Synthesis Y.-L. An et al. Paper

Regioselective Hetero-Michael Addition of Oxygen, Sulfur, and Nitrogen Nucleophiles to Maleimides Catalyzed by BF_3·OEt_2

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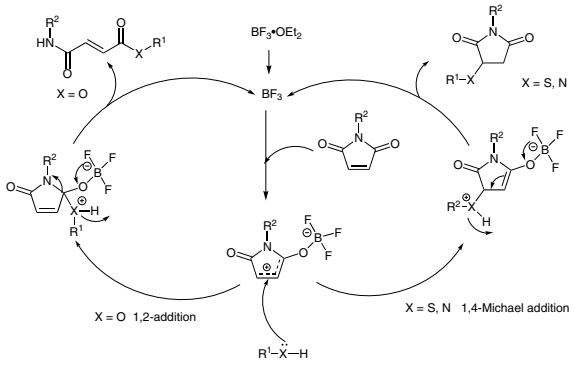

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Abstract A practical BF_3·OEt_2-catalyzed regioselective 1,2-addition or 1,4-hetero-Michael addition of oxygen, sulfur, and nitrogen nucleophiles to maleimides has been developed for the synthesis of alkyl fumarate derivatives or 3-substituted succinimides, respectively. This reaction system has wide substrate scope and gives moderate to excellent yields (up to 96%) of the desired products. In contrast to the base-catalyzed methods, this strategy is very general, simple, environmentally friendly, and tolerant of oxygen.

Key words Michael addition, maleimide, oxygen nucleophiles, sulfur nucleophiles, nitrogen nucleophiles, boron trifluoride diethyl etherate

3-Substituted maleimide and succinimide compounds are versatile building blocks in organic synthesis. They not only constitute as valuable intermediates for the synthesis of various polycyclic compounds[1] and peptide substances,[2] but also serve as key precursors in the synthesis of a variety of natural products[3] and pharmaceuticals (Figure 1).[4] The development of efficient methods for their synthesis has continuously attracted the attentions of many chemists.

In view of the synthetic expediency of 3-substituted succinimides, many methods have been developed for their synthesis. Generally, 3-alkyloxy-substitued succinimides were obtained by base-catalyzed addition and solvolysis reaction of maleimides in alcohol solution.[5] Organocatalytic ring expansion of β-lactam aldehydes was also developed to provide 3-alkoxy-substituted succinimides.[6] However, the above synthetic method gave a low yield and involved tedious procedures. During the past few years, Michael and

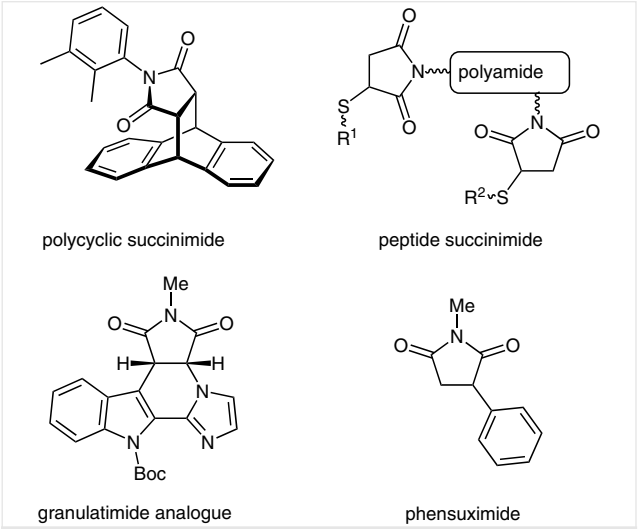
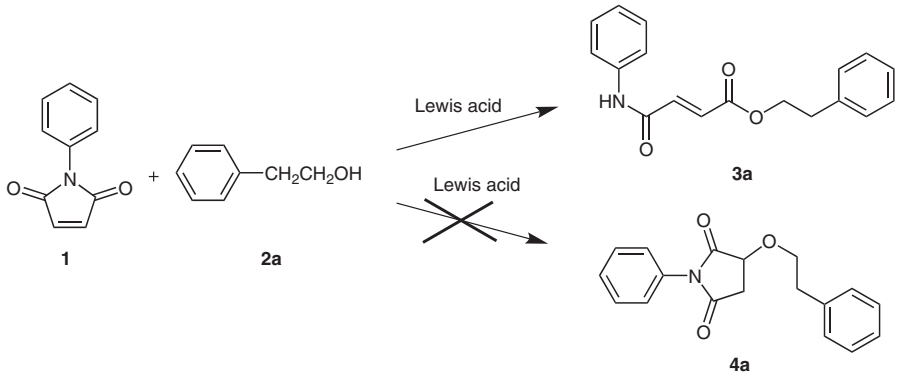


Figure 1 Examples of polycyclic compounds, peptides, natural products, and pharmaceuticals containing 3-substituted succinimide motif

hetero-Michael addition provided a direct protocol for the formation of carbon–carbon and carbon–heteroatom bonds, and attracted much attention.[7] Generally, either the donor or the acceptor component needs to be activated in hetero-Michael addition reactions. Fortunately, important advances have been made with Lewis acids, which activate the acceptor component with catalytic amounts and avoid/reduce the polymerization of starting olefins. $Bi(NO_3)_3$, $Pd(OAc)_2$, $[Rh(COD)_2]BF_4$, $InCl_3$, $Ph_3PAuCl/AgOTf$, $La(OTf)_3$, and related Lewis acids have been used successfully in hetero-Michael addition.[8] Most of the reactions usual-

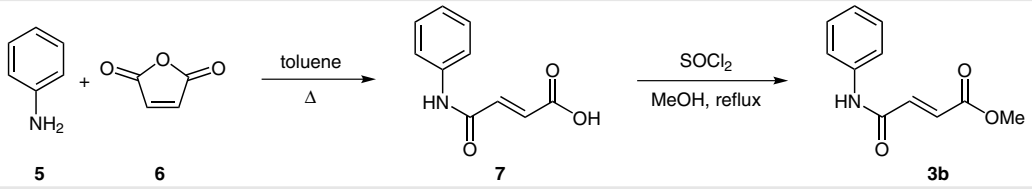
ly demand high catalyst loadings, long reaction times ranging from several hours to several days in some cases, expensive and hazardous reagents, and special reaction conditions to enhance reactivity, such as ultrasounds and ultra-high pressures,[9] microwave irradiation,[10] or ionic liquids.[11] Furthermore, most of the reaction substrates were focused on α,β-unsaturated carbonyl compounds, such as acrylic esters and nitroalkenes. However, only few reports on maleimides serving as Michael addition acceptors using Lewis acid as catalysis have appeared until now. The maleimides are unstable in the presence of strong acids and bases, and are apt to polymerize and decompose. Thus, an efficient, economical and environmentally benign Lewis acid catalyst is highly desirable for this process. In our continued research program directed toward the synthesis of maleimide derivatives in this area,[12] we have successfully developed a highly efficient synthetic strategy for Michael addition of indoles and pyrroles to maleimides using $AlCl_3$ as catalyst.[12d] Thus, we became intrigued by the idea of using catalytic amounts of cheap Lewis acids to catalyze hetero-Michael reactions of maleimides, since β-oxy-, β-thio-, and β-aminocarbonyl functionalities are ubiquitous motifs in

Table 1 Optimization of the Reaction Conditions[a]



Entry	Catalyst	Solvent	Time (h)	Yield (%)[b]
1	–	CH_2Cl_2	12	0
2	$ZnCl_2$	CH_2Cl_2	24	34
3	$ZnBr_2$	CH_2Cl_2	24	42
4	$ZnBr_2$	DCE	24	45
5	$FeCl_3$	CH_2Cl_2	12	trace
6	$AlCl_3$	CH_2Cl_2	12	0[c]
7	$TiCl_4$	CH_2Cl_2	12	0[c]
8	$ZrCl_4$	CH_2Cl_2	12	0
9	$InBr_3$	CH_2Cl_2	12	0
10	$AgBF_4$	CH_2Cl_2	12	0
11	$RuCl_3$	CH_2Cl_2	12	0
12	$Zn(OTf)_2$	CH_2Cl_2	12	34
13	$Y(OTf)_3$	DCE	12	32
14	$BiCl_3$	1,4-dioxane	12	26
15	$BF_3{\cdot}OEt_2$	CH_2Cl_2	12	92
16	$BF_3{\cdot}OEt_2$	DCE	12	89
17	$BF_3{\cdot}OEt_2$	1,4-dioxane	12	0
18	$BF_3{\cdot}OEt_2$	THF	12	0
19	$BF_3{\cdot}OEt_2$	DMF	12	0

[a] Reaction conditions: *N*-phenylmaleimide (**1**; 2.0 mmol), 2-phenylethanol (**2a**; 2.0 mmol), and catalyst (20 mol%) were refluxed in the respective solvent (15 mL) under air.
[b] Isolated yields.
[c] 3-Chloro-1-phenylsuccinimide (**8**) was obtained as the main product in 70% yield.



5 6 7 3b

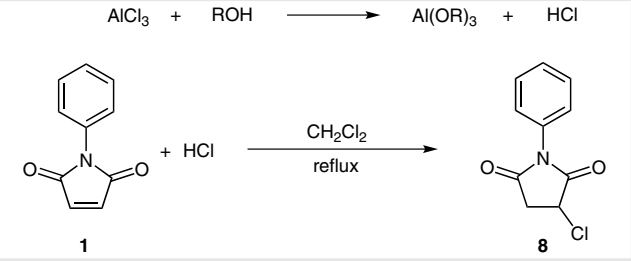
Scheme 1 Synthesis of compound **3b**

most important synthetic intermediates.[13] Boron trifluoride diethyl etherate ($BF_3{\cdot}OEt_2$), an inexpensive Lewis acid, could work well in a series of organic synthesis reaction.[14] Herein, we describe $BF_3{\cdot}OEt_2$-catalyzed regioselective 1,2-addition or 1,4-hetero Michael addition of OH, SH, and NH groups to maleimides in moderate to excellent yields (up to 96%). In addition, the notable advantages of this method are mild conditions, short reaction times, high yields, and lack of any side reaction products.

Our studies were initiated by examining catalyst usefulness and reaction conditions using *N*-phenylmaleimide (**1**) and 2-phenylethanol (**2a**) as a model system because the product is easy to detect and isolate (Table 1). The reaction between **1** and **2a** in the presence of Lewis acid is accomplished by heating the reagents in dichloromethane at reflux for several hours. Under catalyst-free condition, no reaction took place and only the starting material **1** was recovered (Table 1, entry 1). At first, this reaction was run using the classical Lewis acids, such as $ZnCl_2$, $ZnBr_2$, $FeCl_3$, $AlCl_3$, and $TiCl_4$. The product was obtained as a white solid in ca. 40% yield using 0.2 equivalent of $ZnCl_2$ or $ZnBr_2$ as catalyst. The yields cannot be improved by prolonging the reaction time.

Next, this product was analyzed spectroscopically to confirm the formation of the desired 1,4-Michael addition product **4a**. The analysis of NMR spectral data showed seventeen hydrogen and eighteen carbons signals. Furthermore, the EI mass spectrum of this compound showed a molecular ion at 295 (M^+). High-resolution mass spectrum suggested a molecular formula of $C_{18}H_{17}NO_3$. The molecular formula is consistent with the desired compound **4a**. Luckily, chemical shifts in ^1H NMR spectrum gave us a clue to determine the structure of the product. A chemical shift at 10.9 ppm suggested that an active hydrogen should exist in the isolated compound, but it was not found in the isolated compound **4a**. In order to understand this problem, we used methanol as the nucleophile to run this reaction since the desired product was reported in the literature.[7e] Though analytical data similar to Xia' s results were obtained,[7e] the structure could not be assigned to the desired 3-methoxy-1-phenylpyrrolidine-2,5-dione. On the other hand, hydrogen signals at 6.21 and 6.42 ppm with a coupling constant of J = 13.3 Hz suggested that a *trans*-double bond should exist in this isolated compound. Finally, we presumed that a 1,2-addition of maleimide with methanol might have proceeded in this reaction, which subsequently undergoes ring-opening to provide methyl (*E*)-4-oxo-4-(phenylamino)but-2-enoate (**3b**). Fortunately, Bello et al. had reported the data of the 1,2-addition product in their work on antibacterial agents,[15] by preparing it from aniline and maleic anhydride as shown in Scheme 1. Our results were consistent with Bello's data. On the basis of spectral data, we believe that a 1,2-addition reaction had taken place between maleimide and methanol. To the best of our knowledge, this is the first example of Lewis acid catalyzed 1,2-addition to maleimide.

After confirming the structure of the 1,2-addition product, methanol was used as the solvent to obtain only the 1,2-addition product **3b**. No 1,4-Michael addition product was obtained in this reaction. This indicated that the excess oxygen nucleophile did not react with the C=C bond of maleimide to form 3-methoxysuccinimide derivative. Our attention was then turned to continue the screening of the Lewis acids to improve the yield. However, when this reaction was carried out with 0.2 equivalent of $FeCl_3$, only a trace amount of the product was observed (entry 5). The possible reason is that $FeCl_3$ led to the partial polymerization of maleimides due to its oxidation property. Interestingly, 3-chloro-1-phenylsuccinimide (**8**) was obtained in 70% yield in the place of phenethyl (*E*)-4-oxo-4-(phenylamino)but-2-enoate (**3a**) when $AlCl_3$ or $TiCl_4$ was used as catalysts (entries 6, 7). Based on the work of Coskun's group,[16] it is known that *N*-phenylmaleimide (**1**) can directly be converted into 3-chloro-1-phenylsuccinimide (**8**) in the presence of HCl. $TiCl_4$ and $AlCl_3$ can react with alcohol to provide aluminum alkoxide and titanium alkoxide releasing HCl in the reaction system. Then, *N*-phenylmaleimide reacts immediately with HCl to give 3-chloro-1-phenylsuccinimide (**8**) in this reaction medium. It should be noted that without any alcohol, the reaction could not generate any of the product **8**. The results support this hypothesis. A plausible reaction process for the product **8** is proposed in Scheme 2.



Scheme 2 Proposed reaction process for the product **8**

Next, in order to improve the yield, the reaction was performed in the presence of other Lewis acids such as $BiCl_3$, $ZrCl_4$, $InBr_3$, $AgBF_4$, $RuCl_3$, $Zn(OTf)_2$, $Y(OTf)_3$, and $BF_3{\cdot}OEt_2$. Unfortunately, $ZrCl_4$, $InBr_3$, $AgBF_4$, and $RuCl_3$ did not function as catalysts in this reaction (entries 8–11), and the starting materials were recovered. The desired product **3a** was obtained in the presence of $BiCl_3$, $Zn(OTf)_2$, or $Y(OTf)_3$ in a low yield of 30% (entries 12–14). To our delight, use of 0.2 equivalent of $BF_3{\cdot}OEt_2$ afforded the compound **3a** in 92% yield (Table 1, entry 15). Encouraged by this result, the reaction conditions were then optimized. Rapid conversion was observed when the reaction was carried out in dichloromethane (92% yield, entry 15) or 1,2-dichloroethane (89% yield, entry 16). The reaction did not work by using DMF, THF, and 1,4-dioxane as solvent (entries 17–19). The above results demonstrated that $BF_3{\cdot}OEt_2$ is a more effective catalyst in comparison to $ZnCl_2$. It should be noted that without any catalyst, the reaction did not generate the desired product at all.

Subsequently, the influence of the amount of the catalyst on the reaction was also evaluated under identical reaction conditions, as illustrated in Figure 2. Increasing the loading of $BF_3{\cdot}OEt_2$ initially led to a sharp increase in the yield and further to a steady state. The yield approached to 92% by using 20 mol% of $BF_3{\cdot}OEt_2$ as catalyst.

With the above optimal conditions in hand, the present catalyst system was applied to examine the utility and generality of this method for hetero-Michael addition of oxygen, sulfur, and nitrogen nucleophiles to maleimides. First, 1,2-addition of maleimides with oxygen nucleophiles catalyzed by $BF_3{\cdot}OEt_2$ was examined. In some cases, the isolated yields were moderate to excellent (Table 2). It was found that 2-phenylethanol and methanol were better nucleophiles than the secondary alcohols (Table 2, entries 1–8) providing yields around 50–90%. However, tertiary alcohols (e.g., *tert*-butyl alcohol) gave only trace yield and was unsuitable for this method. As the steric hindrance of alkyl chain for alcohol increased, the yields gradually decreased (entries 4–6). In addition, two single broad peak around 5.8 ppm and 8.4 ppm were assigned to the amide group in the ^1H NMR spectra due to hydrogen bonding (NH–O) interaction of compounds **3g** and **3h**.[17]

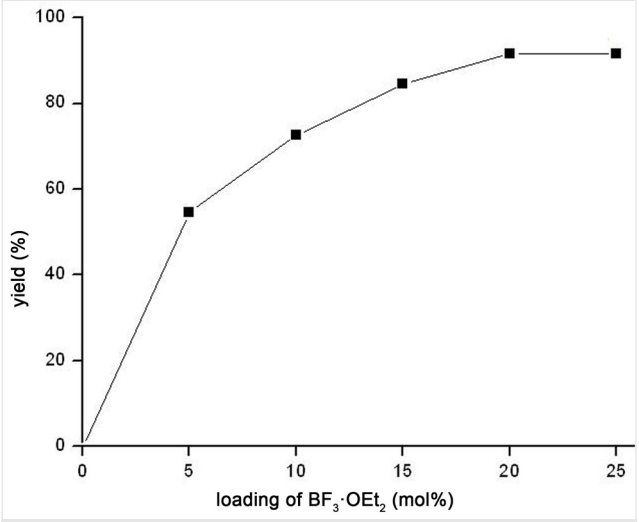
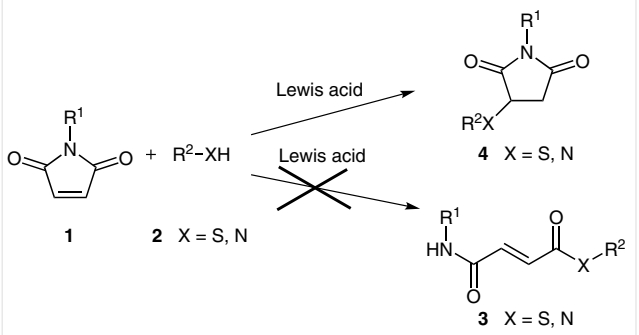


Figure 2 Effect of $BF_3{\cdot}OEt_2$ loading on the yield of **3a**. *Reaction conditions*: *N*-phenylmaleimide (**1**; 2.0 mmol), 2-phenylethanol (**2a**; 2.0 mmol), CH_2Cl_2 (15 mL), 12 h, reflux.

On the other hand, thiols have long been known to act as metal catalyst poisons because of their strong coordinating and adsorptive properties, and often rendered the metal catalytic reactions totally ineffective.[18] Therefore, developing a more efficient catalyst system for S-Michael addition remains open to study. To further illustrate the utility of this method, a series of sulfur and nitrogen nucleophiles including NH-containing heterocycles were applied to this protocol (Table 3). Fortunately, further experiments revealed that the $BF_3{\cdot}OEt_2$-catalyzed reaction system could be applied successfully to Michael addition of thiols and nitrogen nucleophiles to maleimide.

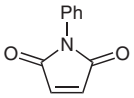
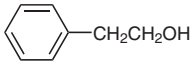
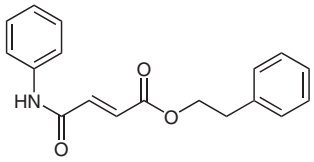
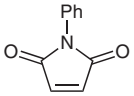
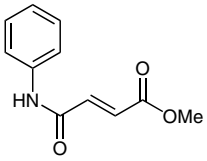
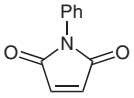
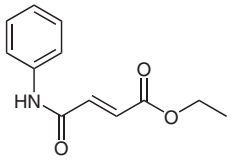
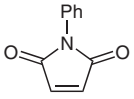
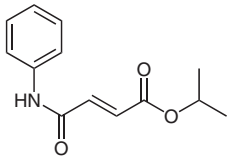
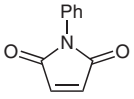
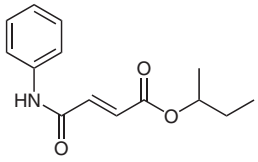
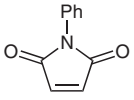
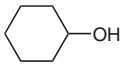
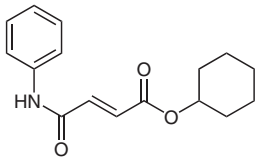
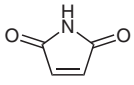
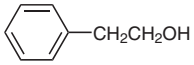
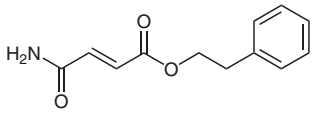
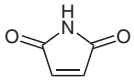
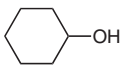
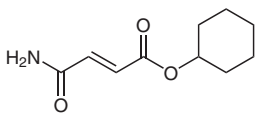
Though the yields were satisfactory, the structures of the products were not assigned as 1,2-addition products by analyzing the NMR spectral data. The reaction, however, proceeded according to our initial hypothesis. Both the sulfur and nitrogen nucleophiles reacted with the C=C double bond of the maleimides in a 1,4-addition manner (Scheme 3), and therefore no 1,2-addition product was observed.



Scheme 3 1,4-Addition of the S and NH nucleophiles to maleimides

It should be noted that without $BF_3{\cdot}OEt_2$, the reaction worked with a poor yield (26% yield, Table 3, entry 1) and the yield was sharply raised under the optimal condition (93% yield, entry 1). Since the reaction did not proceed with the nitrogen nucleophiles in dichloromethane solution in reflux condition, the temperature was increased by using

Table 2 $BF_3{\cdot}OEt_2$-Catalyzed 1,2-Hetero-Michael Addition to Maleimides[a]

Entry	Maleimide	Alcohol	Time (h)	Product	Yield (%)[b]
1			12	**3a**	 92
2		MeOH	12	**3b**	 85
3		EtOH	12	**3c**	 72
4		*i*-PrOH	24	**3d**	 52
5		*s*-BuOH	24	**3e**	 45
6			24	**3f**	 53
7			16	**3g**	 80
8			24	**3h**	 62

[a] Reaction conditions: maleimide (2.0 mmol), alkanol (2.0 mmol), catalyst (20 mol%), CH_2Cl_2 (15 mL), reflux.
[b] Isolated yield.

1,2-dichloroethane as the solvent. The yields went up to 86% (entry 11). The results also revealed that the reactivity decreased with the reducing number of N atoms in azoles (entries 10–12). Besides this, *p*-toluenesulfonamide was also used as the Michael addition acceptor. Unfortunately, the reaction did not work well. By prolonging the refluxing time to 36 hours, only a 34% yield could be obtained (entry 13).

Table 3 $BF_3{\cdot}OEt_2$-Catalyzed 1,4-Hetero-Michael Addition to Maleimides[a]

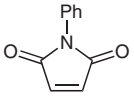
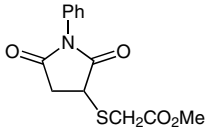
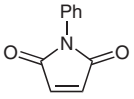
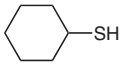
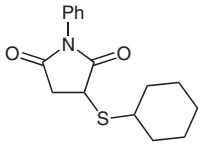
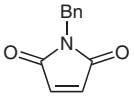
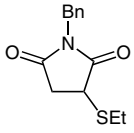
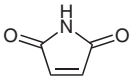
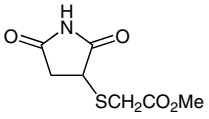
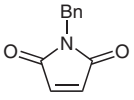
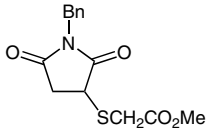
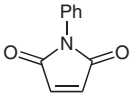
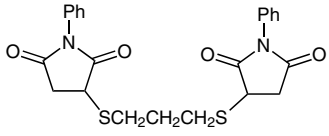
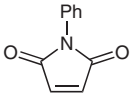
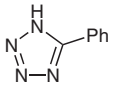
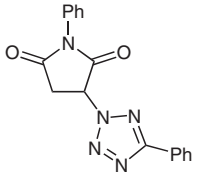
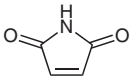
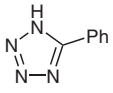
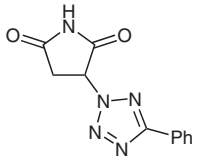
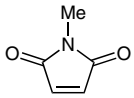
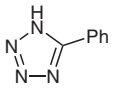
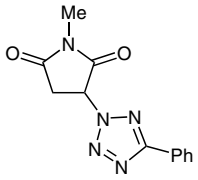
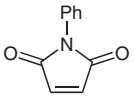
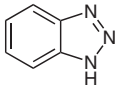
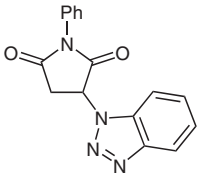
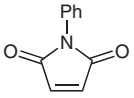
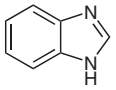
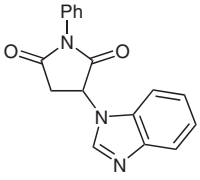
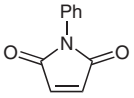
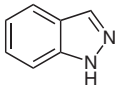
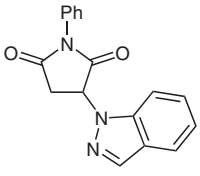
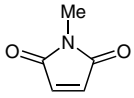
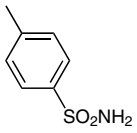
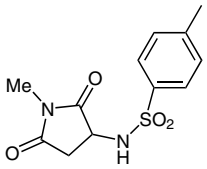
Entry	Maleimide	Nucleophile	Time (h)	Product		Yield (%)[b]
1		$HSCH_2CO_2Me$	12	**4b**		93 26[c]
2			12	**4c**		96
3		EtSH	12	**4d**		90
4		$HSCH_2CO_2Me$	12	**4e**		77
5		$HSCH_2CO_2Me$	12	**4f**		91
6[d]		$HSCH_2CH_2CH_2SH$	12	**4g**		80
7			16	**4h**		63
8			16	**4i**		61

Table 3 (continued)

Entry	Maleimide	Nucleophile	Time (h)	Product	Yield (%)[b]
9			16	**4j**		55
10			16	**4k**		90
11			16	**4l**		86
12			16	**4m**		75
13			36	**4n**		34

[a] Reaction conditions: maleimide (2.0 mmol), S and N nucleophiles (2.0 mmol), catalyst (20 mol%), DCE (15 mL), reflux.
[b] Isolated yield.
[c] Without BF_3·OEt_2.
[d] *N*-Phenylmaleimide (4.0 mmol).

The addition of acrylic acid derivatives to 5-phenyl-1*H*-tetrazole has been reported to provide the addition product at the N2 position of the 1*H*-tetrazoles.[19] In order to confirm the result of 1,4-Michael addition in the same way, single crystal of compound **4i** suitable for X-ray analysis was obtained by slow evaporation of a solution of this compound in ethanol. The X-ray structure is shown in Figure 3. The packing view of **4i** in the unit cell and tables of X-ray crystallographic data can be found in the Supporting Information. The crystal data suggested that 5-phenyl-1*H*-tetrazole rearranged in the reaction and gave the N2-substitution product exclusively (Figure 3). No N1-substitution product and 1,2-addition products were isolated. The target compounds were obtained in moderate to excellent yields with no formation of side products, such as polymers, that are frequently encountered under the influence of strong base.

We believe that BF_3·OEt_2 works well as an efficient catalyst in our selected hetero-Michael addition protocol for oxygen, sulfur, and nitrogen nucleophiles to maleimides. A plausible mechanism for BF_3·OEt_2-catalyzed regioselective hetero-Michael addition is proposed in Scheme 4. Although we do not have additional evidence for this, we assume that BF_3·OEt_2 readily coordinates to the oxygen atom of the carbonyl group.[20] Presumably the intermediate **9** is formed,

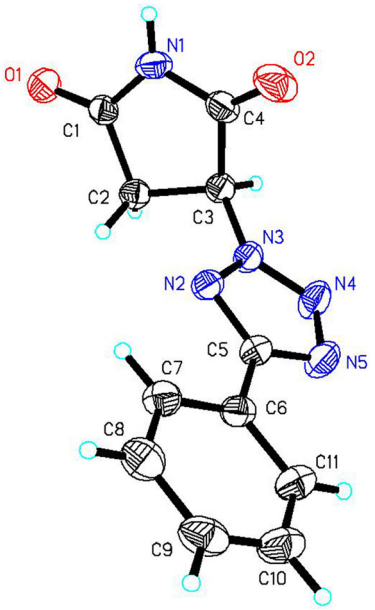
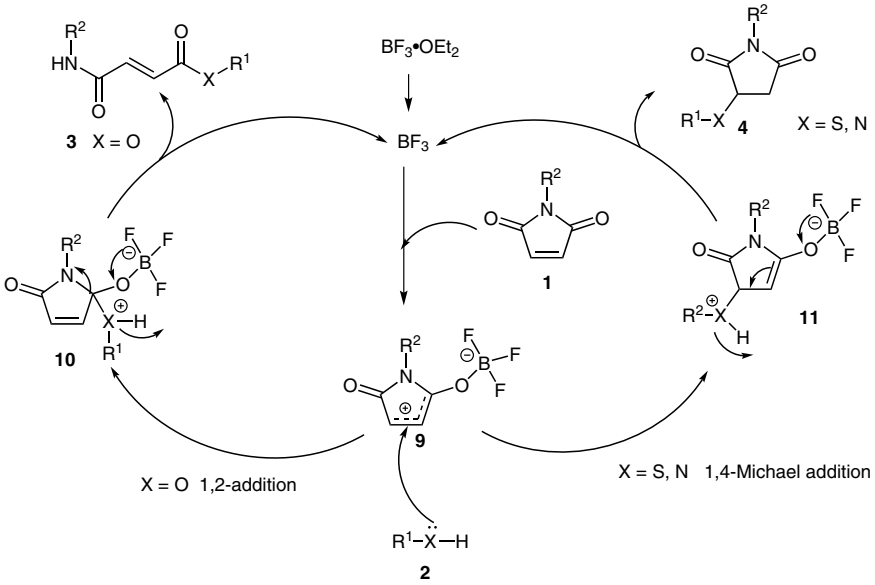


Figure 3 The X-ray crystal structure of 3-(5-phenyl-2*H*-tetrazol-2-yl)pyrrolidine-2,5-dione (**4i**)

which possibly reduces the activation energy required for selective hetero-Michael addition. Next, the nucleophiles are added to labile intermediates **9** in 1,2-addition or 1,4-addition according to the different nucleophilic atoms to furnish the corresponding hetero-Michael adducts **10** and **11**. These adducts upon subsequent electron reorganization followed by hydrogen transfer yield compounds **3** and **4**, respectively, releasing the catalyst for next cycle. In the catalytic cycle, it is thought that BF_3·OEt_2 promotes the reaction by increasing the electrophilic character of enal. A mechanistic study in our laboratory to clarify the pathways for BF_3·OEt_2 employing selected hetero-Michael addition is under way.

In summary, BF_3·OEt_2 has been demonstrated to be an efficient and green catalyst for the regioselective 1,2-addition or 1,4-hetero-Michael addition of oxygen, sulfur, and nitrogen nucleophiles to maleimides. The reactions were performed smoothly to generate the desired products in moderate to excellent yields under safe experimental conditions. Apart from the atom economy, the advantage of this protocol is the use of a cheaper, milder, and more efficient catalyst for the selective 1,2-addition or 1,4-hetero-Michael addition reaction of maleimides. This method offers one of the important motifs for the synthesis of alkyl fumarates and 3-substituted succinimides as natural products, biologically active compounds, and pharmaceutical agents.

Melting points were determined with RY-1 apparatus and are uncorrected. IR spectra were recorded as KBr pellets on a Shimadzu model 470 spectrophotometer. NMR (^{1}H and ^{13}C) spectra were recorded using a Bruker AV 400 MHz spectrometer in $CDCl_3$ with TMS as internal standard. Chemical shifts (δ) are expressed in ppm. EI mass spectra were recorded on Shimadzu QP-2010 GC-MS system and Waters Micromass GCT system. Silica gel (100–200 microns) was used for all chromatographic separations. All materials were obtained from commercial suppliers and were used as received. Petroleum ether (PE) refers to a hydrocarbon mixture with a boiling range of 60–90 °C. The purity of substrates and the monitoring of reactions were performed by TLC on silica gel polygram SILG/UV 254 plates. Crystals of 3-(5-phenyl-2*H*-tetrazol-2-yl)pyrrolidine-2,5-dione (**4i**) were obtained by dissolving **4i** (0.15 g) in EtOH (2 mL) and evaporating the solvent



Scheme 4 Proposed mechanism for regioselective hetero-Michael addition catalyzed by BF_3·OEt_2

slowly at r.t. over a week. The data were collected on CAD-4 diffractometer equipped with graphite-monochromatic MoKα radiation (λ = 0.71073 Å) by using a ω scan mode at 293(2) K. The structure of **4i** is shown in Figure 3. X-ray crystallographic data for compound **4i** can be found in the Supporting Information.

Selective Hetero-Michael Addition of Nucleophiles to Maleimides; General Procedure

A mixture of the nucleophile (2.0 mmol), maleimide **1** (2.0 mmol), $BF_3{\cdot}OEt_2$ (20 mol%, 0.4 mmol) and CH_2Cl_2 (15 mL) was stirred at reflux for the specified time (TLC monitoring, eluent: PE–EtOAc, 4:1). After completion of the reaction, the mixture was cooled to r.t., and H_2O (15 mL) was added. The mixture was extracted with EtOAc (2 × 15 mL), and the combined organic phases were washed with H_2O (2 × 10 mL), and dried (Na_2SO_4). The solvent was removed and the residue was purified by silica gel column chromatography (PE–EtOAc, 6:1) as eluent to yield the pure product. For compounds **4h**–**n**, DCE was used as the solvent instead of CH_2Cl_2. The products were characterized by IR, ^1H NMR, ^{13}C NMR, and HRMS analyses. All the products are known compounds, and the mp, IR, and NMR data are in accordance with those reported in the literature.

Phenethyl (*E*)-4-Oxo-4-(phenylamino)but-2-enoate (3a)

Yield: 542 mg (92%); white solid; mp 100–102 °C.

IR (KBr): 3439, 2913, 1721, 1630, 1545, 1494, 1228, 749 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.07 (t, *J* = 7.0 Hz, 2 H, CH_2), 4.51 (t, *J* = 7.0 Hz, 2 H, CH_2), 6.26 (d, *J* = 13.3 Hz, 1 H, =CH), 6.48 (d, *J* = 13.3 Hz, 1 H, =CH), 7.18 (t, *J* = 7.3 Hz, 1 H_{arom}), 7.27–7.37 (m, 3 H_{arom}), 7.38 (dd, *J* = 16.6, 8.0 Hz, 4 H_{arom}), 7.71 (d, *J* = 7.9 Hz, 2 H_{arom}), 10.92 (s, 1 H, NH).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 34.84, 66.41, 120.10, 124.60, 125.10, 126.87, 128.67, 128.89, 129.02, 137.10, 137.83, 140.61, 161.47, 166.76.

MS (EI): *m*/*z* = 295 $[M]^+$, 191, 173, 146, 105, 91, 77.

HRMS (EI): *m*/*z* calcd for $C_{18}H_{17}NO_3$: 295.1208; found: 295.1203.

Methyl (*E*)-4-Oxo-4-(phenylamino)but-2-enoate (3b)[15,21]

Yield: 348 mg (85%); white solid; mp 72–75 °C.

IR (KBr): 3445, 3137, 2949, 1726, 1670, 1631, 1605, 1544, 1495, 1441, 1232, 1173, 754 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.85 (s, 3 H, CH_3), 6.23 (d, *J* = 13.3 Hz, 1 H, =CH), 6.44 (d, *J* = 13.3 Hz, 1 H, =CH), 7.26 (t, *J* = 7.3 Hz, 1 H_{arom}), 7.35 (t, *J* = 7.6 Hz, 2 H_{arom}), 7.67 (d, *J* = 7.9 Hz, 2 H_{arom}), 10.86 (s, 1 H, NH).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 52.84, 120.12, 124.64, 125.01, 129.03, 137.81, 140.35, 161.51, 167.31.

MS (EI): *m*/*z* = 205 $[M]^+$, 173, 146, 113, 93, 77.

Ethyl (*E*)-4-Oxo-4-(phenylamino)but-2-enoate (3c)[15,22]

Yield: 315 mg (72%); white solid; mp 57–60 °C.

IR (KBr): 3436, 3313, 3129, 2986, 1722, 1671, 1604, 1544, 1494, 1225, 755 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.34 (t, *J* = 7.0 Hz, 3 H, CH_3), 4.30 (q, *J* = 6.9 Hz, 2 H, CH_2), 6.21 (d, *J* = 13.3 Hz, 1 H, =CH), 6.44 (d, *J* = 13.2 Hz, 1 H, =CH), 7.13 (t, *J* = 7.2 Hz, 1 H_{arom}), 7.34 (t, *J* = 7.5 Hz, 2 H_{arom}), 7.67 (d, *J* = 7.8 Hz, 2 H_{arom}), 11.01 (s, 1 H, NH).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 14.02, 62.12, 120.09, 124.59, 125.44, 129.01, 137.85, 140.36, 161.58, 166.88.

MS (EI): *m*/*z* = 219 $[M]^+$, 173, 146, 99, 93, 77.

Isopropyl (*E*)-4-Oxo-4-(phenylamino)but-2-enoate (3d)[15]

Yield: 242 mg (52%); white solid; mp 58–60 °C.

IR (KBr): 3437, 2986, 2929, 1716, 1666, 1545, 1500, 1445, 1232, 1105, 754 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.32 (d, *J* = 6.3 Hz, 6 H, CH_3), 5.10–5.18 (m, 1 H, CH), 6.18 (d, *J* = 13.4 Hz, 1 H, =CH), 6.41 (d, *J* = 13.4 Hz, 1 H, =CH), 7.13 (d, *J* = 7.4 Hz, 1 H_{arom}), 7.34 (t, *J* = 7.9 Hz, 2 H_{arom}), 7.68 (d, *J* = 7.9 Hz, 2 H_{arom}), 11.06 (s, 1 H, NH).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 21.68, 70.03, 120.06, 124.51, 125.83, 128.99, 137.96, 140.32, 161.63, 166.39.

MS (EI): *m*/*z* = 233 $[M]^+$, 191, 174, 146, 120, 99, 93, 77.

HRMS (EI): *m*/*z* calcd for $C_{13}H_{15}NO_3$: 233.1052; found: 233.1055.

sec-Butyl (*E*)-4-Oxo-4-(phenylamino)but-2-enoate (3e)[15]

Yield: 222 mg (45%); white solid; mp 40–42 °C.

IR (KBr): 3432, 2970, 2917, 1715, 1360, 1545, 1390, 1231, 754, 698 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.93 (t, *J* = 7.3 Hz, 3 H, CH_3), 1.30 (d, *J* = 6.1 Hz, 3 H, CH_3), 1.61–1.70 (m, 2 H, CH_2), 4.98–5.01 (m, 1 H, CH), 6.21 (d, *J* = 12.8 Hz, 1 H, =CH), 6.42 (d, *J* = 12.7 Hz, 1 H, =CH), 7.14 (t, *J* = 6.9 Hz, 1 H_{arom}), 7.34 (t, *J* = 7.3 Hz, 2 H_{arom}), 7.68 (d, *J* = 7.6 Hz, 2 H_{arom}), 11.12 (s, 1 H, NH).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 9.60, 19.26, 28.63, 74.61, 120.08, 124.51, 125.79, 128.98, 137.93, 140.44, 161.60, 166.57.

MS (EI): *m*/*z* = 247 $[M]^+$, 191, 174, 146, 120, 93, 77.

HRMS (EI): *m*/*z* calcd for $C_{14}H_{17}NO_3$: 247.1208; found: 247.1211.

Cyclohexyl (*E*)-4-Oxo-4-(phenylamino)but-2-enoate (3f)

Yield: 289 mg (53%); white solid; mp 90–92 °C.

IR (KBr): 3434, 2932, 2851, 1715, 1629, 1547, 1387, 1227, 1024, 750 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.32 (dd, *J* = 36.0, 11.4 Hz, 2 H, CH_2), 1.41–1.52 (m, 4 H, CH_2), 1.75–1.78 (m, 2 H, CH_2), 1.90–1.92(m, 2 H, CH_2), 4.86–4.94 (m, 1 H, CH), 6.21 (d, *J* = 13.4 Hz, 1 H, =CH), 6.43 (d, *J* = 13.3 Hz, 1 H, =CH), 7.13 (d, *J* = 7.4 Hz, 1 H_{arom}), 7.34 (t, *J* = 7.8 Hz, 2 H_{arom}), 7.68 (d, *J* = 7.9 Hz, 2 H_{arom}), 11.15 (s, 1 H, NH).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 23.65, 25.20, 31.39, 74.92, 120.07, 124.53, 125.94, 128.99, 137.94, 140.36, 161.63, 164.21.

MS (EI): *m*/*z* = 273 $[M]^+$, 191, 173, 146, 132, 93, 77.

HRMS (EI): *m*/*z* calcd for $C_{16}H_{19}NO_3$: 273.1365; found: 273.1363.

Phenethyl (*E*)-4-Amino-4-oxobut-2-enoate (3g)

Yield: 350 mg (80%); white solid; mp 50–52 °C.

IR (KBr): 3426, 3182, 1723, 1675, 1424, 1224, 1183, 746 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.02 (t, *J* = 7.0 Hz, 2 H, CH_2), 4.43 (t, *J* = 7.0 Hz, 2 H, CH_2), 5.94 (s, 1 H, NH_2), 6.19 (d, *J* = 13.1 Hz, 1 H, =CH), 6.33 (d, *J* = 13.1 Hz, 1 H, =CH), 7.27 (dd, *J* = 12.4, 6.1 Hz, 3 H_{arom}), 7.35 (t, *J* = 7.3 Hz, 2 H_{arom}), 8.14 (s, 1 H, NH).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 34.82, 66.10, 126.05, 126.82, 128.65, 128.90, 137.24, 137.96, 165.87, 165.99.

MS (EI): *m*/*z* = 219 $[M]^+$, 122, 104, 98, 91, 77.

HRMS (EI): *m*/*z* calcd for $C_{12}H_{13}NO_3$: 219.0895; found: 219.0896.

Cyclohexyl (*E*)-4-Amino-4-oxobut-2-enoate (3h)

Yield: 245 mg (62%); white solid; mp 104–108 °C.

IR (KBr): 3430, 2934, 2855, 1715, 1637, 1386, 1223, 1012 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.19–1.55 (m, 6 H, CH_2), 1.74–1.90 (m, 4 H, CH_2), 4.83–4.87 (m, 1 H, CH), 5.87 (s, 1 H, NH), 6.18 (d, *J* = 13.1 Hz, 1 H, =CH), 6.29 (d, *J* = 13.1 Hz, 1 H, =CH), 8.43 (s, 1 H, NH).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 23.64, 25.22, 31.38, 74.54, 126.93, 137.56, 165.51, 166.02.

MS (EI): *m*/*z* = 198 $[M + H]^+$, 116, 98.

HRMS (EI): *m*/*z* $[M^+ + H]$ calcd for $C_{10}H_{16}NO_3$: 198.1130; found: 198.1132.

3-Chloro-1-phenylpyrrolidine-2,5-dione (8)[16,23]

Yield: 292.6 mg (70%); white solid; mp 114–116 °C.

IR (KBr): 2916, 2848, 1789, 1718, 1499, 1388, 1276, 1179, 952, 744, 695 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.10 (dd, *J* = 18.9, 3.9 Hz, 1 H, CH_2), 3.49 (dd, *J* = 18.9, 8.7 Hz, 1 H, CH_2), 4.79 (dd, *J* = 8.7, 3.9 Hz, 1 H, CH), 7.31 (d, *J* = 7.6 Hz, 2 H_{arom}), 7.44 (t, *J* = 7.2 Hz, 1 H_{arom}), 7.50 (t, *J* = 7.5 Hz, 2 H_{arom}).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 39.43, 48.96, 126.28, 129.17, 129.37, 131.17, 171.97, 172.00.

MS (EI): *m*/*z* = 209 $[M]^+$, 174, 146, 119, 91, 77.

Methyl 2-[(2,5-Dioxo-1-phenylpyrrolidin-3-yl)thio]acetate (4b)[8f]

Yield: 519 mg (93%); light yellow oil.

IR (KBr): 3456, 2945, 1715, 1605, 1495, 1384, 1290, 1182, 743, 698 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.69 (dd, *J* = 18.9, 3.9 Hz, 1 H, CH_2), 3.32 (dd, *J* = 18.9, 9.3 Hz, 1 H, CH_2), 3.43 (d, *J* = 15.9 Hz, 1 H, CH_2), 3.76 (s, 3 H, CH_3), 3.94 (d, *J* = 9.3, 15.9 Hz, 1 H, CH_2), 4.19 (dd, *J* = 9.3, 3.9 Hz, 1 H, CH), 7.27–7.33 (m, 2 H_{arom}), 7.37–7.44 (m, 1 H_{arom}), 7.49 (dd, *J* = 10.3, 4.7 Hz, 2 H_{arom}).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 32.87, 35.49, 38.53, 52.74, 126.44, 128.87, 129.24, 131.53, 170.06, 173.38, 175.19.

MS (EI): *m*/*z* = 279 $[M]^+$, 263, 247, 220, 206, 175, 147, 119, 91.

3-(Cyclohexylthio)-1-phenylpyrrolidine-2,5-dione (4c)[24]

Yield: 555 mg (96%); white solid; mp 102–104 °C.

IR (KBr): 3437, 2929, 2847, 1772, 1714, 1630, 1491, 1381, 1177, 739, 694 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.25–1.49 (m, 5 H, CH_2), 1.59–1.69 (m, 1 H, CH_2), 1.80 (dd, *J* = 12.3, 2.8 Hz, 2 H, CH_2), 1.95 (s, 1 H, CH_2), 2.18 (d, *J* = 11.2 Hz, 1 H, CH_2), 2.68 (dd, *J* = 18.7, 3.6 Hz, 1 H, CH), 3.29 (dt, *J* = 22.9, 11.5 Hz, 2 H, CH_2), 3.97 (dd, *J* = 9.1, 3.5 Hz, 1 H, CH), 7.30 (d, *J* = 7.6 Hz, 2 H_{arom}), 7.40 (t, *J* = 7.4 Hz, 1 H_{arom}), 7.48 (t, *J* = 7.5 Hz, 2 H_{arom}).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 25.68, 25.75, 25.96, 32.91, 33.55, 36.52, 37.75, 43.89, 126.42, 128.72, 129.19, 131.73, 173.88, 175.76.

MS (EI): *m*/*z* = 289 $[M]^+$, 207, 175, 147, 119, 91.

1-Benzyl-3-(ethylthio)pyrrolidine-2,5-dione (4d)

Yield: 448 mg (90%); light yellow solid; mp 58–60 °C.

IR (KBr): 3460, 2970, 2925, 1772, 1705, 1486, 1393, 1345, 1166, 694 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.28 (t, *J* = 7.4 Hz, 3 H, CH_3), 2.53 (dd, *J* = 18.7, 3.6 Hz, 1 H, CH_2), 2.77–2.72 (m, 1 H, CH_2), 2.90–2.85 (m, 1 H, CH_2), 3.13 (dd, *J* = 18.7, 9.1 Hz, 1 H, CH_2), 3.74 (dd, *J* = 9.1, 3.6 Hz, 1 H, CH), 4.62–4.71 (m, 2 H, CH_2), 7.27–7.33 (m, 3 H_{arom}), 7.37–7.38 (m, 2 H_{arom}).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 14.16, 25.80, 36.11, 38.80, 42.61, 128.02, 128.68, 128.70, 135.45, 174.40, 176.32.

MS (EI): *m*/*z* = 249 $[M]^+$, 189, 132, 91, 77.

HRMS (EI): *m*/*z* calcd for $C_{13}H_{15}NO_2S$: 249.0824; found: 249.0827.

Methyl 2-[(2,5-Dioxopyrrolidin-3-yl)thio]acetate (4e)

Yield: 312 mg (77%); light yellow oil.

IR (KBr): 3436, 3252, 2949, 1777, 1714, 1629, 1339, 1282, 1177, 775, 690 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.57 (dd, *J* = 18.9, 4.1 Hz, 1 H, CH_2), 3.21 (dd, *J* = 18.9, 9.3 Hz, 1 H, CH_2), 3.39 (d, *J* = 15.8 Hz, 1 H, CH_2), 3.77 (s, 3 H, CH_3), 3.89 (d, *J* = 15.8 Hz, 1 H, CH_2), 4.08 (dd, *J* = 9.2, 4.1 Hz, 1 H, CH), 8.83 (s, 1 H, NH).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 32.87, 36.57, 39.73, 52.76, 170.14, 174.73, 176.71.

MS (EI): *m*/*z* = 203 $[M]^+$, 171, 144, 130, 99.

HRMS (EI): *m*/*z* calcd for $C_7H_9NO_4S$: 203.0252; found: 203.0253.

Methyl-2-[(1-Benzyl-2,5-dioxopyrrolidin-3-yl)thio]acetate (4f)

Yield: 533 mg (91%); light yellow oil.

IR (KBr): 3456, 2945, 1704, 1495, 1395, 1165, 739, 700 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.51 (dd, *J* = 18.8, 3.9 Hz, 1 H, CH_2), 3.13 (dd, *J* = 18.8, 9.2 Hz, 1 H, CH_2), 3.35 (d, *J* = 15.9 Hz, 1 H, CH_2), 3.73 (s, 3 H, CH_3), 3.90 (d, *J* = 15.9 Hz, 1 H, CH_2), 4.02 (dd, *J* = 9.2, 3.9 Hz, 1 H, CH), 4.61–4.69 (m, 2 H, CH_2), 7.27–7.31 (m, 3 H_{arom}), 7.35–7.37 (m, 2 H_{arom}).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 32.85, 35.41, 38.38, 42.66, 52.66, 128.08, 128.71, 135.34, 170.02, 174.01, 176.01.

MS (EI): *m*/*z* = 293 $[M]^+$, 261, 234, 220, 189, 160, 132, 106, 91, 78.

HRMS (EI): *m*/*z* calcd for $C_{14}H_{15}NO_4S$: 293.0722; found: 293.0725.

3,3′-[Propane-1,3-diylbis(sulfanediyl)]bis(1-phenylpyrrolidine-2,5-dione) (4g)

Yield: 726 mg (80%); light yellow solid; mp 107–109 °C.

IR (KBr): 3447, 2917, 1781, 1712, 1637, 1495, 1382, 1177, 1029, 743, 690 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.12–2.04 (m, 2 H, CH_2), 2.66 (dd, *J* = 18.8, 3.5 Hz, 2 H, CH_2), 2.95–2.90 (m, 2 H, CH_2), 3.12–3.17 (m, 2 H, CH_2), 3.30 (dd, *J* = 18.8, 9.2 Hz, 2 H, CH_2), 3.92–3.86 (m, 2 H, CH), 7.29 (d, *J* = 7.4 Hz, 4 H_{arom}), 7.36–7.44 (m, 2 H_{arom}), 7.48 (t, *J* = 7.5 Hz, 4 H_{arom}).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 28.17, 28.42, 30.60, 30.75, 36.00, 38.93, 39.11, 126.41, 128.83, 129.23, 131.60, 173.55, 175.39.

MS (EI): *m*/*z* = 454 $[M]^+$, 280, 208, 175, 146, 119, 91.

HRMS (EI): *m*/*z* calcd for $C_{23}H_{22}N_2O_4S_2$: 454.1021; found: 454.1025.

1-Phenyl-3-(5-phenyl-2*H*-tetrazol-2-yl)pyrrolidine-2,5-dione (4h)

Yield: 366 mg (63%); white solid; mp 154–156 °C.

IR (KBr): 3437, 1726, 1634, 1495, 1454, 1387, 1192, 743, 694 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.57 (dd, *J* = 18.4, 5.7 Hz, 1 H, CH_2), 3.66 (dd, *J* = 18.5, 9.4 Hz, 1 H, CH_2), 6.19 (dd, *J* = 9.2, 5.9 Hz, 1 H, CH), 7.40 (d, *J* = 7.5 Hz, 2 H_{arom}), 7.45–7.53 (m, 6 H_{arom}), 8.18–8.17 (m, 2 H_{arom}).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 35.39, 59.82, 126.29, 126.56, 127.12, 129.02, 129.40, 129.46, 130.94, 166.27, 168.99, 171.31.

MS (EI): *m*/*z* = 319 $[M]^+$, 263, 234, 208, 180, 144, 119, 104, 91, 77.

HRMS (EI): *m*/*z* [$M^+ - N_2$] calcd for $C_{17}H_{13}N_3O_2$: 291.1008; found: 291.1011.

3-(5-Phenyl-2*H*-tetrazol-2-yl)pyrrolidine-2,5-dione (4i)

Yield: 296 mg (61%); white solid; mp 160–162 °C.

IR (KBr): 3442, 3227, 2953, 1797, 1711, 1454, 1384, 1274, 1163, 935, 714, 677 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.43–3.59 (m, 2 H, CH_2), 6.08 (t, *J* = 8.0 Hz, 1 H, CH), 7.51 (s, 3 H_{arom}), 8.15 (s, 2 H_{arom}), 8.36 (s, 1 H, NH).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 36.31, 60.64, 126.49, 127.11, 129.03, 130.97, 166.29, 169.27, 171.38.

MS (EI): *m*/*z* = 243 $[M]^+$, 215, 186, 159, 144, 116, 104, 89, 77.

HRMS (EI): *m*/*z* calcd for $C_{11}H_9N_5O_2$: 243.0756; found: 243.0758.

1-Methyl-3-(5-phenyl-2*H*-tetrazol-2-yl)pyrrolidine-2,5-dione (4j)

Yield: 282 mg (55%); white solid; mp 134–136 °C.

IR (KBr): 3448, 2921, 1771, 1643, 1440, 1383, 1282, 1117, 792, 735, 681 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.18 (s, 3 H, CH_3), 3.40 (dd, *J* = 18.3, 5.6 Hz, 1 H, CH_2), 3.49 (dd, *J* = 18.3, 9.3 Hz, 1 H, CH_2), 6.03 (dd, *J* = 9.2, 5.7 Hz, 1 H, CH), 7.47–7.55 (m, 3 H_{arom}), 8.20–8.08 (m, 2 H_{arom}).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 25.79, 35.29, 59.73, 126.59, 127.08, 128.97, 130.86, 166.17, 169.98, 172.26.

MS (EI): *m*/*z* = 257 $[M]^+$, 229, 200, 172, 144, 115, 104, 89, 77.

HRMS (EI): *m*/*z* calcd for $C_{12}H_{11}N_5O_2$: 257.0913; found: 257.0917.

3-(1*H*-Benzotriazol-1-yl)-1-phenylpyrrolidine-2,5-dione (4k)[25]

Yield: 525 mg (90%); white solid; mp 146–148 °C.

IR (KBr): 3440, 2925, 1723, 1629, 1495, 1387, 1194, 745, 696 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.64 (dd, *J* = 18.5, 9.6 Hz, 1 H, CH_2), 3.86 (dd, *J* = 18.4, 5.4 Hz, 1 H, CH_2), 5.97 (dd, *J* = 9.5, 5.6 Hz, 1 H, CH), 7.37 (d, *J* = 7.6 Hz, 2 H_{arom}), 7.40–7.55 (m, 4 H_{arom}), 7.56–7.71 (m, 2 H_{arom}), 8.13 (d, *J* = 8.4 Hz, 1 H_{arom}).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 34.87, 55.67, 108.99, 120.63, 124.76, 126.32, 128.57, 129.24, 129.39, 131.13, 133.19, 146.24, 170.69, 171.93.

MS (EI): *m*/*z* = 292 $[M]^+$, 263, 236, 117, 103, 91, 76.

3-(1*H*-Benzimidazol-1-yl)-1-phenylpyrrolidine-2,5-dione (4l)[26]

Yield: 500 mg (86%); light brown solid; mp 176–178 °C.

IR (KBr): 3436, 2917, 1719, 1632, 1493, 1384, 1183, 747, 697 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$); δ = 3.25 (dd, *J* = 18.6, 5.8 Hz, 1 H, CH_2), 3.56 (dd, *J* = 18.6, 9.7 Hz, 1 H, CH_2), 5.62 (dd, *J* = 9.5, 6.0 Hz, 1 H, CH), 7.18–7.25 (m, 1 H_{arom}), 7.37 (dd, *J* = 10.8, 6.1 Hz, 4 H_{arom}), 7.46–7.53 (dt, *J* = 25.7, 7.3 Hz, 3 H_{arom}), 7.87–7.88 (m, 1 H_{arom}), 8.06 (s, 1 H_{arom}).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 35.19, 53.82, 109.16, 121.33, 123.34, 124.12, 126.17, 129.36, 129.48, 131.07, 131.97, 142.28, 144.08, 171.27, 171.66.

MS (EI): *m*/*z* = 291 $[M]^+$, 173, 144, 118, 91, 77.

3-(1*H*-Indazol-1-yl)-1-phenylpyrrolidine-2,5-dione (4m)

Yield: 436 mg (75%); white solid; mp 158–160 °C.

IR (KBr): 3437, 2929, 1789, 1721, 1629, 1503, 1384, 1188, 747, 694 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.49 (dd, *J* = 18.3, 9.3 Hz, 1 H, CH_2), 3.86 (dd, *J* = 18.4, 4.9 Hz, 1 H, CH_2), 5.56 (dd, *J* = 9.0, 5.0 Hz, 1 H, CH), 7.12–7.19 (m, 1 H_{arom}), 7.28–7.60 (m, 6 H_{arom}), 7.68 (t, *J* = 8.9 Hz, 2 H_{arom}), 8.17 (s, 1 H_{arom}).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 35.61, 60.10, 117.61, 120.38, 121.85, 122.54, 124.75, 126.43, 127.06, 129.06, 129.28, 131.37, 149.66, 171.26, 172.59.

MS (EI): *m*/*z* = 291 $[M]^+$, 173, 144, 118, 91, 77.

HRMS (EI): *m*/*z* calcd for $C_{17}H_{13}N_3O_2$: 291.1008; found: 291.1002.

4-Methyl-*N*-(1-methyl-2,5-dioxopyrrolidin-3-yl)benzenesulfonamide (4n)

Yield: 191 mg (34%); white solid; mp 154–156 °C.

IR (KBr): 3440, 3256, 2917, 2847, 1781, 1706, 1605, 1442, 1389, 1335, 1290, 1158, 1029, 816, 661 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.45 (s, 3 H, CH_3), 2.82 (dd, *J* = 18.2, 5.6 Hz, 1 H, CH_2), 2.98 (s, 3 H, CH_3), 3.10 (dd, *J* = 18.3, 8.5 Hz, 1 H, CH_2), 4.09 (s, 1 H, NH), 5.29 (s, 1 H, CH), 7.35 (t, *J* = 9.7 Hz, 2 H_{arom}), 7.80 (t, *J* = 11.3 Hz, 2 H_{arom}).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 21.62, 25.25, 37.07, 51.62, 127.44, 130.08, 135.47, 144.61, 173.63, 174.54.

MS (EI): *m*/*z* = 282 $[M]^+$, 218, 155, 133, 127, 91.

HRMS (EI): *m*/*z* calcd for $C_{12}H_{14}N_2O_4S$: 282.0674; found: 282.0669.

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Supporting Information

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