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Regioselective 1,2-additon of allenamides with *N*-haloimides: synthesis of 2-halo allylic aminal derivatives

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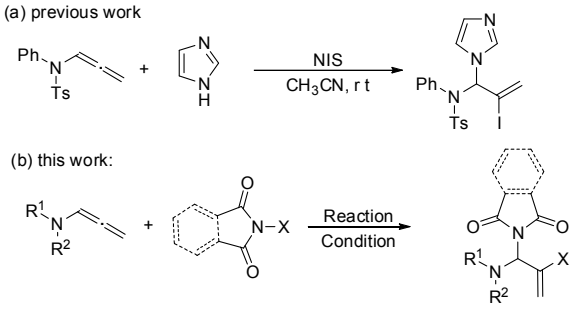
A strategy for the synthesis of 2-halo allylic aminal derivatives through regioselective 1,2-addition of allenamides with *N*-haloimides is presented. This reaction was conducted under very mild conditions and gave up to 99% yield. Moreover, the obtained halides allow functional group diversification by palladium-catalyzed coupling reactions, which could act as potential intermediates for the synthesis of valuable compounds.

Introduction

Protected aminals have been incorporated into peptide chains, and the resulting structures provide the so-called *retro-inverso* mimics.[1] Additionally, various core chiral aminal subunits could be found in natural products[2] and pharmaceuticals.[3] Moreover, aminals have also been involved as partners in transition metal-catalyzed reaction through C–N bond activation.[4] Because of the importance of structural entity, the development of new strategies to construct aminal derivatives has attracted much synthetic effort.

To the best of our knowledge, the addition of amide nucleophiles to doubly activated imines,[5] or catalytic addition of amides to imines[6] has been a popular area of study for the synthesis of aminal derivatives. The regio- and stereo-controlled functionalization of carbon-carbon double bonds has enormous potential in organic synthesis.[7] Among them, allenamides have recently proven to be important synthetic intermediates, undergoing diverse interesting transformations.[8] As a new approach to synthesis this structural entity, Broggini and Baäckvall group reported the transition metal-catalyzed intramolecular hydroamination[9] or carboamination[10] of allenamides to produce cyclo-aminal derivatives. Broggini also found that base could promoted this transformation.[11] However, the utility of this preparation was limited to the intramolecular cyclization of allenamides,. Intermolecular hydroamination of allenamides to synthesis aminal derivatives was seldom reported due to the regioselectivity for the 1,4-addition pathway.[12]

Our research group has focused on the reactions of allenamides,[13] and we found that 2-halo allylic aminal could be synthesized through NIS-madiated intermolecular nucleophilic addition of imidazole and allenamide involved 1,2-addition pathway (Scheme 1a).[14] Encouraged by these achievements and continuing our interest in the halogen mediated reactions of allenamides, we envisioned that N-haloimides could be served as both electrophiles and nucleophiles without extra nucleophilic agents to synthesize 2-halo allylic aminal derivatives through 1,2-addition pathway (Scheme 1b).



Scheme 1 Synthesis of 2-halo allylic aminal derivatives.

Results and discussion

With this idea in mind, we examined the reaction of benzyl substituted allenamide (**1a**) with 1.2 equiv of *N*-chlorosuccinimide (**2a**) in DCM at room temperature. The optimization results are summarized in Table 1. The desired 1,2-addition product **3aa** was isolated in 50% yield after 4 h, along with significant amounts of degradation product 4-methyl-N-phenylbenzenesulfonamide (Table 1, entry 1). An increase in the amount of *N*-chlorosuccinimide to 2.0 equiv afforded **3aa** in 51% yield after 1 h and the yield of **3aa** equaled 51% on increasing the amount of *N*-chlorosuccinimide to 3 equiv (Table 1, entries 2-3). Moreover, the reaction time was shortened to 0.5 h when the amount of **1a** increased to 1.1 equiv, though the yield of **3aa** was also equaled 51% (Table

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Electronic Supplementary Information (ESI) available: Experimental details, compound characterization, NMR spectra. CCDC 1448326 for **3aa**. For ESI and crystallographic data in CIF or other electronic format. See DOI: 10.1039/x0xx00000x

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1, entry 4). Subsequent screening of the solvents led to an increase in the yield to 67% when CH_3Cl and CCl_4 were used as the solvent, whereas DCE, CH_3CN, toluene, and benzene were not as effective. Notably, Only 20% yield of **3aa** was obtained when CH_3CN was used because of the poor solubility of the **2a**. The yield was higher in the solvent with high polarity, providing the evidence of the ion pair mechanism. The N-haloimides were then evaluated. Whereas N-bromosuccinimide (**2b**) and N-iodosuccinimide (**2c**) could give **3ab** and **3ac** in 82% and 85% yield, N-chlorophthalimide (**2d**) exhibited better reactivity, giving **3ad** in 99% yield (Table 1, entries 11–13). When N-bromophthalimide (**2e**) and N-iodophthalimide (**2f**) were used in this reaction, the 1,2-addition products **3ae** and **3af** were isolated in 88% and 43% yield, respectively (Table 1, entries 14–15). At the meantime, the 1,4-addition products **4ae** and **4af** could also obtained in 10% and 14% yield,[15] providing the evidence of the reaction mechanism. The molecular structure of the selective 1,2-addition product was determined by the single-crystal diffraction study of **3aa** (Figure 1).[16]

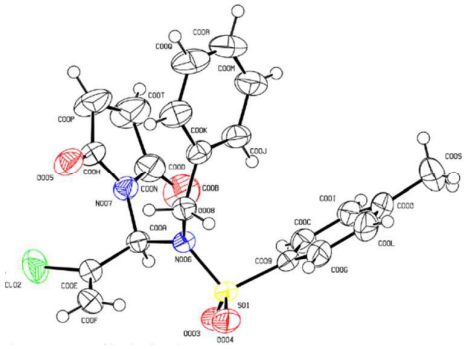
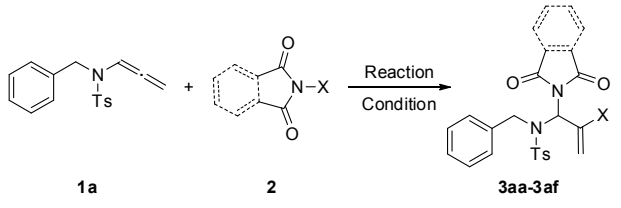


Figure 1 X-ray structure of compound **3aa**.

Table 1 Screening of the optimal conditions.[a]



Entry[a)]	2	1a/2	Solvent	Time (h)	Yield of 3 (%)[b]
1	**2a**	1/1.2	DCM	4	**3aa** (50)
2	**2a**	1/2	DCM	1	**3aa** (51)
3	**2a**	1/3	DCM	1	**3aa** (51)
4	**2a**	1.1/1	DCM	0.5	**3aa** (51)
5	**2a**	1.1/1	DCE	1	**3aa** (47)
6	**2a**	1.1/1	$CHCl_3$	1	**3aa** (67)
7	**2a**	1.1/1	CCl_4	2.5	**3aa** (67)
8	**2a**	1.1/1	CH_3CN	1	**3aa** (20)
9	**2a**	1.1/1	Toluene	3	**3aa** (63)
10	**2a**	1.1/1	Benzene	3	**3aa** (65)
11	**2b**	1.1/1	$CHCl_3$	1	**3ab** (82)
12	**2c**	1.1/1	$CHCl_3$	1	**3ac** (85)
13	**2d**	1.1/1	$CHCl_3$	1	**3ad** (99)
14[c]	**2e**	1.1/1	$CHCl_3$	1	**3ae** (88)
15[d]	**2f**	1.1/1	$CHCl_3$	1	**3af** (43)

[a]Unless otherwise noted, all reactions were carried out at 0.11 mmol of **1a** and 0.1 mmol of **2** in 3 mL solvent at room temperature. [b]Yield of isolated product. [c]10% yield of 1,4-addition product **4ae** was isolated. [d]14% yield of 1,4-addition product **4af** was isolated.

After having established the optimized conditions for the present reaction, various allenamide derivatives were subjected to the above conditions, as summarized in Table 2. 4-F- or 4-MeO-substituted benzyl allenamides were suitable for accessing 2-chloro allylic aminal derivatives **3bd** and **3cd** in 99% and 92% yield in the presence of *N*-chlorophthalimide (**2d**). Phenyl allenamide **1d** also provided the desired product **3dd** in 98% yield. Subsequently, the substitution effect on the aryl ring of phenyl allenamide was examined. At first, several para-substituted phenyl allenamides were investigated. The reactions of substrates **1e** and **1f** both bearing an electron donating-group at the para position of the aromatic ring resulted in the corresponding products **3ed** and **3fd** in 90% yield. The yields of **3jd**, **3hd** and **3id** increased with an increase in electronegativity of substituents at the para positions of the aromatic rings. 2-F-substituted phenyl allenamide **1j** could also give the corresponding product **3jd** in 91% yield. Subsequently, substrates **1k-1m** with different substituent at the meta positions of the aromatic rings were designed. The corresponding products **3kd**–**3md** were obtained in good yields. In the meantime, the reaction also worked well with the substrates **1n** which had two substituents on the same aryl group, furnishing the expected products **3nd** in 77% yield. Furthermore, the reactivity of different aliphatic substituted allenamides was also investigated. Both phenethyl and n-butyl substituted allenamides produced products **3od** and **3pd** in 98% yield, respectively. The reaction was also efficient with allenamides when mesyl and acyl were used in the place of tosyl as the amino protecting group. Thus, the reaction of phenyl allenamide **1q** with a mesyl substituent afforded **3qd** in 98% yield, **1r** with an acyl substituent furnished **3rd** in 91% yield, 2-oxazolidinone allenamide **1s** also provided the corresponding adduct **3sd** in 92% yield. For the allenamides with phenyl and dimethyl in the allene, the corresponding products **3td** and **3ud** were both obtained in 98% yield.

On the basis of our experimental results and precedents in the literature,[17] we propose a mechanism for the reaction as shown in Scheme 2. The reaction of **1a** and *N*-haloimide leads initially to an ion pair **5** composed of an σ-complex and the conjugate base of the imide. Subsequently, the mutual attraction between the σ-complex sulfimide ion species and

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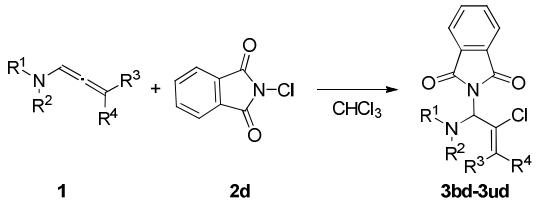
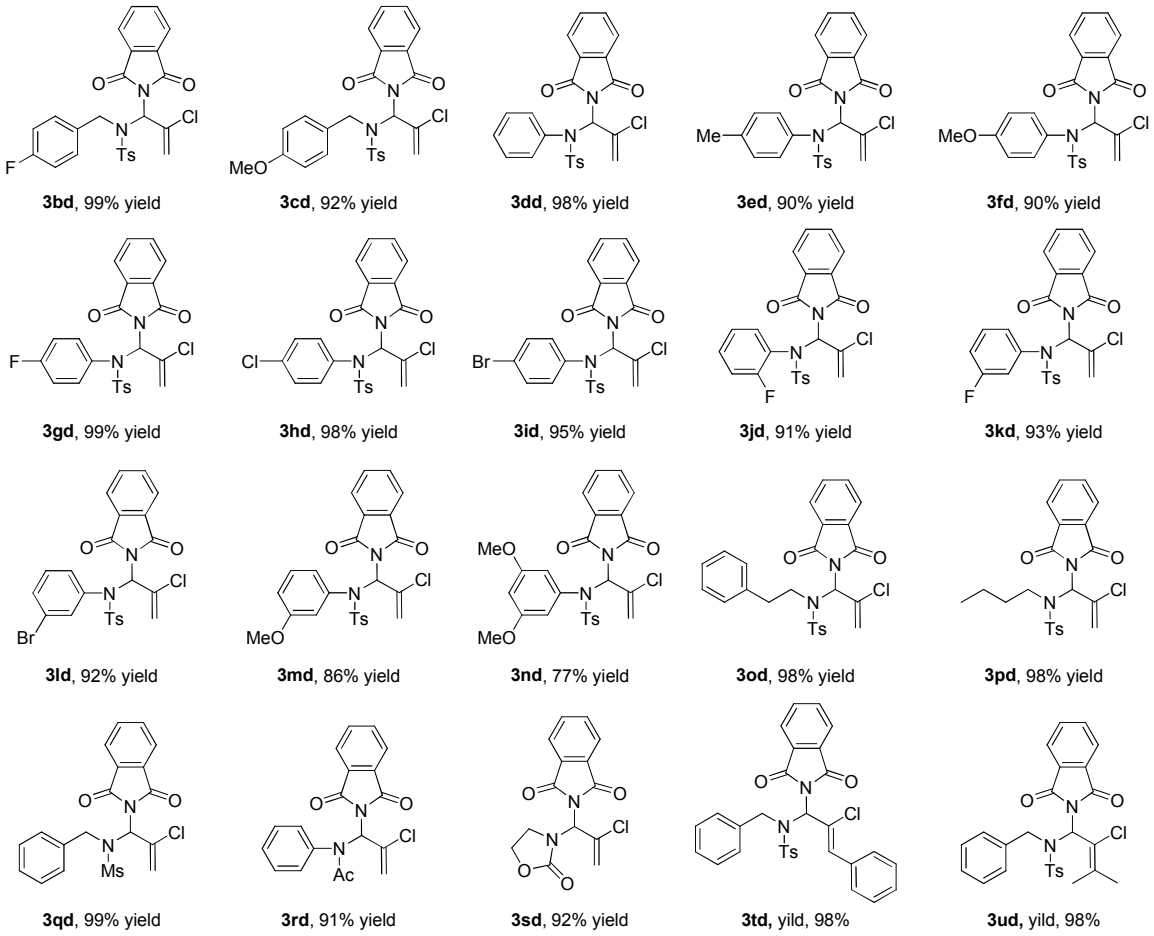
the conjugate base promoted the 1,2-addition pathway to give 2-halo allylic aminal derivatives **3**. The formation of 1,4-addition product **4ae** and **4af** could also indicate that the σ-complex is the conjugated sulfimide ion species.

Table 2 Substrate scope[a,b]



1 **2d** **3bd-3ud**



3bd, 99% yield **3cd**, 92% yield **3dd**, 98% yield **3ed**, 90% yield **3fd**, 90% yield

3gd, 99% yield **3hd**, 98% yield **3id**, 95% yield **3jd**, 91% yield **3kd**, 93% yield

3ld, 92% yield **3md**, 86% yield **3nd**, 77% yield **3od**, 98% yield **3pd**, 98% yield

3qd, 99% yield **3rd**, 91% yield **3sd**, 92% yield **3td,** yild, 98% **3ud,** yild, 98%

[a]Reaction conditions: **1** (0.11 mmol), **2d** (0.1 mmol), $CHCl_3$ (3 mL), r t. [b]Yield of isolated product.

To prove the practicality of this reaction, a gram-scale synthesis of the 2-chloro allylic aminal **3ad** was performed When 1.65 g of allenamide **1a** (5.5 mmol) was used, 2.35 g of the desired product **3ad** was obtained in 98% yield within 1 h, indicating that this transformation is easy to scale up to the gram scale without loss in efficiency (Scheme 3). To further demonstrate the potential application of this protocol, **3ac** and **3ae** were reacted with phenylacetylene under Sonagashira cross-coupling conditions,[18] the corresponding coupling products **6ac** and **6ae** were isolated in 83% and 84% yield, respectively.

Conclusions

In conclusion, a new and mild protocol for the synthesis of 2-halo allylic aminal derivatives has been established. The *N*-

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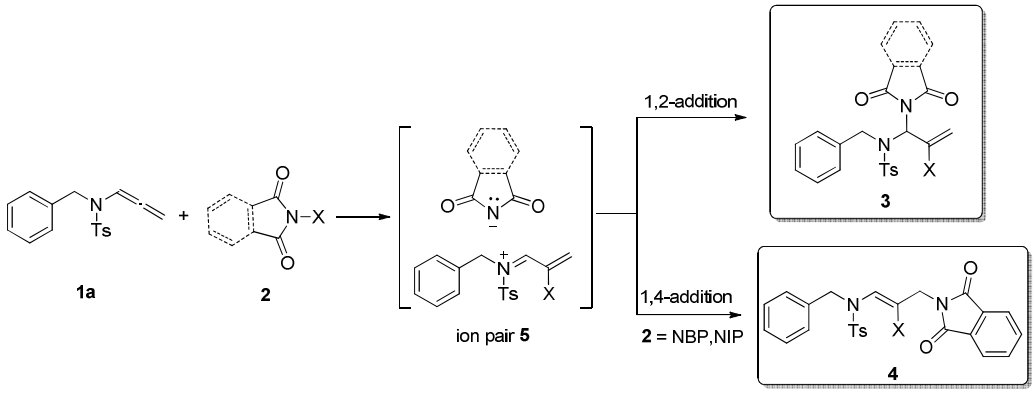
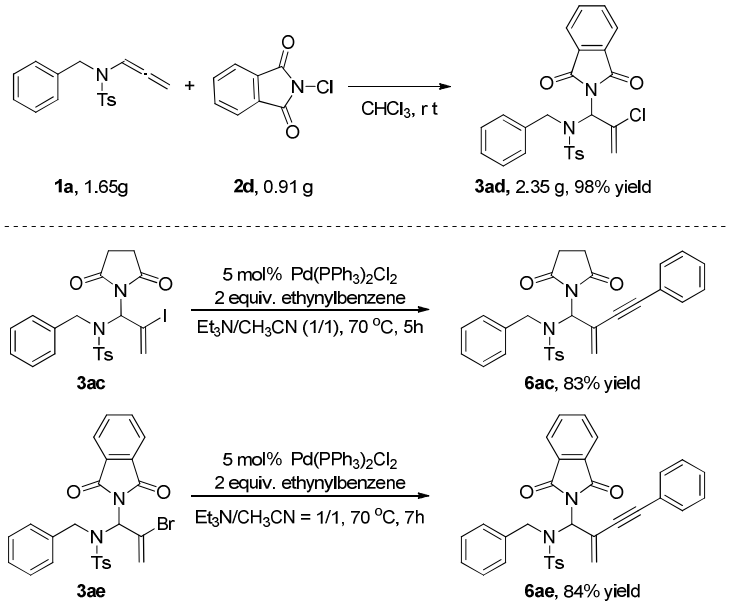
haloimides were served as both electrophiles and nucleophiles in this reaction. The resulting 2-halo allylic aminals are readily elaborated to more products by using known organopalladium chemistry, which may be essential intermediates for building delicate and sophisticated natural products. The potential utilization and extension of this interesting synthetic methodology are currently underway.



Scheme 2 Proposed reaction mechanism.



Scheme 3 Gram-scale synthesis and synthetic application.

Experimental

General information

All reactions were conducted under open air at room temperature. THF、toluene and DCM、DCE、$CHCl_3$ were freshly distilled over sodium/benzophenone and calcium hydride, respectively. Commercial reagents were used as supplied or were purified by standard techniques where necessary. Column chromatography was performed using Qingdao Haiyang Chemical Co., Ltd silica gel (200–300 mesh) with the appropriate solvent system, as determined by TLC analysis (Qingdao Haiyang Chemical Co., Ltd, silica gel F254) using UV light and $KMnO_4$ stain to visualize the reaction components. Melting points were determined from the solids obtained from column chromatography using a WRS-1B digital melting point instrument. IR spectra were recorded on a Nicoletisso FTIR spectrometer using KBr disks. Unless otherwise noted, nuclear magnetic resonance spectra were recorded at room temperature on an Agilent 400 MHz spectrometer using $CDCl_3$ as the solvent and TMS as the internal reference. Chemical shifts for ^{13}C NMR spectra were recorded in parts per million relative to tetramethylsilane using the central peak of deuterochloroform (77.0 ppm) as the internal standard. HRMS was performed using a Bruker Daltonics Bio TOF mass spectrometer. *N*-haloimides **2a-2e** were obtained commercially

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and used without further purification. *N*-iodophthalimide **2f** was prepared according to the published method.[19]

General procedure for allenamides 1a-1t synthesis via base-induced isomerizations.[20]

To a solution of N-tosyl propargylamine (5.0 mmol, 1.0 equiv) in 15 ml of anhydrous THF under N_2 atmosphere at 0℃ was added in portions 169 mg of ^{t}BuOK (30 mol%, 1,5 mmol). The reaction was allowed to stir at room temperature. After 12 h the mixture was diluted with 10 mL of Et_2O, and then filtrated over celite. The residue was washed with diethyl ether. The collected filtrate was concentrated in vacuo and the residue purified by flash column chromatography on silica gel (gradient eluent: EtOAc in hexane), affording the desired N-tosylallenamides.

N-benzyl-4-methyl-N-(3-phenylpropa-1,2-dien-1-yl)benzenesulfonamide (1t). White solid (1125 mg, 60%). M p 111-112℃. ^{1}H NMR (400 MHz, DMSO) δ 7.86 (d, *J* = 8.1 Hz, 2H), 7.51 (d, *J* = 7.9 Hz, 2H), 7.25 – 7.11 (m, 9H), 6.81 (d, *J* = 7.1 Hz, 2H), 6.67 (d, *J* = 5.9 Hz, 1H), 4.28 (s, 2H), 2.46 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ 197.05, 144.20, 136.00, 133.14, 130.12, 128.36, 128.31, 127.92, 127.56, 127.36, 127.24, 127.18, 127.04, 105.78, 102.83, 49.86, 21.10. IR (neat) 3040, 2934, 2863, 1498, 1450, 758, 699, 545 cm^{-1}. HRMS (ESI) calcd for $C_{21}H_{21}NO_2SNa$ $[M+Na]^+$ 386.1191; found: 386.1192.

General procedure for allenamide 1u synthesis via Cu (I) catalysed cross-coupling.[21]

A solution of amide (1.2 equiv), CuCN (10 mol%), Cs_2CO_3 (2.0 equiv), *N, N*'-dimethylethylenediamine (20 mol%) and allenyl iodide (1 equiv) in toluene (0.1 M) was heated to 50 °C for 18 h before being cooled to rt. After filtration through CeliteTM, the filtrate was concentrated under reduced pressure. Separation and purification of the resulting crude residue via silica gel flash column chromatography (hexane/EtOAc = 4/1) afforded the desired allenamide **1u** in 30% yield.

General procedure for selective 1, 2-additon of allenamide 1a with *N*-chlorophthalimide 2d.

To a suspension of **1a** (0.11 mmol) in $CHCl_3$ (3 mL) was added **2d** (0.1 mmol) in one portion. Then the reaction mixture was stirred at room temperature for 1 h until complete consumption of starting material as monitored by TLC. Concentration of the reaction mixture in vacuo followed by purification through flash chromatography on silica gel column (hexane/EtOAc = 5/1 as the eluent) afforded **3ad** (47.6 mg, 99% yield) as a white solid.

N-benzyl-N-(2-chloro-1-(2,5-dioxopyrrolidin-1-yl)allyl)-4-methylbenzenesulfonamide (3aa). White solid (29.0 mg, 67%). M p 148-149℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.2 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.12 – 7.10 (m, 3H), 6.80 (brs, 2H), 6.71 (s, 1H), 5.61 – 5.60 (m, 1H), 5.54 – 5.52 (m, 1H), 5.03 (d, *J* = 17.6 Hz, 1H), 4.59 (d, *J* = 17.7 Hz, 1H), 2.44 (s, 3H), 2.09 – 1.93 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.42, 144.20, 136.94, 136.82, 133.68, 129.69, 128.08, 127.83, 127.05, 126.09, 116.01, 65.76, 48.38, 27.44, 21.58. IR (neat) 3038, 2934, 2861, 1501, 1454, 758, 702, 545 cm^{-1}. HRMS (ESI) calcd for $C_{21}H_{21}ClN_2O_4SNa$ $[M+Na]^+$ 455.0803; found: 455.0800.

N-benzyl-N-(2-bromo-1-(2,5-dioxopyrrolidin-1-yl)allyl)-4-methylbenzenesulfonamide (3ab). White solid (39.1 mg, 82%). M p 146-147℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.1 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.12 – 7.10 (m, 3H), 6.79 (d, *J* = 5.8 Hz, 2H), 6.73 (s, 1H), 5.94 (s, 1H), 5.82 (s, 1H), 5.02 (d, *J* = 17.7 Hz, 1H), 4.59 (d, *J* = 17.7 Hz, 1H), 2.43 (s, 3H), 2.12 – 1.93 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.32, 144.18, 136.93, 136.74, 129.68, 128.07, 127.83, 127.03, 126.09, 124.67, 120.31, 67.07, 48.39, 27.43, 21.56. IR (neat) 3041, 2934, 2861, 1499, 1454, 758, 545 cm^{-1}. HRMS (ESI) calcd for $C_{21}H_{21}BrN_2O_4SNa$ $[M+Na]^+$ 499.0298; found: 499.0298.

N-benzyl-N-(1-(2,5-dioxopyrrolidin-1-yl)-2-iodoallyl)-4-methylbenzenesulfonamide (3ac). White solid (44.3 mg, 85%). M p 129-131℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 7.8 Hz, 2H), 7.30 (d, *J* = 7.9 Hz, 2H), 7.11 – 7.09 (m, 3H), 6.77 (d, *J* = 6.9 Hz, 2H), 6.69 (s, 1H), 6.36 (s, 1H), 6.07 (s, 1H), 5.02 (d, *J* = 17.7 Hz, 1H), 4.58 (d, *J* = 17.7 Hz, 1H), 2.43 (s, 3H), 2.08 – 1.92 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.27, 144.11, 136.86, 136.55, 129.64, 128.57, 128.02, 127.77, 126.98, 126.05, 101.30, 69.60, 48.39, 27.38, 21.53. IR (neat) 3041, 2934, 2861, 1499, 1457, 758, 545 cm^{-1}. HRMS (ESI) calcd for $C_{21}H_{21}IN_2O_4SNa$ $[M+Na]^+$ 547.0159; found: 547.0151.

N-benzyl-N-(2-chloro-1-(1,3-dioxoisoindolin-2-yl)allyl)-4-methylbenzenesulfonamide (3ad). White solid (47.6 mg, 99%). M p 126-127℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.0 Hz, 2H), 7.61 (s, 4H), 7.23 (d, *J* = 8.0 Hz, 2H), 6.92 (s, 1H), 6.82 – 6.75 (m, 4H), 6.72 – 6.70 (m, 1H), 5.66 – 5.65 (m, 2H), 5.03 (d, *J* = 17.3 Hz, 1H), 4.73 (d, *J* = 17.4 Hz, 1H), 2.38 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.55, 143.86, 137.15, 136.20, 134.42, 134.10, 130.77, 129.54, 127.76, 127.67, 126.36, 123.36, 116.41, 65.92, 48.94, 21.51. IR (neat) 3038, 2934, 2861, 1499, 1454, 758, 700, 545 cm^{-1}. HRMS (ESI) calcd for $C_{25}H_{21}ClN_2O_4SNa$ $[M+Na]^+$ 503.0803; found: 503.0801.

N-benzyl-N-(2-bromo-1-(1,3-dioxoisoindolin-2-yl)allyl)-4-methylbenzenesulfonamide (3ae). White solid (45.8 mg, 88%). M p 130-132℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.0 Hz, 2H), 7.64 – 7.57 (m, 4H), 7.23 (d, *J* = 8.0 Hz, 2H), 6.95 (s, 1H), 6.80 – 6.68 (m, 5H), 6.06 (s, 1H), 5.88 (s, 1H), 5.03 (d, *J* = 17.3 Hz, 1H), 4.73 (d, *J* = 17.3 Hz, 1H), 2.38 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.49, 143.87, 137.19, 136.14, 134.09, 130.79, 129.55, 127.77, 127.72, 126.36, 125.46, 123.39, 120.70, 109.99, 67.26, 48.91, 21.53. IR (neat) 3041, 2934, 2861, 1499, 1454, 758, 702, 545 cm^{-1}. HRMS (ESI) calcd for $C_{25}H_{21}BrN_2O_4SNa$ $[M+Na]^+$ 547.0298; found: 547.0293.

(Z)-N-benzyl-N-(2-bromo-3-(1,3-dioxoisoindolin-2-yl)prop-1-en-1-yl)-4-methylbenzenesulfonamide (4ae). White solid (5.2 mg, 10%). M p 157-158℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 – 7.84 (m, 2H), 7.79 – 7.70 (m, 4H), 7.29 (d, *J* = 8.1 Hz, 2H), 7.25 (brs, 2H), 7.23 – 7.17 (m, 3H), 6.63 (s, 1H), 4.62 (s, 2H), 4.47 (s, 2H), 2.41 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.07, 143.83, 135.82, 135.36, 134.16, 131.74, 129.66, 129.01, 128.58, 128.26, 127.70, 127.50, 123.48, 120.61, 52.34, 44.00, 21.55. IR(neat) 3038, 2934, 2861, 1496, 1459, 758, 702, 542 cm^{-1}. $C_{25}H_{21}BrN_2O_4SNa$ $[M+Na]^+$ 547.0298; found: 547.0297.

N-benzyl-N-(1-(1,3-dioxoisoindolin-2-yl)-2-iodoallyl)-4-methylbenzenesulfonamide (3af). White solid (24.5 mg, 43%).

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M p 150-151℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.4 Hz, 2H), 7.60 (brs, 4H), 7.23 (d, *J* = 7.7 Hz, 2H), 6.90 (s, 1H), 6.78 – 6.71 (m, 4H), 6.69 – 6.67 (m, 1H), 6.48 (s, 1H), 6.13 (s, 1H), 5.02 (d, *J* = 17.3 Hz, 1H), 4.71 (d, *J* = 17.4 Hz, 1H), 2.38 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.40, 143.82, 137.11, 135.96, 134.08, 130.68, 129.53, 128.92, 127.72, 127.67, 126.28, 123.37, 102.11, 69.82, 48.86, 21.50. IR(neat) 3041, 2934, 2861, 1499, 1454, 758, 702, 545 cm^{-1}. HRMS (ESI) calcd for $C_{25}H_{21}IN_2O_4SNa$ [M+Na]$^+$ 595.0159; found: 595.0151.

(Z)-N-benzyl-N-(3-(1,3-dioxoisoindolin-2-yl)-2-iodoprop-1-en-1-yl)-4-methylbenzenesulfonamide (4af). White solid (8 mg, 14%). M p 153-154℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 – 7.85 (m, 2H), 7.78 – 7.73 (m, 4H), 7.33 – 7.27 (m, 4H), 7.25 – 7.17 (m, 3H), 6.38 (s, 1H), 4.54 (s, 2H), 4.50 (s, 2H), 2.42 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.07, 143.89, 135.54, 134.95, 134.73, 134.19, 131.76, 129.68, 129.24, 128.27, 127.84, 127.79, 123.53, 103.67, 53.41, 46.79, 21.58. IR(neat) 3037, 2934, 2863, 1495, 1459, 760, 702, 542 cm^{-1}. HRMS (ESI) calcd for $C_{25}H_{21}IN_2O_4SNa$ [M+Na]$^+$ 595.0159; found: 595.0163.

N-(2-chloro-1-(1,3-dioxoisoindolin-2-yl)allyl)-N-(4-fluorobenzyl)-4-methylbenzenesulfonamide (3bd). White solid (49.1 mg, 99%). M p 134-135℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.1 Hz, 2H), 7.66 (brs, 4H), 7.22 (d, *J* = 7.9 Hz, 2H), 6.90 (s, 1H), 6.85 – 6.77 (m, 2H), 6.52 (t, *J* = 8.6 Hz, 2H), 5.63 (s, 1H), 5.58 (s, 1H), 4.97 (d, *J* = 17.1 Hz, 1H), 4.72 (d, *J* = 17.1 Hz, 1H), 2.37 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.57, 161.43 (d, *J* = 245.9 Hz), 144.01, 137.03, 134.35, 134.30, 132.03 (d, *J* = 3.1 Hz), 130.73, 129.57, 128.27 (d, *J* = 8.1 Hz), 127.60, 123.46, 116.56, 114.59 (d, *J* = 21.5 Hz), 66.03, 48.45, 21.50. IR (neat) 3041, 2934, 2861, 1499, 1454, 758, 700, 545 cm^{-1}. HRMS (ESI) calcd for $C_{25}H_{20}ClFN_2O_4SNa$ [M+Na]$^+$ 521.0709; found: 521.0708.

N-(2-chloro-1-(1,3-dioxoisoindolin-2-yl)allyl)-N-(4-methoxybenzyl)-4-methylbenzenesulfonamide (3cd). White solid (47.1 mg, 92%). M p 172-173℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 7.9 Hz, 2H), 7.63 (brs, 4H), 7.23 (d, *J* = 7.9 Hz, 2H), 6.89 (s, 1H), 6.70 (d, *J* = 8.2 Hz, 2H), 6.32 (d, *J* = 8.3 Hz, 2H), 5.64 (d, *J* = 8.5 Hz, 2H), 4.96 (d, *J* = 17.0 Hz, 1H), 4.64 (d, *J* = 17.0 Hz, 1H), 3.48 (s, 3H), 2.38 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.56, 158.14, 143.76, 137.22, 134.45, 134.02, 130.89, 129.49, 128.09, 127.84, 127.65, 123.37, 116.38, 113.17, 65.91, 54.96, 48.45, 21.50. IR (neat) 3038, 2934, 2861, 1499, 1454, 758, 545 cm^{-1}. HRMS (ESI) calcd for $C_{26}H_{23}ClN_2O_5SNa$ [M+Na]$^+$ 533.0908; found: 533.0908.

N-(2-chloro-1-(1,3-dioxoisoindolin-2-yl)allyl)-4-methyl-N-phenylbenzenesulfonamide (3dd). White solid (45.8 mg, 98%). M p 164-165℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 – 7.70 (m, 4H), 7.66 (d, *J* = 8.1 Hz, 2H), 7.26 - 7.22 (m, 3H), 7.11 (t, *J* = 7.6 Hz, 2H), 7.04 (s, 1H), 6.89 (brs, 2H), 6.47 (s, 1H), 5.86 (s, 1H), 2.40 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.56, 158.14, 143.76, 137.22, 134.45, 134.02, 130.89, 129.49, 128.09, 127.84, 127.65, 123.37, 116.38, 113.17, 65.91, 54.96, 48.45, 21.50. IR (neat) 3038, 2934, 2861, 1499, 1454, 761, 545 cm^{-1}. HRMS (ESI) calcd for $C_{24}H_{19}ClN_2O_4SNa$ [M+Na]$^+$ 489.0646; found: 489.0644.

N-(2-chloro-1-(1,3-dioxoisoindolin-2-yl)allyl)-4-methyl-N-(p-tolyl)benzenesulfonamide (3ed). White solid (43.3 mg, 90%). M p 157-158℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 – 7.69 (m, 4H), 7.66 (d, *J* = 8.1 Hz, 2H), 7.23 (d, *J* = 7.8 Hz, 2H), 7.02 (s, 1H), 6.89 (d, *J* = 7.7 Hz, 2H), 6.75 (brs, 2H), 6.45 (s, 1H), 5.85 (s, 1H), 2.40 (s, 3H), 2.23 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.92, 143.89, 139.45, 135.99, 135.78, 134.43, 131.99, 131.86, 130.88, 129.62, 129.23, 128.37, 123.76, 116.89, 67.08, 21.59, 21.17. IR (neat) 3041, 2934, 2861, 1499, 1454, 758, 700, 545 cm^{-1}. HRMS (ESI) calcd for $C_{25}H_{21}ClN_2O_4SNa$ [M+Na]$^+$ 503.0803; found: 503.0798.

N-(2-chloro-1-(1,3-dioxoisoindolin-2-yl)allyl)-N-(4-methoxyphenyl)-4-methylbenzenesulfonamide (3fd). White solid (44.5 mg, 90%). M p 79-80℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 – 7.67 (m, 4H), 7.65 (d, *J* = 8.0 Hz, 2H), 7.22 (d, *J* = 8.0 Hz, 2H), 7.01 (s, 1H), 6.76 (brs, 2H), 6.59 (d, *J* = 7.8 Hz, 2H), 6.43 (s, 1H), 5.84 (s, 1H), 3.71 (s, 3H), 2.40 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.93, 159.84, 143.91, 136.07, 135.72, 134.45, 133.43, 130.87, 129.26, 128.37, 126.85, 123.79, 116.81, 114.07, 67.12, 55.25, 21.60. IR (neat) 3041, 2934, 2861, 1499, 1454, 758, 700, 545 cm^{-1}. HRMS (ESI) calcd for $C_{25}H_{21}ClN_2O_5SNa$ [M+Na]$^+$ 519.0752; found: 519.0750.

N-(2-chloro-1-(1,3-dioxoisoindolin-2-yl)allyl)-N-(4-fluorophenyl)-4-methylbenzenesulfonamide (3gd). White solid (47.5 mg, 99%). M p 154-155℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 – 7.69 (m, 4H), 7.65 (d, *J* = 8.0 Hz, 2H), 7.24 (d, *J* = 8.1 Hz, 2H), 7.02 (s, 1H), 6.87 (brs, 2H), 6.80 (t, *J* = 8.1 Hz, 2H), 6.38 (s, 1H), 5.84 (s, 1H), 2.40 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.92, 162.69 (d, *J* = 250.4 Hz), 144.24, 135.85, 135.43, 134.61, 134.25 (d, *J* = 11.1 Hz), 130.76, 130.63 (d, *J* = 3.3 Hz), 129.41, 128.32, 123.87, 116.98, 116.00 (d, *J* = 22.8 Hz), 67.12, 21.61. IR (neat) 3038, 2934, 2861, 1496, 1451,758, 545 cm^{-1}. HRMS (ESI) calcd for $C_{24}H_{18}ClFN_2O_4SNa$ [M+Na]$^+$ 507.0552; found: 507.0551.

N-(2-chloro-1-(1,3-dioxoisoindolin-2-yl)allyl)-N-(4-chlorophenyl)-4-methylbenzenesulfonamide (3hd). White solid (49.0 mg, 98%). M p 136-137℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 – 7.71 (m, 4H), 7.65 (d, *J* = 8.1 Hz, 2H), 7.24 (d, *J* = 8.0 Hz, 2H), 7.10 (d, *J* = 8.4 Hz, 2H), 7.01 (s, 1H), 6.84 (d, *J* = 7.7 Hz, 2H), 6.36 (s, 1H), 5.83 (s, 1H), 2.41 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.94, 144.30, 135.76, 135.59, 135.41, 134.64, 133.63, 133.38, 130.78, 129.45, 129.22, 128.32, 123.93, 117.11, 67.14, 21.63. IR (neat) 3038, 2934, 2861, 1499, 1451, 758, 542 cm^{-1}. HRMS (ESI) calcd for $C_{24}H_{18}Cl_2N_2O_4SNa$ [M+Na]$^+$ 523.0257; found: 523.0256.

N-(4-bromophenyl)-N-(2-chloro-1-(1,3-dioxoisoindolin-2-yl)allyl)-4-methylbenzenesulfonamide (3id). White solid (51.9 mg, 95%). M p 152-153℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 – 7.71 (m, 4H), 7.65 (d, *J* = 8.0 Hz, 2H), 7.25 (dd, *J* = 8.2, 3.1 Hz, 4H), 7.01 (s, 1H), 6.78 (d, *J* = 7.8 Hz, 2H), 6.35 (s, 1H), 5.83 (s, 1H), 2.41 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.93, 144.31, 135.73, 135.39, 134.65, 133.95, 133.92, 132.20, 130.77, 129.45, 128.31, 123.93, 123.90, 117.13, 67.11, 21.63. IR (neat) 3038, 2934, 2861, 1499, 1454, 758, 700, 545 cm^{-1}. HRMS (ESI) calcd for $C_{24}H_{18}BrClN_2O_4SNa$ [M+Na]$^+$ 566.9751; found: 566.9748.

N-(2-chloro-1-(1,3-dioxoisoindolin-2-yl)allyl)-N-(2-fluorophenyl)-4-methylbenzenesulfonamide (3jd). White solid (44 mg, 91%). M p 178-179℃. ^{1}H NMR (400 MHz, $CDCl_3$)

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δ 7.73 - 7.65 (m, 8H), 7.26 – 7.20 (m, 4H), 7.14 (s, 1H), 6.38 (s, 1H), 5.84 (s, 1H), 2.39 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.86, 160.22 (d, *J* = 249.6 Hz), 144.11, 136.06, 135.84, 134.46 (d, *J* = 14.2 Hz), 132.90, 131.86 (d, *J* = 8.5 Hz), 130.92, 129.30 (d, *J* = 18.3 Hz), 128.29 (d, *J* = 26.8 Hz), 125.11, 123.71, 116.66, 115.89 (d, *J* = 21.4 Hz), 109.95, 66.45, 21.59. IR (neat) 3041, 2934, 2861, 1499, 1454, 758, 545 cm^{-1}. HRMS (ESI) calcd for $C_{24}H_{22}ClFN_3O_4S$ $[M+NH_4]^+$ 502.0998; found: 502.0992.

N-(2-chloro-1-(1,3-dioxoisoindolin-2-yl)allyl)-N-(3-fluorophenyl)-4-methylbenzenesulfonamide (3kd). White solid (45.0 mg, 93%). M p 175-176℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 – 7.74 (m, 2H), 7.73 – 7.69 (m, 2H), 7.66 (d, *J* = 8.2 Hz, 2H), 7.25 (d, *J* = 8.2 Hz, 2H), 7.09 – 7.05 (m, 1H), 7.02 (s, 1H), 6.97 (t, *J* = 8.3 Hz, 1H), 6.69 (t, *J* = 8.4 Hz, 2H), 6.36 (s, 1H), 5.84 (s, 1H), 2.41 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.94, δ 162.18 (d, *J* = 248.6 Hz), 144.36, 136.28 (d, *J* = 9.6 Hz), 135.67, 135.43, 134.62, 130.81, 129.73 (d, *J* = 9.1 Hz), 129.45, 128.32, 128.20 (d, *J* = 3.3 Hz), 123.88, 119.84 (d, *J* = 22.0 Hz), 117.15, 116.72 (d, *J* = 20.9 Hz), 109.99, 67.19, 21.62. IR (neat) 3038, 2934, 2861, 1499, 1454, 758, 700, 545 cm^{-1}. HRMS (ESI) calcd for $C_{24}H_{18}ClFN_2O_4SNa$ $[M+Na]^+$ 507.0552; found: 507.0559.

N-(3-bromophenyl)-N-(2-chloro-1-(1,3-dioxoisoindolin-2-yl)allyl)-4-methylbenzenesulfonamide (3ld). White solid (50.2 mg, 92%). M p 179-180℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 – 7.70 (m, 4H), 7.65 (d, *J* = 8.1 Hz, 2H), 7.38 (d, *J* = 8.0 Hz, 1H), 7.26 (s, 1H), 7.24 (s, 1H), 7.05 – 6.97 (m, 3H), 6.87 (d, *J* = 8.0 Hz, 1H), 6.35 (s, 1H), 5.84 (s, 1H), 2.41 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.94, 144.42, 136.19, 135.56, 135.26, 134.62, 132.57, 131.11, 130.80, 129.98, 129.44, 128.34, 123.90, 121.89, 117.21, 109.99, 67.18, 21.64. IR (neat) 3038, 2934, 2861, 1501, 1454, 758, 702, 545 cm^{-1}. HRMS (ESI) calcd for $C_{24}H_{18}BrClN_2O_4SNa$ $[M+Na]^+$ 566.9751; found: 566.9750.

N-(2-chloro-1-(1,3-dioxoisoindolin-2-yl)allyl)-N-(3-methoxyphenyl)-4-methylbenzenesulfonamide (3md). White solid (42.5 mg, 86%). M p 155-156℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 – 7.67 (m, 6H), 7.26 – 7.23 (m, 2H), 7.01 (brs, 2H), 6.77 (d, *J* = 7.8 Hz, 1H), 6.44 – 6.38 (m, 3H), 5.86 (s, 1H), 3.44 (s, 3H), 2.40 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.90, 159.55, 144.02, 135.91, 135.66, 134.49, 130.91, 129.34, 129.25, 128.45, 124.54, 123.75, 117.54, 116.95, 115.66, 109.98, 67.20, 54.96, 21.60. IR (neat) 3041, 2934, 2861, 1499, 1457, 758, 700, 545 cm^{-1}. HRMS (ESI) calcd for $C_{25}H_{21}ClN_2O_5SNa$ $[M+Na]^+$ 519.0752; found: 519.0743.

N-(2-chloro-1-(1,3-dioxoisoindolin-2-yl)allyl)-N-(3,5-dimethoxyphenyl)-4-methylbenzenesulfonamide (3nd). White solid (40.5 mg, 77%). M p 209-210℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 – 7.70 (m, 6H), 7.25 (d, *J* = 8.0 Hz, 2H), 6.98 (s, 1H), 6.40 (s, 1H), 6.30 (s, 1H), 5.99 (brs, 2H), 5.85 (s, 1H), 3.40 (s, 6H), 2.40 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.86, 160.23, 144.02, 136.14, 135.86, 135.73, 134.50, 130.94, 129.20, 128.51, 123.71, 116.92, 110.30, 102.05, 67.28, 55.03, 21.56. IR (neat) 3038, 2934, 2861, 1499, 1454, 758, 545 cm^{-1}. HRMS (ESI) calcd for $C_{26}H_{23}ClN_2O_6SNa$ $[M+Na]^+$ 549.0858; found: 549.0859.

N-(2-chloro-1-(1,3-dioxoisoindolin-2-yl)allyl)-4-methyl-N-phenethylbenzenesulfonamide (3od). White solid (48.6 mg, 98%). M p 110-111℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 – 7.84 (m, 4H), 7.77 – 7.75 (m, 2H), 7.26 (d, *J* = 7.8 Hz, 2H), 7.14 (t, *J* = 7.3 Hz, 2H), 7.01 (t, *J* = 8.7 Hz, 3H), 6.81 (s, 1H), 5.64 – 5.57 (m, 2H), 3.83 – 3.71 (m, 2H), 2.86 – 2.71 (m, 2H), 2.36 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.79, 143.95, 138.24, 136.93, 134.80, 134.58, 131.09, 129.61, 128.73, 128.34, 127.68, 126.19, 123.82, 116.91, 66.50, 48.20, 36.33, 21.48. IR (neat) 3041, 2934, 2861, 1496, 1454, 758, 542 cm^{-1}. HRMS (ESI) calcd for $C_{26}H_{23}ClN_2O_4SNa$ $[M+Na]^+$ 517.0959; found: 517.0959.

N-butyl-N-(2-chloro-1-(1,3-dioxoisoindolin-2-yl)allyl)-4-methylbenzenesulfonamide (3pd). White solid (43.7 mg, 98%). M p 88-89℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 – 7.86 (m, 2H), 7.81 (d, *J* = 8.1 Hz, 2H), 7.78 – 7.76 (m, 2H), 7.23 (d, *J* = 7.9 Hz, 2H), 6.78 (s, 1H), 5.67 (s, 1H), 5.65 (s, 1H), 3.55 (t, *J* = 8.2 Hz, 2H), 2.35 (s, 3H), 1.53 – 1.44 (m, 1H), 1.36 – 1.25 (m, 1H), 1.15 – 1.06 (m, 2H), 0.74 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.81, 143.67, 137.19, 134.98, 134.64, 131.09, 129.48, 127.60, 123.85, 116.80, 66.50, 46.43, 31.86, 21.47, 20.13, 13.48. IR (neat) 3041, 2934, 2861, 1499, 1454, 758, 702, 542 cm^{-1}. HRMS (ESI) calcd for $C_{22}H_{23}ClN_2O_4SNa$ $[M+Na]^+$ 469.0959; found: 469.0959.

N-benzyl-N-(2-chloro-1-(1,3-dioxoisoindolin-2-yl)allyl)methanesulfonamide (3qd). White solid (40.0 mg, 99%). M p 92-93℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 2.4 Hz, 2H), 7.76 (d, *J* = 2.5 Hz, 2H), 7.11 (d, *J* = 7.2 Hz, 2H), 7.07 (t, *J* = 7.3 Hz, 2H), 7.04 – 6.97 (m, 1H), 6.66 (s, 1H), 5.90 (s, 1H), 5.79 (s, 1H), 4.96 (d, *J* = 16.4 Hz, 1H), 4.81 (d, *J* = 16.4 Hz, 1H), 2.87 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.96, 135.88, 134.66, 134.59, 130.77, 128.39, 127.42, 127.38, 123.78, 116.55, 66.07, 49.00, 42.09. IR (neat) 3038, 2934, 2861, 1499, 1454, 758, 548 cm^{-1}. HRMS (ESI) calcd for $C_{19}H_{17}ClN_2O_4SNa$ $[M+Na]^+$ 427.0490; found: 427.0486.

N-(2-chloro-1-(1,3-dioxoisoindolin-2-yl)allyl)-N-phenylacetamide (3rd). White solid (32.1 mg, 91%). M p 121-122℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 – 7.73 (m, 2H), 7.70 – 7.68 (m, 2H), 7.48 – 7.00 (m, 6H), 5.90 (s, 1H), 5.74 (s, 1H), 1.89 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.53, 166.23, 138.29, 134.51, 134.35, 130.89, 129.85, 129.37, 129.10, 123.55, 115.30, 64.88, 23.18. IR (neat) 3038, 2934, 2861, 1499, 1454, 758, 542 cm^{-1}. HRMS (ESI) calcd for $C_{19}H_{15}ClN_2O_3Na$ $[M+Na]^+$ 377.0663; found: 377.0661.

2-(2-chloro-1-(2-oxooxazolidin-3-yl)allyl)isoindoline-1,3-dione (3sd). Colorless oil liquid (28.2 mg, 92%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 -7.90 (m, 2H), 7.82 – 7.97 (m, 2H), 6.74 (s, 1H), 5.66 (s, 1H), 5.56 (s, 1H), 4.46 – 4.36 (m, 2H), 4.04 – 3.98 (m, 1H), 3.97 – 3.87 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.74, 157.46, 134.74, 133.56, 131.22, 123.92, 116.34, 62.77, 62.45, 42.86. IR (neat) 3038, 2934, 2861, 1499, 1454, 758, 700, 545 cm^{-1}. HRMS (ESI) calcd for $C_{14}H_{11}ClN_2O_4Na$ $[M+Na]^+$ 329.0299; found: 329.0299.

(Z)-N-benzyl-N-(2-chloro-1-(1,3-dioxoisoindolin-2-yl)-3-phenylallyl)-4-methylbenzenesulfonamide (3td). White solid (54.6 mg, 98%). M p 195-196℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 – 7.59(m, 4H), 7.52 (d, *J* = 7.8 Hz, 2H), 7.46 (s, 1H), 7.37 –

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7.28 (m, 5H), 7.24 (d, *J* = 7.6 Hz, 2H), 7.09 (t, *J* = 7.3 Hz, 2H), 7.05 – 6.99 (m, 1H), 6.94 (d, *J* = 7.9 Hz, 2H), 6.69 (s, 1H), 5.28 (d, *J* = 17.4 Hz, 1H), 5.06 (d, *J* = 17.3 Hz, 1H), 2.17 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.23, 143.37, 137.60, 137.01, 135.10, 134.01, 133.34, 131.05, 129.19, 128.63, 128.44, 128.25, 127.87, 127.32, 127.27, 126.82, 123.56, 123.11, 63.40, 51.22, 21.32. IR (neat) 3041, 2931, 2861, 1499, 1457, 758, 700, 545 cm^{-1}. HRMS (ESI) calcd for $C_{31}H_{25}ClN_2O_4SNa$ $[M+Na]^+$ 579.1116; found, 579.1111.

N-benzyl-N-(2-chloro-1-(1,3-dioxoisoindolin-2-yl)-3-methylbut-2-en-1-yl)-4-methylbenzenesulfonamide (3ud). White solid (49.9 mg, 98%). M p 164-165℃.^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 – 7.64 (m, 4H), 7.53 (d, *J* = 7.3 Hz, 4H), 7.30 (t, *J* = 7.4 Hz, 2H), 7.22 (s, 1H), 7.19 (t, *J* = 7.2 Hz, 1H), 6.84 (d, *J* = 8.0 Hz, 2H), 5.18 (d, *J* = 17.0 Hz, 1H), 5.10 (d, *J* = 17.0 Hz, 1H), 2.02 (s, 3H), 1.67 (s, 3H), 1.29 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.55, 143.24, 138.83, 138.61, 136.98, 133.95, 131.29, 129.10, 127.79, 127.26, 127.08, 126.98, 123.03, 119.23, 64.28, 51.65, 21.89, 21.15, 20.58. IR (neat) 3041, 2934, 2861, 1499, 1451, 758, 700 cm^{-1}. HRMS (ESI) calcd for $C_{27}H_{25}ClN_2O_4SNa$ $[M+Na]^+$ 531.1116; found, 531.1113.

General Procedure for the Sonogashira cross-coupling reaction of 3ac with phenylacetylene .

To a suspension of **3ac** (0.1 mmol) in anhydrous CH_3CN (1.5 mL) were added Et_3N (1.5 mL), $PdCl_2(PPh_3)_2$ (3.5 mg, 5 mol %) and phenylacetylene (15.3 mg, 1.5 equiv). The reaction vial was flushed with Ar, and the reaction mixture was stirred for 5 h at 70 °C. Then, the mixture was concentrated under reduced pressure. The crude material was purified by flash column chromatography (hexane/EtOAc = 2.5/1 as the eluent) to give **6ac** (41.3 mg, 83% yield) as a white solid.

N-benzyl-N-(1-(2,5-dioxopyrrolidin-1-yl)-2-methylene-4-phenylbut-3-yn-1-yl)-4-methylbenzenesulfonamide (6ac). White solid (41.3 mg, 83%). M p 125-126℃. ^{1}H NMR (400 MHz, DMSO) δ 7.65 (d, *J* = 8.2 Hz, 2H), 7.44 – 7.37 (m, 3H), 7.34 – 7.33 (m, 4H), 7.17 – 7.15 (m, 3H), 7.03 (d, *J* = 7.4 Hz, 2H), 6.67 (s, 1H), 5.74 (s, 1H), 5.52 (s, 1H), 4.99 (d, *J* = 17.7 Hz, 1H), 4.72 (d, *J* = 17.7 Hz, 1H), 2.40 – 2.38 (m, 2H), 2.34 (s, 3H), 2.15 – 2.20 (m, 2H). ^{13}C NMR (100 MHz, DMSO) δ 176.72, 144.39, 137.84, 137.03, 131.84, 130.21, 129.62, 129.19, 128.29, 127.63, 127.20, 126.92, 125.42, 121.91, 91.28, 86.72, 65.89, 49.79, 27.99, 21.48. IR (neat) 3038, 2934, 2861, 1499, 1454, 758, 702, 540 cm^{-1}. HRMS (ESI) calcd for $C_{29}H_{26}N_2O_4SNa$ $[M+Na]^+$ 521.1505; found: 521.1507.

N-benzyl-N-(1-(1,3-dioxoisoindolin-2-yl)-2-methylene-4-phenylbut-3-yn-1-yl)-4-methylbenzenesulfonamide (6ae). White solid (46.0 mg, 84%). M p 57-58 ℃. ^{1}H NMR (400 MHz, DMSO) δ 7.83 – 7.79 (m, 2H), 7.76 – 7.74 (m, 2H), 7.64 (d, *J* = 8.2 Hz, 2H), 7.33 (d, *J* = 7.2 Hz, 1H), 7.28 (t, *J* = 7.3 Hz, 2H), 7.21 (d, *J* = 8.0 Hz, 2H), 7.10 (d, *J* = 6.9 Hz, 2H), 7.03 (d, *J* = 7.4 Hz, 2H), 6.96 (t, *J* = 7.3 Hz, 2H), 6.91 (d, *J* = 7.1 Hz, 1H), 6.87 (s, 1H), 5.79 (s, 1H), 5.60 (s, 1H), 5.08 (d, *J* = 17.7 Hz, 1H), 4.86 (d, *J* = 17.7 Hz, 1H), 2.22 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ 166.57, 143.75, 137.20, 136.54, 135.08, 131.03, 130.67, 130.19, 129.60, 129.11, 128.62, 127.57, 127.00, 126.35, 125.21, 123.46, 121.17, 109.54, 91.00, 86.18, 65.42, 49.40, 20.86. IR (neat) 3038, 2934, 2861, 1499, 1454, 758, 702, 540 cm^{-1}. HRMS (ESI) calcd for $C_{33}H_{26}N_2O_4SNa$ $[M+Na]^+$ 569.1505; found: 569.1503.

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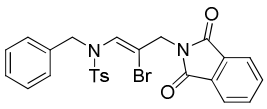
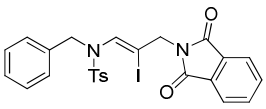
15 **4ae** and **4af** were isolated through flash chromatography on silica gel column (hexane/EtOAc = 3/1 as the eluent).



4ae



4af

16 **3aa**'s molecular structure was confirmed by its X-ray diffraction. Other product's structure was also deduced from **3aa**. CCDC 1448326 contains the supplementary crystallographic data for compound **3aa**, which can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.Uk/data_request/cif.

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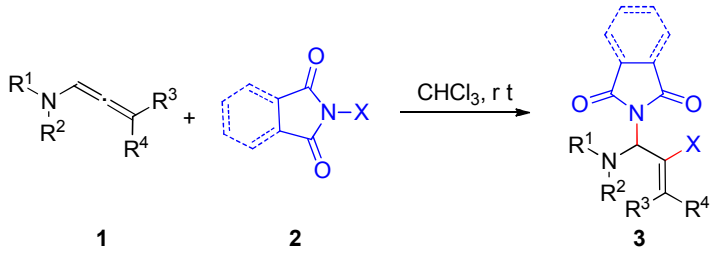
Graphical Abstract

An efficient new method was developed to synthesis of 2-halo allylic aminal derivatives through regioselective 1,2-addition of allenamides with *N*-haloimides.



1 **2** **3**

R^1 = Aryl, Benzyl, Alkyl; R^2 = Ts, Ms, Ac

R^3 = H, R^4 = Ph; R^3 = R^4 = Me

X = Cl, Br, I

26 examples, up to 99% yield