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Synthesis of 2-Imidazolines via Palladium-Catalyzed Cyclization Reaction of 2,3-Allenyl Amines and Aryl Iodides

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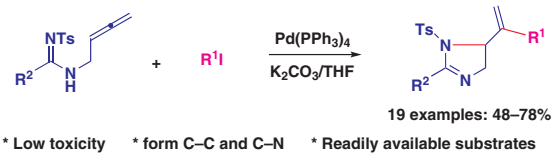

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Abstract An effective method for the synthesis of polysubstituted 2-imidazoline derivatives via palladium-catalyzed cyclization of 2,3-allenyl amines with aryl iodides is described. This pure domino process allows the formation of new carbon–carbon and carbon–nitrogen bonds in a single synthetic operation.

Key words allenes, amines, cyclization, imidazoline, palladium

2-Imidazoline heterocyclic compounds have high medicinal value and a variety of catalytic applications in biology. Indeed, anti-hypertensive,[1] antihyperglycemic,[2] antidepressive,[3] antihypercholesterolemic,[4] and anti-inflammatory[5] activities have been reported for these compounds. Illustrative examples include P2X7 ion channel blocker **I** for treating inflammation conditions,[6] estrogen receptor modulator **II** for oncology applications,[7] proteasome inhibitor **III** for multiple myeloma,[8] and nutlin-3 (**IV**),[9] which disrupts oncogenic p53-mdm2 protein–protein interactions (Figure 1).

The group of Shunsuke Chiba explored a new strategy of organic catalysis to synthesize 2-imidazolines with $Cu(OAc)_2$ as a catalyst in the presence of K_3PO_4 and $PhI(OAc)_2$ (Scheme 1, Eq. 1).[10] The authors subsequently reported a copper-catalyzed synthesis of 2-imidazolines through amination with amidoximes (Scheme 1, Eq. 2).[11] Zhou's group reported a convenient method for the synthesis of a variety of imidazolines and tetrahydropyrimidines by lanthanide-catalyzed direct cycloamidination of aminoalkenes and nitriles (Scheme 1, Eq. 3).[12]

In recent years, the synthesis of various heterocyclic compounds from functionalized allenes has attracted the interest of many scientists.[13–16] Among the approaches, palladium-catalyzed functionalization of allenes to synthesize imidazolines remains extremely challenging. Inspired by our group's reported synthesis of imidazolidines derivatives via Pd-catalyzed cyclization reaction,[15] in this article we describe the application of a Pd-catalyzed cyclization reaction to synthesize polysubstituted 2-imidazoline derivatives from 2,3-allenyl amines and aryl iodides (Scheme 1, Eq 4).

Initially, we investigated the cyclization reaction of *N*-(buta-2,3-dien-1-yl)-*N*′-tosylbenzimidamide (**1a**) and iodobenzene (**2a**), using $Pd(PPh_3)_4$ as the catalyst and K_2CO_3 as the base, to obtain 2-imidazoline **3aa** with a isolated yield of 61% (Table 1, entry 1). Subsequently, the effects of palladium catalysts were examined; thus, $Pd(OAc)_2$, $Pd(PPh_3)_2Cl_2$, $Pd(CF_3COO)_2$ and $Pd(dppf)Cl_2$, were examined, but the yields were slightly lower (entries 2–5). Our research confirmed that the reaction did not proceed without Pd catalyst (entry 6). The influence of the solvent and temperature were then studied (entries 7–11 and 17), and THF was determined to be the most suitable solvent for the

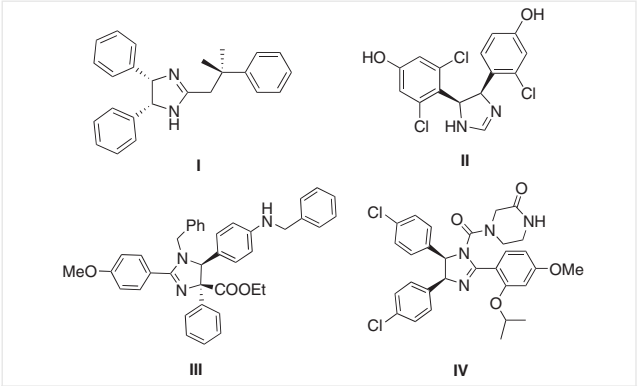

Figure 1 Examples of biologically active 2-imidazolines

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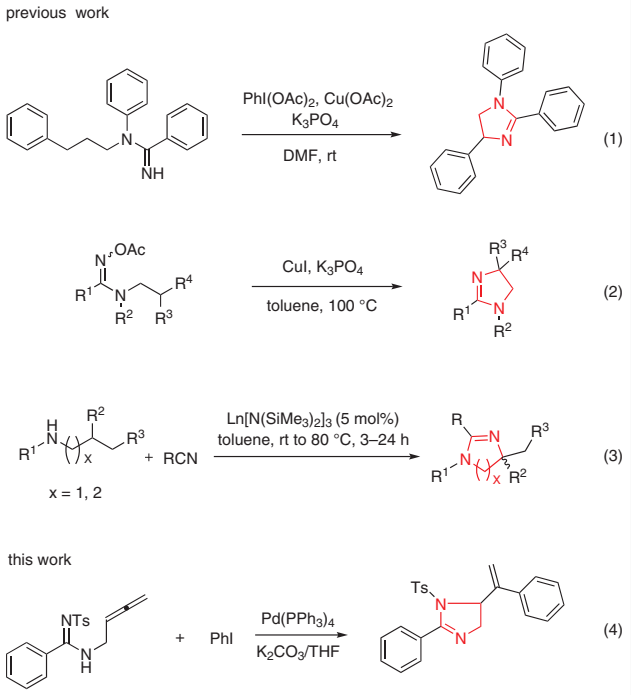


Scheme 1 Selected synthetic methods for 2-imidazolines

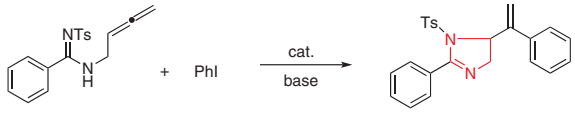
reaction. To further improve the efficiency of the reaction, a range of bases were investigated (entries 12–16). During screening, neither weaker (entries 12–13) nor stronger base (entries 14–16) produced more of the desired target compound **3aa**. Accordingly, it was established that the optimized reaction conditions were **1a** (1.0 equiv) and **2a** (1.2 equiv) with K_2CO_3 (3.0 equiv) in THF at 85 °C using [$Pd(PPh_3)_4$] (5 mol%) as catalyst.

After establishing appropriate reaction conditions, we further explored the scope of the method. The results of the coupling–cyclization of **1a** with various aryl iodides **2** are summarized in Scheme 2. We found that aryl iodides are good model coupling partners, which can produce the desired products in moderate to good yields. Herein, we specifically describe the effect of different substituents on the phenyl ring on the reaction.

Generally, electron-donating substituents on the phenyl ring, such as methoxy (Scheme 2, **3ab–ac**) and methyl groups (**3ad–af**), increased the yield, while electron-withdrawing substituents, such as halides (**3ag–ai**), reduced the yield. The reaction with the aryl iodide of carbonyl group also proceeded smoothly, and the desired product **3aj** was obtained in 61% yield, indicating that the conversion was not affected by the $COCH_3$ group. It was also found that even with a strong electron-withdrawing substituent (CF_3) on the aromatic ring, the reaction proceeded smoothly to give the desired product (**3ak**). We also found that the different positions of the substitution on the aromatic ring had only a slight effect on the reaction (**3ab–af**), thus providing the possibility of further conversion. It is worth noting that when the phenyl ring was substituted with 2-thienyl (**3al**, 78%), the yield of the reaction increased. In addition to aryl iodides, we also tested aliphatic iodides, such as methyl iodide and *n*-butyl iodide (**3am**), but did not obtain the corresponding product.

We then investigated the Pd-catalyzed cyclization reaction using iodobenzene (**2a**) and different 2,3-allenyl amines **1** under the standard conditions (Scheme 3). Irrespective of whether electron-withdrawing or electron-donating substituents were present, the corresponding compounds were obtained in moderate yield. In general, electron-donating substituents on the phenyl ring, such as methoxyl (**3ba**), tended to reduce the yield, whereas electron-withdrawing substituents such as halogen (**3ca–da**) or CF_3 (**3fa**), enhanced the yield. The reaction with the aryl group having a sensitive ester group also proceeded smoothly, and the desired product **3ea** was obtained in 65% yield. In addition, 2-thienyl-substituted and 1-iodonaphthalene-substituted 2,3-allenyl amine were also tested on the reaction and the expected products **3ga** and **3ha** were

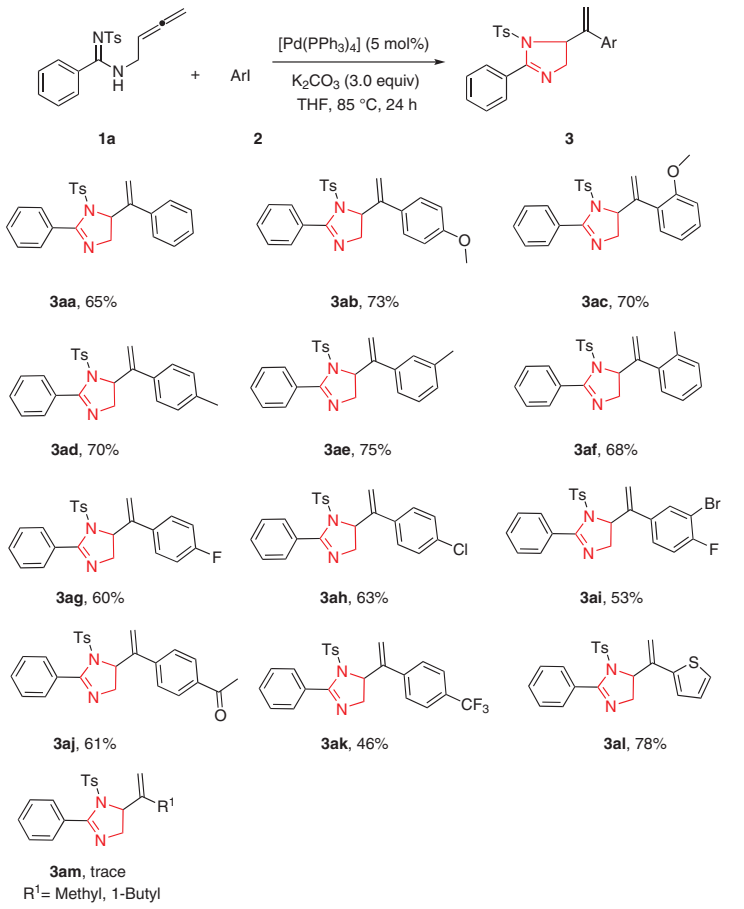
Table 1 Optimization of Reaction Conditions[a]



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

Entry	Cat	Base	Solvent	Yield (%)[b]
1	$Pd(PPh_3)_4$	K_2CO_3	THF	61
2	$Pd(OAc)_2$	K_2CO_3	THF	46
3	$Pd(PPh_3)_2Cl_2$	K_2CO_3	THF	43
4	$Pd(CF_3COO)_2$	K_2CO_3	THF	50
5	$Pd(dppf)Cl_2$	K_2CO_3	THF	52
6	–	K_2CO_3	THF	n.d.[c]
7	$Pd(PPh_3)_4$	K_2CO_3	DCM	trace
8	$Pd(PPh_3)_4$	K_2CO_3	toluene	35
9	$Pd(PPh_3)_4$	K_2CO_3	dioxane	55
10	$Pd(PPh_3)_4$	K_2CO_3	DMF	37
11	$Pd(PPh_3)_4$	K_2CO_3	H_2O	28
12	$Pd(PPh_3)_4$	CsF	THF	31
13	$Pd(PPh_3)_4$	Cs_2CO_3	THF	42
14	$Pd(PPh_3)_4$	*t*-BuOLi	THF	25
15	$Pd(PPh_3)_4$	NaOH	THF	n.d.[c]
16	$Pd(PPh_3)_4$	NaH	THF	23
17	$Pd(PPh_3)_4$	K_2CO_3	THF[d]	65

[a] Reaction conditions: Under a N_2 atmosphere, **1a** (0.25 mmol, in 3 mL THF), PhI (1.2 equiv), base (3.0 equiv), and [Pd^0] (5 mol%) at reflux.
[b] Isolated yield.
[c] n.d.= not detected.
[d] Reaction carried out in a tube with a screw cap in 85 °C.



Scheme 2 Substrate scope of aryl iodides. *Reagents and conditions*: **1a** (0.22 mmol, in 3 mL THF), $Pd(PPh_3)_4$ (5 mol%), **2** (1.2 equiv), K_2CO_3 (3.0 equiv), N_2 atmosphere. Isolated yields given.

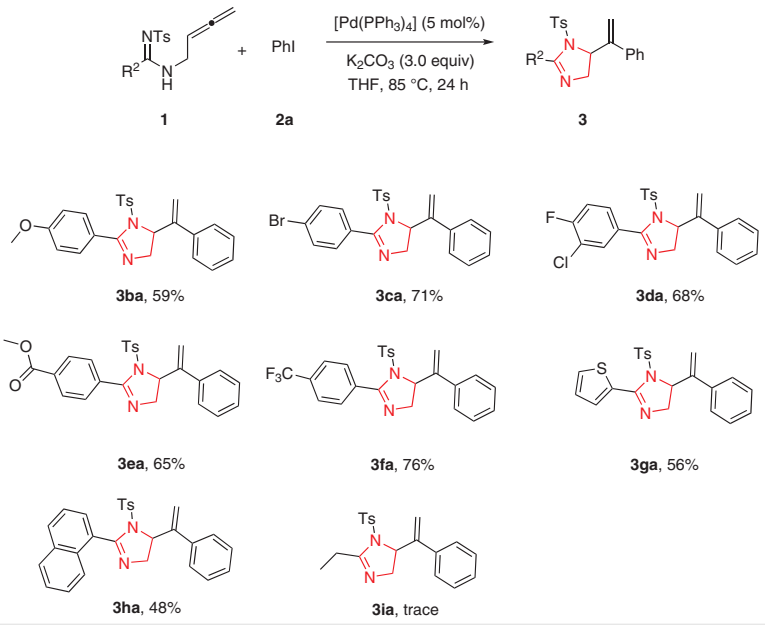
obtained in 56% and 48% yields, respectively. Aliphatic-substituted 2,3-allenyl amine was not suitable for this process and the corresponding imidazoline **3ia** was not obtained. This indicated that aliphatic-substituted allenyl amines are not good coupling partners.

To investigate the mechanism of the cyclization reaction, we conducted a number of control experiments. When a radical scavenger (TEMPO or BHT) was added to the reaction system under the standard conditions, the reaction still proceeded smoothly (Scheme 4, Eq. 1 and Eq. 2) to give the product. These results indicate that the reaction does not proceed via a radical mechanism.

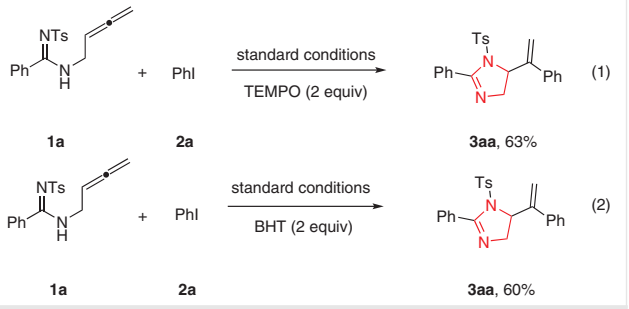
Pd^0-catalyzed cyclization reactions of functionalized allenes leading to heterocyclic compounds has been studied extensively.[13–16] In some of these reactions, the allylpalladium intermediate was captured by intramolecular nucleophiles and formed the target product.[15,16] In this reaction, the sulfonyl group is a slightly stronger electron-withdrawing group, which can generate a nitrogen anion under base conditions, followed by intramolecular nucleophilic attack. Therefore, based on experimental results and on previous reports,[13–16] a reaction mechanism is proposed in Scheme 5. First, oxidative addition of the aryl iodide to Pd^0 affords aryl-Pd species **A**, which adds to the central carbon of allene moiety to provide π-allyl species **B**. The intermediate **B** under base conditions then affords the intermediate **C**. Finally, intermediate **C** undergoes intramolecular nucleophilic attack of the nitrogen atom to afford the product **3**, thereby releasing the active catalytic species.

In summary, we have developed an efficient method to synthesize polysubstituted 2-imidazoline derivatives. The reaction has a good tolerance range and provides a synthetic route to important heterocyclic compounds, thereby promoting the development of catalysis of allenes. Further research on allene chemistry to extend the range of heterocyclic chemistry is ongoing in our laboratory.

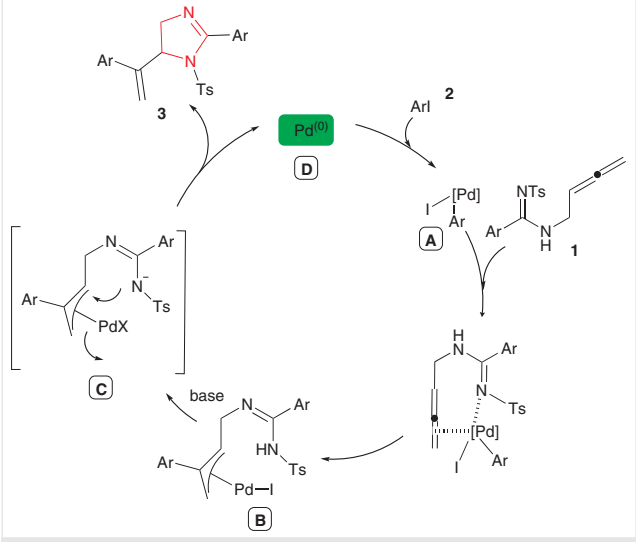
Unless otherwise indicated, all commercial reagents and solvents were used without additional purification. Reactions were monitored by thin-layer chromatography (TLC) on silica plates (GF-254) and visualized under UV light. The melting point was measured on an WRS-1C melting point (Shanghai ShenGuang Instrument Co., Ltd.) apparatus



Scheme 3 Substrate scope of 2,3-allenyl amine. *Reagents and conditions*: **1** (0.22 mmol, in 3 mL THF), $Pd(PPh_3)_4$ (5 mol%), **2a** (1.2 equiv), K_2CO_3 (3.0 equiv), N_2 atmosphere. Isolated yields given.



Scheme 4 Experiments for mechanistic study



Scheme 5 Proposed mechanism

with the thermometer unadjusted. ^1H and ^{13}C NMR spectra were acquired on a Bruker Avance III 400 MHz spectrometer with DMSO-d_6 as the solvent and tetramethylsilane (TMS) as the internal standard. HRMS was carried out by ESI on a TOF mass analyzer. The reagents aryl Iodides (**2a–m**), $Pd(PPh_3)_4$, were commercially obtained.

Typical Procedure

2,3-Allenyl amine **1a** (50 mg, 0.22 mmol) and iodobenzene **2a** (38 mg, 0.26 mmol, 1.2 equiv) were added consecutively to a sealed tube charged with a mixture of potassium carbonate (64 mg, 0.66 mmol, 3.0 equiv), and $[Pd(PPh_3)_4]$ (8.9 mg, 0.011 mmol, 5 mol%) in THF (3 mL) under an argon atmosphere. The resulting mixture was stirred at 85 °C for 24 h and the progress of the reaction was monitored by TLC. Upon completion, H_2O (8 mL) was added and the solution was extracted with CH_2Cl_2. After evaporation of the solvent, the crude product was added to silica gel and the mixture was purified by silica gel column chromatography (PE/EtOAc = 4:1) to afford the desired product **3aa**.

2-Phenyl-5-(1-phenylvinyl)-1-tosyl-4,5-dihydro-1*H*-imidazole (3aa)

Prepared according to the General Procedure; the crude material was purified by flash column chromatography (PE/EtOAc = 4:1) to afford **3aa**.

Yield: 40 mg (65%); light-yellow solid; mp 80.2–81.3 °C.

^1H NMR (400 MHz, DMSO-d_6): δ = 7.82–7.26 (m, 13 H), 5.59 (s, 2 H), 5.43 (d, *J* = 7.5 Hz, 1 H), 3.68 (dd, *J* = 16.5, 9.4 Hz, 1 H), 3.46 (d, *J* = 16.5 Hz, 1 H), 2.41 (s, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 158.72, 146.57, 145.31, 137.18, 135.20, 131.97, 131.57, 130.73, 130.55, 129.72, 129.26, 128.29, 127.63, 121.98, 113.72, 63.10, 60.76, 21.56.

HRMS (ESI-Q-TOF): *m*/*z*[M + Na]$^+$ calcd for $C_{24}H_{22}N_2O_2S$: 425.1402; found: 425.1460

5-(1-(4-Methoxyphenyl)vinyl)-2-phenyl-1-tosyl-4,5-dihydro-1*H*-imidazole (3ab)

Prepared according to the General Procedure; the crude material was purified by flash column chromatography (PE/EtOAc = 4:1) to afford **3ab**.

Yield: 48 mg (73%); light-yellow solid; mp 155.3–156.1 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.64 (d, *J* = 7.4 Hz, 2 H), 7.55 (d, *J* = 7.9 Hz, 3 H), 7.44 (m, 6 H), 6.96 (d, *J* = 8.5 Hz, 2 H), 5.46 (d, *J* = 8.2 Hz, 2 H), 5.40 (d, *J* = 8.0 Hz, 1 H), 3.78 (s, 3 H), 3.67 (dd, *J* = 16.3, 9.5 Hz, 1 H), 3.43 (dd, *J* = 16.3, 2.2 Hz, 1 H), 2.41 (s, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 159.70, 158.78, 146.86, 145.27, 135.26, 131.56, 130.85, 130.57, 130.12, 129.72, 128.31, 128.22, 127.63, 114.50, 110.90, 63.21, 60.95, 55.64, 21.56.

HRMS (ESI-Q-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{25}H_{24}N_2O_3S$: 455.1508; found: 455.1560.

5-(1-(2-Methoxyphenyl)vinyl)-2-phenyl-1-tosyl-4,5-dihydro-1*H*-imidazole (3ac)

Prepared according to the General Procedure; the crude material was purified by flash column chromatography (PE/EtOAc = 5:1) to afford **3ac**.

Yield: 46 mg (70%); light-yellow solid; mp 154.9–155.6 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.68 (d, *J* = 7.2 Hz, 2 H), 7.58–7.41 (m, 7 H), 7.33 (t, *J* = 7.4 Hz, 1 H), 7.16 (d, *J* = 7.1 Hz, 1 H), 7.06–6.92 (m, 2 H), 5.55 (s, 1 H), 5.43–5.34 (m, 1 H), 5.18 (s, 1 H), 3.81 (s, 3 H), 3.51–3.44 (m, 1 H), 3.30–3.20 (m, 1 H), 2.41 (s, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 156.68, 147.17, 145.25, 135.13, 131.52, 131.24, 131.05, 130.63, 130.07, 129.64, 128.34, 127.89, 127.48, 121.17, 114.53, 111.92, 63.13, 60.00, 55.99, 21.57.

HRMS (ESI-Q-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{25}H_{24}N_2O_3S$: 455.1508; found: 455.1568.

2-Phenyl-5-(1-(*p*-tolyl)vinyl)-1-tosyl-4,5-dihydro-1*H*-imidazole (3ad)

Prepared according to the General Procedure; the crude material was purified by flash column chromatography (PE/EtOAc = 5:1) to afford **3ad**.

Yield: 45 mg (70%); light-yellow solid; mp 140.1–141.4 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.64 (d, *J* = 6.9 Hz, 2 H), 7.55 (d, *J* = 7.0 Hz, 3 H), 7.51–7.30 (m, 7 H), 7.21 (d, *J* = 7.0 Hz, 2 H), 5.51 (d, *J* = 6.7 Hz, 2 H), 5.41 (d, *J* = 7.7 Hz, 1 H), 3.67 (dd, *J* = 16.7, 9.6 Hz, 1 H), 3.42 (d, *J* = 16.7 Hz, 1 H), 2.41 (s, 3 H), 2.32 (s, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 158.76, 147.28, 145.27, 138.07, 135.25, 134.99, 131.57, 130.57, 129.70, 128.30, 127.62, 126.87, 111.82, 63.21, 60.89, 21.56, 21.17.

HRMS (ESI-Q-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{25}H_{24}N_2O_2S$: 439.1558; found: 439.1530.

2-Phenyl-5-(1-(*m*-tolyl)vinyl)-1-tosyl-4,5-dihydro-1*H*-imidazole (3ae)

Prepared according to the General Procedure; the crude material was purified by flash column chromatography (PE/EtOAc = 5:1) to afford **3ae**.

Yield: 48 mg (75%); light-yellow solid; mp 96.1–97.2 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.64 (d, *J* = 7.2 Hz, 2 H), 7.56 (d, *J* = 8.1 Hz, 3 H), 7.44 (m, 4 H), 7.28 (dd, *J* = 15.3, 7.6 Hz, 3 H), 7.17 (d, *J* = 6.7 Hz, 1 H), 5.52 (d, *J* = 5.3 Hz, 2 H), 5.43 (d, *J* = 8.0 Hz, 1 H), 3.69 (dd, *J* = 16.2, 9.5 Hz, 1 H), 3.45 (dd, *J* = 16.2, 2.6 Hz, 1 H), 2.41 (s, 3 H), 2.33 (s, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 158.72, 147.72, 145.27, 138.28, 137.97, 135.29, 131.55, 130.82, 130.56, 129.70, 129.32, 128.98, 128.29, 127.67, 127.63, 124.18, 112.68, 63.35, 60.88, 21.56, 21.51.

HRMS (ESI-Q-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{25}H_{24}N_2O_2S$: 439.1558; found: 439.1522.

2-Phenyl-5-(1-(*o*-tolyl)vinyl)-1-tosyl-4,5-dihydro-1*H*-imidazole (3af)

Prepared according to the General Procedure; the crude material was purified by flash column chromatography (PE/EtOAc = 5:1) to afford **3af**.

Yield: 43 mg (68%); light-yellow solid; mp 151.2–152.1 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.60 (d, *J* = 7.2 Hz, 2 H), 7.53 (dd, *J* = 15.9, 7.9 Hz, 3 H), 7.43 (dd, *J* = 19.7, 7.8 Hz, 4 H), 7.20 (m, 4 H), 5.66 (s, 1 H), 5.12 (d, *J* = 8.7 Hz, 1 H), 5.08 (s, 1 H), 3.60 (dd, *J* = 16.2, 2.0 Hz, 1 H), 3.33 (m, 1 H), 2.39 (s, 3 H), 2.33 (s, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 158.80, 147.89, 145.28, 138.76, 135.99, 135.16, 131.57, 130.84, 130.70, 130.63, 129.72, 129.43, 128.26, 128.19, 127.48, 126.06, 115.16, 64.66, 59.54, 21.54, 20.01.

HRMS (ESI-Q-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{25}H_{24}N_2O_2S$: 439.1558; found: 439.1577.

5-(1-(4-Fluorophenyl)vinyl)-2-phenyl-1-tosyl-4,5-dihydro-1*H*-imidazole (3ag)

Prepared according to the General Procedure; the crude material was purified by flash column chromatography (PE/EtOAc = 4:1) to afford **3ag**.

Yield: 39 mg (60%); light-yellow solid; mp 117.2–118.3 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.63 (d, *J* = 7.2 Hz, 2 H), 7.56 (d, *J* = 7.8 Hz, 5 H), 7.44 (m, 4 H), 7.24 (t, *J* = 8.6 Hz, 2 H), 5.54 (d, *J* = 5.9 Hz, 2 H), 5.43 (d, *J* = 8.0 Hz, 1 H), 3.69 (dd, *J* = 16.1, 9.5 Hz, 1 H), 3.46 (m, 1 H), 2.41 (s, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 163.70, 161.26, 158.73, 146.60, 145.30, 135.23, 134.38, 131.57, 130.77, 130.56, 129.72, 129.28, 129.20, 128.29, 127.65, 116.02, 115.81, 113.07, 63.28, 60.78, 21.55.

HRMS (ESI-Q-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{24}H_{21}FN_2O_2S$: 443.1308; found: 443.1336.

5-(1-(4-Chlorophenyl)vinyl)-2-phenyl-1-tosyl-4,5-dihydro-1*H*-imidazole (3ah)

Prepared according to the General Procedure; the crude material was purified by flash column chromatography (PE/EtOAc = 4:1) to afford **3ah**.

Yield: 42 mg (63%); light-yellow solid; mp 130.1–131.2 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.63 (d, J = 7.3 Hz, 2 H), 7.54 (t, J = 7.0 Hz, 5 H), 7.44 (m, 6 H), 5.59 (s, 2 H), 5.44 (d, J = 9.5 Hz, 1 H), 3.69 (dd, J = 16.2, 9.5 Hz, 1 H), 3.46 (d, J = 16.2 Hz, 1 H), 2.41 (s, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 158.72, 146.49, 145.32, 136.78, 135.20, 133.35, 131.59, 130.73, 130.56, 129.73, 129.06, 128.97, 128.30, 127.65, 113.68, 63.12, 60.76, 21.56.

HRMS (ESI-Q-TOF): m/z [M + Na]$^+$ calcd for $C_{24}H_{21}ClN_2O_2S$: 459.1012; found: 459.1055.

5-(1-(3-Bromo-4-chlorophenyl)vinyl)-2-phenyl-1-tosyl-4,5-dihydro-1*H*-imidazole (3ai)

Prepared according to the General Procedure; the crude material was purified by flash column chromatography (PE/EtOAc = 5:1) to afford **3ai**.

Yield: 37 mg (53%); light-yellow solid; mp 114.2–115.1 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.74 (dd, J = 6.9, 1.5 Hz, 1 H), 7.56 (m, 6 H), 7.43 (m, 5 H), 5.61 (s, 2 H), 5.48 (d, J = 9.5 Hz, 1 H), 3.71 (dd, J = 16.3, 9.5 Hz, 1 H), 3.50 (dd, J = 16.3, 2.6 Hz, 1 H), 2.41 (s, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 158.61, 145.70, 145.32, 135.27, 131.60, 130.67, 130.52, 129.71, 129.28, 128.29, 127.69, 117.58, 117.37, 114.68, 63.18, 60.60, 40.60, 40.39, 40.19, 39.98, 39.77, 39.56, 39.35, 21.56.

HRMS (ESI-Q-TOF): m/z [M + Na]$^+$ calcd for$C_{24}H_{20}ClFN_2O_2S$: 477.0918; found: 477.0946.

1-(4-(1-(2-Phenyl-1-tosyl-4,5-dihydro-1*H*-imidazol-5-yl)-vinyl)phenyl)ethan-1-one (3aj)

Prepared according to the General Procedure; the crude material was purified by flash column chromatography (PE/EtOAc = 5:1) to afford **3aj**.

Yield: 42 mg (61%); light-yellow solid; mp 157.1–158.3 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.97 (d, J = 8.1 Hz, 2 H), 7.65 (m, 4 H), 7.56 (d, J = 8.0 Hz, 3 H), 7.44 (dd, J = 21.1, 7.7 Hz, 4 H), 5.71 (s, 1 H), 5.67 (s, 1 H), 5.50 (d, J = 7.1 Hz, 1 H), 3.72 (dd, J = 16.2, 9.6 Hz, 1 H), 3.46 (dd, J = 16.2, 2.3 Hz, 1 H), 2.60 (s, 3 H), 2.41 (s, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 197.95, 158.75, 146.89, 145.35, 142.45, 136.73, 135.18, 131.62, 130.71, 130.58, 129.74, 128.99, 128.32, 127.67, 127.37, 114.89, 63.07, 60.83, 27.26, 21.57.

HRMS (ESI-Q-TOF): m/z [M + Na]$^+$ calcd for $C_{26}H_{24}N_2O_3S$: 467.1508; found: 467.1562.

2-Phenyl-1-tosyl-5-(1-(4-(trifluoromethyl)phenyl)vinyl)-4,5-dihydro-1*H*-imidazole (3ak)

Prepared according to the General Procedure; the crude material was purified by flash column chromatography (PE/EtOAc = 4:1) to afford **3ak**.

Yield: 33 mg (46%); light-yellow solid; mp 110.5–111.3 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.75 (q, J = 8.4 Hz, 4 H), 7.58 (m, 6 H), 7.44 (dd, J = 19.9, 7.8 Hz, 4 H), 5.68 (d, J = 5.6 Hz, 2 H), 5.48 (m, 1 H), 3.71 (dd, J = 16.3, 9.5 Hz, 1 H), 3.49 (dd, J = 16.3, 2.6 Hz, 1 H), 2.41 (s, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 157.47, 145.51, 140.86, 137.03, 136.03, 134.88, 130.76, 130.33, 129.68, 129.48, 129.30, 128.86, 128.55, 127.69, 126.96, 125.15, 67.60, 60.31, 21.56.

HRMS (ESI-Q-TOF): m/z [M + Na]$^+$ calcd for $C_{25}H_{21}F_3N_2O_2S$: 493.1276; found: 493.1210.

2-Phenyl-5-(1-(thiophen-2-yl)vinyl)-1-tosyl-4,5-dihydro-1*H*-imidazole (3al)

Prepared according to the General Procedure; the crude material was purified by flash column chromatography (PE/EtOAc = 5:1) to afford **3al**.

Yield: 49 mg (78%); light-yellow solid; mp 131.2–132.1 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.91 (s, 1 H), 7.67 (d, J = 8.0 Hz, 2 H), 7.42 (tt, J = 18.0, 8.7 Hz, 7 H), 7.20 (d, J = 2.7 Hz, 1 H), 6.70 (s, 1 H), 5.51 (s, 2 H), 5.38 (s, 1 H), 3.73 (dd, J = 16.3, 9.4 Hz, 1 H), 3.43 (d, J = 9.4 Hz, 1 H), 2.40 (s, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 149.29, 146.93, 146.51, 145.33, 143.97, 137.69, 135.38, 130.60, 129.14, 128.71, 127.66, 126.97, 116.96, 112.70, 112.23, 63.15, 60.48, 21.55.

HRMS (ESI-Q-TOF): m/z [M + Na]$^+$ calcd for $C_{22}H_{20}N_2O_2S_2$: 431.0966; found: 431.0924.

2-(4-Methoxyphenyl)-5-(1-phenylvinyl)-1-tosyl-4,5-dihydro-1*H*-imidazole (3ba)

Prepared according to the General Procedure; the crude material was purified by flash column chromatography (PE/EtOAc = 4:1) to afford **3ba**.

Yield: 39 mg (59%); light-yellow solid; mp 59.2–60.5 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.63 (d, J = 8.7 Hz, 2 H), 7.56 (d, J = 8.2 Hz, 2 H), 7.48 (d, J = 7.1 Hz, 2 H), 7.39 (m, 5 H), 7.01 (d, J = 8.7 Hz, 2 H), 5.53 (d, J = 7.9 Hz, 2 H), 5.41 (d, J = 8.1 Hz, 1 H), 3.84 (s, 3 H), 3.56 (dd, J = 16.0, 9.3 Hz, 1 H), 3.41 (d, J = 2.4 Hz, 1 H), 2.41 (s, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 163.27, 160.79, 145.76, 145.03, 144.97, 138.97, 134.65, 134.55, 134.34, 134.30, 132.92, 132.88, 132.79, 131.59, 130.50, 130.37, 129.00, 128.63, 128.13, 127.67, 117.91, 116.84, 116.59, 115.27, 115.05, 72.99, 61.88, 51.90, 21.65, 21.62.

HRMS (ESI-Q-TOF): m/z [M + Na]$^+$ calcd for $C_{25}H_{24}N_2O_3S$:455.1508; found: 455.1546.

2-(4-Bromophenyl)-5-(1-phenylvinyl)-1-tosyl-4,5-dihydro-1*H*-imidazole (3ca)

Prepared according to the General Procedure; the crude material was purified by flash column chromatography (PE/EtOAc = 5:1) to afford **3ca**.

Yield: 52 mg (71%); light-yellow solid; mp 131.7–132.6 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.59 (m, 7 H), 7.44 (m, 6 H), 5.59 (d, J = 3.1 Hz, 2 H), 5.42 (d, J = 7.7 Hz, 1 H), 3.68 (dd, J = 16.2, 9.5 Hz, 1 H), 3.46 (dd, J = 16.2, 2.6 Hz, 1 H), 2.41 (s, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 144.93, 144.85, 144.79, 143.47, 138.75, 134.19, 133.66, 130.52, 130.41, 128.96, 128.53, 128.22, 127.99, 127.90, 127.80, 127.08, 116.71, 73.56, 62.45, 52.59, 21.60, 21.58.

HRMS (ESI-Q-TOF): m/z [M + Na]$^+$ calcd for $C_{24}H_{21}BrN_2O_2S$: 503.0507, 505.0487; found: 503.0545, 505.0495.

2-(3-Chloro-4-fluorophenyl)-5-(1-phenylvinyl)-1-tosyl-4,5-dihydro-1*H*-imidazole (3da)

Prepared according to the General Procedure; the crude material was purified by flash column chromatography (PE/EtOAc = 5:1) to afford **3da**.

Yield: 47 mg (68%); colorless oil.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.74 (dd, J = 7.0, 1.6 Hz, 1 H), 7.55 (ddd, J = 10.6, 9.7, 4.9 Hz, 6 H), 7.43 (m, 5 H), 5.60 (s, 2 H), 5.48 (d, J = 8.1 Hz, 1 H), 3.71 (dd, J = 16.3, 9.5 Hz, 1 H), 3.50 (dd, J = 16.3, 2.6 Hz, 1 H), 2.41 (s, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 158.61, 156.25, 145.70, 145.31, 135.91, 135.28, 131.58, 130.68, 130.52, 129.70, 129.28, 128.28, 128.10, 128.03, 127.69, 120.33, 120.15, 117.57, 117.36, 114.67, 63.18, 60.60, 21.56.

HRMS (ESI-Q-TOF): m/z [M + Na]$^+$ calcd for $C_{24}H_{20}ClFN_2O_2S$: 477.0918; found: 477.0978.

4-(5-(1-Phenylvinyl)-1-tosyl-4,5-dihydro-1*H*-imidazol-2-yl)phenyl acetate (3ea)

Prepared according to the General Procedure; the crude material was purified by flash column chromatography (PE/EtOAc = 5:1) to afford **3ea**.

Yield: 46 mg (65%); light-yellow solid; mp 117.1–118.0 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.97 (d, J = 8.3 Hz, 2 H), 7.65 (dd, J = 13.7, 7.8 Hz, 4 H), 7.56 (d, J = 8.1 Hz, 3 H), 7.44 (m, 4 H), 5.69 (d, J = 12.7 Hz, 2 H), 5.50 (d, J = 7.9 Hz, 1 H), 3.87 (s, 3 H), 3.74 (dd, J = 16.2, 7.1 Hz, 1 H), 3.48 (dd, J = 16.2, 2.7 Hz, 1 H), 2.41 (s, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 166.36, 158.72, 146.84, 145.34, 142.60, 138.15, 135.19, 131.61, 131.42, 130.69, 130.57, 129.89, 129.74, 129.60, 128.31, 127.66, 127.47, 115.00, 67.26, 63.08, 52.69, 21.56.

HRMS (ESI-Q-TOF): m/z [M + Na]$^+$ calcd for $C_{26}H_{24}N_2O_4S$: 483.1457; found: 483.1413.

5-(1-Phenylvinyl)-1-tosyl-2-(4-(trifluoromethyl)phenyl)-4,5-dihydro-1*H*-imidazole (3fa)

Prepared according to the General Procedure; the crude material was purified by flash column chromatography (PE/EtOAc = 3:1) to afford **3fa**.

Yield: 55 mg (76%); light-yellow solid; mp 123.6–124.4 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.94 (s, 2 H), 7.72 (m, 2 H), 7.52 (m, 4 H), 7.39 (m, 5 H), 5.55 (s, 2 H), 5.51 (m, 1 H), 3.83 (dd, J = 16.4, 9.7 Hz, 1 H), 3.56 (dd, J = 16.4, 2.9 Hz, 1 H), 2.41 (s, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 157.49, 147.63, 145.58, 137.91, 135.07, 133.68, 131.61, 130.66, 129.79, 129.09, 128.70, 127.61, 127.13, 113.13, 63.63, 61.28, 21.53.

HRMS (ESI-Q-TOF): m/z [M + Na]$^+$ calcd for $C_{25}H_{21}F_3N_2O_2S$: 493.1276; found: 493.1230.

5-(1-Phenylvinyl)-2-(thiophen-2-yl)-1-tosyl-4,5-dihydro-1*H*-imidazole (3ga)

Prepared according to the General Procedure; the crude material was purified by flash column chromatography (PE/EtOAc = 5:1) to afford **3ga**.

Yield: 35 mg (56%); light-yellow solid; mp 105.8–106.6 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.63 (m, 2 H), 7.54 (m, 4 H), 7.44 (m, 4 H), 7.26 (dd, J = 3.6, 1.0 Hz, 1 H), 7.10 (dd, J = 5.1, 3.7 Hz, 1 H), 5.56 (s, 1 H), 5.43 (s, 1 H), 5.37 (dd, J = 9.7, 3.4 Hz, 1 H), 3.89 (dd, J = 16.3, 9.7 Hz, 1 H), 3.57 (dd, J = 16.3, 3.4 Hz, 1 H), 2.41 (s, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 158.66, 145.36, 141.58, 140.90, 135.09, 131.57, 130.57, 129.74, 128.42, 128.30, 127.67, 126.65, 125.59, 111.11, 63.26, 61.33, 21.57.

HRMS (ESI-Q-TOF): m/z [M + Na]$^+$ calcd for $C_{22}H_{20}N_2O_2S_2$: 431.0966; found: 431.0910.

2-(Naphthalen-1-yl)-5-(1-phenylvinyl)-1-tosyl-4,5-dihydro-1*H*-imidazole (3ha)

Prepared according to the General Procedure; the crude material was purified by flash column chromatography (PE/EtOAc = 6:1) to afford **3ha**.

Yield: 33 mg (48%); light-yellow solid; mp 159.3–160.2 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.09 (d, J = 8.1 Hz, 1 H), 7.97 (d, J = 7.9 Hz, 1 H), 7.90 (d, J = 8.2 Hz, 1 H), 7.59 (p, J = 6.7 Hz, 2 H), 7.50 (t, J = 7.2 Hz, 6 H), 7.44–7.35 (m, 5 H), 5.88 (s, 1 H), 5.25 (d, J = 14.1 Hz, 2 H), 3.68 (dd, J = 16.3, 1.8 Hz, 1 H), 3.38 (d, J = 16.3 Hz, 1 H), 2.37 (s, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 158.69, 146.76, 145.34, 135.05, 133.73, 131.51, 130.78, 130.66, 129.68, 128.80, 128.60, 128.19, 127.45, 126.96, 126.53, 125.80, 125.67, 116.79, 65.24, 59.56, 21.54.

HRMS (ESI-Q-TOF): m/z [M + Na]$^+$ calcd for $C_{28}H_{24}N_2O_2S$: 475.1558; found: 475.1510.

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Supporting Information

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