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Copper-Catalyzed Intermolecular Thioamination of Maleimides with Thiols and Formamides: A One-Step Construction of 3-Amino-4-thiomaleimides Using Formamides as Nitrogen Sources

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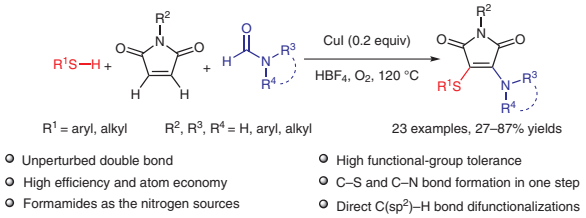

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Abstract A highly efficient copper-catalyzed intermolecular C(sp^2)–H thioamination of maleimides with thiols and formamides in the presence of fluoroboric acid is reported using various readily available formamides as nitrogen sources and solvents. A diverse range of 3-amino-4-thiomaleimides is obtained with good yields under mild conditions, involving C–N and C–S bond formation. This methodology enriches current C–N and C–S bond formation chemistry and features operational simplicity and excellent functional-group tolerance.

Key words copper catalysis, thioamination, maleimides, thiols, formamides

Maleimides constitute the core structure of numerous natural products and pharmaceuticals with diverse biological activities.[1] They can also be converted into diverse, important heterocyclic frameworks such as succinimides, pyrrolidines, lactims, and γ-lactams.[2] Thus, a great deal of attention has been focused on the development of new synthetic routes to access functionalized maleimides.[3] In particular, as a result of their antibacterial and antitumor activities, the development of more concise and efficient methods to construct 3-amino-4-thiomaleimides has particular significance in organic synthesis and the pharmaceutical industry.[4] However, to the best of our knowledge, an intermolecular thioamination of maleimides using formamides as nitrogen sources has not yet been reported. The most likely reason is that dimethylamine is a poisonous, flammable gas with a strong pungent odor. It is extremely dangerous and is difficult to manipulate at high temperatures. Thus, the further development of novel and practical nitrogen sources for the one-step construction of 3-amino-4-thiomaleimides still remains a considerable challenge.

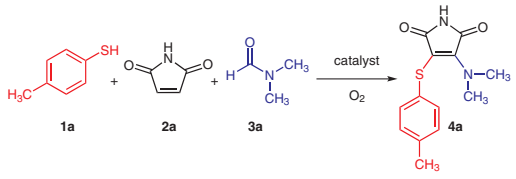
Metal-catalyzed direct functionalization of C–H bonds has gained enormous attention over the past few decades as a powerful and straightforward method to construct new C–X bonds (X = heteroatom).[5] In particular, copper-catalyzed aerobic oxidative reactions have become increasingly attractive.[6] In addition, *N*,*N*-dimethylformamide (DMF) is a polar solvent that has been used as a precursor for $-NMe_2$, $-CONMe_2$, $-CHNMe_2$ and –CN groups.[7] Among these transformations, the decarbonylation of DMF as a source of $-NMe_2$ has elicited the attention of chemists.[8] Replacement of pungent and toxic dimethylamine by DMF is highly desirable from the standpoint of green chemistry. In consideration of our previous studies on maleimides[9] and the importance of the introduction of nitrogen and sulfur functional groups,[10] we herein present an extremely practical and highly efficient method for preparing 3-amino-4-thiomaleimides via copper-catalyzed intermolecular thioamination of maleimides using formamides as nitrogen sources and solvents.

Initially, *p*-thiocresol (**1a**), maleimide (**2a**) and DMF (**3a**) were used as the model substrates to optimize the reaction conditions. The reaction was performed at 120 °C in the presence of CuCl as the catalyst and acetic acid as an additive under air for 8 hours. The desired product **4a** was isolated in 18% yield (Table 1, entry 1). The yield of **4a** dramatically increased to 43% when the reaction was conducted under an atmosphere of pure oxygen (Table 1, entry 2). Clearly, O_2 was beneficial to the efficient formation of **4a**. We next altered several parameters to improve the yield of the desired product. First, several copper salts were examined, among which CuI showed the best activity (Table 1, entries 2–5). In addition, no reaction occurred in the absence of a catalyst (Table 1, entry 6), and none of the desired product was obtained when the copper catalyst was replaced with other metal catalysts such as $AgNO_3$ or $FeCl_3$ (Table 1, entries 7 and 8). The use of $Mn(OAc)_3$ as the cata-

lyst resulted in only a 18% yield of product **4a** (Table 1, entry 9). This implies that Cu plays an important role in this reaction. Subsequently, a series of additives was examined (Table 1, entries 10–14). HBF_4 afforded the best result for this transformation. Moreover, when different amounts of HBF_4 were used (Table 1, entries 14–16), one equivalent of HBF_4 was found to provide the highest yield. None of the desired product was obtained in the absence of an additive (Table 1, entry 17), suggesting the importance of acid in the reaction. Subsequent experiments varying the amount of CuI showed that 20 mol% of CuI was optimal (Table 1, entries 18–20). Finally, examination of the effect of the reaction temperature indicated that 120 °C was ideal for successful product formation (Table 1, entries 19, 21 and 22).

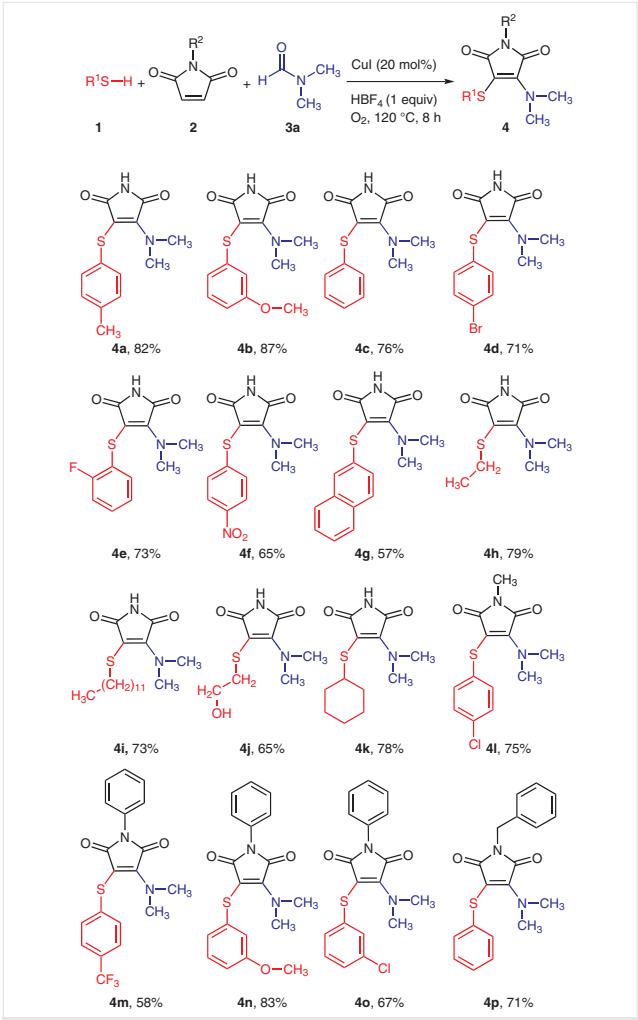
With optimized reaction conditions in hand, we next investigated the substrate scope with regard to the thiol component. As shown in Scheme 1, the reactions proceeded smoothly in moderate to good yields with substrates containing electron-donating groups and electron-withdrawing groups. In general, thiophenols bearing electron-withdrawing groups produced lower yields. For example, when 3-methoxythiophenol was treated with maleimide and DMF under the optimized conditions, the isolated yield of **4b** was 87%, whereas a thiophenol with a strong electron-withdrawing 4-NO_2 group furnished a lower yield (65%) of **4f**. Halogens were all well tolerated, and the corresponding products (**4d**, **4e**, **4l**, and **4o**) could be applied in further reactions. Product **4e** was crystallized and X-ray crystal struc-

Table 1 Optimization of the Reaction Conditions[a]



Entry	Catalyst (equiv)	Additive	Temp (°C)	Yield (%)[b]
1[c]	CuCl (1.0)	AcOH	120	18
2	CuCl (1.0)	AcOH	120	43
3	CuBr (1.0)	AcOH	120	51
4	CuI (1.0)	AcOH	120	66
5	$CuCl_2$ (1.0)	AcOH	120	27
6	–	AcOH	120	0
7	$AgNO_3$	AcOH	120	0
8	$FeCl_3$	AcOH	120	0
9	$Mn(OAc)_3$	AcOH	120	18
10	CuI (1.0)	HCl	120	25
11	CuI (1.0)	L-proline	120	39
12	CuI (1.0)	benzoic acid	120	65
13	CuI (1.0)	HI	120	47
14	CuI (1.0)	HBF_4	120	76
15[d]	CuI (1.0)	HBF_4	120	36
16[e]	CuI (1.0)	HBF_4	120	71
17	CuI (1.0)	–	120	0
18	CuI (0.5)	HBF_4	120	79
19	CuI (0.2)	HBF_4	120	82
20	CuI (0.1)	HBF_4	120	54
21	CuI (0.2)	HBF_4	100	69
22	CuI (0.2)	HBF_4	140	75

[a] Reaction conditions: **1a** (2.1 mmol), **2a** (2.0 mmol), **3a** (6.0 mL), catalyst, additive (2.0 mmol), O_2 balloon, 8 h.
[b] Yield of isolated product.
[c] Air atmosphere.
[d] HBF_4 (1.0 mmol).
[e] HBF_4 (3.0 mmol).



Scheme 1 Cu-catalyzed C–H difunctionalization of maleimides with thiols and dimethyl formamide. *Reagents and conditions*: **1** (2.1 mmol), **2** (2.0 mmol), **3** (6 mL), CuI (20 mol%), HBF_4 (1 equiv), O_2 balloon, 8 h.

ture analysis unambiguously confirmed the structure of the thioamination product (Figure 1).[11] Steric effects had minimal influence on the transformation, as shown by the comparable yields of the products **4e** (73%) and **4o** (67%) obtained from the 2-F and 3-Cl substrates, respectively. Moreover, aliphatic thiols also underwent smooth conversion to give products **4h–k** in yields of 65–79%. Importantly, N-substituted maleimides (methyl, phenyl, and benzyl) showed no significant impact on the reaction yields, affording compounds **4l–p** in 58–83% yield. We also tested the functional group tolerance in the reaction of thioglycol, maleimide, and DMF, observing that a hydroxy substituent had no marked effect on the reaction, with product **4j** being obtained in 65% yield. However, no reaction occurred when the maleimide was replaced with other alkenes such as maleic anhydride, benzoquinone, styrene or norbornene.

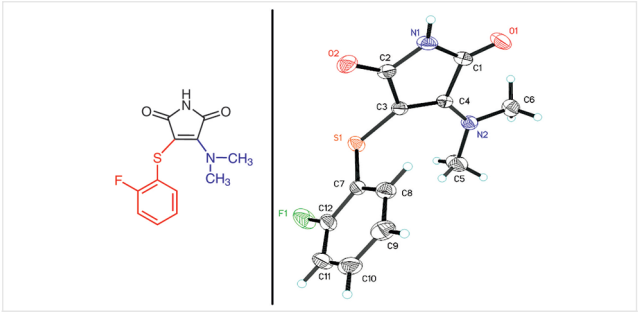
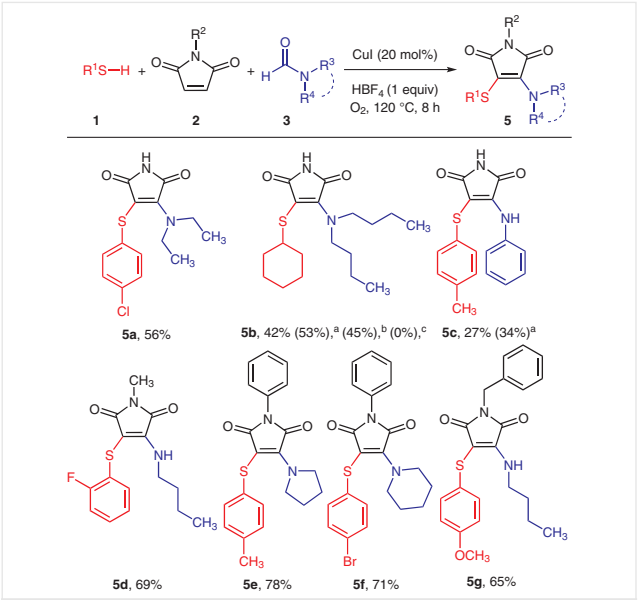


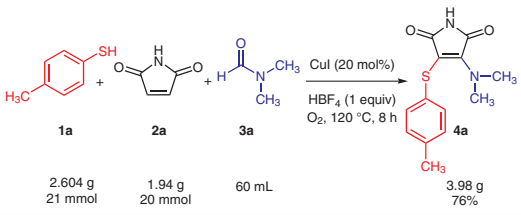
Figure 1 ORTEP representation of the X-ray crystal structure of **4e**



Scheme 2 Cu-catalyzed C–H difunctionalization of maleimides with thiols and various formamides. *Reagents and conditions*: **1** (2.1 mmol), **2** (2.0 mmol), **3** (6 mL), CuI (20 mol%), HBF_4 (1 equiv), O_2 balloon, 8 h, unless otherwise indicated. [a] *Reagents and conditions*: **1** (2.1 mmol), **2** (2.0 mmol), dibutylamine or aniline (2.1 mmol), DMA (6 mL), CuI (20 mol%), HBF_4 (1 equiv), O_2 balloon, 8 h. [b] *Reagents and conditions*: **1** (2.1 mmol), **2** (2.0 mmol), dibutylamine (2.1 mmol), DMSO (6 mL), CuI (20 mol%), HBF_4 (1 equiv), O_2 balloon, 8 h. [c] *Reagents and conditions*: **1** (2.1 mmol), **2** (2.0 mmol), dibutylamine (2.1 mmol), toluene (6 mL), CuI (20 mol%), HBF_4 (1 equiv), O_2 balloon, 8 h.

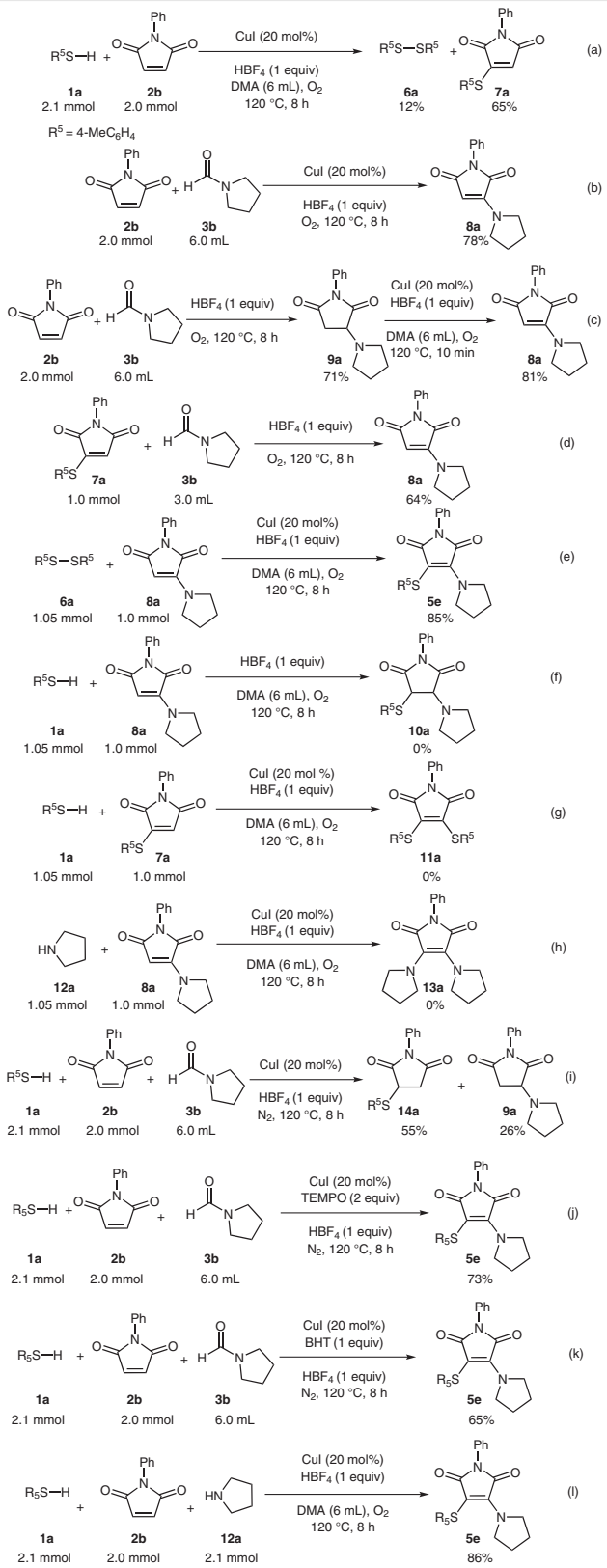
A series of formamides was also examined to expand the synthetic utility of this protocol (Scheme 2). With N,N-disubstituted formamides, lower yields of products (**4a** vs **5a** and **5b**) were obtained when longer alkyl chains were present. These results could be attributed to increased steric hindrance surrounding the formamide nitrogen. Meanwhile, the formamides derived from cyclic amines produced higher yields (**5e** and **5f**) compared with those derived from linear amines. Again, substituents (methyl, phenyl, and benzyl) on the maleimide nitrogen had no obvious impact on the reaction yield. Finally, we used dibutylamine instead of *N*,*N*-dibutylformamide in several typical solvents (DMA, DMSO and toluene). DMA was slightly superior to the others and proved to be the best solvent for this transformation. However, the yields of the desired products **5b** and **5c** were not improved to any great extent when formamides were replaced with amines. The results can be attributed to the larger steric hindrance of dibutylamine and weaker nucleophilicity of aniline.

To further demonstrate the value of this synthetic method, a gram-scale copper-catalyzed intermolecular C(sp^2)–H thioamination of maleimide (**2a**) with *p*-thiocresol (**1a**) and formamide **3a** in the presence of fluoroboric acid was performed. The reaction proceeded smoothly, delivering the 3-amino-4-thiomaleimide **4a** in 76% yield under the optimized reaction conditions (Scheme 3).



Scheme 3 Gram-scale synthesis 3-amino-4-thiomaleimide **4a**

To acquire insight into the mechanism, various control experiments were conducted. First, a small amount of bis(4-methylphenyl)disulfide (**6a**) was obtained in the reaction between *p*-thiocresol (**1a**) and *N*-phenylmaleimide (**2b**) under standard conditions in DMA (6 mL), in addition to the thio-Michael addition oxidative dehydrogenation product **7a** (65%) (Scheme 4, eq a). Second, *N*-phenylmaleimide (**2b**) was reacted with 1-formylpyrrolidine (**3b**) to produce 1-phenyl-3-(pyrrolidin-1-yl)-1*H*-pyrrole-2,5-dione (**8a**) in 78% yield (Scheme 4, eq b). We also found that the aza-Michael addition product **9a** could be easily oxidized to **8a** in good yield in ten minutes (Scheme 4, eq c). At



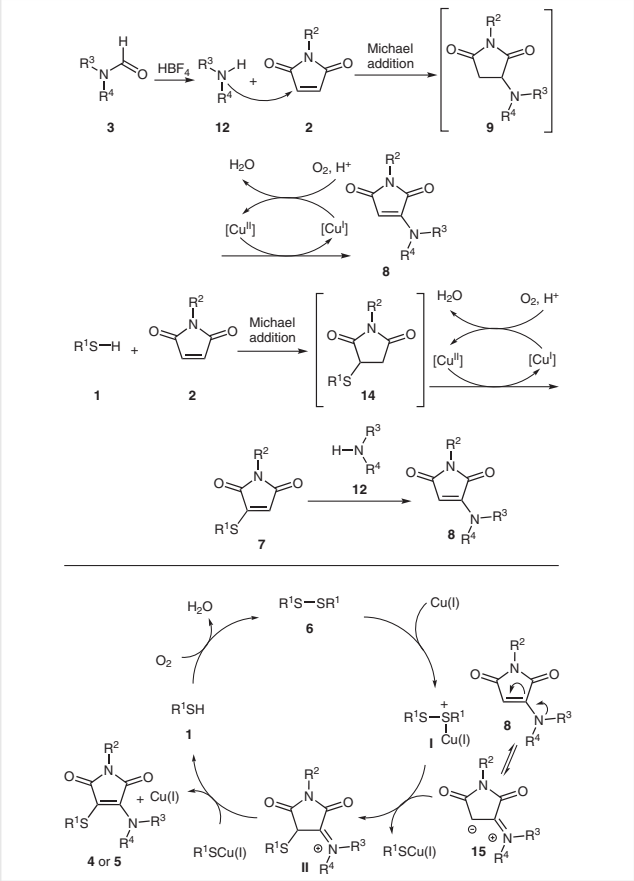
Scheme 4 Control experiments

the same time, the product **7a** could further react with 1-formylpyrrolidine (**3b**) by nucleophilic substitution to produce **8a** in 64% yield (Scheme 4, eq d). Subsequent treatment of **8a** with bis(4-methylphenyl)disulfide (**6a**) proved that product **5e** could be obtained in good yield (Scheme 4, eq e). However, these Michael addition reactions failed under standard conditions, excluding the possibility of double Michael addition and oxidative dehydrogenation processes in the reaction (Scheme 4, eqs f–h). None of target product **5e** was detected under a N_2 atmosphere (Scheme 4, eq i), suggesting that oxygen plays an important role in the formation of the product. Moreover, when the radical scavengers TEMPO (2.0 equiv) and BHT (2.0 equiv) were added to the reaction mixture, respectively, the thioamination of *N*-phenylmaleimide (**2b**) proceeded smoothly to afford the desired product **5e** in 73% or 65% yield. These results therefore ruled out the possibility of a radical pathway (Scheme 4, eqs j and k). In addition, **5e** was obtained in 86% yield when 1-formylpyrrolidine (**3b**) was replaced with pyrrolidine (**12a**) (Scheme 4, eq l). These results show that the compounds **6a**, **7a**, **8a**, **9a** and **14a** are all intermediates in the reaction, and that **12a** is another intermediate obtained via decarbonylation of 1-formylpyrrolidine (**3b**).

Based on the above experimental data and precedents, a putative mechanism is depicted in Scheme 5. Formamide **3** is decarbonylated by HBF_4 to form amine **12**.[10] Next, the amine **12** undergoes an aza-Michael addition with maleimide **2** to form 3-aminosuccinimide **9**, which could afford 3-aminomaleimide **8** via a copper-catalyzed aerobic oxidative dehydrogenation.[12] Because the reaction is conducted under O_2, the Cu(I) species in this reaction is easily oxidized to Cu(II), showing that the reaction can be catalyzed by a copper species with O_2 as the terminal oxidant.[13] Alternatively, compound **8** could also be easily obtained via the nucleophilic substitution between amine **12** and 3-thiomaleimide **7**,[14] which have also been synthesized by thio-Michael addition and oxidative dehydrogenation processes.[9b] Next, the Cu(I) catalyst interacts with disulfide **6** to generate intermediate **I**.[15] Subsequently, the regioselective electrophilic attack of **I** on 3-aminomaleimide **8** at the 4-position (via its isomer **15**) results in the formation of the intermediate **II**, which undergoes deprotonation to furnish the maleimide product and regenerate the copper catalyst.[16] At the same time, the oxidation of the in situ generated R^1SH species by O_2 reproduces disulfide **6**.[17] Oxygen plays an important role in the regeneration of the catalytically active species and the oxidative dimerization of the thiols.

In summary, we have reported an efficient strategy for the thioamination of maleimides with thiols and formamides in the presence of fluoroboric acid, using various formamides as the nitrogen sources and solvents. Using an inexpensive Cu(I) catalyst, maleimides have been successfully coupled with two different heteroatom-based nucleophiles under mild conditions, offering 3-amino-4-thiomaleimides in good yields. The operational simplicity, inexpensive na-

ture of the reaction components, excellent functional group tolerance and the importance of the heteroatom-functionalized maleimides bode well for the rapid adaptation of this reaction in chemical synthesis and clinical medicine.



Scheme 5 Proposed reaction mechanism

All experiments were carried out under O_2 or N_2 atmospheres. All chemicals and solvents were obtained from commercial suppliers and used without further purification. Melting points were determined with a RY-1 melting point apparatus and are uncorrected. IR spectra were recorded as KBr pellets on a Shimadzu 470 spectrophotometer. NMR (^{1}H and ^{13}C) spectra were recorded using Bruker AV 400 or 600 MHz spectrometers in DMSO-d_6 or $CDCl_3$ with TMS as the internal standard. Chemical shifts (δ) are recorded in ppm. Mass spectra were acquired on Waters Micromass GCT Premier, Agilent Technologies 5973N and Thermo Fisher Scientific LTQ FT Ultra spectrometers.

3-Amino-4-thiomaleimides 4 and 5; Typical Procedure

A solution of CuI (0.4 mmol), thiol **1** (2.1 mmol), maleimide **2** (2.0 mmol), formamide **3** (2.0 mmol) and 40% HBF_4 (6 mL) was stirred at 120 °C for 8 h under O_2. After cooling to room temperature, H_2O (10 mL) was added and the resulting mixture was extracted with EtOAc (3 × 10 mL). The combined organic phase was dried over anhydrous Na_2SO_4, concentrated and purified by silica gel column chromatography (eluent: EtOAc/PE, 1:5~20) to yield the pure product **4** or **5**.

3-(Dimethylamino)-4-[(4-methylphenyl)thio]-1*H*-pyrrole-2,5-dione (4a)

Yield: 0.43 g (82%); yellow crystalline solid; mp 187–189 °C.

IR (KBr): 3180, 1758, 1687, 1605, 1478, 1425, 1338, 1288, 1239, 1117, 1041, 933, 847, 757, 647 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.24 (s, 3 H), 3.38 (s, 6 H), 7.05 (d, *J* = 6.6 Hz, 2 H), 7.10 (d, *J* = 6.7 Hz, 2 H), 10.75 (s, 1 H).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 20.89, 42.04, 86.15, 125.74, 130.22, 134.77, 136.41, 152.33, 167.19, 171.00.

MS (EI): *m*/*z* = 262 [M]$^+$, 229, 190, 135, 105, 91, 65.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{13}H_{14}O_2N_2S$: 262.0776; found: 262.0777.

3-(Dimethylamino)-4-[(3-methoxyphenyl)thio]-1*H*-pyrrole-2,5-dione (4b)

Yield: 0.48 g (87%); yellow crystalline solid; mp 150–152 °C.

IR (KBr): 3177, 1684, 1603, 1484, 1424, 1337, 1241, 1040, 933, 840, 795, 752, 649 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 3.39 (s, 6 H), 3.72 (s, 3 H), 6.68 (d, *J* = 4.0 Hz, 1 H), 6.71 (d, *J* = 4.3 Hz, 2 H), 7.20 (t, *J* = 7.8 Hz, 1 H), 10.78 (s, 1 H).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 42.09, 55.57, 85.30, 99.99, 111.01, 117.64, 130.54, 141.48, 152.59, 160.25, 167.08, 170.92.

MS (EI): *m*/*z* = 278 [M]$^+$, 245, 233, 206, 192, 151, 121, 96, 64.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{13}H_{14}O_3N_2S$: 278.0725; found: 278.0731.

3-(Dimethylamino)-4-(phenylthio)-1*H*-pyrrole-2,5-dione (4c)

Yield: 0.38 g (76%); yellow crystalline solid; mp 188–190 °C.

IR (KBr): 3164, 2375, 1749, 1692, 1605, 1466, 1418, 1336, 1111, 1028, 935, 843, 737, 650 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 3.39 (s, 6 H), 7.11 (d, *J* = 7.3 Hz, 1 H), 7.16 (d, *J* = 7.6 Hz, 2 H), 7.29 (t, *J* = 7.7 Hz, 2 H), 10.78 (s, 1 H).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 42.07, 85.45, 125.41, 125.45, 129.58, 139.99, 152.59, 167.12, 170.94.

MS (EI): *m*/*z* = 248 [M]$^+$, 215, 177, 121, 96, 65.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{12}H_{12}O_2N_2S$: 248.0619; found: 248.0622.

3-[(4-Bromophenyl)thio]-4-(dimethylamino)-1*H*-pyrrole-2,5-dione (4d)

Yield: 0.46 g (71%); yellow crystalline solid; mp 192–194 °C.

IR (KBr): 3213, 1753, 1705, 1605, 1424, 1329, 1242, 1004, 935, 840, 797, 720, 641 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 3.39 (s, 6 H), 7.13 (d, *J* = 8.0 Hz, 2 H), 7.46 (d, *J* = 8.0 Hz, 2 H), 10.83 (s, 1 H).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 42.12, 84.55, 118.13, 127.49, 132.28, 139.79, 152.72, 166.99, 170.81.

MS (EI): *m*/*z* = 326 [M]$^+$, 255, 214, 199, 171, 139, 96, 81.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{12}H_{11}O_2N_2SBr$: 325.9725; found: 325.9727.

3-(Dimethylamino)-4-[(2-fluorophenyl)thio]-1*H*-pyrrole-2,5-dione (4e)

Yield: 0.39 g (73%); yellow crystalline solid; mp 210–212 °C.

IR (KBr): 3161, 2376, 1748, 1691, 1607, 1468, 1414, 1337, 1249, 1120, 1112, 1029, 933, 810, 751, 646 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 3.39 (s, 6 H), 7.13–7.21 (m, 4 H), 10.84 (s, 1 H).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 42.14, 82.22, 115.66 (d, *J* = 20.6 Hz), 125.77 (d, *J* = 3.1 Hz), 127.02 (d, *J* = 3.1 Hz), 127.11, 127.90 (d, *J* = 2.5 Hz), 153.28, 158.24 (d, *J* = 241.0 Hz), 166.89, 170.74.

MS (EI): *m*/*z* = 266 $[M]^+$, 233, 195, 139, 109, 96.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{12}H_{11}O_2N_2FS$: 266.0525; found: 266.0529.

3-(Dimethylamino)-4-[(4-nitrophenyl)thio]-1*H*-pyrrole-2,5-dione (4f)

Yield: 0.38 g (65%); yellow crystalline solid; mp 203–205 °C.

IR (KBr): 3212, 1755, 1704, 1611, 1511, 1424, 1336, 1078, 1042, 935, 844, 740, 647 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 3.39 (s, 6 H), 7.43 (d, *J* = 8.9 Hz, 2 H), 8.11 (d, *J* = 8.9 Hz, 2 H), 10.91 (s, 1 H).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 42.23, 82.80, 124.55, 125.64, 145.09, 150.34, 153.13, 166.77, 170.50.

MS (EI): *m*/*z* = 293 $[M]^+$, 260, 222, 166, 139, 120, 96, 82, 69, 55, 42.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{12}H_{11}O_4N_3S$: 293.0470; found: 293.0474.

3-(Dimethylamino)-4-(2-naphthalenylthio)-1*H*-pyrrole-2,5-dione (4g)

Yield: 0.34 g (57%); yellow crystalline solid; mp 178–180 °C.

IR (KBr): 3213, 3051, 1757, 1702, 1606, 1500, 1426, 1341, 1250, 1199, 1123, 1043, 939, 849, 812, 746, 648 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 3.41 (s, 6 H), 7.34 (d, *J* = 8.5 Hz, 1 H), 7.41–7.50 (m, 2 H), 7.63 (s, 1 H), 7.84 (d, *J* = 6.9 Hz, 3 H), 10.83 (s, 1 H).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 42.13, 85.31, 122.85, 124.38, 125.77, 127.14, 127.34, 128.13, 129.03, 131.41, 134.09, 137.82, 152.86, 167.23, 171.04.

MS (EI): *m*/*z* = 298 $[M]^+$, 265, 253, 226, 184, 171, 141, 127, 115, 96, 81, 69, 55, 42.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{16}H_{14}O_2N_2S$: 298.0776; found: 298.0775.

3-(Dimethylamino)-4-(ethylthio)-1*H*-pyrrole-2,5-dione (4h)

Yield: 0.32 g (79%); yellow crystalline solid; mp 120–122 °C.

IR (KBr): 3161, 3033, 2969, 2927, 1753, 1683, 1604, 1421, 1343, 1251, 1199, 1117, 1046, 931, 844, 763, 635, 592 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 1.13 (t, *J* = 7.4 Hz, 3 H), 2.57 (q, *J* = 7.4 Hz, 2 H), 3.39 (s, 6 H), 10.55 (s, 1 H).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 14.79, 30.16, 42.22, 90.47, 150.56, 167.70, 171.30.

MS (EI): *m*/*z* = 200 $[M]^+$, 185, 172, 157, 139, 125, 115, 100, 85, 70, 57, 42.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_8H_{12}O_2N_2S$: 200.0619; found: 200.0621.

3-(Dimethylamino)-4-(dodecylthio)-1*H*-pyrrole-2,5-dione (4i)

Yield: 0.50 g (73%); yellow crystalline solid; mp 83–85 °C.

IR (KBr): 3252, 2914, 2851, 1765, 1695, 1592, 1463, 1426, 1332, 1247, 1023, 935, 718, 642 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 0.85 (t, *J* = 6.8 Hz, 3 H), 1.23–1.31 (m, 18 H), 1.43–1.50 (m, 2 H), 2.56 (t, *J* = 7.2 Hz, 2 H), 3.39 (s, 6 H), 10.54 (s, 1 H).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 14.44, 22.57, 28.46, 29.03, 29.17, 29.22, 29.40, 29.43, 29.47, 29.49, 31.76, 36.23, 42.10, 91.06, 150.26, 167.70, 171.21.

MS (EI): *m*/*z* = 340 $[M]^+$, 172, 157, 139, 115, 100, 85, 69, 55, 40.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{18}H_{32}O_2N_2S$: 340.2185; found: 340.2187.

3-(Dimethylamino)-4-[(2-hydroxyethyl)thio]-1*H*-pyrrole-2,5-dione (4j)

Yield: 0.28 g (65%); yellow crystalline solid; mp 143–145 °C.

IR (KBr): 3546, 3266, 2921, 1746, 1700, 1605, 1344, 1005, 939, 750, 646 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 2.64 (d, *J* = 6.0 Hz, 2 H), 3.40 (s, 6 H), 3.49 (d, *J* = 5.6 Hz, 2 H), 4.71 (s, 1 H), 10.57 (s, 1 H).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 38.83, 42.21, 60.29, 90.30, 150.52, 167.64, 171.51.

MS (EI): *m*/*z* = 216 $[M]^+$, 198, 183, 172, 153, 139, 127, 115, 100, 85, 70, 57, 42.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_8H_{12}O_3N_2S$: 216.0569; found: 216.0574.

3-(Cyclohexylthio)-4-(dimethylamino)-1*H*-pyrrole-2,5-dione (4k)

Yield: 0.40 g (78%); yellow crystalline solid; mp 160–162 °C.

IR (KBr): 3161, 3038, 2930, 2849, 1755, 1687, 1596, 1427, 1337, 1256, 1198, 1110, 1038, 934, 854, 749, 650 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 1.21 (s, 5 H), 1.55 (s, 1 H), 1.68 (s, 2 H), 1.83 (s, 2 H), 2.81 (s, 1 H), 3.40 (s, 6 H), 10.54 (s, 1 H).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 25.79, 25.92, 33.05, 42.31, 47.58, 89.93, 150.67, 167.74, 171.50.

MS (EI): *m*/*z* = 254 $[M]^+$, 172, 157, 139, 115, 100, 85, 70, 55, 41.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{12}H_{18}O_2N_2S$: 254.1089; found: 254.1090.

3-[(4-Chlorophenyl)thio]-4-(dimethylamino)-1-methyl-1*H*-pyrrole-2,5-dione (4l)

Yield: 0.44 g (75%); yellow crystalline solid; mp 106–108 °C.

IR (KBr): 2937, 1751, 1699, 1609, 1434, 1382, 1254, 1191, 1137, 1092, 1049, 977, 816, 750 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 2.90 (s, 3 H), 3.43 (s, 6 H), 7.22 (d, *J* = 7.5 Hz, 2 H), 7.34 (d, *J* = 7.6 Hz, 2 H).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 24.50, 42.31, 83.45, 127.21, 129.41, 130.02, 139.20, 152.69, 165.72, 170.12.

MS (EI): *m*/*z* = 296 $[M]^+$, 263, 228, 211, 155, 125, 100, 96, 85, 68.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{13}H_{13}O_2N_2SCl$: 296.0386; found: 296.0379.

3-(Dimethylamino)-1-phenyl-4-{[4-(trifluoromethyl)phenyl]thio}-1*H*-pyrrole-2,5-dione (4m)

Yield: 0.45 g (58%); yellow crystalline solid; mp 174–175 °C.

IR (KBr): 3082, 2960, 1754, 1704, 1608, 1498, 1388, 1324, 1205, 1164, 1115, 1007, 961, 828, 745, 694, 624 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 3.48 (s, 6 H), 7.36 (s, 3 H), 7.50 (s, 4 H), 7.63 (s, 2 H).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 42.60, 82.91, 99.98, 125.81, 126.05, 126.27, 127.20 (q, J = 290.0 Hz), 127.50, 129.16, 132.57, 145.82, 152.82, 164.48, 168.88.

MS (EI): m/z = 392 $[M]^+$, 359, 245, 215, 189, 145, 100, 96, 82.

HRMS (EI): m/z $[M]^+$ calcd for $C_{19}H_{15}O_2N_2SF_3$: 392.0806; found: 392.0810.

3-(Dimethylamino)-4-[(3-methoxyphenyl)thio]-1-phenyl-1*H*-pyrrole-2,5-dione (4n)

Yield: 0.59 g (83%); yellow crystalline solid; mp 106–108 °C.

IR (KBr): 2936, 1756, 1706, 1608, 1489, 1425, 1384, 1284, 1239, 1124, 1038, 961, 851, 748, 687, 623, 553 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 3.47 (s, 6 H), 3.74 (s, 3 H), 6.73 (dd, J = 8.2, 2.4 Hz, 1 H), 6.79 (t, J = 2.0 Hz, 1 H), 6.83 (d, J = 7.8 Hz, 1 H), 7.23 (t, J = 8.0 Hz, 1 H), 7.33–7.39 (m, 3 H), 7.47 (t, J = 7.6 Hz, 2 H).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 42.53, 55.60, 84.72, 111.14, 111.21, 117.83, 127.49, 128.00, 129.15, 130.58, 132.64, 141.18, 152.44, 160.31, 164.64, 169.10.

MS (EI): m/z = 354 $[M]^+$, 325, 207, 151, 121, 96, 82, 64, 42.

HRMS (EI): m/z $[M]^+$ calcd for $C_{19}H_{18}O_3N_2S$: 354.1038; found: 354.1034.

3-[(3-Chlorophenyl)thio]-4-(dimethylamino)-1-phenyl-1*H*-pyrrole-2,5-dione (4o)

Yield: 0.48 g (67%); yellow crystalline solid; mp 115–117 °C.

IR (KBr): 2942, 1755, 1706, 1610, 1497, 1384, 1247, 1204, 1120, 1068, 961, 745, 686, 623 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 3.49 (s, 6 H), 7.21 (d, J = 7.7 Hz, 1 H), 7.27 (d, J = 7.8 Hz, 1 H), 7.32–7.40 (m, 5 H), 7.49 (t, J = 7.2 Hz, 2 H).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 42.60, 83.46, 124.22, 124.84, 125.52, 127.49, 128.01, 129.14, 131.17, 132.63, 134.47, 142.53, 152.78, 164.55, 169.01.

MS (EI): m/z = 358 $[M]^+$, 325, 215, 155, 100, 96, 83, 66.

HRMS (EI): m/z $[M]^+$ calcd for $C_{18}H_{15}O_2N_2SCl$: 358.0543; found: 358.0547.

1-Benzyl-3-(dimethylamino)-4-(phenylthio)-1*H*-pyrrole-2,5-dione (4p)

Yield: 0.48 g (71%); yellow crystalline solid; mp 100–102 °C.

IR (KBr): 2932, 1751, 1670, 1608, 1429, 1342, 1246, 1120, 1124, 1068, 1026, 849, 743, 695, 625 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 3.43 (s, 6 H), 4.62 (s, 2 H), 7.13 (t, J = 7.3 Hz, 1 H), 7.18 (d, J = 7.3 Hz, 2 H), 7.23–7.26 (m, 2 H), 7.26–7.35 (m, 5 H).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 41.51, 42.38, 84.19, 125.49, 125.52, 127.73, 127.75, 128.98, 129.61, 137.41, 139.87, 152.47, 165.50, 169.90.

MS (EI): m/z = 338 $[M]^+$, 227, 177, 121, 91, 77, 51.

HRMS (EI): m/z $[M]^+$ calcd for $C_{19}H_{18}O_2N_2S$: 338.1089; found: 338.1093.

3-[(4-Chlorophenyl)thio]-4-(diethylamino)-1*H*-pyrrole-2,5-dione (5a)

Yield: 0.35 g (56%); yellow crystalline solid; mp 150–151 °C.

IR (KBr): 3225, 2978, 1760, 1701, 1590, 1474, 1380, 1339, 1281, 1203, 1128, 1088, 1009, 898, 813, 781, 755, 650 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 1.14 (t, J = 6.9 Hz, 6 H), 3.78 (q, J = 6.8 Hz, 4 H), 7.16 (d, J = 8.5 Hz, 2 H), 7.33 (d, J = 8.5 Hz, 2 H), 10.85 (s, 1 H).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 13.94, 45.80, 83.36, 126.44, 128.95, 129.39, 138.27, 150.35, 166.29, 170.28.

MS (ESI): m/z = 311 $[M + H]^+$.

HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{14}H_{16}O_2N_2ClS$: 311.0616; found: 311.0615.

3-(Cyclohexylthio)-4-(dibutylamino)-1*H*-pyrrole-2,5-dione (5b)

Yield: 0.28 g (42%); yellow crystalline solid; mp 114–116 °C.

IR (KBr): 3242, 2926, 2864, 1751, 1767, 1573, 1446, 1322, 1119, 1034, 920, 732, 654 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 0.90 (t, J = 7.3 Hz, 6 H), 1.20 (s, 5 H), 1.23–1.33 (m, 4 H), 1.52–1.55 (m, 5 H), 1.68 (s, 2 H), 1.83 (s, 2 H), 2.90 (s, 1 H), 3.76–3.80 (m, 4 H), 10.55 (s, 1 H).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 14.07, 19.50, 25.66, 25.78, 30.58, 33.00, 47.29, 50.99, 89.56, 148.84, 167.53, 171.15.

MS (EI): m/z = 338 $[M]^+$, 256, 213, 188, 171, 157, 129, 101, 86, 57.

HRMS (EI): m/z $[M]^+$ calcd for $C_{18}H_{30}O_2N_2S$: 338.2028; found: 338.2031.

3-[(4-Methylphenyl)thio]-4-(phenylamino)-1*H*-pyrrole-2,5-dione (5c)

Yield: 0.17 g (27%); yellow crystalline solid; mp 233–235 °C.

IR (KBr): 3273, 1772, 1702, 1620, 1588, 1541, 1489, 1446, 1351, 1128, 1026, 849, 802, 757, 722, 695, 659 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 2.20 (s, 3 H), 6.78 (d, J = 7.9 Hz, 2 H), 6.96 (d, J = 7.8 Hz, 2 H), 7.02 (d, J = 7.7 Hz, 2 H), 7.07–7.10 (m, 1 H), 7.16 (t, J = 7.3 Hz, 2 H), 9.87 (s, 1 H), 10.92 (s, 1 H).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 20.43, 89.36, 124.16, 125.14, 126.37, 127.57, 129.36, 132.41, 134.47, 136.30, 145.97, 167.42, 171.48.

MS (ESI): m/z = 311 $[M + H]^+$.

HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{17}H_{15}O_2N_2S$: 311.0849; found: 311.0847.

3-(Butylamino)-4-[(2-fluorophenyl)thio]-1-methyl-1*H*-pyrrole-2,5-dione (5d)

Yield: 0.43 g (69%); yellow crystalline solid; mp 98–99 °C.

IR (KBr): 3311, 2963, 2937, 2879, 1766, 1695, 1613, 1503, 1467, 1448, 1397, 1284, 1258, 1210, 1169, 1101, 1064, 1018, 982, 806, 752, 644 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 0.70 (t, J = 7.3 Hz, 3 H), 1.13–1.10 (m, 2 H), 1.37–1.42 (m, 2 H), 2.90 (d, J = 6.5 Hz, 3 H), 3.50–3.53 (m, 2 H), 7.13–7.22 (m, 4 H), 8.67 (t, J = 5.7 Hz, 1 H).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 13.35, 19.15, 24.09, 31.71, 42.20, 75.88, 115.20 (d, J = 20.5 Hz), 125.15 (d, J = 3.0 Hz), 125.72 (d, J = 16.7 Hz), 126.61 (d, J = 7.4 Hz), 127.15 (d, J = 1.9 Hz), 151.57, 157.89 (d, J = 241.5 Hz), 165.27, 170.92.

MS (ESI): m/z = 309 $[M + H]^+$.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{18}O_2N_2FS$: 309.1068; found: 309.1065.

4-[(4-Methylphenyl)thio]-1-phenyl-3-(pyrrolidin-1-yl)-1*H*-pyrrole-2,5-dione (5e)

Yield: 0.57g (78%); yellow crystalline solid; mp 168–170 °C.

IR (KBr): 2981, 2877, 1759, 1711, 1612, 1506, 1493, 1458, 1392, 1355, 1217, 1155, 1094, 1078, 1012, 943, 812, 776, 762, 693, 649 cm^{-1}.

^{1}H NMR (600 MHz, DMSO-d_6): δ = 1.84 (t, *J* = 6.8 Hz, 4 H), 2.24 (s, 3 H), 3.97 (s, 4 H), 7.11 (d, *J* = 8.1 Hz, 2 H), 7.15–7.16 (m, 2 H), 7.33–7.38 (m, 3 H), 7.45–7.48 (m, 2 H).

^{13}C NMR (151 MHz, DMSO-d_6): δ = 21.06, 25.21, 51.79, 84.20, 126.07, 127.52, 128.07, 129.30, 130.38, 132.88, 134.99, 137.13, 150.31, 164.50, 169.65.

MS (ESI): *m*/*z* = 365 [M + H]$^+$.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{21}O_2N_2S$: 365.1318; found: 365.1322.

4-[(4-Bromophenyl)thio]-1-phenyl-3-(piperidin-1-yl)-1*H*-pyrrole-2,5-dione (5f)

Yield: 0.63 g (71%); yellow crystalline solid; mp 133–135 °C.

IR (KBr): 2938, 2856, 1758, 1706, 1598, 1501, 1470, 1452, 1385, 1269, 1206, 1126, 1081, 1005, 953, 810, 751, 690, 627 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.61 (s, 6 H), 4.06 (s, 4 H), 7.12–7.62 (m, 9 H).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 23.37, 26.40, 49.47, 84.28, 117.94, 127.04, 127.30, 127.54, 128.64, 131.86, 132.12, 137.67, 151.12, 164.40, 168.36.

MS (ESI): *m*/*z* = 443 [M + H]$^+$.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{20}O_2N_2BrS$: 443.0423; found: 443.0420.

1-Benzyl-3-(butylamino)-4-[(4-methoxyphenyl)thio]-1*H*-pyrrole-2,5-dione (5g)

Yield: 0.51 g (65%); yellow crystalline solid; mp 149–151 °C.

IR (KBr): 3292, 2925, 1764, 1698, 1620, 1493, 1430, 1406, 1353, 1284, 1239, 1178, 1167, 1120, 1083, 1034, 940, 822, 753, 733, 693, 646 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 0.77 (t, *J* = 7.3 Hz, 3 H), 1.16–1.25 (m, 2 H), 1.42–1.50 (m, 2 H), 3.55–3.60 (m, 2 H), 3.71 (s, 3 H), 4.61 (s, 2 H), 6.88 (d, *J* = 8.7 Hz, 2 H), 7.12 (d, *J* = 8.7 Hz, 2 H), 7.23 (d, *J* = 7.3 Hz, 2 H), 7.28 (d, *J* = 7.0 Hz, 1 H), 7.34 (t, *J* = 7.3 Hz, 2 H), 8.53 (s, 1 H).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 13.53, 19.24, 31.76, 41.05, 42.27, 55.17, 81.09, 114.87, 127.15, 127.31, 127.46, 128.55, 128.98, 136.93, 150.23, 157.52, 165.25, 170.79.

MS (ESI): *m*/*z* = 397 [M + H]$^+$.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{25}O_3N_2S$: 397.1580; found: 397.1579.

1,2-Di-*p*-tolyldisulfane (6a)[18]

A solution of CuI (0.4 mmol), *p*-thiocresol (**1a**) (2.0 mmol), *N*-phenylmaleimide (**2b**) (2.0 mmol) and 40% HBF_4 (2.0 mmol) in DMA (6 mL) was stirred at 120 °C for 8 h under O_2. After cooling to room temperature, H_2O (10 mL) was added and the resulting mixture was extracted with EtOAc (3 × 10 mL). The combined organic phase was dried over anhydrous Na_2SO_4, concentrated and purified by silica gel column chromatography (eluent: EtOAc/PE, 1:40) to yield the pure product **6a**.

Yield: 0.06 g (12%); pale yellow solid; mp 48–49 °C.

IR (KBr): 3082, 2366, 1899, 1653, 1574, 1484, 1391, 1388, 1297, 1123, 1073, 1027, 939, 846, 821, 737, 684 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.33 (s, 6 H), 7.12 (d, *J* = 7.6 Hz, 4 H), 7.40 (d, *J* = 7.5 Hz, 4 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 21.08, 128.48, 129.78, 133.85, 137.42.

MS (EI): *m*/*z* = 246 [M]$^+$.

3-[(4-Methylphenyl)thio]-1-phenyl-1*H*-pyrrole-2,5-dione (7a)[19]

A solution of CuI (0.4 mmol), *p*-thiocresol (**1a**) (2.0 mmol), *N*-phenylmaleimide (**2b**) (2.0 mmol) and 40% HBF_4 (2.0 mmol) in DMA (6 mL) was stirred at 120 °C for 8 h under O_2. After cooling to room temperature, H_2O (10 mL) was added and the resulting mixture was extracted with EtOAc (3 × 10 mL). The combined organic phase was dried over anhydrous Na_2SO_4, concentrated and purified by silica gel column chromatography (eluent: EtOAc/PE, 1:25) to yield the pure product **7a**.

Yield: 0.38 g (65%); yellow crystalline solid; mp 161–163 °C.

IR (KBr): 2906, 1753, 1685, 1552, 1491, 1387, 1200, 1132, 1051, 1001, 811, 749, 665, 621 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.40 (s, 3 H), 5.94 (s, 1 H), 7.36 (d, *J* = 7.5 Hz, 2 H), 7.41 (d, *J* = 6.9 Hz, 3 H), 7.50 (t, *J* = 7.2 Hz, 2 H), 7.59 (d, *J* = 7.5 Hz, 2 H).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 21.19, 119.30, 123.36, 127.12, 128.19, 129.20, 131.35, 131.72, 134.11, 140.81, 151.65, 166.86, 168.14.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{17}H_{13}NO_2S$: 295.0667; found: 295.0669.

1-Phenyl-3-(pyrrolidin-1-yl)-1*H*-pyrrole-2,5-dione (8a)[20]

A solution of CuI (0.4 mmol), *N*-phenylmaleimide (**2b**) (2.0 mmol) and 40% HBF_4 (2.0 mmol) in 1-formylpyrrolidine (**3b**) (6 mL) was stirred at 120 °C for 8 h under O_2. After cooling to room temperature, H_2O (10 mL) was added and the resulting mixture was extracted with EtOAc (3 × 10 mL). The combined organic phase was dried over anhydrous Na_2SO_4, concentrated and purified by silica gel column chromatography (eluent: EtOAc/PE, 1:10) to yield the pure product **8a**.

Yield: 0.38 g (78%); yellow crystalline solid; mp 99–101 °C.

IR (KBr): 3112, 3063, 2994, 2886, 1707, 1635, 1528, 1452, 1395, 1359, 1213, 1137, 1047, 971, 784, 696 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.02 (s, 4 H), 3.35 (s, 2 H), 3.94 (s, 2 H), 4.89 (s, 1 H), 7.30 (d, *J* = 7.2 Hz, 1 H), 7.35 (d, *J* = 8.2 Hz, 2 H), 7.43 (t, *J* = 7.5 Hz, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 23.60, 25.87, 48.63, 49.98, 85.57, 125.82, 126.70, 128.38, 131.65, 147.70, 165.12, 169.94.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{14}H_{14}N_2O_2$: 242.1055; found: 242.1054.

1-Phenyl-3-(pyrrolidin-1-yl)-pyrrolidine-2,5-dione (9a)

A solution of CuI (0.4 mmol), *p*-thiocresol (**1a**) (2.0 mmol), *N*-phenylmaleimide (**2b**) (2.0 mmol) and 40% HBF_4 (2.0 mmol) in 1-formylpyrrolidine (**3b**) (6 mL) was stirred at 120 °C for 8 h under O_2. After cooling to room temperature, H_2O (10 mL) was added and the resulting mixture was extracted with EtOAc (3 × 10 mL). The combined organic phase was dried over anhydrous Na_2SO_4, concentrated and purified by silica gel column chromatography (eluent: EtOAc/PE, 1:5) to yield the pure product **9a**.

Yield: 0.13 g (26%); white crystalline solid; mp 108–110 °C.

IR (KBr): 2953, 2800, 1772, 1707, 1583, 1488, 1464, 1379, 1276, 1162, 963, 902, 770, 743, 687 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 1.71 (s, 4 H), 2.61–2.62 (m, 2 H), 2.81–2.87 (m, 3 H), 3.01 (dd, *J* = 8.6, 17.9 Hz, 1 H), 3.97 (dd, *J* = 4.9, 8.6 Hz, 1 H), 7.26–7.27 (m, 2 H), 7.41–7.44 (m, 1 H), 7.50 (dd, *J* = 4.8, 10.6 Hz, 2 H).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 24.54, 34.64, 51.25, 61.14, 128.54, 129.74, 130.31, 133.70, 170.00, 177.43.

HRMS (EI): *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{17}O_2N_2$: 245.1285; found: 245.1284.

3-[(4-Methylphenyl)thio]-1-phenyl-pyrrolidine-2,5-dione (14a)[21]

A solution of CuI (0.4 mmol), *p*-thiocresol (**1a**) (2.0 mmol), *N*-phenylmaleimide (**2b**) (2.0 mmol) and 40% HBF_4 (2.0 mmol) in 1-formylpyrrolidine (**3b**) (6 mL) was stirred at 120 °C for 8 h under N_2. After cooling to room temperature, H_2O (10 mL) was added and the resulting mixture was extracted with EtOAc (3 × 10 mL). The combined organic phase was dried over anhydrous Na_2SO_4, concentrated and purified by silica gel column chromatography (eluent: EtOAc/PE, 1:8) to yield the pure product **14a**.

Yield: 0.33 g (55%); pale yellow solid; mp 138–140 °C.

IR (KBr): 1786, 1721, 1665, 1642, 1598, 1564, 1547, 1500, 1467, 1389, 1183, 956, 825, 758, 682, 690 cm^{-1}.

^1H NMR (600 MHz, DMSO-d_6): δ = 2.32 (s, 3 H), 2.79 (dd, *J* = 3.8, 18.5 Hz, 1 H), 3.41 (dd, *J* = 9.3, 18.5 Hz, 1 H), 4.43 (dd, *J* = 3.8, 9.3 Hz, 1 H), 7.01–7.04 (m, 2 H), 7.23 (d, *J* = 7.9 Hz, 2 H), 7.39–7.41 (m, 1 H), 7.43–7.47 (m, 4 H).

^{13}C NMR (151 MHz, DMSO-d_6): δ = 21.02, 36.61, 44.25, 127.14, 127.34, 128.75, 129.21, 130.34, 132.45, 134.36, 139.21, 174.34, 175.21.

LC-MS (ESI): *m*/*z* = 298 [M + H]$^+$.

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Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0037-1610536.

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