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芳基碘介导的缺电子烯烃电化学氮杂环丙烷化反应

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摘要 氮杂环丙烷在药物分子的设计合成中有广泛应用. 利用电化学方法合成氮杂环丙烷的研究主要集中于富电子烯烃的底物. 利用芳基碘化物介导, 以邻苯二甲酰肼为氮源, 在连通池中实现了缺电子烯烃的氮杂环丙烷化. 高价碘稳定的氮宾及酰化羟肼可能是原位产生的活性氮源试剂, 它们通过分步的过程实现三元环的构建. 一系列 α,β-不饱和酯、酰胺、腈和酮都可以通过这个电化学方法转化为对应的氮杂环丙烷.

关键词 电化学; 氮杂环丙烷; 高价碘; 缺电子烯烃

Aryl-Iodide-Mediated Electrochemical Aziridination of Electron-Deficient Alkenes

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Abstract A protocol of electrochemical aziridination of electron-deficient alkenes was reported using phthalhydrazide as nitrogen source. The reaction could be conducted in undivided cell, and the ArI is essential to achieve the transformation. Hypervalent-iodine-stablized nitrene and acetyl hydroxyhydrazine were suggested as the *in-situ* generated nitrogen source for the stepwise aziridination. This protocol can be applied to the azirdination of α,β-unsaturated esters, amides, nitrile and ketones to give a series N-containing molecules.

Keywords electrochemistry; aziridination; hypervalent iodine; electron-deficient alkene

1 Introduction

Aziridine is one important 3-membered heterocycle with constrained configuration. The ring tension makes it a reactive precursor in a variety of transformations to produce pharmaceutical products (Scheme 1, a).[1] The aziridination of olefin with reactive nitrogen source, including nitrene or nitrogen radical, is one straightforward approach. This chemistry has been extensively explored with various transition metals, including Cu,[2] Mn,[3] Fe,[4] Ru,[5] Co,[6] Rh[7] and others, as catalysis.[8] Besides these achievements, the aziridinations of alkenes with metal-free-catalysis have been established using a variety of organocatalyst.[9] For example, hypervalent iodines have been successfully applied in the aziridination reactions.[10] On the other hand, despite these advances, these chemistries generally require stoichiometric oxidation to generate nitrene or radical from stable nitrogen precursors. Due to the growing need for green chemistry and chemical engineering,[11] it would be highly desirable to develop a protocol effecting aziridination without the engagement of external oxidant.

In recent few years, the electrochemistry provided a number of innovative approaches for organic synthesis.[12] For example, the well-established hydrogen evolution reaction at cathode could drive the dehydrogenative-cross-coupling reaction.[12g,12l] This method could avoid the use of external oxidant via the cathodic reduction of protonic species. In 2002, Yudin group[13] reported the first example electrochemical aziridination of olefin through a nitrene intermediate. In 2015, Little and Zeng *et al*.[14] reported the iodide-mediated aziridination via a nitrogen radical path-

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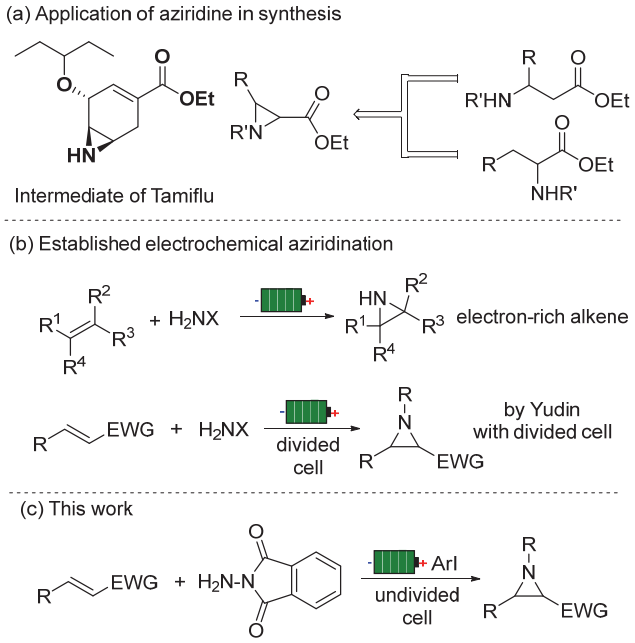
way. In 2018, our group[15] demonstrated the alkene activation protocol in the electrochemical aziridination reaction using sulfamate as redox-inert nitrogen source. Most recently, ammonia was successfully utilized to build aziridination via this pattern.[16] The intramolecular[17] and intermolecular[18] electrochemical C—H activation was also adopted in the aziridination reactions. With these precedents, however, the aziridination of electron-deficient alkene is only marginally explored by Yudin group,[13a] which required a dividing cell (Scheme 1, b). Recently, the electrochemical aryl iodine(III) chemistry exhibited its potential in variety of transformations,[19] including the oxidant-free amination of aromatic compounds.[20] Inspired by these chemistries, we will report the work on the ArI-mediated electrochemical aziridination of electron-deficient alkenes in an undivided cell (Scheme 1, c).

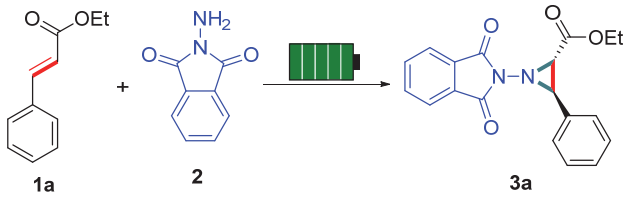


Scheme 1 Reaction design of aziridination of electron-deficient alkene

2 Results and discussion

At the onset of our study, ethyl cinnamate (**1a**) was employed as the model substrate in the reaction with **2** in an undivided cell (Table 1). After a series of optimizations, it was found that, with 0.5 equiv. of 4-methoxy iodobenzene (**4**), the reaction in dichloromethane (DCM) proceeded under a constant current condition at room temperature, giving the desired aziridine **3a** in 67% isolated yield with *trans* configuration as the predominant (*dr* = 10 ∶ 1, by ^{1}H NMR of crude mixture). Other supporting electrolytes were tested. Dramatic drops of reaction yields were observed in the case of *n*-Bu_4NCl (Entry 2) and LiOAc (Entry 3). Only trace conversion was detected when *n*-Bu_4NBF_4 was applied (Entry 4). The variation of current of electrolysis did not give any improvement (Entry 5). Next, the changing of solvent revealed the essential role of DCM in the transformation (Entry 6). When alcoholic solvents, such as EtOH and MeOH, were employed, the desired reaction did not take place. Other solvents, for example, tetrahydrofuran (THF), dimethyl sulfoxide (DMSO) and *N*,*N*-dimethylformamide (DMF), failed to deliver the target product. A 33% yield was detected in MeCN (Entry 7). If 4-$MeOC_6H_4I$ (**4**) was removed from the reaction, compound **3a** was not detected, and instead, phthalimide was isolated as the major side product. When other aryl iodides were used instead of **4**, product **3** was only detected in trace (Entries 9, 10).

Table 1 Optimization of aziridination of cinnamate mediated by ArI[a]



1a 2 3a

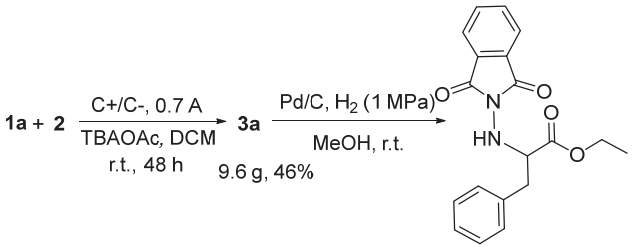
Entry	Deviation from standard conditions	Yield[b]/%
1	None	67
2	^{n}Bu_4NCl instead of ^{n}Bu_4NOAc	33
3	LiOAc instead of ^{n}Bu_4NOAc	37
4	^{n}Bu_4NBF_4 instead of ^{n}Bu_4NOAc	Trace
5	1, 3, 5, 9 mA instead of 7 mA	35～57
6	EtOH, MeOH, THF, DMSO, DMF as solvent	ND
7	MeCN as solvent	33
8	No 4-$MeOC_6H_4I$ (**4**)	ND
9	PhI instead of **4**	Trace
10	4-FC_6H_4I instead of **4**	Trace

[a] Reaction conditions: **1a** (0.2 mmol, 1.0 equiv.), **2** (0.4 mmol, 2.0 equiv.), *n*-Bu_4NOAc (0.2 mmol, 1.0 equiv.), 4-$MeOC_6H_4I$ (**4**, 0.1 mmol, 0.5 equiv.), DCM (5.0 mL), graphene sheet as anode, graphite felt as cathode, undivided cell, 12 h, 7 mA, 25 ℃. [b] Isolated yield based on **1a**. ND = no detected.

With the optimized conditions (Table 1, Entry 1) in hand, a variety of substrates bearing electron-deficient alkenes were subjected to this reaction (Scheme 2). At first, the derivatives of cinnamic acid were investigated. Several *trans*-cinnamate esters **1a**～**1e** were converted to the corresponding aziridines in 51% to 72% yields. It was noted that the obtained azirdines were the mixtures of diastereoisomers in which *cis*-isomers were the minor. These results suggested that the formation of three-membered ring might proceed via a step-wise pathway. This diastereoselectivity was further witnessed in the reaction of amide **1f** that gave rise to product **3f** in 72% isolated yield and 1 ∶ 1 *dr* ratio. Other cinnamides were also subjected to this protocol and the desired products **3g**～**3k** were obtained in decent yields with improved diastereoselectivity in comparison to **3f**. Next, azirdines **3l**～**3n** derived from crotonate esters were generated in moderate yields with *trans*/*cis* ratio ranged from 4 ∶ 1 to 6 ∶ 1. Subsequently, a series of *α*,*β*-unsaturated esters containing heterocycles were examined. It was glad to obtain product **3o** with quinoline, **3p** with benzothiophene and **3q** with pyrimidine in 64%～74% yields with predominant *trans* configurations. Ethyl acrylate **3r**

was also prepared in 56% yield. Next, substrates other than ester were tested. An *α*,*β*-unsaturated nitrile **1s** gave the aziridine **3s** in 63% yield with good diastereoselectivity. *α*,*β*-Unsaturated cyclic ketones were evaluated, and the corresponding products **3t**～**3v** were achieved in moderate yields.

Next, the potential of scale-up for this aziridination reaction was explored. By employing 10 g of **1a** as starting material, the reaction could offer the desired aziridine **3a** in 46% yield. Furthermore, the generated aziridine could be hydrogenated to give the *α*-amino acid derivative **5** in excellent yield at 100 mg scale (Scheme 2).



Scheme 2 Synthetic exploration of electrochemical aziridination reaction

In addition, experiments were carried out to gain some information on the reaction mechanism. At first, cyclic voltammetry analysis was carried out using reactants tending to lose electron at anode (Figure 1). It was found that **2a**, **4**, and supporting electrolyte gave similar redox profiles. Unexpectedly, the ArI could decrease the anodic oxidation current of reagent **2**. These results suggested that some concerted process might take place at anode to produce the activated nitrogen source. So, the reaction mixture of **1a** and

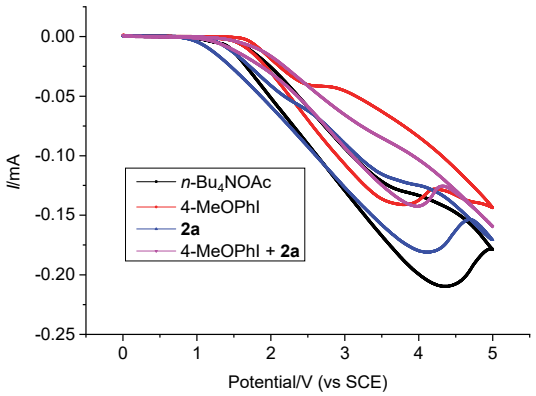
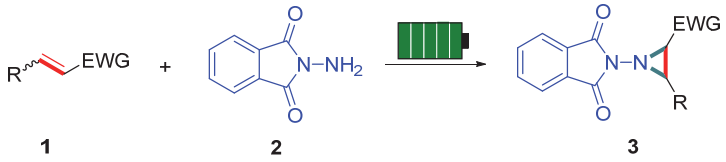
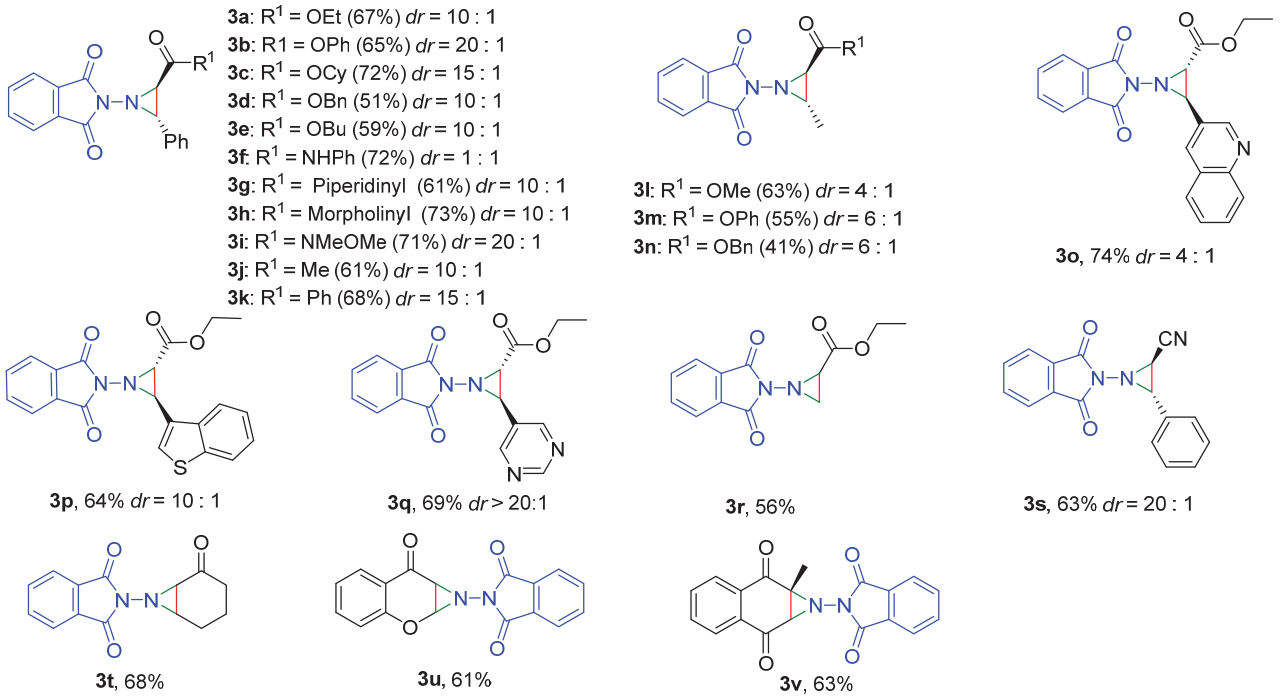


Figure 1 CV analyses of reactants

Table 2 Substrate scope of aziridination of electron-deficient alkene[a]





[a] Reagents and conditions: **1** (0.2 mmol, 1.0 equiv.), **2** (0.4 mmol, 2.0 equiv.), *n*-Bu_4NOAc (0.2 mmol, 1.0 equiv.), 4-$MeOC_6H_4I$ (**4**) (0.1 mmol, 0.5 equiv.), DCM (5.0 mL), graphene sheet as anode, graphite felt as cathode, undivided cell, 12 h, 7 mA, 25 ℃, isolated yield was calculated based on **1a**, *dr* was determined by ^1H NMR.

2 (Table 1, Entry 1) was investigated by the high resolution mass spectroscopy (Scheme 3). Species with molecule weights corresponded to compounds **6** and **7** were detected by HRMS, suggesting that two possible pathways might co-exist in the transformation.

With these observations, a plausible reaction pathway was suggested in Scheme 4. At first, the anodic oxidation took place, giving the hypervalent iodine **A**. Then the I^{III} species would react with **2** to give intermediate **B** incorporating both I—O and I—N bonds. Next, **B** underwent two paths to give compounds **6** and **7**, respectively. Both reagents gave the aziridination in solution, via the stepwise manner.[10c] At cathode, the hydrogen evolution furnished the electron cycle, and regenerated the acetate anion (Scheme 4). So, ArI can facilitate the formation of aziridination reagents **6** and **7**.

3 Conclusions

In summary, an electrochemical aziridination of electron-deficient alkene in undivided cell was mediated by aryl iodide. The reaction proceeded via stepwise pathway with *in-situ* generated iodine nitrene and acetyl hydrazine as aziridination reagent. This protocol could be applied in the aziridination of cinnamate, cinnamide, α,β-unsaturated nitrile, α,β-unsaturated ketones. With this reaction, the scale-up to 10 g could be fulfilled in the same manner, and the product could server as the precursor for α-amino acid.

4 Experimental section

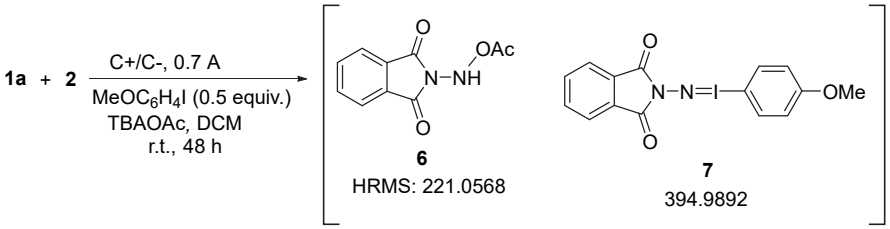
4.1 General Information

Unless otherwise noted, all reactions were carried out under nitrogen or argon atmosphere. All materials were obtained from commercial suppliers and used directly without further purification. The solvents were dried by distillation over the appropriate drying reagents before use. Other chemical reagents were purchased from commercial sources and used without further purification. Flash chromatography utilized 300～400 mesh silica gel from Qingdao Haiyang Chemical Co., Ltd. Reactions were monitored by thin-layer chromatography (TLC) using 254 nm UV light to visualize the progress of the reactions.

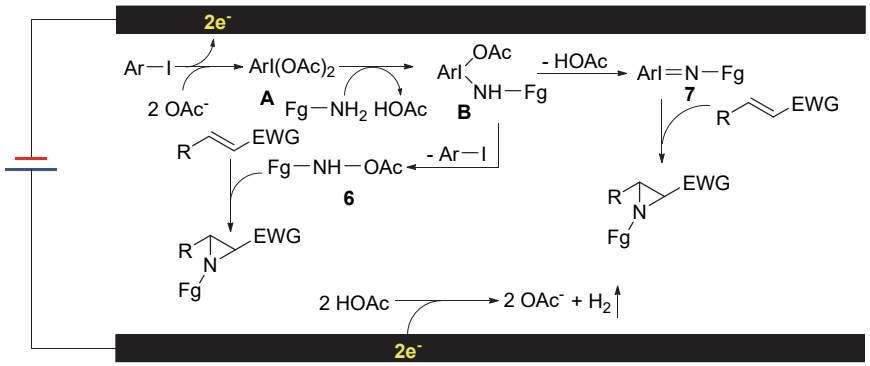
^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance III 400 (400 MHz and 100 MHz) nuclear magnetic resonance instrument. Melting points were measured with digital melting point detector. High-resolution mass spectra (HRMS) were obtained by ESI or EI source and a TOF detector mass spectrometer.

4.2 General procedure of ArI mediated electrochemical aziridination

A 10 mL three-necked flask with a magnetic stir bar was charged with substrate **1** (0.2 mmol), *n*-Bu_4NOAc (0.1 mmol), **2** (0.4 mmol, 2.0 equiv.) and DCM (5 mL) were added by syringe. The flask was equipped with a rubber stopper, graphite sheet (3.0 cm×1 cm×0.1 cm) as anode and graphite felt (1.5 cm×1 cm×0.5 cm) as cathode. The graphite was attached to a platinum wire. The mixture was stirred under room temperature, and constant current electrolysis was conducted for the respective time. After the reaction was completed by monitoring with TLC or GCMS analysis, the mixture was quenched with $Na_2S_2O_3$, and extracted with DCM (5 mL×3). The combined organic layers were dried over Na_2SO_4, filtered and concentrated. The residue was purified by chromatography (eluent: petroleum ether/ethyl acetate, V∶V=5∶1) on silica gel to afford the desire product **3**.



Scheme 3 Experiments to investigate the reaction mechanism



Scheme 4 A plausible reaction mechanism for ArI-mediated electrochemical aziridination

Ethyl 1-(1,3-dioxoisoindolin-2-yl)-3-phenylaziridine-2-carboxylate (**3a**): White solid, 45 mg, 67% yield. m.p. 97～98 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.77 (dd, J=5.6, 3.2 Hz, 2H), 7.68 (dd, J=5.6, 3.2 Hz, 2H), 7.49～7.44 (m, 2H), 7.41～7.35 (m, 3H), 4.39 (d, J=4.8 Hz, 1H), 4.18 (q, J=7.2 Hz, 2H), 3.51 (d, J=4.8 Hz, 1H), 1.28 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.2, 164.6, 134.6 134.3 134.1 134.0, 130.3 128.7 128.6, 127.2, 123.6 123.1, 62.1, 49.5, 46.3, 14.0; HRMS (ESI) calcd for $C_{19}H_{16}N_2O_4Na$ $[M+Na]^+$ 359.1008, found 359.1006.

Phenyl 1-(1,3-dioxoisoindolin-2-yl)-3-phenylaziridine-2-carboxylate (**3b**): White solid, 50 mg, 65% yield. m.p. 145～146 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.78 (dt, J=7.2, 3.6 Hz, 2H), 7.67 (dd, J=5.6, 3.2 Hz, 2H), 7.53 (d, J=6.4 Hz, 2H), 7.45～7.32 (m, 5H), 7.25～7.21 (m, 1H), 7.14 (d, J=8.0 Hz, 2H), 4.48 (d, J=4.8 Hz, 1H), 3.79 (d, J=4.8Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 165.0, 164.7, 150.4, 134.23 134.2, 134.2,134.1, 130.2, 129.5, 128.8, 128.8, 127.30, 126.3, 123.6, 123.2, 121.3, 50.2, 46.2; HRMS (ESI) calcd for $C_{23}H_{16}N_2O_4Na$ $[M+Na]^+$ 407.1008, found 407.1003.

Cyclohexyl 1-(1,3-dioxoisoindolin-2-yl)-3-phenylaziridine-2-carboxylate (**3c**): White solid, 56 mg, 72% yield. m.p. 151～152 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.88～7.86 (m, 1H), 7.78～7.74 (m, 2H), 7.68 (dd, J=5.6, 3.2 Hz, 2H), 7.48～7.46 (m, 2H), 7.39～7.36 (m, 2H), 4.74 (dt, J=9.2, 4.8 Hz, 1H), 4.39 (d, J=5.2 Hz, 1H), 3.51 (d, J=5.2 Hz, 1H), 1.86～1.68 (m, 4H), 1.54～1.49 (m, 3H), 1.36～1.23 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.9, 165.6, 164.6, 134.7, 134.3, 134.0, 132.7, 130.3, 128.6(4), 128.5(9), 127.2, 123.6, 123.1, 74.7, 49.4, 46.7, 31.4, 31.2, 25.2, 23.6, 23.6; HRMS (ESI) calcd for $C_{23}H_{22}N_2O_4Na$ $[M+Na]^+$ 413.1477, found 413.1475.

Benzyl 1-(1,3-dioxoisoindolin-2-yl)-3-phenylaziridine-2-carboxylate (**3d**): White solid, 40 mg, 51% yield. m.p. 94～95 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.81～7.77 (m, 2H), 7.72～7.70 (m, 2H), 7.48 (d, J=7.2 Hz, 2H), 7.38 (d, J=9.2 Hz, 8H), 5.21 (d, J=12.0 Hz, 1H), 5.12 (d, J=12.0 Hz, 1H), 4.44 (d, J=4.8 Hz, 1H), 3.60 (d, J=52 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.1, 164.6, 134.8, 134.4, 134.0, 130.3, 128.6(8), 128.6(6), 128.5(8), 128.5(2), 128.5(1), 127.2, 123.2, 67.9, 49.7, 46.2; HRMS (ESI) calcd for $C_{24}H_{18}N_2O_4Na$ $[M+Na]^+$ 421.1164, found 421.1163.

Butyl 1-(1,3-dioxoisoindolin-2-yl)-3-phenylaziridine-2-carboxylate (**3e**): Pale yellow oil, 43 mg, 59% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.79 (dd, J=5.6, 3.2 Hz, 2H), 7.70 (dd, J=5.6, 3.2 Hz, 2H), 7.51～7.46 (m, 2H), 7.45～7.37 (m, 3H), 4.42 (d, J=4.8 Hz, 1H), 4.19～4.11 (m, 2H), 3.54 (d, J=4.8 Hz, 1H), 1.69～1.60 (m, 2H), 1.46～1.38 (m, 2H), 0.94 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.3, 164.6, 134.6, 134.0, 130.3, 128.6(5), 128.6(2), 127.2, 123.1, 66.0, 49.5, 46.3, 30.4, 19.0, 13.6; HRMS (ESI) calcd for $C_{21}H_{20}N_2O_4Na$ $[M+Na]^+$ 387.1321, found 387.1319.

1-(1,3-Dioxoisoindolin-2-yl)-*N*,3-diphenylaziridine-2-carboxamide (**3f**): White solid, 55 mg, 72% yield. m.p. 368～369 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.86 (s, 1H), 7.66 (d, J=5.6 Hz, 5H), 7.33 (t, J=4.8 Hz, 7H), 7.21 (d, J=7.6 Hz, 2H), 4.68 (d, J=4.8 Hz, 1H), 3.73 (d, J=4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 165.2, 162.4, 137.6, 134.1, 129.7, 129.5, 129.4, 129.0, 128.6, 128.4, 127.4, 124.7, 123.3, 120.3, 48.9, 44.9; HRMS (ESI) calcd for $C_{23}H_{17}N_3O_3Na$ $[M+Na]^+$ 406.1168, found406.1169.

2-(2-Phenyl-3-(piperidine-1-carbonyl)aziridin-1-yl)isoindoline-1,3-dione (**3g**): White solid, 46 mg, 61% yield. m.p. 136～137 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.74 (dd, J=5.6, 3.2 Hz, 2H), 7.64 (dd, J=5.6, 3.2 Hz, 2H), 7.48 (d, J=7.2 Hz, 2H), 7.36 (dt, J=13.6, 6.8 Hz, 3H), 4.72 (d, J=4.8 Hz, 1H), 3.85～3.82 (m, 2H), 3.61 (d, J=4.8 Hz, 1H), 3.51～3.46 (m, 2H), 1.97～1.94 (m, 1H), 1.73～1.61 (m, 4H), 1.57～1.50 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 164.7, 162.1, 135.8, 133.8, 130.5, 128.6, 128.2, 127.2, 123.0, 48.2, 47.6, 45.8, 43.9, 25.9, 25.3, 24.5; HRMS (ESI) calcd for $C_{22}H_{21}N_3O_3Na$ $[M+Na]^+$ 398.1481, found 398.1477.

2-(2-(Morpholine-4-carbonyl)-3-phenylaziridin-1-yl)isoindoline-1,3-dione (**3h**): White solid, 55 mg, 73% yield. m.p. 171～172 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.75 (dd, J=5.6, 3.2 Hz, 2H), 7.66 (dd, J=5.6, 3.2 Hz, 2H), 7.47 (d, J=7.6 Hz, 2H), 7.40～7.30 (m, 3H), 4.71 (d, J=4.8 Hz, 1H), 4.03 (dq, J=11.2, 4.8 Hz, 2H), 3.83～3.76 (m, 2H), 3.72～3.60 (m, 3H), 3.54 (d, J=4.8 Hz, 1H), 3.44～3.36 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 164.7, 162.6, 135.4, 134.0, 130.4, 128.6, 128.4, 127.1, 123.0, 66.4, 66.2, 48.3, 46.8, 45.7, 43.0.

1-(1,3-Dioxoisoindolin-2-yl)-*N*-methoxy-*N*-methyl-3-phenylaziridine-2-carboxamide (**3i**): White solid, 39 mg, 71% yield. m.p. 117～118 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.75 (dd, J=5.6, 3.2 Hz, 2H), 7.65 (dd, J=5.6, 3.2 Hz, 2H), 7.52～7.48 (m, 2H), 7.42～7.34 (m, 3H), 4.54 (d, J=5.2 Hz, 1H), 4.03 (d, J=5.2 Hz, 1H), 4.01 (s, 3H), 3.21 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 164.7, 135.3, 133.9, 130.4, 128.6, 128.4, 127.3, 123.0, 62.0, 48.7, 43.4, 32.8; HRMS (ESI) calcd for $C_{19}H_{17}N_3O_4Na$ $[M+Na]^+$ 374.1117, found 374.1112.

2-(2-Acetyl-3-phenylaziridin-1-yl)isoindoline-1,3-dione (**3j**): White solid, 37 mg, 61% yield. m.p. 181～182 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.77 (dd, J=5.6, 3.2 Hz, 2H), 7.69 (dd, J=5.6, 3.2 Hz, 2H), 7.49～7.45 (m, 2H), 7.44～7.37 (m, 3H), 4.39 (d, J=4.8 Hz, 1H), 3.73 (d, J=4.8 Hz, 1H), 2.57 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 198.6, 164.7, 135.0, 134.3, 134.0, 130.2, 128.6(5), 128.5(7), 127.1, 123.1, 51.1, 50.0, 31.6; HRMS (ESI) calcd for $C_{18}H_{14}N_2O_3Na$ $[M+Na]^+$ 329.0902, found 329.0901.

2-(2-Benzoyl-3-phenylaziridin-1-yl)isoindoline-1,3-dione (**3k**): White solid, 50 mg, 68% yield. m.p. 127～128 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.09 (d, J=7.6 Hz, 2H), 7.72 (dd, J=5.2, 3.2 Hz, 2H), 7.66～7.60 (m, 3H), 7.53 (d, J=7.6 Hz, 4H), 7.44～7.35 (m, 3H), 4.69 (d, J=4.8 Hz, 1H), 4.40 (d, J=4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 190.6, 164.6, 135.2, 134.0, 133.6, 130.3, 128.7(8), 128.7(6), 128.7, 128.6, 127.2, 123.2, 50.6, 48.7; HRMS (ESI) calcd for $C_{23}H_{16}N_2O_3Na$ $[M+Na]^+$ 391.1059, found 391.1057.

Methyl 1-(1,3-dioxoisoindolin-2-yl)-3-methylaziridine-

2-carboxylate (**3l**): White solid, 33 mg, 63% yield. m.p. 101～102 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.77 (dd, J=5.6, 3.2 Hz, 2H), 7.68 (dd, J=5.6, 3.2 Hz, 2H), 3.71 (s, 3H), 3.44～3.35 (m, 1H), 3.07 (d, J=4.8 Hz, 1H), 1.54 (d, J=6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.4, 164.8, 134.3, 133.9, 130.3, 123.0, 52.7, 44.9, 44.8, 16.4; HRMS (ESI) calcd for $C_{13}H_{12}N_2O_4Na$ $[M+Na]^+$ 283.0695, found 283.0691.

Phenyl 1-(1,3-dioxoisoindolin-2-yl)-3-methylaziridine-2-carboxylate (**3m**): White solid, 35 mg, 55% yield. m.p. 106～107 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.89 (dd, J=5.6, 3.2 Hz, 2H), 7.67 (dd, J=5.6, 3.2 Hz, 2H), 7.39～7.35 (m, 2H), 7.25～7.20 (m, 1H), 7.15～7.09 (m, 2H), 3.54～3.45 (m, 1H), 3.33 (d, J=4.8 Hz, 1H), 1.63 (d, J=6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.9, 165.6, 164.7, 150.4, 134.3, 134.0, 132.7, 130.3, 129.5, 126.2, 123.6, 123.1, 121.4, 121.3, 45.4, 45.1, 16.4; HRMS (ESI) calcd for $C_{18}H_{14}N_2O_4Na$ $[M+Na]^+$ 345.0851, found 345.0848.

Benzyl 1-(1,3-dioxoisoindolin-2-yl)-3-methylaziridine-2-carboxylate (**3n**): Pale yellow solid, 28 mg, 41% yield. m.p. 83～84 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.72 (dd, J=5.6, 3.2 Hz, 2H), 7.65 (dd, J=5.6, 3.2 Hz, 2H), 7.33～7.32 (m, 5H), 5.12 (d, J=12.0 Hz, 1H), 5.03 (d, J=12.0 Hz, 1H), 3.44～3.37 (m, 1H), 3.09 (d, J=5.2 Hz, 1H), 1.51 (d, J=5.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.7, 164.8, 135.0, 134.3, 133.9, 130.3, 128.5(3), 128.4(9), 128.4(3), 123.0, 67.6, 45.2, 44.8, 16.4; HRMS (ESI) calcd for $C_{19}H_{16}N_2O_4Na$ $[M+Na]^+$ 359.1008, found 359.1003.

Ethyl 1-(1,3-dioxoisoindolin-2-yl)-3-(quinolin-3-yl)-aziridine-2-carboxylate (**3o**): White solid, 57 mg, 74% yield. m.p. 125～126 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.23 (d, J=8.4 Hz, 1H), 8.10 (d, J=8.8 Hz, 1H), 7.81～7.69 (m, 6H), 7.55 (dd, J=13.2, 5.2 Hz, 2H), 4.67 (d, J=4.8 Hz, 1H), 4.21 (q, J=7.2 Hz, 2H), 3.99 (d, J=4.8 Hz, 1H), 1.30 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.0, 164.6, 154.0, 147.9, 137.0, 134.1, 130.3, 129.8, 129.4, 127.6, 126.8, 123.2, 120.5, 62.2, 50.5, 45.2, 14.0; HRMS (ESI) calcd for $C_{22}H_{17}N_3O_4Na$ $[M+Na]^+$ 410.1117, found 410.1113.

Ethyl 3-(benzo[*b*]thiophen-3-yl)-1-(1,3-dioxoisoindolin-2-yl)aziridine-2-carboxylate (**3p**): White solid, 50 mg, 64% yield. m.p. 179～180 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.08 (d, J=8.0 Hz, 1H), 7.88 (d, J=8.0 Hz, 1H), 7.80 (dd, J=5.6, 3.2 Hz, 2H), 7.70 (dd, J=5.6, 3.2 Hz, 2H), 7.52 (s, 1H), 7.47～7.38 (m, 2H), 4.71 (d, J=4.8 Hz, 1H), 4.22 (q, J=7.2 Hz, 2H), 3.60 (d, J=4.8 Hz, 1H), 1.30 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.2, 164.7, 140.6, 137.8, 134.1, 130.3, 129.9, 125.1, 124.8, 124.5, 123.2, 122.9, 122.0, 62.2, 45.7, 45.1, 14.0; HRMS (ESI) calcd for $C_{21}H_{16}N_2O_4SNa$ $[M+Na]^+$ 415.0728, found415.0728

Ethyl 1-(1,3-dioxoisoindolin-2-yl)-3-(pyrimidin-5-yl)-aziridine-2-carboxylate (**3q**): White solid, 47 mg, 69% yield. m.p. 176～177 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.26 (s, 1H), 8.88 (s, 2H), 7.82 (dd, J=5.6, 3.2 Hz, 2H), 7.74 (dd, J=5.6, 3.2 Hz, 2H), 4.38 (d, J=4.8 Hz, 1H), 4.24 (q, J=6.4 Hz, 2H), 3.58 (d, J=4.8 Hz, 1H), 1.33 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 164.4, 158.7, 156.0, 134.3, 130.1, 128.8, 123.3, 62.6, 45.7, 45.2, 13.9; HRMS (ESI) calcd for $C_{17}H_{14}N_4O_4Na$ $[M+Na]^+$ 361.0913, found 361.0910.

Ethyl 1-(1,3-dioxoisoindolin-2-yl)aziridine-2-carboxylate (**3r**): White solid, 29 mg, 56% yield. m.p. 146～147 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.79 (dd, J=5.6, 3.2 Hz, 2H), 7.70 (dd, J=5.6, 3.2 Hz, 2H), 4.37～4.22 (m, 2H), 3.20～3.16 (m, 1H), 2.89～2.82 (m, 2H), 1.34 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 168.0, 164.5, 134.3, 123.3, 61.9, 40.1, 36.6, 14.1; HRMS (ESI) calcd for $C_{13}H_{12}N_2O_4Na$ $[M+Na]^+$ 283.0695, found 283.0690.

1-(1,3-Dioxoisoindolin-2-yl)-3-phenylaziridine-2-carbonitrile (**3s**): White solid, 36 mg, 63% yield. m.p. 124～125 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.90～7.87 (m, 2H), 7.79～7.77 (m, 2H), 7.44 (qt, J=5.6, 2.0 Hz, 5H), 4.55 (d, J=4.8 Hz, 1H), 3.41 (d, J=4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.9, 164.7, 134.7, 134.3, 132.7, 132.5, 130.1, 129.4, 128.9, 127.1, 123.7, 123.6, 114.7, 49.4, 34.7; HRMS (ESI) calcd for $C_{17}H_{11}N_3O_2Na$ $[M+Na]^+$ 312.0749, found 312.0750.

2-(-2-Oxo-7-azabicyclo[4.1.0]heptan-7-yl)isoindoline-1,3-dione (**3t**): White solid, 35 mg, 68% yield. m.p. 178～179 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.81 (dd, J=5.6, 3.2 Hz, 2H), 7.72 (dd, J=5.6, 3.2 Hz, 2H), 3.48 (dd, J=7.2, 3.2 Hz, 1H), 3.10 (d, J=7.2 Hz, 1H), 2.65～2.50 (m, 2H), 2.20～2.12 (m, 1H), 2.09～1.95 (m, 2H), 1.80～1.71 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 203.1, 164.6, 134.2, 130.2, 123.2, 49.1, 46.2, 37.0, 22.1, 18.3; HRMS (ESI) calcd for $C_{14}H_{12}N_2O_3Na$ $[M+Na]^+$ 279.0746, found 279.0740.

2-(7-Oxo-7,7a-dihydrochromeno[2,3-*b*]azirin-1(1a*H*)-yl)isoindoline-1,3-dione (**3u**): Brown solid, 37 mg, 61% yield. m.p. 172～173 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.91～7.88 (m, 2H), 7.78 (dd, J=5.6, 3.2 Hz, 2H), 7.73 (d, J=9.6 Hz, 1H), 7.56～7.50 (m, 2H), 7.38～7.29 (m, 2H), 6.45 (d, J=9.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.9, 160.8, 154.1, 143.4, 134.3, 132.6, 131.8, 127.8, 124.4, 123.6, 118.9, 116.9, 116.7; HRMS (ESI) calcd for $C_{17}H_9N_2O_4$ $[M-H]^-$ 305.0562, found 305.0559.

1-(1,3-Dioxoisoindolin-2-yl)-1a-methyl-1*H*-naphtho[2,3-*b*]azirine-2,7(1a*H*,7a*H*)-dione (**3v**): White solid, 42 mg, 63% yield. m.p. 227～228 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.17～8.12 (m, 1H), 8.07～8.03 (m, 1H), 7.84 (dd, J=5.6, 3.2 Hz, 2H), 7.77 (ddt, J=8.4, 5.6, 2.4 Hz, 4H), 4.42 (s, 1H), 1.75 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 190.2, 189.4, 164.8, 134.6, 134.5, 134.3, 133.1, 133.0, 130.1, 127.6, 126.8, 123.6, 53.2, 52.6, 11.4; HRMS (ESI) calcd for $C_{19}H_{13}N_2O_4$ $[M+H]^+$ 333.0875, found 333.0869.

Supporting Information Additional optimization, procedures for reaction, investigation of intermediate with HRMS, CV analyses, ^{1}H NMR and ^{13}C NMR spectra. The Supporting Information is available free of charge via the Internet at http://sioc-journal.cn.

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