Catalyzed addition of diazoacetoacetates to imines: synthesis of highly functionalized aziridines†

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Received 7th August 2008, Accepted 14th October 2008
First published as an Advance Article on the web 10th November 2008
DOI: 10.1039/b813763c

The addition of diazoacetoacetates to aromatic imines derived from *p*-methoxyaniline is achieved using dirhodium tetraacetate as the catalyst. Highly functionalized aziridines are obtained in good yield and with excellent stereoselectivity. 2-Diazo-1,3-diketones also provide good yields of aziridines, but dimethyl diazomalonate is inactive in the transformation. The diazoacetoacetates of chiral alcohols are also examined in the reaction and moderate diastereoselectivity is achieved with (*R*)-pantolactone-derived diazoacetoacetate. A reaction mechanism through metal-carbene and azomethine ylide is proposed.

1. Introduction

Aziridines are highly useful synthetic intermediates in organic synthesis and structural units of many natural products and drugs.[1] Various synthetic methods of aziridines,[2] including several asymmetric versions,[3] have been reported. Among them, the addition of carbenes generated from diazo compounds to imines is highly attractive considering the anticipated good yield, high product stereoselectivity, and ease of procedure. Transition metal complexes,[4] Lewis acids,[5] Brønsted acids,[6] lithium perchlorate[7] and ionic liquids[8] have been found to promote efficiently the addition of diazoacetates to imines. The corresponding aziridinecarboxylates are prepared generally in good yields. In addition to diazoacetates, other diazo compounds such as $TMSCHN_2$,[9] diazophosphonates,[10] phenyldiazoactetates and styryldiazoacetates[11] were also successfully applied. On the other hand, addition of diazoacetoacetates to imines is also an attractive research subject and the reaction provides highly functionalized aziridines. They can be used to prepare β-hydroxy-α-amino acids, which are important synthetic intermediates for many natural products and drugs.[12] In addition they are susceptible to ring opening reaction with various nucleophilic agents to provide a number of useful compounds.[13] However, in a previous study the addition of diazoacetoacetates to imines failed to provide desired aziridines, probably due to their lower reactivity compared to diazoacetates.[5g] In this paper we report the rhodium-catalyzed reaction of diazoacetoacetates with imines derived from *p*-methoxyaniline. Highly functionalized aziridines are obtained in good yield and with excellent *cis*-selectivity.

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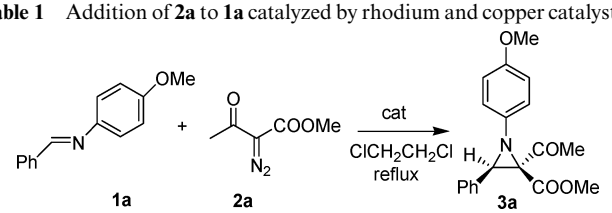
† CCDC reference number 682854. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b813763c

2. Results and discussion

2.1 Study of catalysts and reaction conditions

The reaction of *N*-benzylidene-4-methoxyaniline (**1a**) with methyl diazoacetoacetate (**2a**) was studied in the presence of rhodium and copper catalysts. The results are summarized in Table 1. The use of $Rh_2(OAc)_4$ provided the expected aziridine product in good yield and excellent stereoselectivity. Only the *cis*-isomer **3a** was observed and its relative configuration was determined by NOE experiment. The amount of diazo compound exerted a significant effect on the yield of **3a**. When 1.0 equivalent, 1.5 equivalents and 2.0 equivalents of **2a** were used, the yield of **3a** increased from 69% to 87%, and to 92%, respectively (Table 1, entries 1–3). This result implied the partial loss of **2a** under the reaction conditions. The higher reaction temperature of 1,2-dichloroethane (b.p. 81 °C) was favorable, since lower yield of **3a** was obtained in dichloromethane (b.p. 39 °C) (Table 1, entry 4 *vs.* entry 1).

Table 1 Addition of **2a** to **1a** catalyzed by rhodium and copper catalysts.[a]



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

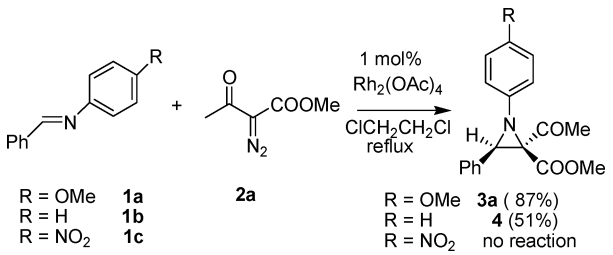
Entry	Catalyst	Time (h)	Yield (%)[b]
1	$Rh_2(OAc)_4$ (1 mol%)	2	87
2	$Rh_2(OAc)_4$ (1 mol%)	2	92[c]
3	$Rh_2(OAc)_4$ (1 mol%)	2	69[d]
4	$Rh_2(OAc)_4$ (1 mol%)	2	35[e]
5	$Cu(hfacac)_2$ (3 mol%)	2	30
6	$Cu(acac)_2$ (3 mol%)	2	30
7	$CuPF_6$ (3 mol%)	3	20
8	$Cu(OTf)_2$ (3 mol%)	6	~0

[a] The reactions were carried out in refluxing 1,2-dichloroethane with **1a** (1 mmol) and **2a** (1.5 mmol). [b] Isolated yield based on **1a**. [c] 2 mmol **2a** was used. [d] 1mmol **2a** was used. [e] CH_2Cl_2 was used as the reaction solvent.

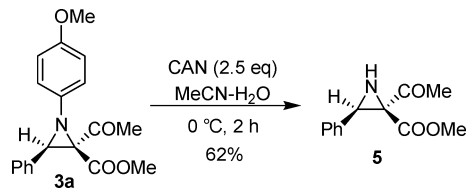
Use of copper salts such as $Cu(hfacac)_2$, $Cu(acac)_2$ and $CuPF_6$ gave low yields of **3a**, but $Cu(OTf)_2$ was totally ineffective in this reaction. Since $Cu(OTf)_2$ is the strongest Lewis acid among the tested copper salts, the result suggested that the reaction did not proceed through the Lewis acid catalytic addition of the diazo compound to the imine. A metal carbene route is consistent with this information.[14]

2.2 The effect of electronic property of imines

Furthermore imines **1a–1c** with different electronic properties were examined in the reaction with **2a**, and the results are illustrated in Scheme 1. The electronic properties of imines show profound effects on the reaction. Imine **1c** with a strong electron-withdrawing group (4-NO_2) was completely inactive. In contrast imine **1a** with an electron-donating group (4-MeO) provided aziridine **3a** in good yield. Unsubstituted imine **1b** gave 51% yield of aziridine **4**. An additional advantage using imine **1a** was that 4-MeO-phenyl could be removed readily by oxidization to provide 1-H aziridines in good yield (Scheme 2).[11]



Scheme 1 The reaction of imines **1a–1c** with **2a**.

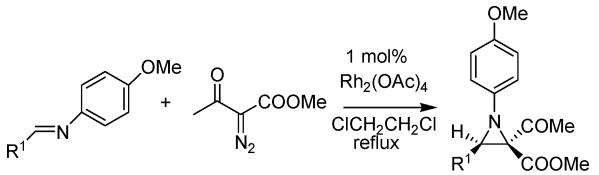


Scheme 2 The reaction of **3a** with cerium(IV) ammonium nitrate (CAN).

2.3 The reaction of methyl diazoacetoacetate with imines

The imines derived from *p*-methoxyaniline and a variety of aldehydes were examined in the reaction with **2a**. The results are summarized in Table 2. The imines prepared from benzaldehydes with *para*- or *ortho*- methoxy substitutent provided *cis*-aziridines in almost quantitative yields (Table 2, entries 2–3). In contrast, *para*-nitro substitution completely inhibited the reaction (Table 2, entries 4). Again the results confirm that the electronic density of imines is of key importance for this transformation. *para*- or *ortho*-Chloro substitution of benzaldehyde was tolerated very well (Table 2, entries 5–6). The imine **1i**, derived from 2-naphthaldehyde, also provided the aziridine in excellent yield. The imine **1j**, derived from picolinaldehyde did not react with **2a**. The deactivation of $Rh_2(OAc)_4$ by a strong coordination with **1j** was proposed in this case. The other imines derived from thiophene-2-carbaldehyde, cinnamaldehyde, isobutyraldehyde and pivalaldehyde, gave a complex mixture of products, and no substantial amount of aziridine products could be isolated.

Table 2 The reaction of **2a** with imines derived from a variety of aldehydes and *p*-methoxy aniline[a]

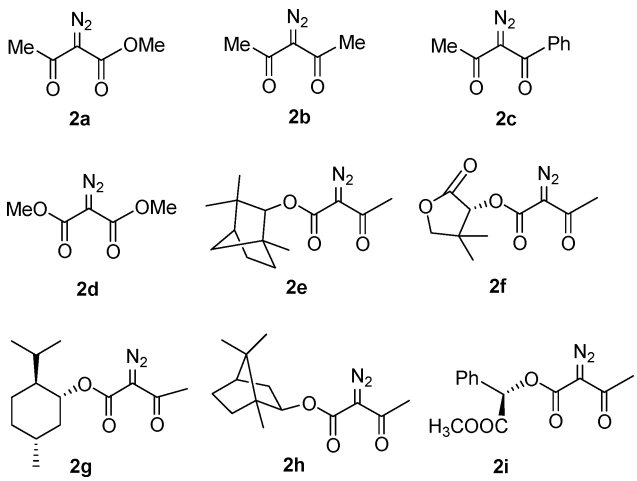


Entry	Imine	R^1	Product (yield (%))[b]
1	**1a**	Ph	**3a** (87)
2	**1d**	*p*-MeO-Ph	**3d** (99)
3	**1e**	*o*-MeO-Ph	**3e** (99)
4	**1f**	*p*-NO_2-Ph	—[c]
5	**1g**	*p*-Cl-Ph	**3g** (94)
6	**1h**	*o*-Cl–Ph	**3h** (89)
7	**1i**	2-naphthyl	**3i** (97)
8	**1j**	2-pyridinyl	—[c]

[a] The reactions were carried out in refluxing 1,2-dichloroethane with **1** (1 mmol) and **2a** (1.5 mmol). [b] Isolated yield based on **1**. [c] No reaction.

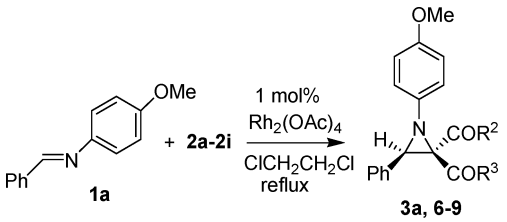
2.4 The reaction of imine 1a with a variety of diazo compounds

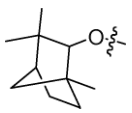
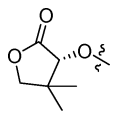
Furthermore diazoacetoacetone (**2b**), 2-diazo-1-phenylbutane-1,3-dione (**2c**), dimethyl diazomalonate (**2d**) and diazoacetoacetate of chiral alcohols (**2e–2i**) were prepared (Scheme 3) and examined in the reaction with **1a**. The results are summarized in Table 3. Both **2b** and **2c** gave the corresponding aziridines in good yield. **2d** was inactive in the reaction. (1*R*)-*endo*-(+)-Fenchol-derived diazoacetoacetate **2e** provided aziridine **6** in 77% yield and low diastereoselectivity (d.r. = 1.3:1). (*R*)-Pantolactone-derived diazoacetoacetate **2f** afforded aziridine **7** in 69% yield and better diastereoselectivity (d.r. = 3:1). (*L*)-Menthol-derived diazoacetoacetate (**2g**) did not afford the corresponding aziridine product, instead an intramolecular C–H insertion product **10** was obtained in 73% yield (Scheme 4).[15], which structure was confirmed by NMR and furthermore by X-Ray diffraction (Fig. 1)[16] The chiral diazoacetoacetates **2h** and **2i** provided complex mixtures



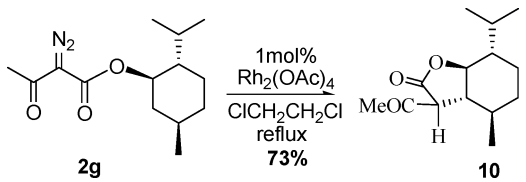
Scheme 3 Diazo compounds **2a-2i**.

Table 3 The reaction of diazo compounds **2a-2g** with **1a**.[a]



Diazo compound	R^2	R^3	Product (yield (%))[b]
2a	Me	OMe	**3a** (87)
2b	Me	Me	**6** (88)
2c	Me	Ph	**7** (84)[c]
2d	MeO	MeO	(0)
2e	Me		**8** (77)[d]
2f	Me		**9** (69)[e]

[a] The reactions were carried out in refluxing dichloroethane with **1a** (1 mmol) and **2a–2i** (1.5 mmol). [b] Isolated yield based on **1a**. [c] Mixture of *cis*/*trans*-aziridine (1/2.2). [d] Two diastereoisomers (1.3/1). [e] Two diastereoisomers (3/1).



Scheme 4 Intramolecular C–H insertion of **2g**.

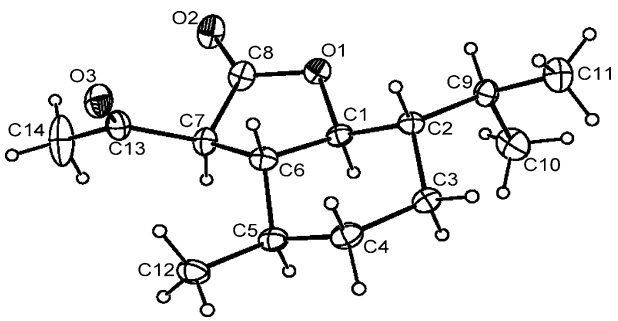
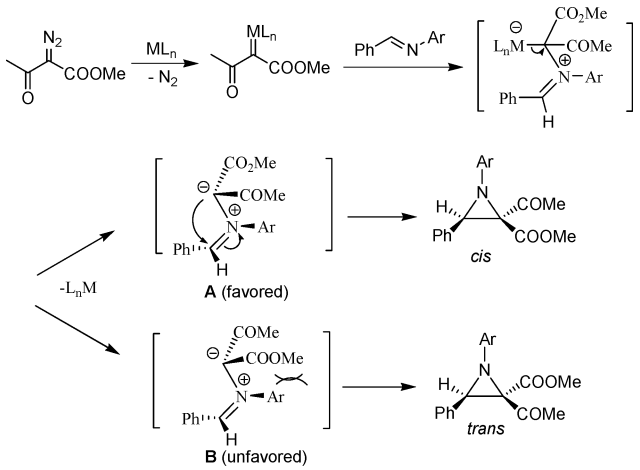


Fig. 1 ORTEP drawing of **10**.

of products, from which no substantial amount of aziridines could be isolated. These results suggest that C–H insertion and other side reactions are competitive with the aziridination reaction for diazoacetoacetates derived from chiral alcohols. The structure of chiral alcohols has great effects on the reactivity of the corresponding diazoacetoacetates. The diazoacetoacetates with available C–H bonds to form insertion products of five-membered rings (**2g**, **2h**) or with aromatic C–H bond (**2i**) failed to give aziridines. For **2e** and **2f**, no C–H bonds are available to form insertion products of five-membered rings, so good yields of aziridines were obtained. A detailed study of C–H insertion reaction of diazoacetoacetates had been reported by Doyle and coworkers.[15]

2.4 Reaction mechanism

A proposed reaction mechanism is illustrated in Scheme 5. Methyl diazoacetoacetate is decomposed by rhodium acetate to generate a metal carbene, which reacts with the imine to provide azomethine ylide. The consequent intramolecular ring-closing step occurs *via* conformation **A** to provide the *cis*-aziridine stereoselectively.[4e,11] Conformation **B** is unfavored due to large steric interactions between the ester group with N-aryl of imine.



Scheme 5 The proposed reaction mechanism.

3. Conclusion

In conclusion, highly functionalized aziridines were prepared in good yields and excellent stereoselectivities by catalyzed addition of diazoacetoacetates to imines derived from *p*-methoxyaniline. Dirhodium tetraacetate is a better catalyst than copper salts in this reaction. Diazoacetoacetates of chiral alcohols were also examined and moderate diastereoselectivity was achieved with (*R*)-pantolactone-derived diazoacetoacetate. The reported reaction provides a new synthetic method of aziridines from diazoacetoacetates and imines.

4. Experimental

General details

NMR spectra were recorded on a Varian Inova 400 MHz instrument and chemical shifts are reported in parts per million (ppm, δ) downfield from the internal standard. Me_4Si (TMS, $\delta = 0$) is used as the internal standard for ^1H NMR spectra. ^{13}C NMR spectral data are reported relative to the central line of the chloroform signal ($\delta = 77.00$ ppm). High-resolution mass spectra were obtained on JEOL HX110A or GCT-TOF spectrometer. Low-resolution mass spectra were obtained on a Finnigan LC-MS spectrometer. Infrared spectra were recorded on Mattson Alpha-Centauri FT-IR spectrometer, either as a thin film, a nujol mull, or a solution on sodium chloride plates. The absorptions are reported in wavenumbers (cm^{-1}). Element analyses were recorded on carlo-Erba

EA1110 CNNO-S instrument. X-ray diffraction was recorded on Rigaku Mercury CCD spectrometer. Thin layer chromatography was performed on Merck Silica Gel 40 F_{254} glass-backed plates. The visualization was achieved with UV, iodine, or phosphomolybdic acid. Flash column chromatography was performed on 40–63 μm, 230–400 mesh, 60Å silica gel. Dichloromethane and 1,2-dichloroethane were distilled over calcium hydride. Other solvents were used as their commercial anhydrous grade. Chemicals were purchased form Aldrich or Acros chemical company. The imines **1a-1j** were prepared by reflux of corresponding aldehydes (1 equivalent) and anilines (1 equivalent) in ethanol for 1–2 hours. Generally crystal imines in good purity were obtained after cooling of the reaction mixture. The diazo compounds **2a-2i** were prepared *via* treatment of corresponding acetoacetates or 1,3-diketones with methanesulfonyl azide and triethylamine according to reported procedures.[15]

Representative experimental procedure for the catalyzed addition of diazoacetoacetates to imines

A solution of methyl diazoacetoacetate **2a** (213 mg, 1.5 mmol) in $ClCH_2CH_2Cl$ (4 mL) was added *via* a syringe pump over one hour to a refluxing solution of $Rh_2(OAc)_4$ 4.4 mg (0.01 mmol) and benzylidene-p-methoxyaniline **1a** (211 mg, 1.0 mmol) in $ClCH_2CH_2Cl$ (8 mL). The resulting solution was allowed to reflux for another hour. The reaction mixture was filtered through a short silica plug, which was washed with $ClCH_2CH_2Cl$ (10 mL). The solvent was removed and the crude product was purified by flash column chromatography on silica gel (hexane: ethyl acetate = 3: 1) afforded **3a** as a colorless oil (284 mg, 87%).

***cis*-Methyl 1-(4-methoxyphenyl)-2-acetyl-3-phenyl-aziridine-2-carboxylate (3a).** IR (film, cm^{-1}): 1744 (s), 1610 (m), 1511 (s), 1245 (m); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.36-7.29 (m, 3 H), 7.28-7.24 (m, 4 H), 6.80 (d, J = 9.0 Hz, 2 H), 4.87 (s, 1 H), 3.73 (s, 3 H), 3.25 (s, 3 H), 1.78 (s, 3 H); ^{13}C NMR ($CDCl_3$, 100 Hz) δ 168.58, 163.49, 156.16, 133.42, 130.75, 128.65, 128.36, 126.60, 118.41, 114.22, 66.06, 65.84, 55.30, 51.66, 17.43; HRMS (FAB) calc. for $C_{19}H_{19}NO_4$ (M^+): 325.1314, found: 325.1330.

***cis*-Mehtyl 2-acetyl-1,3-bis (4-methoxyphenyl)-aziridine-2-carboxylate (3d).** White solid. M. p. 100–102 °C; IR (KBr, cm^{-1}): 1757 (s), 1614 (m), 1514 (s), 1457 (m), 1390 (m); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.27 (d, J = 8.8 Hz, 2H), 7.19 (d, J = 8.8 Hz, 2H), 6.85 (d, J = 8.8 Hz, 2H), 6.81 (d, J = 8.8 Hz, 2H), 4.81 (s, 1H), 3.78 (s, 3H), 3.76 (s, 3H), 3.32 (s, 3H), 1.77 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 Hz) δ 168.8, 163.8, 159.9, 156.2, 130.8, 128.0, 125.2, 118.5, 114.3, 113.9,66.0, 65.9, 55.4, 55.2, 51.8, 17.4; HRMS (EI) calc. for $C_{20}H_{21}O_5N_1$ (M^+): 355.1414, found: 355.1413.

***cis*-Methyl 1-(4-methoxyphenyl)-2-acetyl-3-(2-methoxyphenyl)-aziridine-2-carboxylate (3e).** White solid. M. p. 104–105 °C; IR (KBr, cm^{-1}): 1749 (m), 1637 (s), 1618 (s), 1514 (s), 1455 (m); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.32-7.26 (m, 3H), 7.08 (dd, J = 1.6, 7.6 Hz, 1H), 6.85 (dd, J = 1.2, 8.0 Hz, 1H), 6.85-6.83 (m, 3H), 5.22 (s, 1H), 3.88 (s, 3H), 3.77 (s, 3H), 3.21 (s, 3H), 1.80 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.9, 164.2, 157.3, 156.1, 131.1, 129.3, 127.2, 122.1, 119.9, 118.5, 114.3, 110.3, 65.3, 61.1, 55.5, 55.4, 51.5, 17.0; HRMS (EI) calc. for $C_{20}H_{21}O_5N_1$ (M^+): 355.1414, found: 355.1412.

***cis*-Mehtyl 1-(4-methoxyphenyl)-2-acetyl-3-(4-chlorophenyl)-aziridine-2-carboxylate (3g).** White solid. M. p. 140–142 °C; IR (KBr, cm^{-1}): 1748 (s), 1639 (m), 1618 (m), 1511 (s); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.30-7.22 (m, 6H), 6.82 (d, J = 9.2 Hz, 2H), 4.83 (s, 1H), 3.76 (s, 3H), 3.32 (s, 3H), 1.79 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.5, 163.3, 156.4, 134.7, 132.1, 130.5, 128.7, 128.1, 118.4, 114.4, 66.0, 65.5, 55.4, 51.9, 17.5; HRMS (EI) calc. for $C_{19}H_{18}O_4N_1Cl$ (M^+): 359.0919, found: 359.0917.

***cis*-Methyl 1-(4-methoxyphenyl)-2-acetyl-3-(2-chlorophenyl)-aziridine-2-carboxylate (3h).** White solid. M. p. 116–118 °C; IR (KBr, cm^{-1}): 1749 (m), 1637 (s), 1618 (s), 1514 (m), 1455 (m); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.43 (dd, J = 1.2, 8.0 Hz, 1H), 7.27-7.14 (m, 5H), 6.84 (d, J = 8.8 Hz, 2H), 5.32 (s, 1H), 3.77 (s, 3H), 3.26 (s, 3H), 1.89 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.3, 163.6, 156.4, 133.4, 131.5, 130.6, 129.7, 129.6, 128.1, 126.4, 118.4, 114.4, 65.7, 62.7, 55.4, 51.8, 17.5; HRMS (EI) calc. for $C_{19}H_{18}O_4N_1Cl_1$ (M^+): 359.0919, found: 359.0918.

***cis*-Methyl 1-(4-methoxyphenyl)-2-acetyl-3-(naphthalen-2-yl)-aziridine-2-carboxylate (3i).** White solid. M. p. 142–143 °C; IR (KBr, cm^{-1}): 1753 (s), 1736 (s), 1602 (m), 1511 (s), 1446 (m), 1245 (s); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.82-7.76 (m, 3H), 7.50-7.47 (m, 2H), 7.37 (dd, J = 2.0, 8.8 Hz, 2H), 7.30-7.26 (m, 2H), 6.79 (d, J = 9.2 Hz, 2H), 5.02 (s, 1H), 3.74 (s, 3H), 3.19 (s, 3H), 1.85 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.7, 163.7, 156.2, 133.3, 132.9, 131.1, 130.9, 128.3, 127.9, 127.7, 126.5, 126.4, 126.3, 123.9, 118.5, 114.3, 66.4, 66.1, 65.3, 51.8, 17.7; HRMS (EI) calc. for $C_{23}H_{21}O_4N_1$ (M^+): 375.1465, found: 375.1464.

***cis*-methyl 2-acetyl-1,3-diphenyl-aziridine-2-carboxylate (4).** Colorless oil. ^1H NMR ($CDCl_3$, 400 MHz) δ 7.34-7.32 (m, 5H), 7.29-7.23 (m, 4H), 7.09 (t, J = 7.3 Hz, 1H), 4.90 (s, 1H), 3.26 (s, 3H), 1.80 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.56, 164.15, 137.31, 133.38, 129.09, 128.78, 128.49, 126.65, 124.26, 117.23, 66.14, 65.94, 51.81, 17.58; HRMS (FAB) calc. for $C_{18}H_{18}NO_3$ (M^+ + 1): 296.1287, found: 296.1285.

1-(4-Methoxyphenyl)-2,2-diacetyl-3-phenyl-aziridine (6). Colorless oil. ^1H NMR ($CDCl_3$, 400 MHz) δ 7.45-7.39 (m, 2H), 7.36-7.29 (m, 3H), 7.12 (d, J = 9.0 Hz, 2H), 6.79 (d, J = 9.0 Hz, 2H), 6.42 (s, 1H), 3.72 (s, 3 H), 1.90 (s, 3H), 1.77 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 163.54, 158.58, 137.20, 132.68, 128.97, 128.27, 127.08, 126.82, 113.93, 106.65, 88.91, 55.22, 17.30, 10.24; HRMS (FAB^+) calc. for $C_{19}H_{19}NO_3$ (M^+): 309.1365, found: 309.1367.

1-(4-Methoxyphenyl)-2-acetyl-2-benzoyl-3-phenyl-aziridine (7). Colorless oil, *cis*-isomer. ^1H NMR ($CDCl_3$, 400 MHz) δ 7.56-7.49 (m, 2H), 7.43-7.36 (m, 3H), 7.31-7.18 (m, 5H), 7.14 (d, J = 9.0 Hz, 2H), 6.82 (d, J = 9.0 Hz, 2H), 6.59 (s, 1H), 3.75 (s, 3H), 1.84 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 162.23, 160.92, 157.70, 137.23, 133.35, 132.67, 130.85, 129.29, 128.52, 127.86, 127.23, 126.89, 114.87, 114.10, 90.33, 89.50, 55.42, 18.63; HRMS (FAB^+) calc. for $C_{24}H_{21}NO_3$ (M^+): 371.1521, found: 371.1513.

trans-isomer. ^1H NMR ($CDCl_3$, 400 MHz) δ 7.55 (d, J = 8.4 Hz, 2H), 7.45-7.34 (m, 8 H), 7.19 (d, J = 9.0 Hz, 2H), 6.84 (d, J = 9.0 Hz, 2H), 6.60 (s, 1H), 3.76 (s, 3H), 1.95 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 164.50, 157.76, 156.55, 136.87, 133.05, 132.59, 130.04, 129.31, 129.15, 128.54, 128.11, 127.44, 126.84, 114.14, 107.97, 89.39, 55.39, 12.04; HRMS (FAB^+) calc. for $C_{24}H_{21}NO_3$ (M^+): 371.1521, found: 371.1532.

1,3,3-Trimethylbicyclo[2.2.1]heptan-2-yl 1-(4-methoxyphenyl)-2-acetyl-3-phenyl-aziridine-2-carboxylate (8). Major isomer. IR (KBr, cm^{-1}): 1755 (s), 1716 (s), 1585 (m), 1512 (m), 1458 (m), 1396 (m), 1292 (s), 1176 (m), 1157 (m), 1030 (m), 956 (w), 694 (w); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.31-7.26 (m, 5H), 7.24 (d, J = 8.4 Hz, 2H), 6.80 (d, J = 8.4 Hz, 2H), 4.86 (s, 1H), 3.99 (s, 1H), 3.75 (s, 3H), 1.82 (s, 3H), 1.69-1.42 (m, 2H), 1.39-1.26 (m, 3H), 1.08-0.96 (m, 2H), 0.96 (s, 3H), 0.92 (s, 3H), 0.55 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 164.4, 156.6, 129.3, 127.6, 127.4, 119.1, 114.7, 87.9, 67.0, 55.9, 48.7, 41.7, 39.9, 29.8, 26.8, 26.2, 23.2, 20.7, 19.4, 19.2, 18.7; HRMS (EI^+) calc. for $C_{28}H_{33}NO_4$ (M^+): 447.2410, found: 447.2374; Anal. Calc. for $C_{28}H_{33}NO_4$: C, 75.14; H, 7.43; N, 3.13, found: C, 75.14; H, 7.45; N, 3.13.

Minor isomer. ^1H NMR ($CDCl_3$, 400 MHz) δ 7.31-7.26 (m, 5H), 7.21 (d, J = 8.8 Hz, 2H), 6.78 (d, J = 8.8 Hz, 2H), 4.86 (s, 1H), 3.94 (s, 1H), 3.74 (s, 3H), 1.82 (s, 3H), 1.69-1.42 (m, 2 H), 1.39-1.26 (m, 3H), 1.08-0.96 (m, 2H), 0.98 (s, 3H), 0.67 (s, 3H), 0.43 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 164.4, 156.6, 129.3, 127.6, 127.4, 119.1, 114.7, 87.9, 67.0, 55.9, 48.7, 41.7, 39.9, 29.8, 26.8, 26.2, 23.2, 20.7, 19.4, 19.2, 18.7; HRMS (EI^+) calc. for $C_{28}H_{33}NO_4$ (M^+): 447.2410; found: 447.2374.

Tetrahydro-4,4-dimethyl-2-oxofuran-3-yl 1-(4-methoxyphenyl)-2-acetyl-3-phenyl-aziridine-2-carboxylate (9). Major isomer. IR (KBr, cm^{-1}): 1763 (s), 1734 (s), 1609 (s), 1583 (m), 1510 (m), 1466 (m), 1373 (m), 1292 (m), 1246 (m), 1178 (w), 1161 (m), 823 (m), 594 (w); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.51 (d, J = 6.4 Hz, 2H), 7.28 (d, J = 9.2 Hz, 3H), 6.92 (d, J = 9.2 Hz, 2H), 6.79 (d, J = 9.2 Hz, 2H), 4.99 (s, 1H), 4.58 (s, 1H), 4.21 (d, J = 9.6 Hz, 1H), 4.04 (d, J = 9.6 Hz, 1H), 3.72 (s, 3H), 2.0 (s, 3H), 1.39 (s, 3H), 1.23 (d, J = 8.4 Hz, 3 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 196.9, 164.6, 155.04, 137.2, 133.9, 129.2, 118.8, 115.4, 114.6, 114.5, 83.7, 79.9, 65.5, 60.9, 55.9, 55.8, 40.0, 28.5, 21.7; HRMS (EI^+) calc. for $C_{24}H_{25}NO_6$ (M^+): 423.1682, found: 423.1641; Anal. Calc. for $C_{24}H_{25}NO_6$: C, 68.07; H, 5.95; N, 3.31, found: C, 67.62; H, 6.01; N, 3.27.

Minor isomer. ^1H NMR ($CDCl_3$, 400 MHz) δ 7.59 (d, J = 8.0 Hz, 2H), 7.34 (d, J = 11.4 Hz, 3H), 7.01 (d, J = 9.2 Hz, 2H), 6.79 (d, J = 9.2 Hz, 2H), 5.28 (s, 1H), 4.69 (s, 1H), 4.12 (d, J = 8.4 Hz, 1H), 3.99 (d, J = 8.4 Hz, 1H), 3.74 (s, 3H), 2.05 (s, 3H,), 1.35 (s, 3H), 1.26 (d, J = 8.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 197.9, 164.6, 157.2, 138.2, 135.7, 129.5, 129.0, 128.9, 127.7, 126.0, 114.6, 90.7, 87.0, 86.9, 80.8, 69.5, 40.8, 27.1, 25.4, 20.8; HRMS (EI^+) calc. for $C_{24}H_{25}NO_6$ (M^+): 423.1682, found: 423.1641.

(3*S*,3a*R*,4*R*,7*S*,7a*S*)-3-Acetyl-hexahydro-7-isopropyl-4-methyl-benzofuran-2(3*H*)-one (10). IR (KBr, cm^{-1}): 1755 (s), 1725 (s), 1458 (m), 1385 (m), 1362 (m), 1289 (m), 1238 (m), 1154 (w), 992 (w); ^1H NMR ($CDCl_3$, 400 MHz) δ 3.72 (t, J = 7.2 Hz, 1H), 3.45 (d, J = 12.0 Hz, 1H), 2.42 (s, 3H), 2.37-2.27 (m, 1H), 1.96-1.92 (m, 1H), 1.78 (d, J = 9.6 Hz, 2H), 1.69 (t, J = 10.8 Hz, 1H), 1.47 (t, J = 5.6 Hz, 1H), 1.21-1.12 (m, 2H), 0.95 (d, J = 6.8 Hz, 3H), 0.9 (d, J = 7.2 Hz, 3H), 0.83 (d, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 202.6, 173.0, 84.9, 59.1, 52.5, 47.0, 35.8, 34.8, 31.3, 28.9, 25.3, 20.3, 20.2, 18.2; HRMS (EI^+) calc. for $C_{14}H_{22}O_3$ (M^+): 238.1569, found: 238.1581; Anal. Calc. for $C_{14}H_{22}O_3$: C, 70.56; H, 9.30, found: C, 70.64; H, 9.28.

Reaction of aziridine 3a with cerium(IV) ammonium nitrate

To a solution of **3a** (168 mg, 0.5 mmol) in acetonitrile (7 mL) under an ice-bath was added a solution of cerium(IV) ammonium nitrate (685 mg, 1.25 mmol) in 4 mL of water. The reaction mixture was stirred for 2 hours and 5% aqueous $NaHCO_3$ solution was added at 0 °C until pH of the solution was almost neutral. The resulting mixture was allowed to warm up to room temperature. The solid sodium sulfite was added portionwise until a brown slurry was formed. After AcOEt (10 mL) was added, the organic layer was separated and dried over anhydrous sodium sulfate. The solvent was removed under vacuum and the residue was purified by flash column chromatography on silica gel (hexane: ethyl acetate = 3: 1) to afford *cis*-methyl 2-acetyl-3-phenyl-aziridine-2-carboxylate (**5**) as a white solid (68 mg, 62% yield). M. p. 128–130 °C; IR (KBr, cm^{-1}): 1741 (s), 1600 (m), 1453 (m), 1250 (m); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.32-7.26 (m, 5H), 4.63 (s, 1H), 3.24 (s, 3H), 1.76 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.8, 167.8, 135.6, 128.5, 128.3, 126.1, 67.5, 63.0, 51.7, 17.2; HRMS (FAB) calc. for $C_{12}H_{13}O_3N_1$ (M^+): 219.0890, found: 219.0886.

Acknowledgements

We thank the National Natural Science Foundation of China (No. 20472061, 20772160), NCET plan of Ministry of Education of China, Guangzhou Bureau of Science and Technology for financial support of this study. We also thank Prof. Michael P. Doyle for his help and suggestions.

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16 CCDC-682854 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge *via* www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB21EZ, UK; fax (t44) 1223-336-033; or deposit@ccdc.cam.ac.uk].

