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Scope and limitations of diastereoselective aziridination reactions using stabilised ammonium ylides or α-bromo carbonyl nucleophiles†

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The applicability of easily available ammonium salts to access aziridines *via* an ammonium ylide pathway was carefully investigated and compared with classical *aza*-Darzens approaches using α-bromo carbonyl nucleophiles. Whereas amide-stabilised ammonium ylides could be successfully reacted with aromatic aldimines to obtain the corresponding *trans*-aziridines in good yields and with high diastereoselectivities, α-bromo amides failed. In sharp contrast, acetophenone-based ylides did not give any aziridines while in this specific case α-bromo acetophenone derivatives gave the corresponding *cis*-aziridines in high yields and with excellent diastereoselectivities under optimised conditions.

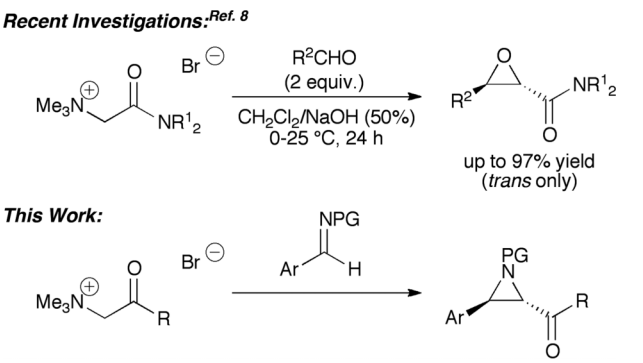
Introduction

Aziridines are versatile highly reactive organic molecules playing an important role in biologically active compounds or as intermediates in multistep syntheses.[1] Thus, numerous approaches for the stereoselective syntheses of aziridines have been reported in the past.[1–4] The addition of easily accessible ylide species to electrophiles is a powerful strategy to obtain three-membered ring compounds.[3–8] Whilst the application of (chiral) sulfur ylides to access aziridines has evolved as one of the most efficient strategies in the past,[4] the use of ammonium ylides for this purpose has been reported only sparingly so far.[5] This comes as a surprise keeping in mind the successful applications of (chiral) ammonium ylides in cyclopropanation[5] and epoxidation reactions.[7,8] Based on our recent development of a highly *trans*-selective protocol for the synthesis of glycidic amides by reacting aldehydes with stabilised amide-derived ammonium ylides[8] (Scheme 1) we have now undertaken systematic investigations concerning the use of carbonyl-stabilised ammonium ylides to access aziridines from easily available starting materials.

Results and discussion

Amide-stabilised ammonium ylides

Based on the knowledge gained in our recent studies concerning the use of amide-stabilised ammonium ylides for epoxidation reactions we first investigated the feasibility of an analogous strategy to obtain aziridines by reacting preformed α-ammonium acetamides with protected aromatic aldimines. As trimethylamine was recently found to be the best-suited amine leaving group[8b] initial investigations to identify the best-suited imine protecting group and the optimum reaction conditions were carried out using the diethylamide-based ammonium salt **1a** as the ylide precursor (Table 1 gives an overview about the most significant results obtained in a thorough screening). Some key-factors of this reaction became obvious very early in our investigations (entries 1–7). First, our recently established liquid/liquid biphasic epoxidation conditions (using CH_2Cl_2 and an excess of 50% aqueous NaOH)[8]



Scheme 1 Recently developed epoxidation protocol and the targeted aziridine formation using carbonyl-stabilised ammonium ylides.

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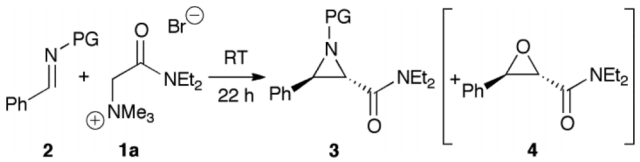
Table 1 Identification of the best-suited protecting group and reaction conditions for the use of ammonium salt **1a** to access aziridines **3**



2 **1a** **3** **4**

Entry	PG	Solv.	Base (eq.)	**1** : **2**	Yield (**3**)[a] (%)	*trans* (%)[b]	**3** : **4**[b]
1	Ph	CH_2Cl_2	NaOH (50%) (60×)	1 : 1	<5[c]	n.d.	1 : 15
2	$PhSO_2$				0	n.d.	**4** only
3			Cs_2CO_3 (2×)		<10[c]	n.d.	**3** only
4	Tosyl				<15[c]	n.d.	**3** only
5	Boc		NaOH (50%) (60×)		26	>98	1 : 1
6			NaOH (1%) (4×)		0	n.d.	n.d.
7			Cs_2CO_3 (2×)		25	>98	**3** only
8			*t*-BuOK (1×)		48	>98	**3** only
9			*t*-BuOK (2×)		58	>98	5 : 1
10			*t*-BuOK (1×)	1 : 2	50	>98	**3** only
11		THF		1 : 1	25	>98	3 : 7
12		DMSO			20	>98	1 : 3
13		CH_2Cl_2	$CsOH·H_2O$ (2×)		44	>98	5 : 1
14			Cs_2CO_3 (10×)		49	>95	**3** only
15	**Boc**	**CH_2Cl_2**	**Cs_2CO_3 (10×)**	**1 : 2**	**73**	**>95**	**3 only**

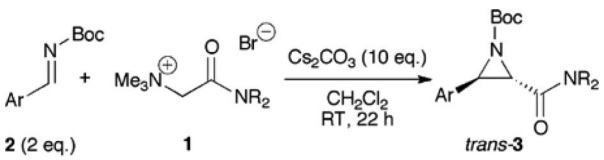
[a] Isolated yield of **3**. [b] Determined by NMR of the crude product.[9] [c] Product could not be isolated.

were found to be too harsh for this approach (entries 1, 2, and 5). Independent of the employed imine protecting group these conditions caused a rapid hydrolysis of **2** to benzaldehyde which then reacted further *via* the epoxidation pathway to give oxirane **4**. The only protecting group, which allowed us to isolate aziridine **3** in small amounts under these strongly basic conditions, was the Boc-group (entry 5). Unfortunately, lowering the amount of base did not result in any conversion any more (entry 6). As hydrolysis of starting imine **2** was therefore supposed to be one of the main obstacles herein we next investigated a variety of liquid/solid base conditions. After a careful screening we first realised that the use of Cs_2CO_3 with the sulfonamide-protected imines **2** did not result in any epoxide **4** formation any more (entries 3 and 4) but also gave very small amounts of aziridines **3** only. Using the Boc-protected imine **2** in the presence of 2 eq. Cs_2CO_3 gave *trans*-**3** in 25% isolated yield and very high diastereoselectivity without any formation of epoxide **4** (entry 7) (*trans* and *cis*-aziridines can be distinguished by their $^3J_{HH}$-coupling constants).[9] As the Boc-group was found to be the best-suited protecting group further optimisation of the reaction conditions were undertaken with Boc-protected benzaldimine **2** only (entries 8–15). Amongst a variety of different other bases that have been screened only *t*-BuOK was found to give *trans*-**3** in reasonable yields. However, neither changing the amount of base nor the stoichiometric ratio of the reagents or the solvent allowed us to isolate **3** in more than 50% yield when *t*-BuOK was used (entries 8–12). In addition, using an excess of *t*-BuOK or more polar solvents like THF or DMSO favoured epoxide-formation again. Changing for solid CsOH in CH_2Cl_2 also did not allow us to increase the yield (entry 13). However, by using a larger access of Cs_2CO_3 in CH_2Cl_2 the aziridine **3** could be obtained in 49% by using equimolar amounts of starting materials and in 73% by using two equivalents of the imine **2**. Noteworthy, in these reactions formation of minute amounts of the *cis*-diastereomer of **3** were observed occasionally,[10] but epoxide-formation could be totally suppressed (entries 14, 15).

Having identified the Boc-protecting group as the best-suited one and the combination of an excess of solid Cs_2CO_3 and CH_2Cl_2 as the most promising reaction conditions for the highly *trans*-selective aziridine formation we next screened the scope of this reaction for differently substituted aromatic aldimines **2** and ammonium acetamides **1** (Table 2).

Whereas differently substituted *tert*-amide-based ammonium salts **1** gave the *trans*-aziridines in comparable yields and with the same high diastereoselectivity as the standard

Table 2 Scope of the ammonium ylide-mediated *trans*-aziridination reaction



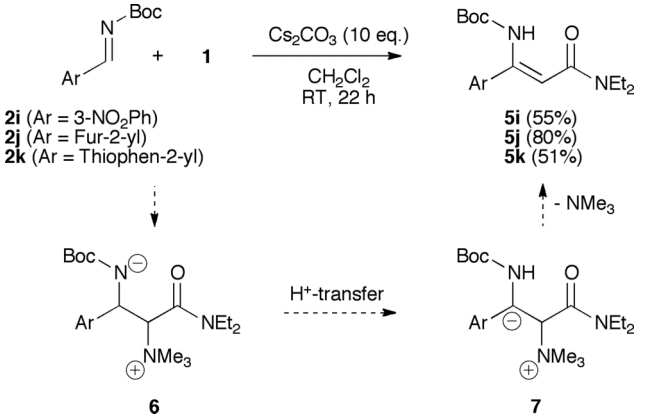
2 (2 eq.) **1** *trans*-**3**

Entry	Ar	NR_2	Product	Yield[a] (%)
1	Ph	NEt_2	**3a**	73
2		NPh_2	**3b**	62
3		Piperidine	**3c**	64
4		NHBn	**3d**	0
5	2-MePh	NEt_2	**3e**	59
6	4-MeOPh		**3f**	72
7	4-BrPh		**3g**	75
8	Naphth-2-yl		**3h**	49
9	3-NO_2Ph		see Scheme 2	
10	Fur-2-yl		see Scheme 2	
11	Thiophen-2-yl		see Scheme 2	

[a] Isolated yields.

diethylamide based salt (compare entries 1–3), *sec*-amides could not be successfully employed (entry 4). These ammonium salts were also significantly less reactive in our recent epoxidation protocol.[8] Using different aromatic aldimines **2** next, we found that electron neutral and electron rich aryl moieties were tolerated well (entries 5–8) although the yields were sometimes slightly lower, especially when the naphthalene-based **2** was used (entry 8). Unexpected results were obtained when the *m*-nitro-substituted benzaldimine **2i** and the heteroaryl-based imines **2j** and **2k** (entries 9–11 and Scheme 2) were used. In all these cases, the major product formed in the reaction were not the aziridines **3**, but the α,β-unsaturated β-amino amides **5** (Scheme 2). Only in the case of the thiophene-based imine **2k** small amounts (<20%) of the aziridine could be detected in the crude product mixture but no improvement was possible by applying different conditions. In addition this aziridine could not be isolated due to its high instability during the isolation procedure. Formation of compounds **5** can be rationalised as illustrated in Scheme 2. Due to the increased acidity of the benzylic position of these aromatic compounds the initially formed betaine intermediate **6** can more easily undergo a deprotonation in the benzylic position (instead of the wanted aziridine forming ring closure reaction) than other more electron rich compounds. The resulting intermediate **7** then rapidly eliminates trimethylamine, thus giving the α,β-unsaturated β-amino amides **5** in reasonable not-optimised yields.[11] Based on these results, we then carefully re-examined the NMR spectra of the crude reaction products of the other successful aziridinations (Table 2, entries 1–8) and found that only in the case of the naphthalene-based **2** small amounts of the olefin **5** were formed, thus explaining the slightly lower yield in this reaction (entry 8).

To prove the necessity of the amine leaving group for this reaction we also carried out an analogous reaction by just using α-bromo acetamide as the nucleophile in a classical *aza*-Darzens fashion under different reaction conditions. However, not even traces of **3** were formed, thus highlighting the potential of this ylide strategy to obtain these valuable building blocks in a highly diastereoselective and reasonably high yielding fashion. With respect to a stereoselective variant of this reaction the use of easily available cinchona alkaloid-based ammonium salts seems reasonable.[12] Although this strategy has been successful for ammonium ylide-mediated cyclopropanation reactions[6] we and others have not been able to apply a similar strategy to epoxidation reactions.[7b,8] However, the Yadav group recently reported a *trans*-selective aziridination reaction starting from α-bromoacetophenone derivatives which, upon reaction with *tert*-amines under basic conditions, proceeds *via* the corresponding ammonium ylides.[5] Therein, they also described the use of cinchona alkaloids to render this reaction stereoselective. Thus we investigated the feasibility of this strategy for our target reaction. Unfortunately we have not been able to obtain even traces of the targeted aziridine **3**, neither using preformed ammonium salts nor using the cinchona alkaloids in catalytic amounts, a result which is in full accordance with our epoxidation experience.



Scheme 2 Formation of the α,β-unsaturated β-amino amides **5**.

The mechanism and the origin of the diastereoselectivity of onium-ylide mediated 3-membered ring forming reactions has been thoroughly investigated in the past.[3,4,7,13] It is known that amide-stabilised sulfur and ammonium ylides give exclusively the *trans*-epoxides upon reacting with aldehydes.[8,13a] Systematic investigations of these epoxidation reactions by Aggarwal *et al.* revealed that for stabilised sulfonium ylides formation of the intermediate *syn*- and *anti*-betaines is reversible, but bond rotation towards the required *antiperiplanar* betaines (which allow for ring closure) is more hindered for *syn*-betaines (which would give *cis*-epoxides) than for *anti*-betaines, thus favouring *trans*-epoxide formation in these cases. As we have not been able to isolate any intermediates (and re-subject them to reaction conditions) in our present aziridination reaction we can not yet prove whether a similar rational can be taken into consideration to explain the high *trans*-selectivity observed herein.[14] However, based on the fact that a similarly high *trans*-selectivity has been observed in all cases where amide-stabilised sulfur or ammonium ylides have been used it seems reasonable that the origin of this high selectivity may be due to similar reasons.

Acetophenone-based nucleophiles

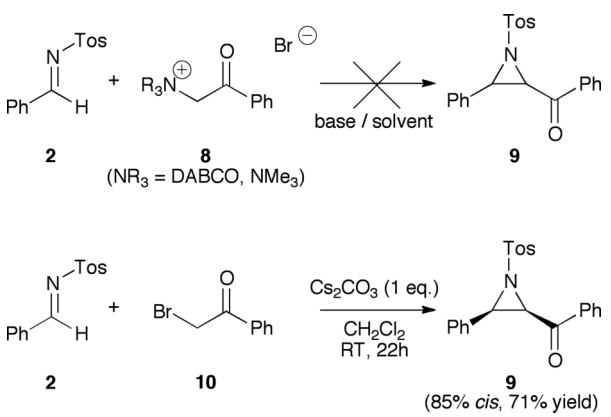
As mentioned above the only (dia)stereoselective aziridination reaction using ammonium ylides has been reported by the Yadav group recently.[5] One interesting fact about this report is that acetophenone-based ammonium salts could be successfully employed to obtain aziridines, whereas a reaction of these nucleophiles with aldehydes does not give any epoxides at all.[15] In addition, also the successful use of cinchona-based acetophenone-stabilised ammonium ylides to carry out this aziridination in a stereoselective fashion was reported,[5] whereas we have not been able to employ cinchona alkaloids for the herein presented reaction using amide-stabilised ammonium ylides. Thus we had a closer look on the reported reaction of acetophenone-based ammonium salts **8** with *N*-tosylated aldimines **2** to access aziridines **9** under different conditions. Unfortunately we have not been able to successfully obtain any aziridines **9** in a reproducible and high yielding fashion under a variety of different conditions. Interestingly, whereas preformed ammonium salts yielded

almost no aziridines **9** at all, the use of α-bromoacetophenone **10** with catalytic amounts of DABCO in the presence of Cs_2CO_3 in CH_2Cl_2 allowed us to obtain **9** in reasonable amounts (>50% yield) and with high *cis*-selectivity, a result which is in sharp contrast to the recently reported approach using Na_2CO_3 in CH_3CN at elevated temperature.[5] To elucidate whether this reaction is catalysed by the *tert*-amine (thus proceeding *via* an ylide pathway) or represents a classical hitherto unknown *aza*-Darzens reaction, the direct addition of **10** to **2** was performed in the presence of 1 eq. Cs_2CO_3 in CH_2Cl_2 as the solvent. Interestingly, the product **9** was obtained in good yield and with high *cis*-selectivity, thus representing the first example of a direct *aza*-Darzens reaction of acetophenone-based nucleophiles to aldimines (Scheme 3).

Encouraged by this result we carried out a screening of different conditions for this reaction next (Table 3 gives an overview of the most significant results). First the tosyl-protecting group was identified to be the best-suited for this reaction.[16] Testing other solid bases we found that the use of Cs_2CO_3 is crucial to obtain the product in reasonable yield, whereas *e.g.* Na_2CO_3 did not give any product at all (entries 3 and 4). To warrant high diastereoselectivities it was necessary to use a small excess of the base first (entry 1 *vs.* 2). Whereas other solvents like THF or toluene were also tolerated well (entries 5 and 6) the stoichiometric ratio of **2** and **10** was found to be crucial with respect to yield and *cis*-selectivity. Whereas a small excess of imine **2** had a beneficial effect, the use of an excess of acetophenone **10** significantly decreased the diastereoselectivity and also the yield (entries 7–11). In addition, using a larger excess of base resulted in full decomposition of the starting materials and the product, thus illustrating a certain sensitivity of **9** and the necessity to carefully balance the reaction conditions.

Having identified the best-suited and reproducible reaction conditions for the *cis*-selective formation of aziridine **9** (Table 3, entry 11) we then investigated the scope of this reaction for differently substituted starting materials. As shown in Table 4 the reaction was found to be tolerant to a variety of different substituents, giving the *cis*-aziridines with excellent diastereoselectivities and in high yields. Only the presence of a substituent *ortho* to the imine (entry 7) and of a strongly electron donating group *para* to the imine (entry 8) resulted in lower yields.[17]

The remarkably high *cis*-selectivity in this approach may be explained by steric factors in the intermediate primary addition products. The α-bromo acetophenone derivative can approach the imine to either give the *syn*- or the *anti*-addition products first (*syn* or *anti* approaches as depicted in Scheme 4). Accordingly four *syn*-intermediates (**A–D**) and two *anti*-intermediates (**E**, **F**) can be formed ((*E*)- and (*Z*)-enolates will give the same intermediates). Due to steric factors intermediates **B**, **C**, and **D** seem to be less favourable than **A** in the *syn*-approach, thus favouring *cis*-aziridine formation. In the *anti*-approach, intermediate **E** would be the preferred one, which



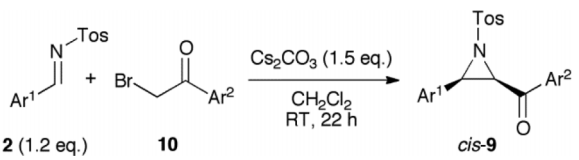
Scheme 3 Results using either acetophenone-based ammonium salts **8** or the α-bromo derivative **10** for the diastereoselective aziridination reaction.

Table 3 Identification of the best-suited reaction conditions for the *cis*-selective aziridination using α-bromo acetophenone **10** and aldimine **2**

Entry	Solv.	Base (eq.)	**10 : 2**	Yield[a] (%)	*cis* (%)[b]
1	CH_2Cl_2	Cs_2CO_3 (1×)	1 : 1	71	85
2		Cs_2CO_3 (1.5×)		74	>98
3	CH_3CN	Na_2CO_3 (1.5×)		0	n.d.
4	CH_2Cl_2			0	n.d.
5	THF	Cs_2CO_3 (1.5×)		73	>98
6	Toluene			67	>98
7	CH_2Cl_2		1.5 : 1	77	80
8		Cs_2CO_3 (4×)		<5[c]	n.d.
9		Cs_2CO_3 (1.5×)	4 : 1	50	65
10			1 : 1.5	76	>98
11	**CH_2Cl_2**	**Cs_2CO_3 (1.5×)**	**1 : 1.2**	**76**	**>98**

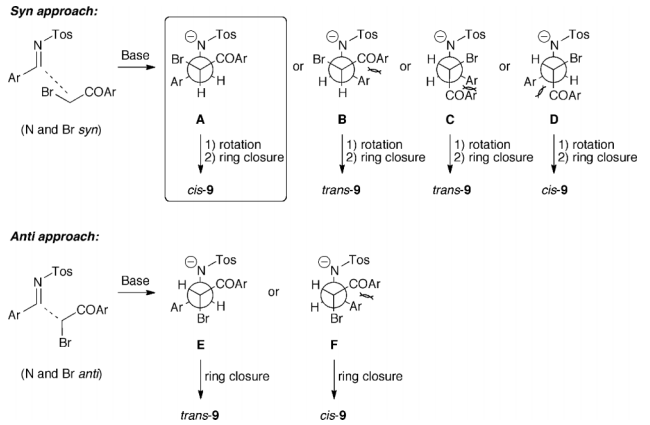
[a] Isolated yield of **9**. [b] Determined by NMR of the crude product.[9] [c] Full decomposition of starting materials and product.

Table 4 Scope of the *cis*-selective *aza*-Darzens reaction using differently substituted α-bromo acetophenone derivatives **10** and aldimines **2**



Entry	Ar^1	Ar^2	Product	Yield[a] (%)
1	Ph	Ph	**9a**	76
2		4-ClPh	**9b**	94
3		4-MePh	**9c**	78
4		4-MeOPh	**9d**	65
5		Naphth-2-yl	**9e**	73
6	4-BrPh	Ph	**9f**	74
7	2-MePh		**9g**	53
8	4-MeOPh		**9h**	41
9	4-ClPh		**9i**	67
10	4-NO_2Ph		**9j**	94

[a] Isolated yields.



Scheme 4 Mechanistic proposal for the preferred formation of *cis*-azridines **9**.

would result in formation of the corresponding *anti*-aziridine. Due to the high *cis*-selectivity observed in our investigations we therefore rationalize that this reaction proceeds *via* a *syn*-approach of the acetophenone to the imine giving the preferred intermediate **A**, which after bond rotation and ring closure thus yields the *cis*-azridines as the major diastereomers.

Conclusions

It was shown that, depending on the nature of the nucleophile either α-ammonium acetamides or α-bromo carbonyl nucleophiles can be successfully employed for highly diastereoselective aziridine formations upon reacting them with differently substituted aromatic aldimines. Whereas amide-stabilised ammonium ylides could be successfully reacted with aromatic aldimines to obtain the corresponding *trans*-aziridines in good yields and with high diastereoselectivities, α-bromo amides failed, thus highlighting the potential of this ylide strategy for this specific case. In sharp contrast, acetophenone-based ylides did not give any aziridines while in this specific case α-bromo acetophenone derivatives gave the corresponding *cis*-aziridines in high yields and with excellent diastereoselectivities under carefully optimised conditions, thus resulting in a novel *aza*-Darzens protocol for the syntheses of these interesting compounds.

Experimental section

General

^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance DRX 500 MHz spectrometer, a Bruker Avance III 300 MHz spectrometer, and on a Bruker Avance III 700 MHz spectrometer with TCI cryoprobe. All NMR spectra were referenced on the solvent peak. High resolution mass spectra were obtained using an Agilent 6510 Q-TOF mass spectrometer with an ESI source. IR spectra were recorded on a Shimadzu IR Affinity-1 FT infrared spectrometer. All chemicals were purchased from commercial suppliers and used without further purification unless otherwise stated. All reactions were performed under an Ar-atmosphere. CH_2Cl_2 was distilled over P_2O_5 and stored under Ar (it was not necessary to dry CH_2Cl_2 prior to every experiment and usually this quality could be used successfully in these reactions over the course of 3–4 weeks after distillation).

General procedure for the *trans*-aziridination using amide-stabilised Me_3N-ammonium salts

To a solution of the ammonium salt **1** (1 mmol) in CH_2Cl_2 (20 mL), 10 equiv. of solid Cs_2CO_3, followed by *N*-Boc-aryl aldimine **2** (2 mmol), were added. The mixture was vigorously stirred for 22 h at room temperature. CH_2Cl_2 and brine were added and the phases separated. The aqueous layer was extracted twice with CH_2Cl_2, the combined organic layers were extracted with brine and the aqueous layer was re-extracted twice with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4, evaporated, and dried *in vacuo*. Column chromatography (silica gel, heptanes/EtOAc = 10 : 1) gave the aziridines **3** in the reported yields.

trans-Aziridine 3a

Obtained in 73% as a colourless oil. ^{1}H NMR (300 MHz, δ, $CDCl_3$, 298 K): 1.19 (t, J = 7.1 Hz, 3H), 1.27 (t, J = 7.1 Hz. 3H), 1.46 (s, 9H), 3.19 (d, J = 2.6 Hz, 1H), 3.35–3.66 (m, 4H), 3.99 (d, J = 2.6 Hz, 1H), 7.29–7.39 (m, 5H) ppm; ^{13}C NMR (75 MHz, δ, $CDCl_3$, 298 K): 13.3, 15.2, 28.0, 41.7, 42.3, 43.3, 44.2, 81.5, 126.6, 128.0, 128.5, 136.3, 159.2, 164.8 ppm; IR (film): $\tilde{V}$ = 2967, 2932, 1732, 1643, 1491, 1456, 1435, 1408, 1366, 1306, 1258, 1227, 1149, 1099, 945, 872, 847, 750 cm^{-1}; HRMS (ESI): m/z calcd for $C_{18}H_{26}N_2O_3$: 357.1575 $[M+K]^+$; found: 357.1580.

General procedure for the *cis*-aziridination using α-bromo acetophenone derivatives

To a solution of 2-bromo-acetophenone **10** (1 mmol) in CH_2Cl_2 (15 mL), 1.5 equivalents of solid Cs_2CO_3, followed by *N*-tosyl-aryl aldimine **2** (1.2 mmol), were added. The mixture was vigorously stirred for 22 h at room temperature. CH_2Cl_2 and brine were added and the phases separated. The aqueous layer was extracted twice with CH_2Cl_2, the combined organic layers were extracted with brine and the aqueous layer was re-extracted twice with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4, evaporated, and dried *in vacuo*. Column chromatography (silica gel, heptanes/EtOAc = 10 : 1) gave the aziridines **9** in the reported yields.

cis-Aziridine 9a

Obtained in 86% as white foam. ^{1}H NMR (300 MHz, δ, $CDCl_3$, 298 K): 2.41 (s, 3H), 4.32 (d, J = 7.7 Hz, 1H), 4.40 (d, J = 7.7 Hz, 1H), 7.06–7.10 (m, 3H), 7.12–7.18 (m, 2H), 7.24–7.33 (m, 4H), 7.44 (t, J = 7.3 Hz, 1H), 7.78 (d, J = 7.3 Hz, 2H), 7.90 (d, J = 8.3 Hz, 2H) ppm; ^{13}C NMR (75 MHz, δ, $CDCl_3$, 298 K): 21.7, 46.5, 48.2, 127.3, 128.1, 128.3, 128.4, 128.5, 128.7, 129.9, 131.2, 133.8, 134.4, 135.7, 145.2, 189.0 ppm; IR (film): $\tilde{V}$ = 3063, 3032, 2926, 1691, 1597, 1449, 1327, 1306, 1229, 1157, 1090, 984, 914, 883, 812, 756, 729 cm^{-1}; HRMS (ESI): m/z calcd for $C_{22}H_{19}NO_3S$: 378.1158 $[M+H]^+$; found: 378.1156.

Acknowledgements

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References

1 (*a*) *Aziridines Epoxides in Organic Synthesis*, ed. A. K. Yudin, Wiley-VCH, Weinheim, 2006; (*b*) D. Tanner, *Angew. Chem., Int. Ed. Engl.*, 1994, **33**, 599–619; (*c*) G. S. Singh, M. D'hooghe and N. De Kimpe, *Chem. Rev.*, 2007, **107**, 2080–2135; (*d*) A. Padwa and S. S. Murphree, *ARKIVOC*, 2006, 6–33; (*e*) D. M. Jenkins, *Synlett*, 2012, **23**, 1267–1270.

2 (*a*) D. Borkin, A. Carlson and B. Török, *Synlett*, 2010, 745–748; (*b*) X. Zeng, X. Zeng, Z. Xu, M. Lu and G. Zhong, *Org. Lett.*, 2009, **11**, 3036–3039; (*c*) E. Gayon, O. Debleds, M. Nicouleau, F. Lamaty, A. van der Lee, E. Vrancken and J.-M. Campagne, *J. Org. Chem.*, 2010, **75**, 6050–6053; (*d*) A. Yoshimura, V. N. Nemykin and V. V. Zhdankin, *Chem.–Eur. J.*, 2011, **17**, 10538–10541; (*e*) S. A. Künzi, B. Morandi and E. M. Carreira, *Org. Lett.*, 2012, **14**, 1900–1901; (*f*) S. C. Valdez and J. L. Leighton, *J. Am. Chem. Soc.*, 2009, **131**, 14638–14639; (*g*) T. Hashimoto, N. Uchiyama and K. Maruoka, *J. Am. Chem. Soc.*, 2008, **130**, 14380–14381; (*h*) S. Minakata, Y. Murakami, R. Tsuruoka, S. Kitanaka and M. Komatsu, *Chem. Commun.*, 2008, 6363–6365; (*i*) T. Akiyama, T. Suzuki and K. Mori, *Org. Lett.*, 2009, **11**, 2445–2447.

3 (*a*) For reviews see: V. K. Aggarwal, in *Comprehensive Asymmetric Catalysis*, ed. E. N. Jacobsen, A. Pfaltz and H. Yamamoto, Springer, New York, 1999, vol. 2, 679; (*b*) E. M. McGarrigle, E. L. Myers, O. Illa, M. A. Shaw, S. L. Riches and V. K. Aggarwal, *Chem. Rev.*, 2007, **107**, 5841–5883.

4 (*a*) For the use of sulfur ylides in aziridine synthesis see: A.-H. Li, L.-X. Dai and X.-L. Hou, *J. Chem. Soc., Perkin Trans. 1*, 1996, 867–869; (*b*) V. K. Aggarwal, M. Ferrara, C. J. O'Brien, A. Thompson, R. V. H. Jones and R. Fieldhouse, *J. Chem. Soc., Perkin Trans. 1*, 2001, 1635–1643; (*c*) R. Robiette, *J. Org. Chem.*, 2006, **71**, 2726–2734; (*d*) T. Saito, M. Sakairi and D. Akiba, *Tetrahedron Lett.*, 2001, **42**, 5451–5454; (*e*) V. K. Aggarwal, E. Alonso, G. Fang, M. Ferrara, G. Hynd and M. Porcelloni, *Angew. Chem., Int. Ed.*, 2001, **40**, 1433–1436; (*f*) V. K. Aggarwal and J.-L. Vasse, *Org. Lett.*, 2003, **5**, 3987–3990; (*g*) M. T. Reetz and W. K. Lee, *Org. Lett.*, 2001, **3**, 3119–3120.

5 For the only report describing an ammonium ylide-mediated aziridination see: L. D. S. Yadav and R. Kapoor Garima, *Synlett*, 2009, 3123–3126.

6 (*a*) M. J. Gaunt and C. C. C. Johansson, *Chem. Rev.*, 2007, **107**, 5596–5605; (*b*) C. C. C. Johansson, N. Bremeyer, S. V. Ley, D. R. Owen, S. C. Smith and M. J. Gaunt, *Angew. Chem., Int. Ed.*, 2006, **45**, 6024–6028; (*c*) C. D. Papageorgiou, M. A. Cubillo de Dios, S. V. Ley and M. J. Gaunt, *Angew. Chem., Int. Ed.*, 2004, **43**, 4641–4644; (*d*) N. Bremeyer, S. C. Smith, S. V. Ley and M. J. Gaunt, *Angew. Chem., Int. Ed.*, 2004, **43**, 2681–2684; (*e*) C. D. Papageorgiou, S. V. Ley and M. J. Gaunt, *Angew. Chem., Int. Ed.*, 2003, **42**, 828–831.

7 (*a*) T. Kimachi, H. Kinoshita, K. Kusaka, Y. Takeuchi, M. Aoe and M. Ju-ichi, *Synlett*, 2005, 842–844; (*b*) H. Kinoshita, A. Ihoriya, M. Ju-ichi and T. Kimachi, *Synlett*, 2010, 2330–2334; (*c*) R. Robiette, M. Conza and V. K. Aggarwal, *Org. Biomol. Chem.*, 2006, **4**, 621–623; (*d*) A. Kowalkowska, D. Sucholbiak and A. Jonczyk, *Eur. J. Org. Chem.*, 2005, 925–933; (*e*) A. Jonczyk and A. Konarska, *Synlett*, 1999, 1085–1087; (*f*) X. Xiao, D. Lin, S. Tong and H. Mo, *Synlett*, 2011, 2823–2826; (*g*) V. K. Aggarwal, J. N. Harvey and R. Robiette, *Angew. Chem., Int. Ed.*, 2005, **44**, 5468–5471.

8 (*a*) M. Waser, R. Herchl and N. Müller, *Chem. Commun.*, 2011, **47**, 2170–2172; (*b*) R. Herchl, M. Stiftinger and M. Waser, *Org. Biomol. Chem.*, 2011, **9**, 7023–7027.

9 The *trans*-aziridines have a characteristic $^{3}J_{HH}$-coupling of less than 4 Hz (6-8 Hz for *cis*-aziridines).

10 The traces of *cis*-aziridines (always clearly less than 5%) could not be isolated in a pure form due to their limited amount.

11 Formation of the (*Z*)-diastereomers was found to be dominant as shown by the observed NOE between the olefinic proton and an aromatic proton.

12 C. E. Song, *Cinchona Alkaloids in Synthesis & Catalysis*, Wiley-VCH, Weinheim, 2009.

13 (*a*) V. K. Aggarwal and J. Richardson, *Chem. Commun.*, 2003, 2644–2651; (*b*) S. L. Riches, C. Saha, N. F. Filgueira, E. Grange, E. M. McGarrigle and V. K. Aggarwal, *J. Am. Chem. Soc.*, 2010, **132**, 7626–7630; (*c*) M. K. Lindvall and A. M. P. Koskinen, *J. Org. Chem.*, 1999, **64**, 4596–4606.

14 We have recently started carrying out additional computational investigations of both, epoxidation and aziridination using amide-stabilised ammonium ylides and the results will be reported in due course.

15 Unpublished investigations showed that acetophenone-based ammonium salts could not be employed in epoxidation reactions. The same comes true for ester-based ones (Ref. 8*b*).

16 Boc-protected imines did not give any product in this reaction.

17 Compound **9h** was found to be highly sensitive towards ring opening specially in the isolation and purification procedure and no analytically pure sample could obtained, thus also explaining the reduced isolated yield.