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Molecular Iodine-Mediated Difunctionalization of Alkenes with Nitriles and Thiols Leading to β-Acetamido Sulfides

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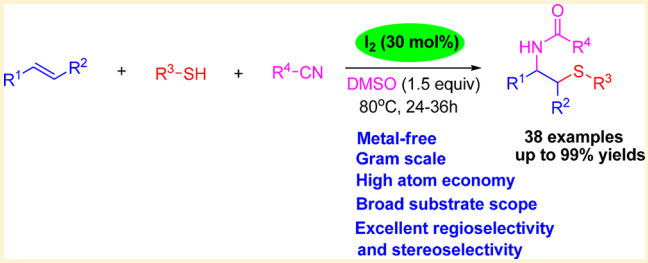
Supporting Information

ABSTRACT: A direct difunctionalization protocol of alkenes with nitriles and thiols toward β-acetamido sulfide derivatives has been proposed under metal-free synthesis conditions. The present protocol provides the facile and highly efficient synthesis of various β-acetamido sulfides in a scaled-up manner with good to excellent yields simply using inexpensive molecular iodine as a catalyst, DMSO as a mild oxidant, and readily available thiols as thiolating reagents.

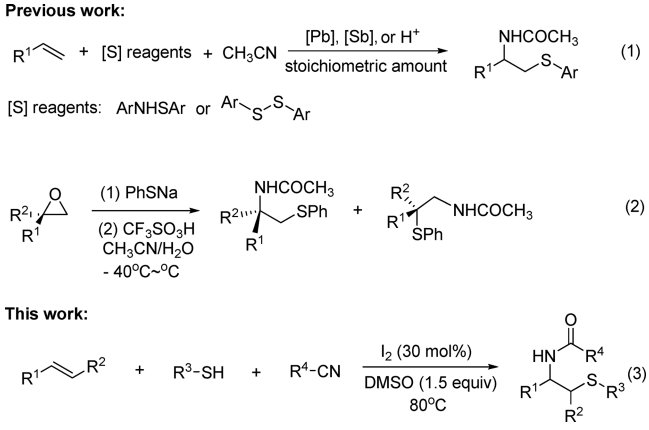


INTRODUCTION

The synthetic pursuit of sulfur-containing compounds has been strong among chemists in both academic and industrial communities due to their extensive applications in organic synthesis,[1] the pharmaceutical industry,[2] and materials science.[3] The introduction of a sulfanyl group to an unsaturated carbon−carbon bond represents one of most powerful and reliable procedures for the synthesis of organosulfur compounds.[4] In particular, the difunctionalization of alkenes with thiolation agents and other functional groups could provide rapid and concise access to diverse sulfur-containing organic materials in a single pot operation.[5−9] Over the past several years, some useful organosulfur compounds have been successfully synthesized through the difunctionalization of alkenes, such as alkoxythiolation,[5] hydroxythiolation,[6] acetoxythiolation,[7] sulfamination,[8] and disulfidation.[9] However, there is still great demand for the development of some convenient and efficient difunctionalization reaction systems to afford structurally diverse functional sulfur compounds of great importance.

β-Acetamido sulfides, an important class of sulfur-containing molecules, are widely presented in various biologically active compounds and natural products.[10] Furthermore, they can also serve as versatile building blocks for various organic transformations toward many useful compounds.[11] Generally, the acetamidosulfidation of alkenes with nitriles and preformed benzenesulfenanilides or disulfides can give β-acetamido sulfide derivatives in the presence of a stoichiometric amount of a transition-metal catalyst or strong acid (Scheme 1, (1)).[12] An alternative method for the synthesis of β-acetamido sulfide derivatives from oxiranes, PhSNa, and nitrile has also been developed (Scheme 1, (2)).[13] Nevertheless, most of these reactions might suffer from certain limitations, such as the need for prefunctionalized thiolating reagents, limited substrate scope, harsh reaction conditions, low atom economy, poor regioselectivity, or toxic metal catalysts. Therefore, it remains a challenging but attractive task to develop more direct, economic, efficient, and environmentally benign methods to construct β-acetamido sulfide derivatives.

Scheme 1. Methods for the Synthesis of β-Acetamido Sulfide Derivatives



From a synthetic standpoint, the direct use of thiols as thiolating reagents for the functionalization of olefins is an ideal method for constructing β-acetamido sulfides because it offers the advantages of easy availability, low cost, and high atom economy.[14] With our continuous interest in metal-free difunctionalization of alkenes,[15] we wish to report here a simple, economic, and efficient method for the selective synthesis of β-acetamido sulfide compounds via direct metal-free difunctionalization of alkenes with various thiols and nitriles (Scheme 1, (3)). A series of biologically important β-acetamido sulfide derivatives were selectively synthesized with

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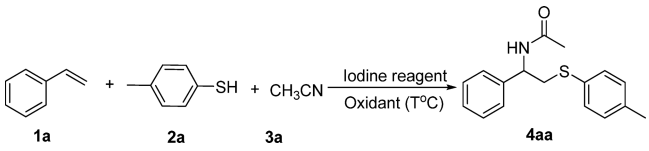
good to excellent yields in a simple way use inexpensive molecular iodine as a catalyst, DMSO as a mild oxidant, and commercially available thiols as thiolating reagents.

RESULTS AND DISCUSSION

Initially, the reaction of styrene (**1a**), 4-methylbenzenethiol (**2a**), and CH_3CN (**3a**) was selected as the model reaction to optimize various reaction conditions. In the absence of a transition-metal catalyst, various iodide-containing reagents were investigated using DMSO as the oxidant. As shown in Table 1, none of the desired product was detected when KI, NaI, or TBAI was separately used as the catalyst (entries 1–3). To our delight, desired β-acetamido sulfide **4aa** was obtained in 83% yield when the reaction was carried out by employing molecular iodine (20 mol %) (entry 4). Further optimization of catalyst loading demonstrated that 30 mol % of iodine was the best choice, affording product **4aa** in 94% yield (entry 8). Moreover, no conversion was observed when the reaction was performed in the absence of molecular iodine (entry 5). The use of other oxidants did not improve the reaction efficiency (entries 11–16). In addition, the reaction efficiency was obviously low with decreasing DMSO loading, and no reaction occurred in the absence of DMSO (entries 17–19). Subsequent investigation on the effect of the reaction temperature proved that 80 °C was appropriate for this reaction (entries 8 and 20–22). Finally, the desired product was obtained in 93% yield when the model reaction was performed in dry nitriles, suggesting that anhydrous reagents have no obvious impact on the reaction efficiency (entry 23).

Table 1. Optimization of the Reaction Conditions[a]



1a 2a 3a 4aa

entry	iodine reagent (mol %)	oxidant (equiv)	T (°C)	yield (%)[b]
1	KI (20)	DMSO (1.5)	80	0
2	NaI (20)	DMSO (1.5)	80	0
3	TBAI (20)	DMSO (1.5)	80	0
4	I_2 (20)	DMSO (1.5)	80	83
5		DMSO (1.5)	80	0
6	I_2 (5)	DMSO (1.5)	80	34
7	I_2 (10)	DMSO (1.5)	80	58
8	**I_2 (30)**	**DMSO (1.5)**	**80**	**94**
9	I_2 (40)	DMSO (1.5)	80	92
10	I_2 (50)	DMSO (1.5)	80	94
11	I_2 (20)	$PhI(AcO)_2$ (1.5)	80	71
12	I_2 (20)	$K_2S_2O_8$ (1.5)	80	53
13	I_2 (20)	H_2O_2 (1.5)	80	72
14	I_2 (20)	Oxone (1.5)	80	62
15	I_2 (20)	$C_{12}H_{25}S(O)Me$ (1.5)	80	42
16	I_2 (20)	O_2	80	<10
17	I_2 (30)	DMSO (1.0)	80	74
18	I_2 (30)	DMSO (0.5)	80	25
19	I_2 (30)		80	0
20	I_2 (30)	DMSO (1.5)	25	trace
21	I_2 (30)	DMSO (1.5)	60	84
22	I_2 (30)	DMSO (1.5)	100	92
23	I_2 (30)	DMSO (1.5)	80	93[c]

[a]Reaction conditions: **1a** (0.25 mmol), **2a** (0.375 mmol), iodine reagent (0–50% equiv), oxidant (0–1.5 equiv), CH_3CN **3a** (2 mL, 47.8 mmol), 25–100 °C, 24 h. [b]Isolated yields based on **1a**. TBAI = $(n\text{-Bu})_4NI$; DMSO = dimethyl sulfoxide. [c]Dry CH_3CN **3a** (2 mL, 47.8 mmol).

Under the optimized conditions, the scope of the difunctionalization reaction of styrene with acetonitrile and various thiols was explored with the results summarized in Table 2. In general, aryl thiols containing electron-rich or -poor groups on the aryl rings could readily participate in the reactions, affording the desired products in good to excellent yields (**4aa**–**4ak**). It was found that the reaction was not significantly affected by the steric effect. The sterically congested ortho- or meta-substituted aryl thiols were also effectively reacted with styrene and acetonitrile to achieve products **4ad**–**4ah** in good yields. 2-Naphthalenethiol could also be used in the reactions to give expected product **4al** in 88% yield. Notably, various alkyl thiols, such as phenylmethanethiol, 2-phenylethanethiol, and thiols with long aliphatic chains, could also be compatible with the reactions to deliver corresponding products **4am**–**4ar** in good yields.

Moreover, the participation of various alkenes and nitriles in this protocol was examined (Table 3). The reactions also proceeded well using aromatic alkenes with an electron-donating or -withdrawing group on the aromatic ring to give the desired products in moderate to good yields (**4ba**–**4ha**). As expected, 2-vinylnaphthalene was also compatible with the reactions with the desired product **4ia** obtained in 64% yield. It is noteworthy that aliphatic alkenes (i.e., cyclooctane, 1-hexene, and 1-octene) were all tolerated in the reactions, yet they might obtain the corresponding products (**4ka**–**4oa**) in moderate yields. Moreover, the difunctionalization reaction proceeded with excellent stereoselectivity when internal alkenes were used in the present reaction system. For example, (*E*)-β-methylstyrene gave **4la** in 40% yield with good stereoselectivity, and cyclooctane, (*E*)-oct-4-ene, and (*Z*)-oct-4-ene gave the corresponding stereospecific products **4ka**–**4ma** in moderate to good yields, respectively. The scope of this difunctionalization reaction was further expanded to a variety of nitriles. In addition to **3a**, herein a series of substituted nitriles containing long aliphatic chains or aromatic ring group were all suitable substrates, generating the corresponding products **4aab**–**4aag** in good yields.

Furthermore, the potential synthetic applicability of this method was investigated on a gram scale using the model reaction. As shown in Scheme 2, the reaction could afford 2.51 g of **4aa** in 88% yield without any significant loss of its efficiency, demonstrating the potential applications of the present method for a large scale synthesis of β-acetamido sulfide derivatives.

For further insights into this reaction to be obtained, two control experiments were newly carried out under the standard conditions (Scheme 3). When thiophenol **2b** was added independently under the standard conditions, the corresponding diphenyl sulfide (**5b**) was isolated in 90% yield at 2 h (Scheme 3, (a)). Furthermore, when styrene (**1a**), diphenyl sulfide (**5b**), and CH_3CN (**3a**) reactions were conducted under the standard conditions in the presence of H_2O (1.5 equiv), desired product **4ab** was isolated in 92% (Scheme 3, (b)). The above result suggested that diphenyl sulfide might be an intermediate in the present reaction system.

A possible reaction pathway was thus proposed as Scheme 4 for this difunctionalization of alkenes. Initially, the interaction

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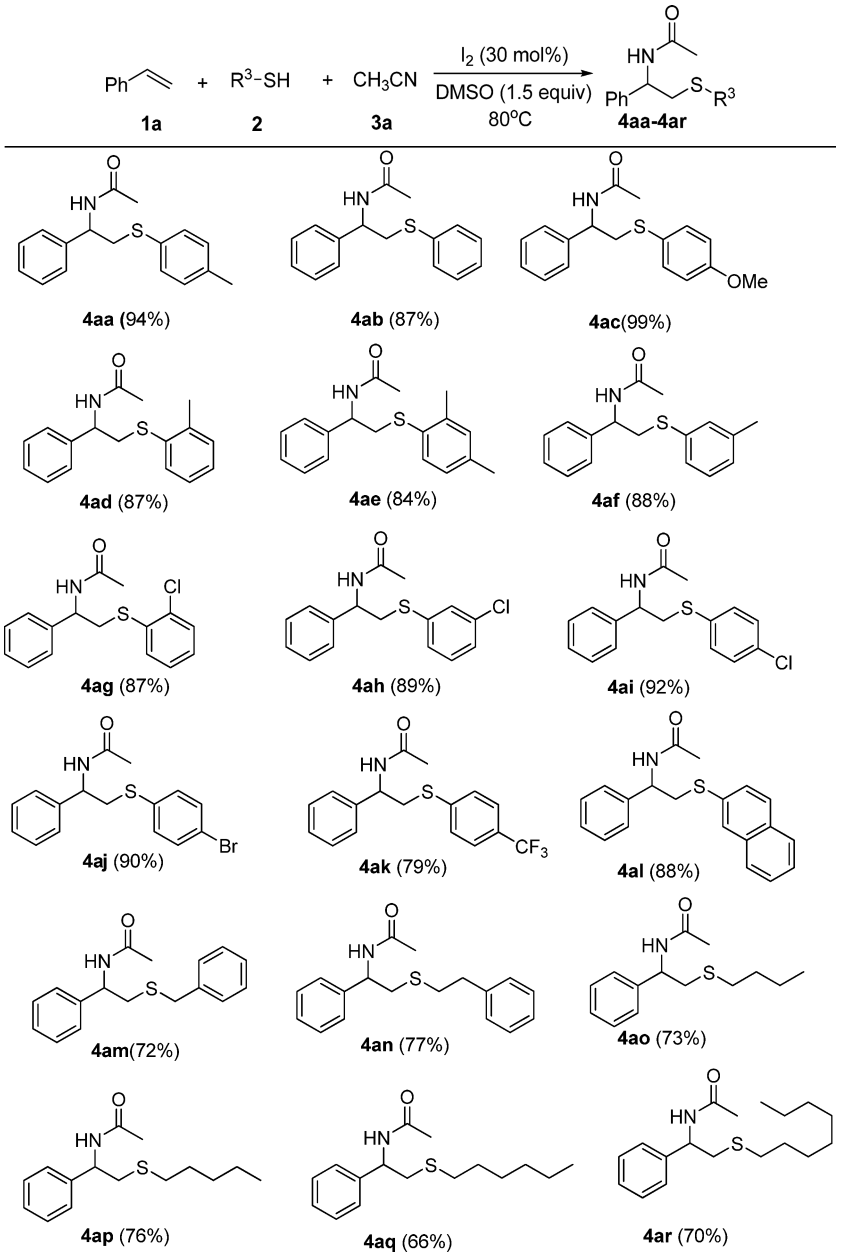
Table 2. Results for the Molecular-Iodine Mediated Difunctionalization of Styrene with Acetonitrile and Various Thiols[a]



[a]Reaction conditions: **1a** (0.25 mmol), **2** (0.375 mmol), **3a** (2.0 mL, 47.8 mmol), I_2 (30 mol %, 0.075 mmol), DMSO (1.5 equiv, 0.375 mmol), 80 °C, 24−30 h. Isolated yields based on **1a**.

of molecular iodine with thiol **2** generated disulfide **5** with the concomitant formation of HI.[16a,d] Formed disulfide **5** reacted with iodine to give electrophilic species R^3−SI **6**.[16] Furthermore, the electrophilic attack of R^3−SI **6** to alkene **1** gave thiiranium ion intermediate **7**.[17] Next, intermediate **7** was selectively attacked by nitrile **3**, followed by hydrolysis (Ritter-type reaction) to produce the desired *β*-acetamido sulfide derivatives with the release of HI.[12a,c,d] It should be noted that the ring opening of a thiiranium ion by an attack of iodide ion followed by displacement of nitrile via an S_N2 reaction might also be involved in this transformation to some extent. Finally, DMSO would oxidize two equiv of HI into molecular iodine to participate in the catalytic cycle along with the generation of water and dimethyl sulfide with a bad smell.[18]

CONCLUSIONS

In conclusion, a facile and atom-economical method has been successfully developed for the synthesis of *β*-acetamido sulfides through the metal-free direct difuctionalization of alkenes with thiols and nitriles. A series of structurally diverse *β*-acetamido sulfide derivatives could be effectively obtained from various readily available starting materials in the I_2/DMSO system by mild heating. The difunctionalization reactions proceeded with good regioselectivity, and no regioisomers were observed in the present reaction system. Taking into account the combination of some desirable features, such as operation simplicity, atom efficiency, good tolerance to scale-up synthesis, good regioselectivity and stereoselectivity, as well as readily available catalyst and oxidant of low toxicity, this synthesis procedure

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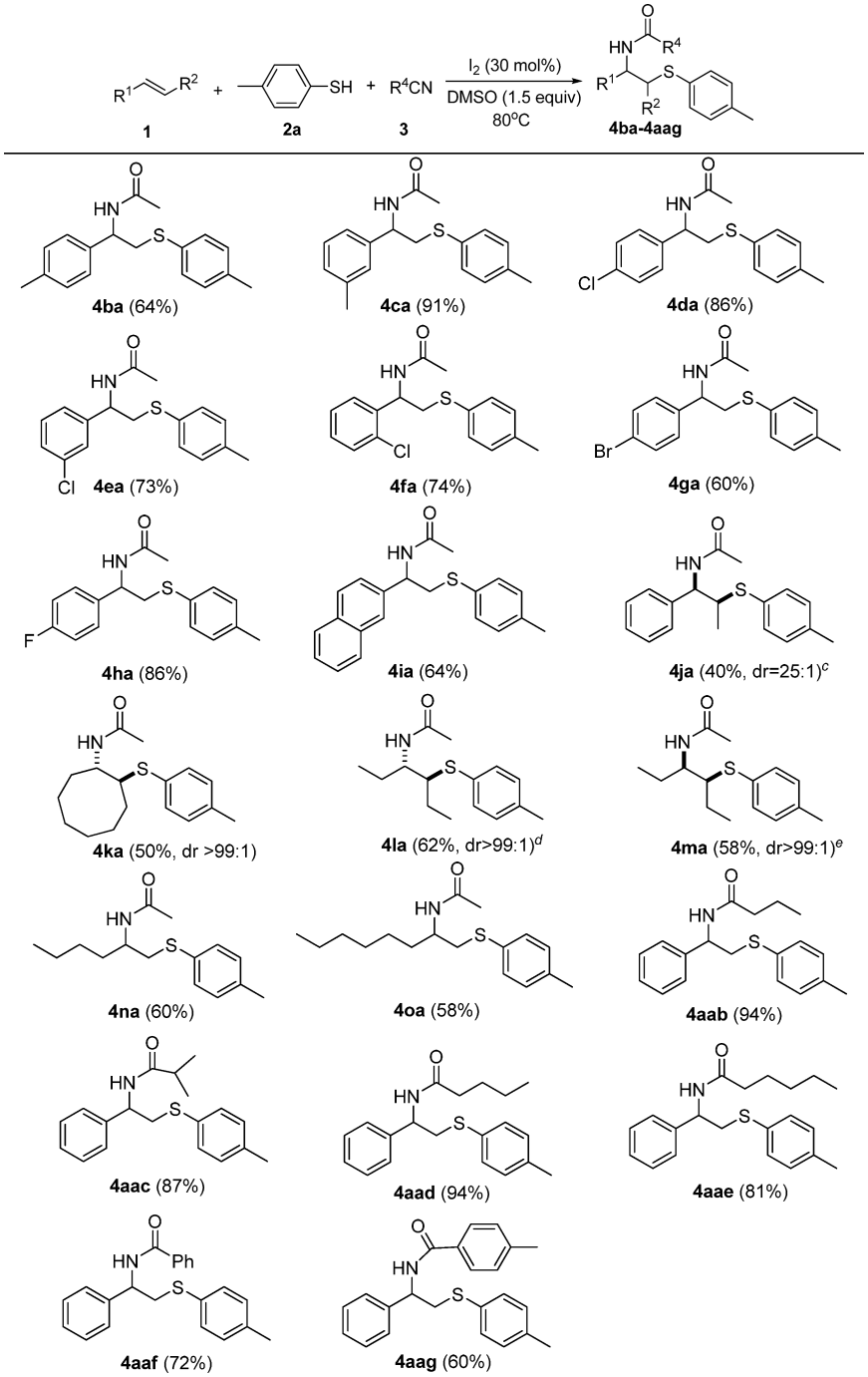
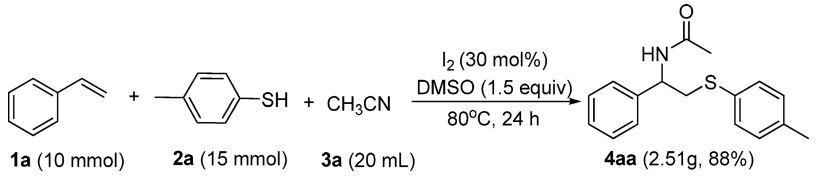
Table 3. Results for the Molecular Iodine-Mediated Difunctionalization of Various Alkenes with Nitriles and 4-Methylbenzenethiol[a,b]



[a]Reaction conditions: **1** (0.25 mmol), **2a** (0.375 mmol), **3** (2 mL: **3a**, 47.8 mmol; **3b**, 23.0 mmol; **3c**, 22.0 mmol; **3d**, 19.1 mmol; **3e**, 16.5 mmol; **3f**, 19.6 mmol; **3g**, 16.7 mmol), I_2 (30 mol %, 0.075 mmol), DMSO (1.5 equiv, 0.375 mmol), 80 °C, 24−36 h. [b]Isolated yields based on **1**; the value of dr was determined by ^{1}H NMR. [c]From (*E*)-*β*-methylstyrene. [d]From (*Z*)-hex-3-ene. [e]From (*E*)-hex-3-ene.

Scheme 2. Gram Scale Reaction



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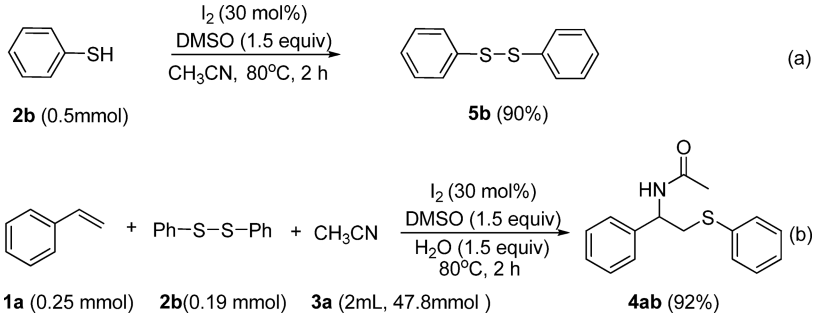
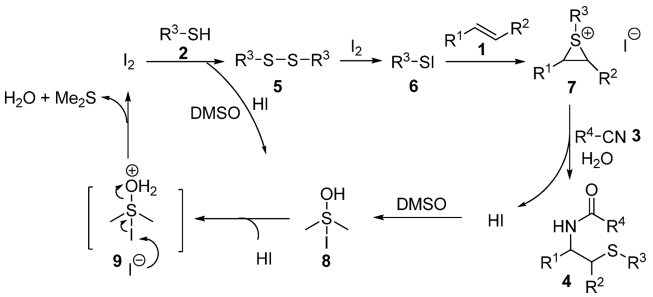
Scheme 3. Control Experiments



Scheme 4. Postulated Reaction Pathway



would serve as a practical and efficient protocol to synthesize β-acetamido sulfide derivatives.

EXPERIMENTAL SECTION

General. Chemicals were commercially available and used without further purification unless otherwise stated. All solvents were used as received without further purification unless otherwise stated. ^{1}H NMR and ^{13}C NMR spectra were obtained in $CDCl_3$ with TMS as theinternal standard (400 or 500 MHz ^{1}H and 100 or 125 MHz ^{13}C) at room temperature; the chemical shifts (δ) were expressed in ppm, and J values were given in Hz. The following abbreviations are used to indicate the multiplicity: singlet (s), doublet (d), triplet (t), quartet (q), doublet of doublets (dd), doublet of triplets (dt), doublet of quartets (dq), and multiplet (m). All first order splitting patterns were assigned on the basis of the appearance of the multiplet. Splitting patterns that could not be easily interpreted were designated as multiplet (m). In a few cases, the number of signals in the ^{13}C NMR spectrum is less than expected, which may be caused by the superimposition of signals. HRMS data were obtained by ESI on a TOF mass analyzer. Column chromatography was performed on silica gel (200−300 mesh).

General Experimental Procedures. To a 25 mL round-bottomed flask was added alkene **1** (0.25 mmol), thiol **2** (0.38 mmol), nitrile **3** (2.0 mL), I_2 (30 mol %, 0.075 mmol), and DMSO (1.5 equiv, 0.38 mmol). The reaction vessel was allowed to stir at 80 °C for 24−36 h. After the reaction, the solvent was removed under a vacuum. The residue was purified by flash column chromatography using a mixture of petroleum ether and ethyl acetate as eluent to give desired product **4**. ***Caution!*** *Thiols and byproduct dimethylsulfide have a bad smell, and ventilation should be used while carrying out this reaction.*

*N-(1-Phenyl-2-(p-tolylthio)ethyl)acetamide (**4aa**).* Compound **4aa**[14] was obtained in 94% yield (67.0 mg) according to the general procedure (acetonitrile: 2 mL, 47.8 mmol; 24 h) as a yellow solid; mp 72.4−74.1 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.35−7.26 (m, 7H), 7.12 (d, J = 8.1 Hz, 2H), 6.36 (d, J = 7.3 Hz, 1H), 5.16 (q, J = 7.2 Hz, 1H), 3.36−3.24 (m, 2H), 2.34 (s, 3H), 1.96 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 169.7, 140.6, 136.8, 131.7, 130.7, 129.9, 128.7, 127.7, 126.6, 53.0, 40.6, 23.2, 21.0. HRMS calcd for $C_{17}H_{20}NOS$ [M + H]$^+$, 286.1266; found, 286.1263.

*N-(1-Phenyl-2-(phenylthio)ethyl)acetamide (**4ab**).* Compound **4ab**[14] was obtained in 87% yield (58.7 mg) according to the general procedure (acetonitrile: 2 mL, 47.8 mmol; 24 h) as a yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.41−7.38 (m, 2H), 7.37−7.33 (m, 2H), 7.32−7.28 (m, 5H), 7.24−7.20 (m, 1H), 6.19 (d, J = 7.2 Hz, 1H), 5.21 (q, J = 6.9 Hz, 1H), 3.42 (dd, J_1 = 7.0 Hz, J_2 = 13.6 Hz, 1H), 3.32 (dd, J_1 = 6.3 Hz, J_2 = 13.6 Hz, 1H), 1.96 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 169.6, 140.3, 135.6, 129.8, 129.1, 128.8, 127.9, 126.7, 126.5, 53.0, 39.8, 23.3. HRMS calcd for $C_{16}H_{18}NOS$ [M + H]$^+$, 272.1109; found, 272.1112.

*N-(2-(4-Methoxyphenylthio)-1-phenylethyl)acetamide (**4ac**).* Compound **4ac**[14] was obtained in 99% yield (74.6 mg) according to the general procedure (acetonitrile: 2 mL, 47.8 mmol; 24 h) as a white solid; mp 98.7−99.7 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.38−7.35 (m, 2H), 7.33−7.32 (m, 2H), 7.29−7.24 (m, 3H), 6.87−6.84 (m, 2H), 6.17 (d, J = 7.4 Hz, 1H), 5.12 (q, J = 7.2 Hz, 1H), 3.81 (s, 3H), 3.28−3.19 (m, 2H), 1.98 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 169.5, 159.3, 140.6, 133.7, 128.7, 127.7, 126.6, 125.5, 114.8, 55.4, 53.0, 41.8, 23.3. HRMS calcd for $C_{17}H_{20}NO_2S$ [M + H]$^+$, 302.1215; found, 302.1217.

*N-(1-Phenyl-2-(o-tolylthio)ethyl)acetamide(**4ad**).* Compound **4ad**[14] was obtained in 87% yield (62.4 mg) according to the general procedure (acetonitrile: 2 mL, 47.8 mmol; 24 h) as a white solid; mp 97.1−99.0 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.42−7.29 (m, 6H), 7.20−7.14 (m, 3H), 6.15 (d, J = 7.2 Hz, 1H), 5.21 (q, J = 7.1 Hz, 1H), 3.39 (dd, J_1 = 7.2 Hz, J_2 = 13.4 Hz, 1H), 3.28 (dd, J_1 = 6.3 Hz, J_2 = 13.4 Hz, 1H), 2.37 (s, 3H), 1.98 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 169.6, 140.5, 138.3, 134.8, 130.3, 129.3, 128.8, 127.9, 126.7, 126.6, 126.5, 53.0, 39.2, 23.3, 20.5. HRMS calcd for $C_{17}H_{20}NOS$ [M + H]$^+$, 286.1266; found, 286.1269.

*N-(2-(2,4-Dimethylphenylthio)-1-phenylethyl)acetamide (**4ae**).* Compound **4ae** was obtained in 84% yield (62.5 mg) according to the general procedure (acetonitrile: 2 mL, 47.8 mmol; 24 h) as a yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.37−7.33 (m, 2H), 7.32−7.27 (m, 4H), 7.03 (s, 1H), 7.00 (t, J = 7.9 Hz, 1H), 6.20 (d, J = 7.3 Hz, 1H), 5.15 (q, J = 7.3 Hz, 1H), 3.30 (dd, J_1 = 7.4 Hz, J_2 = 13.4 Hz, 1H), 3.30 (dd, J_1 = 6.1 Hz, J_2 = 13.4 Hz, 1H), 2.36 (s, 3H), 2.31 (s, 3H), 1.98 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 169.5, 140.7, 138.8, 136.8, 131.3, 130.9, 130.8, 128.7, 127.7, 127.4, 126.6, 53.0, 39.9, 23.3, 20.9, 20.5. HRMS calcd for $C_{18}H_{22}NOS$ [M + H]$^+$, 300.1422; found, 300.1425.

*N-(1-Phenyl-2-(m-tolylthio)ethyl)acetamide (**4af**).* Compound **4af** was obtained in 88% yield (62.8 mg) according to the general procedure (acetonitrile: 2 mL, 47.8 mmol; 24 h) as a yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.37−7.33 (m, 2H), 7.31−7.28 (m, 3H), 7.20−7.17 (m, 3H), 7.04−7.02 (m, 1H), 6.26 (d, J = 7.2 Hz, 1H), 5.22 (q, J = 6.9 Hz, 1H), 3.42−3.37 (dd, J_1 = 7.0 Hz, J_2 = 13.5 Hz, 1H), 3.34−3.29 (dd, J_1 = 6.2 Hz, J_2 = 13.5 Hz, 1H), 2.34 (s, 3H), 1.97 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 169.6, 140.5, 138.9, 135.4, 130.4, 128.9, 128.7, 127.8, 127.4, 126.8, 126.7, 53.0, 39.8, 23.2, 21.3. HRMS calcd for $C_{17}H_{20}NOS$ [M + H]$^+$, 286.1266; found, 286.1271.

*N-(2-(2-Chlorophenylthio)-1-phenylethyl)acetamide (**4ag**).* Compound **4ag**[14] was obtained in 89% yield (67.7 mg) according to the general procedure (acetonitrile: 2 mL, 47.8 mmol; 24 h) as a yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.48 (dd, J_1 = 1.5 Hz, J_2 = 7.8 Hz,

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1H), 7.39−7.30 (m, 6H), 7.23 (dt, J_1 = 1.4 Hz, J_2 = 7.5 Hz, 1H), 7.15 (dt, J_1 = 1.6 Hz, J_2 = 7.8 Hz, 1H), 6.24 (d, J = 7.2 Hz, 1H), 5.22 (q, J = 6.8 Hz, 1H), 3.48−3.43 (dd, J_1 = 6.8 Hz, J_2 = 13.6 Hz, 1H), 3.36−3.31 (dd, J_1 = 6.7 Hz, J_2 = 13.5 Hz, 1H), 2.00 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 169.7, 140.0, 134.7, 134.3, 130.2, 129.8, 128.8, 128.0, 127.4, 127.3, 126.7, 52.7, 38.6, 23.3. HRMS calcd for $C_{16}H_{17}ClNOS$ $[M + H]^+$, 306.0719; found, 306.0721.

*N-(2-(3-Chlorophenylthio)-1-phenylethyl)acetamide (**4ah**).* Compound **4ah** was obtained in 88% yield (67.1 mg) according to the general procedure (acetonitrile: 2 mL, 47.8 mmol; 24 h) as a yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.38−7.28 (m, 6H), 7.26−7.15 (m, 3H), 6.12 (d, J = 7.2 Hz, 1H), 5.22 (q, J = 6.8 Hz, 1H), 3.50−3.45 (dd, J_1 = 6.5 Hz, J_2 = 13.5 Hz, 1H), 3.33−3.28 (dd, J_1 = 6.8 Hz, J_2 = 13.6 Hz, 1H), 2.00 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 169.6, 139.8, 137.9, 134.7, 130.0, 128.9, 128.8, 128.1, 127.2, 126.7, 126.4, 53.0, 39.2, 23.3. HRMS calcd for $C_{16}H_{17}ClNOS$ $[M + H]^+$, 306.0719; found, 306.0723.

*N-(2-(4-Chlorophenylthio)-1-phenylethyl)acetamide (**4ai**).* Compound **4ai** was obtained in 92% yield (70.3 mg) according to the general procedure (acetonitrile: 2 mL, 47.8 mmol; 24 h) as a yellow solid; mp 118.3−119.9 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.37−7.33 (m, 2H), 7.32−7.24 (m, 7H), 6.18 (d, J = 7.3 Hz, 1H), 5.17 (q, J = 7.0 Hz, 1H), 3.42 (dd, J_1 = 6.8 Hz, J_2 = 13.6 Hz, 1H), 3.27 (dd, J_1 = 6.8 Hz, J_2 = 13.6 Hz, 1H), 1.98 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 169.6, 140.0, 134.1, 132.5, 131.1, 129.2, 128.8, 128.0, 126.7, 53.0, 39.8, 23.3. HRMS calcd for $C_{16}H_{17}ClNOS$ $[M + H]^+$, 306.0719; found, 306.0721.

*N-(2-(4-Bromophenylthio)-1-phenylethyl)acetamide (**4aj**).* Compound **4aj** was obtained in 90% yield (78.4 mg) according to the general procedure (acetonitrile: 2 mL, 47.8 mmol; 24 h) as a yellow solid; mp 134.7−137.1 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.42−7.38 (m, 2H), 7.37−7.31 (m, 3H), 7.28−7.23 (m, 4H), 6.13 (d, J = 7.4 Hz, 1H), 5.17 (q, J = 6.9 Hz, 1H), 3.43 (dd, J_1 = 6.7 Hz, J_2 = 13.5 Hz, 1H), 3.27 (dd, J_1 = 6.8 Hz, J_2 = 13.6 Hz, 1H), 1.99 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 169.6, 140.0, 134.8, 132.1, 131.2, 128.9, 128.1, 126.7, 120.4, 52.9, 39.5, 23.3. HRMS calcd for $C_{16}H_{17}BrNOS$ $[M + H]^+$, 350.0214; found, 350.0217.

*N-(1-Phenyl-2-(4-(trifluoromethyl)phenylthio)ethyl)acetamide (**4ak**).* Compound **4ak** was obtained in 79% yield (66.6 mg) according to the general procedure (acetonitrile: 2 mL, 47.8 mmol; 24 h) as a white solid; mp 104.7−105.3 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.42 (d, J = 8.1 Hz, 2H), 7.34 (d, J = 8.1 Hz, 2H), 7.28−7.19 (m, 5H), 6.03 (s, 1H), 5.12 (q, J = 6.8 Hz, 1H), 3.49 (dd, J_1 = 6.2 Hz, J_2 = 13.6 Hz, 1H), 3.24 (dd, J_1 = 7.3 Hz, J_2 = 13.5 Hz, 1H), 1.91 (s, 3H). ^{13}CNMR ($CDCl_3$, 125 MHz): δ 169.8, 141.2, 139.5, 129.0, 128.3, 128.0, 126.8, 125.7 (q, J = 4.1 Hz), 124.1 (q, J = 298.9 Hz), 53.0, 38.0, 23.3. HRMS calcd for $C_{17}H_{17}F_3NOS$ $[M + H]^+$, 340.0983; found, 340.0984.

*N-(2-(Naphthalen-2-ylthio)-1-phenylethyl)acetamide (**4al**).* Compound **4al** was obtained in 88% yield (70.4 mg) according to the general procedure (acetonitrile: 2 mL, 47.8 mmol; 24 h) as a yellow oil. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.73 (s, 1H), 7.70−7.65 (m, 3H), 7.40−7.32 (m, 3H), 7.26−7.17 (m, 5H), 6.11 (s, 1H), 5.17 (q, J = 6.6 Hz, 1H), 3.44 (dd, J_1 = 6.8 Hz, J_2 = 13.6 Hz, 1H), 3.31 (dd, J_1 = 6.4 Hz, J_2 =13.6 Hz, 1H), 1.86 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 169.8, 140.2, 133.8, 133.0, 131.9, 128.8, 128.6, 128.0, 127.7, 127.6, 127.5, 127.2, 126.7, 126.7, 125.9, 53.1, 39.4, 23.3. HRMS calcd for $C_{20}H_{20}NOS$ $[M + H]^+$, 322.1266; found, 322.1269.

*N-(2-(Benzylthio)-1-phenylethyl)acetamide (**4am**).* Compound **4am**[14] was obtained in 72% yield (51.6 mg) according to the general procedure (acetonitrile: 2 mL, 47.8 mmol; 30 h) as a yellow solid; mp 108.1−109.3 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.35−7.29 (m, 5H), 7.26−7.23 (m, 5H), 5.91 (d, J = 6.2 Hz, 1H), 5.17 (q, J = 6.7 Hz, 1H), 3.61−3.54 (m, 2H), 2.89−2.80 (m, 2H), 1.99 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 169.7, 140.8, 138.0, 129.0, 128.7, 128.6, 127.7, 127.2, 126.5, 52.2, 37.2, 36.4, 23.3. HRMS calcd for $C_{17}H_{20}NOS$ $[M + H]^+$, 286.1266; found, 286.1269.

*N-(2-(Phenethylthio)-1-phenylethyl)acetamide (**4an**).* Compound **4an** was obtained in 77% yield (57.5 mg) according to the general procedure (acetonitrile: 2 mL, 47.8 mmol; 30 h) as a yellow oil. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.34 (t, J = 7.5 Hz, 2H), 7.29−7.26 (m, 5H), 7.20 (t, J = 7.2 Hz, 1H), 6.14 (d, J = 7.2 Hz, 2H), 6.08 (s, 1H), 5.17 (q, J = 6.4 Hz, 1H), 3.00−2.91 (m, 2H), 2.82 (t, J = 7.7 Hz, 2H), 2.67−2.64 (m, 2H), 2.03 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 169.6, 140.7, 140.2, 128.8, 128.5, 128.5, 127.8, 126.5, 126.4, 52.5, 38.1, 36.2, 33.9, 23.4. HRMS calcd for $C_{18}H_{22}NOS$ $[M + H]^+$, 300.1422; found, 300.1427.

*N-(2-(Butylthio)-1-phenylethyl)acetamide (**4ao**).* Compound **4ao** was obtained in 70% yield (43.7 mg) according to the general procedure (acetonitrile: 2 mL, 47.8 mmol; 30 h) as a yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.37−7.28 (m, 5H), 6.30 (d, J = 7.2 Hz, 1H), 5.18 (q, J = 6.5 Hz, 1H), 2.99−2.90 (m, 2H), 2.42 (t, J = 7.3 Hz, 2H), 2.03 (s, 3H), 1.54−1.48 (m, 2H), 1.39−1.33 (m, 2H), 0.89 (t, J = 7.4 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 169.6, 140.9, 128.7, 127.7, 126.5, 52.5, 38.1, 32.2, 31.6, 23.3, 21.9, 13.6. HRMS calcd for $C_{14}H_{22}NOS$ $[M + H]^+$, 252.1422; found, 252.1425.

*N-(2-(Pentylthio)-1-phenylethyl)acetamide (**4ap**).* Compound **4ap** was obtained in 76% yield (50.2 mg) according to the general procedure (acetonitrile: 2 mL, 47.8 mmol; 30 h) as a yellow oil. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.34 (t, J = 7.2 Hz, 2H), 7.30−7.26 (m, 3H), 6.04 (d, J = 6.5 Hz, 1H), 5.18 (q, J = 6.4 Hz, 1H), 2.99−2.92 (m, 2H), 2.39 (t, J = 6.9 Hz, 2H), 2.05 (s, 3H), 1.54−1.49 (m, 2H), 1.29−1.26 (m, 4H), 0.88 (t, J = 6.5 Hz, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 169.6, 140.8, 128.7, 127.7, 126.5, 52.5, 38.0, 32.5, 31.0, 29.3, 23.3, 22.2, 14.0. HRMS calcd for $C_{15}H_{24}NOS$ $[M + H]^+$, 266.1579; found, 266.1581.

*N-(2-(Hexylthio)-1-phenylethyl)acetamide (**4aq**).* Compound **4aq** was obtained in 66% yield (46 mg) according to the general procedure (acetonitrile: 2 mL, 47.8 mmol; 30 h) as a yellow oil. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.34 (t, J = 7.4 Hz, 2H), 7.30−7.26 (m, 3H), 6.04 (d, J = 6.2 Hz, 1H), 5.18 (q, J = 6.3 Hz, 1H), 3.00−2.92 (m, 2H), 2.39 (t, J = 7.4 Hz, 2H), 2.05 (s, 3H), 1.52−1.50 (m, 2H), 1.30−1.23 (m, 6H), 0.87 (t, J = 6.7 Hz, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 169.5, 140.8, 128.7, 127.7, 126.5, 52.4, 38.1, 32.6, 31.4, 29.5, 28.5, 23.4, 22.5, 14.0. HRMS calcd for $C_{16}H_{26}NOS$ $[M + H]^+$, 280.1735; found, 280.1739.

*N-(2-(Octylthio)-1-phenylethyl)acetamide (**4ar**).* Compound **4ar** was obtained in 70% yield (53.6 mg) according to the general procedure (acetonitrile: 2 mL, 47.8 mmol; 30 h) as a yellow oil. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.34 (t, J = 7.3 Hz, 2H), 7.30−7.26 (m, 3H), 6.07 (d, J = 5.2 Hz, 1H), 5.18 (q, J = 6.5 Hz, 1H), 2.99−2.92 (m, 2H), 2.39 (t, J = 7.4 Hz, 2H), 2.04 (s, 3H), 1.52−1.48 (m, 2H), 1.29−1.25 (m, 10H), 0.87 (t, J = 6.6 Hz, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 169.5, 140.8, 128.7, 127.7, 126.5, 52.4, 38.1, 32.6, 31.8, 29.5, 29.2, 29.1, 28.8, 23.4, 22.7, 14.1. HRMS calcd for $C_{18}H_{30}NOS$ $[M + H]^+$, 308.2048; found, 308.2051.

*N-(1-p-Tolyl-2-(p-tolylthio)ethyl)acetamide (**4ba**).* Compound **4ba** was obtained in 64% yield (47.8 mg) according to the general procedure (acetonitrile: 2 mL, 47.8 mmol; 24 h) as a yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.30 (d, J = 8.2 Hz, 2H), 7.19−7.11 (m, 6H), 6.09 (d, J = 7.4 Hz, 1H), 5.14 (q, J = 6.9 Hz, 1H), 3.36 (dd, J_1 = 7.0 Hz, J_2 = 13.5 Hz, 1H), 3.26 (dd, J_1 = 6.3 Hz, J_2 = 13.5 Hz, 1H), 2.35 (s, 3H), 2.34 (s, 3H), 1.96 (m, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 169.5, 137.5, 137.4, 136.7, 131.8, 130.6, 129.9, 129.4, 126.5, 52.7, 40.4, 23.3, 21.1, 21.0. HRMS calcd for $C_{18}H_{22}NOS$ $[M + H]^+$, 300.1422; found, 300.1423.

*N-(1-m-Tolyl-2-(p-tolylthio)ethyl)acetamide (**4ca**).* Compound **4ca** was obtained in 91% yield (68.0 mg) according to the general procedure (acetonitrile: 2 mL, 47.8 mmol; 24 h) as a yellow solid; mp 87.0−89.0 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.31 (d, J = 8.2 Hz, 2H), 7.24 (t, J = 7.8 Hz, 1H), 7.13−7.07 (m, 5H), 6.07 (d, J = 7.4 Hz, 1H), 5.13 (q, J = 7.1 Hz, 1H), 3.35 (dd, J_1 = 6.2 Hz, J_2 = 13.6 Hz, 1H), 3.27 (dd, J_1 = 7.2 Hz, J_2 = 13.6 Hz, 1H), 2.35 (s, 3H), 2.34 (s, 3H), 1.98 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 169.5, 140.4, 138.4, 136.8, 131.8, 130.7, 129.9, 128.6, 128.6, 127.4, 123.6, 53.0, 40.5, 23.3, 21.5, 21.0. HRMS calcd for $C_{18}H_{22}NOS$ $[M + H]^+$, 300.1422; found, 300.1425.

*N-(1-(4-Chlorophenyl)-2-(p-tolylthio)ethyl)acetamide (**4da**).* Compound **4da** was obtained in 86% yield (68.9 mg) according to the general procedure (acetonitrile: 2 mL, 47.8 mmol; 24 h) as a yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.29−7.27 (m, 4H), 7.19

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(d, J = 8.4 Hz, 2H), 7.12 (d, J = 8.0 Hz, 2H), 6.22 (d, J = 7.2 Hz, 1H), 5.10 (q, J = 7.0 Hz, 1H), 3.30−3.20 (m, 2H), 2.34 (s, 3H), 1.97 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 169.6, 139.1, 137.2, 133.5, 131.2, 130.9, 130.0, 128.8, 128.0, 52.4, 40.6, 23.2, 21.0. HRMS calcd for $C_{17}H_{19}ClNOS$ $[M + H]^+$, 320.0876; found, 320.0877.

*N-(1-(3-Chlorophenyl)-2-(p-tolylthio)ethyl)acetamide (**4ea**).* Compound **4ea** was obtained in 73% yield (58.4 mg) according to the general procedure (acetonitrile: 2 mL, 47.8 mmol; 24 h) as a white solid; mp 97−99.6 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.30−7.27 (m, 2H), 7.25−7.23 (m, 3H), 7.15−7.11 (m, 3H), 6.25 (d, J = 7.3 Hz, 1H), 5.10 (q, J = 7.0 Hz, 1H), 3.28−3.20 (m, 2H), 2.34 (s, 3H), 1.98 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 169.7, 142.8, 137.2, 134.6, 131.1, 131.1, 131.1, 130.0, 129.9, 127.8, 126.7, 124.9, 52.6, 40.7, 23.2, 21.0. HRMS calcd for $C_{17}H_{19}ClNOS$ $[M + H]^+$, 320.0876; found, 320.0879.

*N-(1-(2-Chlorophenyl)-2-(p-tolylthio)ethyl)acetamide (**4fa**).* Compound **4fa** was obtained in 74% yield (59.1 mg) according to the general procedure (acetonitrile: 2 mL, 47.8 mmol; 24 h) as a white solid; mp 158.7−159.7 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.34−7.29 (m, 4H), 7.25−7.18 (m, 2H), 7.11 (d, J = 8.0 Hz, 2H), 6.36 (d, J = 7.2 Hz, 1H), 5.48−5.43 (m, 1H), 3.37 (q, J = 5.6 Hz, 1H), 3.36 (dd, J_1 = 5.6 Hz, J_2 = 13.8 Hz, 1H), 3.27 (dd, J_1 = 7.8 Hz, J_2 = 13.8 Hz, 1H), 2.34 (s, 3H), 1.99 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 169.5, 137.8, 137.0, 132.7, 131.1, 131.0, 130.0, 129.9, 128.8, 128.2, 127.0, 51.1, 38.9, 23.2, 21.1. HRMS calcd for $C_{17}H_{19}ClNOS$ $[M + H]^+$, 320.0876; found, 320.0879.

*N-(1-(4-Bromophenyl)-2-(p-tolylthio)ethyl)acetamide (**4ga**).* Compound **4ga** was obtained in 60% yield (54.5 mg) according to the general procedure (acetonitrile: 2 mL, 47.8 mmol, 36 h) as a white solid; mp 116.1−118.4 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.44 (d, J = 8.4 Hz, 2H), 7.28 (d, J = 7.6 Hz, 2H), 7.14−7.11 (m, 4H), 6.14 (d, J = 7.2 Hz, 1H), 5.09 (q, J = 7.0 Hz, 1H), 3.31−3.20 (m, 2H), 2.34 (s, 3H), 1.98 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 169.6, 139.6, 137.2, 131.8, 131.2, 131.0, 130.0, 128.3, 121.6, 52.5, 40.5, 23.2, 21.1. HRMS calcd for $C_{17}H_{19}BrNOS$ $[M + H]^+$, 364.0371; found, 364.0374.

*N-(1-(4-Fluorophenyl)-2-(p-tolylthio)ethyl)acetamide (**4ha**).* Compound **4ha** was obtained in 86% yield (64.9 mg) according to the general procedure (acetonitrile: 2 mL, 47.8 mmol; 24 h) as a yellow solid, mp 86.1−87.4 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.28 (d, J = 8.2 Hz, 2H), 7.25−7.21 (m, 2H), 7.12 (d, J = 8.0 Hz, 2H), 7.03−6.99 (m, 2H), 6.21 (d, J = 7.2 Hz, 1H), 5.12 (q, J = 7.0 Hz, 1H), 3.33−3.21 (m, 2H), 2.34 (s, 3H), 1.97 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 169.6, 162.2 (d, J = 244.7 Hz), 137.1, 136.4 (d, J = 3.2 Hz), 131.4, 130.8, 129.9, 128.3 (d, J = 8.1 Hz), 115.5 (d, J = 8.1 Hz), 52.4, 40.7, 23.2, 21.0. HRMS calcd for $C_{17}H_{19}FNOS$ $[M + H]^+$, 304.1171; found, 304.1177.

*N-(1-(Naphthalen-2-yl)-2-(p-tolylthio)ethyl)acetamide (**4ia**).* Compound **4ia** was obtained in 64% yield (53.6 mg) according to the general procedure (acetonitrile: 2 mL, 47.8 mmol; 24 h) as a yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.84−7.80 (m, 3H), 7.72 (s, 1H), 7.50−7.48 (m, 2H), 7.37 (dd, J_1 = 1.8 Hz, J_2 = 8.5 Hz, 1H), 7.31 (d, J = 8.1 Hz, 2H), 7.10 (d, J = 8.0 Hz, 2H), 6.31 (d, J = 7.6 Hz, 1H), 5.34 (q, J = 7.0 Hz, 1H), 3.45−3.33 (m, 2H), 2.33 (s, 3H), 2.00 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 169.7, 137.9, 136.9, 133.3, 132.9, 131.6, 130.8, 129.9, 128.6, 127.9, 127.7, 126.3, 126.1, 125.5, 124.6, 53.1, 40.5, 23.3, 21.0. HRMS calcd for $C_{21}H_{22}NOS$ $[M + H]^+$, 336.1422; found, 336.1425.

*N-(1-Phenyl-2-(p-tolylthio)propyl)acetamide (**4ja**).* Compound **4ja** was obtained in 40% yield (29.9 mg) according to the general procedure (acetonitrile: 2 mL, 47.8 mmol, 36 h) as a yellow solid; mp 136.2−138.9 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.35−7.32 (m, 4H), 7.29−7.27 (m, 3H), 7.13 (d, J = 7.1 Hz, 2H), 6.21 (d, J = 6.2 Hz, 1H), 5.15(dd, J_1 = 4.4 Hz, J_2 = 6.3 Hz, 1H), 3.64−3.55 (m, 1H), 2.33 (s, 3H), 2.00 (s, 3H), 1.19 (d, J = 6.3 Hz, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 169.3, 138.7, 137.7, 132.8, 131.0, 130.0, 128.4, 127.7, 127.4, 56.5, 49.9, 23.4, 21.1, 17.9. HRMS calcd for $C_{18}H_{22}NOS$ $[M + H]^+$, 300.1422; found, 300.1426.

*N-(2-(p-Tolylthio)cyclooctyl)acetamide (**4ka**).* Compound **4ka** was obtained in 50% yield (36.4 mg) according to the general procedure (acetonitrile: 2 mL, 47.8 mmol; 24 h) as a white solid; mp 108.7−109.6 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.33 (d, J = 8.1 Hz, 2H), 7.13 (d, J = 7.9 Hz, 2H), 5.66 (d, J = 8.5 Hz, 1H), 4.06−3.99 (m, 1H), 3.23−3.18 (m, 1H), 2.34 (s, 3H), 2.11−2.05 (m, 1H), 1.93 (s, 3H), 1.90−1.75 (m, 4H), 1.69−1.61 (m, 4H), 1.52−1.42 (m, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 169.3, 137.3, 132.7, 131.3, 129.8, 53.9, 53.2, 31.6, 30.4, 26.2, 26.1, 25.6, 24.9, 23.5, 21.1. HRMS calcd for $C_{17}H_{26}NOS$ $[M + H]^+$, 292.1735; found, 292.1733.

*N-(4-(p-Tolylthio)hexan-3-yl)acetamide (**4la**).* Compound **4la** was obtained in 62% yield (41.1 mg) according to the general procedure (acetonitrile: 2 mL, 47.8 mmol; 24 h) as a white solid; mp 79.6−81.0 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.36 (d, J = 8.2 Hz, 2H), 7.12 (d, J = 7.9 Hz, 2H), 5.54 (d, J = 9.0 Hz, 1H), 4.21−4.16 (m, 1H), 3.10−3.06 (m, 1H), 2.35 (s, 3H), 2.01 (s, 3H), 1.72−1.65 (m, 1H), 1.64−1.53 (m, 3H), 1.11 (t, J = 7.3 Hz, 3H), 0.85 (t, J = 7.4 Hz, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 169.6, 137.1, 132.2, 132.1, 129.8, 56.7, 54.0, 26.6, 26.4, 23.4, 21.1, 12.4, 10.8. HRMS calcd for $C_{15}H_{24}NOS$ $[M + H]^+$, 266.1579; found, 266.1580.

*N-(4-(p-Tolylthio)hexan-3-yl)acetamide (**4ma**).* Compound **4ma** was obtained in 58% yield (38.4 mg) according to the general procedure (acetonitrile: 2 mL, 47.8 mmol; 24 h) as a light yellow oil. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.32 (d, J = 8.2 Hz, 2H), 7.11 (d, J = 7.9 Hz, 2H), 5.57 (d, J = 8.9 Hz, 1H), 4.17−4.11 (m, 1H), 3.22−3.19 (m, 1H), 2.33 (s, 3H), 1.81 (s, 3H), 1.72−1.63 (m, 3H), 1.49−1.42 (m, 1H), 1.10 (t, J = 7.3 Hz, 3H), 0.95 (t, J = 7.4 Hz, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 169.7, 136.8, 133.1, 131.5, 129.9, 58.2, 53.9, 26.7, 23.2, 22.4, 21.0, 12.4, 10.8. HRMS calcd for $C_{15}H_{24}NOS$ $[M + H]^+$, 266.1579; found, 266.1583.

*N-(1-((p-Tolylthio)methyl)pentyl)acetamide (**4na**).* Compound **4na** was obtained in 60% yield (39.8 mg) according to the general procedure (acetonitrile: 2 mL, 47.8 mmol; 24 h) as a white solid; mp 89.3−89.4 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.32 (d, J = 8.2 Hz, 2H), 7.12 (d, J = 8.0 Hz, 2H), 5.47 (d, J = 8.1 Hz, 1H), 4.18−4.13 (m, 1H), 3.14−3.05 (m, 2H), 2.33 (s, 3H), 1.88 (s, 3H), 1.68−1.61 (m, 1H), 1.55−1.47 (m, 1H), 1.33−1.25 (m, 4H), 0.88 (t, J = 6.8 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 169.6, 136.5, 132.6, 130.2, 129.8, 49.1, 39.4, 33.2, 28.1, 23.3, 22.5, 21.0, 13.9. HRMS calcd for $C_{15}H_{24}NOS$ $[M + H]^+$, 266.1579; found, 266.1581.

*N-(1-((p-Tolylthio)methyl)heptyl)acetamide (**4oa**).* Compound **4oa** was obtained in 58% yield (42.7 mg) according to the general procedure (acetonitrile: 2 mL, 47.8 mmol; 24 h) as a white solid; mp 89.1−89.4 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.31 (d, J = 8.2 Hz, 2H), 7.12 (d, J = 8.0 Hz, 2H), 5.47 (d, J = 8.4 Hz, 1H), 4.18−4.12 (m, 1H), 3.14−3.05 (m, 2H), 2.33 (s, 3H), 1.88 (s, 3H), 1.67−1.60 (m, 1H), 1.52−1.49 (m, 1H), 1.32 −1.26 (m, 8H), 0.89 (t, J = 6.6 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 169.6, 136.5, 132.6, 130.2, 129.8, 49.1, 39.3, 33.5, 31.7, 29.1, 25.9, 23.3, 22.6, 21.0, 14.0. HRMS calcd for $C_{17}H_{28}NOS$ $[M + H]^+$, 294.1892; found, 294.1894.

*N-(1-Phenyl-2-(p-tolylthio)ethyl)butyramide (**4aab**).* Compound **4aab** was obtained in 94% yield (73.8 mg) according to the general procedure (butyronitrile: 2 mL, 23 mmol; 24 h) as a white solid; mp 87.0−88.1 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.35−7.27 (m, 7H), 7.12 (d, J = 7.9 Hz, 2H), 6.15 (d, J = 7.4 Hz, 1H), 5.18 (q, J = 7.2 Hz, 1H), 3.37−3.26 (m, 2H), 2.34 (s, 3H), 2.16 (t, J = 7.0 Hz, 2H), 1.70−1.61 (m, 2H), 0.95 (t, J = 7.4 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 172.5, 140.7, 136.8, 131.7, 130.7, 129.9, 128.7, 127.7, 126.6, 52.7, 40.7, 38.6, 21.0, 19.1, 13.8. HRMS calcd for $C_{19}H_{24}NOS$ $[M + H]^+$, 314.1579; found, 314.1583.

*N-(1-Phenyl-2-(p-tolylthio)ethyl)isobutyramide (**4aac**).* Compound **4aac** was obtained in 87% yield (68.5 mg) according to the general procedure (isobutyronitrile: 2 mL, 22.0 mmol; 24 h) as a white solid; mp 144.5−146.7 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.35−7.26 (m, 7H), 7.12 (d, J = 8.0 Hz, 2H), 6.06 (d, J = 7.0 Hz, 1H), 5.16 (q, J = 7.0 Hz, 1H), 3.39−3.27 (m, 2H), 2.42−2.35 (m, 1H), 2.34 (s, 3H), 1.18 (d, J = 6.9 Hz, 3H), 1.15 (d, J = 6.9 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 176.3, 140.7, 136.8, 131.7, 130.7, 129.9, 128.7, 127.7, 126.5, 52.5, 40.7, 35.7, 21.0, 19.6, 19.5. HRMS calcd for $C_{19}H_{24}NOS$ $[M + H]^+$, 314.1579; found, 314.1581.

*N-(1-Phenyl-2-(p-tolylthio)ethyl)pentanamide (**4aad**).* Compound **4aad** was obtained in 94% yield (76.6 mg) according to the general procedure (pentanenitrile: 2 mL, 19.1 mmol; 24 h) as a white

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solid; mp 58.5−59.1 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.36−7.27 (m, 7H), 7.12 (d, J = 8.0 Hz, 2H), 6.10 (d, J = 7.4 Hz, 1H), 5.18 (q, J = 7.1 Hz, 1H), 3.38−3.26 (m, 2H), 2.34 (s, 3H), 2.18 (t, J = 7.5 Hz, 2H), 1.64−1.57 (m, 2H), 1.40−1.30 (m, 2H), 0.93 (t, J = 7.3 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 172.6, 140.7, 136.8, 131.7, 130.7, 129.9, 128.7, 127.7, 126.6, 52.7, 40.6, 36.5, 27.7, 22.4, 21.0, 13.8. HRMS calcd for $C_{20}H_{26}NOS$ $[M + H]^+$, 328.1735; found, 328.1733.

*N-(1-Phenyl-2-(p-tolylthio)ethyl)hexanamide (**4aae**).* Compound **4aae** was obtained in 81% yield (69.2 mg) according to the general procedure (hexanenitrile: 2 mL, 16.5 mmol; 24 h) as a white solid; mp 93.4−96.0 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.32 (t, J = 7.0 Hz, 2H), 7.28−7.24 (m, 5H), 7.09 (d, J = 7.9 Hz, 2H), 5.97 (d, J = 6.4 Hz, 1H), 5.15 (q, J = 6.9 Hz, 1H), 3.35−3.25 (m, 2H), 2.31 (s, 3H), 2.14 (t, J = 7.5 Hz, 2H), 1.62−1.57 (m, 2H), 1.31−1.26 (m, 4H), 0.88 (t, J = 6.8 Hz, H). ^{13}CNMR ($CDCl_3$, 100 MHz): δ 172.6, 140.6, 136.8, 131.7, 130.7, 129.9, 128.7, 127.7, 126.6, 52.7, 40.6, 36.7, 31.5, 25.3, 22.4, 21.0, 14.0. HRMS calcd for $C_{21}H_{28}NOS$ $[M + H]^+$, 342.1892; found, 342.1897.

*N-(1-Phenyl-2-(p-tolylthio)ethyl)benzamide (**4aaf**).* Compound **4aaf** was obtained in 72% yield (62.2 mg) according to the general procedure (benzonitrile: 2 mL, 19.6 mmol; 24 h) as a white solid; mp 156.1−157.5 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.72−7.70 (m, 2H), 7.53−7.49 (m, 1H), 7.43−7.40 (m, 2H), 7.37−7.29 (m, 7H), 7.12 (d, J = 7.9 Hz, 2H), 6.79 (d, J = 7.1 Hz, 1H), 5.37 (q, J = 7.0 Hz, 1H), 3.49−3.40 (m, 2H), 2.34 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 166.9, 140.6, 137.0, 134.2, 131.6, 131.5, 130.9, 130.0, 128.8, 128.5, 127.8, 127.0, 126.6, 53.5, 40.8, 21.1. HRMS calcd for $C_{22}H_{22}NOS$ $[M + H]^+$, 348.1422; found, 348.1423.

*4-Methyl-N-(1-phenyl-2-(p-tolylthio)ethyl)benzamide (**4aag**).* Compound **4aag** was obtained in 60% yield (54.1 mg) according to the general procedure (4-methylbenzonitrile: 2 mL, 16.7 mmol; 24 h) as a white solid; mp 129.0−130.0 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.62 (d, J = 8.2 Hz, 2H), 7.36−7.30 (m, 7H), 7.21 (d, J = 8.0 Hz, 2H), 7.12 (d, J = 8.0 Hz, 2H), 6.74 (d, J = 7.1 Hz, 1H), 5.36 (q, J = 7.0 Hz, 1H), 3.49−3.39 (m, 2H), 2.42 (s, 3H), 2.34 (s, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 166.8, 142.0, 140.7, 137.0, 131.6, 131.4, 130.9, 130.0, 129.2, 128.8, 127.7, 127.0, 126.6, 53.4, 40.8, 21.5, 21.0. HRMS calcd for $C_{23}H_{24}NOS$ $[M + H]^+$, 362.1579; found, 362.1581.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b02579.

^{1}H and ^{13}C NMR spectra for all compounds (PDF)

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Notes

The authors declare no competing financial interest.

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