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Thio-Michael addition of α,β-unsaturated amides catalyzed by Nmm-based ionic liquids†

Yawei Liu,‡[a] Zhenzhen Lai,‡[a] Pengkun Yang,‡[a] Yuanqing Xu,[a] Wenkai Zhang,[a] Baoying Liu,[a] Minghua Lu,[a] Haibo Chang,[a] Tao Ding*[a] and Hao Xu*[ab]

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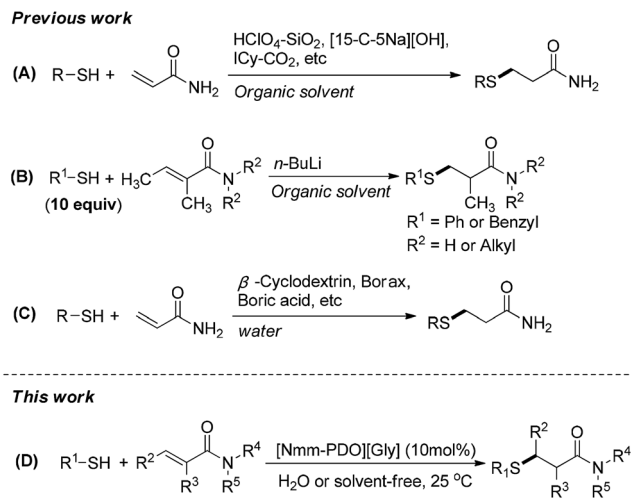
A simple and practical thio-Michael addition of α,β-unsaturated amides catalyzed by Nmm-based ionic liquids with a 1,2-propanediol group has been developed. All the α,β-unsaturated amides without substituents at the carbon end could smoothly react with sulfur-nucleophiles in water. Meanwhile for thio-Michael addition of α,β-unsaturated amides with substituents at the carbon end, the relevant product could also be obtained successfully under solvent-free conditions at 55 °C. Furthermore, the IL-catalyst is recyclable and applicable for gram-scale synthesis.

Introduction

Ionic liquids (ILs) are acknowledged as eco-friendly alternatives to volatile organic solvents, because of their unique properties like negligible vapor pressure, high thermal stability, excellent dissolving capacity and ease of recyclability. In the past few years, many functional ILs have been also employed as catalysts for various reactions such as Michael addition,[1] Knoevenagel condensation[2] and Mannich reaction.[3] Furthermore, well-designed ILs could significantly improve the reactivity and selectivity of reactions by modifying distinct cations and anions.[4] Therefore, it is highly desirable to explore rationally-designed and readily available IL catalysts for different reactions.

Thio-Michael reaction is one of the most important carbon–sulfur bond forming reactions, and plays a key role in the synthesis of many bioactive molecules.[5] Traditionally, the reaction is performed in organic solvent under base-mediated or Lewis acid-mediated conditions.[6] In recent years, some catalytic methods have been developed in the presence of catalysts including organic bases,[7] Lewis or Brønsted acids,[8] ionic liquids,[9] enzymes[10] and N-heterocyclic carbine.[11] Although these methods above are efficient, the range of Michael acceptors was limited to relatively active substrates such as acrylonitrile, nitroalkenes, α,β-unsaturated ketones and esters. Several examples attempted to employ α,β-unsaturated amides as Michael acceptors (Scheme 1A and B),[1c,8c,11,12] but only the acrylamide without substituents at carbon end could be transformed into the corresponding thio-Michael adduct easily because of less steric hindrance. Therefore, the systematical research on thio-Michael addition of α,β-unsaturated amides is very necessary.

"The best solvent is no solvent and if a solvent is needed it should preferably be water" stated by R. A. Sheldon.[13] Thio-Michael addition in water is environmentally benign because water is cheap and safe. Recently, several examples conducted in water have been reported by employing catalysts including $NiFeO_4$ nanoparticle,[14] boric acid,[15] borax[16] and β-cyclodextrin (Scheme 1C).[17] However, the poor tolerance for different α,β-unsaturated amides is still the main hurdle with thio-Michael addition in water, and only unsubstituted acrylamide was tolerated for its less steric hindrance. Furthermore, the reaction catalyzed by ionic liquid in water has not been found in the literature. In our previous work, a serial of novel ionic liquids



Scheme 1 Thio-Michael addition of α,β-unsaturated amides.

[a]College of Chemistry and Chemical Engineering, Henan University, Kaifeng 475004, P. R. China. E-mail: xuhao@henu.edu.cn; dingtao@henu.edu.cn

[b]Key Laboratory of Natural Medicine and Immuno-Engineering, Henan University, Kaifeng 475004, P. R. China

† Electronic supplementary information (ESI) available: ^{1}H, ^{13}C NMR spectra of these synthesized compounds. See DOI: 10.1039/c7ra08956b

‡ These authors contributed equally to this work.

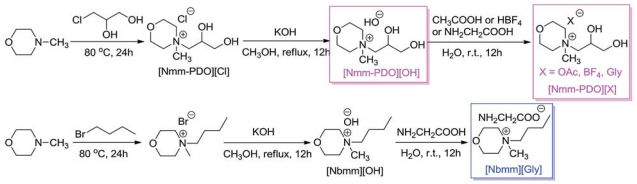
based on N-methyl morpholine (Nmm) and 3-chloro-1,2-propanediol were synthesized and applied successfully in Knoevenagel condensation.[2a] In continuation of our endeavors to develop simple and practical methodology for organic synthesis,[18] herein we report a thio-Michael addition of α,β-unsaturated amides catalyzed by Nmm-based ionic liquids in water (Scheme 1D), and most of the substrates could provide good yields in water. In addition, the catalysts are recyclable and applicable for the gram-scale synthesis.

Results and discussion

Five Nmm-based ionic liquids were synthesized by our previous methods (Scheme 2).[2a]

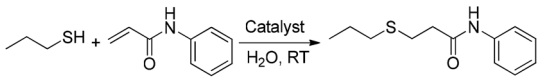
Initially, the thio-Michael addition of propanethiol (**1a**) with *N*-phenylacrylamide (**2c**) was chosen as the model reaction to optimize conditions including catalysts, solvents and the amount of catalyst. As shown in Table 1, four Nmm-based IL catalysts were screened using water as the solvent at room temperature for 10 hours (Table 1, entries 1–4), and [Nmm-PDO][Gly] afforded the highest yield (entry 4). The reaction did not work in the absence of IL catalysts, even reaction time was extended to 24 h (entry 6). [Nbmm][Gly] was also used as the catalyst for comparison, but it was inferior to [Nmm-PDO][Gly] although the same glycine (Gly) anion existed in the two IL catalysts (compare entry 4 with entry 5); the results hinted the hydrogen bonding interaction between carbonyl group of *N*-phenylacrylamide (**2c**) and hydroxyl groups in the cation of [Nmm-PDO][Gly], which could increase the electrophilicity of the amide as Michael acceptor. The effect of solvents was also investigated (entries 4, 7, 8), and H_2O was more suitable, perhaps because of its better dissolving ability for IL-catalysts. When the reaction was performed under solvent-free condition, an excellent yield could also be obtained (entry 9). Furthermore, the effect of catalyst loading was also investigated; when the amount of catalyst was decreased, the product (**3n**) could still be generated in moderate to good yield, but more reaction time was needed (entries 10, 11).

With the optimized conditions in hand (10 mol% of [Nmm-PDO][OAc] as the catalyst, water as solvent, room temperature), the scope of thio-Michael addition of α,β-unsaturated amides catalyzed by Nmm-based ionic liquids in water was investigated; and most of the substrates provided good yields as shown in Table 2. For α,β-unsaturated amides, the steric hindrance had a great impact on their reactivity; the substrates with larger substituents showed lower reactivity (entries 1–5, 14–18).



Scheme 2 Synthesis of the [Nmm-PDO][X] and [Nbmm][Gly] ionic liquids.

Table 1 Thio-Michael addition of propanethiol (**1a**) with *N*-phenylacrylamide (**2c**) catalyzed by Nmm-based ionic liquids: optimization of conditions[a]



1a **2c** **3n**

Entry	Cat.	Solvent	Time (h)	Yield[b] (%)
1	[Nmm-PDO][OH]	H_2O	10	95
2	[Nmm-PDO][OAc]	H_2O	10	85
3	[Nmm-PDO][BF_4]	H_2O	10	65
4	**[Nmm-PDO][Gly]**	**H_2O**	**10**	**96**
5	[Nbmm][Gly]	H_2O	10	60
6	Catalyst free	H_2O	24	Trace
7	[Nmm-PDO][Gly]	CH_2Cl_2	10	83
8	[Nmm-PDO][Gly]	CH_3CN	10	73
9	[Nmm-PDO][Gly]	Neat	10	90
10[c]	[Nmm-PDO][Gly]	H_2O	24	86
11[d]	[Nmm-PDO][Gly]	H_2O	48	52

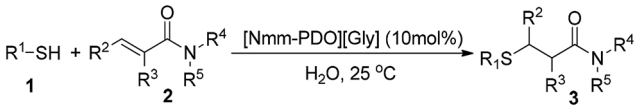
[a] Reaction conditions: propanethiol (0.5 mmol, 45 μL), *N*-phenylacrylamide (0.5 mmol, 74 mg), catalyst (10 mol%), H_2O (1 mL), room temperature. [b] Isolated yield. [c] Catalyst (5 mol%). [d] Catalyst (1 mol%).

Especially for the substituted acrylamides with substituents at carbon end, only trace amount of products could be monitored by TLC; fortunately, the corresponding products could be obtained in good yields under solvent-free conditions at 55 °C (entries 26–30). Furthermore, substituted propynamide could also be transformed into relevant thio-Michael adduct in 42% yield under solvent-free conditions (entry 31), and the reaction is highly stereoselective for the *Z*-geometry. For the sulfur-nucleophile, the reactivity of thiols was also affected by the steric hindrance. Meanwhile the aromatic sulfur-nucleophile could react with α,β-unsaturated amides smoothly too (entry 6–9, 12–13, 19–21, 27), perhaps because the proton (H^+) could be removed more easily than thiols although the steric hindrance of phenyl group was relatively larger. In addition, thiols with hydroxyl group or carbon–carbon double bond could be tolerated as well (entries 22, 23, 28).

The reaction of propanethiol (**1a**) with *N*,*N*-dimethylacrylamide (**2b**) was chosen to examine the recyclability of IL-catalysts and applicability in the large-scale synthesis. The result showed that the catalyst still kept a high catalytic activity even in the third run (see Table S1 in the ESI†). Furthermore, the scaled-up experiment was performed on a gram-scale, and 2.90 g of **3j** were prepared in 82% yield (**2g** of **2b** was used); the result demonstrated that [Nmm-PDO][Gly] was also efficient catalyst for gram-scale synthesis.

A possible mechanism is proposed in Scheme 3 for the [Nmm-PDO][Gly] catalyzed thio-Michael addition (herein, reaction of propanethiol **1a** with *N*,*N*-dimethylacrylamide **2b** is chosen as the example). Firstly, the hydrogen-bonding interactions between the hydroxyl groups of [Nmm-PDO][Gly] and the carbonyl group of **2b** can be formed, which making **2b** more vulnerable by **1a**. Then nucleophilic attack of thiol **1a** on the

Table 2 Thio-Michael addition of α,β-unsaturated amides catalyzed by [Nmm-PDO][Gly][a]



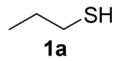
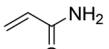
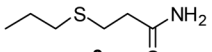
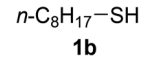
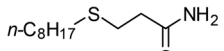
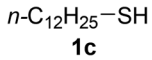
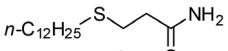
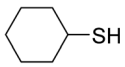
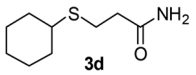
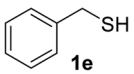
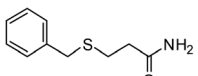
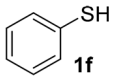
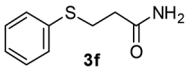
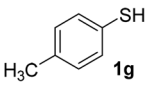
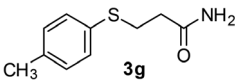
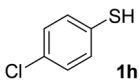
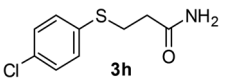
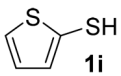
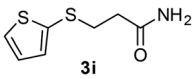
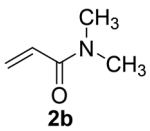
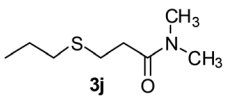
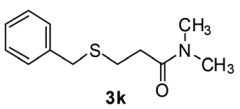
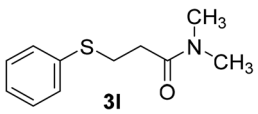
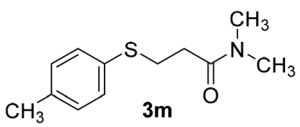
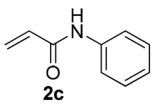
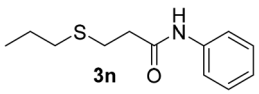
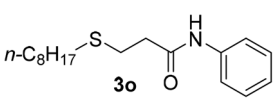
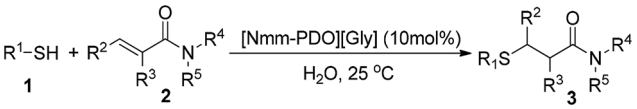
Entry	1	2	3	t/h	Yield[b]/%
1	 1a	 2a	 3a	6	98
2	 1b	2a	 3b	6	92
3	 1c	2a	 3c	25	50(91[c])
4	 1d	2a	 3d	6	88
5	 1e	2a	 3e	6	87
6	 1f	2a	 3f	6	78
7	 1g	2a	 3g	6	82
8	 1h	2a	 3h	6	88
9	 1i	2a	 3i	6	72
10	1a	 2b	 3j	6	90
11	1e	2b	 3k	6	92
12	1f	2b	 3l	6	94
13	1g	2b	 3m	6	96
14	1a	 2c	 3n	10	96
15	1b	2c	 3o	10	80

Table 2 (*Contd.*)



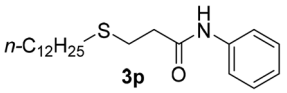
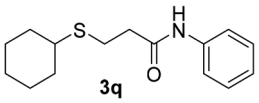
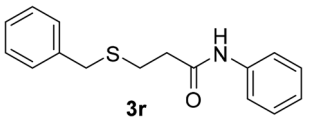
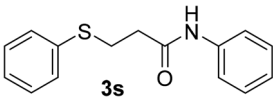
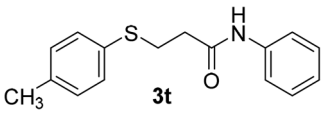
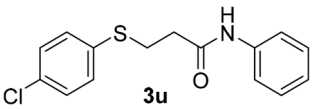
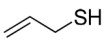
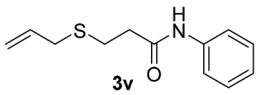
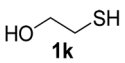
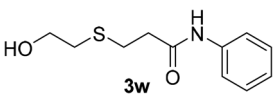
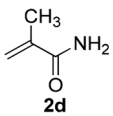
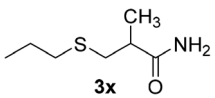
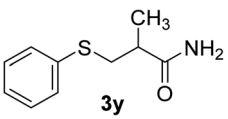
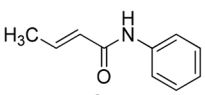
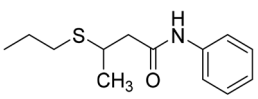
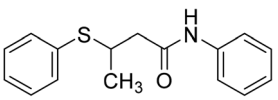
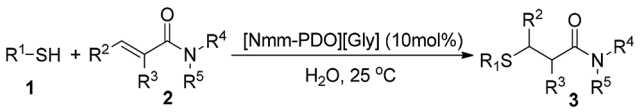
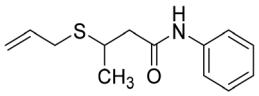
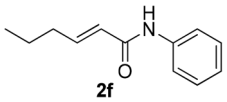
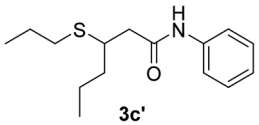
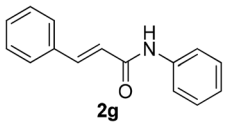
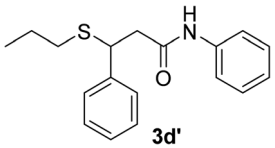
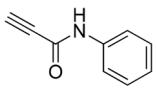
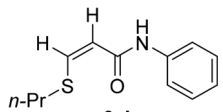
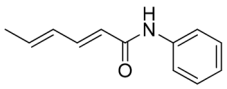
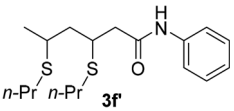
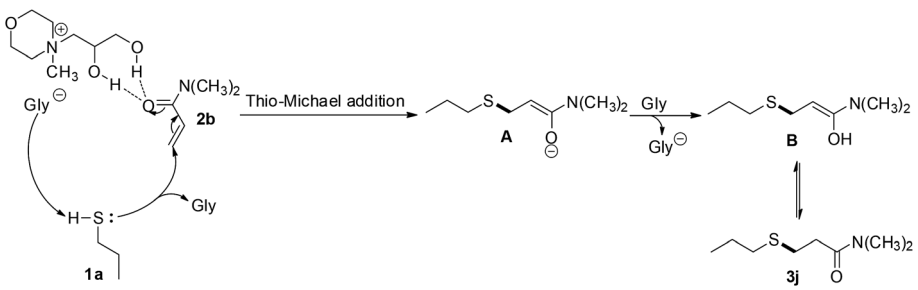
Entry	1	2	3	*t*/h	Yield[b]/%
16	**1c**	**2c**	 **3p**	25	44(81[c])
17	**1d**	**2c**	 **3q**	10	85
18	**1e**	**2c**	 **3r**	10	86
19	**1f**	**2c**	 **3s**	10	91
20	**1g**	**2c**	 **3t**	10	88
21	**1h**	**2c**	 **3u**	10	91
22	 **1j**	**2c**	 **3v**	10	34(60[c])
23	 **1k**	**2c**	 **3w**	10	95
24	**1a**	 **2d**	 **3x**	6	98
25	**1f**	**2d**	 **3y**	6	90
26	**1a**	 **2e**	 **3z**	10	78[c]
27	**1f**	**2e**	 **3a'**	20	60[c]

Table 2 (*Contd.*)



Entry	1	2	3	*t*/h	Yield[b]/%
28	**1j**	**2e**	 **3b'**	10	42[c]
29	**1a**	 **2f**	 **3c'**	16	88[c]
30	**1a**	 **2g**	 **3d'**	25	75[c]
31	**1a**	 **2h**	 **3e'**	15	42
32	**1a**	 **2i**	 **3f'**	20	62[d]

[a] Reaction conditions: sulfur-nucleophile **1** (0.5 mmol), α,β-unsaturated amides **2** (0.5 mmol), catalyst [Nmm-PDO][Gly] (10 mol%), water (1 mL), room temperature. [b] Isolated yield. [c] Solvent-free at 55 °C. [d] Sulfur-nucleophile **1a** (1 mmol).



Scheme 3 Possible mechanism for the thio-Michael addition catalyzed by [Nmm-PDO][Gly] between propanethiol (**1a**) and *N*,*N*-dimethylacrylamide (**2b**).

β-carbon of *N*,*N*-dimethylacrylamide **2b** lead to the intermediate A. Intermediate A take the proton from glycine (Gly), generating the thio-Michael product **3j**.

Additionally, we compared the FTIR spectrum of the *N*,*N*-dimethylacrylamide with *N*,*N*-dimethylacrylamide-[Nmm-PDO][Gly] mixture, and the results were shown in Fig. 1. It was found that the absorption peak of carbonyl group in *N*,*N*-dimethylacrylamide was at 1648 cm^{-1}, while it was red-shifted to 1568 cm^{-1} in the mixture; meanwhile we also compared the ^{13}C NMR spectrum of *N*,*N*-dimethylacrylamide with *N*,*N*-dimethylacrylamide-[Nmm-PDO][Gly] mixture (Fig. S1 and S2 in the ESI†); the chemical shift of carbonyl group in *N*-phenylacrylamide was 165.23, while it was 165.47 in the mixture. All the results hinted the existence of the hydrogen bonding interactions between the carbonyl group of the *N*,*N*-dimethylacrylamide and the hydroxyl groups in [Nmm-PDO][Gly].

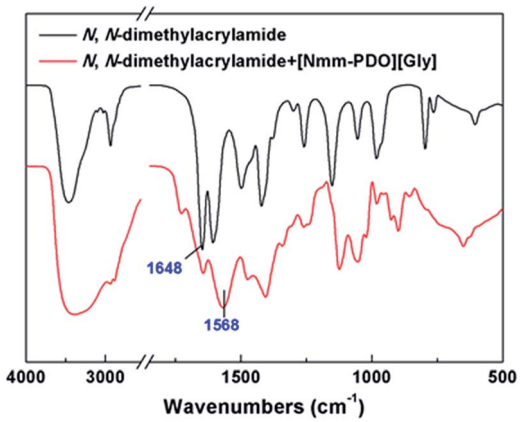


Fig. 1 FTIR comparison of *N*,*N*-dimethylacrylamide with *N*,*N*-dimethylacryl-amide + [Nmm-PDO][Gly] mixture.

Conclusion

Readily available and eco-friendly Nmm-based ILs are developed as the practical and recyclable catalysts for the thio-Michael addition of α,β-unsaturated amides. All the α,β-unsaturated amides without substituents at carbon end could smoothly react with sulfur-nucleophile in water, and only unsubstituted acrylamide was tolerated in water by the previous methods. Meanwhile for thio-Michael addition of α,β-unsaturated amides with substituents at carbon end, the relevant product could be obtained successfully under solvent-free condition at 55 °C, which was hard to be prepared *via* thio-Michael addition in the previous methods. Furthermore, the IL-catalyst is recyclable and applicable for the gram-scale synthesis. All the results above represent an efficient and eco-friendly IL-catalyst for the thio-Michael addition of α,β-unsaturated amides.

General experimental procedures

The reaction is carried out at room temperature in water or solvent-free. NMR spectra were recorded on Bruker AVANCE III HD 400 MHz; proton and carbon magnetic resonance spectra (^{1}H NMR and ^{13}C NMR) were recorded using tetramethylsilane (TMS) in the solvent of $CDCl_3$ as the internal standard (^{1}H NMR: TMS at 0.00 ppm, $CHCl_3$ at 7.26 ppm; ^{13}C NMR: $CDCl_3$ at 77.16 ppm) or were recorded using tetramethylsilane (TMS) in the solvent of DMSO-d_6 as the internal standard (^{1}H NMR: TMS at 0.00 ppm, DMSO at 2.50 ppm; ^{13}C NMR: DMSO at 39.51 ppm).

[Nmm-PDO][X] and [Nbmm][Gly]

Ionic liquids was synthesized by our previous method.[2a]

[Nmm-PDO][Cl]

White solid; ^{1}H NMR (D_2O, 400 MHz, 25 °C): δ 4.44–4.22 (m, 1H), 4.03 (s, 4H), 3.72–3.46 (m, 8H), 3.30 (s, 3H). ^{13}C NMR (D_2O, 100 MHz, 25 °C): δ 66.4, 65.7, 63.7, 61.1, 60.9, 60.5, 48.4. ESI-MS $[Nmm\text{-}PDO]^+$ 176.12.

[Nmm-PDO][OH]

Colourless liquid; ^{1}H NMR (D_2O, 400 MHz, 25 °C): δ 4.43–4.23 (m, 1H), 4.04 (s, 4H), 3.73–3.46 (m, 8H), 3.30 (s, 3H). ^{13}C NMR (D_2O, 100 MHz, 25 °C) δ 66.5, 65.7, 63.7, 61.1, 60.7, 60.5, 48.4. ESI-MS $[Nmm\text{-}PDO]^+$ 176.12.

[Nmm-PDO][OAc]

Colourless liquid; ^{1}H NMR (D_2O, 400 MHz, 25 °C): δ 4.22–4.11 (m, 1H), 3.89 (s, 4H), 3.61–3.32 (m, 8H), 3.16 (s, 3H), 1.77 (s, 3H). ^{13}C NMR (D_2O, 100 MHz, 25 °C): δ 180.0, 66.4, 65.6, 63.6, 60.9, 60.6, 60.3, 48.3, 23.1. ESI-MS $[Nmm\text{-}PDO]^+$ 176.12; ESI-MS $[CH_3COO]^-$ *m*/*z* 59.06.

[Nmm-PDO][BF_4]

Colourless liquid; ^{1}H NMR (D_2O, 400 MHz, 25 °C): δ 4.47–4.32 (m, 1H), 4.12 (s, 4H), 3.81–3.51 (m, 8H), 3.37 (s, 3H). ^{13}C NMR (D_2O, 100 MHz, 25 °C) δ 66.6, 65.8, 63.8, 61.2, 60.7, 60.5, 48.3. ESI-MS $[Nmm\text{-}PDO]^+$ 176.12; ESI-MS $[BF_4]^-$ 87.03.

[Nmm-PDO][Gly]

Colourless liquid; ^{1}H NMR (D_2O, 400 MHz, 25 °C): δ 4.30–4.20 (m, 1H), 3.97 (s, 4H), 3.66–3.39 (m, 8H), 3.23 (s, 3H), 1.81 (s, 2H). ^{13}C NMR (D_2O, 100 MHz, 25 °C) δ 181.1, 66.4, 65.6, 63.6, 61.0, 60.6, 60.4, 48.3, 23.4. ESI-HRMS $[Nmm\text{-}PDO]^+$ *m*/*z* calcd for $C_8H_{18}NO_3$ 176.1281, found 176.1284; ESI-MS $[Nmm\text{-}PDO]^+$ 176.12; ESI-MS $[NH_2CH_2COO]^-$ *m*/*z* 74.01.

[Nbmm][Gly]

Colourless liquid; ^{1}H NMR (D_2O, 300 MHz, 25 °C): δ 3.95 (s, 4H), 3.50–3.31 (m, 6H), 3.10 (s, 3H), 1.82 (s, 2H), 1.76–1.61 (m, 2H), 1.41–1.24 (m, 2H), 0.88 (t, 3H). ^{13}C NMR (D_2O, 100 MHz, 25 °C) δ 180.5, 65.1, 60.4, 59.5, 46.7, 44.6, 23.6, 22.9, 19.1, 12.9. ESI-MS $[Nbmm]^+$ *m*/*z* 158.25; ESI-MS $[NH_2CH_2COO]^-$ *m*/*z* 74.01.

General procedure for synthesis of compounds 3a–w

Sulfur-nucleophile (0.5 mmol), α,β-unsaturated amides (0.5 mmol), IL catalyst (10 mol%) and water (1 mL) was added into 25 mL Schlenk tube and stirred at room temperature. Upon completion of the reaction (monitored by TLC), the reaction mixture was extracted with ethyl acetate (3 × 5 mL), the organic and aqueous layers were separated, and the aqueous layer was extracted with EtOAc (2 × 5 mL). The combined organic layers were dried over anhydrous Na_2SO_4, concentrated and purified by column chromatography on silica gel employing petroleum ether/ethyl acetate as eluent to afford target product **3** [the products of **3z–3d′**, **3f′** were prepared at 55 °C under solvent-free condition; upon completion of the reaction, the reaction mixture was extracted with ethyl acetate (3 × 5 mL). The combined organic layers were dried over anhydrous Na_2SO_4, they were purified by column chromatography on silica gel using petroleum ether/ethyl acetate as the eluent].

3-(Propylthio)propanamide (3a).[19] Eluent: petroleum ether/ethyl acetate (4 : 1). Yield 72 mg (98%). White solid, mp 62–63 °C (lit.[19] mp 59–61 °C). ^{1}H NMR (d_6-DMSO, 400 MHz, 25 °C)

δ 7.33 (s, 1H), 6.83 (s, 1H), 2.64 (t, J = 7.4 Hz, 2H), 2.47 (t, J = 7.2 Hz, 2H), 2.31 (t, J = 7.4 Hz, 2H), 1.59–1.47 (m, 2H), 0.93 (t, J = 7.3 Hz, 3H). ^{13}C NMR (d_6-DMSO, 100 MHz, 25 °C) δ 173.0, 36.1, 33.5, 27.3, 22.9, 13.7. ESI-MS $[M + H]^+$ m/z 148.25; $[M + Na]^+$ 170.19.

3-(Octylthio)propanamide (3b).[19] Eluent: petroleum ether/ethyl acetate (4 : 1). Yield 100 mg (92%). White solid, mp 90–91 °C (lit.[19] mp 92–93 °C). ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C) δ 5.79 (s, 2H), 2.81 (t, J = 7.2 Hz, 2H), 2.60–2.45 (m, 4H), 1.64–1.53 (m, 2H), 1.42–1.23 (m, 10H), 0.88 (t, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz, 25 °C) δ 173.8, 36.0, 32.4, 31.8, 29.6, 29.2, 28.9, 27.5, 22.7, 14.1. ESI-MS $[M + H]^+$ m/z 218.28; $[M + Na]^+$ 240.29.

3-(Dodecylthio)propanamide (3c). Eluent: petroleum ether/ethyl acetate (4 : 1). Yield 68 mg (50%), solvent-free condition yield 124 mg (91%). White solid, mp 84–86 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C) δ 5.60 (d, J = 94.4 Hz, 2H), 2.81 (t, J = 7.2 Hz, 2H), 2.53 (m, J = 14.2, 7.3 Hz, 4H), 1.67–1.53 (m, 5H), 1.41–1.19 (m, 19H), 0.88 (t, J = 6.7 Hz, 3H). ^{13}C NMR (d_6-DMSO, 100 MHz, 25 °C) δ 173.1, 36.0, 31.8, 31.5, 29.6, 29.5, 29.2, 29.1, 28.7, 27.4, 22.6. ESI-HRMS $[M + H]^+$ m/z calcd for $C_{15}H_{32}NOS$ 274.2199, found 274.2210.

3-(Cyclohexylthio)propanamide (3d).[17] Eluent: petroleum ether/ethyl acetate (4 : 1). Yield 82 mg (88%). White solid, mp 74–75 °C. ^{1}H NMR (d_6-DMSO, 400 MHz, 25 °C) δ 7.35 (s, 1H), 6.85 (s, 1H), 2.66 (t, J = 7.4 Hz, 3H), 2.30 (t, J = 7.4 Hz, 2H), 1.89 (t, J = 10.2, 4.9 Hz, 2H), 1.76–1.62 (m, 2H), 1.62–1.50 (m, 1H), 1.24 (m, J = 14.3, 13.3, 7.1 Hz, 5H). ^{13}C NMR (d_6-DMSO, 100 MHz, 25 °C) δ 173.1, 43.0, 36.4, 33.7, 25.9, 25.7. ESI-MS $[M + H]^+$ m/z 188.12; $[M + Na]^+$ 210.11.

3-(Benzylthio)propanamide (3e).[19] Eluent: petroleum ether/ethyl acetate (4 : 1). Yield 85 mg (87%). White solid, mp 110–111 °C(lit.[19] mp 104–105 °C). ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C) δ 7.35–7.22 (m, 5H), 5.73 (d, J = 69.6 Hz, 2H), 3.74 (s, 2H), 2.72 (t, J = 7.2 Hz, 2H), 2.41 (t, J = 7.2 Hz, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz, 25 °C) δ 173.5, 138.2, 128.9, 128.6, 127.2, 36.7, 35.7, 27.0. ESI-MS $[M + H]^+$ m/z 196.14; $[M + Na]^+$ 218.12.

3-(Phenylthio)propanamide (3f).[14] Eluent: petroleum ether/ethyl acetate (4 : 1). Yield 71 mg (78%). White solid, mp 116–118 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C) δ 7.40–7.34 (m, 2H), 7.33–7.27 (m, 2H), 7.24–7.18 (m, 1H), 5.71 (d, J = 68.2 Hz, 2H), 3.20 (t, J = 7.3 Hz, 2H), 2.52 (t, J = 7.3 Hz, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz, 25 °C) δ 173.3, 135.2, 129.8, 129.1, 126.5, 35.3, 29.1. ESI-MS $[M + H]^+$ m/z 182.18; $[M + Na]^+$ 204.15.

3-(*p*-Tolylthio)propanamide (3g).[17] Eluent: petroleum ether/ethyl acetate (4 : 1). Yield 80 mg (82%). White solid, mp 111–113 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C) δ 7.28 (d, 2H), 7.12 (d, J = 7.9 Hz, 2H), 5.69 (d, J = 53.8 Hz, 2H), 3.15 (t, J = 7.3 Hz, 2H), 2.49 (t, J = 7.3 Hz, 2H), 2.33 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz, 25 °C) δ 173.38, 136.84, 131.30, 130.68, 129.87, 35.39, 29.89, 21.05. ESI-MS $[M + H]^+$ m/z 196.14; $[M + Na]^+$ 218.12.

3-[(4-Chlorophenyl)thio]propanamide (3h).[17] Eluent: petroleum ether/ethyl acetate (4 : 1). Yield 95 mg (88%). White solid, mp 116–117 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C) δ 7.34–7.23 (m, 4H), 5.63 (d, J = 60.2 Hz, 2H), 3.19 (t, J = 7.3 Hz, 2H), 2.51 (t, J = 7.3 Hz, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz, 25 °C) δ 172.9, 133.9, 132.5, 131.1, 129.2, 35.2, 29.3. ESI-MS $[M + H]^+$ m/z 216.11; $[M + Na]^+$ 238.09.

3-(Thiophen-2-ylthio)propanamide (3i). Eluent: petroleum ether/ethyl acetate (4 : 1). Yield 67 mg (72%). Yellow solid, mp 88–90 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C) δ 7.30 (d, J = 5.4, 1.3 Hz, 1H), 7.08 (d, J = 3.5, 1.3 Hz, 1H), 6.92 (t, J = 5.4, 3.5 Hz, 1H), 5.75 (d, J = 120.5 Hz, 2H), 2.98 (t, J = 7.2 Hz, 2H), 2.44 (t, J = 7.2 Hz, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz, 25 °C) δ 173.3, 134.4, 133.6, 129.8, 127.7, 35.49, 33.98. ESI-HRMS $[M + H]^+$ m/z calcd for $C_7H_{10}NOS_2$ 188.0198, found 188.0210.

***N*,*N*-Dimethyl-3-(propylthio)propanamide (3j).** Eluent: petroleum ether/ethyl acetate (4 : 1). Yield 79 mg (90%). Yellow liquid. ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C) δ 2.79 (s, 3H), 2.70 (s, 3H), 2.55 (t, 2H), 2.36 (t, J = 7.6 Hz, 2H), 2.27 (t, J = 7.3, 1.5 Hz, 2H), 1.43–1.30 (m, 2H), 0.73 (t, J = 7.4, 1.4 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz, 25 °C) δ 171.0, 36.9, 35.1, 34.2, 33.6, 27.1, 22.7, 13.2. ESI-HRMS $[M + H]^+$ m/z calcd for $C_8H_{18}NOS$ 176.1104, found 176.1115.

3-(Benzylthio)-*N*,*N*-dimethylpropanamide (3k).[20] Eluent: petroleum ether/ethyl acetate (4 : 1). Yield 103 mg (92%). Yellow liquid. ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C) δ 7.34–7.26 (m, 4H), 7.24–7.19 (m, 1H), 3.73 (s, 2H), 2.89 (d, J = 8.4 Hz, 6H), 2.74 (t, J = 8.2, 6.9 Hz, 2H), 2.48 (t, J = 7.5 Hz, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz, 25 °C) δ 171.1, 138.6, 128.8, 128.5, 127.0, 36.9, 35.4, 33.5, 27.0. ESI-HRMS $[M + H]^+$ m/z calcd for $C_{12}H_{18}NOS$ 224.1104, found 224.1109.

***N*,*N*-Dimethyl-3-(phenylthio)propanamide (3l).** Eluent: petroleum ether/ethyl acetate (4 : 1). Yield 98 mg (94%). Yellow liquid. ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C) δ 7.26 (d, J = 7.4 Hz, 2H), 7.19 (t, J = 7.7 Hz, 2H), 7.08 (t, J = 7.3 Hz, 1H), 3.15 (t, J = 7.5 Hz, 2H), 2.83 (d, J = 6.8 Hz, 6H), 2.54 (t, J = 7.5 Hz, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz, 25 °C) δ 170.9, 136.0, 129.1, 129.0, 126.0, 37.0, 35.4, 33.1, 28.9. ESI-HRMS $[M + H]^+$ m/z calcd for $C_{11}H_{16}NOS$ 210.0947, found 210.0947.

***N*,*N*-Dimethyl-3-(*p*-tolylthio)propanamide (3m).** Eluent: petroleum ether/ethyl acetate (4 : 1). Yield 107 mg (96%). Yellow liquid. ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C) δ 7.18 (d, J = 8.0 Hz, 2H), 7.01 (d, J = 7.9 Hz, 2H), 3.14–3.05 (t, 2H), 2.83 (d, J = 5.2 Hz, 6H), 2.51 (t, J = 7.5 Hz, 2H), 2.22 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz, 25 °C) δ 171.0, 136.2, 132.1, 130.0, 129.7, 37.0, 35.4, 33.3, 29.6, 21.0. ESI-HRMS $[M + H]^+$ m/z calcd for $C_{12}H_{18}NOS$ 224.1104, found 224.1109.

***N*-Phenyl-3-(propylthio)propanamide (3n).** Eluent: petroleum ether/ethyl acetate (10 : 1). Yield 107 mg (96%). White solid, mp 42–44 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C) δ 8.53 (s, 1H), 7.43 (d, J = 7.5 Hz, 2H), 7.17 (t, J = 7.9 Hz, 2H), 6.98 (t, J = 7.4 Hz, 1H), 2.74 (t, J = 7.2 Hz, 2H), 2.53 (t, J = 7.3 Hz, 2H), 2.38 (t, J = 7.3 Hz, 2H), 1.55–1.40 (m, 2H), 0.85 (t, J = 7.4 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz, 25 °C) δ 170.4, 138.0, 128.9, 124.4, 120.4, 37.6, 34.4, 27.7, 22.9, 13.5. ESI-HRMS $[M + H]^+$ m/z calcd for $C_{12}H_{18}NOS$ 224.1104, found 224.1088.

3-(Octylthio)-*N*-phenylpropanamide (3o). Eluent: petroleum ether/ethyl acetate (10 : 1). Yield 117 mg (80%). White solid, mp 57–58 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C) δ 7.76 (s, 1H), 7.52 (d, 2H), 7.31 (t, J = 7.9 Hz, 2H), 7.10 (t, J = 7.4 Hz, 1H), 2.89 (t, J = 7.0 Hz, 2H), 2.63 (t, J = 7.0 Hz, 2H), 2.56 (t, J = 7.4 Hz, 2H), 1.64–1.54 (m, 2H), 1.41–1.20 (m, 10H), 0.88 (t, J = 6.7 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz, 25 °C) δ 169.7, 137.8, 129.0, 124.4, 119.9,

37.8, 32.5, 31.8, 29.6, 29.2, 28.9, 27.7, 22.7, 14.1. ESI-HRMS [M + H]$^+$ *m*/*z* calcd for $C_{17}H_{28}NOS$ 294.1886, found 294.1890.

3-(Dodecylthio)-*N*-phenylpropanamide (3p). Eluent: petroleum ether/ethyl acetate (10 : 1). Yield 77 mg (44%), solvent-free condition yield 142 mg (81%). White solid, mp 75–77 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C) δ 7.66–7.42 (m, 3H), 7.33 (t, J = 7.9 Hz, 2H), 7.11 (t, J = 7.4 Hz, 1H), 2.90 (t, J = 7.0 Hz, 2H), 2.64 (t, J = 7.0 Hz, 2H), 2.57 (t, J = 7.4 Hz, 2H), 1.65–1.56 (m, 2H), 1.46–1.16 (m, 18H), 0.88 (t, J = 6.7 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz, 25 °C) δ 169.8, 169.6, 137.8, 129.0, 124.4, 120.0, 119.9, 50.9, 37.8, 37.7, 32.5, 31.9, 29.7, 29.6, 29.5, 29.4, 29.3, 28.9, 27.7, 22.7, 14.2. ESI-HRMS [M + H]$^+$ *m*/*z* calcd for $C_{21}H_{36}NOS$ 350.2512, found 350.2517.

3-(Cyclohexylthio)-*N*-phenylpropanamide (3q). Eluent: petroleum ether/ethyl acetate (10 : 1). Yield 112 mg (85%). White solid, mp 85–86 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C) δ 7.78 (s, 1H), 7.52 (d, 2H), 7.31 (t, J = 7.9 Hz, 2H), 7.11 (t, 1H), 2.91 (t, J = 7.1 Hz, 2H), 2.75–2.66 (m, 1H), 2.62 (t, J = 7.1 Hz, 2H), 2.03–1.94 (m, 2H), 1.80–1.73 (m, 2H), 1.65–1.57 (m, 1H), 1.38–1.22 (m, 5H). ^{13}C NMR ($CDCl_3$, 100 MHz, 25 °C) δ 169.7, 137.8, 129.0, 124.4, 119.9, 44.0, 38.0, 33.6, 26.1, 25.8, 25.7. ESI-HRMS [M + H]$^+$ *m*/*z* calcd for $C_{15}H_{22}NOS$ 264.1417, found 264.1416.

3-(Benzylthio)-*N*-phenylpropanamide (3r). Eluent: petroleum ether/ethyl acetate (10 : 1). Yield 117 mg (86%). White solid, mp 80–82 °C. ^{1}H NMR (d_6-DMSO, 400 MHz, 25 °C) δ 9.98 (s, 1H), 7.59 (d, J = 8.0 Hz, 2H), 7.35–7.22 (m, 7H), 7.03 (t, J = 7.4 Hz, 1H), 3.78 (s, 2H), 2.66 (t, J = 6.3 Hz, 2H), 2.61 (t, J = 6.2 Hz, 2H). ^{13}C NMR (d_6-DMSO, 100 MHz, 25 °C) δ 167.0, 139.6, 139.0, 129.3, 129.2, 128.9, 127.3, 123.6, 119.5, 36.8, 35.4, 26.9. ESI-HRMS [M + H]$^+$ *m*/*z* calcd for $C_{16}H_{18}NOS$ 272.1104, found 272.1100.

***N*-Phenyl-3-(phenylthio)propanamide (3s).**[21] Eluent: petroleum ether/ethyl acetate (10 : 1). Yield 117 mg (91%). White solid, mp 84–85 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C) δ 7.48 (d, 2H), 7.42 (s, 1H), 7.38 (d, J = 7.4 Hz, 2H), 7.34–7.27 (m, 4H), 7.22 (t, 1H), 7.10 (t, J = 7.4 Hz, 1H), 3.28 (t, J = 7.1 Hz, 2H), 2.64 (t, J = 7.2 Hz, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz, 25 °C) δ 169.4, 137.7, 135.2, 129.7, 129.2, 129.0, 126.6, 124.5, 120.1, 37.1, 29.3. ESI-MS [M + H]$^+$ *m*/*z* 258.23; [M + Na]$^+$ 280.21.

***N*-Phenyl-3-(*p*-tolylthio)propanamide (3t).** Eluent: petroleum ether/ethyl acetate (10 : 1). Yield 119 mg (88%). White solid, mp 94–96 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C) δ 7.64–7.41 (m, 3H), 7.34–7.25 (m, 4H), 7.10 (t, J = 7.9 Hz, 3H), 3.22 (t, J = 7.2 Hz, 2H), 2.59 (t, J = 7.1 Hz, 2H), 2.31 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz, 25 °C) δ 169.5, 137.7, 136.9, 131.3, 130.7, 129.9, 129.0, 124.4, 120.1, 37.2, 30.1, 21.1. ESI-HRMS [M + H]$^+$ *m*/*z* calcd for $C_{16}H_{18}NOS$ 272.1104, found 272.1100.

3-[(4-Chlorophenyl)thio]-*N*-phenylpropanamide (3u). Eluent: petroleum ether/ethyl acetate (10 : 1). Yield 133 mg (91%). White solid, mp 91–93 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C) δ 7.53–7.42 (m, 2H), 7.38–7.20 (m, 8H), 7.12 (t, J = 7.4 Hz, 1H), 3.28 (t, J = 7.1 Hz, 2H), 2.64 (t, J = 7.1 Hz, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz, 25 °C) δ 168.8, 137.5, 133.7, 132.6, 131.1, 129.3, 129.1, 124.6, 119.9, 37.1, 29.6. ESI-HRMS [M + H]$^+$ *m*/*z* calcd for $C_{15}H_{15}ClNOS$ 292.0557, found 292.0554.

3-(Allylthio)-*N*-phenylpropanamide (3v). Eluent: petroleum ether/ethyl acetate (10 : 1). Yield 38 mg (34%), solvent-free condition yield 66 mg (60%). White solid, mp 38–40 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C) δ 7.91 (s, 1H), 7.44 (d, J = 7.9 Hz, 2H), 7.22 (t, J = 7.8 Hz, 2H), 7.02 (t, J = 7.4 Hz, 1H), 5.79–5.61 (m, 1H), 5.14–4.91 (m, 2H), 3.08 (d, J = 7.2 Hz, 2H), 2.74 (t, J = 7.1 Hz, 2H), 2.53 (t, J = 7.1 Hz, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz, 25 °C) δ 169.9, 137.8, 134.0, 129.0, 124.4, 120.1, 117.5, 37.4, 35.1, 26.4. ESI-HRMS [M + H]$^+$ *m*/*z* calcd for $C_{12}H_{16}NOS$ 222.0947, found 222.0952.

3-[(2-Hydroxyethyl)thio]-*N*-phenylpropanamide (3w). Eluent: petroleum ether/ethyl acetate (10 : 1). Yield 107 mg (95%). White solid, mp 74–76 °C. ^{1}H NMR ($CDCl_3$, 300 MHz, 25 °C) δ 7.92 (s, 1H), 7.54 (d, J = 7.9 Hz, 2H), 7.33 (t, J = 7.6 Hz, 2H), 7.13 (t, J = 7.4 Hz, 1H), 3.80 (t, J = 5.4 Hz, 2H), 2.94 (t, J = 6.9 Hz, 2H), 2.85 (s, 1H), 2.77 (t, J = 5.8 Hz, 2H), 2.67 (t, J = 6.9 Hz, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz, 25 °C) δ 169.7, 137.7, 129.0, 124.5, 120.0, 61.0, 37.8, 35.6, 27.5. ESI-HRMS [M + H]$^+$ *m*/*z* calcd for $C_{11}H_{16}NO_2S$ 226.0896, found 226.0897.

2-Methyl-3-(propylthio)propanamide (3x). Eluent: petroleum ether/ethyl acetate (6 : 1). Yield 79 mg (98%). Yellow solid, mp 46–47 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C) δ 6.46–5.84 (d, 2H), 2.87–2.77 (m, 1H), 2.62–2.43 (m, 4H), 1.67–1.53 (m, 2H), 1.29–1.21 (d, 3H), 1.04–0.91 (t, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz, 25 °C) δ 177.7, 41.3, 35.9, 35.0, 23.0, 17.6, 13.5. ESI-HRMS [M + H]$^+$ *m*/*z* calcd for $C_7H_{16}NOS$ 162.0947, found 162.0947.

2-Methyl-3-(phenylthio)propanamide (3y).[6d] Eluent: petroleum ether/ethyl acetate (6 : 1). Yield 88 mg (90%). Yellow solid, mp 55–56 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C) δ 7.32–7.26 (m, 2H), 7.26–7.18 (m, 2H), 7.17–7.09 (m, 1H), 5.62 (d, J = 76.1 Hz, 2H), 3.25–3.10 (m, 1H), 2.94–2.84 (m, 1H), 2.47–2.36 (m, 1H), 1.20 (d, J = 6.9 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz, 25 °C) δ 177.0, 135.8, 129.6, 129.1, 126.4, 40.4, 37.3, 17.6. ESI-MS [M + H]$^+$ *m*/*z* 196.16; [M + Na]$^+$ 218.14.

***N*-Phenyl-3-(propylthio)butanamide (3z).** Eluent: petroleum ether/ethyl acetate (10 : 1). Yield 93 mg (78%). Yellow liquid. ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C) δ 8.26 (s, 1H), 7.45 (d, J = 8.0 Hz, 2H), 7.21 (t, J = 7.8 Hz, 2H), 7.01 (t, J = 7.4 Hz, 1H), 3.28–3.11 (m, 1H), 2.57–2.39 (m, 4H), 1.59–1.46 (m, 2H), 1.27 (d, J = 6.8 Hz, 3H), 0.89 (t, J = 7.4 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz, 25 °C) δ 169.6, 137.9, 129.0, 124.4, 120.2, 45.2, 36.9, 33.1, 23.1, 21.8, 13.6. ESI-HRMS [M + H]$^+$ *m*/*z* calcd for $C_{13}H_{20}NOS$ 238.1260, found 238.1268.

***N*-Phenyl-3-(phenylthio)butanamide (3a′).** Eluent: petroleum ether/ethyl acetate (10 : 1). Yield 81 mg (60%). White solid, mp 60–61 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C) δ 7.80 (d, J = 25.2 Hz, 1H), 7.41 (d, J = 8.0 Hz, 2H), 7.34 (d, J = 7.1 Hz, 2H), 7.26–7.10 (m, 6H), 7.01 (t, J = 7.4 Hz, 1H), 3.76–3.59 (m, 1H), 2.67–2.50 (m, 1H), 2.49–2.27 (m, 1H), 1.29 (d, J = 6.8 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz, 25 °C) δ 169.1, 137.7, 133.9, 132.4, 129.1, 129.0, 127.5, 124.5, 120.1, 44.5, 40.0, 21.0. ESI-HRMS [M + H]$^+$ *m*/*z* calcd for $C_{16}H_{18}NOS$ 272.1104, found 272.1110.

3-(Allylthio)-*N*-phenylbutanamide (3b′). Eluent: petroleum ether/ethyl acetate (10 : 1). Yield 49 mg (42%). Yellow solid, mp 55–56 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C) δ 7.81 (s, 1H), 7.52 (d, J = 7.2 Hz, 1H), 7.32 (t, J = 7.9 Hz, 2H), 7.11 (t, J = 7.4 Hz, 1H), 5.94–5.72 (m, 1H), 5.16 (d, J = 16.9, 1.6 Hz, 1H), 5.11 (d, J = 10.0 Hz, 1H), 3.33–3.17 (m, 3H), 2.67–2.57 (m, 1H), 2.57–2.46 (m, 1H), 1.37 (d, J = 6.8 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz,

25 °C) δ 169.0, 137.8, 134.3, 129.0, 124.4, 120.0, 117.4, 45.1, 36.0, 34.3, 21.6. ESI-HRMS $[M + H]^+$ *m*/*z* calcd for $C_{16}H_{18}NOS$ 236.1104, found 236.1110.

***N*-Phenyl-3-(propylthio)hexanamide (3c′).** Eluent: petroleum ether/ethyl acetate (10 : 1). Yield 117 mg (88%). White solid, mp 55–57 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C) δ 8.33 (s, 1H), 7.46 (d, 2H), 7.21 (t, J = 7.7 Hz, 2H), 7.00 (t, J = 7.4 Hz, 1H), 3.11–2.96 (m, 1H), 2.58–2.37 (m, 4H), 1.60–1.28 (m, 6H), 0.88 (t, J = 7.3 Hz, 3H), 0.82 (t, J = 7.1 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz, 25 °C) δ 169.9, 138.0, 128.9, 124.3, 120.1, 44.0, 42.5, 37.7, 33.3, 23.2, 20.1, 13.9, 13.6. ESI-HRMS $[M + H]^+$ *m*/*z* calcd for $C_{16}H_{18}NOS$ 266.1573, found 266.1574.

***N*-3-Diphenyl-3-(propylthio)propanamide (3d′).** Eluent: petroleum ether/ethyl acetate (10 : 1). Yield 112 mg (75%). White solid, mp 55–56 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C) δ 7.36–7.09 (m, 9H), 7.02–6.93 (m, 1H), 4.27 (t, J = 7.5 Hz, 1H), 2.89–2.67 (m, 2H), 2.32–2.13 (m, 2H), 1.53–1.30 (m, 2H), 0.79 (t, J = 7.3 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz, 25 °C) δ 167.6, 140.8, 136.6, 127.8, 127.6, 126.6, 126.4, 123.4, 119.2, 44.9, 44.0, 32.5, 21.5, 12.4. ESI-HRMS $[M + H]^+$ *m*/*z* calcd for $C_{18}H_{22}NOS$ 300.1417, found 300.1425.

***N*-Phenyl-3-(propylthio)acrylamide (3e′).** Eluent: petroleum ether/ethyl acetate (10 : 1). Yield 46 mg (42%). Yellow solid, mp 55–56 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C) δ 7.51 (d, J = 8.0 Hz, 2H), 7.29 (s, 1H), 7.21 (t, 2H), 7.00 (t, J = 7.4 Hz, 1H), 6.91 (d, J = 9.9 Hz, 1H), 5.86 (d, J = 10.0 Hz, 1H), 2.65 (t, J = 7.3 Hz, 2H), 1.67–1.58 (m, 2H), 0.95 (t, J = 7.3 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz, 25 °C) δ 163.5, 146.8, 137.1, 127.9, 122.9, 118.5, 114.3, 37.5, 22.6, 12.1. ESI-HRMS $[M + H]^+$ *m*/*z* calcd for $C_{12}H_{16}NOS$ 222.0947, found 222.0952.

***N*-Phenyl-3,5-bis(propylthio)hexanamide (3f′).** Eluent: petroleum ether/ethyl acetate (10 : 1). Yield 105 mg (62%). Yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J = 6.4 Hz, 1H), 7.46 (t, J = 8.0, 4.9 Hz, 2H), 7.24 (t, J = 7.7 Hz, 2H), 7.03 (t, J = 7.4 Hz, 1H), 3.42–3.15 (m, 1H), 3.07–2.86 (m, 1H), 2.62–2.39 (m, 6H), 1.81–1.44 (m, 6H), 1.23 (t, J = 6.7, 5.4 Hz, 3H), 0.96–0.85 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 137.9, 137.8, 129.0, 128.9, 124.3, 124.2, 120.0, 119.9, 99.9, 44.4, 43.8, 42.6, 42.5, 40.8, 40.3, 37.8, 37.1, 33.5, 33.1, 32.3, 31.9, 23.3, 23.2, 23.1, 22.6, 21.4, 13.7, 13.6. ESI-HRMS $[M + H]^+$ *m*/*z* calcd for $C_{18}H_{30}NOS_2$ 340.1763, found 340.1773.

Conflicts of interest

There are no conflicts to declare.

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