Studies on the synthesis of α-iodoaziridines and improved conditions for the synthesis of alkyl-α-iodoaziridines using $ClMgCHI_2$

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ABSTRACT

α-Iodoaziridines are unusual motifs and intriguing structures for further functionalisation of the intact aziridine. The preparation of *N*-protected α-iodoaziridines is achieved through an addition-cyclisation reaction of $LiCHI_2$ with imines. The effects of varying the *N*-group and using different carbenoids are investigated. Excellent *cis*-stereochemistry is achieved, except for *N*-carbamates containing aryl groups. Using the mixed carbenoid LiCHICl, the iodide leaving group is selected for cyclisation affording chloroaziridines only, as a *cis*/*trans* mixture. More convenient and higher yielding conditions for the preparation of alkyl *N*-Ts α-iodoaziridines are developed, using $ClMgCHI_2$. Additionally, the formation of the problematic primary alkyl α-iodoaziridines is achieved.

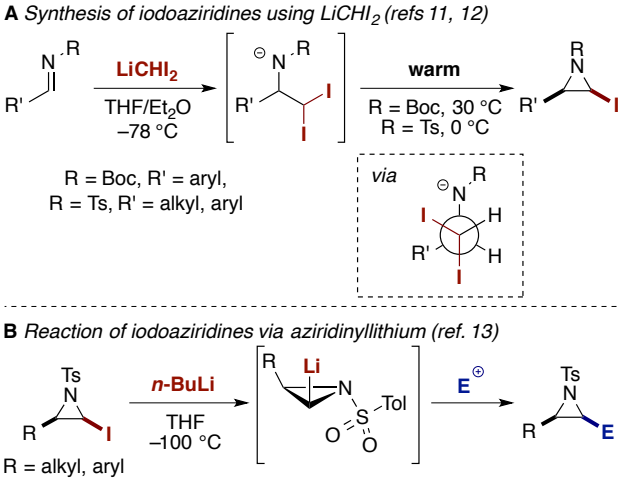
Keywords:

Aziridines; Carbenoids ; Diiodomethyllithium; Diiodomethylmagnesium chloride; Cyclisation;

1. Introduction

Aziridines are important motifs in organic chemistry as a result of the inherent strain in the 3-membered heterocycle.[1] This feature is central to their use as synthetic intermediates in ring opening processes to provide important nitrogen-containing compounds,[2,3] and also to the mode of biological action of aziridine containing natural products.[4] For the synthetic chemist the small ring structure of aziridines is a fascinating target for new methodology development, and there continues to be important advances in the stereoselective synthesis of aziridines.[5] Conceptually there are several strategies for the preparation of aziridine derivatives. These include the transfer of carbenoid reagents or equivalents to imines.[6] The direct nitrogen transfer to alkenes can be achieved using nitrenoid derivatives.[7] Aziridines can also be accessed by cyclisation of β-functionalised amines,[8] which may be formed effectively via addition of nucleophiles to α-haloimines.[9] An alternative, divergent strategy is to prepare an aziridine by one of these approaches, and then to couple that intact aziridine, forming a bond directly to the aziridine ring.[10] This has been achieved by metalation of aziridines and reaction with electrophiles,[11,12] as well as palladium-catalysed cross-coupling of the intact aziridines.[13]

Inspired by this latter approach, we hypothesised that iodo-substituted aziridines might provide interesting precursors for the further functionalisation of intact aziridine rings. Towards this goal, we have recently developed protocols for the synthesis of *N*-Boc[14] and *N*-Ts[15] α-iodoaziridines, the first examples of this functional group (Scheme 1A). Both of these methods employ the addition of diiodomethyllithium, formed via the deprotonation of diiodomethane with LiHMDS, to *N*-protected imines, often formed in situ from their sulfinic acid adducts, followed by highly stereoselective cyclisation.



Scheme 1. Synthesis of α-iodoaziridines and functionalisation via aziridinyllithium.

The formation of *N*-Boc α-iodoaziridines was successful for aryl substituted imines.[14] With *N*-Ts imines, both alkyl and aryl substituted α-iodoaziridines could be accessed in moderate to good yields, though unbranched, primary alkyl imines only afforded very low yields.[15a] The temperature at which cyclisation occurred varied depending on the nature of the *N*-protecting group, but excellent *cis*-selectivity was achieved in all cases. These α-iodoaziridines were shown to be stable on isolation and could be purified by chromatography when the stationary phase was judiciously selected.[15] Furthermore, we demonstrated that *N*-Ts α-iodoaziridines could be used to generate aziridinyllithium species by Li–I exchange (Scheme 1B).[16] The aziridinyllithium was then trapped with electrophiles, affording *N*-sulfonyl aziridine derivatives in high yields and with complementary regio- and stereochemistry to deprotonation approaches.

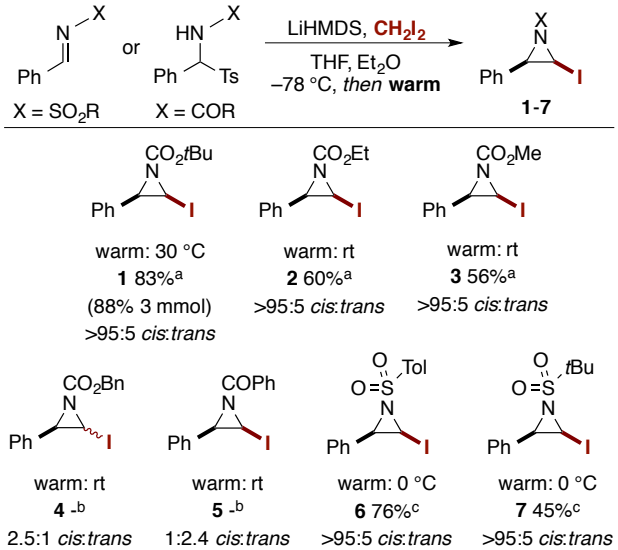
Halomethylmetal reagents, in particular chloromethyllithium, have received significant attention in synthetic chemistry, as they can display both nucleophilic and electrophilic reactivity.[17,18,19] Dihalomethylmetal reagents have been investigated to a lesser degree.[20,21,22] Integral to the approach to α-iodoaziridines has been the use of diiodomethyllithium.[14,15] Unlike traditional aza-Darzens reactions, whereby the diastereoselectivity of aziridine products is determined in the initial carbenoid addition step, here due to the symmetrical nature of $LiCHI_2$, the cyclisation step is diastereodetermining. We considered that using alternative reagents (changing either the nature of the *N*-group, or the nature of the carbenoid reagent ($MCHI_2$)), could afford a different stereochemical outcome, provide improved yields for the more challenging substrates, or provide insight into the factors that affect stereoselectivity.

Here we report our investigations into the effect of variation of the *N*-protecting group and the carbenoid reagents employed in the synthesis of α-iodoaziridines, and relevance to the stereochemical outcome. We report an improved procedure for the preparation of alkyl substituted *N*-Ts α-iodoaziridines with improved yields, through the use of $ClMgCHI_2$, and study the problematic unbranched primary alkyl α-iodoaziridine examples.

2. Results and Discussion

2.1. Role of N-protecting group

We first assessed the effect of changing the *N*-protecting group on the α-iodoaziridine reaction, using imines formed from benzaldehyde. Diiodomethyllithium was formed by deprotonation of CH_2I_2 with LiHMDS over 20 min in a THF/Et_2O mixture at −78 °C, prior to the addition of the imine–HSO_2Tol adduct. Within the carbamate series (2.4 equiv CH_2I_2, 2.6 equiv LiHMDS), the reaction with the *N*-Boc imine gave 83% isolated yield of α-iodoaziridine **1**.[14] The reaction required warming to 30 °C to give full cyclisation and prevent elimination from the intermediate diiodide.[23] Only the *cis*-α-iodoaziridine was observed. In moving to the ethyl and methyl carbamates, the products (**2** and **3** respectively) were obtained in reduced yields, presumably due to attack of the nucleophile at the carbonyl. However, very high diastereoselectivity was maintained, despite the decrease in steric bulk; again only the *cis*–product was observed. Rapid warming from −78 °C to ambient temperatures was required to minimize the formation of unwanted side products and to ensure full cyclisation of the amino *gem*-diiodide intermediates. The reaction with phenyl carbamate yielded a complex mixture of products. The imine formed from *N*-benzyl carbamate also afforded a complicated mixture of products under the reaction conditions. Elimination of iodide from the *gem*-diiodide intermediate to form the corresponding vinyl iodide was a major reaction pathway. The Cbz-protected α-iodoaziridine **4** was observed in the ^1H NMR spectrum of the crude reaction mixture, as a mixture of diastereoisomers (*cis*:*trans*, 2.5:1), but could not be isolated (CHI: *cis*, δ 4.76, J = 5.4 Hz *vs*. *trans*, δ 4.31, J = 1.9 Hz). In both cases, isolation of aziridine-like products proved problematic, with decomposition apparent on a variety of stationary phases. Interestingly, the use of the benzoyl *N*-protecting group (COPh) led to a reverse in the diastereoselectivity of the cyclisation step, with the *trans*-product now the major product **5** (*trans*:*cis* = 2.4:1). Unfortunately, decomposition again occurred on attempted purification and the aziridine products could not be isolated.



Scheme 2. Effect of *N*-protecting group on α-iodoaziridine formation. [a] Reaction conditions: imine–HO_2STol adduct (0.50-0.65 mmol), CH_2I_2 (3.0 equiv), LiHMDS (2.6 equiv), THF:Et_2O (3:1), –78 ºC (10 min), *then warm* (10 min). [b] Product not isolated, unstable to chromatography . [c] Reaction conditions: imine (0.50 mmol), CH_2I_2 (3.4 equiv), LiHMDS (3 equiv), THF:Et_2O (3:1), –78 ºC (10 min), *then warm* (15 min).

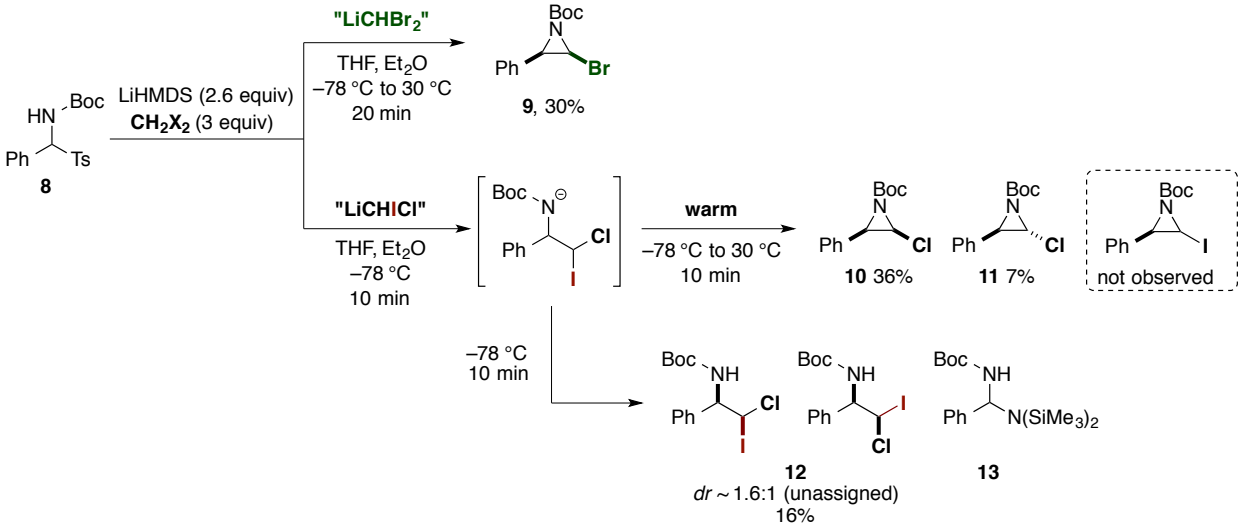
Our hypothesis for the *cis*-stereochemical outcome of the cyclisation is that interactions of the non-displaced iodide with the *N*-protecting groups disfavour the *trans*-aziridine cyclisation transition state (Scheme 1A).[14] In all of the cases depicted in Scheme 2, we observed exclusively the *cis*-α-iodoaziridines, apart from when *N*-groups containing aromatic rings were employed (Cbz and benzylamide). This suggests a favourable π-π interaction between the aryl groups may be occurring, promoting formation of the *trans*-compound in these cases.

We next assessed bulky sulfonyl protecting groups, under slightly different reaction conditions; 1.0 equiv imine, 3.4 equiv CH_2I_2, 3.0 equiv LiHMDS. We had previously reported *N*-Ts α-iodoaziridine **6**, formed in 76% on warming the reaction mixture to 0 ºC to

promote cyclisation, exclusively as the *cis*-aziridine. The *tert*-butylsulfonyl protecting group, in similar fashion, also gave rise exclusively to the *cis*-α-iodoaziridine **7** in 45% yield.

2.2. Mixed halo-carbenoids: chloroiodomethyllithium

Reacting $LiCHBr_2$, in place of $LiCHI_2$, with imine−HSO_2Tol adduct **8** afforded *cis*-*N*-Boc bromoaziridine **9** in 30% yield (Scheme 3).[14] Deyrup demonstrated that chloroaziridines also show a complete preference for *cis*-stereochemistry.[20] However, mixed dihalocarbenoid systems of the form LiCHXY (X≠Y) have not been previously investigated, posing interesting questions about the reactivity of the proposed intermediate and the diastereoselectivity. Chloroiodomethane was chosen as a suitable carbenoid precursor to investigate this, due to cost and availability. Being unsymmetrical, the initial nucleophilic addition of LiCHICl would determine the relative stereochemistry of a particular product, however, there would be a choice for the cyclisation. Preference for *cis*-configuration in the aziridine products would give a mixture of *cis*-chloro and *cis*-α-iodoaziridines. On the other hand, preference for the displacement of iodide from the dihalogenated intermediate as the better leaving group would give exclusively chloroaziridines, as a mixture of *cis*- and *trans*-substituted products.



Scheme 3. Effect of using mixed dihalocarbenoids on chemo- and diastereoselectivity in formation of α-haloaziridines.

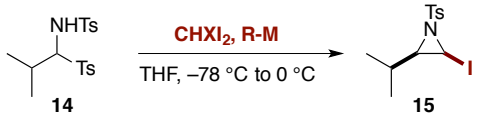
To test this, using phenyl *N*-Boc imine precursor **8**, LiCHICl was formed using LiHMDS and CH_2ICl under reaction conditions developed for α-iodoaziridines (Scheme 3). Both *cis*- and *trans*-substituted α-chloroaziridines were formed (**10** and **11**), but none of the corresponding α-iodoaziridines (CHCl: *cis*, δ 4.77, J = 5.1 Hz *vs*. *trans*, δ 4.53, J = 1.8 Hz). This indicated a preference for the system to displace the better leaving group, rather than for the *cis*-stereochemistry. However, the yield for the *cis*-product was higher than that for the *trans* (*dr* = 3.3:1 **10**:**11** in crude reaction mixture). The intermediate dihalides (**12**) were formed in 1.6:1 *dr* when the reaction was quenched at low temperature, and were isolated in low yield.[24] The *dr* enhancement in the formation of the *cis*-α-chloroaziridine, suggests that the cyclisation to the *cis*-product may remain a lower energy pathway. Finally, the observation of aminal species **13**, suggests the chloroiodomethane is not fully deprotonated under the reaction conditions. The corresponding product was also observed in our studies with *N*-Ts α-iodoaziridines.[15]

2.3. Using diiodomethylmagnesium: an improved protocol for the preparation of alkyl-α-iodoaziridines.

In our studies to date, the use of LiHMDS to deprotonate diiodomethane had provided the highest yield of α-iodoaziridines. In the synthesis of *N*-Ts α-iodoaziridines, the addition of LiHMDS directly to the imine was a significant side product,[25] implying incomplete deprotonation of diiodomethane in the 20 min reaction time prior to addition of the imine. This was confirmed by deuteration studies, whereby treatment of diiodomethane with LiHMDS under our standard protocol and quenching with d_4-MeOD after 20 minutes, revealed only 30% D-incorporation. However, increasing the deprotonation time led to lower overall yields of α-iodoaziridines. Furthermore, the presence of the aminal side-product required a more involved purification of the α-iodoaziridines. Degradation of the aminal to benzaldehyde occurred upon silica gel, which co-eluted with the desired *N*-Ts α-iodoaziridines during chromatography. Therefore purification was performed with deactivated basic alumina.

Due to ongoing further studies using the *N*-Ts α-iodoaziridines in particular, we required multi gram-quantities of alkyl *N*-Ts α-iodoaziridines. Consequently, a more facile procedure to improve both the yield and ease of purification of the reaction was required. Therefore we examined alternative protocols for the formation of $MCHI_2$ reagents, where full formation of the reagent could be achieved.

Table 1. Optimisation of improved procedure for *N*-Ts α-iodoaziridine formation varying diiodomethyl-metal rea-gents.

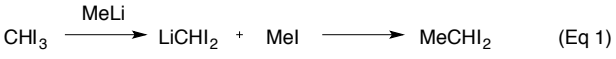


entry [a]	$CHXI_2$ (equiv)	R-M (equiv)	yield **15** (%)[b]

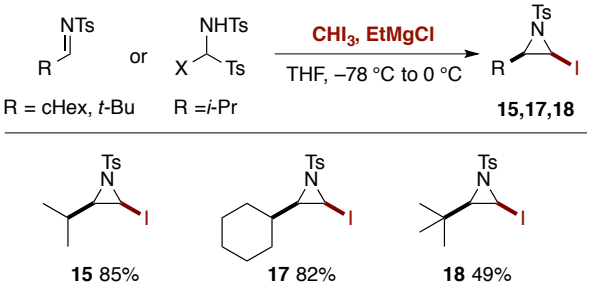
1[c]	CH_2I_2 (4.4)	LiHMDS (4.0)	63
2	CHI_3 (4.0)	*n*-BuLi (4.0)	(65)[d]
3	CHI_3 (4.0)	MeLi (4.0)	0[e]
4	CHI_3 (4.0)	*i*-PrMgCl (4.0)	75
5	CHI_3 (4.0)	EtMgCl (4.0)	87
6	CHI_3 (3.0)	EtMgCl (3.0)	85

[a] Reaction conditions unless specified: imine–HO_2STol adduct (0.50 mmol), CHI_3, R-M, THF (0.26 M at exchange), –78 ºC to 0 ºC. [b] Yield determined by ^1H NMR spectroscopy with reference to an internal standard (1,3,5-trimethoxybenzene). [c] Reaction conditions: imine–HO_2STol adduct (0.50 mmol), *n*-BuLi (2.00 mmol), HMDS (2.00 mmol), CH_2I_2 (2.20 mmol), THF:Et_2O (0.16 M at deprotonation), –78 ºC to 0 ºC. [d] Isolated yield. [e] Diiodoethane formed (see Equation 1).

Under the standard conditions involving deprotonation of CH_2I_2, a 63% yield of α-iodoaziridine **15** was obtained (Table 1, entry 1).[15] The product could also be obtained starting from iodoform, employing *n*-BuLi at low temperature to generate diiodomethyllithium by Li–I exchange, over 3 min prior to the addition of the imine (entry 2). While the yield was comparable, in the absence of LiHMDS, we found that α-iodoaziridine **15** could now be purified using conventional silica gel chromatography. Using MeLi provided no desired α-iodoaziridine under the reaction conditions (entry 3). Interestingly 1,1-diiodoethane (**16**) was observed as the only reaction product due to the reaction of MeI with diiodomethyllithium after the initial Li–I exchange with iodoform (Equation 1).

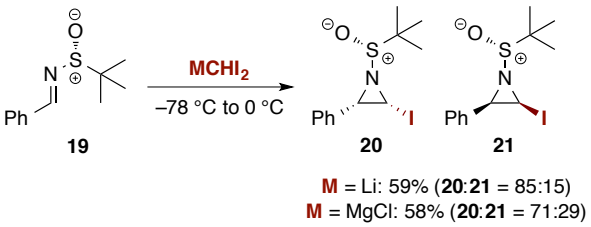


Next we considered magnesium carbenoids, which display similar reactivity to lithium carbenoids but may show increased thermal and configurational stability.[17b,c,26] Methodology developed by Seyferth and Lambert[18b] to form $ClMgCHI_2$ by Mg−I exchange between iodoform and *i*-PrMgCl at low temperature, has recently been adapted by Schmidt for addition to aldehydes.[26a] Formation of $ClMgCHI_2$ using 4.0 equiv of both *i*-PrMgCl and CHI_3 at –78 ºC, followed by addition of the imine precursor **14** and cyclisation by warming (10 min, −78 °C, then 15 min, 0 °C) was very promising (entry 4). We observed an improved yield of 75% for α-iodoaziridine **15**. This was further improved when employing EtMgCl under otherwise identical reaction conditions (entry 5). Finally, we were able to reduce the equivalents of both iodoform and EtMgCl (entry 6), and maintain a good yield of **15**. The previously employed dual solvent system (THF/Et_2O) was not required for the formation and stability of the magnesium carbenoid, meaning THF alone could be used, simplifying the protocol. α-Iodoaziridine **15** was isolated in 85% yield on 3 mmol scale (vs 63% using $LiCHI_2$).[15] These improved conditions were applied to other secondary and tertiary-alkyl *N*-Ts imines enabling the preparation of *N*-Ts α-iodoaziridines **17** and **18** in high yield and purity, exclusively as their *cis*-diastereoisomers (Scheme 4). Notably the excellent *cis*-stereoselectivity remained for the *tert*-butyl example **18**.



Scheme 4. Scope of secondary alkyl substituted α-iodoaziridines utilizing Mg-carbenoids. Reaction conditions: imine−HO_2STol adduct/imine (3.00 mmol), CHI_3 (9.00 mmol), EtMgCl (9.00 mmol), THF (0.26 M at exchange), –78 ºC to 0 ºC.

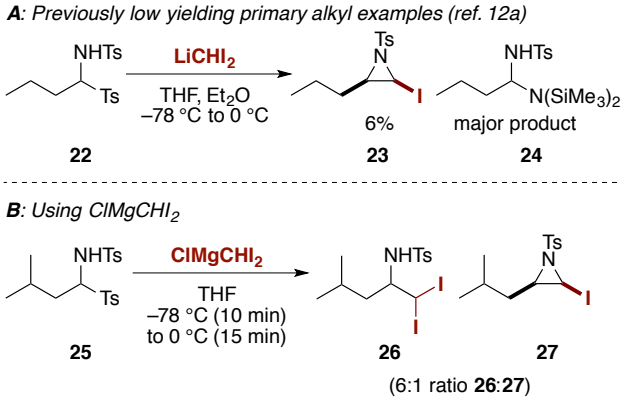
Next we examined the effect of employing $ClMgCHI_2$ with chiral imine **19**, bearing Ellman's auxiliary (Scheme 5). Using $LiCHI_2$ gave rise to a mixture of two enantiopure *cis*-α-iodoaziridines, **20** and **21**, in an 85:15 diastereomeric ratio.[15a] Treatment of imine **19** with $ClMgCHI_2$ afforded a mixture of aziridines **20** and **21**, exclusively the *cis*-diastereoisomers. The major isomer **20** was the same in both cases, here with a reduced 71:29 ratio of diastereoisomers. The addition is proposed to occur via an open transition state.[27] With the Grignard reagent, a chelated, cyclic transition state is plausible, which is likely to reduce the *dr*, though not dominate due to competing coordination of the THF solvent.



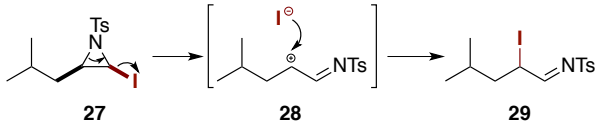
Scheme 5. Effect of changing $MCHI_2$ reagent on the reaction with chiral imines.

2.4. Primary alkyl α-iodoaziridines.

Under our reaction conditions for the formation of *N*-Ts α-iodoaziridines, primary alkyl imine-sulfinic acid adducts suffered from very poor yields and competing nucleophilic addition by LiHMDS, (6% yield for the imine derived from butanal, Scheme 6A). However, generating $LiCHI_2$ by Li–I exchange using *n*-BuLi/CHI_3 only gave a very slight improvement in yield (13% as determined by ^{1}H NMR). We were pleased to find that the use of diiodomethylmagnesium chloride afforded excellent conversion of imine precursor **25** to the corresponding diiodide **26** after 15 min at 0 °C, though only minor conversion to α-iodoaziridine **27** was observed (Scheme 6B). However, a sampling study indicated that while prolonged reaction times at 0 °C did increase conversion to α-iodoaziridine **27**, the rate of cyclisation was slow and the desired α-iodoaziridine product rearranged to iodo-imine **29** (Scheme 7).[28]



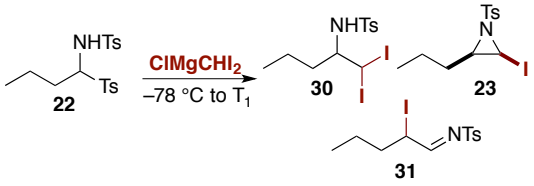
Scheme 6. Formation of primary alkyl α-iodoaziridines using $ClMgCHI_2$.



Scheme 7. Postulated mechanism for rearrangement of α-iodoaziridine **27** to iodo-imine **29**.

This rearrangement is presumed to occur via a unimolecular aziridine-ring opening process, affording cation **28**,[29] which is subsequently trapped with iodide affording iodo-imine **29**. Similar aziridine rearrangements have previously been reported by Yudin, converting bromoaziridines to bromohydrazones,[30] and ourselves in the rearrangement of electron rich *N*-Ts α-iodoaziridines to iodo-imines.[15a,31] Attempting to control the conversion to the desired α-iodoaziridine and prevent rearrangement to the corresponding iodo-imine, we examined the influence of reaction time at different temperatures with imine–HSO_2Tol adduct **22** (Table 2).

Table 2. Optimisation of improved procedure for primary *N*-Ts α-iodoaziridine using $ClMgCHI_2$.



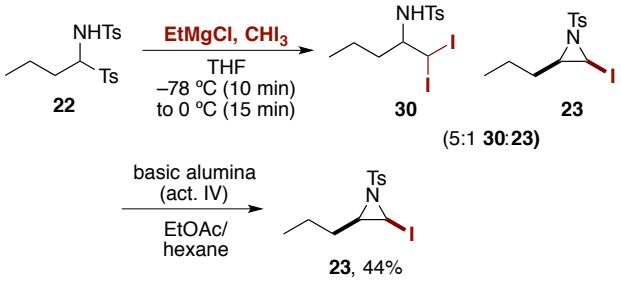
entry[a]	T_1 / °C	t_1 (min)	yield (%)[b]		
			30	**23**	**31**
1	0	15	81	16	0
2	0	30	77	22	0
3	0	45	69	31	0
4	15	15	41	18	5
5	30	15	15	7	10

[a] Reaction conditions: imine–HO_2STol adduct (0.50 mmol), CHI_3 (4.0 equiv), *i*-PrMgCl (4.0 equiv), THF (0.26 M at exchange). [b] Yield determined by ^{1}H NMR spectroscopy with reference to an internal standard (1,3,5-trimethoxybenzene).

Increasing the time at 0 ºC from 15 min to 45 min led to an increase in the proportion of cyclised product (entries 1-3). However, increased times led to degradation and rearrangement. Unfortunately, warming to 15 °C (entry 4), led to significant degradation of the reaction mixture, with a lower recovery observed. The thermal instability of the reaction mixture was further evident with warming to 30 °C for 15 min (entry 5), with α-iodoaziridine **23** rearranging to iodo-imine **31**.

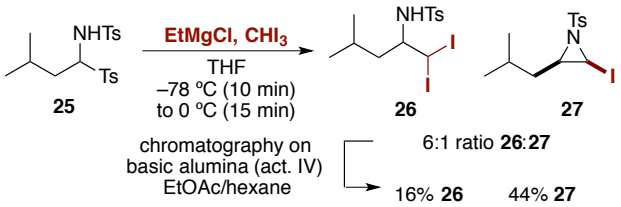
We therefore examined the possibility of isolating diiodide **30** to perform cyclisation in a second step. Under conditions outlined in Table 2 (entry 1), the crude reaction mixture (5:1 **30**:**23**) was subjected to purification using deactivated basic alumina (activity IV). To

our surprise, this resulted in cyclization to the desired α-iodoaziridine, promoted by the basic solid phase, in a modest, but much improved, 44% yield (Scheme 8).



Scheme 8. Formation of primary alkyl *N*-Ts α-iodoaziridine **23** via treatment with deactivated basic alumina (activity IV).

Pleasingly this was similarly successful with imine adduct **25** (Scheme 9). With warming to 0 ºC we observed minimal cyclisation in the crude reaction mixture with diiodide **26** as the major product. Passing this mixture through a column of basic alumina (activity IV) again promoted cyclisation to the desired α-iodoaziridine **27** in a 44% isolated yield. Small quantities of remaining diiodide **26** were also isolated. This approach represents a significant improvement to the reaction protocol for primary imines versus the same imine–HSO_2Tol adduct with $LiCHI_2$, which only yielded 6% of corresponding α-iodoaziridine **23**.



Scheme 9. Formation of primary alkyl *N*-Ts α-iodoaziridine **27** via treatment with deactivated basic alumina (activity IV).

3. Conclusion

In conclusion we have demonstrated that a variety of *N*-groups (carbamate, sulfonyl and sulfinyl) are suitable for the synthesis of α-iodoaziridines, often in excellent *cis*-selectivity. The exception is when carbamates contain aromatic rings, which afforded an increase in the *trans*-product possibly due to π-π interactions. The use of LiCHICl also led to the formation of aziridines, as a mixture of *cis* and *trans*-chloroaziridines. The corresponding iodides are not observed indicating a strong preference for cyclisation through the better leaving group, rather than an essential preference for *cis*-stereochemistry. These observations are supportive of our model that the usual *cis* preference is due to unfavourable steric interactions in the transition state that would lead to the *trans*-product.

The use of $ClMgCHI_2$ has been shown to be superior to the use of $LiCHCI_2$ for the synthesis of alkyl *N*-Ts α-iodoaziridines. A modified, more straightforward procedure provided improved yields and workup procedure. The perfect *cis*-selectivity is maintained. This protocol has enabled the synthesis of primary, secondary and tertiary alkyl substituted α-iodoaziridines. Further reactivity of these α-iodoaziridines will be reported in due course.

4. Experimental Section

All nonaqueous reactions were run under an inert atmosphere (argon) with flame-dried glassware using standard techniques. Anhydrous solvents were obtained by filtration through drying columns (THF, Et_2O, CH_2Cl_2, hexane). Flash column chromatography was performed using 230-400 mesh silica or 50-200 μm Brockmann basic alumina (activity IV) with the indicated solvent system according to standard techniques. Analytical thin-layer chromatography (TLC) was performed on precoated, glass-backed silica gel plates. Visualisation of the developed chromatogram was performed by UV absorbance (254 nm), aqueous potassium permanganate stain, ninhydrin solution in ethanol, phosphomolybdic acid solution in ethanol, or a vanillin solution. Infrared spectra (ν_{max}, FTIR ATR) were recorded in reciprocal centimeters (cm^{-1}). Nuclear magnetic resonance spectra were recorded on 400 MHz spectrometers. Chemical shifts for ^1H NMR spectra are recorded in parts per million from tetramethylsilane with the solvent resonance as the internal standard (chloroform, δ = 7.27 ppm). Data is reported as follows: chemical shift [multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet and br = broad), coupling constant in Hz, integration, assignment]. ^{13}C NMR spectra were recorded with complete proton decoupling. Chemical shifts are reported in parts per million from tetramethylsilane with the solvent resonance as the internal standard ($^{13}CDCl_3$: 77.0 ppm). *J* values are reported in Hz. Assignments of $^1H/^{13}C$ spectra were made by the analysis of δ/*J* values, and COSY, HSQC, and HMBC experiments as appropriate. α-Iodoaziridines and diiodides decomposed upon heating (>100 °C), therefore accurate melting points have not been determined. *Reagents*: HMDS was freshly distilled over KOH pellets under an Ar atmosphere prior to use. All other commercial reagents were used as supplied, or purified by standard techniques where necessary. *Procedure for obtaining deactivated basic alumina:* Commercial alumina is classed as activity I. To alter the activity to basic alumina (activity IV), 10% w/v water must be added to basic alumina (activity I) and evenly distributed.[15,32] *Imine synthesis*: *N*-Carbamate imine–HSO_2Tol adducts were prepared according to the procedure of Jacobsen.[33] *N*-[(*E*)-Phenylmethylidene]-4-methyl-benzenesulfonamide was prepared according to the method of Chemla.[34,15] 2-Methyl-*N*-(phenylmethylidene)-propane-2-sulfonamide was prepared by oxidation of (*R*)-(+)-2-methyl-*N*-(phenylmethylidene)propane-2-sulfinamide **19**[35] according to the procedure of Ruano.[36]

4.1. General Procedure A: Synthesis of N-carbamate α-Iodoaziridines using LiHMDS.

Diiodomethane (145 μL, 1.80 mmol, 3.0 equiv) in THF (1.6 mL) was added dropwise to a solution of LiHMDS (1 M solution in THF, 1.56 mL, 1.56 mmol, 2.6 equiv) in THF (6.0 mL) and Et_2O (3.0 mL) at −78 °C in the dark. After 20 minutes at −78 °C, a solution of the imine−HSO_2Tol adduct (0.60 mmol, 1.0 equiv) in THF (2.0 mL) was added dropwise to the reaction mixture. After 10 minutes at −78 °C, the reaction flask was transferred to a water bath at the specified temperature for 10 minutes and then quenched by the addition of saturated aqueous sodium bicarbonate solution (30 mL). The aqueous mixture was extracted with CH_2Cl_2 (3 × 30 mL). The organic extracts were combined, dried (Na_2SO_4), filtered and the solvent removed under reduced pressure. Purification by flash chromatography afforded the *cis*-α-iodoaziridine.

*4.1.1. cis-(±)-2-Iodo-3-phenyl-1-tert-butoxycarbonylaziridine (**1**).*

Prepared according to General Procedure A described above, starting from imine–HO_2STol adduct **8** (217 mg, 0.60 mmol), warming to 30 °C. Purification by flash chromatography (10% Et_2O/hexane) afforded *cis*-α-iodoaziridine **1** (172 mg, 83%) as a colourless oil: R_f = 0.37 (20% Et_2O/hexane); ν_{max} (film)/cm^{-1} 2981, 1724 (C=O), 1610, 1496, 1478, 1458, 1399, 1372, 1320, 1306, 1285, 1258, 1230, 1147, 1078, 1029; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43–7.34 (m, 5H, 5 × Ph-H), 4.72 (d, J = 5.4 Hz, 1H, CHI), 3.59 (d, J = 5.4 Hz, 1H, CHPh), 1.51 (s, 9H, C(CH_3)$_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.6 (C=O quat.), 134.8 (Ph-C quat.), 128.4 (Ph-C), 128.0 (2 × Ph-C), 127.5 (2 × Ph-C), 82.9 (*C*(CH_3)$_3$ quat.), 43.1 (PhCHN), 27.9 (C(*C*H_3)$_3$), 18.2 (CHI); HRMS (ESI$^+$) *m/z* Calculated for $C_{13}H_{17}INO_2^+$ [M+H]$^+$: 346.0298; Found: 346.0295.

*4.1.2. cis-(±)-2-Iodo-3-phenyl-1-ethoxycarbonylaziridine (**2**).*

Prepared according to General Procedure A described above, starting from [(phenyl-(toluene-4-sulfonyl)-methyl]-ethyl-carbamate (200 mg, 0.60 mmol, 1.0 equiv), warming to rt. Purification by flash chromatography (10% Et_2O/hexane) afforded *cis*-α-iodoaziridine **2** (114 mg, 60%) as a colourless oil: R_f = 0.32 (20% EtOAc/hexane); ν_{max} (film)/cm^{-1} 2989, 1727 (C=O), 1610, 1458, 1401, 1369, 1301, 1268, 1226, 1183, 1100, 1025, 757, 698; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43–7.34 (m, 5H, 5 × Ph-H), 4.76 (d, J = 5.4 Hz, 1H, CHI), 4.29 (q, J = 7.1 Hz, 2H, OC*H*$_2$CH$_3$), 3.65 (d, J = 5.4 Hz, 1H, CHPh), 1.34 (t, J = 7.1 Hz, 3H, OCH$_2$C*H*$_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.8 (C=O quat.), 134.4 (Ph-C quat.), 128.5 (Ph-C), 128.1 (2 × Ph-C), 127.4 (2 × Ph-C), 63.4 (O*C*H$_2$CH$_3$), 43.2 (PhCHN), 17.8 (CHI), 14.3 (OCH$_2$*C*H$_3$); HRMS (ESI$^+$) *m/z* Calculated for $C_{11}H_{13}INO_2^+$ [M+H]$^+$: 317.9991; Found: 317.9998.

*4.1.3. cis-(±)-2-Iodo-3-phenyl-1-methoxycarbonylaziridine (**3**).*

Prepared according to General Procedure A described above, starting from [(phenyl-(toluene-4-sulfonyl)-methyl]-methyl-carbamate[37] (202 mg, 0.63 mmol), warming to rt. Purification by flash chromatography (10% Et_2O/hexane) afforded *cis*-α-iodoaziridine **3** (107 mg, 56%) as a colourless oil: R_f = 0.32 (20% EtOAc/hexane); ν_{max} (film)/cm^{-1} 2956, 1725 (C=O), 1508, 1437, 1403, 1319, 1301, 1270, 1225, 1196, 1015, 963, 915, 813, 750, 698; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41–7.34 (m, 5H, 5 × Ph-H), 4.77 (d, J = 5.4 Hz, 1H, CHI), 3.83 (s, 3H, OCH_3), 3.67 (d, J = 5.4 Hz, 1H, CHPh); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.2 (C=O quat.), 134.2 (Ph-C quat,), 128.5 (Ph-C), 128.1 (2 × Ph-C), 127.4 (2 × Ph-C), 54.1 (OCH_3), 43.2 (PhCHN), 17.6 (CHI); HRMS (ESI$^+$) *m/z* Calculated for $C_{10}H_{11}INO_2$ [M+H]$^+$: 303.9834; Found: 303.9848.

*4.1.4. cis-(±)-2-Bromo-3-phenyl-1-tert-butoxycarbonylaziridine (**9**).*

Prepared according to General Procedure A described above, starting from dibromomethane (126 μL, 1.80 mmol, 3.0 equiv) and imine−HSO_2Tol adduct **8** (217 mg, 0.60 mmol, 1.0 equiv), warming to 30 °C. Purification by flash chromatography (10% EtOAc/hexane) afforded *cis*-α-bromoaziridine **9** (53 mg, 30%) as a colourless oil: R_f = 0.25 (10% EtOAc/hexane); ν_{max} (film)/cm^{-1} 2982, 1726 (C=O), 1303, 1279, 1257, 1233, 1156, 907, 730, 698; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43–7.35 (m, 5H, 5 × Ph-H), 4.87 (d, J = 5.1 Hz, 1H, CHBr), 3.75 (d, J = 5.1 Hz, 1H, CHPh), 1.52 (s, 9H, C(CH_3)$_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.3 (C=O quat.), 133.2 (Ph-C quat.), 128.4 (Ph-C), 128.0 (2 × Ph-C), 127.8 (2 × Ph-C), 83.0 (*C*(CH_3)$_3$ quat.), 44.7 (CHBr), 44.1 (CHN), 27.9 (C(*C*H_3)$_3$); HRMS (CI) *m/z* Calculated for $C_{13}H_{17}{}^{79}Br\,NO_2^+$ [M+H]$^+$: 298.0443; Found: 298.0450.

*4.1.5. cis-(±)-2-Chloro-3-phenyl-1-tert-butoxycarbonylaziridine (**10**)* and *trans-(±)-2-chloro-3-phenyl-1-tert-butoxycarbonylaziridine (**11**).*

Prepared according to General Procedure A described above, starting from chloroiodomethane (131 μL, 1.80 mmol, 3.0 equiv) and imine−HSO_2Tol adduct **8** (217 mg, 0.60 mmol, 1.0 equiv), warming to 30 °C. Purification by flash chromatography (hexane grading to 10% EtOAc/hexane) afforded *trans*-α-chloroaziridine **11** (11 mg, 7%) as a yellow oil, followed by *cis*-α-chloroaziridine **10** (55 mg, 36%) as a yellow oil.

11: R_f = 0.44 (10% EtOAc/hexane); ν_{max} (film)/cm^{-1} 2878, 1726 (C=O), 1483, 1457, 1394, 1369, 1309, 1252, 1228, 1154, 1080, 1042, 942, 841, 733, 697; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.33 (m, 3H, 3 × Ph-H), 7.27–7.25 (m, 2H, 2 × Ph-H), 4.53 (d, J = 1.8 Hz, 1H, CHCl), 3.67 (d, J = 1.8 Hz, 1H, CHPh), 1.42 (s, 9H, C(CH_3)$_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.9 (C=O quat.), 133.7 (Ph-C quat.), 128.64 (Ph-C), 128.62 (2 × Ph-C), 126.8 (2 × Ph-C), 82.9 (*C*(CH_3)$_3$ quat.), 52.1 (CHCl), 477 (CHN), 27.8 (C(*C*H_3)$_3$); HRMS (CI) *m/z* Calculated for $C_{13}H_{20}ClN_2O_2^+$ [M+NH_4]$^+$: 271.1206; Found: 271.1213.

10: R_f = 0.30 (10% EtOAc/hexane); ν_{max} (film)/cm^{-1} 2982, 1728 (C=O), 1396, 1370, 1321, 1283, 1257, 1150, 853, 748, 696; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42–7.35 (m, 5H, 5 × Ph-H), 4.77 (d, J = 5.1 Hz, 1H, CHCl), 3.78 (d, J = 5.1 Hz, 1H, CHPh), 1.52 (s, 9H, C(CH_3)$_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.4 (C=O quat.), 132.3 (Ph-C quat.), 128.3 (Ph-C), 128.1 (2 × Ph-C), 127.9 (2 × Ph-C), 83.0 (*C*(CH_3)$_3$ quat.), 54.4 (CHCl), 44.9 (CHN), 27.9 (C(*C*H_3)$_3$); HRMS (CI) *m/z* Calculated for $C_{13}H_{17}ClNO_2^+$ [M+H]$^+$: 254.0948; Found: 254.0946.

4.2. General Procedure B: Synthesis of N-Sulfonyl α-Iodoaziridines using LiHMDS.

n-BuLi (1.50 mmol, 3.0 equiv) was added dropwise to a solution of hexamethyldisilazane (315 μL, 1.50 mmol, 3.0 equiv) in THF (5.7 mL) and Et_2O (2.7 mL) at –78 °C. After 30 minutes, diiodomethane (135 μL, 1.70 mmol, 3.4 equiv) in THF (1.0 mL) was added dropwise to the reaction mixture at –78 °C in the dark. After 20 minutes at −78 °C, a solution of the appropriate imine (0.50 mmol, 1.0

equiv) in THF (2.0 mL) was added dropwise to the reaction mixture over 5 minutes. The reaction was then immediately warmed to 0 °C in an ice bath and left at this temperature for 15 minutes. The reaction was then quenched by the addition of saturated aqueous sodium bicarbonate solution (40 mL). The aqueous solution was extracted with CH_2Cl_2 (3 × 30 mL), then the combined organic layers were dried (Na_2SO_4), filtered and the solvent removed under reduced pressure. Purification by flash chromatography on deactivated basic alumina (activity IV or activity V) afforded the *cis*-**α**-iodoaziridine.

*4.2.1. cis-(±)-2-Iodo-3-phenyl-1-(4-tolylsulfonyl)aziridine (**6**).*

Prepared according to General Procedure B described above, starting from *N*-[(*E*)-phenylmethylidene]-4-methyl-benzene-sulfonamide (130 mg, 0.50 mmol). Purification by flash chromatography (10% EtOAc/hexane) on deactivated basic alumina (activity IV) afforded *cis*-α-iodoaziridine **6** (152 mg, 76%) as a yellow oil: R_f = 0.24 (15% Et_2O/hexane); ν_{max} (film)/cm^{-1} 3035, 2928, 1600, 1499, 1453, 1330, 1157, 1088, 902, 813, 763, 727, 696, 683, 666; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 8.5 Hz, 2H, 2 × SO_2Tol-H), 7.42−7.33 (m, 5H, 3 ×Ph-H and 2 × SO_2Tol-H), 7.31−7.25 (m, 2H, 2 × Ph-H), 4.89 (d, J = 6.1 Hz, 1H, CHI), 3.89 (d, J = 6.1 Hz, 1H, CHPh), 2.47 (s, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.3 (SO_2C-Tol quat.), 134.1 (SO_2Tol*C*-CH_3 quat.), 132.9 (PhC quat.), 129.9 (2 × SO_2Tol-C), 128.7 (Ph-C), 128.1 (2 × SO_2Tol-C), 127.8 (2 × Ph-C), 127.5 (2 × Ph-C), 44.9 (PhCN), 21.7 (SO_2Tol-CH_3), 16.4 (CHI); HRMS (ESI$^+$) *m/z* Calculated for $C_{15}H_{15}INO_2S^+$ $[M+H]^+$ 399.9863; Found 399.9856.

*4.2.2. cis-(±)-2-Iodo-1-(2-methylpropane-2-sulfonyl)-3-phenylaziridine (**7**).*

Prepared according to General Procedure B described above, starting from 2-methyl-*N*-(phenylmethylidene)propane-2-sulfonamide (113 mg, 0.50 mmol). Purification by flash chromatography (5% EtOAc/hexane) on deactivated basic alumina (activity IV) afforded *cis*-α-iodoaziridine **7** (82 mg, 45%) as a yellow oil: R_f = 0.24 (15% Et_2O/hexane); ν_{max} (film)/cm^{-1} 2987, 1457, 1314, 1249, 1175, 1126, 905, 862, 765, 730, 699, 670; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46−7.35 (m, 5H, 5 × Ph-H), 4.90 (d, J = 6.0 Hz, 1H, CHI), 3.86 (d, J = 6.0 Hz, 1H, CHPh), 1.58 (s, 9H, C(CH_3)$_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 133.1 (Ph-C quat.), 128.9 (Ph-C), 128.3 (2 × Ph-C), 127.7 (2 × Ph-C), 60.1 (*C*(CH_3)$_3$ quat.), 43.3 (CHN), 24.0 (C(*C*H_3)$_3$), 19.0 (CHI); HRMS (ESI$^+$) *m/z* Calculated for $C_{12}H_{17}INO_2S^+$ $[M+H]^+$ 366.0019; Found 366.0021.

4.3. General Procedure C: Synthesis of N-Sulfonyl Iodoaziridines using ClMgCHI$_2$.

EtMgCl (2 M in THF, 4.50 mL, 9.00 mmol, 3.0 equiv) was added dropwise over 2 minutes to a solution of iodoform (3.54 g, 9.00 mmol, 3.0 equiv) in THF (34 mL) at −78 °C in the dark. After 10 minutes at −78 °C, a solution of the appropriate imine or imine−HSO_2Tol adduct (3.00 mmol, 1.0 equiv) in THF (8 mL) was added dropwise over 3 minutes. The reaction was left for 10 minutes at −78 °C and then warmed to 0 °C in an ice/water bath. After 15 minutes at 0 °C, the reaction was quenched by the addition of saturated aqueous sodium bicarbonate solution (100 mL). The aqueous solution was extracted with CH_2Cl_2 (3 × 100 mL) and the organic extracts were combined, dried (Na_2SO_4), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (silica, hexane grading to 10% EtOAc/hexane) afforded the *cis*-α-iodoaziridine**.**

*4.3.1. cis-(±)-2-Iodo-3-(propan-2-yl)-1-(4-tolylsulfonyl)aziridine (**15**).*

Prepared according to General Procedure C described above, starting from imine−HO_2STol adduct **14** (1.14 g, 3.00 mmol). Purification by flash chromatography (10% EtOAc/hexane) afforded *cis*-α-iodoaziridine **15** (930 mg, 85%) as a yellow solid: R_f = 0.21 (10% EtOAc/hexane); ν_{max} (film)/cm^{-1} 2963, 2931, 2874, 1597, 1466, 1403, 1329, 1244, 1156, 1089, 1026, 954, 885, 831, 813, 734, 684, 667; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, J = 8.3 Hz, 2H, 2 × SO_2Tol-H), 7.36 (d, J = 8.3 Hz, 2H, 2 × SO_2Tol-H), 4.54 (d, J = 5.9 Hz, 1H, CHI), 2.46 (s, 3H, SO_2Tol-CH_3), 2.20 (dd, J = 9.7, 5.9 Hz, 1H, CHN), 1.92 (dqq, J = 9.7, 6.7, 6.7 Hz, 1H, C*H*(CH_3)$_2$), 0.99 (d, J = 6.7 Hz, 3H, CH(C*H*$_3$)$_2$), 0.92 (d, J = 6.7 Hz, 3H, CH(C*H*$_3$)$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.1 (SO_2Tol-C quat.), 134.3 (SO_2Tol*C*-CH_3 quat.), 129.8 (2 × SO_2Tol-C), 128.0 (2 × SO_2Tol-C), 49.3 (CHN), 31.5 (*C*H(CH_3)$_2$), 21.7 (SO_2Tol-CH_3), 20.0 (CH_3), 17.9 (CH_3), 13.8 (CHI); HRMS (ESI$^+$) *m/z* Calculated for $C_{12}H_{17}INO_2S^+$ $[M+H]^+$: 366.0019; Found: 366.0034.

*4.3.2. cis-(±)-2-Iodo-3-cyclohexyl-1-(4-tolylsulfonyl)aziridine (**17**).*

Prepared according to General Procedure C described above, starting from *N*-[(*E*)-cyclohexylmethylidene]-4-methyl-benzene-sulfonamide (796 mg, 3.00 mmol). Purification by flash chromatography (10% EtOAc/hexane) afforded *cis*-α-iodoaziridine **17** (999 mg, 82%) as a yellow solid: R_f = 0.18 (10% Et_2O/hexane); ν_{max} (film)/cm^{-1} 2926, 2851, 1598, 1450, 1330, 1242, 1158, 1090, 968, 900, 883, 814, 732, 669; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, J = 8.2 Hz, 2H, 2 × SO_2Tol-H), 7.37 (d, J = 8.2 Hz, 2H, 2 × SO_2Tol-H), 4.53 (d, J = 6.0 Hz, 1H, CHI), 2.47 (s, 3H, SO_2Tol-CH_3), 2.26 (dd, J = 9.4, 6.0 Hz, 1H, CHCy), 1.84−1.71 (m, 2H, 2 × Cy-H), 1.70−1.62 (m, 2H, 2 × Cy-H), 1.60−1.53 (m, 1H, Cy-H), 1.33−0.99 (m, 6H, 6 × Cy-H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.0 (SO_2Tol-C quat.), 134.4 (SO_2Tol*C*-CH_3 quat.), 129.8 (2 × SO_2Tol-C), 128.0 (2 × SO_2Tol-C), 47.8 (CHN), 40.1 (CH), 30.3 (CH_2), 28.3 (CH_2), 25.9 (CH_2), 25.2 (CH_2), 25.1 (CH_2), 21.7 (SO_2Tol-CH_3), 13.5 (CHI); HRMS (ESI$^+$) *m/z* Calculated for $C_{15}H_{21}INO_2S^+$ $[M+H]^+$: 406.0332; Found: 406.0328.

*4.3.3. cis-(±)-2-Iodo-3-(tert-butyl)-1-(4-tolylsulfonyl)aziridine (**18**).*

Prepared according to General Procedure C described above, starting from *N*-[(*E*)-2,2-dimethylpropylidene]-4-methyl-benzenesulfonamide (718 mg, 3.00 mmol, 1.0 equiv). Purification by flash chromatography (hexane grading to 10% EtOAc/hexane) afforded *cis*-α-iodoaziridine **18** (553 mg, 49%) as a yellow oil: R_f = 0.31 (10% EtOAc/hexane); ν_{max} (film)/cm^{-1} 2964, 2874, 1600, 1330, 1258, 1158, 1089, 953, 931, 852, 734, 677, 667; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, J = 8.2 Hz, 2H, 2 × SO_2Tol-H), 7.36 (d, J = 8.2 Hz, 2H, 2 × SO_2Tol-H), 4.36 (d, J = 6.4 Hz, 1H, CHI), 2.45 (s, 3H, SO_2Tol-CH_3), 2.43 (d, J = 6.4, 1H, HCC(CH_3)$_3$), 0.98 (s, 9H, C(C*H*$_3$)$_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.0 (SO_2Tol-C quat.), 134.1 (SO_2Tol*C*-CH_3 quat.), 129.7 (2 × SO_2Tol-C), 128.0 (2 × SO_2Tol-C), 50.2 (H*C*C(CH_3)$_3$), 31.4 (*C*(CH_3)$_3$ quat.), 27.0 (C(*C*H_3)$_3$), 21.7 (SO_2Tol-CH_3), 6.6 (CHI); HRMS (ESI$^+$) *m/z* Calculated for $C_{13}H_{19}INO_2S^+$ $[M+H]^+$ 380.0181; Found 380.0203.

*4.3.4. (2R,3S)-2-Iodo-1-[(R)-2-methylpropane-2-sulfinyl]-3-phenylaziridine (major, **20**)* and *(2S,3R)-2-Iodo-1-[(R)-2-methylpropane-2-sulfinyl]-3-phenylaziridine (minor, **21**).*

Using $ClMgCHI_2$: Prepared according to General Procedure C described above, starting from imine **19** (105 mg, 0.50 mmol). Purification by flash chromatography (hexane grading to 10% EtOAc/hexane) on silica gel afforded a mixture of *cis*-α-iodoaziridines (71:29 major:minor) **20** and **21** (101 mg, 58%) as a yellow oil:

Using $LiCHI_2$: Prepared according to General Procedure B described above, starting from imine **19** (105 mg, 0.50 mmol). Purification by flash chromatography (5% EtOAc/hexane) on deactivated basic alumina (activity V) afforded a mixture of *cis*-α-iodoaziridines (85:15 major:minor) **20** and **21** (103 mg, 59%) as a yellow oil.

R_f = 0.36 (25% EtOAc/hexane); $[\alpha]_D^{18}$ –21.3° (*c* 0.66, $CHCl_3$; 85:15 major:minor); ν_{max} (film)/cm^{-1} 2960, 2867, 1605, 1495, 1475, 1454, 1363, 1312, 1238, 1170, 1080, 1026, 906, 847, 817, 791, 758, 699, 676; **20:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43–7.33 (m, 5H, 5 × Ph-H), 4.54 (d, *J* = 6.0 Hz, 1H, CHI), 3.71 (d, *J* = 6.0 Hz, 1H, CHPh), 1.20 (s, 9H, C(CH_3)$_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 133.8 (Ph-C quat.), 128.5 (Ph-C), 128.2 (2 × Ph-C), 128.1 (2 × Ph-C), 57.5 (CHPh), 35.4 (*C*(CH_3)$_3$), 22.6 (C(*C*H_3)$_3$), 17.8 (CHI); **21:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43–7.33 (m, 5H, 5 × Ph-H), 4.83 (d, *J* = 5.9 Hz, 1H, CHI), 3.30 (d, *J* = 5.9 Hz, 1H, CHPh), 1.41 (s, 9H, C(CH_3)$_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 134.7 (Ph-C quat.), 128.4 (Ph-C), 128.0 (2 × Ph-C), 127.7 (2 × Ph-C), 58.6 (CHPh), 38.6 (*C*(CH_3)$_3$), 23.3 (C(*C*H_3)$_3$), 15.4 (CHI); HRMS (ESI^+) *m/z* Calculated for $C_{12}H_{17}INOS^+$ $[M+H]^+$ 350.0070; Found 350.0078.

*4.3.5. cis-(±)-2-Iodo-3-propyl-1-(4-tolylsulfonyl)aziridine (**23**).*

EtMgCl (2 M in THF, 0.75 mL, 1.50 mmol, 3.0 equiv) was added dropwise over 2 minutes to a solution of iodoform (591 mg, 1.50 mmol, 3.0 equiv) in THF (6 mL) at −78 °C in the dark. After 10 minutes at −78 °C, a solution of imine−HO_2STol adduct **22** (191 mg, 0.50 mmol) in THF (2 mL) was added dropwise over 3 minutes. The reaction was left for 10 minutes at −78 °C and then warmed to 0 °C in an ice/water bath. After 15 minutes at 0 °C, the reaction was quenched by the addition of saturated aqueous sodium bicarbonate solution (20 mL). The aqueous solution was extracted with CH_2Cl_2 (3 × 30 mL) and the organic extracts were combined, dried (Na_2SO_4), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (hexane grading to 10% EtOAc/hexane) on deactivated basic alumina (activity IV) afforded *cis*-α-iodoaziridine **23** (80 mg, 44%) as a yellow oil: R_f = 0.23 (10% EtOAc/hexane); ν_{max} (film)/cm^{-1} 2960, 2931, 2873, 1598, 1331, 1245, 1160, 1090, 902, 717; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.3 Hz, 2H, 2 × SO_2Tol-H), 7.37 (d, *J* = 8.3 Hz, 2H, 2 × SO_2Tol-H), 4.55 (d, *J* = 6.0 Hz, 1H, CHI), 2.60−2.55 (m, 1H, CHN), 2.47 (s, 3H, SO_2Tol-CH_3), 1.57−1.40 (m, 4H, 2 × CH_2), 0.95 (t, *J* = 7.3 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.0 (SO_2Tol-C quat.), 134.5 (SO_2Tol*C*-CH_3 quat.), 129.8 (2 × SO_2Tol-C), 127.9 (2 × SO_2Tol-C), 43.6 (CHN), 33.5 (CH_2), 21.7 (SO_2Tol-CH_3), 19.7 (CH_2), 14.5 (CH_3), 13.6 (CHI); HRMS (ESI^+) *m/z* Calculated for $C_{12}H_{17}INO_2S^+$ $[M+H]^+$: 366.0019; Found: 366.0031.

*4.3.6. cis-(±)-2-Iodo-3-(2-methylpropyl)-1-(4-tolylsulfonyl)aziridine (**27**) and N-(1,1-Diiodo-4-methylpentan-2-yl)-4-tolyl-1-sulfonamide (**26**).*

EtMgCl (2 M in THF, 0.75 mL, 1.50 mmol, 3.0 equiv) was added dropwise over 2 minutes to a solution of iodoform (591 mg, 1.50 mmol, 3.0 equiv) in THF (6 mL) at −78 °C in the dark. After 10 minutes at −78 °C, a solution of imine−HO_2STol adduct **25** (198 mg, 0.50 mmol) in THF (2 mL) was added dropwise over 3 minutes. The reaction was left for 10 minutes at −78 °C and then warmed to 0 °C in an ice/water bath. After 15 minutes at 0 °C, the reaction was quenched by the addition of saturated aqueous sodium bicarbonate solution (20 mL). The aqueous solution was extracted with CH_2Cl_2 (3 × 30 mL) and the organic extracts were combined, dried (Na_2SO_4), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (hexane grading to 10% EtOAc/hexane) on deactivated basic alumina (activity IV) afforded *cis*-α-iodoaziridine **27** (83 mg, 44%) as a yellow oil, followed by amino *gem*-diiodide **26** (40 mg, 16%) as a white solid.

26: R_f = 0.17 (10% EtOAc/hexane); ν_{max} (film)/cm^{-1} 3243, 2959, 1417, 1330, 1162, 1093, 1036, 962, 917, 814, 665; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 7.9 Hz, 2H, 2 × SO_2Tol-H), 7.34 (d, *J* = 7.9 Hz, 2H, 2 × SO_2Tol-H), 5.27−5.26 (m, 1H, CHI_2), 4.93 (d, *J* = 8.3 Hz, 1H, NH), 2.91−2.84 (m, 1H, CHN), 2.46 (s, 3H, SO_2Tol-CH_3), 1.70−1.60 (m, 1H, CH), 1.47−1.35 (m, 2H, CH_2), 0.88 (t, *J* = 6.4 Hz, 3H, CH_3), 0.66 (t, *J* = 6.3 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.1 (SO_2Tol-C quat.), 137.3 (SO_2Tol*C*-CH_3 quat.), 129.9 (2 × SO_2Tol-C), 127.1 (2 × SO_2Tol-C), 59.1 (CHN), 43.2 (CH_2), 24.1 (CH), 23.3 (CH_3), 21.6 (SO_2Tol-CH_3), 21.2 (CH_3), −11.6 (CHI_2).

27: R_f = 0.31 (10% EtOAc/hexane); ν_{max} (film)/cm^{-1} 2956, 2872, 1597, 1467, 1329, 1246, 1158, 1089, 999, 904, 813, 714; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.3 Hz, 2H, 2 × SO_2Tol-H), 7.36 (d, *J* = 8.3 Hz, 2H, 2 × SO_2Tol-H), 4.54 (d, *J* = 5.9 Hz, 1H, CHI), 2.63 (dt, *J* = 7.0, 6.1 Hz, 1H, CHN), 2.46 (s, 3H, SO_2Tol-CH_3), 1.77−1.67 (m, 1H, CH), 1.51−1.42 (m, 2H, CH_2), 0.98 (t, *J* = 6.7 Hz, 3H, CH_3), 0.95 (t, *J* = 6.7 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.0 (SO_2Tol-C quat.), 134.5 (SO_2Tol*C*-CH_3 quat.), 129.8 (2 × SO_2Tol-C), 127.8 (2 × SO_2Tol-C), 42.6 (CHN), 40.1 (CH_2), 26.3 (CH), 22.5 (CH_3), 22.3 (CH_3), 21.7 (SO_2Tol-CH_3), 14.9 (CHI); HRMS (ESI^+) *m/z* Calculated for $C_{13}H_{19}INO_2S^+$ $[M+H]^+$: 380.0176; Found: 380.0195.

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24. Compound **12** was isolated in a low yield as an inseparable 1.6:1 mixture of diastereoisomers, which were rotameric on the NMR timescale at rt. The relative configuration of the isomers was not assigned. Assignment of the *dr* was determined by examination of the 1H NMR spectrum of the complex crude mixture and integration of signals at δ 5.53 and δ 5.39 presumed to correspond to the CHICl protons. See Supporting Information for 1H NMR spectrum.

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