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A New Synthesis of Aziridine-2-carboxylates: Reaction of Hexahydro-1,3,5-triazines or *N*-Methoxymethylanilines with Alkyl Diazoacetates in the Presence of Lewis Acid[1]

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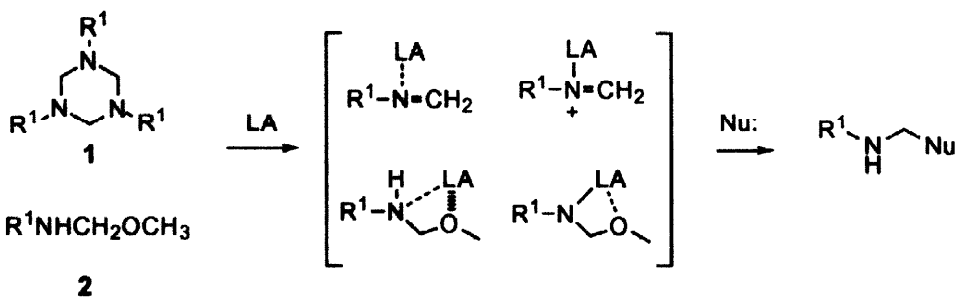
Abstract: Aziridine-2-carboxylates were prepared from the reaction of hexahydro-1,3,5-triazines or *N*-methoxymethylanilines with alkyl diazoacetates in the presence of Lewis acid catalyst in high yield.

INTRODUCTION

A series of our previous reports shows that *N*-methyleneamine equivalents could be generated *in situ* from hexahydro-1,3,5-triazines (**1**) or *N*-methoxymethylamines (**2**) in the presence of Lewis acid and reacted with various nucleophiles for the synthesis of noble aminomethylated products.[1,2]



Scheme 1

We apply this synthetic method to prepare aziridine-2-carboxylates (**3**), from the reaction of *N*-methyleneamine equivalents with alkyl diazoacetates as nucleophiles.[3] Aziridine-2-carboxylates attract great attentions as useful building blocks for the synthesis of α- and β-amino esters, β-lactams and alkaloids.[4] A few methods for aziridine synthesis were reported based on three different approaches as shown in Scheme 2, i) nucleophilic displacement of nitrogen with removal of the leaving group at α-position[5], ii) 1,2-addition of nitrogen to olefins[6] and iii) 1,2-addition of carbon to imines[7]. All three approaches will allow to yield products in certain degree of stereoselectivity. Only two methods ii and iii are available for the catalytic version of the reaction. However catalytic efficacy and applicability is quite limited until now. Therefore catalytic version of the reaction is essential for the future development toward efficient and stereoselective synthesis of aziridine.

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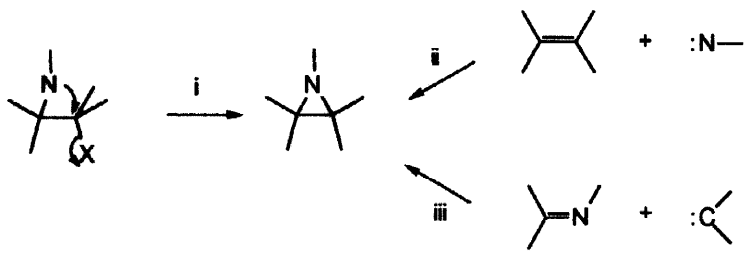
Recently $Cu(OTf)_2$ catalyzed synthesis of aziridine-2-carboxylates were reported by Jorgensen from 1 and alkyldiazoacetate.[7b] This reaction proceeded in the manner of iii of the Scheme 2 with the formation of carbene intermediate from alkyl diazoacetate that gave self-adducts of maleate and fumarate as by-products. Therefore excessive use of alkyl diazoacetate and the removal of self-adducts are required for the reaction. However, Lewis acid catalysts with the generation of *N*-methyleneamine equivalents can give a way to overcome those limitations.

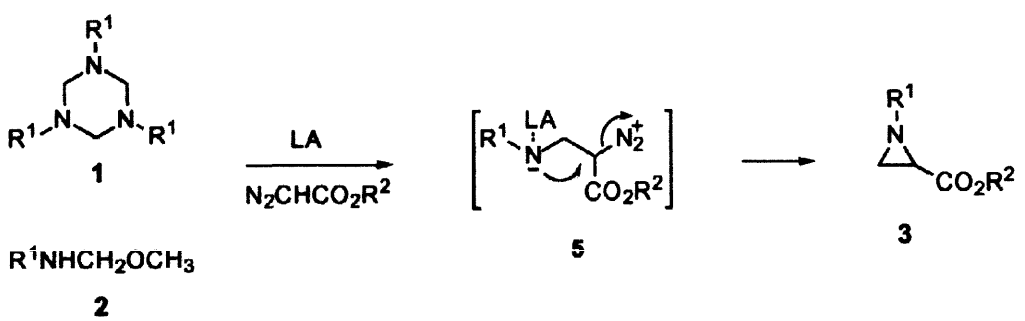


Scheme 2

In this paper we describe the effective synthesis of aziridine-2-carboxylates (3) from the reaction of hexahydro-1,3,5-triazines (1) or *N*-methoxymethylanilines (2) with alkyl diazoacetate in the presence of Lewis acid as a catalyst in high yield.

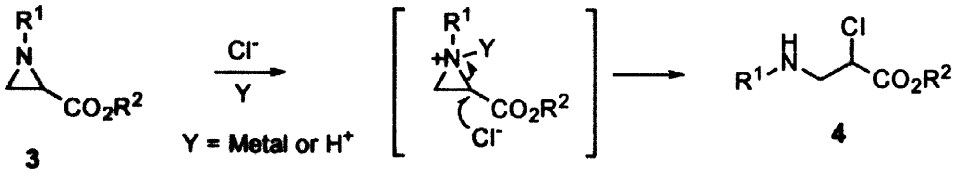
RESULTS AND DISCUSSION

Our earlier studies enable formation of *N*-methyleneamine equivalents shown in the bracket of Scheme 1 from hexahydro-1,3,5-triazines (1) or *N*-methoxymethylanilines (2). The adduct of *N*-methyleneamine equivalents with the nucleophile of alkyl diazoacetate was formed as 5. Then the nucleophilic nitrogen of amine pushed N_2 out as the leaving group with the formation of three membered ring to give aziridines. Trials to trap the intermediate 5 were not succeeded with maleate or other Michael acceptor before releasing nitrogen to form aziridine ring. The initial adduct seems quite reactive toward intramolecular cyclization instead of any further intermolecular addition. This overall reaction to make aziridine ring can be classified as the pathway iii in Scheme 2 when we consider the condensation of formaldehyde imine equivalent with carbon nucleophile. However, the intermediacy of 5 and the releasing of N_2 from the initial adduct is quite similar to the pathway i. Therefore this reaction is quite unique and distinctive from other methods from the synthetic point of view.[8]



Scheme 3

For the best result we have tried with several different Lewis acids. When $TiCl_4$ or $AlCl_3$ was used as a catalyst ring opened product **4** was obtained in 62 and 20% yields with the expected product in 21 and 64% yields respectively. 3-Amino-2-chloropropionate was originated from the metal catalyzed ring opening reaction of aziridine. This was confirmed that the isolated product of *N*-phenylaziridine-2-carboxylate (**3**) was converted to **4** in good yield with $TiCl_4$. This type of ring opening reactions was succeeded with $MgBr_2$.[9]



Scheme 4

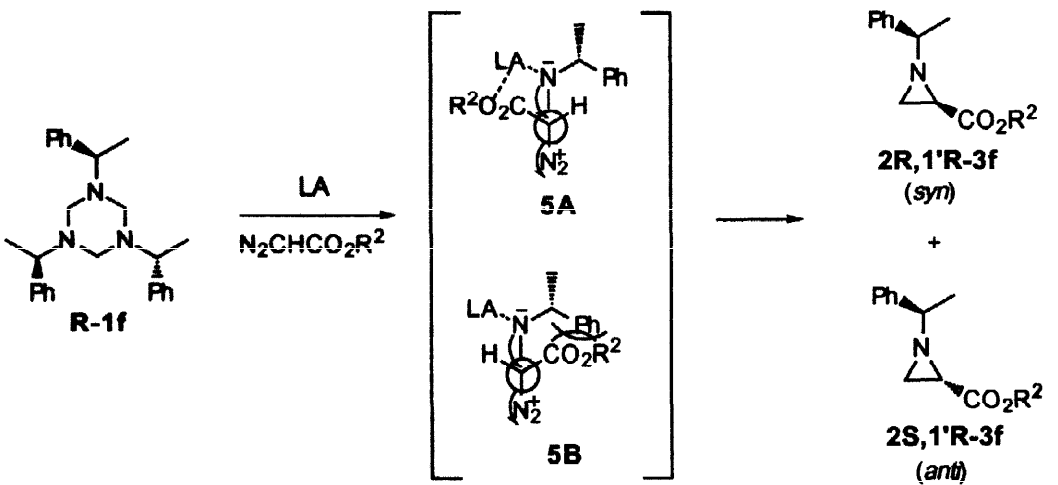
Table 1. Reactions of 1,3,5-trisubstituted hexahydro-1,3,5-triazine (**1**) or *N*-methoxymethylanilines (**2**) with alkyl diazoacetate in the presence of Lewis Acid.

Substrate	R^1	R^2	Lewis Acid	mol %	T/°C	Time(h)	Yield(%)[a]	
1a	Ph	Et	$TiCl_4$	20	-78	0.2	21	(62)[b]
1a	Ph	Et	$SnCl_4$	20	-78	0.2	80	(5)[b]
1a	Ph	Me	$SnCl_4$	20	-78	0.2	86	
1a	Ph	Et	$AlCl_3$	20	-78	0.3	64	(20)[b]
1a	Ph	Et	$BF_3{\cdot}OEt_2$	20	-78	0.3	58	
1b	2-CH_3-C_6H_4	Et	$SnCl_4$	20	-78	3	76	
1c	2-CH_3O-C_6H_4	Et	$SnCl_4$	20	-78	3	50	
1d	2,5-Cl_2-C_6H_3	Et	$SnCl_4$	20	-78	3	62	
1e	4-F-C_6H_4	Et	$SnCl_4$	20	-78	3	82	
R-**1f**	(R)-Ph(CH_3)CH	Et	$SnCl_4$	100	-15	3	71	(67:33)[c]
R-**1f**	(R)-Ph(CH_3)CH	Et	$AlCl_3$	100	-15	3	47	(59:41)[c]
R-**1f**	(R)-Ph(CH_3)CH	Et	$BF_3{\cdot}OEt_2$	100	-15	3	74	(60:40)[c]
R-**1f**	(R)-Ph(CH_3)CH	Et	$SnCl_4$	20	-15	3	67	(64:36)[c]
R-**1f**	(R)-Ph(CH_3)CH	Me	$SnCl_4$	100	-15	3	71	(61:39)[c]
R-**1f**	(R)-Ph(CH_3)CH	Me	$BF_3{\cdot}OEt_2$	100	-15	3	87	(55:45)[c]
R-**1f**	(R)-Ph(CH_3)CH	t-Bu	$SnCl_4$	100	-15	3	57	(76:24)[c]
R-**1f**	(R)-Ph(CH_3)CH	t-Bu	$BF_3{\cdot}OEt_2$	100	-15	3	59	(69:31)[c]
2a	Ph	Et	$SnCl_4$	20	-78	0.2	58	(34)[b]
2a	Ph	Et	$BF_3{\cdot}OEt_2$	20	-15	0.2	84	
2b	2-CH_3-C_6H_4	Et	$SnCl_4$	20	-78	3	49	(38)[b]
2b	2-CH_3-C_6H_4	Et	$BF_3{\cdot}OEt_2$	20	-15	3	78	
2c	2-CH_3O-C_6H_4	Et	$SnCl_4$	20	-78	3	68	
2c	2-CH_3O-C_6H_4	Et	$BF_3{\cdot}OEt_2$	20	-15	3	74	
2d	2,5-Cl_2-C_6H_3	Et	$SnCl_4$	20	-78	3	66	

a. Yield of isolated pure product. b. The yield of **4**. c. Diastereomeric ratio of *syn* and *anti*.

Among Lewis acids we tested $SnCl_4$ was the best for the preparation of diverse *N*-arylaziridine-2-carboxylates. $BF_3{\cdot}OEt_2$ was also equally effective catalyst for **1a**. The reaction with 20 mol% of $SnCl_4$ as a catalyst was quite successful for the starting 1,3,5-triphenylhexahydro-1,3,5-triazine with diverse substituents of 2-Me (**1b**), 2-OMe (**1c**), 2,5-Cl_2 (**1d**) and 4-F (**1e**) on the benzene ring. The same reactions from the chiral

N-methyleneamine equivalents derived from 1,3,5-tris-(*R*)-phenylethylhexahydro-1,3,5-triazines (*R*-**1f**) yielded a diastereomeric mixture of *N*-phenylethylaziridine-2-carboxylates. This substrate showed relatively lower reactivity compared to **1** not to be reacted at -78°C. Therefore we elevated the reaction temperature to -15°C. The preference of the Lewis acid to $SnCl_4$ for the best result was the same as others. A little better yield without change of diastereomeric ratio was obtained with one mole equivalent of $SnCl_4$. The ratio depends on the R^2 measured by either isolation of each diastereomer by flash column chromatography or by ^1H NMR. The stereochemistry was determined by comparison of the spectral data reported in the literature.[5c] When we used methyl or ethyl diazoacetate the ratio of **2*R*,1'*R*-3f** (*syn*) and **2*S*,1'*R*-3f** (*anti*) was about 2:1with 20 mol% of $SnCl_4$ at -15°C. With bigger alkyl group of t-butyl *syn*:*anti* ratio was obtained as 3:1. The similar result as in the Table 1 was obtained from the reaction of 1,3,5-tris-(*S*)-phenylethylhexahydro-1,3,5-triazine and ethyl diazoacetate to yield **2*S*,1'*S*-3f** (*syn*) and **2*R*,1'*S*-3f** (*anti*) as the ratio of 62:38 with 20 mol% of $SnCl_4$ at -15°C. This implies that formation of intermediate **5A** is preferred to **5B** starting from 1,3,5-tris-(*R*)-phenylethylhexahydro-1,3,5-triazine. **5A** allows possible coordination of carboxylate with Lewis acid and minimization of steric hindrance between carboxylate and phenylethyl groups. Similar yields were obtained for most reactions with one mole equivalents of $BF_3{\cdot}OEt_2$ with relatively poor diasteromeric ratio. This suggests that the coordination with Lewis acid in the reaction pathway is one of the important factors to discriminate two possible intermediates.



Scheme 5

We also have tried for the possible enantioselective synthesis from **1a** with chiral Lewis acid catalyst of $Eu(hfc)_3$. The reaction did not proceeded at all even at the room temperature just recovering all starting material because it was not strong enough to break down the hexahydro-1,3,5-triazine to yield *N*-methyleneamine equivalents.

The similar reaction starting from *N*-methoxymethylanilines (**2**) with alkyl diazoacetate also succeeded to yield *N*-phenylaziridine-2-carboxylate (**3**) with the same catalyst of $SnCl_4$. However, the yields were relatively lower compared to the reaction from the corresponding 1,3,5-triphenylhexahydro-1,3,5-triazines. From this reaction we obtained ring opened products of **4a** and **4b** from **2a** and **2b** in 34 and 38% yield respectively. This implies that the internal proton bearing the starting *N*-methoxymethylanilines promoted the ring opening with $SnCl_4$ as $TiCl_4$ does well in most cases as in Scheme 4. This ring opening can be prevented

a little with starting *N*-silylated *N*-methoxymethylanilines. When *N*-trimethylsilyl-*N*-methoxymethylaniline without internal proton was used, aziridine 2-carboxylate was given in 72% yield. With $BF_3 \cdot OEt_2$ we could prevent the formation of ring opened product to improve the yield 84% and 78% yields from **1a** and **1b**. For the substrates **2c** and **2d** both catalysts of $SnCl_4$ and $BF_3 \cdot OEt_2$ are good enough for the reactions to be succeeded in the similar yields. This reaction can be served as a general method to prepare the synthetically valuable *N*-substituted aziridine-2-carboxylates.

CONCLUSION

This work extends the utility of *N*-methyleneamine equivalents generated from hexahydro-1,3,5-triazines or *N*-methoxymethylanilines. Synthetically valuable aziridine-2-carboxylates were prepared in high yields from *N*-methyleneamine equivalents with alkyl diazoacetates as a nucleophile in the presence of Lewis acid catalyst.

EXPERIMENTAL

^{1}H-NMR and ^{13}C-NMR spectra were recorded on a Gemini 200 (200 MHz for ^{1}H and 50.3 MHz for ^{13}C). Chemical shifts were given in ppm using TMS as internal standard. Mass spectra were obtained using a Hewlett Packard Model 5985B spectrometer or a Kratos Concept 1-S double focusing mass spectrometer. Elemental analysis was taken on a Perkin-Elmer 240 DS elemental analyzer. Optical rotation was measured with Rudolph Research Autopole 3 polarimeter. The silica gel used for column chromatography was Merck 200-230 mesh. Thin layer chromatography was carried out with Merck 60F-254 plates with 0.25 mm thickness. *N*-Methoxymethylanilines were prepared by the reported method.[2b] All the other chemicals were reagent grade and used without further purification. 1,3,5-Trisubstituted hexahydro-1,3,5-triazines were obtained by the conventional method with amine and formaldehyde. Some of the *N*-methoxymethylanilines and 1,3,5-triphenylhexahydro-1,3,5-triazines were inter-convertible.[2c]

General Procedure for the Synthesis of Aziridine-2-carboxylates: To a stirred solution of 1,3,5-trisubstituted hexahydro-1,3,5-triazine (**1**) (3.0 mmol) or *N*-methoxymethylanilines (**2**) (9.0 mmol) in CH_2Cl_2 under nitrogen atmosphere was added the Lewis acid at the specified temperature in the Table. After being stirred for 10 min alkyl diazoacetate (9.0 mmol) was added to it. The resulting solution was stirred at the specified temperature until all starting material was consumed on TLC. The reaction mixture was poured into ice-water. The resulting solution was neutralized with cold sat. $NaHCO_3$ solution. The reaction product was extracted with CH_2Cl_2. Organic layer was washed successively with water and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude reaction product was purified by flash chromatography on silica gel eluting with 4:1 *n*-Hexane-EtOAc to give aziridine-2-carboxylates.

Methyl 1-phenylaziridine-2-carboxylate: δ_H (200 MHz; $CDCl_3$) 2.34 (1H, dd, J = 6.4 and 1.6 Hz), 2.68 (1H, dd, J = 3.4 and 1.6 Hz), 2.81 (1H, dd, J = 6.4 and 3.4 Hz), 3.82 (3H, s), 6.92 - 7.07 (3H, m) and 7.21 - 7.31 (2H, m); δ_C (50.3 MHz, $CDCl_3$) 33.7, 37.4, 52.4, 120.6, 123.4, 129.1, 152.4 and 170.6; m/z 177 (M^+, 57%), 162 (54), 104 (100), 91 (80) and 77 (65). [HREIms. Found: 177.0783. $C_{10}H_{11}NO_2(M^+)$ requires: 177.0790].

Ethyl 1-phenylaziridine-2-carboxylate: δ_H (200 MHz; $CDCl_3$) 1.14 (3H, t, J = 6.6 Hz), 2.09 (1H, dd, J = 6.2 and 1.6 Hz), 2.52 (1H, dd, J = 3.0 and 1.6 Hz), 2.61 (1H, dd, J = 6.2 and 3.0 Hz), 3.95 - 4.13 (2H, m), 6.80 - 6.87 (3H, m) and 7.01 - 7.09 (2H, m); δ_C (50.3 MHz, $CDCl_3$) 12.4, 32.0, 35.8, 59.8, 119.0, 121.7, 127.4, 150.9 and 168.5; m/z 191 (M^+, 33%), 162 (70), 132 (13), 118 (22) and 104 (100). [HREIms. Found: 191.0949. $C_{11}H_{13}NO_2(M^+)$ requires: 191.0946].

t-Butyl 1-phenylaziridine-2-carboxylate: δ_H (200 MHz; $CDCl_3$) 1.47 (9H, s), 2.24 (1H, dd, J = 6.2 and 1.8 Hz), 2.59 (1H, dd, J = 3.2 and 1.8 Hz), 2.69 (1H, dd, J = 6.2 and 3.2 Hz), 6.94 - 7.01 (3H, m) and 7.18 - 7.29 (2H, m); δ_C (50.3 MHz, $CDCl_3$) 27.9, 33.3, 38.4, 81.9, 120.7, 123.1, 129.0, 152.7 and 169.1; m/z 219 (M^+, 28%), 163 (60), 118 (100), 117 (34), 104 (32) and 91 (80). [HREIms. Found: 219.1247. $C_{13}H_{17}NO_2(M^+)$ requires: 219.1259].

Ethyl 1-(1-methylphenyl)-aziridine-2-carboxylate: δ_H (200 MHz; $CDCl_3$) 1.30 (3H, t, J = 7.2 Hz), 2.25 - 2.32 (1H, m), 2.29 (3H, s), 2.61 - 2.66 (2H, m), 4.15 - 4.32 (2H, m) and 6.77 - 7.11 (4H, m); δ_C (50.3 MHz, $CDCl_3$) 12.4, 16.0, 31.8, 36.3, 59.6, 117.3, 121.6, 124.9, 128.9, 130.0, 148.3 and 168.6; m/z 205 (M^+, 48%), 176 (22), 132 (100), 118 (73) and 117 (40), 105 (17), 91 (25). [HREIms. Found: 205.1113. $C_{12}H_{15}NO_2(M^+)$ requires: 205.1103].

Ethyl 1-(1-methoxyphenyl)-aziridine-2-carboxylate: δ_H (200 MHz; $CDCl_3$) 1.30 (3H, t, J = 7.0 Hz), 2.28 (1H, dd, J = 7.2 and 0.8 Hz), 2.65 - 2.71 (2H, m), 3.83 (3H, s), 4.15 - 4.35 (2H, m) and 6.78 - 7.03 (4H, m); δ_C (50.3 MHz, $CDCl_3$) 12.5, 32.3, 36.3, 53.8, 59.5, 109.3, 118.5, 119.0, 122.1, 139.2, 150.6 and 168.7; m/z 221 (M^+, 65%), 192 (70), 148 (28), 134 (100) and 120 (17), 117 (15). [HREIms. Found: 221.1047. $C_{12}H_{15}NO_3(M^+)$ requires: 221.1052].

Ethyl 1-(2,4-dichlorophenyl)-aziridine-2-carboxylate (4d): δ_H (200 MHz; $CDCl_3$) 1.24 (3H, t, J = 7.2), 2.39 (1H, dd, J = 6.2 and 1.0 Hz), 2.69 (1H, dd, J = 3.2 and 1.0 Hz), 2.78 (1H, dd, J = 6.2 and 3.2 Hz), 4.12 - 4.28 (2H, m), 6.86 (1H, s), 6.88 (1H, d, J = 8.2 Hz) and 7.19 (1H, d, J = 8.4 Hz); δ_C (50.3 MHz, $CDCl_3$) 14.0, 34.1, 38.4, 61.5, 121.3, 124.0, 125.5, 130.7, 132.8, 148.9 and 169.2; m/z 261 (M^++2, 13%), 259 (M^+, 20), 232 (22), 230 (33), 174 (65), 172 (100), 151 (41), and 109 (29). [HREIms. Found: 259.0173. $C_{11}H_{11}NO_2Cl_2(M^+)$ requires: 259.0167].

Ethyl 1-(4-fluorophenyl)-aziridine-2-carboxylate: δ_H (200 MHz; $CDCl_3$) 1.22 (3H, t, J = 7.2 Hz), 2.16 - 2.21 (1H, m), 2.53 - 2.56 (1H, m), 2.64 - 2.68 (1H, m), 4.10 - 4.22 (2H, m) and 6.78 - 6.88 (4H, m); δ_C (50.3 MHz, $CDCl_3$) 12.3, 32.0, 36.1, 59.7, 113.7, 114.1, 120.0, 120.1, 146.9, 147.0, 154.8, 159.6 and 168.2; m/z 209 (M^+, 15%), 180 (37), 136 (18), 122 (100) and 109 (47), 95 (38). [HREIms. Found: 209.0854. $C_{11}H_{12}NO_2F(M^+)$ requires: 209.0852].

Methyl (2*R*, 1'*R*)-1-(1'-phenylethyl)-aziridine-2-carboxylate : $[\alpha]_D^{21}$ +101.2° (c 0.5, CH_2Cl_2); δ_H (200 MHz; $CDCl_3$) 1.48 (3H, d, J = 6.6 Hz), 1.62 (1H, dd, J = 6.2 and 1.4 Hz), 2.14 (1H, dd, J = 3.1 and 1.4 Hz), 2.22 (1H, dd, J = 6.2 and 3.1 Hz), 2.54 (1H, q, J = 6.6 Hz), 3.75 (3H, s) and 7.25 - 7.41 (5H, m); δ_C (50.3 MHz, $CDCl_3$) 22.9, 33.8, 37.9, 52.1, 69.7, 126.8, 127.2, 128.3, 143.3 and 171.3; m/z 204 (M^+-H, 3%), 190 (15), 146 (14), 131 (17), 105 (100), and 77 (58). [HREIms. Found: 204.1013. $C_{12}H_{14}NO_2(M^+$-H) requires: 204.1025].

Methyl (2*S*, 1'*R*)-1-(1'-phenylethyl)-aziridine-2-carboxylate : $[\alpha]_D^{21}$ -50.5° (c 0.9, CH_2Cl_2); δ_H (200 MHz; $CDCl_3$) 1.47 (3H, d, J = 6.6 Hz), 1.79 (1H, dd, J = 6.4 and 1.0 Hz), 2.09 (1H, dd, J = 6.8, 3.0 Hz), 2.34 (1H, dd, J = 3.2, 0.8 Hz), 2.57 (1H, q, J = 6.6 Hz), 3.68 (3H, s) and 7.27 - 7.35 (5H, m); δ_C (50.3 MHz, $CDCl_3$) 23.3, 34.9, 36.8, 52.1, 69.7, 126.5, 127.2, 128.5, 143.6 and 171.2; m/z 204 (M^+-H,

39%), 190 (53), 105 (100), 103 (29) and 77 (59). [HREIms. Found: 204.1033. $C_{12}H_{14}NO_2(M^+-H)$ requires: 204.1025].

Ethyl (2*R*, 1'*R*)-1-(1'-phenylethyl)-aziridine-2-carboxylate: $[\alpha]_D^{21}$ +83.6° (c 0.8, CH_2Cl_2); δ_H (200 MHz; $CDCl_3$) 1.22 (3H, t, J = 7.2Hz), 1.40 (3H, d, J = 6.6 Hz), 1.51 (1H, dd, J = 6.4 and 0.8 Hz), 2.05 (1H, d, J = 2.4 Hz), 2.13 (1H, dd, J = 6.2 and 3.0 Hz), 2.46 (1H, dd, J = 6.2 and 3.0 Hz), 2.46 (1H, q, J = 6.6 Hz), 4.10 - 4.21 (2H, m) and 7.16 - 7.35 (5H, m); δ_C (50.3 MHz, $CDCl_3$) 14.0, 23.0, 33.8, 38.0, 61.0, 69.8, 126.9, 127.2, 128.3, 143.4 and 170.9; m/z 218 (M^+-H, 6%), 204 (23), 190 (25), 146 (10) and 105 (100). [HREIms. Found: 218.1184. $C_{13}H_{16}NO_2(M^+-H)$ requires: 218.1181].

Ethyl (2*S*, 1'*R*)-1-(1'-phenylethyl)-aziridine-2-carboxylate: $[\alpha]_D^{21}$ -48.9° (c 0.7, CH_2Cl_2); δ_H (200 MHz; $CDCl_3$) 1.21 (3H, t, J = 7.2Hz), 1.46 (3H, d, J = 6.6 Hz), 1.78 (1H, dd, J = 6.6 and 1.2 Hz), 2.05 (1H, dd, J = 6.6 and 3.2 Hz), 2.34 (1H, dd, J = 3.2 and 1.2 Hz), 2.57 (1H, q, J = 6.6 Hz), 4.14 (2H, q, J = 6.6 Hz) and 7.21 - 7.38 (5H, m); δ_C (50.3 MHz, $CDCl_3$) 14.0, 23.4, 34.8, 37.0, 60.9, 69.7, 126.5, 127.2, 128.5, 143.8 and 170.7; m/z 218 (M^+-H, 4%), 204 (4), 190 (3), 146 (19), 131 (13) and 105 (100). [HREIms. Found: 218.1178. $C_{13}H_{16}NO_2(M^+-H)$ requires: 218.1181.

t-Butyl (2*R*, 1'*R*)-1-(1'-phenylethyl)-aziridine-2-carboxylate: $[\alpha]_D^{21}$ +72.3° (c 0.8, CH_2Cl_2); δ_H (200 MHz; $CDCl_3$) 1.25 - 1.49 (13H, m), 2.05 - 2.12 (2H, m), 2.51 (1H, q, J = 6.6 Hz) and 7.21 - 7.43 (5H, m); δ_C (50.3 MHz, $CDCl_3$) 23.1, 27.9, 33.6, 38.8, 69.7, 81.2, 126.9, 127.2, 128.3, 143.7 and 170.1; m/z 246 (M^+-H, 1%), 190 (46), 176 (26), 146 (9) and 105 (100). [HREIms. Found: 246.1485. $C_{15}H_{20}NO_2(M^+-H)$ requires: 246.1494.

t-Butyl (2*S*, 1'*R*)-1-(1'-phenylethyl)-aziridine-2-carboxylate: $[\alpha]_D^{21}$ -24.4° (c 0.6, CH_2Cl_2); δ_H (200 MHz; $CDCl_3$) 1.27 - 1.46 (12H, m), 1.69 (1H, d, J = 6.4 Hz), 1.93 (1H, dd, J = 6.4 and 3.2 Hz), 2.29 (1H, d, J = 3.2 Hz), 2.54 (1H, q, J = 6.6 Hz) and 7.20 - 7.37 (5H, m); δ_C (50.3 MHz, $CDCl_3$) 23.5, 27.8, 34.3, 37.8, 69.4, 81.0, 126.5, 127.0, 128.3, 144.2 and 169.9; m/z 246 (M^+-H, 1%), 232 (1), 190 (53), 176 (38), 146 (7) and 105 (100). [HREIms. Found: 246.1491. $C_{15}H_{20}NO_2(M^+-H)$ requires: 246.1494].

General Procedure for Ethyl 3-Anilino-2-chloropropanoate 4a- b: To a stirred solution of ethyl *N*-phenylaziridine-2-carboxylate (3) (117 mg, 61 mmol) in CH_2Cl_2 under nitrogen atmosphere was slowly added the $TiCl_4$ (116 mg, 61 mmol) at -78°C. After the reaction was completed (TLC monitoring) the reaction mixture was poured into ice-water. The resulting solution was neutralized with cold sat. $NaHCO_3$ solution. The reaction product was extracted with CH_2Cl_2. Organic layer was washed successively with water and brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The crude reaction product was purified by flash chromatography on silica gel eluting with 4:1 *n*-Hexane-EtOAc to give ethyl 3-anilino-2-chloropropanoate in 85% yield.

Ethyl 3-anilino-2-chloropropanoate: δ_H (200 MHz; $CDCl_3$) 1.32 (3H, t, J = 7.0 Hz), 3.61 (1H, dd, J = 6.6 and 6.2 hz), 3.85 (1H, dd, J = 6.4 and 5.8 Hz), 4.27 (2H, q, J = 7.0 Hz), 4.51 (1H, t, J = 6.6 Hz), 6.67 - 6.82 (3H, m), 7.21 - 7.30 (2H, m); δ_C (50.3 MHz, $CDCl_3$) 12.3, 45.7, 53.2, 60.7, 111.6, 116.9, 128.0, 144.9 and 167.2; Anal. Calcd. for $C_{11}H_{15}NO_2Cl$: C, 58.0; H, 6.20; N, 6.15. Found: C, 57.8; H, 6.42; N, 6.01.

Ethyl 2-chloro-3-toluidylpropanoate: δ_H (200 MHz; $CDCl_3$) 1.19 (3H, t, J = 7.0 Hz), 2.04 (3H, s), 3.45 - 3.98 (3H, m), 4.14 (2H, q, J = 3.0 Hz), 4.14 (1H, t, J = 6.4 Hz), 6.53 - 6.61 (2H, m), 6.96 - 7.04 (2H, m); δ_C (50.3 MHz, $CDCl_3$) 13.8, 17.1, 47.1, 54.6, 62.2, 109,8, 118.0, 122.7, 127.2, 130.5,

144.4, and 168.7; Anal. Calcd. for $C_{12}H_{16}NO_2Cl$: C, 59.6; H, 6.67; N, 5.79. Found: C, 59.3; H, 6.82; N, 5.66.

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