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Construction of sulfur-containing *N*-vinylimides: *N*-addition of imides to propargyl sulfonium salts†

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An *N*-addition reaction between imides and propargyl sulfonium salts was developed to afford sulfur-containing *N*-vinylimides with moderate to excellent yields. Under the activation of NaOAc·3H_2O, imides could undergo deprotonation and propargyl sulfonium salts could isomerize to allenic sulfonium salts. The *N*-nucleophilic attack initiates the reaction and gives the desired products. Various imides, including arylimides, aliphatic imides and *N*-(arylsulfonyl) alkyl acylamides, and even bioactive saccharin, thalidomide and pomalidomide could provide organosulfur *N*-vinylimides compounds. The simple, mild and metal-free reaction conditions, the broad scope of substrates, gram-scale synthesis and convenient transformation embody the synthetic superiority of this process.

N-vinylimides represent crucial structural motifs due to the importance of these frameworks (Fig. 1), which are the core structure found in biologically active structures,[1] functional materials[2] and natural products such as the parazoanthines A–E.[3] They can also serve as versatile synthetic intermediates in the synthesis of β-2-amino acid derivatives[4] and other complex structures.[5]

Due to the importance of these *N*-vinylimides frameworks, the growing interest in this featured moiety has catalyzed a recent spurt of attention for methodology appropriate for its construction. Conventionally, protocols for the synthesis of this important substrate class included transition-metal-catalyzed en-imidic C(sp^2)–N bond formation reactions of imides with vinyl halides, pseudohalides or alkynes. The main strategies involved Cu-catalyzed Chan–Lam–Evans reactions,[6] Ru-catalyzed hydroimidation reaction of imide with alkyne[7] and Pd-catalyzed oxidative amination of alkenes.[8] In 2021, Sandtorv's group reported Cu-catalyzed Chan–Lam–Evans reaction for coupling cyclic imides and alkenylboronic acids by forming C(sp^2)–N-bonds, enables the practical and mild preparation of (*E*)-enimides (Scheme 1a).[6a] In 2020, Schaub's group reported Ru-phosphine catalyzed hydroimidation reaction of cyclic amides with acetylene under low pressure, affording new method for synthesis of *N*-vinylimides (Scheme 1b).[7a] Hull's group reported Pd-catalyzed anti-Markovnikov oxidative amination reaction, alkenes are shown to react with imides in the presence of a palladate catalyst to generate the terminal imide, providing mild and robust complementary routes (Scheme 1c).[8a] Besides, rarely examples of organo-catalytic conjugate additions of imides to acetylene can also provide methods for the synthesis of *N*-vinylimides.[9]

The previously reported synthesis strategies mainly involved the use of expensive Ru and Pd-catalysts, otherwise toxic copper catalyst, and the structural limitations imposed to phthalimide and therefore specialized. Considering the limitation in generality, the harsh reaction condition, and the use of metal-catalysis decreased the attractiveness for synthetic applications, the development of new kind of vinylation reagents and their application of building *N*-vinylimides in a simple, mild, metal-free and efficient manner are highly desirable.

Our earlier work inspired our interest in synthesis of *N*-vinylimides by employing propargyl sulfonium salts as vinylation reagent. We have been exploring new reaction patterns of sulfonium salts and developed propargyl sulfonium salts involved [3 + 2] annulation/substitution reaction and *N*-addition/[2,3]-sigmatropic rearrangement reaction in an acyclic

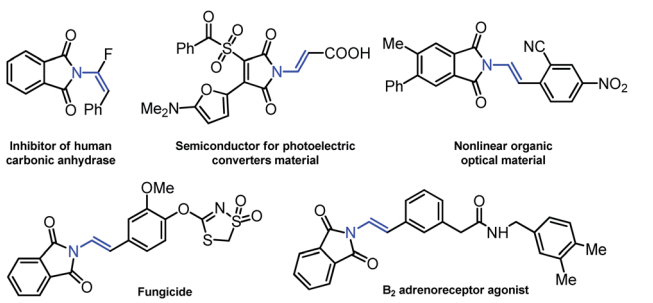

Fig. 1 Representative functional *N*-vinylimides scaffolds.

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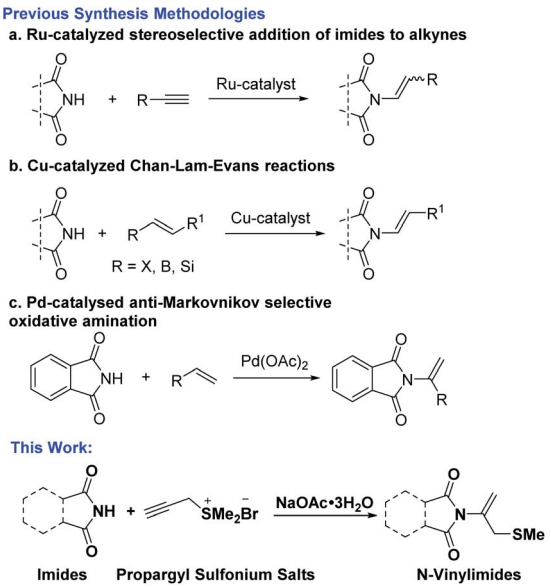
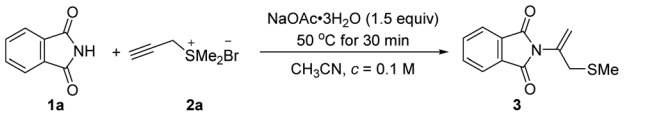


Scheme 1 Approaches for vinylation of imides.

model.[10] Based on our processive interests on constructing *N*-functionalized vinylation reaction and exploring the diverse reactive pathway of propargyl sulfonium salts, we herein report the realization of inorganic base promoted *N*-addition reaction of imides and propargyl sulfonium salts, delivering potential bioactive sulfur-containing *N*-vinylimides in moderate to excellent yields (Scheme 1).

We began our investigation by selecting phthalimide **1a** and propargyl sulfonium salt **2a** as model substrates (Table 1). When phthalimide **1a** (0.3 mmol, 1.0 equiv.), $NaOAc\cdot 3H_2O$ (0.45 mmol, 1.5 equiv.) in CH_3CN (3.0 mL, c = 0.1 M) were mixed, the reaction mixture was stirred for 10 min at 22 °C and propargyl sulfonium salt **2a** (0.45 mmol, 1.5 equiv.) was added in one portion. The reaction was stirred for 6 h continuously, phthalimide **1a** was consumed completely and afforded *N*-addition product **3a** with 71% yield (Table 1). Extensive exploration of a range of bases indicated that $NaOAc\cdot 3H_2O$ was the most efficient to promote the process. Replacement of $NaOAc\cdot 3H_2O$ with anhydrous NaOAc, Na_2CO_3, K_2CO_3, Cs_2CO_3, KOH and lithium carbonate gave related product with 24–46% yields (Table 1, entries 1–7). Replacement of either stronger inorganic bases such as NaH and KO^tBu, or organic base Et_3N and DBU could not promote the reaction efficiently (Table 1, entries 8–11, yields from 33 to 40%). Screening of solvents including THF, $CHCl_3$, DCE, DCM, and toluene did not give better yield (Table 1, entries 12–16, yields from trace to 37%). Temperature affected the reaction greatly and the desired product was obtained only in 11% yield when the reaction was conducted at 22 °C (entry 17 in Table 1). As the temperature was risen to 30 and 60 °C, the product **3a** was obtained gradually to 23 and 61%, respectively (Table 1, entries 18 and 19). When the temperature was risen to 80 and 90 °C, the reaction efficiency was slightly decreased to 51 and 49%, respectively (entries 20 and 21 in Table 1). We also probed the influence of the ratio of

Table 1 Optimization of the reaction conditions[a]

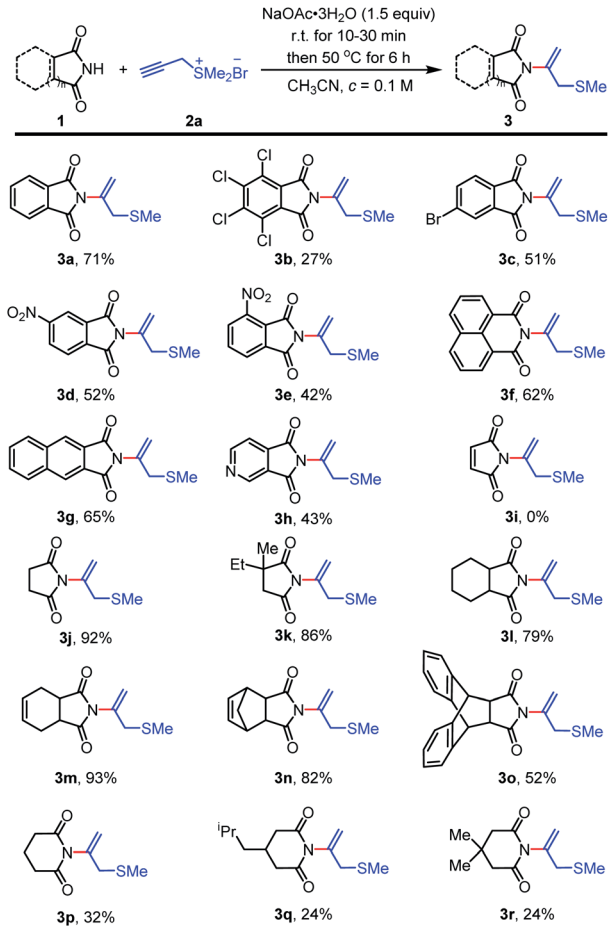


Entry	Base	Solvent	Temp. (°C)	Yield[b] (%)
1	NaOAc	CH_3CN	50	45
2	Na_2CO_3	CH_3CN	50	42
3	K_2CO_3	CH_3CN	50	46
4	Cs_2CO_3	CH_3CN	50	39
5	KOH	CH_3CN	50	24
6	$LiOAc\cdot 2H_2O$	CH_3CN	50	33
7	LiOAc	CH_3CN	50	42
8	NaH	CH_3CN	50	40
9	KO^tBu	CH_3CN	50	37
10	Et_3N	CH_3CN	50	36
11	DBU	CH_3CN	50	33
12	$NaOAc\cdot 3H_2O$	THF	50	37
13	$NaOAc\cdot 3H_2O$	$CHCl_3$	50	34
14	$NaOAc\cdot 3H_2O$	DCE	50	28
15	$NaOAc\cdot 3H_2O$	DCM	50	35
16	$NaOAc\cdot 3H_2O$	Toluene	50	Trace
17[c]	$NaOAc\cdot 3H_2O$	CH_3CN	22	11
18[c]	$NaOAc\cdot 3H_2O$	CH_3CN	30	23
19[c]	$NaOAc\cdot 3H_2O$	CH_3CN	60	61
20[c]	$NaOAc\cdot 3H_2O$	CH_3CN	80	51
21[c]	$NaOAc\cdot 3H_2O$	CH_3CN	90	49

[a] Unless otherwise noted, the reactions were performed under air and imide **1a** (0.3 mmol, 1.0 equiv.), base (0.45 mmol, 1.5 equiv.) in solvent (3.0 mL, c = 0.1 M) were mixed, the reaction mixture was stirred for 10 min at 22 °C. Then propargyl sulfonium salt **2a** (0.45 mmol, 1.5 equiv.) was added in one portion. The reaction was stirred at 50 °C for 6 h until starting material **1a** was fully consumed (monitored by TLC). [b] Isolated yield. DCE: 1,2-dichloroethane; DCM: dichloromethane. [c] With the ratio of **1a** : **2a** : $NaOAc\cdot 3H_2O$ = 1 : 1.5 : 1.5.

sulfonium salts **2a** and $NaOAc\cdot 3H_2O$ (for reaction details, see ESI†).

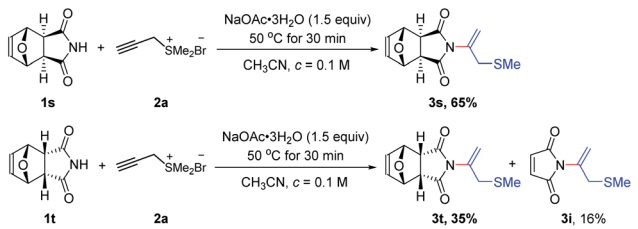
Having established the optimized conditions, we commenced to explore the substrate scope of the reaction. A selection of arylimides and aliphatic imides was next investigated with propargyl sulfonium salt **2a** in Scheme 2. Generally, arylimides containing electron-withdrawing group such as tetrachloro-, 4-bromo-, 4-nitro- and 3-nitrophthalimide provided desired *N*-vinylimides products **3b–3e** with moderate yields (Scheme 2, **3b–3e**, with yields of 27–52%), probably due to the electron withdrawing effect of substituents. 1,8-Naphthalimide and 2,3-naphthalimide were well-tolerated to provide *N*-vinylimide products **3f** and **3g** with 62 and 65% yields, respectively. 3,4-Pyridinedicarboximide could also be engaged in the reaction to obtain **3h** with yield of 43%. Subsequently, we went on to evaluate the reactivity of aliphatic imides. Unexpected, maleimide could not provide the desired *N*-nucleophilic addition product under the optimized conditions with recovering of the starting material. Oppositely, the method was high yielding and tolerable to succinimide and substituted succinimides. Succinimide and substituted succinimides worked well to deliver *N*-



Scheme 2 Scope of imides[a]. [a]Unless otherwise noted, the reactions were performed under air and imide 1 (0.3 mmol, 1.0 equiv.), NaOAc·3H$_2$O (0.45 mmol, 1.5 equiv.) in CH$_3$CN (3.0 mL, c = 0.1 M) were mixed, the reaction mixture was stirred for 10 min at 22 °C. Then propargyl sulfonium salt **2a** (0.45 mmol, 1.5 equiv.) was added in one portion. The reaction was stirred at 50 °C for 6 h until starting material 1 was fully consumed (monitored by TLC). [b]Isolated yield.

vinylimides products **3j–3o** with moderate to excellent yields of 52–93%.[11] Continuously, we evaluated the reactive effectiveness of glutarimide and substituted glutarimides. Under optimized conditions, glutarimide and substituted glutarimides could also react with 2a and give desired products **3p**, **3q** and **3r** with yields of 32, 24 and 24%, respectively.

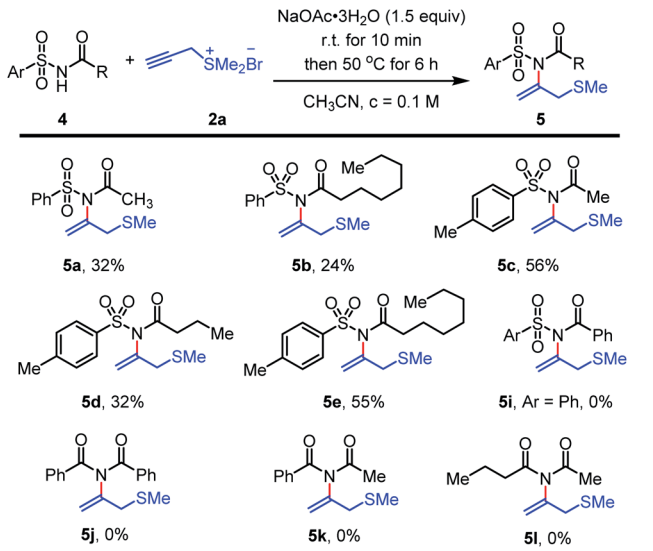
Surprising reaction appeared when we explored the reaction of tetrahydro-1*H*-4,7-epoxyisoindole-1,3(2*H*)-dione **1s** and **1t** (Scheme 3).[12] Under the optimized conditions, **1s** worked well with propargyl sulfonium salt **2a** to deliver the corresponding product **3s** with yield of 65%. Under the same conditions, compound **1t** gave the desired *N*-vinylimide product **3t** with yield of 35%, meanwhile with the unexpected *N*-vinylimide product **3i** with yield of 16%, which unavailable in the reaction of maleimide with propargyl sulfonium salt **2a**, probably due to the retro-Diels–Alder reaction of **1t** with generation of maleimide intermediate.



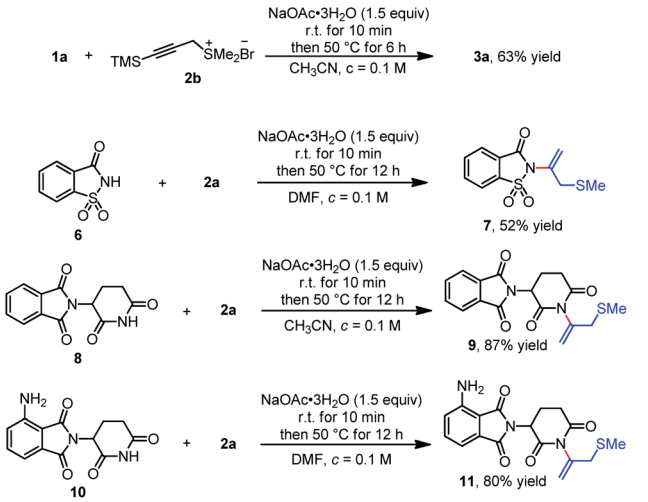
Scheme 3 Scope of imides.

The reaction performance could also be adapted to *N*-(arylsulfonyl) alkyl acylamides (Scheme 4). The method smoothly transferred electron-deficient aryl sulfonyl acylamides to form *N*-vinylimide products such as **5a–5e** in moderate yields. In contrast, when *N*-(arylsulfonyl) aryl acylamides **5i** and *N*-(arylacyl) alkyl acylamides **5j–5l** were involved, the reaction was sluggish and no desired *N*-vinylimide products could be obtained probably due to its low nucleophilicity (Scheme 4, **5i–5l**).

To further broaden the scope of the reaction, other representative propargyl sulfonium salts were also investigated (Scheme 5). Trimethylsilyl contained propargyl sulfonium salt **2b** could be applied to the reaction and the desilylation product **3a** was obtained with a yield of 63%. The method was high yielding and tolerable to diverse bioactive molecules, such as saccharin, thalidomide and pomalidomide. Saccharin derivatives have been reported as good hCAs inhibitors,[13] and thalidomide and pomalidomide belongs to an important class of molecules known as immunomodulatory imide drugs (IMiDs).[14] We found that under optimized conditions, saccharin, thalidomide and pomalidomide were also compatible with propargyl sulfonium salt **2a** and provided the



Scheme 4 Scope of aryl sulfonyl amides and carbonimides[a]. [a]Unless otherwise noted, the reactions were performed under air and imide **4** (0.3 mmol, 1.0 equiv.), NaOAc·3H$_2$O (0.45 mmol, 1.5 equiv.) in CH$_3$CN (3.0 mL, c = 0.1 M) were mixed, the reaction mixture was stirred for 10 min at 22 °C. Then propargyl sulfonium salt **2a** (0.45 mmol, 1.5 equiv.) was added in one portion. The reaction was stirred at 50 °C for 6 h until starting material **4** was fully consumed (monitored by TLC). [b]Isolated yield.



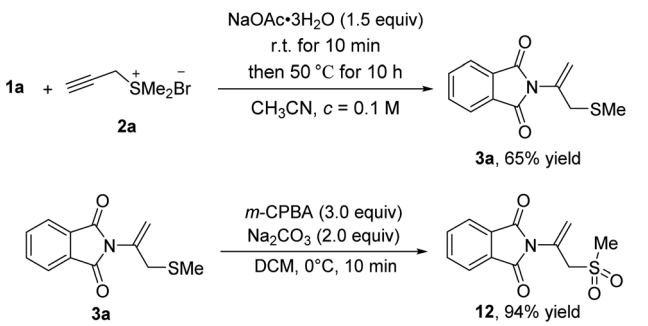
Scheme 5 Scope of propargyl sulfonium salts and bioactive molecules.

corresponding products **7**, **9** and **11** with 52, 87, and 80% yields, respectively (Scheme 5).

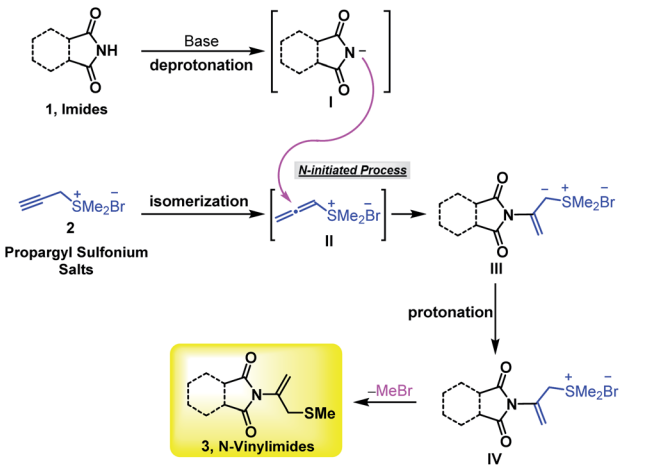
To demonstrate the synthetic utility of this protocol, we performed the gram-scale operation using phthalimide **1a** (1.01 g, 6.8 mmol) and propargyl sulfonium salt **2a** (1.5 equiv.) as the representative substrates under the optimized conditions, providing the related product **3a** (1.03 g) with 65% yield (Scheme 6). The typical transformation was also conducted by oxidation of compound **3a** with *m*-chloro peroxybenzoic acid (3.0 equiv.) and sulfonyl product **12** was obtained with 94% yield.

According to the previous reports on α-alkylidene pyrazolinones and propargyl sulfonium ylides,[10b,c] a possible mechanism is proposed to account for the formation of *N*-vinylimides **3** (Scheme 7). Under the activation of inorganic base $NaOAc\cdot 3H_2O$, the imides **1** may undergo deprotonation to form intermediate **I** and propargyl sulfonium salt **2a** can isomerize to allenic sulfonium salts **II**. The *N*-nucleophilic attack of **I** to allenic sulfonium salts **II** initiates the reaction and gives intermediate **III**. Subsequently, protonation of the species **III** and release of MeBr provided the desired product **3**.

In summary, we have developed $NaOAc\cdot 3H_2O$ promoted *N*-addition reaction between imides and propargyl sulfonium



Scheme 6 Gram-scale synthesis and further transformation.



Scheme 7 Plausible reaction mechanism.

salts, delivering potentially bioactive *N*-vinylimides in moderate to excellent yields. Various imides, including arylimides, aliphatic imides and *N*-(arylsulfonyl) alkyl acylamides, even bioactive saccharin, thalidomide and pomalidomide could tolerate and function to provide organosulfur *N*-vinylimides compounds. Gram-scale synthesis and convenient transformations are also furnished. The simple, mild, metal-free and efficient reaction condition, the broad scope of substrates, gram-scale synthesis and convenient transformation embody the synthetic superiority of this reaction process.

Experimental

General information

All reactions were performed in oven-dried or flame-dried round-bottom flasks and vials. Stainless steel syringes and cannula were used to transfer air- and moisture-sensitive liquids. Flash chromatography was performed using silica gel 60 (230–400 mesh) from Aladdin.

General procedure for substrates

To a flame-dried sealable 3-dram vial equipped with a stir bar was added imides **1** (0.3 mmol, 1.0 equiv.), $NaOAc\cdot 3H_2O$ (0.45 mmol, 1.5 equiv.), subsequently treated CH_3CN (3 mL, c = 0.1 M) was added to vial *via* syringe, the reaction mixture was stirred for 10–30 min at 22 °C. Then propargyl sulfonium salt **2a** (0.45 mmol, 1.5 equiv.) was added in one portion. The reaction was stirred at 50 °C for 6–12 h until imides **1** was fully consumed (monitored by TLC). The organic solvent was removed under reduced pressure and purified through column chromatography (eluent: petroleum ether and EtOAc) to afford the desired product **3**.

Characterization data for the products

2-(3-(Methylthio)prop-1-en-2-yl)isoindoline-1,3-dione (3a). The reaction was carried out on a 0.3 mmol scale by following the general procedure A. The product **3a** was purified through column chromatography (PE/EtOAc from 35 : 1 to 25 : 1) as

colorless oil (33 mg, 71% yield). IR ν_{max} (neat)/cm^{-1}: 3465, 3437, 2925, 2848, 1768, 1711, 1635, 1460, 1375, 1087, 717; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.82 (dd, J = 0, 0.6 Hz, 2H), 7.69 (dd, J = 0, 0.6 Hz, 2H), 5.39 (s, 1H), 5.24 (s, 1H), 3.53 (s, 2H), 1.97 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 167.1, 134.3, 134.0, 131.7, 123.7, 116.8, 37.1, 11.5. HRMS (ESI, m/z): calcd for $C_{12}H_{12}NO_2S^+$, $[M + H]^+$, 234.0583, found 234.0585.

4,5,6,7-Tetrachloro-2-(3-(methylthio)prop-1-en-2-yl)isoindoline-1,3-dione (3b). The reaction was carried out on a 0.3 mmol scale by following the general procedure A. The product **3b** was purified through column chromatography (PE/EtOAc from 50 : 1 to 35 : 1) as colorless oil (20 mg, 27% yield). IR ν_{max} (neat)/cm^{-1}: 3452, 3437, 2974, 2925, 2855, 1719, 1648, 1388, 1368, 1157, 1116, 730; ^{1}H NMR (600 MHz, $CDCl_3$): δ 5.53 (s, 1H), 5.35 (s, 1H), 3.57 (s, 2H), 2.05 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 162.3, 140.5, 133.4, 130.1, 127.2, 117.9, 36.9, 14.6. HRMS (ESI, m/z): calcd for $C_{12}H_8Cl_4NO_2S^+$, $[M + H]^+$, 369.9024, found 369.9025.

5-Bromo-2-(3-(methylthio)prop-1-en-2-yl)isoindoline-1,3-dione (3c). The reaction was carried out on a 0.3 mmol scale by following the general procedure A. The product **3c** was purified through column chromatography (PE/EtOAc from 50 : 1 to 25 : 1) as colorless oil (32 mg, 51% yield). IR ν_{max} (neat)/cm^{-1}: 3465, 3445, 2961, 2910, 2848, 1753, 1712, 1648, 1375, 1087, 892; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.02 (s, 1H), 7.89 (dd, J = 0.6, 7.8 Hz, 1H), 7.75 (d, J = 8.4 Hz, 1H), 5.47 (s, 1H), 5.30 (s, 1H), 3.57 (s, 2H), 2.02 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 166.3, 165.7, 137.3, 133.8, 133.3, 130.2, 129.2, 127.0, 125.0, 117.0, 37.0, 14.5. HRMS (ESI, m/z): calcd for $C_{12}H_{11}BrNO_2S^+$, $[M + H]^+$, 311.9688, found 311.9687.

2-(3-(Methylthio)prop-1-en-2-yl)-5-nitroisoindoline-1,3-dione (3d). The reaction was carried out on a 0.3 mmol scale by following the general procedure A. The product **3d** was purified through column chromatography (PE/EtOAc from 15 : 1 to 5 : 1) as colorless oil (29 mg, 52% yield). IR ν_{max} (neat)/cm^{-1}: 3465, 3437, 3108, 2939, 2910, 2856, 1782, 1720, 1648, 1537, 1375, 1339, 1087, 926, 722; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.73 (d, J = 1.8 Hz, 1H), 8.66 (dd, J = 1.8, 7.8 Hz, 1H), 8.11 (d, J = 7.8 Hz, 1H), 5.54 (s, 1H), 5.38 (s, 1H), 3.60 (s, 2H), 2.05 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 165.0, 164.7, 151.9, 136.0, 133.6, 133.1, 129.5, 124.9, 119.1, 117.5, 36.9, 14.5. HRMS (ESI, m/z): calcd for $C_{12}H_{11}N_2O_4S^+$, $[M + H]^+$, 279.0434, found 279.0436.

2-(3-(Methylthio)prop-1-en-2-yl)-4-nitroisoindoline-1,3-dione (3e). The reaction was carried out on a 0.3 mmol scale by following the general procedure A. The product **3e** was purified through column chromatography (PE/EtOAc from 15 : 1 to 6 : 1) as colorless oil (23 mg, 42% yield). IR ν_{max} (neat)/cm^{-1}: 3470, 3430, 3111, 2942, 2915, 2858, 1789, 1727, 1653, 1543, 1381, 1343, 1092, 933, 726; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.16 (t, J = 9.0 Hz, 2H), 7.97 (t, J = 7.8 Hz, 1H), 5.54 (s, 1H), 5.37 (s, 1H), 3.58 (s, 2H), 2.05 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 164.6, 161.6, 145.4, 135.6, 133.7, 133.5, 128.8, 127.4, 123.3, 117.8, 36.9, 14.5. HRMS (ESI, m/z): calcd for $C_{12}H_{11}N_2O_4S^+$, $[M + H]^+$, 279.0434, found 279.0437.

2-(3-(Methylthio)prop-1-en-2-yl)-1*H*-benzo[de]isoquinoline-1,3(2*H*)-dione (3f). The reaction was carried out on a 0.3 mmol scale by following the general procedure A. The product **3f** was purified through column chromatography (PE/EtOAc from 15 : 1 to 4 : 1) as colorless oil (35 mg, 62% yield). IR ν_{max} (neat)/cm^{-1}: 3430, 2910, 2897, 1704, 1663, 1593, 1347, 1242, 899, 779; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.63 (d, J = 7.2 Hz, 2H), 8.25 (d, J = 8.4 Hz, 2H), 7.78 (t, J = 7.8 Hz, 2H), 5.75 (s, 1H), 5.38 (s, 1H), 3.57 (s, 2H), 2.23 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 163.7, 137.6, 134.2, 131.7, 131.5, 128.5, 126.9, 122.7, 118.4, 38.0, 15.6. HRMS (ESI, m/z): calcd for $C_{16}H_{14}NO_2S^+$, $[M + H]^+$, 284.0740, found 284.0742.

2-(3-(Methylthio)prop-1-en-2-yl)-1*H*-benzo[*f*]isoindole-1,3(2*H*)-dione (3g). The reaction was carried out on a 0.3 mmol scale by following the general procedure A. The product **3g** was purified through column chromatography (PE/EtOAc from 25 : 1 to 1 : 1) as colorless oil (37 mg, 65% yield). IR ν_{max} (neat)/cm^{-1}: 3458, 3424, 2967, 2925, 2856, 1768, 1712, 1368, 1095, 758; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.41 (s, 2H), 8.09 (dd, J = 3.6, 6.0 Hz, 2H), 7.73 (dd, J = 3.6, 6.0 Hz, 2H), 5.54 (s, 1H), 5.40 (s, 1H), 3.66 (s, 2H), 2.09 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 167.0, 135.6, 134.2, 130.3, 129.3, 127.4, 125.2, 117.0, 37.1, 14.6. HRMS (ESI, m/z): calcd for $C_{16}H_{14}NO_2S^+$, $[M + H]^+$, 284.0740, found 284.0744.

2-(3-(Methylthio)prop-1-en-2-yl)-1*H*-pyrrolo[3,4-*c*]pyridine-1,3(2*H*)-dione (3h). The reaction was carried out on a 0.3 mmol scale by following the general procedure A. The product **3h** was purified through column chromatography (PE/EtOAc from 15 : 1 to 5 : 1) as colorless oil (20 mg, 43% yield). IR ν_{max} (neat)/cm^{-1}: 3437, 2918, 2848, 1720, 1648, 1607, 1417, 1362, 1095, 892; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.23 (s, 1H), 9.13 (d, J = 3.0 Hz, 1H), 7.82 (d, J = 4.8 Hz, 1H), 5.53 (s, 1H), 5.36 (s, 1H), 3.59 (s, 2H), 2.05 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 165.9, 165.6, 155.8, 145.3, 139.0, 133.6, 125.6, 117.6, 117.1, 37.0, 14.5. HRMS (ESI, m/z): calcd for $C_{11}H_{11}N_2O_2S^+$, $[M + H]^+$, 235.0536, found 235.0537.

1-(3-(Methylthio)prop-1-en-2-yl)-1*H*-pyrrole-2,5-dione (3i). The product **3t** was purified through column chromatography (PE/EtOAc from 8 : 1 to 1 : 1) as colorless oil (18 mg, 35% yield), **3i** was also detected in the reaction colorless oil (6 mg, 16% yield). IR ν_{max} (neat)/cm^{-1}: 3475, 3434, 2928, 2848, 1707, 1638, 1624, 1391, 1378, 1198; ^{1}H NMR (600 MHz, $CDCl_3$): δ 6.77 (s, 2H), 5.37 (s, 1H), 5.22 (s, 1H), 3.50 (s, 2H), 2.01 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 169.3, 134.1, 133.4, 116.1, 36.9, 14.4. HRMS (ESI, m/z): calcd for $C_8H_{10}NO_2S^+$, $[M + H]^+$, 184.0427, found 184.0429.

1-(3-(Methylthio)prop-1-en-2-yl)pyrrolidine-2,5-dione (3j). The reaction was carried out on a 0.3 mmol scale by following the general procedure A. The product **3j** was purified through column chromatography (PE/EtOAc from 8 : 1 to 4 : 1) as colorless oil (34 mg, 92% yield). IR ν_{max} (neat)/cm^{-1}: 3473, 3430, 2925, 1704, 1635, 1622, 1388, 1375, 1193; ^{1}H NMR (600 MHz, $CDCl_3$): δ 5.45 (s, 1H), 5.22 (s, 1H), 3.47 (s, 2H), 2.82 (s, 4H), 2.03 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 175.9, 134.4, 117.2, 36.4, 28.3, 14.6. HRMS (ESI, m/z): calcd for $C_8H_{12}NO_2S^+$, $[M + H]^+$, 186.0583, found 186.0584.

3-Ethyl-3-methyl-1-(3-(methylthio)prop-1-en-2-yl)pyrrolidine-2,5-dione (3k). The reaction was carried out on a 0.3 mmol scale by following the general procedure A. The product **3k** was purified through column chromatography (PE/EtOAc from

15 : 1 to 2 : 1) as colorless oil (39 mg, 86% yield). IR ν_{max} (neat)/cm^{-1}: 3478, 3435, 2929, 1710, 1637, 1652, 1381, 1370, 1198, 630; ^{1}H NMR (600 MHz, $CDCl_3$): δ 5.42 (s, 1H), 5.19 (s, 1H), 3.46 (s, 2H), 2.61 (ABQ, J = 18.6 Hz, 2H), 2.01 (s, 3H), 1.83–1.77 (m, 1H), 1.68–1.62 (m, 1H), 1.36 (s, 3H), 0.95 (t, J = 7.8 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 181.7, 174.9, 134.3, 117.0, 44.2, 40.5, 36.4, 31.0, 24.1, 14.5, 8.7. HRMS (ESI, m/z): calcd for $C_{11}H_{18}NO_2S^+$, $[M + H]^+$, 228.1053, found 228.1055.

2-(3-(Methylthio)prop-1-en-2-yl)hexahydro-1*H*-isoindole-1,3(2*H*)-dione (3l). The reaction was carried out on a 0.3 mmol scale by following the General Procedure A. The product **3l** was purified through column chromatography (PE/EtOAc from 15 : 1 to 5 : 1) as colorless oil (38 mg, 79% yield). IR ν_{max} (neat)/cm^{-1}: 3457, 3437, 2972, 2919, 1714, 1645, 1375, 1193, 684, 605; ^{1}H NMR (600 MHz, $CDCl_3$): δ 5.40 (s, 1H), 5.19 (s, 1H), 3.49 (s, 2H), 2.95 (s, 2H), 2.03 (s, 3H), 1.90 (s, 4H), 1.49 (d, J = 2.4 Hz, 4H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 178.5, 134.3, 116.7, 40.1, 36.5, 23.9, 21.9, 14.5. HRMS (ESI, m/z): calcd for $C_{12}H_{18}NO_2S^+$, $[M + H]^+$, 240.1053, found 240.1054.

2-(3-(Methylthio)prop-1-en-2-yl)-3a,4,7,7a-tetrahydro-1*H*-isoindole-1,3(2*H*)-dione (3m). The reaction was carried out on a 0.3 mmol scale by following the general procedure A. The product **3m** was purified through column chromatography (PE/EtOAc from 10 : 1 to 5 : 1) as colorless oil (44 mg, 93% yield). IR ν_{max} (neat)/cm^{-1}: 3452, 3437, 2961, 2925, 2848, 1712, 1648, 1375, 1208, 694; ^{1}H NMR (600 MHz, $CDCl_3$): δ 5.93 (s, 2H), 5.39 (s, 1H), 5.15 (s, 1H), 3.41 (s, 2H), 3.15 (t, J = 3.0 Hz, 2H), 2.61 (d, J = 15.6 Hz, 2H), 2.29 (d, J = 13.8 Hz, 2H), 1.98 (s, 3H); ^{13}C NMR (600 MHz, $CDCl_3$): δ 179.0, 134.4, 117.0, 39.0, 36.3, 23.5, 14.5. HRMS (ESI, m/z): calcd for $C_{12}H_{16}NO_2S^+$, $[M + H]^+$, 238.0896, found 238.0898.

2-(3-(Methylthio)prop-1-en-2-yl)-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoisoindole-1,3(2*H*)-dione (3n). The reaction was carried out on a 0.3 mmol scale by following the general procedure A. The product **3n** was purified through column chromatography (PE/EtOAc from 15 : 1 to 8 : 1) as colorless oil (41 mg, 82% yield). IR ν_{max} (neat)/cm^{-1}: 3458, 3437, 2982, 2918, 1704, 1648, 1375, 1355, 1193, 604; ^{1}H NMR (600 MHz, $CDCl_3$): δ 6.20 (s, 2H), 5.35 (s, 1H), 5.05 (s, 1H), 3.45 (s, 2H), 3.35 (t, J = 1.2 Hz, 2H), 3.32 (s, 2H), 2.01 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 176.6, 134.7, 134.3, 117.1, 52.1, 45.8, 45.2, 36.4, 14.5. HRMS (ESI, m/z): calcd for $C_{13}H_{16}NO_2S^+$, $[M + H]^+$, 250.0896, found 250.0898.

13-(3-(Methylthio)prop-1-en-2-yl)-11,15-dihydro-9*H*-9,10-[3,4] epipyrroloanthracene-12,14(10*H*,13*H*)-dione (3o). The reaction was carried out on a 0.3 mmol scale by following the general procedure A. The product **3o** was purified through column chromatography (PE/EtOAc from 13 : 1 to 4 : 1) as colorless oil (38 mg, 52% yield). IR ν_{max} (neat)/cm^{-1}: 3458, 3429, 2961, 2925, 1768, 1712, 1648, 1473, 1375, 1208, 766; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.42 (dd, J = 3.6, 5.4 Hz, 2H), 7.32 (dd, J = 3.0, 5.4 Hz, 2H), 7.21 (dd, J = 3.0, 5.4 Hz, 2H), 7.18 (dd, J = 3.0, 5.4 Hz, 2H), 5.18 (s, 1H), 4.83 (s, 2H), 4.27 (s, 1H), 3.31 (s, 2H), 3.03 (s, 2H), 1.94 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 175.7, 141.3, 138.7, 134.2, 127.0, 126.7, 125.0, 124.2, 116.9, 46.9, 45.7, 36.0, 14.6. HRMS (ESI, m/z): calcd for $C_{22}H_{20}NO_2S^+$, $[M + H]^+$, 362.1209, found 362.1212.

1-(3-(Methylthio)prop-1-en-2-yl)piperidine-2,6-dione (3p). : The reaction was carried out on a 0.3 mmol scale by following the general procedure A. The product **3p** was purified through column chromatography (PE/EtOAc from 8 : 1 to 5 : 1) as colorless oil (13 mg, 32% yield). IR ν_{max} (neat)/cm^{-1}: 3465, 3360, 2988, 2925, 2904, 1671, 1586, 1285, 1213, 1102, 779; ^{1}H NMR (600 MHz, $CDCl_3$): δ 5.53 (s, 1H), 5.11 (s, 1H), 3.32 (s, 2H), 2.73 (t, J = 6.6 Hz, 4H), 2.09 (s, 3H), 2.05–2.00 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 171.9, 137.0, 118.1, 37.8, 32.9, 17.2, 15.4. HRMS (ESI, m/z): calcd for $C_9H_{14}NO_2S^+$, $[M + H]^+$, 200.0740, found 200.0743.

4-Isobutyl-1-(3-(methylthio)prop-1-en-2-yl)piperidine-2,6-dione (3q). The reaction was carried out on a 0.3 mmol scale by following the general procedure A. The product **3q** was purified through column chromatography (PE/EtOAc from 20 : 1 to 4 : 1) as colorless oil (12 mg, 24% yield). IR ν_{max} (neat)/cm^{-1}: 3465, 3430, 2975, 2920, 2894, 1736, 1673, 1486, 1281, 1233, 1132, 734; ^{1}H NMR (600 MHz, $CDCl_3$): δ 5.53 (s, 1H), 5.11 (s, 1H), 3.36 (s, 2H), 2.84 (dd, J = 4.2, 16.8 Hz, 2H), 2.39 (dd, J = 10.2, 16.8 Hz, 2H), 2.27–2.23 (m, 1H), 2.09 (s, 3H), 1.72–1.68 (m, 1H), 1.28 (dd, J = 7.8, 15.0 Hz, 2H), 0.94 (s, 3H), 0.93 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 171.7, 137.0, 118.2, 44.0, 39.2, 37.9, 27.1, 24.8, 22.5, 15.4. HRMS (ESI, m/z): calcd for $C_{13}H_{22}NO_2S^+$, $[M + H]^+$, 256.1366, found 256.1369.

4,4-Dimethyl-1-(3-(methylthio)prop-1-en-2-yl)piperidine-2,6-dione (3r). The reaction was carried out on a 0.3 mmol scale by following the general procedure A. The product **3r** was purified through column chromatography (PE/EtOAc from 10 : 1 to 5 : 1) as colorless oil (11 mg, 24% yield). IR ν_{max} (neat)/cm^{-1}: 3465, 3437, 2961, 2918, 2856, 1725, 1676, 1355, 1270, 1242, 1131, 625; ^{1}H NMR (600 MHz, $CDCl_3$): δ 5.52 (s, 1H), 5.10 (s, 1H), 3.36 (s, 2H), 2.59 (s, 4H), 2.10 (s, 3H), 1.18 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 171.4, 136.9, 118.2, 46.5, 37.9, 29.3, 27.8, 15.3. HRMS (ESI, m/z): calcd for $C_{11}H_{18}NO_2S^+$, $[M + H]^+$, 228.1053, found 228.1056.

(3a*R*,4*S*,7*R*,7a*S*)-2-(3-(Methylthio)prop-1-en-2-yl)-3a,4,7,7a-tetrahydro-1*H*-4,7-epoxyisoindole-1,3(2H)-dione (3s). The reaction was carried out on a 0.3 mmol scale by following the general procedure A. The product **3s** was purified through column chromatography (PE/EtOAc from 8 : 1 to 2 : 1) as colorless oil (33 mg, 65% yield). IR ν_{max} (neat)/cm^{-1}: 3465, 3424, 2918, 2910, 1776, 1712, 1648, 1375, 1193, 871; ^{1}H NMR (600 MHz, $CDCl_3$): δ 6.55 (s, 2H), 5.44 (s, 1H), 5.34 (s, 1H), 5.21 (s, 1H), 3.42 (s, 2H), 2.94 (s, 2H), 2.03 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 175.0, 136.6, 134.2, 117.3, 47.4, 36.4, 14.7. HRMS (ESI, m/z): calcd for $C_{12}H_{14}NO_3S^+$, $[M + H]^+$, 252.0689, found 252.0692.

(3a*R*,4*R*,7*S*,7a*S*)-2-(3-(Methylthio)prop-1-en-2-yl)-3a,4,7,7a-tetrahydro-1*H*-4,7-epoxyisoindole-1,3(2*H*)-dione (3t). The reaction was carried out on a 0.3 mmol scale by following the general procedure A. The product **3t** was purified through column chromatography (PE/EtOAc from 8 : 1 to 1 : 1) as colorless oil (18 mg, 35% yield), **3i** was also detected in the reaction colorless oil (6 mg, 16% yield). IR ν_{max} (neat)/cm^{-1}: 3456, 2443, 3031, 2984, 2908, 1762, 1701, 1654, 1372, 1153, 1132, 905, 865, 706, 618; ^{1}H NMR (600 MHz, $CDCl_3$): δ 6.51 (s,

2H), 5.39–5.38 (m, 2H), 5.36 (s, 1H), 5.06 (s, 1H), 3.61 (dd, J = 1.8, 3.6 Hz, 2H), 3.33 (s, 2H), 2.01 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 173.7, 134.8, 134.0, 117.3, 79.7, 46.0, 36.3, 14.5. HRMS (ESI, m/z): calcd for $C_{12}H_{14}NO_3S^+$, $[M + H]^+$, 252.0689, found 252.0687.

General procedure B: to a flame-dried sealable 3-dram vial equipped with a stir bar was added imides **4** (0.3 mmol, 1.0 equiv.), $NaOAc \cdot 3H_2O$ (0.45 mmol, 1.5 equiv.), subsequently treated CH_3CN (3 mL, c = 0.1 M) was added to vial *via* syringe, the reaction mixture was stirred for 10 min at 22 °C. Then propargyl sulfonium salt **2a** (0.45 mmol, 1.5 equiv.) was added in one portion. The reaction was stirred at 50 °C for 6–12 h until imides **4** was fully consumed (monitored by TLC). The organic solvent was removed under reduced pressure and purified through column chromatography (eluent: petroleum ether and EtOAc) to afford the desired product **5**.

***N*-(3-(Methylthio)prop-1-en-2-yl)-*N*-(phenylsulfonyl)acetamide (5a).** The reaction was carried out on a 0.3 mmol scale by following the general procedure B. The product **5a** was purified through column chromatography (PE/EtOAc from 10 : 1 to 5 : 1) as colorless oil (18 mg, 32% yield). IR ν_{max} (neat)/cm^{-1}: 3478, 2430, 2925, 2918, 1704, 1635, 1362, 1339, 1249, 1172, 1080, 722, 623; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.06 (d, J = 7.8 Hz, 2H), 7.66 (t, J = 7.2 Hz, 1H), 7.56 (t, J = 7.8 Hz, 1H), 5.72 (s, 1H), 5.26 (s, 1H), 3.54 (s, 2H), 2.23 (s, 3H), 2.20 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 169.9, 141.1, 138.7, 133.9, 129.0, 128.7, 120.6, 39.8, 23.8, 15.9. HRMS (ESI, m/z): calcd for $C_{12}H_{16}NO_3S_2^+$, $[M + H]^+$, 286.0566, found 286.0569.

***N*-(3-(methylthio)prop-1-en-2-yl)-*N*-(phenylsulfonyl)octanamide (5b).** The reaction was carried out on a 0.3 mmol scale by following the general procedure B. The product **5b** was purified through column chromatography (PE/EtOAc from 35 : 1 to 18 : 1) as colorless oil (18 mg, 24% yield). IR ν_{max} (neat)/cm^{-1}: 3474, 2454, 2925, 2895, 1705, 1635, 1352, 1339, 1270, 1172, 1080, 823, 722, 623; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.07 (d, J = 8.4 Hz, 2H), 7.65 (t, J = 7.2 Hz, 1H), 7.56 (t, J = 7.8 Hz, 2H), 5.74 (s, 1H), 5.26 (s, 1H), 3.54 (s, 2H), 2.46 (t, J = 7.8 Hz, 2H), 2.01 (s, 3H), 1.56 (dd, J = 7.2, 13.8 Hz, 2H), 1.27–1.23 (m, 8H), 0.86 (t, J = 6.6 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 172.7, 140.6, 139.0, 133.8, 129.0, 128.7, 120.6, 39.9, 35.4, 31.5, 28.9, 28.8, 24.5, 22.5, 16.0, 14.0. HRMS (ESI, m/z): calcd for $C_{18}H_{28}NO_3S_2^+$, $[M + H]^+$, 370.1505, found 370.1506.

***N*-(3-(Methylthio)prop-1-en-2-yl)-*N*-(phenylsulfonyl)acetamide (5c).** The reaction was carried out on a 0.3 mmol scale by following the general procedure B. The product **5c** was purified through column chromatography (PE/EtOAc from 10 : 1 to 4 : 1) as colorless oil (34 mg, 56% yield). IR ν_{max} (neat)/cm^{-1}: 3445, 3416, 2954, 2925, 2869, 1691, 1642, 1339, 1265, 1157, 1136, 1087, 941, 799, 681, 617; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.95 (d, J = 8.4 Hz, 2H), 7.35 (d, J = 8.4 Hz, 2H), 5.71 (s, 1H), 5.25 (s, 1H), 3.53 (s, 2H), 2.46 (s, 3H), 2.22 (s, 3H), 2.20 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 169.9, 145.1, 141.2, 135.8, 130.0, 129.3, 129.1, 127.3, 120.4, 39.8, 23.9, 21.7, 15.9. HRMS (ESI, m/z): calcd for $C_{13}H_{18}NO_3S_2^+$, $[M + H]^+$, 300.0723, found 300.0726.

***N*-(3-(Methylthio)prop-1-en-2-yl)-*N*-(phenylsulfonyl)butyramide (5d).** The reaction was carried out on a 0.3 mmol scale by following the general procedure B. The product **5d** was purified through column chromatography (PE/EtOAc from 15 : 1 to 4 : 1) as colorless oil (21 mg, 32% yield). IR ν_{max} (neat)/cm^{-1}: 3445, 2954, 2925, 2869, 1699, 1642, 1339, 1270, 1172, 1157, 1087, 807, 681, 617; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.95 (d, J = 8.4 Hz, 2H), 7.34 (d, J = 7.8 Hz, 2H), 5.73 (s, 1H), 5.25 (s, 1H), 3.53 (s, 2H), 2.45 (t, J = 6.6 Hz, 2H), 2.21 (s, 3H), 2.07 (s, 3H), 1.61 (dd, J = 7.2, 15.0 Hz, 2H), 0.87 (t, J = 7.8 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 172.5, 145.0, 140.7, 136.0, 129.3, 129.1, 120.5, 39.9, 37.2, 21.7, 18.0, 16.0, 13.5. HRMS (ESI, m/z): calcd for $C_{15}H_{22}NO_3S_2^+$, $[M + H]^+$, 328.1036, found 328.1038.

***N*-(3-(Methylthio)prop-1-en-2-yl)-*N*-tosyloctanamide (5e).** The reaction was carried out on a 0.3 mmol scale by following the general procedure B. The product **5e** was purified through column chromatography (PE/EtOAc from 15 : 1 to 4 : 1) as colorless oil (42 mg, 55% yield). IR ν_{max} (neat)/cm^{-1}: 3474, 2454, 2923, 2895, 1705, 1635, 1352, 1339, 1270, 1172, 1080, 813, 728, 625; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.94 (d, J = 7.8 Hz, 2H), 7.33 (d, J = 7.8 Hz, 2H), 5.72 (s, 1H), 5.25 (s, 1H), 3.52 (s, 2H), 2.45 (t, J = 7.2 Hz, 5H), 2.20 (s, 3H), 1.55 (t, J = 7.2 Hz, 2H), 1.28–1.22 (m, 8H), 0.86 (t, J = 6.6 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 172.7, 144.9, 140.6, 136.0, 129.3, 129.0, 120.5, 39.9, 35.3, 31.5, 28.9, 28.8, 24.5, 22.5, 21.6, 15.9, 14.0. HRMS (ESI, m/z): calcd for $C_{19}H_{30}NO_3S_2^+$, $[M + H]^+$, 384.1662, found 384.1665.

To a flame-dried sealable 3-dram vial equipped with a stir bar was added imides **1a** (0.3 mmol, 1.0 equiv.), $NaOAc \cdot 3H_2O$ (0.45 mmol, 1.5 equiv.), subsequently treated CH_3CN (3 mL, c = 0.1 M) was added to vial *via* syringe, the reaction mixture was stirred for 10 min at 22 °C. Then propargyl sulfonium salt **2b** (0.45 mmol, 1.5 equiv.) was added in one portion. The reaction was stirred at 50 °C for 6 h until imide **1a** was fully consumed (monitored by TLC). The organic solvent was removed under reduced pressure and purified through column chromatography (eluent: petroleum ether and EtOAc) to afford the desired product **3a.**

To a flame-dried sealable 3-dram vial equipped with a stir bar was added saccharin **6** (0.3 mmol, 1.0 equiv.), $NaOAc \cdot 3H_2O$ (0.45 mmol, 1.5 equiv.), anhydrous DMF (3 mL, c = 0.1 M) was added to vial *via* syringe, the reaction mixture was stirred for 10 min at 22 °C. Then **2a** (0.45 mmol, 1.5 equiv.) was added in one portion. The reaction was stirred at 50 °C for 12 h until saccharin **6** was fully consumed (monitored by TLC). The organic solvent was removed under reduced pressure and purified through column chromatography (eluent: petroleum ether and EtOAc) to afford the desired product **7**.

2-(3-(Methylthio)prop-1-en-2-yl)benzo[*d*]isothiazol-3(2*H*)-one 1,1-dioxide (7). The reaction was carried out on a 0.3 mmol scale by following the general procedure. The product **7** was purified through column chromatography (PE/EtOAc from 15 : 1 to 4 : 1) as colorless oil (28 mg, 52% yield). IR ν_{max} (neat)/cm^{-1}: 3452, 3093, 3072, 3038, 2925, 1733, 1607, 1473, 1319, 1172, 982, 751, 591; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.91 (dd, J = 3.0, 5.4 Hz, 2H), 7.77 (dd, J = 2.4, 5.4 Hz, 2H), 5.49 (s, 1H), 5.33 (s, 1H), 3.61 (s, 2H), 2.06 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 158.0, 137.7, 135.0, 134.4, 133.5, 126.8, 125.5, 121.1, 117.2, 36.9, 14.8. HRMS (ESI, m/z): calcd for $C_{11}H_{12}NO_3S_2^+$, $[M + H]^+$, 270.0253, found 270.0255.

To a flame-dried sealable 3-dram vial equipped with a stir bar was added thalidomide **8** (0.3 mmol, 1.0 equiv.), $NaOAc \cdot 3H_2O$ (0.45 mmol, 1.5 equiv.), subsequently treated CH_3CN (3 mL, c = 0.1 M) was added to vial *via* syringe, the reaction mixture was stirred for 10 min at 22 °C. Then propargyl sulfonium salt **2a** (0.45 mmol, 1.5 equiv.) was added in one portion. The reaction was stirred at 50 °C for 12 h until thalidomide **8** was fully consumed (monitored by TLC). The organic solvent was removed under reduced pressure and purified through column chromatography (eluent: petroleum ether and EtOAc) to afford the desired product **9**.

2-(1-(3-(Methylthio)prop-1-en-2-yl)-2,6-dioxopiperidin-3-yl) isoindoline-1,3-dione (9). The reaction was carried out on a 0.3 mmol scale by following the general procedure. The product **9** was purified through column chromatography (PE/EtOAc from 8 : 1 to 1 : 1) as colorless oil (60 mg, 87% yield). IR ν_{max} (neat)/cm^{-1}: 3445, 3407, 2961, 2925, 2848, 1720, 1684, 1388, 1262, 1193, 1116, 722; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.90 (dd, J = 3.6, 5.4 Hz, 2H), 7.79–7.78 (m, 2H), 5.57 (s, 1H), 5.23 (s, 1H), 5.99 (dd, J = 6.0, 12.6 Hz, 1H), 3.33 (dd, J = 15.0, 22.8 Hz, 2H), 3.04 (dd, J = 2.4, 13.2 Hz, 1H), 2.90–2.87 (m, 2H), 2.20–2.17 (m, 1H), 2.08 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 170.3, 167.9, 167.3, 136.9, 134.4, 131.8, 123.7, 118.4, 50.1, 37.5, 32.1, 22.1, 15.3. HRMS (ESI, m/z): calcd for $C_{17}H_{17}N_2O_4S^+$, $[M + H]^+$, 345.0904, found 345.0905.

To a flame-dried sealable 3-dram vial equipped with a stir bar was added pomalidomide **10** (0.3 mmol, 1.0 equiv.), $NaOAc \cdot 3H_2O$ (0.45 mmol, 1.5 equiv.), subsequently treated DMF (3 mL, c = 0.1 M) was added to vial *via* syringe, the reaction mixture was stirred for 10 min at 22 °C. Then propargyl sulfonium salt **2a** (0.45 mmol, 1.5 equiv.) was added in one portion. The reaction was stirred at 50 °C for 12 h until pomalidomide **10** was fully consumed (monitored by TLC). The organic solvent was removed under reduced pressure and purified through column chromatography (eluent: petroleum ether and EtOAc) to afford the desired product **11**.

3-Amino-2-(1-(3-(methylthio)prop-1-en-2-yl)-2,6-dioxopiperidin-3-yl)isoindoline-1,3-dione (11). The reaction was carried out on a 0.3 mmol scale by following the general procedure. The product **11** was purified through column chromatography (PE/EtOAc from 8 : 1 to 1 : 1) as colorless oil (58 mg, 80% yield). IR ν_{max} (neat)/cm^{-1}: 3432, 3397, 2958, 2925, 2851, 1725, 1681, 1378, 1256, 1191, 1107, 718; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.43 (t, J = 7.8 Hz, 1H), 7.16 (d, J = 7.2 Hz, 1H), 6.88 (d, J = 8.4 Hz, 1H), 5.57 (s, 1H), 5.28 (s, 2H), 5.23 (s, 1H), 5.31 (dd, J = 4.8, 12.0 Hz, 1H), 3.33 (dd, J = 15.0, 21.6 Hz, 2H), 3.06–2.98 (m, 1H), 2.90–2.82 (m, 2H), 2.16–2.15 (m, 1H), 2.09 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 170.5, 168.9, 168.3, 167.5, 145.6, 136.9, 135.5, 132.3, 121.4, 118.4, 113.1, 110.8, 49.6, 37.5, 32.1, 22.1, 15.3. HRMS (ESI, m/z): calcd for $C_{17}H_{18}N_3O_4S^+$, $[M + H]^+$, 360.1013, found 360.1016.

To a flame-dried 100 mL round bottom flask equipped with a stir bar was added phthalimide **1a** (1.01 g, 6.8 mmol, 1.0 equiv.), $NaOAc \cdot 3H_2O$ (1.39 g, 10.2 mmol, 1.5 equiv.), subsequently treated CH_3CN (68 mL, c = 0.1 M) was added to vial *via* syringe, the reaction mixture was stirred for 10 min at 22 °C. Then propargyl sulfonium salt **2a** (1.85 g, 10.2 mmol, 1.5 equiv.) was added in one portion. The reaction was stirred at 50 °C for 10 h until phthalimide **1a** was fully consumed (monitored by TLC). The organic solvent was removed under reduced pressure and purified through column chromatography (eluent: petroleum ether and EtOAc) to afford the desired product **3** with yield of 65% (1.03 g).

To a flame-dried sealable 2-dram vial equipped with a stir bar was added phthalimide **3a** (50 mg, 0.2 mmol, 1.0 equiv.), Na_2CO_3 (42.4 mg, 0.4 mmol, 2.0 equiv.) and CH_2Cl_2 (3 mL, c = 0.2 M). After stirred at 0 °C for 2 min, *m*-CPBA (103.5 mg, 0.6 mmol, 75%, 3.0 equiv.) was added in portions to the mixture. The reaction mixture was kept stirring for 10 min at 0 °C until **3a** was fully consumed (monitored by TLC). The reaction was quenched with aqueous Na_2CO_3 and extracted with CH_2Cl_2 (5 mL × 3). The combined organic solvent was dried with anhydrous Na_2SO_4, removed under reduced pressure and purified through column chromatography (eluent: petroleum ether and EtOAc) to afford the desired product **12** (50 mg, 94%).

2-(3-(Methylsulfonyl)prop-1-en-2-yl)isoindoline-1,3-dione (12). The product **12** was purified through column chromatography (eluent: petroleum ether and EtOAc) as colorless oil (50 mg, 94% yield). IR ν_{max} (neat)/cm^{-1}: 3486, 3416, 3129, 3023, 2995, 2925, 1776, 1720, 1648, 1362, 1311, 1123, 1080, 877, 722, 485; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.91 (d, J = 3.0 Hz, 2H), 7.79 (dd, J = 3.0, 5.4 Hz, 2H), 5.77 (s, 1H), 5.66 (s, 1H), 4.27 (s, 2H), 3.00 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 166.7, 134.6, 131.5, 127.9, 124.0, 122.8, 57.5, 39.3. HRMS (ESI, m/z): calcd for $C_{12}H_{12}NO_4S^+$, $[M + H]^+$, 266.0482, found 266.0481.

Conflicts of interest

The authors declare no conflicts of interest.

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