Metal-catalysed reactions of imines with ethyl diazoacetate leading to aziridines

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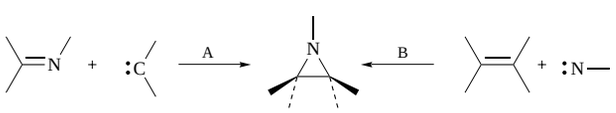
The metal-catalysed aziridination of imines with ethyl diazoacetate as the carbene fragment donor using various Lewis acids as the catalyst has been investigated. The catalytic properties of different Lewis acid complexes have been tested and it has been found that both main-group complexes, such as $BF_3{\cdot}OEt_2$, early- and late-transition metal complexes, such as $TiCl_2(O\text{-}Pr^i)_2$, $Cu(OTf)_2$ and $Zn(OTf)_2$ and rare-earth metal complexes, such as $Yb(OTf)_3$, can catalyse the formation of aziridines. The aziridination gives mainly the *cis*-aziridines as the major diastereoisomer, but the selectivity is dependent on the substrate, catalyst and solvent. $Zn(OTf)_2$ and $Yb(OTf)_3$ have been shown to be general catalysts for the formation of various aziridines using different imines and a variety of reaction conditions. Both $Zn(OTf)_2$ and $Yb(OTf)_3$, as well as some of the other Lewis acids, in combination with various chiral ligands, have been tested as catalysts for the formation of optically active aziridines, but only low ees are obtained. The $Zn(OTf)_2$- and $Yb(OTf)_3$-catalysed reactions have been investigated for imines having both electron-donating and -withdrawing substituents, and in reactions containing diethyl fumarate as a trapping reagent, in attempts to obtain insight into the mechanism of the aziridination.

Introduction

The development of catalysts for selective organic synthesis is a field in rapid progress. An attractive area in catalytic chemistry is the metal-catalysed coupling of 'simple' organic molecules to give higher functionalised molecules. Until now the formation of epoxides from alkenes and an oxygen donor has received considerable interest, whereas the catalytic formation of the nitrogen analogue, aziridines has been less examined.

Aziridines can be used as versatile precursors for the synthesis of a variety of organic compounds such as the unnatural amino acids and other nitrogen-compounds of biological importance.[1] Various methods are available for the preparation of enantiomerically pure aziridines, but most of them are laborious multi-step reactions, where either optically pure starting materials or stoichiometric amounts of a chiral auxiliary are used.[2–5]

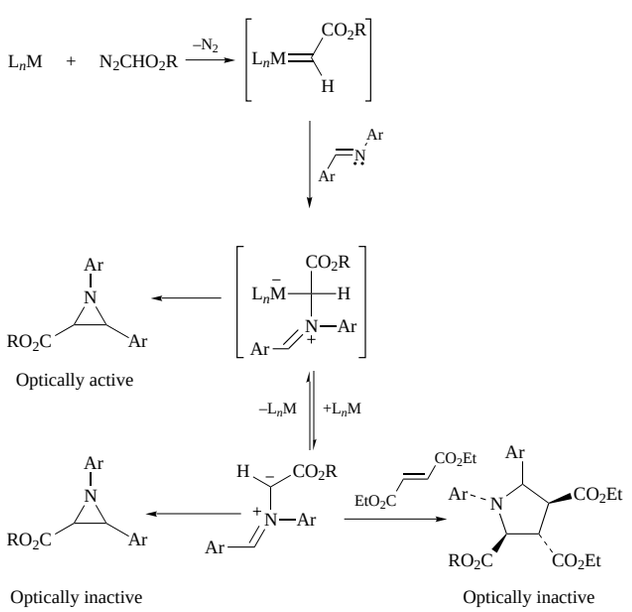
The simplest catalytic formation of aziridines is, in principle, either the addition of a carbene fragment to an imine (Scheme 1, route A) or the addition of a nitrene fragment to an alkene (Scheme 1, route B).



Scheme 1

The catalytic preparation of aziridines as outlined in Scheme 1 has been achieved. The formation of aziridines from alkenes and nitrenes (Scheme 1, route B) has been studied by several groups. Probably the most successful approach has been the catalytic activation of (*p*-tolylsulfonylimino)phenyliodinane, PhI=NTs, using various copper salts,[6] bis(4,4′-disubstituted oxazoline)copper complexes[6] and chiral copper-Schiff bases[7] as the catalysts. Other metal complexes, such as iron porphyrin,[8] manganese salens[9,10] and rhodium acetate[11] were found to be less active compared with the copper complexes. In the case of rhodium acetate, it has been found that using (*p*-nitrophenylsulfonylimino)phenyliodinane, PhI=NNs, instead of PhI=NTs leads to a smooth formation of the corresponding aziridine in good yields; however, no enantiomeric excess (ee) was obtained when chiral ligands were used in combination with the rhodium catalyst.[11]

The formation of aziridines from imines and diazoacetates by route B (Scheme 1) has received much less attention compared with route A (Scheme 1).[12] The first attempts were based on the use of copper salts in combination with chiral (bis)dihydrooxazoles and ethyl diazoacetate as the carbene fragment donor.[13,14] The aziridines were formed in relatively good yields (10–90%), but the ee was low, except in a few cases.[13,14] The formation of aziridines according to route A, Scheme 1 has also been pursued using rhodium acetate and other rhodium complexes as the catalyst with ethyl diazoacetate as the carbene fragment donor, but here also only a moderate yield of the aziridine was obtained.[15] Based on the relatively low ee, and trapping experiments using diethyl fumarate or dimethyl maleate as the trapping reagent, both in the copper- and the rhodium-catalysed aziridination, the mechanism outlined in Scheme 2 was proposed (*vide infra*).[13,15] Very recently

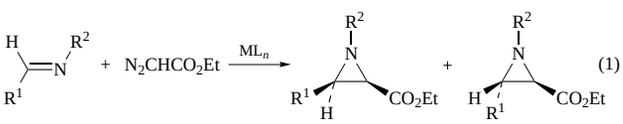


Scheme 2

hexahydro-1,3,5-triazines were found to react with different alkyl diazoacetates in the presence of $SnCl_4$ as the catalyst to give aziridine-2-carboxylates,[16] and similar aziridines were formed when methylrhenium trioxide was used as a catalyst for the reaction of imines and ethyl diazoacetate (EDA).[17]

The first step in the mechanism in Scheme 2 is the formation of a transient metal–carbene species; this species can react with the imine by a nucleophilic attack of the imine-nitrogen lone pair electrons at the carbon atom of the metal–carbene species to form a metal-complexed azomethine ylide. This ylide can either undergo intramolecular ring closure to form the aziridine, or it may dissociate from the metal–ligand complex. If the former reaction takes place enantioselectivity can be introduced in this step if a chiral ligand is coordinated to the metal. If the latter reaction takes place, the ylide formed can, by an intramolecular cyclisation, form the optically inactive aziridine or be trapped by diethyl fumarate—if present—to give the pyrrolidine. The reaction of diethyl fumarate is an important test for the presence of an ylide during the reaction course.[13]

This paper presents a general study of the Lewis acid-catalysed reaction of imines with EDA (route A, Scheme 1) [eqn. (1)]. We will focus on the aziridination catalysed by differ-



1a–f **2** **3a–f** **4a–f**

a $R^1 = R^2 = Ph$
b $R^1 = Ph$, $R^2 = p\text{-}MeOC_6H_4$
c $R^1 = Ph$, $R^2 = Bu^t$
d $R^1 = Ph$, $R^2 = p\text{-}ClC_6H_4$
e $R^1 = Ph$, $R^2 = o\text{-}HOC_6H_4$
f $R^1 = Bu^t$, $R^2 = Ph$

ent Lewis acids and compare the results obtained with the results for mainly the copper-catalysed aziridination.

Results and discussion

The catalytic properties of various metal salts for the formation of the aziridines **3** and **4** have been tested for the reaction of *C*,*N*-diphenyl imine **1a** ($R^1 = R^2 = Ph$) with EDA **2**. The yield and diastereoselectivity of the aziridines **3a** ($R^1 = R^2 = Ph$) and **4a** ($R^1 = R^2 = Ph$) are presented in Table 1.

The results in Table 1 show that of the metal complexes studied, $BF_3{\cdot}Et_2O$, $TiCl_2(Pr^iO)_2$, $Zn(OTf)_2$ and $Yb(OTf)_3$ act also, together with $Cu(OTf)_2$ and $Rh_2(OAc)_4$, as catalysts for the formation of the aziridines **3a** and **4a** using EDA as the carbene fragment donor and the imine **1a** as the substrate. The reactions have all been carried out under a standard set of conditions with no attempts to optimise the yield. The yield of **3a** and **4a** are comparable but, more importantly, a significantly improvement of the diastereoselectivity is often observed, especially when $Yb(OTf)_3$ is used as the catalyst (Table 1, entry 5). The low yield in the reaction catalysed by $TiCl_2(Pr^iO)_2$ (entry 3) is due to the instability of the aziridine, which is found to undergo titanium(IV)-catalysed nucleophilic ring-opening by the chloride ion.

The Lewis acids $Zn(OTf)_2$ and $Yb(OTf)_3$ were found to be the best catalysts of those tested for the aziridination. Thus, we have used these two Lewis acids as catalysts for the reaction of some representative imines **1b**,**c** and **f** with EDA. The results (not optimised) are presented in Table 2.

Use of the imines **1b** and **1f**, both *N*-phenyl substituted imines, as the substrate, gave the aziridines **3b** and **f**, **4b** and **f** in a total yield of 40–48%, whereas use of the imine **1c**, an *N*-*tert*-butyl substituted imine, gave only traces of **3c** using $Zn(OTf)_2$ as the catalyst. The diastereoselectivity is greatly affected by the

Table 1 The catalytic properties of various metal salts for the formation of the aziridines **3a** and **4a** have been tested for the reaction of the imine **1a** with EDA **2** in CH_2Cl_2

Entry	Catalyst	Reac. temp. (°C)	**3a**:**4a**[a]	Total yield[b] (%)
1	$Cu(OTf)_2$	−25	1.7:1	(80)
2	$BF_3{\cdot}OEt_2$	−30	8:1	55
3	$TiCl_2(OPr^i)_2$	20	>20:1	(10)
4	$Zn(OTf)_2$	20	1.4:1	50
5	$Yb(OTf)_3$	0	25:1	52

[a] Determined by ^{1}H NMR spectroscopy of the crude product. [b] Isolated yield. Yields in brackets were determined by ^{1}H NMR spectroscopy of the crude product.

Table 2 The catalytic properties of various metal salts for the formation of the aziridines **3b**,**c** and **f** and **4b**,**c** and **f** have been tested for the reaction of the imine **1b**,**c** and **f** with EDA **2** in CH_2Cl_2

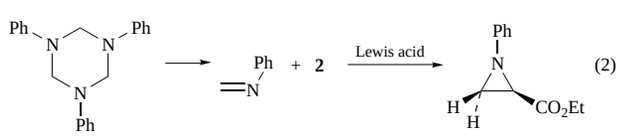
Entry	Imine	Catalyst	Reac. temp. (°C)	**3**:**4**[a]	Total yield (%)
1	**1b**	$Zn(OTf)_2$	20	2.3:1	40
2	**1b**	$Yb(OTf)_3$	0	16:1	45
3	**1c**	$Zn(OTf)_2$	20	>25:1	(2)
4	**1c**	$Yb(OTf)_3$	0	—	—
5	**1f**	$Zn(OTf)_2$	20	1:1.8	48
6	**1f**	$Yb(OTf)_3$	0	1:2	41

[a] Determined by ^{1}H NMR spectroscopy of the crude product. [b] Isolated yield. Yields in brackets were determined by ^{1}H NMR spectroscopy of the crude product.

Table 3 The catalytic properties of various metal salts for the formation of *N*-phenylaziridine-2-carboxylate **3g** have been tested for the reaction of the imine **1g** (= **5**) with EDA **2** in CH_2Cl_2

Entry	Catalyst	Reac. temp. (°C)	Yield[a] (%)
1	$BF_3{\cdot}OEt_2$	−30	63
2	$Zn(OTf)_2$	20	76
3	$Yb(OTf)_3$	0	70

[a] Isolated yield.



5 **1g** **3g**

imine substituents and the catalyst. The imines derived from benzaldehyde **1a**,**b** and **c** gave the *cis*-aziridine as the major product, whereas the *trans*-aziridine is the major product of the imine derived from trimethylacetaldehyde **1f**. For the reaction of **1a** (see Table 1) and **b** the diastereoselectivity is highly dependent on the catalyst as $Zn(OTf)_2$ gives a *cis*:*trans* ratio of the aziridine of 1.4:1 and 2.3:1, respectively, whereas $Yb(OTf)_3$ gives 25:1 and 16:1, respectively.

The reaction of the imine **1g**, which exists as a trimeric compound **5**, with EDA in the presence of different Lewis acids as catalysts was also examined [eqn. (2)]. The results (not optimised) using $BF_3{\cdot}Et_2O$, $Zn(OTf)_2$ and $Yb(OTf)_3$ as the catalyst are presented in Table 3.

The results in Table 3 show that $BF_3{\cdot}Et_2O$, $Zn(OTf)_2$ and $Yb(OTf)_3$ all catalyse the formation of ethyl *N*-phenylaziridine-2-carboxylate **3g** in good yield, an interesting reaction, since nucleophilic ring-opening of the aziridine can lead to α- and β-amino esters, β-lactams and alkaloids. The catalytic properties of the Lewis acids $BF_3{\cdot}Et_2O$, $Zn(OTf)_2$ and $Yb(OTf)_3$ for the reaction in eqn. (2) are comparable to the use of $Cu(OTf)_2$,[14] but the Lewis acids react probably by a different mechanism compared with $Cu(OTf)_2$ (*vide infra*).

Table 4 The catalytic properties of $Zn(OTf)_2$ for the formation of the aziridines **3a**, **4a**, **3b** and **4b** have been tested for the reaction of the imines **1a** and **1b** with EDA **2** in different solvents

Entry	Imine	Solvent	Reac. temp. (°C)	**3**:**4**[a]	Total yield[b] (%)
1	**1a**	CH_2Cl_2	20	1.4:1	50
2	**1a**	Heptane	20	>25:1	43
3	**1a**	$MeNO_2$	0	6:1	50
4	**1b**	CH_2Cl_2	20	2.3:1	40
5	**1b**	Heptane	20	7:1	27
6	**1b**	$MeNO_2$	0	9:1	65

[a] Determined by ^{1}H NMR spectroscopy of the crude product. [b] Isolated yield.

The influence of the solvent in the Lewis acid-catalysed aziridination has also been investigated. The results of the reaction of the imines **1a** and **1b** with EDA catalysed by $Zn(OTf)_2$ in CH_2Cl_2, heptane and $MeNO_2$, respectively are presented in Table 4.

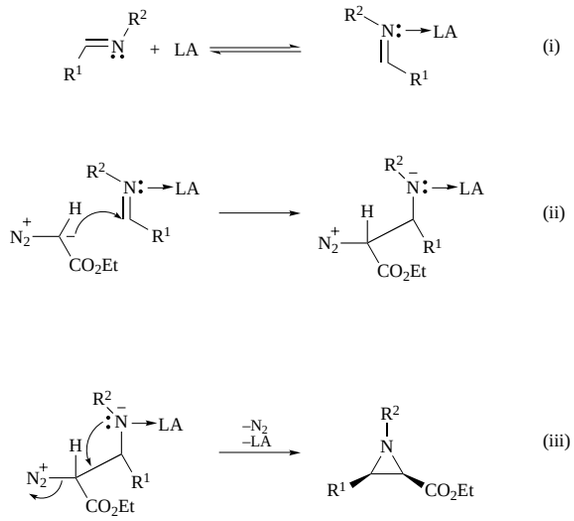
Use of heptane as the solvent gave slightly lower yields for both imines examined compared with the reactions in CH_2Cl_2 and $MeNO_2$; the latter solvent gives the highest yield of the aziridines of the different solvents tested. That the diastereoselectivity in the aziridination is dependent on the solvent is shown by the fact that both heptane and $MeNO_2$ increase the *cis*-diastereoselectivity compared with CH_2Cl_2 as the solvent. The reaction rate is also dependent on the solvent as it decreases with heptane and increases with $MeNO_2$.

The reaction of imine **1a** with EDA in the presence of $Zn(OTf)_2$ and $Yb(OTf)_3$ as the catalyst has been studied in the presence of diethyl fumerate in an attempt to trap an azomethine ylide, if formed, during the reaction course (see Scheme 2). Using the same reaction conditions as used for the $Cu(PF_6)(MeCN)_4$-[13] and $Rh_2(OAc)$[15]-catalysed aziridination, where the azomethine ylide was trapped by diethyl fumerate or dimethyl maleate to form the pyrrolidine, *no* spectroscopic evidence for the formation of the pyrrolidine is observed in the present reactions. Futhermore, the aziridines **3a** and **4a** are formed to the same extent, and with the same diastereoselecitivity, as in the reactions in the absence of diethyl fumarate. It is also important to notice that under the present reaction conditions products formed from dimerisation of EDA, diethyl fumarate and diethyl maleate, are *not* observed. These observations might indicate that the reaction mechanism for the formation of the aziridines catalysed by $Zn(OTf)_2$ and $Yb(OTf)_3$ probably is different compared with the $Cu(PF_6)(MeCN)_4$-[13] and $Rh_2(OAc)_4$[15]-catalysed aziridination.

The reaction of the imines **1a**,**b**,**d** and **e** with EDA in the presence of $Yb(OTf)_3$ in [$^2H_3$]-MeCN has also been studied in an attempt to investigate the influence of electron-donating and -withdrawing substituents on the reaction rate. The formation of the corresponding aziridines **3a**,**b**,**d** and **e** and **4a**,**b**,**d** and **e** was followed by ^{1}H NMR spectroscopy. The spectroscopic studies show that the unsubstitued aziridines **3a** and **4a** and the *p*-chloro substituted aziridines **3d** and **4d** are formed with comparable rates, whereas the *p*-methoxy substituted aziridines **3b** and **4b** are formed significantly slower. On the other hand, the *o*-hydroxy substituted aziridines **3e** and **4e** are formed faster than the other aziridines studied, indicating that the *o*-hydroxy substitutent is important for the catalytic process (*vide infra*). It should also be noted that in all the reactions the **3**:**4** ratio was ≈2:1, showing that the electronic factor on the diastereoselectivity is diminishing.

Based on the trapping- and reaction-rate experiments we propose the reaction mechanism outlined in Scheme 3 for the $Zn(OTf)_2$ and $Yb(OTf)_3$ catalysed aziridination.

The first step (i) in the mechanism outlined in Scheme 3 is the coordination of the Lewis acid [LA = $Zn(OTf)_2$ or $Yb(OTf)_3$] to the nitrogen atom in the imine. The next step (ii), which

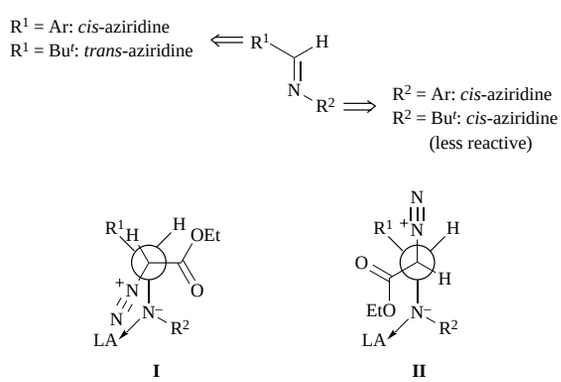


Scheme 3

probably is the rate-determining step (an electron-donating substituent in the *para*-position decreases the reaction rate), is a nucleophilic attack of EDA on the C=N double bond followed by (iii) a nucleophilic attack of the nitrogen atom on the carbon atom with N_2 as the leaving group. The mechanism in Scheme 3 is very different from the one proposed in Scheme 2 for the $Cu(PF_6)(MeCN)_4$-[13] and $Rh_2(OAc)_4$[15]-catalysed aziridination, as the Lewis acid activates the imine in the present aziridinations, while in Scheme 2 the metal complex reacts with EDA with elimination of N_2 and the formation of a metal–carbene species.

The diastereoselectivity of the aziridination is dependent both on the substitutents of the imine, the catalyst and the reaction conditions. With regard to the imine we have found the following trends for the diastereoselectivity.

For imines having $R^1 = R^2 = Ar$ and $R^2 = Bu^t$, it is proposed that the nucleophilic attack of the carbon atom of EDA takes place with the ethyl ester group of the incoming EDA placed over the C-hydrogen atom of the imine to reduce the steric repulsion (Scheme 4, I). In order for the nitrogen atom to per-

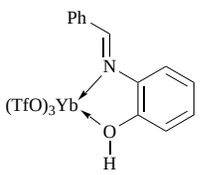


Scheme 4

form the nucleophilic attack on the carbon atom with N_2 as the leaving group a rotation around the newly formed carbon–carbon bond is necessary placing the ester- and R^1 substituent *cis* as outlined in Scheme 4, II. This approach thus leads to the formation of *cis*-aziridines and seems to be *substrate dependent*. To account for the formation of the *trans*-aziridines as the major diastereoisomer when $R^1 = Bu^t$ and $R^2 = Ar$, the hydrogen atom and the ester group in EDA in Scheme 4, I and II have to be exchanged. We propose that the reaction path leading to *trans*-aziridines is *product dependent*, as the last step, the nucleophilic attack of the nitrogen atom at the carbon atom, leads to a minimum steric repulsion between the ethyl substitu-

ent of the ester group and the *tert*-butyl (R^1) substituent, compared with the proposal outlined in Scheme 4, I and II, where a significant steric repulsion between the ester group and the *tert*-butyl (R^1) substituent will be present in the product aziridine.

The increase in reaction rate of the *o*-hydroxy-substituted imine **1e** compared with the corresponding *p*-methoxy substituted imine **1b**, is proposed to be caused by a coordination of the catalyst, such as $Yb(OTf)_3$ to both the nitrogen- and oxygen atoms of **1e** leading to **6**.



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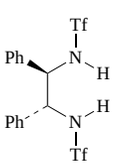
The bidentate coordination of **1e** to $Yb(OTf)_3$ changes the electronic properties of the hydroxy substituent in **1e**. To account for the increased reactivity of **1e** it is proposed that the coordination of the Lewis acid to **1e** leads to an increase in the removal of electron density from the carbon atom of the imine making it more prone to the nucleophilic attack by EDA, compared with the other imines.

The aziridination using aluminium-, boron-, zinc- and ytterbium complexes as catalyst has also been performed in the presence of various chiral ligands in an attempt to obtain optically active aziridines. The chiral ligands studied are the C_2-symmetric ligands **7**–**11**.



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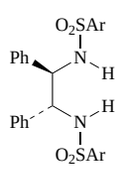
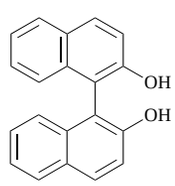


8a R = C_6H_4Me-*p*
8b R = $C_6H_4NO_2$-*p*



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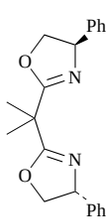

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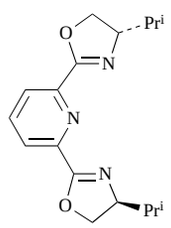

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Attempts to perform asymmetric aziridinations using the above mentioned Lewis acids as catalysts for the reaction of mainly *C*,*N*-diphenyl imine **1a** with EDA were performed under a variety of reaction conditions for the following combinations of the catalyst and ligand: $ZnMe_2$·**7**, $AlMe_3$·**9**, BBr_3·**8a**, BBr_3·**9**, $Zn(OTf)_2$·**10**, $ZnMe_2$·**8a**, $ZnMe_2$·**8b**, $ZnMe_2$·**9**, $Yb(OTf)_3$·**9** and $Yb(OTf)_3$·**11**. Although it was assumed that higher ees could be achieved if the formation of the achiral ylide intermediate was suppressed discouraging results were obtained. Generally the ees were all in the range 5–15% and, furthermore, a reduced catalytic activity of the metal complexes was often observed.

Note added in proof. After the submission of the manuscript two papers have appeared in *Journal of Organic Chemistry* dealing with metal-catalysed aziridination.[19,20] Tempelton, Brookhart *et al.* describe the use of BF_3·OEt_2, $AlCl_3$ and $TiCl_4$ for the synthesis of aziridines,[19] while Aggarwal *et al.* use a combination of sulfur ylides and metal complexes for catalytic asymmetric aziridination.[20]

Experimental

The ^{1}H NMR and ^{13}C NMR spectra were obtained in a Varian Gemini at 300 MHz and 75 MHz, respectively. Chemical shifts for ^{1}H NMR and ^{13}C NMR are recorded in $CDCl_3$ and reported in ppm downfield from tetramethylsilane (TMS). Enantiomeric excess was determined by HPLC using a 4.6 mm × 25 cm DAICEL CHIRALCEL OD column and 1% Pr^iOH in hexane as the eluent.

Materials

The imines were prepared from the corresponding amines and aldehydes.[18] Compounds **1a**,**b**,**d**,**e** and **5** were recrystallised from EtOH. Compounds **1c** and **f** were dried with $MgSO_4$ and distilled before use. $TiCl_2(OPr^i)_2$ was made from $TiCl_4$ (2.5 mmol) and $Ti(O^iPr)_4$ (2.5 mmol) mixed in dry CH_2Cl_2 to a total volume of 50.0 ml. EDA, $AlMe_3$, BF_3·Et_2O, $Zn(OTf)_2$, $ZnMe_2$ and $Yb(OTf)_3$ were commercially available from Aldrich and used as received. CH_2Cl_2 and $MeNO_2$ were dried over CaH_2. Heptane was dried over Na. The solvents were distilled before use.

General procedure for the reaction of imines with EDA catalysed by various Lewis acids

The Lewis acid (0.1 mmol) was added to a 10-ml Schlenk flask which was evacuated and filled twice with Ar. The solvent (4 ml) was added followed by the imine (1.5 mmol) and EDA (1.0 mmol). In the reactions where BF_3·Et_2O was used as the catalyst, the solvent was added to the flask before adding the catalyst. In the reactions at other temperatures than 20 °C the reaction mixture was cooled before the addition of EDA. When the evolution of N_2 ceased the reaction mixture was filtered through a plug of silica gel, which was washed with additional CH_2Cl_2 (3 ml). When using $MeNO_2$ as solvent the reaction mixture was poured onto ice and the product was extracted with a mixture of light petroleum and Et_2O. The organic phase was dried (Na_2SO_4), filtered, and evaporated *in vacuo* to give the crude product which was analysed by ^{1}H NMR spectroscopy. The crude product was then purified by flash chromatography on silica gel using 2–10% EtOAc–light petroleum as eluent to give the pure aziridines.

^{1}H and ^{13}C NMR data

Ethyl *cis*-1,3-diphenylaziridine-2-carboxylate 3a.[13] δ_H 0.99 (t, *J* 7.2, 3 H), 3.20 (d, *J* 6.6, 1 H), 3.60 (d, *J* 6.6, 1 H), 3.95–4.09 (m, 2 H), 7.03–7.10 (m, 3 H), 7.24–7.39 (m, 5 H) and 7.49–7.54 (m, 2 H); δ_C 13.9, 45.5, 47.1, 61.0, 119.9, 123.6, 127.7, 127.9, 128.1, 129.2, 134.6, 152.4 and 167.7.

Ethyl *trans*-1,3-diphenylaziridine-2-carboxylate 4a.[13] δ_H 1.16 (t, *J* 7.1, 3 H), 3.23 (d, *J* 2.2, 1 H), 3.80 (d, *J* 2.2, 1 H), 4.12 (q, *J* 7.1, 2 H), 6.85–6.91 (m, 2 H), 6.94–7.02 (m, 1 H), 7.18–7.26 (m, 2 H) and 7.32 (br s, 5 H); δ_C 14.0, 45.8, 46.3, 61.3, 119.9, 122.8, 126.8, 128.0, 128.5, 128.8, 136.2, 148.4 and 167.6.

Ethyl *cis*-1-(*p*-methoxyphenyl)-3-phenylaziridine-2-carboxylate 3b.[19] δ_H 0.98 (t, *J* 7.1, 3 H), 3.14 (d, *J* 6.9, 1 H), 3.53 (d, *J* 6.9, 1 H), 3.76 (s, 3 H), 3.93–4.08 (m, 2 H), 6.82 (d, *J* 9.3, 2 H), 7.00 (d, *J* 9.3, 2 H), 7.27–7.37 (m, 3 H) and 7.49–7.52 (m 2 H); δ_C 13.8, 45.8, 48.4, 56.4, 60.9, 114.3, 120.7, 127.6, 127.7, 128.0, 134.4, 145.7, 155.8 and 167.7; *m/z* 297 (26%), 251 (22%) and 224 (100%).

Ethyl *trans*-1-(*p*-methoxyphenyl)-3-phenylaziridine-2-carboxylate 4b. δ_H 1.19 (t, *J* 7.2, 3 H), 3.21 (d, *J* 2.2, 1 H), 3.74 (s, 3 H), 3.78 (d, *J* 2.2, 1 H), 4.13 (q, *J* 7.2, 2 H), 6.75–6.84 (m, 4 H) and 7.31 (br s, 5 H); δ_C 14.1, 45.9, 46.5, 55.4, 61.3, 114.2, 120.8, 126.9, 128.0, 128.4, 136.1, 141.6, 155.3 and 167.7; *m/z* 297 (41%), 251 (22%) and 224 (100%).

Ethyl *cis*-1-(*p*-chlorophenyl)-3-phenylaziridine-2-carboxylate 3d. ν_{max}(film)/cm^{-1} 1748, 1490 and 1190; δ_H 0.99 (t, *J* 7.1, 3 H), 3.18 (d, *J* 6.8, 1 H), 3.57 (d, *J* 6.8, 1 H), 3.95–4.09 (m, 2 H), 6.98–7.03 (m, 2 H), 7.21–7.38 (m, 5 H) and 7.48–7.51 (m, 2 H); δ_C 13.9, 45.7, 47.3, 61.1, 121.2, 127.6, 128.0, 128.1, 128.5, 129.2,

134.2, 151.0 and 167.3; *m/z* 301.084 ($C_{17}H_{16}ClNO_2$ requires 301.086, 17%), 272 (9%), 256 (24%) and 228 (100%).

Ethyl *trans*-1-(*p*-chlorophenyl)-3-phenylaziridine-2-carboxylate 4d. ν_{max}(film)/cm^{-1} 1735, 1490 and 1189; δ_H 1.20 (t, *J* 7.1, 3 H), 3.23 (d, *J* 2.2, 1 H), 3.76 (d, *J* 2.2, 1 H), 4.15 (q, *J* 7.1, 2 H), 6.81 (d, *J* 8.8, 2 H), 7.17 (d, *J* 8.8, 2 H) and 7.27–7.37 (m, 5 H); δ_C 14.1, 45.8, 46.6, 61.5, 121.2, 126.8, 127.8, 128.2, 128.6, 128.9, 135.6, 147.1 and 167.4; *m/z* 301.084 ($C_{17}H_{16}ClNO_2$ requires 301.086, 16%), 272 (8%), 256 (25%) and 228 (100%).

Ethyl *cis*-1-(*o*-hydroxyphenyl)-3-phenylaziridine-2-carboxylate 3e. ν_{max}(film)/cm^{-1} 1727, 1495, 1274 and 752; δ_H 1.02 (t, *J* 7.1, 3 H), 3.00 (d, *J* 6.6, 1 H), 3.83 (d, *J* 6.6, 1 H), 4.05 (q, *J* 7.1, 2 H), 6.62 (s, 1 H) 6.82–6.84 (m, 2 H), 6.95–7.03 (m, 2 H), 7.29–7.37 (m, 3 H) and 7.47–7.50 (m, 2 H); δ_C 13.9, 45.1, 47.7, 61.6, 115.4, 117.5, 120.2, 125.2, 127.2, 128.1, 128.3, 134.0, 137.2, 150.9 and 167.6; *m/z* 283.121 ($C_{17}H_{17}NO_3$ requires 283.120, 50%) and 210 (100%).

Ethyl *cis*-3-*tert*-butyl-1-phenylaziridine-2-carboxylate 3f.[19] δ_H 1.08 (s, 9 H), 1.34 (t, *J* 7.2, 3 H), 2.22 (d, *J* 7.1, 1 H), 2.76 (d, *J* 7.1, 1 H), 4.19–4.38 (m, 2 H), 6.98–7.02 (m, 3 H) and 7.22–7.26 (m, 2 H); δ_C 14.1, 27.4, 31.9, 43.1, 55.4, 61.2, 119.9, 122.9, 129.0, 153.6 and 169.6.

Ethyl *trans*-3-*tert*-butyl-1-phenylaziridine-2-carboxylate 4f.[19] δ_H 1.03 (s, 9 H), 1.06 (t, *J* 7.1, 3 H), 2.63 (d, *J* 2.8, 1 H), 3.02 (d, *J* 2.8, 1 H), 4.00 (q, *J* 7.1, 2 H), 6.81–6.87 (m, 2 H), 6.90–6.98 (m, 1 H) and 7.16–7.24 (m, 2 H); δ_C 13.9, 26.7, 30.8, 39.1, 54.1, 60.9, 119.6, 122.3, 128.7, 149.8 and 168.2.

Ethyl 1-phenylaziridine-2-carboxylate 3g. ν_{max}(film)/cm^{-1} 1744, 1492 and 1194; δ_H 1.32 (t, *J* 7.2, 3 H), 2.30 (dd, *J* 1.6, 6.6, 1 H), 2.65 (dd, *J* 1.6, 2.7, 1 H), 2.79 (dd, *J* 2.7, 6.1, 1 H), 4.18–4.30 (m, 2 H), 6.96–7.04 (m, 3 H) and 7.20–7.27 (m, 2 H); δ_C 14.1, 33.6, 37.5, 61.3, 120.5, 123.2, 128.1, 152.3 and 169.9; *m/z* 191.096 ($C_{11}H_{13}NO_2$ requires 191.094, 60%), 162 (97%) and 104 (100%).

References

1 D. Tanner, *Angew. Chem., Int. Ed. Engl.*, 1994, **33**, 599.
2 See *e.g.*: J. W. Kelly, N. L. Eskew and S. A. Evans, *J. Org. Chem.*, 1986, **51**, 95.
3 See *e.g.*: (*a*) J. Legters, L. Thijs and B. Zwanenburg, *Tetrahedron Lett.*, 1989, **30**, 4881; (*b*) D. Tanner and P. Somfai, *Tetrahedron Lett.*, 1987, **28**, 1211.
4 See *e.g.*: T. Satoh, T. Sato, T. Oohara and K. Yamakawa, *J. Org. Chem.*, 1989, **54**, 3973.
5 See *e.g.*: J. L. G. Ruano, I. Fernández and C. Hamdouchi, *Tetrahedron Lett.*, 1995, **36**, 295.
6 (*a*) D. A. Evans, M. M. Faul and M. T. Bilodeau, *J. Am. Chem. Soc.*, 1994, **116**, 2742; (*b*) *J. Org. Chem.*, 1991, **56**, 6744; (*c*) D. A. Evans, M. M. Faul, M. T. Bilodeau, B. A. Anderson and D. M. Barnes, *J. Am. Chem. Soc.*, 1993, **115**, 5328; (*d*) D. A. Evans, K. A. Woerpel, M. M. Hinman and M. M. Faul, *J. Am. Chem. Soc.*, 1991, **113**, 726; (*e*) A. M. Harm, J. G. Knight and G. Stemp, *Tetrahedron Lett.*, 1996, **37**, 6189.
7 (*a*) Z. Li, K. R. Conser and E. N. Jacobsen, *J. Am. Chem. Soc.*, 1993, **115**, 5326; (*b*) W. Zhang, N. H. Lee and E. N. Jacobsen, *J. Am. Chem. Soc.*, 1994, **116**, 116; (*c*) Z. Li, R. W. Quan and E. N. Jacobsen, *J. Am. Chem. Soc.*, 1995, **117**, 5889.
8 J.-P. Mahy, G. Bedi, P. Battioni and D. Mansuy, *J. Chem. Soc., Perkin Trans.* 2, 1988, 1517.
9 K. J. O'Conner, S.-J. Wey and C. J. Burrows, *Tetrahedron Lett.*, 1992, **33**, 1001.
10 K. Noda, N. Hosoya, R. Irie and T. Katsuki, *Synlett*, 1993, 469.
11 P. Müller, C. Baud and Y. Jacueier, *Tetrahedron*, 1996, **52**, 1543.
12 It should be noted that aziridines have been observed previously when an imine is mixed with a diazoacetate in the presence of a metal complex: (*a*) P. Baret, H. Buffet and J.-L. Pierre, *Bull. Soc. Chim. Fr.*, 1972, 2493; (*b*) A. J. Hubert, A. Feron, R. Warin and P. Teyssi, *Tetrahedron Lett.*, 1976, 1317; (*c*) R. Bartnik and G. Mloston, *Synthesis*, 1983, 924.
13 K. B. Hansen, N. S. Finney and E. N. Jacobsen, *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 676.
14 K. G. Rasmussen and K. A. Jørgensen, *J. Chem. Soc., Chem. Commun.*, 1995, 1401.
15 M. Moran, G. Bernardinelli and P. Müller, *Helv. Chem. Acta*, 1996, **78**, 2048.
16 H.-J. Ha, K.-H. Kang, J.-M. Suh and Y.-G. Ahn, *Tetrahedron Lett.*, 1996, **37**, 7069.
17 (*a*) Z. Zhu and J. H. Esperson, *J. Am. Chem. Soc.*, 1996, **118**, 9901; (*b*) *J. Org. Chem.*, 1995, **60**, 7090.
18 L. A. Bigalow and H. Eatough, *Org. Synth.*, Coll. Vol. I, 1932, 73.
19 L. Casarrubios, J. A. Pérez, M. Brookhart and J. L. Tempelton, *J. Org. Chem.*, 1996, **61**, 8358.
20 V. K. Aggarwal, A. Thompson, R. V. H. Jones and M. C. H. Standen, *J. Org. Chem.*, 1996, **61**, 8368.

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