towards nucleophilic reagents.[7,8]

Among the reactions of aziridines, the deamination of aziridines has been attractive for mechanistic, structural, thermodynamic and theoretical reasons. Several methods have been described for the deamination of a variety of aziridines.[9–11]

We have explored different reactions of 2-aroyl-3-aryl aziridines affording functionalised and other valuable N-containing compounds.[12–20] In continuation of our research activities in the field of the reactions of aziridines, we have found that N-bromosuccinimide (NBS)/cerium (IV) ammonium nitrate (CAN) is a suitable reagent for deamination of N–H, N-aryl and N-aroyl 2-benzoyl-3-phenyl aziridines. This study shows that substituents on C1 and C2 aziridines have a more important role in determining the reactions, deamination or oxidation, with NBS/CAN rather than substituents on the N-atom of the aziridine ring.



Scheme 1 Reaction of 2-benzoyl-3-phenyl aziridine with NBS/CAN.



Scheme 2 Transformation of *trans*-2-benzoyl-3-phenylaziridine (**1**) to the corresponding *trans*-chalcone (**2**).

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Initially, a variety of N–H 2-benzoyl-3-aryl aziridines (**1a**–**f**) was prepared *via* the Gabriel–Cromwell procedure[21] by bromination of the related α,β-unsaturated carbonyl compounds followed by the reaction of ammonia solution (30%) in methanol at room temperature.[15,21] The aziridines were identified by comparison of their melting points and spectroscopic data with those from the literature.[22,23]

We examined the reaction of **1a** with NBS in CH_3CN/H_2O which afforded a chalcone by a the deamination reaction in low yield. The reaction of aziridine with NBS/CAN (1 : 0.2) in CH_3CN/H_2O (9 : 1) was also examined. This gave *trans*-chalcone in excellent yield by the deamination reaction (Scheme 1).

In further investigations, the deamination reaction in the presence of NBS/CAN (1 : 0.2) was then extended to a variety of N–H 2-benzoyl-3-aryl aziridines (**1a**–**f**). The results are summarised in Table 1. We observed the formation of the *trans*-alkenes (**2a**–**f**) as exclusive products of the deamination reaction (Scheme 2). The products were characterised by their spectral data (^{13}C NMR, ^{1}H NMR, IR and melting point) and in the case of known products by comparison of their melting points and spectroscopic data with reported values.[24,25]

After successful application of this methodology to non-activated aziridines, in order to investigate the scope of the reaction, the reaction of *trans*-1,2-dibenzoyl-3-aryl aziridine (**3a**,**b**),[15] and *trans*-1-benzyl-2-benzoyl-3-aryl aziridine (**4a**,**b**),[14] were subsequently examined under the same conditions (Scheme 3). These reactions afforded only *trans*-chalcone by the deamination reaction.

Another striking feature of this reaction was that other aziridines in the presence of NBS/CAN (1 : 1) in CH_3CN/H_2O resulted in carbonyl compounds. Both aryl aziridines and aliphatic aziridines in the presence of NBS/CAN have been oxidised (Scheme 4). A related report uses β-cyclodextrins in

Table 1 Deamination of *trans*-2-benzoyl-3-aryl aziridines (**1**) with NBS/CAN

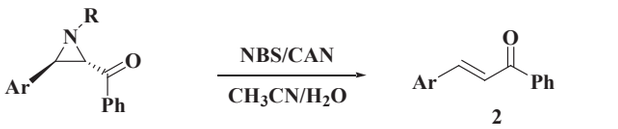
Entry	Ar[1]	Time/h	Yield/%[a,b]	M.p./°C	M.p./°C
1a	C_6H_5	1	91	55–57[d]	56–58[c]
1b	4-$NO_2C_6H_4$	1.5	86	165–166[d]	164–166[c]
1c	2,4-$Cl_2C_6H_3$	1	94	210[d]	209–211[c]
1d	2-$NO_2C_6H_4$	1.5	88	111–112[d]	108–111[c]
1e	4-$OMeC_6H_4$	1	81	115–116[d]	114–115[c]
1f	4-ClC_6H_4	1	89	113–115	113–115

[a]Isolated yield after purification.

[b]All the products were identified by spectroscopic (IR, ^{1}H NMR, ^{13}C NMR) and elemental analyses.

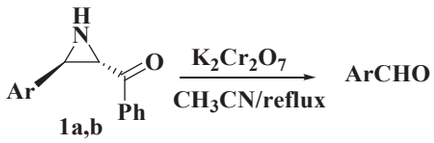
[c]Identified by comparison of their melting points and spectroscopic data with those reported.[24,25]

[d]Literature experimental melting points.[24,25]



R= PhCOCl, Ar=Ph (**3a**), 4-$NO_2C_6H_4$ (3b)[15] **2a** (83%) **2b**(89%)
R= BzCl, Ar=Ph (**4a**), 4-$NO_2C_6H_4$ (4b)[14] **2a** (87%) **2b**(81%)

Scheme 3 Transformation of N-alkyl, N-benzoyl 2-benzoyl-3-phenyl aziridines to the corresponding *trans*-chalcone with NBS/CAN.



Scheme 5 The reaction of ketoaziridine with a strong oxidising agent.

addition to NBS to catalyse the same transformation. These reaction conditions also work well for epoxides to provide the corresponding α-hydroxy ketones.[26,27]

A comparison of the reactions in Scheme 4 shows that the substituents on C2 of the aziridines ring have a more important role than substituents on the nitrogen atom of the aziridines ring in determining the reactions, oxidation or deamination of aziridine. By changing the substituents such as benzoyl, alkyl, tosyl or H on the nitrogen atom of the ketoaziridines ring (A, Scheme 4), the reaction afforded only *trans*-chalcone of the deamination reaction. On the other hand, replacing of hydrogen atom on C2 of the aziridine ring with tosyl on the nitrogen atom of aziridine ring (**B** and **C**, Scheme 4) led to α-tosyl amino carbonyl compounds of the oxidation reaction.

In another attempt, to investigate the possibility of oxidation reaction with this class of compounds, we examined the reaction of 2-benzoyl-3-aryl aziridines in the presence of some oxidising agents such MnO_2 and $KMnO_4$ in acetonitrile. No reaction between **1a** and MnO_2 or $KMnO_4$ occurs even under refluxing conditions. The reaction of aziridine (**1a**,**b**) with $K_2Cr_2O_7$ was also examined at room temperature, which afforded benzaldehyde in 67 and 74% yield (Scheme 5).

In conclusion, this work describes a novel method for the deamination of *trans*-1-alkyl (H or benzoyl)-2-aroyl aziridines in a completely stereo-controlled reaction in the presence of NBS/CAN. In comparison with the previous work, this reaction reveals a substituent-reactivity relationship and an important role of the substituent on the C1 and C2 in determining whether a deamination or a oxidation reaction occurs.

Experimental

All yields refer to isolated products after purification by column chromatography or distillation in vacuum. Products were characterised by IR, ^{1}H NMR and ^{13}C NMR spectra, TLC, melting points. NMR spectra were recorded on a Bruker AMX-400 spectrometer (^{1}H at 400 MHz and ^{13}C at 100 MHz) in $CDCl_3$with chemical shift values in ppm downfield from TMS and IR spectra were recorded on a FTIR spectroscope JASCO, FT/IR-6300. All solvents used were dried and distilled according to standard procedures.

*Deamination of ketoaziridines (***1a**–**f***); general procedure*

CAN (0.2 mmol) was added into a solution of acetonitrile: water (9 : 1) (10 mL), NBS (1 mmol), N–H 2-benzoyl-3-phenyl aziridine (**1a**–**f**) (1 mmol) and the mixture was left stirring at room temperature (Scheme 2). After completion of the reaction, the solvent was removed the reaction mixture was diluted with water and extracted with ether (3 × 10 mL). The crude product was purified by column chromatography on silica gel using n-hexane/ethyl acetate as eluent, provided the corresponding *trans*-chalcone **2** (81–94%) (Table 1).

*Deamination of N-benzoyl and/or N-benzyl ketoaziridines (***3a**–**b***) and (***4a**–**b***); general procedure*

CAN (0.2 mmole) was added to a solution of acetonitrile: water (9 : 1) (10 mL), NBS (1 mmol), N-benzoyl and/or N-benzyl 2-benzoyl-3-phenyl aziridine (1 mmol) and the mixture was left stirring at room temperature (Scheme 3). After completion of the reaction, the solvent was removed the reaction mixture was diluted with water and extracted with ether (3 × 10 mL). The crude product was purified by column chromatography on silica gel using *n*-hexane/ethyl acetate as eluent, to provide the corresponding *trans*-chalcone **2** (81–89%) (Scheme 3).

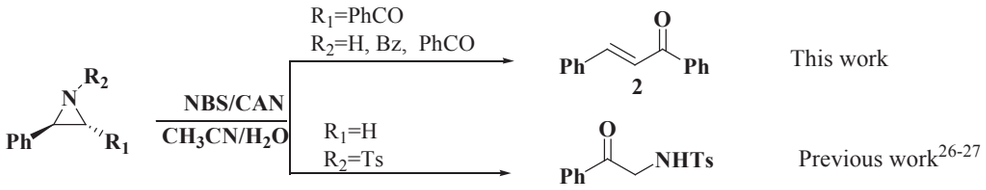
(E)-*1,3-Diphenylprop-2-en-1-one* (**2a**): Pale yellow solid; m.p. 56–58 °C; IR (KBr): 3042, 3021, 1682, 1593, 883, 774, 699, 682. ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm): 8.10–7.98 (m, 2H), 7.74 (d, *J* = 15.6 Hz, 1H), 7.65–7.35 (m, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) (δ, ppm): 190.5, 144.6, 138.2, 134.9, 132.8, 130.5, 128.9, 128.6, 128.5, 128.4, 122.2.

(E)-*3-(4-Nitrophenyl)-1-phenylprop-2-en-1-one* (**2b**): Pale brown solid; m.p. 164–166 °C; IR (KBr): 3062, 1660, 1597, 1518. ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm): 7.55–7.58 (t, *J* = 7.62, 7.67 Hz, 2H), 7.64–7.67 (t, *J* = 7.55 Hz, 1H), 7.66–7.69 (d, *J* = 15.88 Hz, 1H), 7.82 (d, *J* = 8.7 Hz, 2H), 7.83–7.87 (d, *J* = 15.88 Hz, 1H), 7.07 (d, *J* = 7.69 Hz, 2H), 8.31 (d, *J* = 8.59 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) (δ, ppm): 189.4, 141.4, 141.2, 137.7, 133.3, 128.8, 128.7, 128.6, 125.7, 124.2.

(E)-*3-(2,4-Dichlorophenyl)-1-phenylprop-2-en-1-one* (**2c**): Yellow solid; m.p. 209–211 °C; IR (KBr): 3037, 1658, 1596. ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm): 8.50 (s, 1H), 8.14 (dd, *J* = 7.6, 1.98 Hz, 1H), 8.03 (d, *J* = 8.3 Hz, 1H), 7.80 (d, *J* = 15.82 Hz, 1H), 7.66 (d, *J* = 15.82 Hz, 1H), 7.61–7.70 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$) (δ, ppm): 189.8, 138.1, 136.7, 134.8, 133.2, 128.1, 123.3.

(E)-*3-(2-nitrophenyl)-1-phenylprop-2-en-1-one* (**2d**): Off yellow solid; m.p. 108–111 °C; IR (KBr): 3049, 1661, 1605, 1580, 1524, 858, 780, 743, 682, 666. ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm): 8.49 (s, 1H), 8.26–8.28 (dt, *J* = 2.1, 8.1 Hz, 1H)., 8.0 (q, *J* = 1.4, 7.2 Hz, 2H), 7.9 (d, *J* = 7.7 Hz, 1H), 7.80–7.86 (d, *J* = 15.6 Hz, 1H), 7.65–7.67 (d, *J* = 15.6 Hz, 1H), 7.62–7.63 (m, 2H), 7.52–7.56 (q, *J* = 0.6, 7.5 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) (δ, ppm): 189.6, 148.7, 141.5, 137.5, 136.6, 134.3, 133.3, 130.0, 128.8, 128.6, 124.6, 124.5, 122.4.

(E)-*3-(4-Methoxyphenyl)-1-phenylprop-2-en-1-one* (**2e**): Pale yellow solid; m.p. 114–115 °C; IR (KBr): 3056, 2935, 1658, 1596, 1268. ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm): 8.03 (dd, *J* = 8.4 Hz, *J* = 1.9, 2H), 7.80 (d, *J* = 15.8 Hz, 1H), 7.63 (d, *J* = 8.6 Hz, 2H), 7.53–7.46 (m, 3H), 7.43 (d, *J* = 15.6 Hz, 1H), 6.91 (d, *J* = 8.6 Hz, 2H), 3.83 (s, 3H).



Scheme 4 The substituent effect on the deamination or oxidation reaction of aziridines with NBS/CAN.

^{13}C NMR (100 MHz, $CDCl_3$) (δ, ppm): 190.6, 161. 6, 144.9, 138.4, 132.4, 130.6, 130.3, 128.5, 128.4, 127.8, 119.7.

(E)-*3-(4-Chlorophenyl)-1-phenylprop-2-en-1-one* (**2f**): Yellow crystals; m.p. 113–115 °C; IR (KBr): 3041, 1655, 1591. ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm): 8.1 (dd, J = 7.6, 2.01 Hz, 2H), 7.74 (d, J = 15.7 Hz, 1H), 7.58 (m, 2H), 7.55 (dd, J = 7.7, 1.9 Hz, 1H), 7.50 (m, 3H), 7.70 (m, 2H).190.1, 143.2, 138.1, 136.4, 133.4, 132.8, 129.5, 129.2, 128.7, 128.4, 122.5.

*Oxidation of ketoaziridines (***1a**–**b***); general procedure*

$K_2Cr_2O_7$ (0.5 mmole) was added to a solution of acetonitrile: water (4 : 1) (10 mL), and N–H 2-benzoyl-3-phenyl aziridine (1 mmole) and the mixture was refluxed. After completion of the reaction, the solvent was removed and the reaction mixture was diluted with water and extracted with ether (3 × 10 mL). The crude product was purified by column chromatography on silica gel using *n*-hexane/ethyl acetate as eluent to provide the corresponding benzaldehyde (Scheme 5) (67–74%).

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