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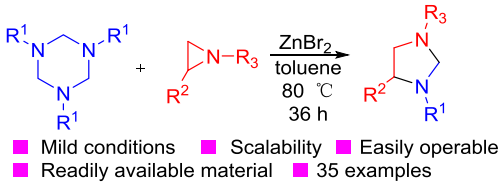
Access to Imidazolidines via 1,3-Dipolar Cycloadditions of 1,3,5-Triazinanes with Aziridines

Liang Tu,[†,⊥] Zhenghui Li,[†,⊥] Tao Feng,[†,⊥] Shuyan Yu,[‡] Rong Huang,[†] Jing Li,[†] Wenxuan Wang,[†] Yongsheng Zheng,[*,†] and Jikai Liu[*,†]

[†]School of Pharmaceutical Sciences, National Demonstration Center for Experimental Ethnopharmacology Education, South-Central University for Nationalities, Wuhan 430074, China

[‡]College of Pharmacy, Inner Mongolia Medical University, Hohhot 010010, China



ABSTRACT: The unprecedented 1,3-dipolar cycloaddition of 1,3,5-triazinanes and aziridines has been described. With readily available starting material, this method offers efficient access to a wide range of functionalized imidazolidine derivatives in moderate to good yields (up to 92%) under mild conditions. Preliminary mechanistic investigations show that the ring opened zwitterionic pathway product dominated over the S_N2-like product. This protocol is very promising because the reaction is scalable, and the versatile transformation of the products into other functionalized imidazolidines.

■ INTRODUCTION

Imidazolidine frameworks are ubiquitous in a myriad of natural alkaloids (e. g., (-)-Chaetominine[1]) and chiral ligands or catalysts in organic catalysis (e. g., MacMillan's catalyst)[2]. They also constitute important structural motifs in synthetic biologically active compounds[3] and could find great potential in drug discovery, such as antipyretic agents[4] and cannabinoid CB2 receptor agonist (Figure 1.)[5]. Although the importance of imidazolidines has stimulated considerable interest from chemists, limited approaches for the synthesis of imidazolidines have been developed. Among the developed strategies, the 1,3-dipolar cycloaddition of azomethine ylides with imines is the most straightforward and convenient method for the synthesis of functionalized imidazolines (Scheme 1a).[6] Re cently, Punniyamurthy reported the copper catalyzed nucleophilic ring opening, oxidative sp^3 C–H functionalization, and

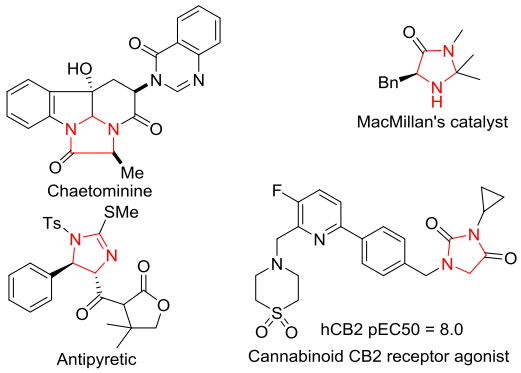
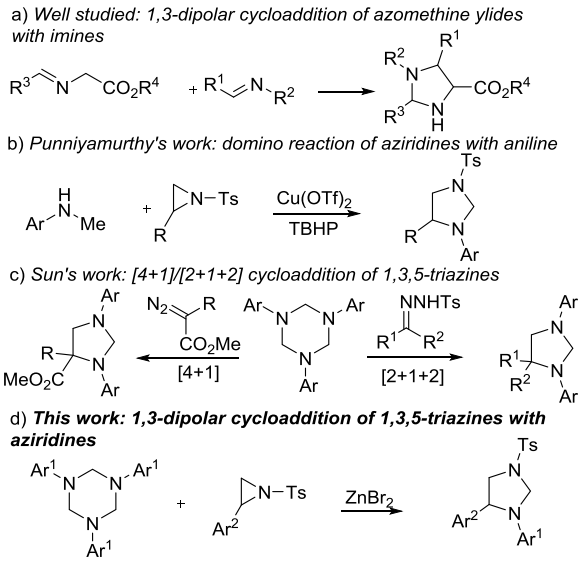


Figure 1. Representive biologically active compounds and catalyst

Scheme 1. Imidazolidines synthesis and our work



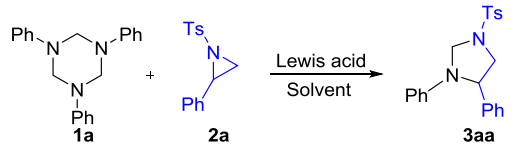
C–N bond formation of aziridines with *N*-alkylanilines for the synthesis of imidazolidines (Scheme 1b).[7] The Sun group described the [4+1]/[2+1+2] cycloaddition of 1,3,5-triazines with diazo esters and tosylhydrazones to form imidazolidines, respectively (Scheme 1c).[8] In addition, Wang and Zhang developed the [3+2] cycloaddition of imines with donor-acceptor aziridines via C-C bond cleavages, respectively.[9] Despite these significant progresses in this field, most strategies reported so far were limited to a few special substrates, mainly due to the dimerization of the azomethine ylides[6a-6c] and the low electrophilicity of imines[6d-6f]. Therefore, the development of novel

method to access imidazolidines is challenge and highly desirable.

Aziridines are versatile synthons in 1,3-dipolar or zwitterion cycloaddition for the synthesis of heterocyclic ring system.[10] On the other hand, 1,3,5-triazinanes are bench stable precursors of formaldimines which bear a nucleophilic nitrogen and an electrophilic carbon atom, has been widely utilized in various nitrogen-containing heterocycles construction and aminomethylation reaction.[11] Our group has recently reported the first inverse-electron-demand [4+2]-cycloaddition of 1,3,5-triazinanes for the efficient synthesis of tetrahydroquinazolines.[12] As our ongoing research program in the 1,3,5-triazinanes chemistry, we envisioned that the 1,3-dipolar cycloadditions of 1,3,5-triazinanes with aziridines would afford a novel approach to the synthesis of biologically active imidazolidines. This protocol represents the first example of 1,3-dipolar cycloaddition of 1,3,5-triazinanes and aziridines.

■ RESULTS AND DISCUSSION

Table 1. Optimization of Reaction Conditions[a]



1a 2a 3aa

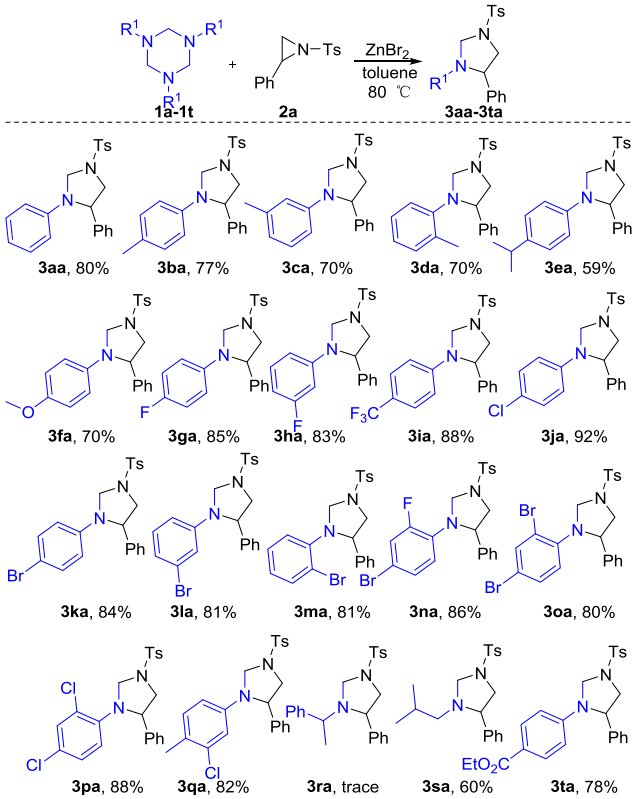
entry	Lewis acid	solvent	*t* (h)	yield
1	$FeCl_3$	toluene	24	30
2	$Sc(OTf)_3$	toluene	48	NR
3	$AlCl_3$	toluene	22	34
4	$Cu(OTf)_2$	toluene	10	52
5	$Cu(OAc)_2$	toluene	48	NR
6	BF_3	toluene	48	NR
7	$Zn(OTf)_2$	toluene	24	46
8	$ZnBr_2$	toluene	36	78
9	$ZnCl_2$	toluene	20	67
10	$Zn(OAc)_2$	toluene	36	NR
11[b]	$ZnBr_2$	toluene	63	71
12[c]	$ZnBr_2$	toluene	63	78
13	$ZnBr_2$	dioxane	36	56
14	$ZnBr_2$	DCE	48	36
15	$ZnBr_2$	MeCN	48	42
16[d]	$ZnBr_2$	toluene	36	69

[a]The reactions were performed with **1a** (0.2 mmol), **2a** (0.24 mmol), and Lewis acid (0.04 mmol) in solvent (2.0 mL) at 80 ℃. [b]The reaction was ran at 60 ℃. [c]The reaction was ran at 70 ℃. [d]**1a** (0.067 mmol) and **2a** (0.20 mmol) were used.

Initially, 1,3,5-triphenyl-1,3,5-triazinane **1a** and 2-phenyl-1-tosylaziridine **2a** were chosen as the substrates for the reaction optimization. As shown in Table 1, the desired product imidazoline **3aa** could be obtained in 30% yield in the presence of 20% $FeCl_3$ in toluene at 80 ℃ (Table 1, entry 1). Because Lewis acids can facilitate the nucleophilic ring opening of the *N*-tosylaziridines and the formation of formaldimines from 1,3,5-triazinanes, a variety of Lewis acids were screened to improve the reaction efficiency (Table 1, entries 2-10). $ZnBr_2$ was found to be the most efficient catalyst and afforded the desired product in 78 % yield (Table 1, entry 8), whereas others resulted in a drop of the yield (Table 1, entries 3, 4, 7 and 9) or no reaction (Table 1, entries 2, 5, 6 and 10). The reaction efficiency was significantly decreased when the reaction was conducted under lower temperature (Table 1, entry 8 vs entries 11-12). For the solvent, dioxane, DCM and MeCN all led to dramatically decreased yields, compared to that with toluene (Table 1, entries 13-15 vs entry 8).

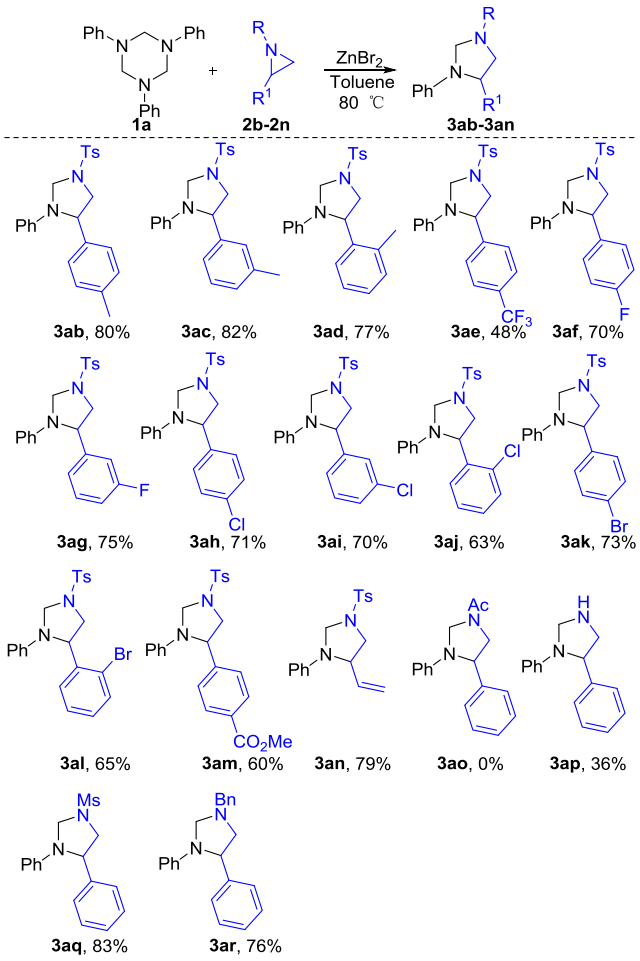
Having established the optimal reaction conditions, we thereby examined the substrate scope of this protocol by employing a variety of 1,3,5-triazinanes **1**, and the results are summarized in Scheme 2. First, 1,3,5-triazinanes with electron-donating groups were well tolerated, providing the corresponding imidazolidines with decent yields (Scheme 2, **3ba-3fa**). However, the substrates with electron-donating substituents gave lower yields than the electron-neutral one did (Scheme 2, **3ba-3fa** vs **3aa**). Next, several substrates with electron-withdrawing groups were investigated under the reaction conditions. Satisfyingly, the imidazolidines **3ga-3oa** were obtained in good to excellent yields, probably because of the relative high electrophilicity of the corresponding formaldimines generated *in situ*. Polysubstituted 1,3,5-triazinanes could also be compatible (Scheme 2, **3na-3pa**). Moreover, 1,3,5-triazinanes with groups at *ortho* position reacted well to yield the desired products without any losses of yield compared to the *meta*- or *para*-substituted ones (Scheme 2, **3da** vs **3ba-3ca**, **3ma-3pa** vs **3ga-3la**). Notably, the 1,3,5-triisobutyl-1,3,5-triazinane could also be subjected to the cyclization reaction to give the desired product **3sa**, albeit in slightly low yields. However, no product was isolated and most of the substrate decomposed when 1,3,5-tris(1-phenylethyl)-1,3,5-triazinane was employed, and only trace of product was detected by HRMS. Last, 1,3,5-triazinanes with ester group was also suitable substrate to afford desired product **3ta** in 78% yield.

Scheme 2. Scope of 1,3,5-triazianes[a]



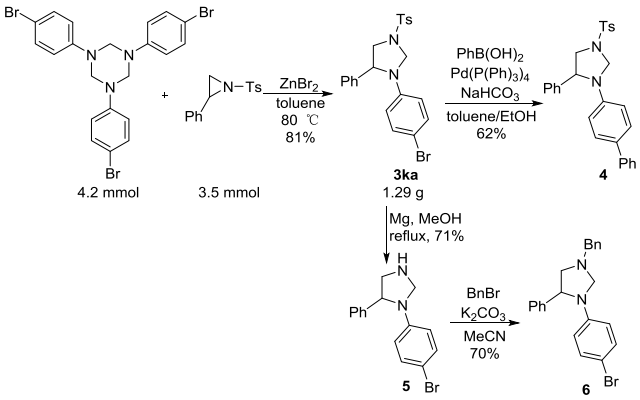
[a]Reaction condition: **1** (0.2 mmol), **2a** (0.24 mmol), and $ZnBr_2$ (0.04 mmol) in toluene (2.0 mL) at 80 ℃ for 36 h.

Scheme 3. Scope of aziridines[a]



[a]Reaction condition: **1** (0.2 mmol), **2a** (0.24 mmol), and $ZnBr_2$ (0.04 mmol) in toluene (2.0 mL) at 80 ℃ for 36 h.

Scheme 4. Gram scale experiment and product derivation

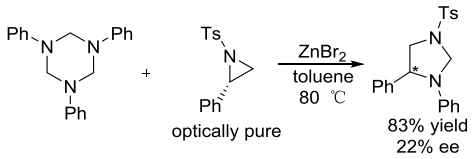


Subsequently, a variety of substituted aziridines was tested for the imidazolidines formation. As shown in Scheme 3. The substrates bearing electron-donating or electron-withdrawing groups could take part in this transformation smoothly, affording the corresponding products (**3ab**−**3an**) in moderate to high yields. It was noteworthy that aziridines with electron-donating groups were more efficient than substrates bearing electron-withdrawing groups (Scheme 3, **3ab-3ad** vs **3ae-3al**). Furthermore, strong electron-withdrawing substituent, such as trifluoromethyl group, has significant adverse effect to the reaction efficiency (Scheme 3, **3ae**), presumably due to the electronic effects. Negligible steric effect of substitutent on the aromatic ring of 1,3,5-triazinanes on the reaction efficiency has been observed. Sterically more bulky group on the phenyl ring of aziridines did not conspicuously influence the reaction efficiency (Scheme 3, **3ad, 3aj** and **3al**). Reaction with substrate bearing ester group also proceeded smoothly to afford the desired product **3am**. Vinyl substituted aziridines also could be well tolerated under the conditions and gave the product in 79% yield. Then aziridines bearing other functional groups such as acetyl, Boc, Ms and Bn were examined. *N*-Ms and *N*-Bn aziridines gave the corresponding product in 83% and 76% yield (**3aq** and **3ar**), respectively. However, the *N*-acetyl aziridine is totally inactive under the reaction conditions (**3ao**). The *N*-Boc aziridine gave the Boc-deprotected imidazolidine in 36% yield under the acidic condition (**3ap**).

To further explore the synthetic application of this transformation, we performed the reaction of **1k** with **2a** on a 4.2 mmol scale and isolated the **3ka** in 81% yield, which could be converted to **4** via Suzuki coupling (Scheme 4). The *N*-Ts group of cycloadduct **3ka** could be easily removed with magnesium in methanol to give the imidazolidine **5** in 71% yield, which could be further converted to a pharmaceutically important imidazolidine **6** in 70% yield.

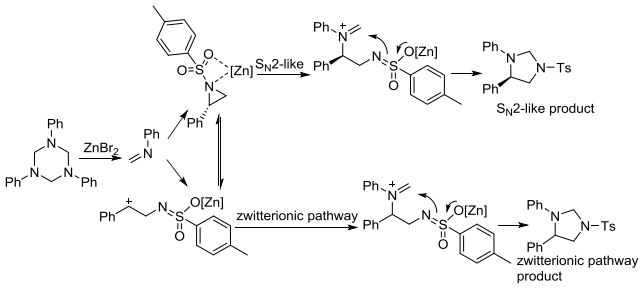
To gather information for a mechanistic study, we conducted this 1,3-dipolar cycloaddition reaction using enantioenriched aziridines **2a** to explore the stereochemistry of this transformation (Scheme 5). The corresponding **3aa** was obtained in 83% yield with 22% ee, a significant loss in the stereochemical purity from the enantioriched aziridine.

Scheme 5. Stereochemistry and mechanistic investigation.



Based on these obtained results and literature information,[13] we proposed a mechanism. As depicted in Scheme 6, the formaldimine was first generated in the presence of Lewis acid. Next, formaldimine attacked the activated aziridine through an S_N2-like pathway, leading to the inversion of configuration and the ring open of the aziridine. Meanwhile, the racemic product was generated through the ring opened zwitterion, which served as both a nucleophile and an electrophile to react with *N*-phenyl formaldimine. The ee value of **3aa** suggested that the ring opened zwitterionic pathway product dominated over the S_N2-like product.

Scheme 6. A Plausible Reaction Mechanism



In summary, we have established an unprecedented 1,3-dipolar cycloadditions of 1,3,5-triazinanes with aziridines under mild conditions, providing an efficient access to functionalized imidazolidines. Preliminary mechanistic studies were also conducted to elucidate the mechanism. This protocol is

very promising because the reaction is scalable, and the products can be readily converted to other functionalized imidazolidines.

■ EXPERIMENTAL SECITON

General Information. Unless otherwise specified, all reactions were carried out under a nitrogen atmosphere in anhydrous conditions. All chemicals and solvents which are commercially available were used without further purification. Analytical thin-layer chromatography (TLC) was performed on silica gel plates (GF-254) using UV-light (254 and 365 nm). Flash chromatography was conducted on silica gel (200-300 mesh). NMR spectra were recorded at ambient temperature in $CDCl_3$ on a Bruker AMX600 (^{1}H NMR at 600 MHz and $^{13}C\{^1H\}$ NMR at 150MHz) spectrometer. Chemical shifts were reported in parts per million (ppm) downfield from an internal standard, tetramethylsilane (0 ppm). All high resolution mass spectra were obtained on a Agilent 6200 Q-TOF MS. Melting points were determined on a WRX-4 melting point apparatus. 1,3,5-Triazinanes[12,14], *N*-Ts aziridines[15], *N*-Benzyl aziridine[16], *N*-Boc aziridine[17] and *N*-Ms aziridine[18] were prepared according to the literature procedures.

General procedure for the synthesis of 3. To a dried test tube with a magnetic stirring bar under N_2 at room temperature were added 1,3,5-triazinane **1a** (0.24 mmol, 75.6 mg) and aziridine **2a** (0.20 mmol, 54.6 mg), followed by the addition of $ZnBr_2$ (0.04 mmol, 9.0 mg). Then toluene (2.00 mL) was introduced by syringe, and the mixture was stirred at 80 ℃ in an oil bath for 36 h. The reaction was then quenched with an aqueous Na_2CO_3 solution (10 mL) and extracted with ethyl acetate (15 mL) for three times. The combined organic layer was washed with brine (15 mL × 3), dried over Na_2SO_4 and the solvent was removed by rotary evaporation. The residue was purified by column chromatography on silica gel (petroleum: ethyl acetate = 10:1 to 5:1) to afford the desired product **3aa**.

*3,4-Diphenyl-1-tosylimidazolidine **(3aa)***. White solid (60.7 mg, yield: 80 %); mp 110-111 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.67 (d, J = 8.2 Hz, 2H), 7.24-7.21 (m, 5H), 7.12-7.09 (m, 4H), 6.72 (t, J = 7.3 Hz, 1H), 6.36 (d, J = 8.1 Hz, 2H), 5.02 (d, J = 5.9 Hz, 1H), 4.74 (d, J = 5.9 Hz, 1H), 4.58-4.43 (m, 1H), 3.91 (dd, J = 10.4, 7.4 Hz, 1H), 3.44 (dd, J = 10.4, 5.2 Hz, 1H), 2.38 (s, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 144.8 , 144.4, 140.4, 132.7, 129.9 , 129.1, 128.9, 127.9, 127.7, 125.9, 118.3, 113.0, 66.1, 61.5, 55.5, 21.6; IR 3028.2, 2918.3, 1599, 1508, 1346, 1159, 1030, 747, 667, 550; HRMS (ESI) m/z calcd for $C_{22}H_{23}N_2SO_2^+$ $[M+H]^+$ 379.1475, found 379.1473.

*4-Phenyl-3-(p-tolyl)-1-tosylimidazolidine **(3ba)***. White solid (60.4 mg, yield: 77 %); mp 130-131 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.67 (d, J = 8.0 Hz, 2H), 7.27-7.15 (m, 5H), 7.09 (d, J = 7.2 Hz, 2H), 6.91 (d, J = 8.2 Hz, 2H), 6.29 (d, J = 8.3 Hz, 2H), 5.02 (d, J = 5.7 Hz, 1H), 4.69 (d, J = 5.7 Hz, 1H), 4.49 (t, J = 6.3 Hz, 1H), 3.90 (dd, J = 10.2, 7.5 Hz, 1H), 3.41 (dd, J = 10.3, 5.4 Hz, 1H), 2.38 (s, 3H), 2.18 (s, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 144.3, 142.7, 140.5, 132.8, 129.9, 129.7, 128.9, 127.9, 127.6, 127.6 125.9, 113.4, 66.5, 61.7, 55.6, 21.6, 20.4; IR 3030, 2920, 1618, 1524, 1348, 1163, 1028, 799, 669, 588; HRMS (ESI) m/z calcd for $C_{23}H_{25}N_2SO_2^+$ $[M+H]^+$ 393.1631, found 393.1630.

*4-Phenyl-3-(m-tolyl)-1-tosylimidazolidine **(3ca)***. White solid (54.9 mg, yield: 70 %); mp 126-127 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.67 (d, J = 8.1 Hz, 2H), 7.26-7.19 (m, 5H), 7.10 (d, J = 6.4 Hz, 2H), 6.97 (t, J = 7.8 Hz, 1H), 6.54 (d, J = 7.4 Hz, 1H), 6.21 (s, 1H), 6.15 (d, J = 8.1 Hz, 1H), 5.02 (d, J = 5.8 Hz, 1H), 4.72 (d, J = 5.8 Hz, 1H), 4.60-4.35 (m, 1H), 3.88 (dd, J = 10.2, 7.5 Hz, 1H), 3.44 (dd, J = 10.3, 5.0 Hz, 1H), 2.38 (s, 3H), 2.21 (s, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 144.9, 144.3, 140.6, 138.9, 132.7, 129.9, 129.9, 128.9, 127.9, 127.6, 125.9, 119.2, 113.7, 110.3, 66.1, 61.4, 55.6, 21.8, 21.6; IR 3032, 2918, 1603, 1489, 1344, 1159, 1030, 853, 665, 550; HRMS (ESI) m/z calcd for $C_{23}H_{25}N_2SO_2^+$ $[M+H]^+$ 393.1631, found 393.1629.

*4-Phenyl-3-(o-tolyl)-1-tosylimidazolidine **(3da)***. A white solid (54.9 mg, yield: 70 %); mp 118-119 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.75 (d, J = 8.1 Hz, 2H), 7.32 (d, J = 8.0 Hz, 2H), 7.16-7.14 (m, 3H), 7.12-7.05 (m, 3H), 6.96 (t, J = 7.3 Hz, 1H), 6.90 (t, J = 7.1 Hz, 1H), 6.79 (d, J = 7.9 Hz, 1H), 4.85 (d, J = 6.8 Hz, 1H), 4.58 (t, J = 7.4 Hz, 1H), 4.22 (d, J = 6.8 Hz, 1H), 3.96 (dd, J = 9.9, 6.6 Hz, 1H), 3.34-3.26 (m, 1H), 2.46 (s, 3H), 2.16 (s, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$); δ 144.1, 143.9, 137.8, 133.6, 133.2, 131.2, 129.9, 128.6, 127.9, 127.8, 126.9, 126.6, 124.2, 119.9, 68.9, 63.9, 54.8, 21.7, 18.6; IR 2976, 2830, 1597, 1495, 1341, 1167, 1094, 665, 592, 546; HRMS (ESI) m/z calcd for $C_{23}H_{25}N_2SO_2^+$ $[M+H]^+$ 393.1631, found 393.1629.

*3-(4-Isopropylphenyl)-4-phenyl-1-tosylimidazolidine **(3ea)***. White solid (49.2 mg, yield: 59 %); mp 100-101 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.67 (d, J = 8.2 Hz, 2H), 7.25-7.21 (m, 5H), 7.11 (d, J = 7.8 Hz, 2H), 6.98 (d, J = 8.6 Hz, 2H), 6.33 (d, J = 8.6 Hz, 2H), 5.04 (d, J = 5.8 Hz, 1H), 4.68 (d, J = 5.8 Hz, 1H), 4.50 (dd, J = 7.2, 5.5 Hz, 1H), 3.88 (dd, J = 10.3, 7.5 Hz, 1H), 3.43 (dd, J = 10.3, 5.3 Hz, 1H), 2.83-2.65 (m, 1H), 2.39 (s, 3H), 1.15 (d, J = 3.6 Hz, 3H), 1.14 (d, J = 3.6 Hz, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 144.3, 143.1, 140.7, 138.8, 132.7, 129.9, 128.9, 127.9, 127.6, 127.0, 125.9, 113.1, 66.4, 61.9, 55.6, 33.1, 24.2, 24.2, 21.6; IR 1616, 1522, 1387, 1350, 1163, 814, 698, 667, 590, 548; HRMS (ESI) m/z calcd for $C_{25}H_{29}N_2SO_2^+$ $[M+H]^+$ 421.1944, found 421.1943.

*3-(4-Methoxyphenyl)-4-phenyl-1-tosylimidazolidine **(3fa)***. White solid (56.9 mg, yield: 70 %); mp 135-136 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.69 (d, J = 8.1 Hz, 2H), 7.25-7.22 (m, 5H), 7.09 (d, J = 7.5 Hz, 2H), 6.69 (d, J = 8.9 Hz, 2H), 6.35 (d, J = 9.0 Hz, 2H), 5.03 (d, J = 5.8 Hz, 1H), 4.65 (d, J = 5.8 Hz, 1H), 4.44 (t, J = 6.6 Hz, 1H), 3.93 (dd, J = 10.3, 7.5 Hz, 1H), 3.68 (s, 3H), 3.38 (dd, J = 10.4, 6.0 Hz, 1H), 2.40 (s, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 152.7, 144.3, 140.3, 139.4, 132.9, 129.9, 128.9, 127.9, 127.7, 126.0, 114.8, 114.6, 67.1, 62.2, 55.6, 21.6; IR 2916, 2849, 1514, 1348, 1242, 1161, 1034, 812, 667, 548; HRMS (ESI) m/z calcd for $C_{23}H_{25}N_2SO_3^+$ $[M+H]^+$ 409.1580, found 409.1578.

*3-(4-Fluorophenyl)-4-phenyl-1-tosylimidazolidine **(3ga)***. White solid (67.4 mg, yield: 85 %); mp 138-139 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.68 (d, J = 8.2 Hz, 2H), 7.28-7.21 (m, 5H), 7.13-7.04 (m, 2H), 6.81 (t, J = 8.7 Hz, 2H), 6.29 (dd, J = 9.1, 4.2 Hz, 2H), 5.00 (d, J = 5.9 Hz, 1H), 4.71 (d, J = 5.9 Hz, 1H), 4.44 (t, J = 6.6 Hz, 1H), 3.95 (dd, J = 10.5, 7.4 Hz, 1H), 3.40 (dd, J = 10.5, 5.9 Hz, 1H), 2.40 (s, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 156.20 (d, J = 237.1 Hz), 144.4, 141.4 (d, J = 1.7 Hz), 140.0, 132.8, 129.9, 128.9, 127.9, 125.9, 115.6 (d, J = 22.3 Hz), 114.1 (d, J = 7.5 Hz), 66.7, 62.0, 55.7, 21.6;

IR 2920, 1518, 1344, 1227, 1161, 1030, 814, 669, 588, 548; HRMS (ESI) m/z calcd for $C_{22}H_{22}FN_2SO_2^+$ $[M+H]^+$ 397.1381, found 397.1381.

3-(3-Fluorophenyl)-4-phenyl-1-tosylimidazolidine ***(3ha)***. White solid (65.4 mg, yield: 83 %); mp: 148-151 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.67 (d, J = 8.2 Hz, 2H), 7.26-7.22 (m, 5H), 7.10 (d, J = 7.7 Hz, 2H), 7.04 (dd, J = 15.1, 8.1 Hz, 1H), 6.40 (m, 1H), 6.13 (d, J = 8.3 Hz, 1H), 6.01 (d, J = 11.8 Hz, 1H), 4.97 (d, J = 6.1 Hz, 1H), 4.76 (d, J = 6.1 Hz, 1H), 4.56-4.38 (m, 1H), 3.94 (dd, J = 10.6, 7.4 Hz, 1H), 3.45 (dd, J = 10.7, 5.3 Hz, 1H), 2.39 (s, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 163.59 (d, J = 243.5 Hz), 146.3 (d, J = 10.6 Hz), 144.5, 139.8, 132.7, 130.3 (d, J = 10.1 Hz), 129.9, 129.0, 127.9 (d, J = 16.7 Hz), 125.8, 108.6 (d, J = 2.2 Hz), 104.8 (d, J = 21.5 Hz), 100.1 (d, J = 26.2 Hz), 65.9, 61.5, 55.6, 21.6; IR 1622, 1584, 1506, 1385, 1344, 1196, 1159, 816, 671, 550; HRMS (ESI) m/z calcd for $C_{22}H_{22}FN_2SO_2^+$ $[M+H]^+$ 397.1381, found 397.1380.

4-Phenyl-1-tosyl-3-(4-(trifluoromethyl)phenyl)imidazolidine ***(3ia)*****.** White solid (78.1 mg, yield: 88 %); mp: 133-135 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.59 (d, J = 8.1 Hz, 2H), 7.24 (d, J = 8.5 Hz, 2H), 7.18-7.16 (m, 3H), 7.12 (d, J = 8.0 Hz, 2H), 7.01 (dd, J = 15.5, 9.4 Hz, 2H), 6.27 (d, J = 8.6 Hz, 2H), 4.90 (dd, J = 18.2, 6.3 Hz, 1H), 4.77 (d, J = 6.4 Hz, 1H), 4.46-4.41 (m, 1H), 3.91 (dd, J = 10.7, 7.4 Hz, 1H), 3.40 (dd, J = 10.8, 5.3 Hz, 1H), 2.29 (s, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 145.8, 143.6, 138.4, 131.6, 128.9, 128.1, 127.0, 126.7, 125.3, 125.3, 125.3, 124.7, 111.1, 64.5, 60.2, 54.6, 20.5; IR 1618, 1533, 1335, 1167, 1105, 1071, 820, 669, 610, 552; HRMS (ESI) m/z calcd for $C_{23}H_{22}N_2F_3SO_2^+$ $[M+H]^+$ 447.1349, found 447.1347.

3-(4-Chlorophenyl)-4-phenyl-1-tosylimidazolidine ***(3ja)***. White solid (75.8 mg, yield: 92 %); mp 140-142 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.59 (d, J = 8.1 Hz, 2H), 7.17-7.13 (m, 5H), 6.99 (d, J = 7.6 Hz, 2H), 6.95 (d, J = 8.9 Hz, 2H), 6.17 (d, J = 8.9 Hz, 2H), 4.89 (d, J = 6.1 Hz, 1H), 4.66 (d, J = 6.1 Hz, 1H), 4.45-4.30 (m, 1H), 3.87 (dd, J = 10.6, 7.4 Hz, 1H), 3.34 (dd, J = 10.6, 5.5 Hz, 1H), 2.30 (s, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 143.4, 142.2, 138.7, 131.6, 128.9, 127.9, 127.9, 126.8, 126.7, 124.8, 122.1, 113.0, 65.0, 60.4, 54.6, 20.5; IR 1599, 1503, 1348, 1161, 1098, 1028, 810, 669, 611, 554; HRMS (ESI) m/z calcd for $C_{22}H_{22}ClN_2SO_2^+$ $[M+H]^+$ 413.1085, found 413.1085.

3-(4-Bromophenyl)-4-phenyl-1-tosylimidazolidine ***(3ka)***. White solid (76.2 mg, yield: 84 %); mp: 145-147 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.67 (d, J = 8.2 Hz, 2H), 7.27-7.21 (m, 5H), 7.17 (d, J = 9.0 Hz, 2H), 7.08 (d, J = 7.7 Hz, 2H), 6.21 (d, J = 9.0 Hz, 2H), 4.96 (d, J = 6.1 Hz, 1H), 4.74 (d, J = 6.1 Hz, 1H), 4.51-4.38 (m, 1H), 3.96 (dd, J = 10.6, 7.4 Hz, 1H), 3.43 (dd, J = 10.7, 5.6 Hz, 1H), 2.40 (s, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 144.5, 143.7, 139.7, 132.7, 131.8, 129.9, 129.0, 127.9, 127.8, 125.8, 114.6, 110.4, 65.9, 61.5, 55.6, 21.6; IR 1595, 1491, 1387, 1350, 1165, 808, 704, 669, 610, 552; HRMS (ESI) m/z calcd for $C_{22}H_{22}BrN_2SO_2^+$ $[M+H]^+$ 457.0580, found 457.0580.

3-(2-Bromophenyl)-1-tosyl-1,2,3,4-tetrahydroquinazoline ***(3la)***. White solid (73.4 mg, 81 %); mp: 130-133 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.67 (d, J = 8.1 Hz, 2H), 7.29-7.20 (m, 5H), 7.09 (d, J = 7.4 Hz, 2H), 6.93 (t, J = 8.1 Hz, 1H), 6.83 (d, J = 7.8 Hz, 1H), 6.46 (s, 1H), 6.24 (d, J = 8.2 Hz, 1H), 4.96 (d, J = 6.2 Hz, 1H), 4.77 (d, J = 6.2 Hz, 1H), 4.50-4.35 (m, 1H), 3.95 (dd, J = 10.6, 7.4 Hz, 1H), 3.44 (dd, J = 10.7, 5.4 Hz, 1H), 2.40 (s, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 145.9, 144.5, 139.6, 132.6, 130.3, 129.9, 129.0, 127.9, 127.7, 125.8, 123.1, 121.0, 115.5, 111.5, 65.9, 61.2, 55.6, 21.6; IR 1593, 1487, 1346, 1159, 1092, 1028, 849, 762, 669, 550; HRMS (ESI) m/z calcd for $C_{22}H_{22}BrN_2SO_2^+$ $[M+H]^+$ 457.0580, found 457.0580.

3-(2-Bromophenyl)-4-phenyl-1-tosylimidazolidine ***(3ma)*****.** White solid (74.2 mg, yield: 81 %); mp: 130-132 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.76 (d, J = 8.2 Hz, 2H), 7.46 (d, J = 7.9 Hz, 1H), 7.29 (d, J = 8.0 Hz, 2H), 7.19-7.14 (m, 5H), 7.03 (dd, J = 11.9, 4.8 Hz, 1H), 6.81 (dd, J = 11.9, 4.6 Hz, 1H), 6.77 (d, J = 8.1 Hz, 1H), 5.24 (d, J = 6.9 Hz, 1H), 4.70 (dd, J = 8.1, 6.8 Hz, 1H), 4.34 (d, J = 6.9 Hz, 1H), 4.02 (dd, J = 10.0, 6.5 Hz, 1H), 3.23 (dd, J = 9.9, 8.5 Hz, 1H), 2.43 (s, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 144.2, 144.1, 137.4, 134.0, 133.5, 129.9, 128.7, 128.1, 128.0, 127.9, 126.9, 125.2, 121.4, 119.1, 68.5, 63.4, 54.8, 21.7; IR 2922, 2851, 1514, 1348, 1244, 1161, 1032, 814, 667, 546; HRMS (ESI) m/z calcd for $C_{22}H_{22}BrN_2SO_2^+$ $[M+H]^+$ 457.0580, found 457.0579.

3-(4-Bromo-2-fluorophenyl)-4-phenyl-1-tosylimidazolidine ***(3na)***. White solid (81.1 mg, yield: 86 %); mp: 150-152 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.72 (d, J = 8.1 Hz, 2H), 7.27 (d, J = 8.0 Hz, 2H), 7.22-7.16 (m, 3H), 7.11 (d, J = 12.2 Hz, 1H), 7.07-7.02 (m, 2H), 6.85 (dd, J = 8.6, 0.9 Hz, 1H), 6.17 (t, J = 8.9 Hz, 1H), 5.15 (dd, J = 7.4, 2.5 Hz, 1H), 4.69 (dd, J = 7.4, 2.2 Hz, 1H), 4.47 (t, J = 7.5 Hz, 1H), 4.07 (dd, J = 10.9, 7.1 Hz, 1H), 3.19 (dd, J = 10.9, 8.2 Hz, 1H), 2.41 (s, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 153.11 (d, J = 247.5 Hz), 144.5, 138.1, 133.2, 132.7 (d, J = 10.2 Hz), 130.0, 129.0, 128.1, 128.0, 127.2 (d, J = 3.1 Hz), 126.2, 119.53 (d, J = 23.9 Hz), 118.5 (d, J = 4.2 Hz), 111.8 (d, J = 9.2 Hz), 67.8 (d, J = 11.4 Hz), 62.0, 55.0, 21.7; IR 1607, 1506, 1341, 1163, 1092, 968, 791, 762, 667, 546; HRMS (ESI) m/z calcd for $C_{22}H_{21}FBrN_2SO_2^+$ $[M+H]^+$ 475.0486, found 475.0486.

3-(2,4-Dibromophenyl)-4-phenyl-1-tosylimidazolidine ***(3oa)***. White solid (85.4 mg, yield: 80 %); mp: 133-136 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.68 (d, J = 8.1 Hz, 2H), 7.53 (d, J = 2.0 Hz, 1H), 7.23 (d, J = 7.9 Hz, 2H), 7.12-7.10 (m, 3H), 7.07-7.04 (m, 3H), 6.51 (d, J = 8.7 Hz, 1H), 5.14 (d, J = 7.0 Hz, 1H), 4.57 (t, J = 7.5 Hz, 1H), 4.26 (d, J = 7.0 Hz, 1H), 3.96 (dd, J = 10.1, 6.6 Hz, 1H), 3.16-3.13 (m, 1H), 2.37 (s, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 143.3, 142.3, 135.9, 135.1, 132.3, 129.8, 128.8, 127.8, 127.1, 126.9 125.8, 121.2, 118.2, 115.7, 67.2, 62.2, 53.7, 20.6; IR 2916, 2849, 1597, 1474, 1341, 1161, 1092, 812, 664, 592; HRMS (ESI) m/z calcd for $C_{22}H_{21}Br_2N_2SO_2^+$ $[M+H]^+$ 534.9685, found = 534.9687.

3-(2,4-Dichlorophenyl)-4-phenyl-1-tosylimidazolidine ***(3pa)***. White solid (78.4 mg, yield: 88 %); mp: 155-157 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.68 (d, J = 8.1 Hz, 2H), 7.23 (d, J = 8.0 Hz, 2H), 7.20 (d, J = 2.3 Hz, 1H), 7.12-7.10 (m, 3H), 7.03 (d, J = 7.6 Hz, 2H), 6.84 (dd, J = 8.7, 2.2 Hz, 1H), 6.49 (d, J = 8.8 Hz, 1H), 5.14 (d, J = 7.2 Hz, 1H), 4.55-4.53 (m, 1H), 4.34 (d, J = 7.2 Hz, 1H), 3.98 (dd, J = 10.4, 6.7 Hz, 1H), 3.12 (dd, J = 9.9, 9.2 Hz, 1H), 2.37 (s, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 143.3, 140.4, 136.1, 132.3, 129.3, 128.9, 127.9, 127.4, 127.1, 127.0 126.2, 125.6, 119.9, 67.1, 61.8, 53.7, 20.6; IR 2943, 2884, 1597, 1476, 1346, 1165, 1090, 669, 610, 550; HRMS (ESI) m/z calcd for $C_{22}H_{21}Cl_2N_2SO_2^+$ $[M+H]^+$ 447.0695, found 447.0696.

3-(3-Chloro-4-methylphenyl)-4-phenyl-1-tosylimidazolidine ***(3qa)***. Yellow solid (70.1 mg, yield: 82 %); mp: 148-150 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.67 (d, J = 8.1 Hz, 2H), 7.25-7.22 (m, 5H), 7.09-7.06 (m, 2H), 6.91 (d, J = 8.4 Hz, 1H), 6.35 (d, J = 2.3 Hz, 1H), 6.15 (dd, J = 8.4, 2.3 Hz, 1H), 4.96 (d, J = 6.1 Hz, 1H), 4.72 (d, J = 6.1 Hz, 1H), 4.43 (t, J = 6.4 Hz, 1H), 3.94 (dd, J = 10.6, 7.4 Hz, 1H), 3.41 (dd, J = 10.6, 5.6 Hz, 1H), 2.39 (s, 3H), 2.19 (s, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 144.5, 143.9, 139.9, 134.8, 132.8, 131.2, 129.9, 129.0, 127.9, 127.8, 125.9, 125.3, 113.5, 111.7, 66.2, 61.5, 55.6, 21.6, 18.9; IR 1613, 1508, 1346, 1161, 816, 791, 762, 700, 669, 550; HRMS (ESI) m/z calcd for $C_{23}H_{24}ClN_2SO_2^+$ $[M+H]^+$ 427.1242, found 427.1241.

3-Isobutyl-4-phenyl-1-tosylimidazolidine ***(3sa)***. Yellow solid (43.1 mg, yield: 60 %); mp: 70-72 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.76 (d, J = 8.2 Hz, 2H), 7.36 (d, J = 8.0 Hz, 2H), 7.25-7.19 (m, 3H), 7.01 (dd, J = 6.4, 2.9 Hz, 2H), 4.65 (d, J = 6.8 Hz, 1H), 3.72 (dd, J = 9.9, 7.0 Hz, 1H), 3.65 (d, J = 6.8 Hz, 1H), 3.45 (dd, J = 9.0, 7.2 Hz, 1H), 3.07 (t, J = 9.6 Hz, 1H), 2.48 (s, 3H), 2.02-1.84 (m, 2H), 1.61-1.47 (m, 1H), 0.72 (d, J = 6.7 Hz, 6H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 142.8, 137.5, 132.7, 128.6, 127.5, 127.0, 126.9, 126.6, 69.2, 67.5, 58.5, 54.0, 26.2, 20.6, 20.0, 18.9; IR 2963, 2805, 1599, 1337, 1165, 1107, 1011, 667, 588, 548; HRMS (ESI) m/z calcd for $C_{20}H_{27}N_2SO_2^+$ $[M+H]^+$ 359.1788, found 359.1785.

Ethyl 4-(5-phenyl-3-tosylimidazolidin-1-yl)benzoate ***(3ta)***. White solid (70.1 mg, yield: 78 %); mp: 170-172 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.72 (d, J = 8.8 Hz, 2H), 7.60 (d, J = 8.2 Hz, 2H), 7.19-7.17 (m, 3H), 7.15 (d, J = 8.1 Hz, 2H), 7.02-7.00 (m, 2H), 6.24 (d, J = 8.8 Hz, 1H), 4.94 (d, J = 6.4 Hz, 1H), 4.79 (d, J = 6.4 Hz, 1H), 4.48 (dd, J = 7.0, 5.3 Hz, 1H), 4.21 (qd, J = 7.0, 1.3 Hz, 2H), 3.89 (dd, J = 10.7, 7.4 Hz, 1H), 3.42 (dd, J = 10.7, 5.0 Hz, 1H), 2.31 (s, 3H), 1.25 (t, J = 7.1 Hz, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 166.6, 147.7, 144.6, 139.6, 132.6, 131.6, 131.1, 130.0, 129.1, 128.0, 127.8, 125.8, 119.7, 113.8, 111.9, 65.4, 61.1, 60.4, 55.6, 21.6, 14.4; IR 2984, 1701, 1611, 1344, 1283, 1159, 1109, 770, 671, 554; HRMS (ESI) m/z calcd for $C_{25}H_{27}N_2SO_4^+$ $[M+H]^+$ 451.1685, found 451.1685.

3-Phenyl-4-(p-tolyl)-1-tosylimidazolidine ***(3ab)***. White solid (63.0 mg, yield: 80 %); mp: 160-162 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.59 (d, J = 8.0 Hz, 2H), 7.13 (d, J = 7.9 Hz, 2H), 7.02 (t, J = 7.7 Hz, 2H), 6.96 (d, J = 7.7 Hz, 2H), 6.91 (d, J = 7.8 Hz, 2H), 6.62 (t, J = 7.2 Hz, 1H), 6.28 (d, J = 8.0 Hz, 2H), 4.92 (d, J = 5.8 Hz, 1H), 4.66 (d, J = 5.8 Hz, 1H), 4.40 (t, J = 6.1 Hz, 1H), 3.84-3.77 (m, 1H), 3.34 (dd, J = 10.3, 5.2 Hz, 1H), 2.30 (s, 3H), 2.21 (s, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 144.9, 144.3, 137.4, 132.7, 129.9, 129.6, 129.1, 127.9, 125.9, 118.2, 113.0, 66.1, 61.3, 55.7, 21.6, 21.2; IR 1599, 1508, 1350, 1163, 1028, 812, 745, 667, 600, 550; HRMS (ESI) m/z calcd for $C_{23}H_{25}N_2SO_2^+$ $[M+H]^+$ 393.1631, found 393.1631.

3-Phenyl-4-(m-tolyl)-1-tosylimidazolidine ***(3ac)***. White solid (64.2 mg, yield: 82 %); mp: 158-160 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.59 (d, J = 8.2 Hz, 2H), 7.14 (d, J = 8.1 Hz, 2H), 7.06-7.00 (m, 3H), 6.98-6.89 (m, 2H), 6.87-6.80 (m, 1H), 6.64 (t, J = 6.1 Hz, 1H), 6.35-6.17 (m, 2H), 4.93 (dd, J = 8.6, 5.9 Hz, 1H), 4.66 (d, J = 5.9 Hz, 1H), 4.43-4.35 (m, 1H), 3.81 (dd, J = 10.3, 7.5 Hz, 1H), 3.40-3.30 (m, 1H), 2.30 (s, 3H), 2.20 (d, J = 15.4 Hz, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 144.9, 144.9, 144.3, 140.5, 138.6, 137.4, 137.4, 132.7, 129.9, 129.6, 129.1, 128.8, 128.6, 127.9, 127.9, 126.5, 125.9, 123.0, 118.2, 118.2, 113.0, 66.1, 66.1, 61.6, 61.2, 55.7, 55.6, 21.6, 21.5, 21.2; IR 2920, 2860, 1599, 1506, 1350, 1163, 1092, 748, 664, 548; HRMS (ESI) m/z calcd for $C_{23}H_{25}N_2SO_2^+$ $[M+H]^+$ 393.1631, found 393.1632.

3-Phenyl-4-(o-tolyl)-1-tosylimidazolidine ***(3ad)***. White solid (60.1 mg, yield: 77 %); mp: 150-152 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.66 (d, J = 8.1 Hz, 2H), 7.20 (d, J = 8.0 Hz, 2H), 7.15-7.08 (m, 4H), 7.00-6.89 (m, 2H), 6.71 (t, J = 7.3 Hz, 1H), 6.25 (d, J = 8.1 Hz, 2H), 5.04 (d, J = 6.2 Hz, 1H), 4.81 (d, J = 6.2 Hz, 1H), 4.68-4.46 (m, 1H), 3.98 (dd, J = 10.5, 7.5 Hz, 1H), 3.36 (dd, J = 10.5, 5.6 Hz, 1H), 2.38 (s, 3H), 2.32 (s, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 144.8, 144.4, 137.8, 134.1, 132.8, 130.8, 129.9, 129.1, 127.8, 127.4, 126.7, 125.3, 118.2, 112.8, 66.1, 58.7, 54.1, 21.6, 19.3; IR 1599, 1508, 1385, 1346, 1157, 1094, 1034, 747, 667, 598; HRMS (ESI) m/z calcd for $C_{23}H_{25}N_2SO_2^+$ $[M+H]^+$ 393.1631, found 393.1630.

3-Phenyl-1-tosyl-4-(4-(trifluoromethyl)phenyl)imidazolidine ***(3ae)***. Thick liquid (42.5 mg, yield: 48 %); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.65 (d, J = 8.1 Hz, 2H), 7.47 (d, J = 8.0 Hz, 2H), 7.20 (d, J = 7.3 Hz, 4H), 7.14 (t, J = 7.9 Hz, 2H), 6.76 (t, J = 7.3 Hz, 1H), 6.34 (d, J = 8.1 Hz, 2H), 5.07 (d, J = 5.9 Hz, 1H), 4.74 (d, J = 5.9 Hz, 1H), 4.62 (dd, J = 7.0, 4.7 Hz, 1H), 3.94 (dd, J = 10.5, 7.6 Hz, 1H), 3.50 (dd, J = 10.6, 4.5 Hz, 1H), 2.39 (s, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 144.7, 144.5, 144.4, 132.8, 129.9, 129.3, 127.8, 126.3, 125.9, 125.8 118.7, 113.0, 65.9, 61.1, 55.2, 21.5; IR 2920, 2851, 1601, 1506, 1325, 1163, 1067, 750, 665, 596; HRMS (ESI) m/z calcd for $C_{23}H_{22}F_3N_2SO_2^+$ $[M+H]^+$ 447.1349, found 447.1347.

4-(4-Fluorophenyl)-3-phenyl-1-tosylimidazolidine ***(3af)***. White solid (57.6 mg, yield: 70 %); mp: 168-170 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.66 (d, J = 8.1 Hz, 2H), 7.22 (d, J = 8.0 Hz, 2H), 7.11 (t, J = 7.9 Hz, 2H), 7.09-7.04 (m, 2H), 6.90 (t, J = 8.6 Hz, 2H), 6.73 (t, J = 7.3 Hz, 1H), 6.35 (d, J = 8.1 Hz, 2H), 5.03 (d, J = 5.8 Hz, 1H), 4.70 (d, J = 5.8 Hz, 1H), 4.56-4.48 (m, 1H), 3.87 (dd, J = 10.4, 7.4 Hz, 1H), 3.43 (dd, J = 10.4, 4.8 Hz, 1H), 2.38 (s, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 162.2 (d, J = 246.0 Hz), 144.5 (d, J = 16.7 Hz), 136.2 (d, J = 3.0 Hz), 132.7, 129.9, 129.2, 127.8, 127.6 (d, J = 8.2 Hz), 118.5, 115.8 (d, J = 21.6 Hz), 113.0, 65.9, 60.8, 55.6, 21.6; IR 3065, 2920, 1601, 1508, 1346, 1163, 1028, 829, 667, 550; HRMS (ESI) m/z calcd for $C_{22}H_{22}FN_2SO_2^+$ $[M+H]^+$ 397.1381, found 397.1380.

4-(3-Fluorophenyl)-3-phenyl-1-tosylimidazolidine ***(3ag).*** White solid (61.7 mg, yield: 75 %); mp: 165-166 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.58 (d, J = 8.1 Hz, 2H), 7.17-7.13 (m, 3H), 7.05 (t, J = 7.9 Hz, 2H), 6.85-6.80 (m, 2H), 6.67 (t, J = 7.3 Hz, 1H), 6.62 (d, J = 9.5 Hz, 1H), 6.28 (d, J = 8.1 Hz, 2H), 4.97 (d, J = 6.0 Hz, 1H), 4.64 (d, J = 6.0 Hz, 1H), 4.53-4.35 (m, 1H), 3.84 (dd, J = 10.5, 7.6 Hz, 1H), 3.39 (dd, J = 10.6, 4.8 Hz, 1H), 2.31 (s, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 163.1 (d, J = 247.0 Hz), 144.6, 143.4 (d, J = 6.5 Hz), 132.7, 130.5 (d, J = 8.2 Hz), 129.9, 129.2, 127.8, 121.6 (d, J = 2.7 Hz), 118.6, 114.7 (d, J = 21.2 Hz), 113.1, 112.80 (d, J = 22.3 Hz), 66.0, 61.1 (d, J = 1.3 Hz), 55.3, 21.6; IR 2924, 1603, 1508, 1346, 1159, 1028, 750, 667, 590, 552; HRMS (ESI) m/z calcd for $C_{22}H_{22}FN_2SO_2^+$ $[M+H]^+$ 397.1381, found 397.1380.

4-(4-Chlorophenyl)-3-phenyl-1-tosylimidazolidine ***(3ah)***. Yellow solid (58.1 mg, yield: 71 %); mp: 174-177 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.55 (d, J = 8.2 Hz, 2H), 7.13-7.06 (m, 4H), 7.02 (t, J = 7.9 Hz, 2H), 6.92 (d, J = 8.4 Hz, 2H),

6.64 (t, *J* = 7.3 Hz, 1H), 6.24 (d, *J* = 8.1 Hz, 2H), 4.93 (d, *J* = 5.9 Hz, 1H), 4.61 (d, *J* = 5.9 Hz, 1H), 4.42 (dd, *J* = 7.1, 4.8 Hz, 1H), 3.79 (dd, *J* = 10.5, 7.5 Hz, 1H), 3.40-3.29 (m, 1H), 2.29 (s, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 144.5, 144.5, 139.1, 133.3, 132.8, 129.9, 129.3, 129.0, 127.8, 127.4, 118.5, 113.0, 65.9, 60.8, 55.4, 21.6; IR 1601, 1506, 1344, 1159, 1088, 820, 750, 667, 600, 550; HRMS (ESI) m/z calcd for $C_{22}H_{22}ClN_2SO_2^+$ $[M+H]^+$ 413.1085, found 413.1085. I

4-(3-Chlorophenyl)-3-phenyl-1-tosylimidazolidine ***(3ai)***. White solid (57.7 mg, yield: 70 %); mp: 169-170 °C. ^1H NMR (600 MHz, $CDCl_3$): δ 7.59 (d, *J* = 8.2 Hz, 2H), 7.17-7.08 (m, 4H), 7.06 (dd, *J* = 8.5, 7.5 Hz, 2H), 6.97 (s, 1H), 6.94 (d, *J* = 6.9 Hz, 1H), 6.68 (t, *J* = 7.3 Hz, 1H), 6.28 (d, *J* = 8.0 Hz, 2H), 4.97 (d, *J* = 6.0 Hz, 1H), 4.64 (d, *J* = 6.0 Hz, 1H), 4.41 (dd, *J* = 7.4, 5.0 Hz, 1H), 3.82 (dd, *J* = 10.6, 7.5 Hz, 1H), 3.38 (dd, *J* = 10.6, 4.9 Hz, 1H), 2.32 (s, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 144.5, 144.5, 142.8, 134.8, 132.6, 130.3, 129.9, 129.3, 128.0, 127.8, 126.0, 124.2, 118.6, 113.1, 66.0, 61.1, 55.3, 21.6; IR 1601, 1508, 1385, 1348, 1163, 1090, 748, 689, 667, 552; HRMS (ESI) m/z calcd for $C_{22}H_{22}ClN_2SO_2^+$ $[M+H]^+$ 413.1085, found 413.1085.

4-(2-Chlorophenyl)-3-phenyl-1-tosylimidazolidine ***(3aj)***. White solid (52.1 mg, yield: 63 %); mp: 110-111 °C. ^1H NMR (600 MHz, $CDCl_3$): δ 7.58 (d, *J* = 8.2 Hz, 2H), 7.28 (d, *J* = 7.5 Hz, 1H), 7.14-7.07 (m, 3H), 7.04 (t, *J* = 7.9 Hz, 2H), 6.95 (t, *J* = 7.4 Hz, 1H), 6.93-6.89 (m, 1H), 6.66 (t, *J* = 7.3 Hz, 1H), 6.19 (d, *J* = 8.1 Hz, 2H), 5.00 (d, *J* = 6.0 Hz, 1H), 4.75 (dd, *J* = 7.4, 4.3 Hz, 1H), 4.65 (d, *J* = 6.0 Hz, 1H), 3.91 (dd, *J* = 10.8, 7.6 Hz, 1H), 3.46 (dd, *J* = 10.8, 4.3 Hz, 1H), 2.29 (s, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 144.4, 1144.3, 137.4, 132.6, 132.2, 129.9, 129.7, 129.3, 128.9, 127.8, 127.4, 127.3, 118.4, 112.7, 65.8, 58.8, 53.9, 21.6; IR 1603, 1508, 1391, 1348, 1159, 1032, 758, 667, 604, 550; HRMS (ESI) m/z calcd for $C_{22}H_{22}ClN_2SO_2^+$ $[M+H]^+$ 413.1085, found 413.1087.

4-(4-Bromophenyl)-3-phenyl-1-tosylimidazolidine ***(3ak)***. White solid (66.8 mg, yield: 73 %); mp: 170-171 °C. ^1H NMR (600 MHz, $CDCl_3$): δ 7.64 (d, *J* = 7.8 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.20 (d, *J* = 7.7 Hz, 2H), 7.12 (t, *J* = 7.5 Hz, 2H), 6.95 (d, *J* = 8.0 Hz, 2H), 6.73 (t, *J* = 7.1 Hz, 1H), 6.34 (d, *J* = 7.9 Hz, 2H), 5.02 (s, 1H), 4.71 (d, *J* = 5.7 Hz, 1H), 4.53-4.47 (m, 1H), 3.93-3.85 (m, 1H), 3.48-3.41 (m, 1H), 2.39 (s, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 144.5, 144.5, 139.6, 132.8, 132.0, 129.9, 129.3, 127.8, 127.7, 121.5, 118.6, 113.0, 65.9, 60.9, 55.3, 21.7; IR 1601, 1506, 1344, 1159, 1030, 816, 748, 667, 600, 550; HRMS (ESI) m/z calcd for $C_{22}H_{22}BrN_2SO_2^+$ $[M+H]^+$ 457.0580, found 457.0580.

4-(2-Bromophenyl)-3-phenyl-1-tosylimidazolidine ***(3al)***. White solid (59.4 mg, yield: 65 %); mp: 175-176 °C. ^1H NMR (600 MHz, $CDCl_3$): δ 7.67 (d, *J* = 8.2 Hz, 2H), 7.54 (dd, *J* = 7.5, 1.4 Hz, 1H), 7.19 (d, *J* = 8.0 Hz, 2H), 7.15-7.05 (m, 4H), 6.99 (dd, *J* = 7.3, 1.9 Hz, 1H), 6.73 (t, *J* = 7.3 Hz, 1H), 6.25 (d, *J* = 8.0 Hz, 2H), 5.09 (d, *J* = 6.1 Hz, 1H), 4.78 (dd, *J* = 7.4, 4.4 Hz, 1H), 4.74 (d, *J* = 6.1 Hz, 1H), 4.00 (dd, *J* = 10.8, 7.6 Hz, 1H), 3.52 (dd, *J* = 10.9, 4.4 Hz, 1H), 2.37 (s, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 144.4, 144.2, 138.9, 133.0, 132.7, 129.9, 129.3, 129.2, 128.0, 127.8, 127.5, 122.1, 118.4, 112.7, 66.0 61.1, 54.0, 21.6; IR 1601, 1510, 1387, 1352, 1159, 1034, 818, 747, 665, 550; HRMS (ESI) m/z calcd for $C_{22}H_{22}BrN_2SO_2^+$ $[M+H]^+$ 457.0580, found 457.0580.

Methyl 4-(3-phenyl-1-tosylimidazolidin-4-yl)benzoate ***(3am)***. White solid (52.4 mg, yield: 60 %); mp: 170-171 °C. ^1H NMR (600 MHz, $CDCl_3$): δ 7.90 (d, *J* = 8.2 Hz, 2H), 7.65 (d, *J* = 8.2 Hz, 2H), 7.21 (d, *J* = 8.0 Hz, 2H), 7.16 (d, *J* = 8.2 Hz, 2H), 7.12 (t, *J* = 8.0 Hz, 2H), 6.74 (t, *J* = 7.3 Hz, 1H), 6.34 (d, *J* = 8.1 Hz, 2H), 5.06 (d, *J* = 6.0 Hz, 1H), 4.75 (d, *J* = 6.0 Hz, 1H), 4.59 (dd, *J* = 7.3, 5.0 Hz, 1H), 3.95 (dd, *J* = 10.6, 7.6 Hz, 1H), 3.90 (s, 3H), 3.55-3.43 (m, 1H), 2.39 (s, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 166.7, 145.7, 144.5, 144.5, 132.8, 130.2, 129.9, 129.9, 129.6, 129.3, 127.8, 125.9, 118.6, 113.0, 66.0, 61.3, 55.2, 52.2, 21.6; IR 2924, 1724, 1508, 1350, 1283, 1161, 1028, 667, 600, 550; HRMS (ESI) m/z calcd for $C_{24}H_{25}N_2SO_4^+$ $[M+H]^+$ 437.1530, found 437.1529.

3-Phenyl-1-tosyl-4-vinylimidazolidine ***(3an)***. White solid (52.0 mg, yield: 79 %); mp: 157-158 °C. ^1H NMR (600 MHz, $CDCl_3$): δ 7.61 (d, *J* = 8.2 Hz, 2H), 7.15 (d, *J* = 8.1 Hz, 2H), 7.08 (dd, *J* = 8.3, 7.6 Hz, 2H), 6.65 (t, *J* = 7.3 Hz, 1H), 6.36 (d, *J* = 8.0 Hz, 2H), 5.46 (ddd, *J* = 17.0, 10.2, 6.7 Hz, 1H), 5.03 (dd, *J* = 33.1, 13.7 Hz, 2H), 4.67 (d, *J* = 5.7 Hz, 1H), 4.48 (d, *J* = 5.7 Hz, 1H), 3.96 (dd, *J* = 11.1, 6.8 Hz, 1H), 3.53 (dd, *J* = 10.2, 7.2 Hz, 1H), 3.31 (dd, *J* = 10.3, 4.2 Hz, 1H), 2.28 (s, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 144.8, 144.4, 136.0, 132.7, 129.9, 129.2, 127.9, 118.2, 117.6, 113.0, 65.0 59.7, 52.8, 21.6; IR 2826, 1510, 1385, 1350, 1159, 932, 747, 665, 600, 550; HRMS (ESI) m/z calcd for $C_{18}H_{21}N_2SO_2^+$ $[M+H]^+$ 329.1318, found 329.1318;

1,5-Diphenylimidazolidine ***(3ap)***. Pink oil (16.1 mg, yield: 36 %). ^1H NMR (600 MHz, $CDCl_3$): δ 7.44-7.30 (m, 3H), 7.21 (d, *J* = 6.5 Hz, 2H), 7.10 (t, *J* = 7.8 Hz, 2H), 6.71 (t, *J* = 7.3 Hz, 1H), 6.57 (d, *J* = 7.9 Hz, 2H), 4.95 (dd, *J* = 14.5, 5.2 Hz, 1H), 4.73 (t, *J* = 8.3 Hz, 1H), 4.46 (t, *J* = 8.9 Hz, 1H), 4.19 (dd, *J* = 14.6, 7.5 Hz, 1H), 4.10 (s, 1H), 4.02-3.91 (m, 1H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 157.3, 144.2, 136.4, 128.5, 128.4, 126.0, 117.9, 112.3, 69.1, 57.6, 50.9; IR 3412, 1732, 1653, 1603, 1495, 1215, 814, 748, 692, 505; HRMS (ESI) m/z calcd for $C_{15}H_{17}N_2^+$ $[M+H]^+$ 225.1386, found 225.1385.

1-(Methylsulfonyl)-3,4-diphenylimidazolidine ***(3aq)***. Light red solid (50.2 mg, yield: 83%); mp: 135-136 °C. ^1H NMR (600 MHz, $CDCl_3$): δ 7.24 (d, *J* = 7.2 Hz, 2H), 7.19 (dd, *J* = 7.7, 3.9 Hz, 3H), 7.08 (dd, *J* = 8.6, 7.4 Hz, 2H), 6.69 (t, *J* = 7.3 Hz, 1H), 6.43 (d, *J* = 7.9 Hz, 2H), 5.01 (d, *J* = 6.3 Hz, 1H), 4.79 (dd, *J* = 7.2, 5.2 Hz, 1H), 4.75 (d, *J* = 6.3 Hz, 1H), 4.01 (dd, *J* = 10.9, 7.5 Hz, 1H), 3.49 (dd, *J* = 10.9, 5.0 Hz, 1H), 2.68 (s, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 143.6, 139.3, 128.3, 128.0, 126.9, 125.0, 117.6, 112.4, 64.7, 60.6, 54.5, 35.3; IR 1601, 1508, 1329, 1221, 1153, 1034, 955, 748, 698, 525; HRMS (ESI) m/z calcd for $C_{16}H_{19}N_2O_2S^+$ $[M+H]^+$ 303.1162, found 303.1160.

1-Benzyl-3,4-diphenylimidazolidine ***(3ar)***. White solid (47.8mg, yield: 76%); mp 100-101 °C. ^1H NMR (600 MHz, $CDCl_3$): δ 7.35-7.27 (m, 9H), 7.27-7.20 (m, 2H), 7.15 (d, *J* = 8.8 Hz, 2H), 6.26 (d, *J* = 8.9 Hz, 2H), 4.67 (dd, *J* = 6.5, 5.2 Hz, 1H), 4.39 (d, *J* = 4.6 Hz, 1H), 4.05 (d, *J* = 4.6 Hz, 1H), 3.71 (q, *J* = 13.0 Hz, 2H), 3.29 (dd, *J* = 9.2, 7.2 Hz, 1H), 2.89 (dd, *J* = 9.4, 4.9 Hz, 1H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 145.0, 142.2, 138.1, 131.7, 128.8, 128.7, 128.6, 127.5, 127.4, 126.3, 114.1, 108.8, 72.0, 62.4, 62.3, 58.3; IR 3030, 2872, 1599, 1508, 1452, 1368, 1219, 1186, 748, 692; HRMS (ESI) m/z calcd for $C_{22}H_{23}N_2^+$ $[M+H]^+$ 315.1856, found 315.1856.

3-([1,1'-Biphenyl]-4-yl)-4-phenyl-1-tosylimidazolidine ***(4)***. To a solution of **3ak** (200 mg, 0.630 mmol) in toluene (10 mL) under a nitrogen atmosphere was added $Pd(P(Ph)_3)_4$ (73 mg, 0.063 mmol). After stirring 30 min, a solution of phenyl-

boronic acid in ethanol (5mL) and saturated $NaHCO_3$ (3mL) was added. Then mixture was heated to reflux for 24 h. After cooling to room temperature, the mixture was added saturated aqueous NaCl solution and extracted with ethyl acetate. The organic layer was combined, washed with saturated brine, dried with anhydrous Na_2SO_4, and concentrated. The residue was chromatographed on silica gel to give the desired product **4** as a white solid (180 mg, yield: 62 %). mp: 135-136 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.68 (d, J = 8.2 Hz, 2H), 7.46 (d, J = 7.4 Hz, 2H), 7.38-7.32 (m, 4H), 7.23 (dd, J = 19.7, 7.6 Hz, 6H), 7.12 (d, J = 6.5 Hz, 2H), 6.42 (d, J = 8.7 Hz, 2H), 5.05 (d, J = 6.0 Hz, 1H), 4.80 (d, J = 6.0 Hz, 1H), 4.61-4.49 (m, 1H), 3.93 (dd, J = 10.4, 7.4 Hz, 1H), 3.46 (dd, J = 10.5, 5.2 Hz, 1H), 2.37 (s, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 144.4, 144.2, 140.8, 140.3, 132.7, 131.1, 130.0, 129.0, 128.8, 128.7, 127.9, 127.8, 127.8, 126.4, 126.4, 126.0, 113.4, 66.1, 61.6, 55.6, 21.6; IR 2918, 1614, 1526, 1489, 1346, 1161, 818, 760, 669, 548; HRMS (ESI) m/z calcd for $C_{28}H_{27}N_2SO_2^+$ $[M+H]^+$ 455.1788, found 455.1787.

1-(4-Bromophenyl)-5-phenylimidazolidine **(5)**. To a solution of **3ak** (200 mg, 0.438 mmol) in MeOH (20 mL) were added Mg turnings (105 mg, 4.38 mmol), the resulting mixture was refluxed until confirmed to be complete by TLC. The mixture was added 1 N HCl to remove excess Mg, then NaOH was added to adjust pH of aqueous to pH = 10. The aqueous layer was extracted with ethyl acetate. The organic layer was combined, washed with saturated brine, dried with anhydrous Na_2SO_4, and concentrated. The residue was chromatographed on silica gel to give the desired product **5** as a white solid (93.9 mg, yield: 71 %). mp: 128-129 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.35-7.31 (m, 2H), 7.28-7.25 (m, 2H), 7.24-7.20 (m, 3H), 6.31 (dd, J = 20.0, 9.0 Hz, 2H), 4.64 (d, J = 7.6 Hz, 1H), 4.56 (dd, J = 7.1, 2.0 Hz, 1H), 4.25 (d, J = 7.6 Hz, 1H), 3.55 (dd, J = 12.0, 7.2 Hz, 1H), 3.15 (dd, J = 12.0, 2.3 Hz, 1H), 2.07 (s, 1H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 144.5, 142.5, 131.9, 128.9, 127.4, 125.7, 114.2, 108.7, 66.6, 62.4, 57.0; IR 2847, 1734, 1593, 1493, 1370, 1074, 806, 750, 700, 502; HRMS (ESI) m/z calcd for $C_{15}H_{16}BrN_2^+$ $[M+H]^+$ 303.0491, found 303.0490.

1-Benzyl-3-(4-bromophenyl)-4-phenylimidazolidine **(6)**. To a solution of 1-(4-bromophenyl)-5-phenylimidazolidine **5** (100 mg, 0.331 mmol) in 15 mL of CH_3CN was added K_2CO_3 (914 mg, 0.662 mmol) followed by addition of BnBr (0.047 mL , 0.397 mmol). Then the reaction mixture was stirred at room temperature for 2 hours. The solvent was evaporated under reduced pressure. The residue was mixed with water and extracted with ethyl acetate. The extract was washed with brine, dried over Na_2SO_4 and solvent was removed by rotary evaporation. The crude product was purified by column chromatography using petroleum/ethyl acetate mixture as eluent to afford **6** as a white solid (90.8 mg, yield: 70 %). Mp: 150-151 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.01 (dd, J = 7.8, 1.4 Hz, 1H), 7.88 (d, J = 8.1 Hz, 1H), 7.64 (td, J = 8.1, 1.5 Hz, 1H), 7.44-7.40 (m, 1H), 7.38 (t, J = 7.9 Hz, 2H), 7.29-7.24 (m, 3H), 7.11 (d, J = 8.1 Hz, 2H), 7.00 (d, J = 7.7 Hz, 2H), 5.58 (s, 2H), 2.37 (s, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 161.1, 144.8, 139.6, 138.3, 134.9, 133.4, 129.8, 129.1, 128.9, 127.4, 127.3, 126.6, 125.4, 125.1, 123.9, 63.8, 21.7; IR 2810, 1589, 1487, 1343, 1173, 1076, 806, 760, 702, 505; HRMS (ESI) m/z calcd for $C_{22}H_{22}N_2Br^+$ $[M+H]^+$ 393.0961, found 393.0961.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI:
Copies of ^{1}H, ^{13}C NMR spectra data for all compounds (PDF)

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: zhysh@mail.scuec.edu.cn (Y.-S.Z.)
*E-mail: liujikai@mail.scuec.edu.cn (J.-K.L.)

Author Contributions

⊥These authors contributed equally.

Notes

The authors declare no competing financial interest

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