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Addition reactions to chiral aziridine-2-carboxaldimine toward various enantiopure nitrogen-containing heterocycles

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Abstract—Chiral (2*R*,1′*R*)-(1′-phenylethyl)aziridine-2-carboxaldimine was utilized as a nitrogen-containing starting substrate for the preparation of various enantiopure nitrogen-containing heterocycles. The additions of nucleophiles including organomagnesium reagents, cyanotrimethylsilane and ketene acetal to the chiral (2*R*,1′*R*)-(1′-phenylethyl)aziridine-2-carboxaldimine proceeded in highly stereoselective manner via chelation controlled transition states. Subsequent treatment of adducts with triphosgene and NaH yielded 5-substituted-4-chloromethylimidazolidin-2-ones. This imine was also served as either aza-diene or aza-dienophile with olefin or diene to provide hetero-Diels–Alder adducts 2-aziridinylpiperidines or 1,2,3,4-tetrahydroquinolines.

1. Introduction

Commercial success to produce both enantiomers of aziridine-2-carboxylates in optically pure forms enables us to provide enantiomerically pure α- or β-amino ester and their derivatives.[1,2] We would like to extend their synthetic utilities for the construction of enantiopure diamine compounds based on the reaction of the substrate aziridin-2-carboxaldimine that is readily available from aziridine-2-carboxylate. The additions to the chiral (2′*R*,1″*R*)-(4-methoxyphenyl){[1-(1″-phenylethyl)aziridin-2′-yl]methylene}amine (**1**) would afford amino alkyl aziridines (**2** and **3**), 2-aziridinylpiperidines (**4**) and 1,2,3,4-tetrahydroquinolines (**5**) via many different reaction pathways including nucleophilic additions and Diels–Alder reactions shown in Scheme 1. The subsequent chemical transformations of aziridine ring of the adduct by the known methods[1] can afford various enantiopure nitrogen-containing cyclic and acyclic molecules.

Throughout the study we had an insight into the transition state conformation with better understanding the factors governing the stereochemical pathways of the addition reactions.

2. Results and discussion

(2′*R*,1″*R*)-(4-Methoxyphenyl){[1-(1″-phenylethyl)aziridin-2′-yl]methylene}amine (**1**) was prepared from the condensation of (2*R*,1′*R*)-(1′-phenylethyl)aziridine-2-carboxaldehyde and *p*-anisidine. *p*-Methoxyphenyl moiety is readily removed to give free amine after the reaction with cerium(IV) ammonium nitrate.[3] Nucleophilic addition to imines[4] is a useful synthetic route toward the amines with expectation of certain degree of stereoselectivity. Addition of organometallic compounds including MeMgBr and MeLi without any additive did not provide the addition product even at room temperature for 15 h and all the starting imine was recovered unreacted. This suggests that the starting imine is not reactive enough toward alkyl metal compounds whose reactivity can be increased by the addition of a suitable Lewis acid. Among all tested Lewis acids $BF_3 \cdot OEt_2$ was the best to promote the reactivity without breaking the aziridine ring. The best result was obtained with the addition of four equivalents of MeMgBr at −10 °C with $BF_3 \cdot OEt_2$ to give the methylated product **2a** in 86% yield[5] (entry 5). Lower temperatures or smaller amounts of MeMgBr resulted in either no reaction or lower yield

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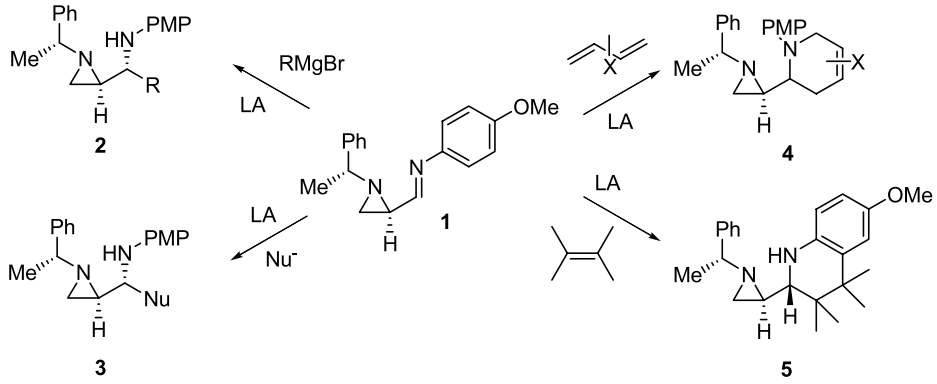


Scheme 1.

(entries 1–4). Addition of MeLi provided a slightly lower yield (76%, entry 6). The addition of a methyl group proceeded in a completely stereoselective manner to give a single isomer judging from ^{1}H NMR and HPLC regardless of the source of the organometallic reagents.

Under the same reaction conditions were added various alkyl and arylmagnesium reagents (Table 1). Ethyl magnesium bromide gave **2b** in a similar yield (82%) in a completely stereoselective manner (entry 7). This was further tested by addition of vinyl magnesium bromide resulting **2c** in 71% yield with diastereoselectivity of 97:3 based on ^{1}H NMR integration (entry 8). Much lower stereoselectivity was observed in the addition of allyl- and *n*-butylmagnesium bromide with diastereoselectivities of 62:38 (**2d** and **2d′**) and 91:9 (**2e** and **2e′**), even though the reaction yields were 82 and 72%, respectively (entries 9 and 10). Changing the alkylating agent to *n*-butyllithium form *n*-butylmagnesium bromide showed lower selectivity of 84:16 in 63% yield (entry 11). Addition of aryl magnesium reagents such as PhMgBr, *p*-tolyl-MgBr, *p*-FPhMgBr was completely stereoselective to give products **2f**, **2g**, and **2h** in 75, 68, and 71% yields, respectively (entries 12–14).

The utility of imines can be expanded by the addition of nucleophile other than organometallic reagents as shown in Table 2.[6] The addition of nitrile to imine as in Strecker reaction was studied using cyanotrimethylsilane (**6**).[7] The substrate we used, (2*R*,1′*R*)-(1′-phenylethyl)aziridine-2-carboxaldimine, was inert without any additives. However, reaction with cyanotrimethylsilane in CH_2Cl_2 with 50 mol% of $BF_3\cdot OEt_2$ at room temperature for 3 h yielded the products **3a** and **3a′** as a diastereomeric mixture with the ratio of 69:31 in 91% yield with *threo* isomer **3a** as the major product (entry 1). Trials to improve the diastereoselectivity by changing Lewis acids such as $ZnCl_2$, $Sc(OTf)_3$, $Ti(O\textit{i}\text{-}Pr)_4$, TMSTf, $CeCl_3$ were not successful to show similar stereoselectivity in a little lower yield. When we used CsF that is known to be a good catalyst[7c] in the addition of imine, the reaction showed a little better ratio of 78:22 in 85% yield (entry 2). It is also noteworthy that the reaction with TMSCl as an additive gave products **3a** and **3a′** with the ratio of 45:55 in 62% yield (entry 3).

Another nucleophile ketene silyl acetal (**7**)[8] was added to (2*R*,1′*R*)-(1′-phenylethyl)aziridine-2-carboxaldimine (**1**) in the presence of 50 mol% of $BF_3\cdot OEt_2$ to afford β-amino-carboxylated **3b** as a single isomer with aziridine ring conserved in 87% yield (entry 4).

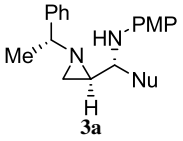
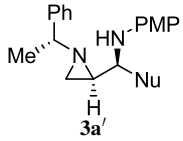
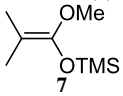
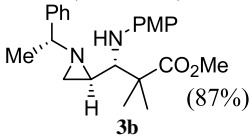
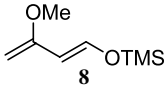
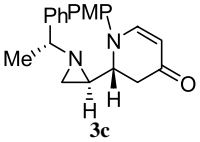
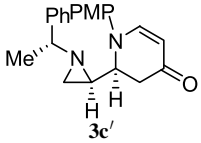
All of adducts aminomethylaziridines **2** and **3** were converted to other cyclic or acyclic dinitrogen containing compounds by the known methods.[1] We wished to convert them to the valuable enantiopure 4,5-disubstituted imidazolin-2-ones, some of which have important biological activities.[9] This was achieved with triphosgene and NaH to give 5-alkyl or 5-aryl-4-chloromethylimidazolidin-2-one (**9**) in good yield (Scheme 2 and Table 3).[10] The reaction

Table 1. The addition of organometallic reagents to chiral (2′*R*,1″*R*)-(4-methoxyphenyl){[1-(1″-phenylethyl)aziridin-2′-yl]methylene}amine (**1**)

Entries	Reagents	Equiv	Temperature (°C)	Time (h)	Yield	Product	Ratio
1	MeMgBr	2	−78	10	No rxn		
2	MeMgBr	2	−10	10	40 (60)		
3	MeMgBr	4	−78	4	45 (55)	**2a**	>99:<1
4	MeMgBr	2	−10	3	65 (10)	**2a**	>99:<1
5	MeMgBr	4	−10	3	86	**2a**	>99:<1
6	MeLi	4	−78	5	76	**2a**	>99:<1
7	EtMgBr	4	−10	4	82	**2b**	>99:<1
8	VinylMgBr	4	−10	3	71	**2c**, **2c′**	97:3
9	AllylMgBr	4	−10	3	82	**2d**, **2d′**	62:38
10	*n*-BuMgBr	4	−10	3	72	**2e**, **2e′**	91:9
11	*n*-BuLi	4	−10	3	63	**2e**, **2e′**	84:16
12	PhMgBr	3	−10	3	75	**2f**	>99:<1
13	*p*-TolylMgBr	3	−10	3	68	**2g**	>99:<1
14	*p*-FPhMgBr	3	−10	3	71	**2h**	>99:<1

All reactions were carried out in the presence of 1 mol equiv of $BF_3\cdot OEt_2$. Isolated yield. Determined by ^{1}H NMR.

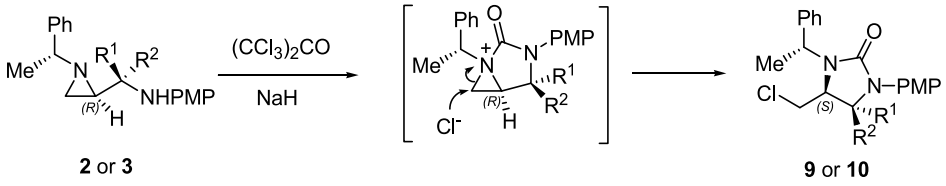
Table 2. The addition of nucleophiles to chiral (2′*R*,1″*R*)-(4-methoxyphenyl){[1-(1″-phenylethyl)aziridin-2′-yl]methylene}amine

Entry	Nucleophile	Lewis acid[a]	Products (% yield, ratio)[b,c]	
1	TMSCN (**6**)	$BF_3 \cdot OEt_2$	 **3a**	 **3a′** (91%, 69:31)
2	TMSCN (**6**)	CsF		(85%, 78:22)
3	TMSCN (**6**)	TMSCI		(62%, 45:55)
4	 **7**	$BF_3 \cdot OEt_2$	 **3b** (87%)	
5	 **8**	$BF_3 \cdot OEt_2$	 **3c**	 **3c′** (81%, 71:29)

[a] Lewis acid (0.5 mol equiv) was added.
[b] Yields were not optimized.
[c] The ratio was determined by ^{1}H NMR spectrum.

proceeded smoothly with the formation of the aziridium ion intermediate shown in the bracket of Scheme 2 that was known from our early observations. All of the alkyl or aryl addition products (**2a**–**2h**) yielded the corresponding chloromethylimidazolidin-2-ones (**9a**–**9h**) in high yields between 97 and 71% yields regardless of the stereochemistry as either *threo* or *erythro*. This reaction also worked with other addition products **3a**, **3a′**, and **3b** to afford chloromethylimidazolidin-2-ones **10a**, **10a′**, and **10b** in 75, 82, and 67% yields, respectively. These transformations from aminomethylaziridine (**2** or **3**) to 4-chloromethylimidazolidin-2-one (**9**) provide a useful tool to determine the initial stereochemical outcomes of the original adducts **2** or **3** with nucleophlies whether they are *threo* or *erythro*.

The stereochemistry of the addition product **2a** (R^1=Me, R^2=H) was identified after its conversion to 5-methyl-4-chloromethylimidazolidin-2-one (**9a**) by treatment with triphosgene and NaH in THF. The coupling constant of the two adjacent imidazolidinone ring protons at C-4 and C-5 was measured to be 3.2 Hz (entry 1), which corresponds to trans-relationship. This implies that methyl addition occurred from *re*-face via a chelation controlled transition state. The stereochemistry of the initial addition products **2b**



2 or **3** **9** or **10**

Scheme 2.

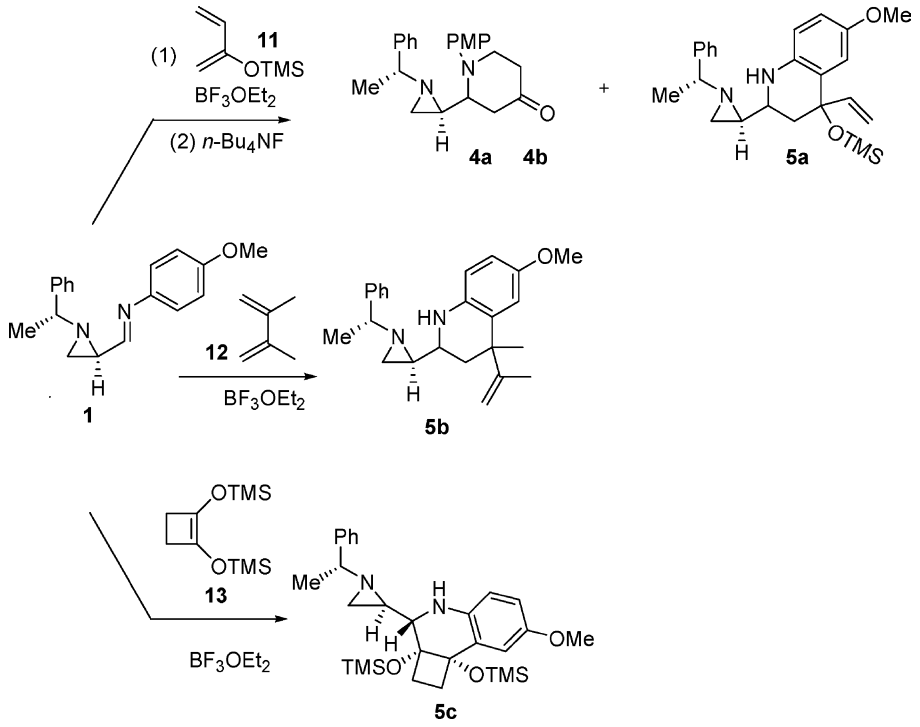
Table 3. Preparation of 5-alkyl or 5-aryl-4-chloromethylimidazolidin-2-one (**9**) from the reactions of the corresponding 2-aminomethylaziridine (**2** and **3**) with triphosgene and NaH

Entry	Substrate	R^1	R^2	Product	Yield (%)[a]	*J* (Hz)[b]
1	**2a**	Me	H	**9a**	94	3.2
2	**2b**	Et	H	**9b**	91	3.0
3	**2c**	Vinyl	H	**9c**	87	3.4
4	**2d**	Allyl	H	**9d**	79	2.6
5	**2d′**	H	Allyl	**9d′**	71	6.4
6	**2e**	*n*-Bu	H	**9e**	96	3.2
7	**2e′**	H	*n*-Bu	**9e′**	83	6.6
8	**2f**	Ph	H	**9f**	97	3.0
9	**2g**	Tolyl	H	**9g**	92	3.2
10	**2h**	*p*-FPh	H	**9h**	89	2.6
11	**3a**	CN	H	**10a**	75	3.0
12	**3a′**	H	CN	**10a′**	82	7.1
13	**3b**	CMe_2CO_2Me	H	**10b**	67	3.4

[a] All reactions were carried out at −78 °C for 2 h.
[b] Coupling constants of the imidazoline ring protons at C-4 and C-5.

and **2c** were identified as *threo* by judging the coupling constants of the two imidazolidinone ring protons at C-4 and C-5 of **9b** and **9c** as 3.0 and 3.4 Hz, respectively (entries 2 and 3). The stereochemistry of all major products **2d**, **2e**, **2f**, **2g** and **2h** were confirmed to be *threo* from the observed coupling constants of 2.6–3.2 Hz corresponding to *trans* relationship of two neighboring imidazolidinone ring protons of compounds **9d**, **9e**, **9f**, **9g**, **9h** (entries 4, 6, 8, 9, and 10). The minor *erythro* isomers **2d′** and **2e′** isolated from the addition of allyl- and *n*-butylMgBr were converted by the same method to *cis*-5-chloromethylimidazolidin-2-ones **9d′** and **9e′** whose coupling constants between two ring protons at C-4 and C-5 were 6.4 and 6.6 Hz, respectively (entries 5 and 7). The initial adduct of nitrile to imine was obtained as inseparable diastreomeric mixture of **3a** and **3a′**, which were also converted to 5-chloromethylimidazolidin-2-ones **10a** and **10a′** at which stage two diastereomers were separated by column chromatography. The similar stereochemical relationship was observed from the coupling constants between two protons at C-4 and C-5 as 3.0 Hz for the major isomer and 7.1 Hz for the minor isomer, respectively (entries 11 and 12). The single isomer **10b** showed 3.4 Hz of coupling constant to indicate that the original adduct of ketene acetal **3b** was *threo* as expected.

The success of the addition of ketene silyl acetal **7** in entry 4 of the Table 2 prompted us to expand the reaction with another electron rich nucleophile 3-methoxytrimethylsilyloxybutadiene (**8**) known as the Danishefsky diene. The reaction with the additive, 50 mol% $BF_3 \cdot OEt_2$, was successful to give 4-oxopiperidines (**3c** and **3c′**) as a diastereomeric mixture with the ratio of 71:29 in 81% yields (entry 5 of Table 2). Formation of cyclic adducts 4-oxopiperidines would be explained by the addition of 3-methoxytrimethylsilyloxybutadiene (**8**) as a nucleophile to the imine like Mannich-type reaction followed by intramolecular cyclization.[11] The same reaction product can be formed from aza-Diels–Alder reaction between the imine (**1**) and 3-methoxytrimethylsilyloxybutadiene (**8**) as an aza-dienophile and a diene, respectively.[12] This prompted us to expand the utility of the imine substrate (1″*R*,2′*R*)-(4-methoxyphenyl){[1-(1″-phenylethyl)aziridin-2′-yl]methylene}amine (**1**) for aza-Diels–Alder reactions with a different diene to provide 2-aziridinylpiperidines **4** (Schemes 1 and 3). Addition of 2-trimethylsilyloxybutadiene (**11**) to the imine in the presence of 50 mol% $BF_3 \cdot OEt_2$ yielded cycloadducts as an inseparable mixture. Those adducts were subsequently treated with *n*-Bu_4F to remove TMS to afford separable adducts **4a**, **4b**, and **5a**. The ratio of two diasteromers **4a** and **4b** was 83:17 in 48% yield while unexpected product **5a** also obtained in 32% yield as a single stereoisomer. Formation of 4-oxopiperidines (**4a** and **4b**) can be explained by aza-Diels–Alder reactions between the imine (**1**) and 2-trimethylsilyloxybutadiene (**11**) in the same manner as observed in the formation of the ring compound in entry 5 of the Table 2, followed by desilylation. However, formation of 1,2,3,4-tetrahydroquinolines (**5**) bearing aziridine ring at C-2 indicates that the imine substrate can perform as an azadiene with an electron rich olefin in a reverse electron demand aza-Diels–Alder reaction.[12,13] Reactions with electron rich olefins such as 2,3-dimethyl-1,3-butadiene (**12**) and bis-1,2-trimethylsilyloxycyclobutene (**13**) afforded 1,2,3,4-tetrahydroquinolines **5b** and **5c** in 62 and 68% yields, respectively (Scheme 3). Even though 1,2,3,4-tetrahydroquinoline **5b** was obtained as a single stereoisomer, the absolute stereochemistry of newly formed C–C bonds could not be identified. Fortunately adduct **5c** coming from the reaction with bis-1,2-trimethylsilyloxycyclobutene was obtained as a single crystal whose structure was fully identified by X-ray crystallography as shown in Figure 1.[14] The configuration of C-2 of 1,2,3,4-tetrahydroquinoline in **5c** showed *R*, which



Scheme 3.

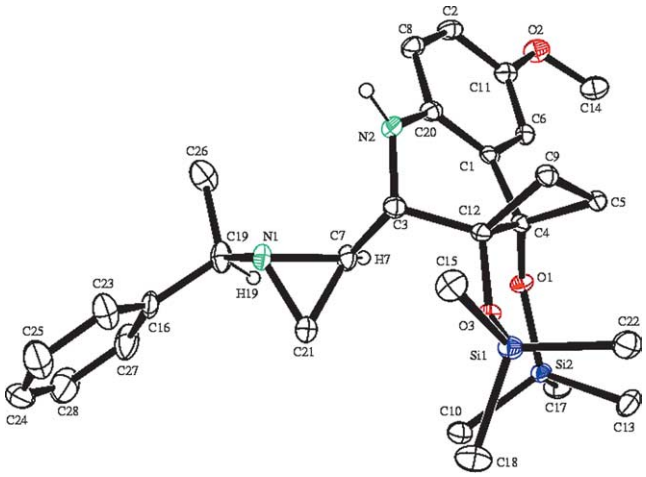


Figure 1.

came from the same facial selectivity as in the nucleophilic addition reactions for the preparation of **2** and **3** in the Scheme 1. This draws a conclusion that initial bond formation on the imine carbon and the coming counterpart approaches from *re*-face via a chelation controlled transition state. All of these successful reactions informed us that (2′*R*,1″*R*)-(4-methoxyphenyl){[1-(1″-phenylethyl)aziridin-2′-yl]methylene}amine (**1**) may have dual role as an azadiene and also an azadienophile in the reactions with proper dienophiles and dienes to yield either 2-aziridinylpiperidines (**4**) or 1,2,3,4-tetrahydroquinolines (**5**).

All of the addition reactions to (2*R*,1′*R*)-(1′-phenylethyl) aziridine-2-carboxaldimine with various nucleophiles, dienes and dienophiles yielded *threo* products with chelation controlled transition state that is quite general for the addition reaction of alkyl metal reagents to α,β-epoxyimine without any additives.[15] However, in the presence of $BF_3 \cdot OEt_2$ as a Lewis acid non-chelation controled product was dominant on the addition reaction of alkyl Grignard to α,β-epoxyimine.[15a,16] We have learned that the same addition reaction of α,β-aziridinylimine (**1**) led chelation controlled product. Because the Lewis acid $BF_3 \cdot OEt_2$ we used in the reactions has dual roles, that is, activating the imine and chelating the two nitrogens of the substrate as shown in **14** of Figure 2. Therefore, the transition state becomes quite rigid and the coming nucleophile attacks the substrate from *re*-face more favorably than from *si*-face. The rigidity of the transition state is supported by the observation of the strong binding between boron and aziridine ring nitrogen in a single crystal

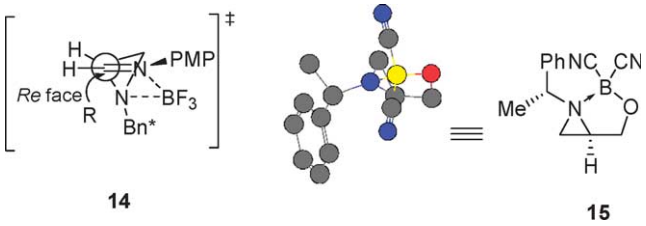


Figure 2. The possible transition state (**14**) to lead the major isomer of the nucleophilic addition from *re*-face to (2*R*,1′*R*)-(1′-phenylethyl)aziridine-2-carboxaldimine and the X-ray structure (**15**) of dicyano[[(1*R*)-(1-phenylethyl)-aziridin-2-yl]methanolato-*O,N*]boron.

structure of dicyano[[(1*R*)-(1-phenylethyl)-aziridin-2-yl]methanolato-*O,N*]boron (**15**) shown in Figure 2.[17] This crystalline structure features that there is a quite strong chelation between boron and nitrogen without altering the aziridine ring conformation. Therefore, we assume that the transition state conformation of the addition reaction is quite similar to the structure **15** and is rigid enough for the coming nucleophile or olefin to approach from the *re*-face more favorably.

The same stereochemical pathway was observed during the reduction of 2-acylaziridine with $NaBH_4$ and $ZnCl_2$ in methanol. High stereoselectivity was observed from the tight binding between the nitrogen of aziridine ring and the carbonyl oxygen by Zn^{+2} metal.[18]

In conclusion, the enantiomerically pure (2′*R*,1″*R*)-(4-methoxyphenyl){[1-(1″-phenylethyl)aziridin-2′-yl]methylene}amine plays a multi-role substrate for the reactions with nucleophiles, dienes and olefins to yield aminomethylaziridines, 2-aziridinylpiperidines and 1,2,3,4-tetrahydroquinolines, respectively. High stereoselectivity was observed throughout these addition reactions via a chelation controlled transition state with *re*-face preference.

3. Experimental

3.1. General methods

^1H and ^{13}C NMR spectra were recorded on a Varian 200 or 500 (300 or 500 MHz for ^1H and 50.3 or 125.7 MHz for ^{13}C). Chemical shifts were given in ppm using TMS as an 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. Melting point was measured by Mel-II capillary melting point apparatus. Optical rotation was measured with Rudolph Research Autopole 3 polarimeter. The silica gel used for column chromatography was Merck 230–400 mesh. Thin-layer chromatography was carried out with Merck 60F-254 plates with 0.25 mm thickness.

3.1.1. (2′*R*,1″*R*)-(4-Methoxyphenyl){[1-(1″-phenylethyl) aziridin-2′-yl]methylene}amine (1). (2*R*,1′*R*)-(1′-phenylethyl)aziridine-2-carboxaldehyde (175 mg, 1 mmol) in 5 mL CH_2Cl_2 was added dropwise into *p*-anisidine solution (123 mg, 1 mmol) in 20 mL CH_2Cl_2 with anhydrous $MgSO_4$ (1.20 g, 10 mmol). This solution was stirred for 5 h at room temperature until all the starting material was consumed. The reaction mixture was filtered and the filtrate was evaporated under reduced pressure. The product was purified by recrystallization from EtOH to give 272 mg of product in 97% yield. This product should be kept under dry condition not for longer than a week.

Yellowish solid. Mp 68–69 °C. ^1H NMR (200 MHz, $CDCl_3$) δ 1.46 (d, $J=6.2$ Hz, 3H), 1.73 (d, $J=6.6$ Hz, 1H), 1.92 (d, $J=1.8$ Hz, 1H), 2.48–2.52 (m, 1H), 2.56 (q, $J=6.2$ Hz, 1H), 3.79 (s, 3H), 6.84–7.13 (m, 4H), 7.24–7.43 (m, 6H). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 23.0, 33.4, 42.8, 55.4, 69.7,

114.2, 122.0, 126.7, 127.2, 128.4, 143.8, 143.9, 159.2, 162.9. HRMS (EI) calcd for $C_{18}H_{20}N_2O$: 280.1576, found 280.1572.

3.2. General procedure for addition reactions of alkyl or aryl magnesium bromide

Into the solution of (2′*R*,1″*R*)-(4-methoxyphenyl){[1-(1″-phenylethyl)aziridin-2′-yl]methylene}amine (**1**, 280 mg, 1 mmol) in 10 mL of ethyl ether was added ethereal solution of alkyl or aryl magnesium bromide (3 mmol) and $BF_3 \cdot OEt_2$ (0.15 mL, 1.0 mmol). The resultant solution was stirred under −10 °C for the completion before the reaction was quenched by adding ice-water. The reaction product was isolated with ethyl ether (15 mL×4). The ethereal solution was washed with brine twice. The organic layer was dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. Purification by silica gel flash column chromatography provided the analytically pure addition product.

3.2.1. (1*R*,2′*R*,1″*R*)-(4-Methoxyphenyl){1-[1′-(1″-phenylethyl)aziridin-2′-yl]ethyl}amine (2a). Liquid. $[\alpha]_D$ 33.5 (*c* 2.0 in EtOAc); ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.14 (d, J=4.2 Hz, 3H), 1.28 (d, J=6.2 Hz, 3H), 1.24–1.62 (m, 2H), 2.36 (q, J=6.6 Hz, 1H), 3.32–3.41 (m, 1H), 3.40 (q, J=6.8 Hz, 1H), 3.63 (s, 3H), 6.52–6.71 (m, 4H), 7.14–7.31 (m, 5H). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 19.5, 23.49, 30.37, 44.2, 48.9, 55.6, 69.3, 114.6, 114.6, 126.6, 126.7, 128.1, 141.8, 144.8, 151.6. HRMS (EI) calcd for $C_{19}H_{24}N_2O$: 296.1889, found 296.1883. Anal. Calcd for $C_{19}H_{24}N_2O$: C, 77.0; H, 8.16; N, 9.45. Found: C, 76.8; H, 8.09; N, 9.42.

3.2.2. (1*R*,2′*R*,1″*R*)-(4-Methoxyphenyl){1-[1′-(1″-phenylethyl)aziridin-2′-yl]propyl}amine (2b). Liquid. $[\alpha]_D$ 70.0 (*c* 0.2 in EtOAc); ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.06 (t, J=7.2 Hz, 3H), 1.19 (d, J=5.8 Hz 1H), 1.38 (d, J=6.6 Hz, 3H), 1.51–1.68 (m, 4H), 2.45 (q, J=6.6 Hz, 1H), 3.17 (td, J=6.6 Hz, 3.4 Hz, 1H), 3.72 (s, 3H), 6.61–6.78 (m, 4H), 7.24–7.41 (m, 5H). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 10.8, 23.4, 27.4, 30.4, 42.7, 55.3, 55.6, 69.3, 114.3, 114.6, 126.6, 126.7, 128.1, 142.6, 144.6, 151.4. HRMS (EI) calcd for $C_{20}H_{26}N_2O$: 310.2045, found 310.2042.

3.2.3. (1*R*,2′*R*,1″*R*)-(4-Methoxyphenyl){1-[1′-(1″-phenylethyl)aziridin-2′-yl]prop-2-enyl}amine (2c). Liquid. $[\alpha]_D$ 34.5 (*c* 0.5 in EtOAc); ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.21–1.25 (m, 1H), 1.38 (d, J=6.6 Hz, 3H), 1.58–1.71 (m, 2H), 2.42 (q, J=6.6 Hz, 1H), 3.70 (s, 3H), 3.2–3.76 (m, 1H), 5.20 (d, J=9 Hz, 1H), 5.26 (d, J=16 Hz, 1H), 5.81 (ddd, J=16.0, 9.0, 6.0 Hz, 1H), 6.56–6.79 (m, 4H), 7.16–7.41 (m, 5H). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 23.6, 30.3, 37.3, 42.8, 56.5, 69.0, 114.5, 114.7, 115.6, 126.6, 126.8, 128.1, 134.8, 141.5, 144.4, 151.7. HRMS (EI) calcd for $C_{20}H_{24}N_2O$: 308.1889, found 308.1892.

3.2.4. (1*R*,2′*R*,1″*R*)-(4-Methoxyphenyl){1-[1′-(1″-phenylethyl)aziridin-2′-yl]but-3-enyl}amine (2d). Liquid. $[\alpha]_D$ 2.98 (*c* 3.0 in EtOAc); ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.29–1.33 (m, 1H), 1.41 (d, J=6.6 Hz, 3H), 1.61–1.77 (m, 2H), 2.38–2.54 (m, 3H), 3.14 (q, J=6.6 Hz, 1H), 3.72 (s, 3H), 5.16 (d, J=10 Hz, 1H), 5.18 (d, J=16 Hz, 1H), 5.80–6.10 (m, 1H), 6.57–6.76 (m, 4H), 7.24–7.33 (m, 5H). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 14.1, 23.4, 32.7, 42.1, 55.5, 56.7, 68.0, 114.5, 114.7, 115.7, 126.7, 126.9, 128.2, 138.7, 141.7, 144.4, 151.8. HRMS (EI) calcd for $C_{21}H_{26}N_2O$: 322.2045, found 322.2038.

3.2.5. (1*S*,2′*R*,1″*R*)-(4-Methoxyphenyl){1-[1′-(1″-phenylethyl)aziridin-2′-yl]but-3-enyl}amine (2d′). Liquid. $[\alpha]_D$ 40.1 (*c* 3.0 in EtOAc); ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.30–1.41 (m, 1H), 1.65 (d, J=6.6 Hz, 3H), 1.68–1.72 (m, 2H), 2.35–2.40 (m, 3H), 3.30 (q, J=6.6 Hz, 1H), 3.72 (s, 3H), 5.15 (d, J=10 Hz, 1H), 5.18 (d, J=16 Hz, 1H), 5.80–6.01 (m, 1H), 6.61–6.79 (m, 4H), 7.21–7.40 (m, 5H). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 14.1, 23.5, 30.5, 34.3, 42.5, 53.6, 55.7, 69.4, 114.6, 114.7, 117.3, 126.7, 126.8, 128.2, 135.4, 142.2, 144.6, 151.7. HRMS (EI) calcd for $C_{21}H_{26}N_2O$: 322.2045, found 322.2044.

3.2.6. (1*R*,2′*R*,1″*R*)-(4-Methoxyphenyl){1-[1′-(1″-phenylethyl)aziridin-2′-yl]pentyl}amine (2e). Viscous oil. ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.79 (t, J=7.0 Hz, 3H), 1.09–1.42 (m, 7H), 1.27 (d, J=6.6 Hz, 3H), 1.43–1.68 (m, 2H), 2.33 (q, J=6.6 Hz, 1H), 3.12 (q, J=6.4 Hz, 1H), 3.64 (s, 3H), 6.50–6.80 (m, 4H), 7.15–7.30 (m, 5H). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 14.1, 22.8, 23.5, 28.6, 32.2, 33.8, 44.1, 53.7, 55.9, 69.4, 114.3, 114.7, 126.7, 126.8, 128.2, 142.7, 144.7, 151.4. HRMS (EI) calcd for $C_{22}H_{30}N_2O$: 338.2358, found 338.2364.

3.2.7. (1*S*,2′*R*,1″*R*)-(4-Methoxyphenyl){1-[1′-(1″-phenylethyl)aziridin-2′-yl]pentyl}amine (2e′). Viscous oil. ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.78 (t, J=7.0 Hz, 3H), 1.08–1.45 (m, 7H), 1.26 (d, J=6.6 Hz, 3H), 1.50–1.72 (m, 2H), 2.36 (q, J=6.6 Hz, 1H), 3.12–3.21 (m, 1H), 3.64 (s, 3H), 6.48–6.68 (m, 4H), 7.16–7.25 (m, 5H). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 14.1, 22.8, 23.3, 28.0, 32.6, 33.0, 44.0, 53.7, 55.8, 69.7, 114.7, 114.9, 126.7, 126.9, 128.2, 142.1, 144.4, 151.8. HRMS (EI) calcd for $C_{22}H_{30}N_2O$: 338.2358, found 338.2360.

3.2.8. (1*R*,2′*R*,1″*R*)-(4-Methoxyphenyl){1-[1′-(1″-phenylethyl)aziridin-2′-yl]-1-[phenyl]methyl}amine (2f). Liquid. $[\alpha]_D$ 18.9 (*c* 3.0 in EtOAc); ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.08 (d, J=6.8 Hz, 3H), 1.19 (d, J=6.2 Hz, 1H), 1.66–1.78 (m, 2H), 2.25 (q, J=6.6 Hz, 1H), 3.55 (s, 3H), 4.04–4.08 (m, 1H), 6.35–6.57 (m, 4H), 7.10–7.33 (m, 10H). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 23.6, 31.5, 45.4, 55.6, 58.9, 69.1, 114.6, 114.8, 126.5, 126.7, 127.0, 127.1, 128.3, 128.5, 141.5, 142.8, 144.3, 151.7. HRMS (EI) calcd for $C_{24}H_{26}N_2O$: 358.2045, found 358.2049.

3.2.9. (1*R*,2′*R*,1″*R*)-(4-Methoxyphenyl){1-[1′-(1″-phenylethyl)aziridin-2′-yl]-1-[*p*-tolyl]methyl}amine (2g). Liquid. $[\alpha]_D$ 5.3 (*c* 5.0 in EtOAc); ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.23–1.29 (m, 4H), 1.82–1.94 (m, 2H), 2.26 (s, 3H), 2.28–2.41 (m, H), 3.59 (s, 3H), 4.08 (bs, 1H), 6.45–6.66 (m, 4H), 7.05–7.33 (m, 9H). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 20.9, 23.5, 31.4, 45.5, 55.4, 58.8, 69.0, 114.4, 114.8, 126.6, 126.8, 128.1, 129.1, 136.5, 138.5, 139.5, 140.5, 141.5, 144.1, 151.6. HRMS (EI) calcd for $C_{25}H_{28}N_2O$: 372.2202, found 372.2204.

3.2.10. (1*R*,2′*R*,1″*R*)-(4-Methoxyphenyl){1-[1′-(1″-phenylethyl)aziridin-2′-yl]-1-[*p*-fluorophenyl]methyl}-amine (2h). Liquid. $[\alpha]_D$ 30.8 (*c* 2.0 in EtOAc); ^{1}H NMR

(200 MHz, $CDCl_3$) δ 1.12 (d, J=6.6 Hz, 3H), 1.23 (d, J=6.4 Hz, 1H), 1.71–1.80 (m, 2H), 2.33 (q, J=6.6 Hz, 1H), 3.59 (s, 3H), 4.11 (d, J=4.4 Hz, 1H), 6.36–6.62 (m, 4H), 6.90–7.34 (m, 9H). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 23.6, 31.3, 45.2, 55.6, 58.0, 69.0, 114.6, 114.8, 115.2, 115.6, 126.7, 127.0, 127.9, 128.0, 128.2, 128.3, 138.4, 138.5, 141.2, 144.2, 151.8, 159.5, 164.3. HRMS (EI) calcd for $C_{24}H_{25}FN_2O$: 376.1951, found 376.1948.

3.3. General Procedure for the preparation of 3

To a solution of (2′*R*,1″*R*)-(4-methoxyphenyl){[1-(1″-phenylethyl)aziridin-2′-yl]methylene}amine (**1**, 414 mg, 1.48 mmol) in 20 mL of CH_2Cl_2 under nitrogen atmosphere was added the nucleophile (1.48 mmol) at −10 °C. The mixture was stirred at room temperature for 2–3 h until the reaction was completed. Then the reaction was quenched by adding water at 0 °C and warmed to room temperature. The aqueous layer was extracted with CH_2Cl_2 (15 mL×5). The combined extracts was dried over anhydrous $MgSO_4$ and the solvent was evaporated to give the crude product, which was purified by silica gel flash chromatography to obtain analytically pure product.

3.3.1. (2*R*,2′*R*,1″*R*)-2-(*p*-Methoxyphenylamino)-2-[1′-(1″-phenylethyl)aziridin-2′-yl]acetonitrile (3a). Liquid. ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.39–1.49 (m, 1H), 1.47 (d, J=6.6 Hz, 3H), 1.90 (d, J=4.0 Hz, 1H), 2.09 (dd, J=5.8, 2.2 Hz, 1H), 2.55 (d, J=6.6 Hz, 1H), 3.70 (s, 3H), 4.29 (q, J=6.6 Hz, 1H), 6.60–6.87 (m, 4H), 7.18–7.32 (m, 5H). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 23.6, 29.7, 39.2, 46.6, 55.6, 68.8, 114.9, 115.9, 119.0, 126.7, 127.3, 128.4, 138.3, 143.6, 153.6. HRMS (EI) calcd for $C_{19}H_{21}N_3O$: 307.1685, found 307.1691.

3.3.2. (3*R*,2′*R*,1″*R*)-2,2-Dimethyl-3-(4-methoxyphenylamino)-3-[1′-(1″-phenylethyl)aziridin-2′-yl]propionic acid methyl ester (3b). Liquid. ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.07 (d, J=6.2 Hz, 1H), 1.31 (s, 9H), 1.43 (d, J=2.4 Hz, 1H), 1.58–1.62 (m, 1H), 2.47 (q, J=6.6 Hz, 1H), 3.38 (s, 1H), 3.59 (s, 3H), 3.64 (s, 3H), 3.98 (s, 1H), 6.63–6.73 (m, 4H), 7.14–7.26 (m, 5H). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 21.6, 22.9, 30.2, 40.2, 47.4, 51.4, 55.2, 61.6, 69.0, 114.3, 114.4, 126.6, 128.0, 143.2, 144.2, 151.5, 177.0. HRMS (EI) calcd for $C_{23}H_{30}N_2O_3$: 382.2256, found 382.2251.

3.3.3. (2*R*,2′*R*,1″*R*)-1-(4-Methoxyphenyl)-2-[1′-(1″-phenylethyl)aziridin-2′-yl]-2,3-dihydro-1*H*-pyridin-4-one (3c). Liquid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.28 (d, J=6.5 Hz, 1H), 1.36 (d, J=3.5 Hz, 1H), 1.44 (d, J=6.5 Hz, 3H), 2.00–2.04 (m, 1H), 2.41 (q, J=6.5 Hz, 1H), 2.84 (dd, J=16.5, 2.5 Hz, 1H), 3.05 (dd, J=16.5, 7.0 Hz, 1H), 3.62 (td, J=7.0, 2.5 Hz, 1H), 3.80 (s, 3H), 5.21 (d, J=8.0 Hz, 1H), 6.87 (d, J=7.0 Hz, 2H), 7.11 (d, J=9.0 Hz, 2H), 7.21–7.23 (m, 1H), 7.26–7.30 (m, 5H). ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 23.5, 34.1, 38.5, 39.7, 55.7, 62.6, 69.5, 100.8, 114.8, 124.0, 126.8, 127.2, 128.5, 138.5, 144.2, 149.8, 157.8, 191.1. HRMS (EI) calcd for $C_{22}H_{24}N_2O_2$: 348.1838, found 348.1834.

3.3.4. (2*S*,2′*R*,1″*R*)-1-(4-Methoxyphenyl)-2-[1′-(1″-phenylethyl)aziridin-2′-yl]-2,3-dihydro-1*H*-pyridin-4-one (3c′). Liquid. ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.23 (d, J=6.5 Hz, 3H), 1.47 (d, J=6.5 Hz, 1H), 1.62 (d, J=3.0 Hz, 1H), 2.37–2.46 (m, 2H), 3.02 (dd, J=16.5, 6.0 Hz, 1H), 3.59 (t, J=7.5 Hz, 1H), 3.83 (s, 3H), 4.12 (q, J=6.5 Hz, 1H), 5.28 (dd, J=6.5, 1.0 Hz, 1H), 6.94 (d, J=9.0 Hz, 2H), 7.26–7.30 (m, 1H), 7.33–7.38 (m, 4H), 7.45 (dd, J=7.0, 1.5 Hz, 1H), 7.59 (d, J=8.5 Hz, 2H). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 23.7, 32.3, 39.1, 39.3, 55.8, 63.2, 70.1, 102.0, 114.6, 121.6, 126.9, 127.4, 128.6, 138.4, 144.3, 147.5, 156.9, 191.3. HRMS (EI) calcd for $C_{22}H_{24}N_2O_2$: 348.1838, found 348.1840.

3.4. General procedure for 5-alkyl or 5-aryl-4-chloromethylimidazolidin-2-one (9 and 10)

To a solution of (2′*R*,1″*R*)-(4-methoxyphenyl){[1-(1″-phenylethyl)aziridin-2′-yl]alkyl}amine (**2** or **3**, 310 mg, 1.05 mmol) in 15 mL of THF under nitrogen atmosphere was added NaH (144 mg, 6 mmol) at −10 °C. The mixture was stirred for 1 h at −10 °C. To the mixture was slowly added triphosgene solution (0.356 g, 1.2 mmol) in THF (5 mL) at −10 °C. The mixture was stirred for 2 h at −10 °C. The reaction was quenched with water at −10 °C and warmed to room temperature. The aqueous layer was extracted with CH_2Cl_2 (10 mL×5). The combined organic extracts was dried over $MgSO_4$ and the solvent was evaporated in vacuo to give the crude product as a white solid, which was purified by silica gel flash chromatography to give analytically pure product.

3.4.1. (4*S*,5*R*,1′*R*)-4-Chloromethyl-1-(4-methoxyphenyl)-5-methyl-3-(1′-phenylethyl)imidazolidin-2-one (9a). Liquid. ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.82 (d, J=6.2 Hz, 3H), 1.50 (d, J=7.4 Hz, 3H), 2.92 (dt, J=7.0, 3.2 Hz, 1H), 3.32 (dd, J=11.4, 7.6 Hz, 1H), 3.42 (dd, J=11.4, 3.2 Hz, 1H), 3.65 (s, 3H), 3.90 (qd, J=6.2, 3.2 Hz, 1H), 5.25 (q, J=7.4 Hz, 1H), 6.72–6.78 (m, 2H), 7.11–7.27 (m, 7H). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 18.7, 19.4, 45.5, 51.2, 54.6, 55.4, 58.8, 114.1, 123.1, 127.3, 127.7, 128.6, 131.4, 139.8, 156.2, 156.8. HRMS (EI) calcd for $C_{20}H_{23}ClN_2O_2$: 358.1448, found 358.1453.

3.4.2. (4*S*,5*R*,1′*R*)-4-Chloromethyl-5-ethyl-1-(4-methoxyphenyl)-3-(1′-phenylethyl)imidazolidin-2-one (9b). Liquid. ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.45 (t, v=6.6 Hz, 3H), 1.01–1.53 (m, 2H), 1.50 (d, J=6.2 Hz, 3H), 3.05 (q, J=2.8 Hz, 1H), 3.29–3.55 (m, 2H), 3.63 (s, 3H), 3.78 (dt, J=7.8, 3.0 Hz, 1H), 5.23 (q, J=6.6 Hz, 1H), 6.61–6.76 (m, 2H), 7.11–7.27 (m, 7H). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 7.61, 18.7, 24.6, 46.1, 51.4, 55.3, 55.6, 59.4, 114.0, 123.2, 127.3, 127.7, 128.5, 131.4, 139.6, 156.1, 156.8. HRMS (EI) calcd for $C_{21}H_{25}ClN_2O_2$: 372.1605, found 372.1594.

3.4.3. (4*S*,5*R*,1′*R*)-4-Chloromethyl-1-(4-methoxyphenyl)-3-(1′-phenylethyl)-5-vinylimidazolidin-2-one (9c). Liquid. ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.59 (d, J=7.4 Hz, 3H), 3.11 (td, J=4.4, 3.4 Hz, 1H), 3.45 (d, J=4.4 Hz, 3H), 3.70 (s, 3H), 4.31 (dd, J=6.0, 3.4 Hz, 1H), 5.01 (d, J=8.2 Hz, 1H), 5.15 (d, J=18.0 Hz, 1H), 5.21–5.45 (m, 1H), 6.76–6.81 (m, 2H), 7.18–7.35 (m, 7H). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 18.5, 45.1, 51.3, 55.3, 58.0, 61.0, 113.9, 118.3, 122.3, 127.3, 127.7, 128.6, 132.1, 135.8,

139.4, 155.9, 157.1. HRMS (EI) calcd for $C_{21}H_{23}ClN_2O_2$: 370.1448, found 370.1441.

3.4.4. (4*S*,5*R*,1′*R*)-5-Allyl-4-chloromethyl-1-(4-methoxyphenyl)-3-(1′-phenylethyl)imidazolidin-2-one (9d). Liquid. ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.51 (d, J=7.0 Hz, 3H), 2.47 (d, J=7.2 Hz, 2H), 3.47–3.71 (m, 3H), 3.76 (s, 3H), 4.12 (dt, J=7.2, 2.6 Hz, 1H), 4.93–5.02 (m, 2H), 5.38 (q, J=7.0 Hz, 1H), 5.50–5.57 (m, 1H), 6.85 (d, J=8.8 Hz, 2H), 7.20–7.31 (m, 7H). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 18.4, 31.1, 41.8, 50.7, 55.4, 55.6, 56.7, 114.1, 118.0, 125.1, 127.3, 127.6, 128.7, 130.9, 133.4, 139.1, 156.8, 158.7. HRMS (EI) calcd for $C_{22}H_{25}ClN_2O_2$: 384.1605, found 384.1603.

3.4.5. (4*S*,5*S*,1′*R*)-5-Allyl-4-chloromethyl-1-(4-methoxyphenyl)-3-(1′-phenylethyl)imidazolidin-2-one (9d′). Liquid. ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.52 (d, J=7.4 Hz, 3H), 1.60–1.75 (m, 1H), 2.02–2.09 (m, 1H), 3.10–3.13 (m, 1H), 3.35–3.41 (m, 2H), 3.37 (s, 3H), 3.85 (dt, J=6.4, 3.4 Hz, 1H), 4.52 (d, J=17.0 Hz, 1H), 4.78 (d, J=8.4 Hz, 1H), 5.16–5.33 (m, 2H), 6.77 (d, J=8.8 Hz, 2H), 7.11–7.27 (m, 7H). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 18.7, 36.5, 45.9, 51.4, 55.1, 55.4, 58.0, 114.2, 119.5, 123.5, 127.5, 127.8, 128.6, 131.2, 131.5, 139.7, 156.3, 156.8. HRMS (EI) calcd for $C_{22}H_{25}ClN_2O_2$: 384.1605, found 384.1611.

3.4.6. (4*S*,5*R*,1′*R*)-5-*n*-Butyl-4-chloromethyl-1-(4-methoxyphenyl)-3-(1′-phenylethyl)imidazolidin-2-one (9e). Liquid. ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.47 (t, J=7.0 Hz, 3H), 0.65–1.13 (m, 4H), 1.35–1.45 (m, 2H), 1.38 (d, J=6.4 Hz, 3H), 3.09 (dt, J=7.4, 3.2 Hz, 1H), 3.28–3.47 (m, 2H), 3.61 (s, 3H), 3.69–3.77 (m, 1H), 5.15 (q, J=6.4 Hz, 1H), 6.69–6.73 (m, 2H), 7.05–7.19 (m, 7H). HRMS (EI) calcd for $C_{23}H_{29}ClN_2O_2$: 400.1918, found 400.1916.

3.4.7. (4*S*,5*S*,1′*R*)-5-*n*-Butyl-4-chloromethyl-1-(4-methoxyphenyl)-3-(1′-phenylethyl)imidazolidin-2-one (9e′). Liquid. ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.44 (t, J=7.0 Hz, 3H), 0.78–1.20 (m, 4H), 1.46–1.49 (m, 2H), 1.49 (d, J=6.4 Hz, 3H), 3.06 (td, J=7.0, 6.6 Hz, 1H), 3.25–3.52 (m, 2H), 3.65 (s, 3H), 3.71–3.82 (m, 1H), 5.16 (q, J=6.4 Hz, 1H), 6.71–6.78 (m, 2H), 7.11–7.27 (m, 7H). HRMS (EI) calcd for $C_{23}H_{29}ClN_2O_2$: 400.1918, found 400.1921.

3.4.8. (4*S*,5*R*,1′*R*)-4-Chloromethyl-1-(4-methoxyphenyl)-5-phenyl-3-(1′-phenylethyl)imidazolidin-2-one (9f). Liquid. ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.58 (d, J=7.0 Hz, 3H), 3.21–3.27 (m, 1H), 3.50–3.64 (m, 1H), 3.64 (s, 3H), 4.85 (d, J=3.0 Hz, 2H), 5.33 (q, J=7.0 Hz, 1H), 6.66–7.00 (m, 4H), 7.12–7.27 (m, 10H). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 18.6, 45.5, 51.5, 55.3, 60.8, 62.2, 113.9, 121.7, 125.8, 127.1, 128.0, 128.2, 128.8, 129.4, 132.1, 139.4, 139.9, 155.6, 157.3. HRMS (EI) calcd for $C_{25}H_{25}ClN_2O_2$: 420.1605, found 420.1602.

3.4.9. (4*S*,5*R*,1′*R*)-4-Chloromethyl-1-(4-methoxyphenyl)-5-(4-methylphenyl)-3-(1′-phenylethyl)imidazolidin-2-one (9g). Liquid. ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.57 (d, J=6.6 Hz, 3H), 2.18 (s, 3H), 3.21–3.26 (m, 1H), 3.48 (d, J=4.4 Hz, 2H), 3.61 (s, 3H), 4.80 (d, J=3.2 Hz, 1H), 5.32 (q, J=7.4 Hz, 1H), 6.67 (d, J=8.6 Hz, 2H), 6.86–6.95 (m, 4H), 7.13–7.25 (m, 7H). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 18.6, 20.9, 45.4, 51.5, 55.2, 60.9, 62.0, 113.8, 121.8, 125.8, 127.1, 127.6, 128.5, 129.4, 132.1, 136.9, 137.7, 139.4, 155.6, 157.3. HRMS (EI) calcd for $C_{26}H_{27}ClN_2O_2$: 434.1761, found 434.1762.

3.4.10. (4*S*,5*R*,1′*R*)-4-Chloromethyl-5-(4-fluorophenyl)-1-(4-methoxyphenyl)-3-(1′-phenylethyl)imidazolidin-2-one (9h). Liquid. ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.57 (d, J=7.8 Hz, 3H), 3.19–3.34 (m, 1H), 3.59 (s, 3H), 3.64 (d, J=3.4 Hz, 2H), 4.83 (d, J=2.6 Hz, 1H), 5.32 (q, J=7.4 Hz, 1H), 6.58–6.88 (m, 4H), 6.89–7.21 (m, 9H). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 18.6, 45.5, 51.6, 56.9, 60.7, 61.7, 114.0, 115.5, 121.7, 126.9, 127.1, 127.4, 127.6, 128.1, 128.6, 128.8, 135.7, 138.2, 139.5, 155.8, 157.9. HRMS (EI) calcd for $C_{25}H_{24}ClFN_2O_2$: 438.1510, found 438.1513.

3.4.11. (4*S*,5*S*,1′*R*)-4-Chloromethyl-5-cyano-3-(4-methoxyphenyl)-1-(1′-phenylethyl)imidazolidin-2-one (10a). Liquid. ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.50 (d, J=7.0 Hz, 3H), 3.28–3.40 (m, 1H), 3.51–3.63 (m, 2H), 3.61 (s, 3H), 4.50 (d, J=3.0 Hz, 1H), 5.17 (q, J=7.0 Hz, 1H), 6.78 (d, J=8.8 Hz, 4H), 7.10–7.30 (m, 5H). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 18.4, 44.4, 49.9, 51.7, 55.2, 56.3, 114.3, 116.4, 124.0, 127.1, 128.1, 128.7, 129.5, 138.2, 155.6, 157.5. Anal. Calcd HRMS (EI) calcd for $C_{20}H_{20}ClN_3O_2$: 369.1244, found 369.1241.

3.4.12. (4′*S*,5′*R*,1″*R*)-2-[4′-Chloromethyl-1′-(4-methoxyphenyl)-2-oxo-3- (1″-phenylethyl)imidazolidin-5′-yl]-2,2-dimethylpropionate acid methyl ester (10b). Liquid. ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.74 (s, 3H), 0.82 (s, 3H), 1.58 (d, J=7.2 Hz, 3H), 3.10–3.19 (m, 1H), 3.12 (s, 3H), 3.45 (dd, J=11.0, 1.8 Hz, 1H), 3.55 (dd, J=11.0, 4.2 Hz, 1H), 3.65 (s, 3H), 4.27 (d, J=2.2 Hz, 1H), 5.13 (q, J=7.2 Hz, 1H), 6.75 (d, J=8.8 Hz, 2H), 7.20–7.34 (m, 7H). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 18.6, 19.9, 20.1, 46.2, 47.9, 51.3, 52.1, 54.2, 55.0, 63.6, 113.5, 126.7, 127.4, 127.7, 128.4, 131.4, 139.0, 157.1, 157.2, 175.3. HRMS (EI) calcd for $C_{24}H_{29}ClN_2O_4$: 444.1816, found 444.1823.

3.5. Cycloaddition reaction with 2-trimethylsilyloxy-1,3-butadiene (4a, 4b and 5a)

Into the solution of (2′*R*,1″*R*)-(4-methoxyphenyl){[1-(1″-phenylethyl)aziridin-2′-yl]methylene}amine (**1**, 280 mg, 1.0 mmol) in 10 mL of CH_2Cl_2 were added 2-trimethylsilyloxy-1,3-butadiene (**11**, 142 mg, 1.0 mmol) and $BF_3\cdot OEt_2$ (56 mg, 0.4 mmol) at room temperature. The resultant solution was stirred for 0.5 h until all the starting material was consumed. Then the reaction was quenched by adding water. The reaction product was isolated with CH_2Cl_2 (20 mL×4). The solution was washed with brine twice. The organic layer was dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was dissolved in 10 mL THF. Into this solution was added ethereal solution n-Bu_4NF (4 mmol). The reaction mixture was stirred for 30 min and quenched by adding water. The organic layer was treated in the standard protocol. The crude reaction mixture was obtained after removal of solvent under reduced pressure. Careful chromatographic separation and purification yielded the analytically pure products **4a** (137 mg), **4b** (21 mg) and **5a** (13 mg).

3.5.1. 1-4-Methoxyphenyl)-2-[1′-(1″-phenylethyl)aziridin-2′-yl]piperidin-4-one, major isomer (4a). Viscous liquid. $[\alpha]_D$ 3.85 (*c* 1.5 in EtOAc); ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.23 (d, J=6.2 Hz, 3H), 1.37–1.84 (m, 3H), 2.45–2.87 (m, 5H), 3.34–3.97 (m, 3H), 3.76 (s, 3H), 6.81–7.02 (m, 4H), 7.21–7.30 (m, 5H). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 23.4, 33.9, 40.8, 41.2, 44.9, 47.4, 55.6, 63.8, 69.8, 114.4, 121.1, 126.8, 127.2, 128.4, 143.7, 144.3, 154.9, 208.9. HRMS (EI) calcd for $C_{22}H_{26}N_2O_2$: 350.1994, found 350.1991.

3.5.2. 1-4-Methoxyphenyl)-2-[1′-(1″-phenylethyl)aziridin-2′-yl]piperidin-4-one, minor isomer (4b). Viscous liquid. $[\alpha]_D$ 9.40 (*c* 5 in EtOAc); ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.43 (d, J=6.2 Hz, 3H), 1.27–1.84 (m, 3H), 2.39–2.98 (m, 5H), 3.21–3.77 (m, 3H), 3.87 (s, 3H), 6.76–7.48 (m, 9H). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 23.3, 31.4, 40.5, 41.6, 42.8, 44.9, 55.8, 59.1, 69.9, 114.7, 117.7, 126.9, 127.1, 128.4, 143.9, 144.5, 153.4, 209.4. HRMS (EI) calcd for $C_{22}H_{26}N_2O_2$: 350.1994, found 350.1208.

3.5.3. 6-Methoxy-2-[1′-(1″-phenylethyl)aziridin-2′-yl]-4-trimethylsilanyloxy-4-vinyl-1,2,3,4-tetrahydroquinoline (5a). Gummy liquid. $[\alpha]_D$ 2.55 (*c* 1.0 in EtOAc); ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.07 (s, 9H), 1.27 (d, J=6.8 Hz, 3H), 1.31–1.87 (m, 4H), 1.57 (dd, 2H), 2.51 (q, J=6.6 Hz, 1H), 3.57–3.83 (m, 2H), 3.75 (s, 3H), 5.30 (dd, J=7.8, 1.8 Hz, 1H), 5.56 (dd, J=15.2, 1.8 Hz, 1H), 6.06 (dd, J=15.2, 7.8 Hz, 1H), 6.97–6.83 (m, 3H), 7.28–7.46 (m, 5H). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 1.93, 2.01, 23.6, 29.8, 41.6, 43.0, 47.8, 56.0, 56.1, 69.6, 74.0, 113.4, 114.9, 115.2, 116.5, 122.7, 126.9, 127.2, 128.5, 128.6, 139.1, 144.1, 144.8, 150.7. HRMS (EI) calcd for $C_{25}H_{34}N_2O_2Si$: 422.2390, found 422.2383.

3.5.4. 6-Methoxy-4-methyl-4-(1-methylethenyl)-2-[1′-(1″-phenylethyl)aziridin-2′-yl]-1,2,3,4-tetrahydroquinoline (5b). The starting imine (2′*R*,1″*R*)-(4-methoxyphenyl){[1-(1″-phenylethyl)aziridin-2′-yl]methylene}-amine (**1**, 403 mg, 1.35 mmol) was dissolved in 10 mL of CH_2Cl_2 and then were added excess amount of 2,3-dimethyl-1,3-butadiene (**12**, 123 mg, 1.50 mmol) and $BF_3\cdot OEt_2$ (85 mg, 0.6 mmol) at 0 °C. T he resultant solution was stirred for 2 h at room temperature. After the reaction was completed according to TLC the reaction was quenched by adding saturated $NaHCO_3$ solution. The reaction product was isolated with CH_2Cl_2 (15 mL×4), which was washed with brine twice. The organic layer was dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. Product was further purified by flash column chromatography to afford the titled products 224 mg as a diastereomeric mixture in 49% yield.

Gummy liquid. ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.15–1.83 (m, 5H), 1.28 (s, 3H), 1.89–2.12 (m, 2H), 2.52 (q, J=6.7 Hz, 1H), 2.95 (tq, J=6.7, 3.4 Hz, 1H), 3.74 (s, 3H), 4.12–4.25 (m, 1H), 4.75–5.12 (m, 1H), 6.54–6.78 (m, 2H), 7.28–7.64 (m, 2H). 13C NMR (50.3 MHz, $CDCl_3$) δ 14.35, 20.25, 21.23, 23.67, 30.30, 31.50, 38.06, 42.73, 45.39, 52.72, 55.72, 60.55, 69.51, 111.93, 112.95, 113.44, 116.12, 126.90, 127.26, 128.44, 128.56, 129.25, 138.18, 144.37, 151.46, 152.45. HRMS (EI) calcd for $C_{24}H_{30}N_2O$: 362.2358, found 362.2351.

3.5.5. (2a*R*,3*S*,8b*S*,2′*R*,1″*R*)-7-Methoxy-3-[1′-(1″-phenylethyl)aziridin-2′-yl]-2a,8b-bistrimethylsilyloxy-1,2,2a,3,4,8b-hexahydrocyclobuta[*c*]quinoline (5c). The starting imine (2′*R*,1″*R*)-(4-methoxyphenyl){[1-(1″-phenylethyl)-aziridin-2′-yl]methylene}amine (**1**, 350 mg, 1.25 mmol) was dissolved in 15 mL of CH_2Cl_2 and then were added bis-1,2-trimethylsilyloxycyclobutene (**13**, 290 mg, 1.25 mmol) and $BF_3\cdot OEt_2$ (71 mg, 0.5 mmol) at −78 °C. The resultant solution was stirred for 2 h at −78 °C. After the reaction was completed according to TLC the reaction was quenched by adding saturated $NaHCO_3$ solution. The reaction product was isolated with CH_2Cl_2 (15 mL×4), which was washed with brine twice. The organic layer was dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. Analytically pure product 433 mg was obtained after flash column chromatography in 68% yield.

White soild. Mp 140–141 °C. $[\alpha]_D$ −2.30 (*c* 3.0 in EtOAc); ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.12–0.31 (s, 18H), 1.29 (d, J=4.2 Hz, 3H), 1.50 (d, J=6.2 Hz, 2H), 1.72 (d, J=3.6 Hz, 1H), 1.88–2.16 (m, 4H), 2.33 (q, J=6.6 Hz, 1H), 3.81 (s, 3H), 6.57 (d, J=8.8 Hz, 1H), 6.72 (dd, J=8.8 Hz, 2.1 Hz, 1H), 6.95 (d, J=3.0 Hz, 1H), 7.24–7.37 (m, 5H). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 2.39, 2.94, 23.6, 24.2, 34.7, 36.9, 40.9, 55.7, 59.7, 69.5, 74.7, 83.9, 112.9, 115.1, 116.8, 126.1, 127.1, 128.5, 131.0, 135.6, 144.5, 152.8. HRMS (EI) calcd for $C_{28}H_{41}N_2O_3Si_2$: 509.2656, found 509.2651. Anal. Calcd for $C_{28}H_{41}N_2O_3Si_2$: C, 66.0; H, 8.11; N, 5.49. Found: C, 66.2; H, 8.03; N, 5.52.

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