Article

A Concise Approach to *N*-Substituted Rhodanines through a Base-Assisted One-Pot Coupling and Cyclization Process

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Abstract: An efficient approach to obtain functionalized rhodanines was developed through a base-assisted one-pot coupling and continuous cyclization of a primary amine, carbon disulfide, and methyl (2-chloroacetyl)carbamate. This conversion tolerates a broad range of functional groups and can be used to scale the preparation of *N*-substituted rhodanines in excellent yields.

Keywords: base; one-pot; coupling; cyclization; metal-free

1. Introduction

The exploration of effective approaches to access privileged structural motifs is one of the most important and urgent requirements in modern organic and pharmaceutical chemistry [1–4]. As a prime example, *N*-substituted rhodanines serve as versatile and useful subunits for numerous biological compounds, which are used in several pharmaceutical agents [5–9]. *N*-substituted rhodanines and their related heterocycles have been identified as synthetic building blocks and structural scaffolds which possess a unique biomolecular interaction profile [10–14]. However, as pan-assay interference compounds (PAINS), *N*-substituted rhodanines have been discovered in screening campaigns that have often been overinterpreted in the past [15]. Epalrestat, an aldose reductase inhibitor which has been used for the treatment of diabetic neuropathy in clinical practice, exemplifies the importance of these heterocycles [16,17]. Furthermore, *N*-substituted rhodanines have been demonstrated to have many biological activities, such as antiviral [18], antimalarial [19], anti-inflammatory [20], and anticancer activities (Figure 1) [21]. In addition, *N*-substituted rhodanines have been utilized in analytical chemistry to detect heavy metal ions [22,23]. Owing to the importance of *N*-substituted rhodanine scaffolds in pharmaceutical chemistry, synthesis methods have attracted a great deal of attention, and a number of powerful approaches have been reported. Even so, the development of an efficient and concise process to obtain *N*-substituted rhodanines is still a challenge in organic and pharmaceutical synthetic chemistry.
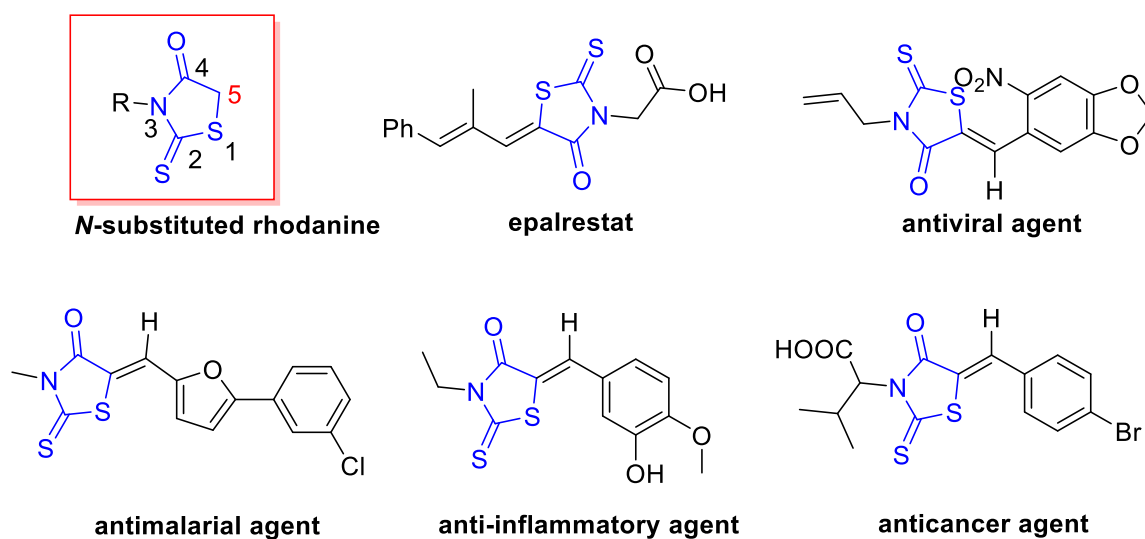
Figure 1. Selected pharmaceuticals and representative compounds bearing *N*-substituted rhodanines.

Multicomponent processes are undoubtedly one of the most efficient approaches to forming several important motifs in modern organic synthesis and pharmaceutical synthesis [24–26]. For example, rhodanines have been successfully synthesized through multicomponent processes [27–33]. However, almost all known methods involving multicomponent reactions cannot achieve the synthesis of 5-unsubstituted rhodanines. Moreover, the known method for obtaining 5-unsubstituted rhodanines requires long reaction times and harsh reaction conditions (Scheme 1a−d) [32,34–36]. As a continuation of drug synthesis and interest in the synthetic methodology of *N*-substituted rhodanines, we decided to investigate the multicomponent reaction of a primary amine **1**, carbon disulphide **2**, and methyl (2-chloroacetyl)carbamate **3i** to form 5-unsubstituted rhodanines. To the best of our knowledge, no results through base-assisted one-pot coupling and a continuous cyclization process to obtain 5-unsubstituted rhodanines by the reactions of a primary amine, carbon disulfide, and methyl (2-chloroacetyl)carbamate have previously been reported (Scheme 1e).

Previous works.
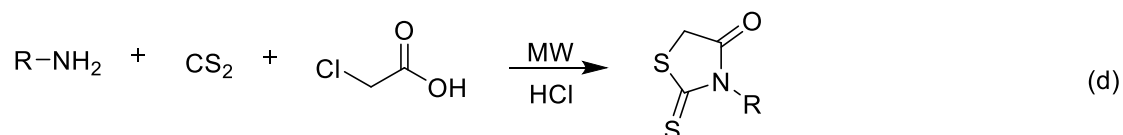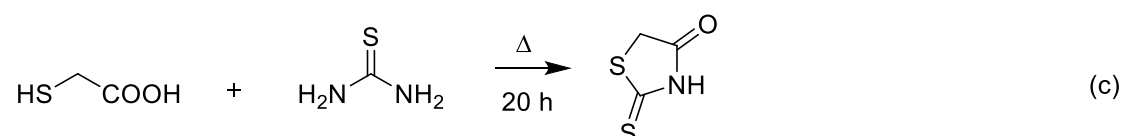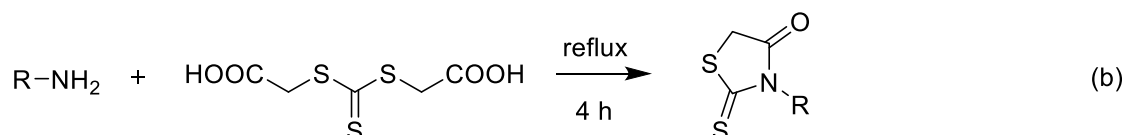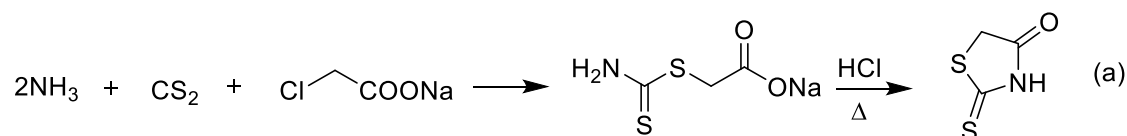
This Work.
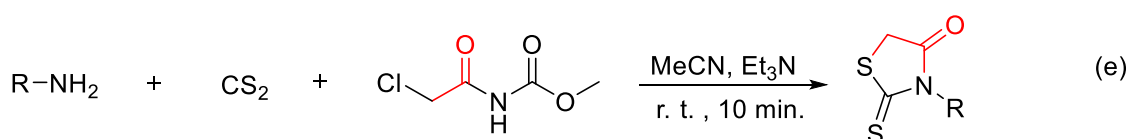
Scheme 1. Synthesis of 5-unsubstituted rhodanines. (**1a–d**) previous works. (**1e**) our work.

2. Results and Discussion

2.1. Optimization of Reaction Conditions

Our investigation started with the three-component reaction of 4-Methylbenzylamine **1a**, carbon disulphide **2**, and 4-methoxyphenyl (2-chloroacetyl)carbamate **3a** (Table 1). First, when the mixture was treated with 1,8-diazabicyclo[5.4.0]undec-7-ene in MeCN, the desired product **4a** was produced in 74% yield (Table 1, Entry 1). Then, various bases, including *N,N*-diisopropylethylamine, Et$_3$N, K$_2$CO$_3$, Na$_2$CO$_3$, K$_3$PO$_4$, and 4-dimethylaminopyridine, were screened, and the results are summarized in Table 1 (Entries 2−7). The results showed that most of these bases could promote the reaction, and Et$_3$N was able to generate **4a** in 94% yield (Entry 3). Other solvents were also investigated, and the results showed that when MeCN was used, the yield of **4a** was up to 94% (Entries 8−17). It is worth mentioning that the base has a great influence on this process. When the reaction was treated in the absence of the base, the desired product **4a** did not form (Entry 18).
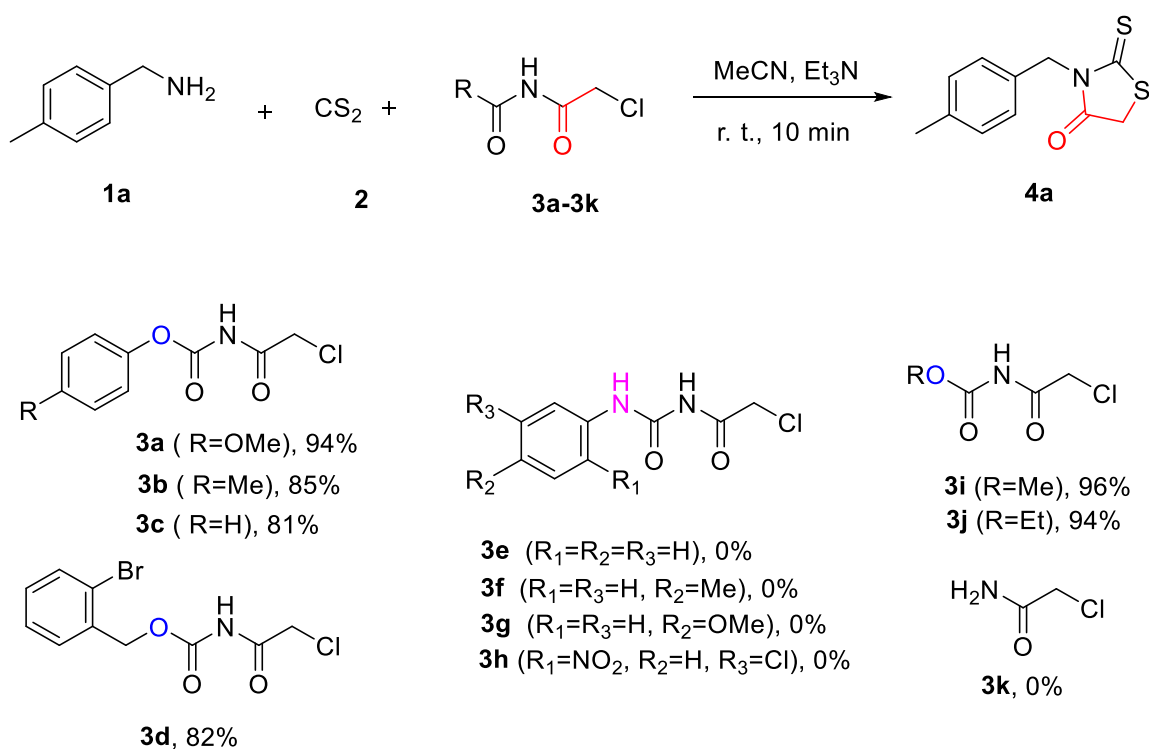
Table 1. Optimization of reaction conditions [a].
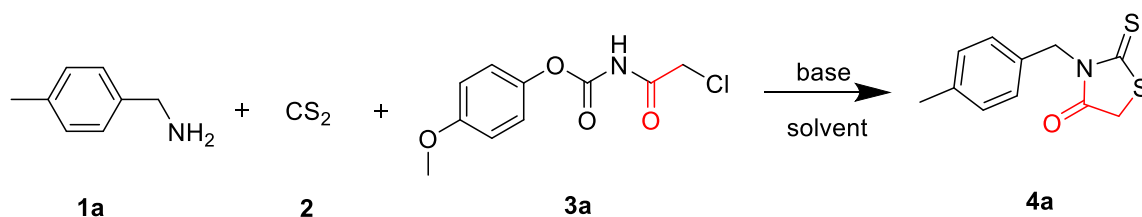
Entry	Solvent	Base	Yield [b] (%)
1	MeCN	DBU	74
2	MeCN	DIPEA	90
3	MeCN	Et$_3$N	94
4	MeCN	K$_2$CO$_3$	82
5	MeCN	Na$_2$CO$_3$	84
6	MeCN	K$_3$PO$_4$	88
7	MeCN	DMAP	80
8	DMSO	Et$_3$N	81
9	DMA	Et$_3$N	84
10	EA	Et$_3$N	86
11	acetone	Et$_3$N	88
12	toluene	Et$_3$N	82
13	DCM	Et$_3$N	84
14	DCE	Et$_3$N	88
15	MeOH	Et$_3$N	76
16	EtOH	Et$_3$N	74
17	DMF	Et$_3$N	76
18	MeCN	–	0

[a] Reaction conditions: **1a** (0.5 mmol), **2** (0.5 mmol), **3a** (0.5 mmol), base (0.6 mmol), solvent (3 mL), r. t., 10 min. [b] Isolated yield based on **1a**. DMSO = dimethyl sulfoxide; DMA = *N,N*-dimethylacetamide; EA = ethyl acetate; DCM = dichloromethane; DCE = dichloroethane; DMF = *N,N*-dimethylformamide; DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene; DIPEA = *N,N*-diisopropylethylamine; DMAP = 4-dimethylaminopyridine.

2.2. Optimization of Substrate Conditions

To further investigate the limitations of this three-component system, various *N*-acetyl-2-chloroacetamides **3a**–**3k** were examined under the above-optimized reaction conditions (Scheme 2). When contacting esters **3a**–**3d** were used, the desired product **4a** was obtained in excellent yield. However, when contacting amides **3e**–**3h** were used, the reaction would not progress. In contrast, when methoxy group- (MeO-) and ethoxy group-(EtO-)substituted *N*-acetyl-2-chloroacetamides **3i** and **3j** were examined, an excellent yield of **4a** was obtained. However, 2-chloroacetamide **3k** could not promote this three-component reaction. Finally, as a low-cost and effective substrate, **3i,** was selected to investigate the scope of primary amines.

Scheme 2. Optimization of substrate conditions. Reaction conditions: **1a** (0.5 mmol), **2** (0.5 mmol), **3a–3k** (0.5 mmol), Et$_3$N (0.6 mmol), MeCN (3 mL), r. t., 10 min. Isolated yield based on **1a**.
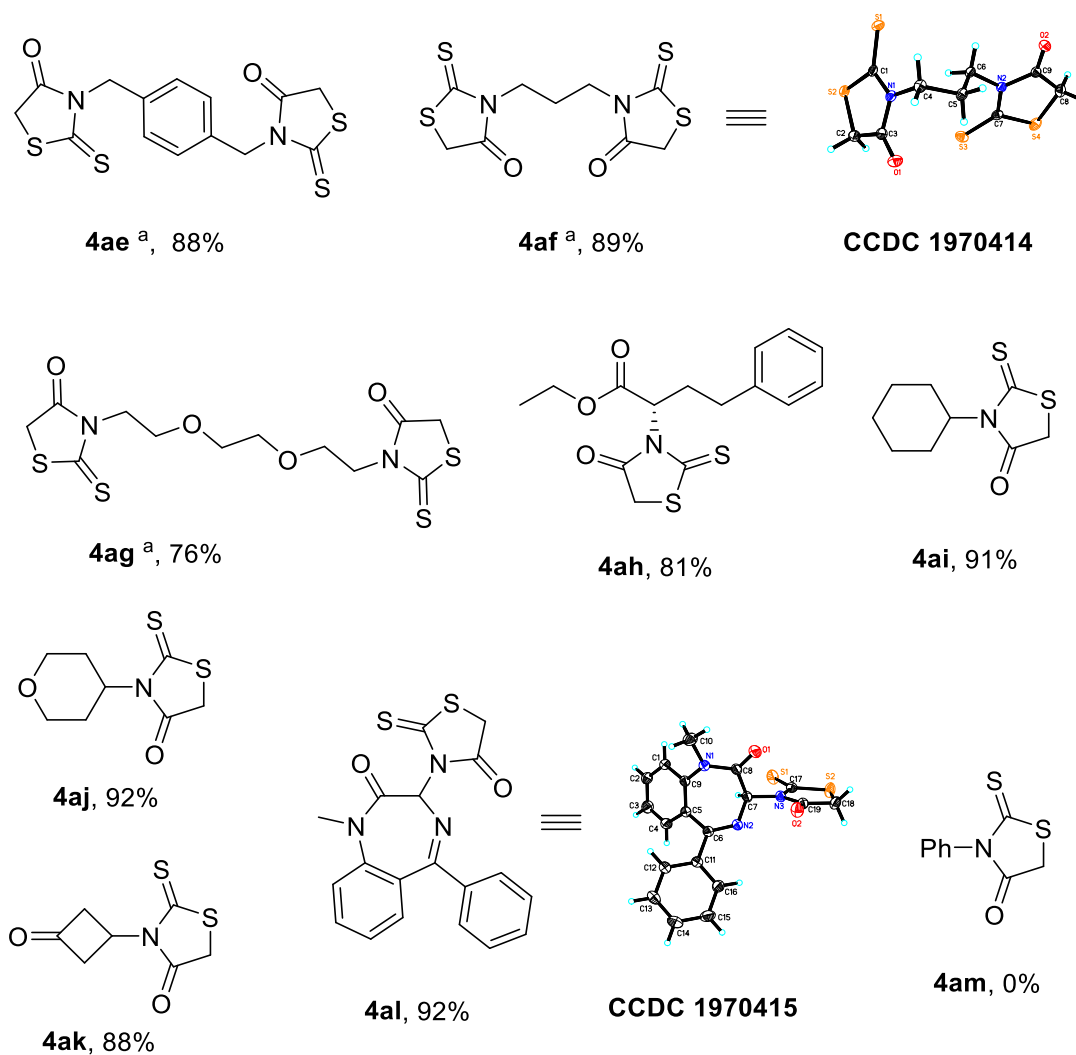
2.3. Substrate Scope Study

Next, we turned our attention to investigate the scope and limitations of three-component reactions of a primary amine **1**, carbon disulphide **2**, and methyl (2-chloroacetyl)carbamate **3i**. First, different substituted benzyl amines **1a–1m** were examined under the optimal conditions, as summarized in Scheme 3. In general, the three-component reactions with various substituted benzyl amines proceeded smoothly with excellent yields (**4a–4m**). Other benzyl-type amines **1n–1r** were also investigated in this process. The results showed that compounds **4n–4r** were also obtained in excellent yields. Various substituted ethylamines **1s–1w** were also examined, and the desired compounds, **4s–4w,** were successfully obtained in excellent yields. A series of linear primary amines **1x–1ad** were examined, and the desired 5-unsubstituted rhodanines **4x–4ad** were also generated in excellent yields. Notably, 1,4-phenylenedimethanamine, propane-1,3-diamine, and 2,2′-(ethane-1,2-diylbis(oxy))bis(ethan-1-amine) afforded **4ae**, **4af**, and **4ag** in 88%, 89%, and 76% yields, respectively. When several secondary amines, including 1ah and cyclic secondary amines **1ai–1al,** were investigated, the desired compounds, **4ah** and **4ai–4al,** were also produced in excellent yields. It is worth noting that when aniline was investigated, the desired compound, **4am,** was not obtained. The structures of 5-unsubstituted rhodanines **4af** (CCDC 1970414) and **4al** (CCDC 1970415) were unambiguously confirmed by X-ray crystallographic analysis**.**

R−NH₂ + CS₂ + (3i) → (4a-4am)

1a-1am   **2**   **3i**   MeCN, Et₃N, r. t. , 10 min.   **4a-4am**

4a (R=4-Me), 96%
4b (R=4-OMe), 91%
4c (R=4-*n*-Bu), 72%
4d (R=4-Ph), 94%
4e (R=4-F), 92%
4f (R=4-CF₃), 90%
4g (R=4-OCF₃), 90%
4h (R=4-CN), 84%
4i (R=3-Ph), 81%
4j (R=3-NH₂), 91%
4k (R=3-Cl), 89%
4l (R=2-Cl), 94%
4m (R=2-Me), 96%

4n, 91%

4o, 91%

4p, 89%

4q, 91%

4r, 81%

4s, 92%

4t, 93%

4u, 92%

4v, 91%

4w, 89%

4x (n=0), 96%
4y (n=3), 94%
4z (n=5), 94%
4aa (n=9), 92%
4ab (n=11), 88%

4ac, 91%

4ad, 88%

Scheme 3. *Cont.*

4ae [a], 88%   **4af** [a], 89%   **CCDC 1970414**

4ag [a], 76%   **4ah**, 81%   **4ai**, 91%

4aj, 92%

4ak, 88%   **4al**, 92%   **CCDC 1970415**   **4am**, 0%
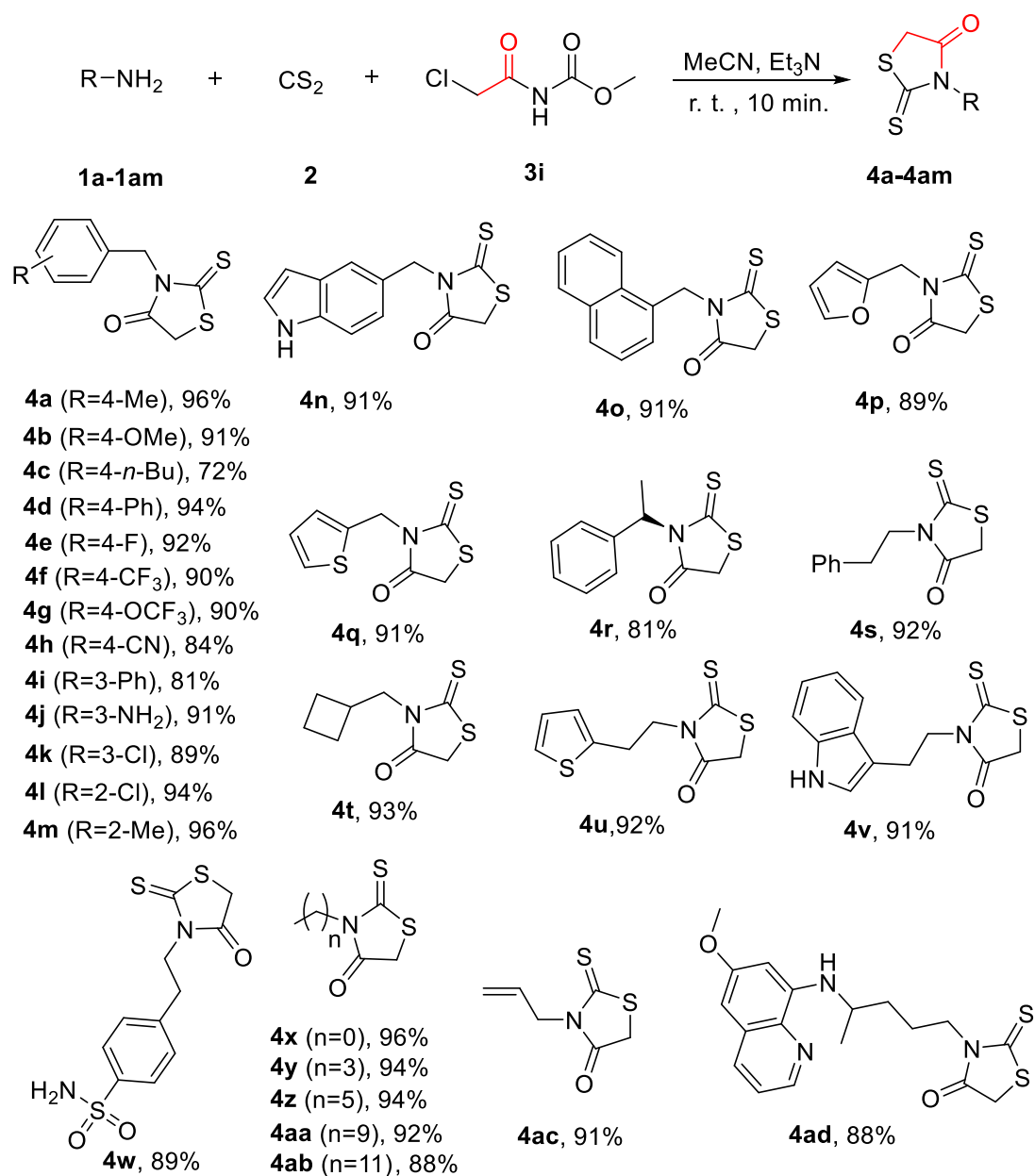
**Scheme 3.** Scope of amines. Reaction conditions: **1a**–**1am** (0.5 mmol), **2** (0.5 mmol), **3i** (0.5 mmol), Et$_3$N (0.6 mmol), MeCN (3 mL), r. t., 10 min. Isolated yield based on **1**. [a] **1** (0.25 mmol).

2.4. Mechanism Study

To elucidate the mechanism, mechanistic studies were performed (Scheme 4). When **1a**, **2**, and **3a** were stirred under standard conditions in the absence of Et$_3$N, the result showed that the reaction did not proceed (Table 1, Entry 18). Furthermore, when we scaled Et$_3$N up to 0.50 or 0.75 equiv., the desired product **4a** was not yet formed. We found that activity returned after increasing from 1 equiv. to 1.10 equiv. Et$_3$N (Scheme 4b, 90% yield). In the model reaction progress, we obtained the carbamate product, **5a,** in 80% yield (Scheme 4a). The structure of **5a** (CCDC 1970413) was confirmed by X-ray crystallographic analysis.
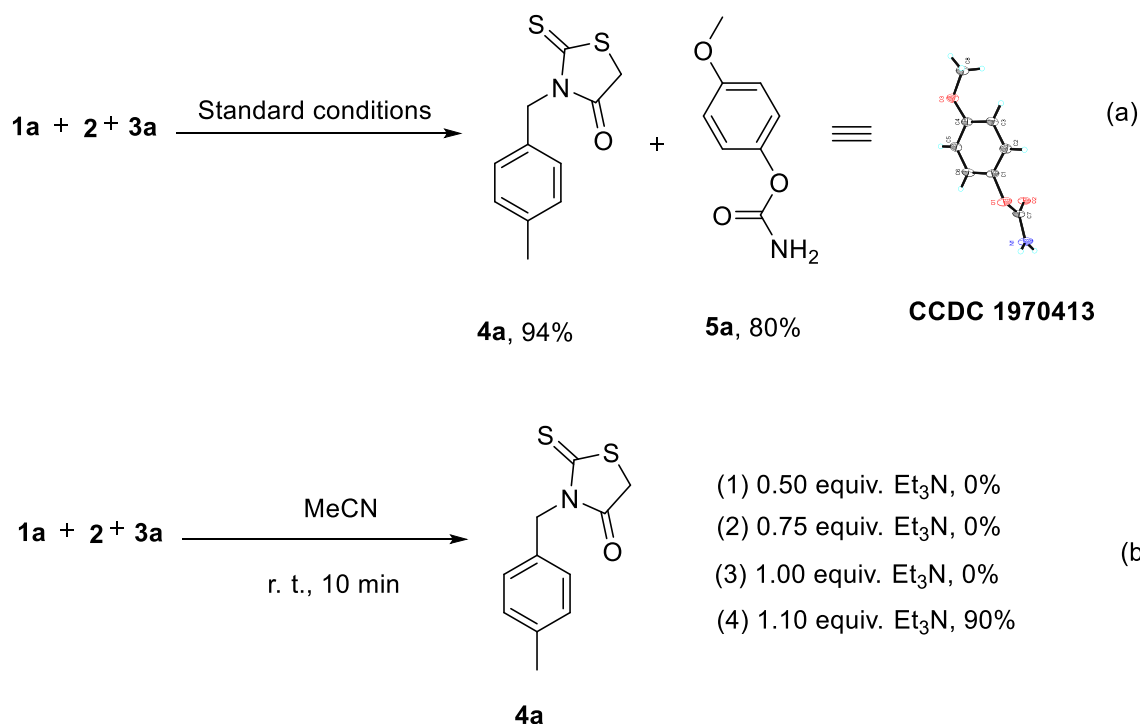
Scheme 4. Mechanism study. (**a**) the model reaction. (**b**) comparison with different conditions in the model reaction.

2.5. Plausible Mechanism

On the basis of the mechanistic studies and previous results [37,38], a possible mechanism is proposed in Scheme 5. The initial step in this reaction is the nucleophilic attack of amine **1** on carbon disulphide **2** to afford the key intermediate **A**, which subsequently reacts with **3** to form another intermediate, **B**, releasing 1 equiv. of protons from the reaction between **1** and **2**. Thus, at least 1 equiv. of Et_3N is needed to scavenge this 1 equiv. of protons being released, and additional excess Et_3N is then available to catalyze **B** to **D**. Considering the fact that the desired product **4a** was not obtained when replacing **3a**–**3d** (contacting ester) with **3e**–**3h** (contacting amide), the key lies in the difference in electronegativity and polarity between O atom and NH group. The O atom of the ester group does not affect the isomerization of imide, while NH group does, containing an active hydrogen atom, which may be the reason why the reaction of **3e**–**3h** could not progress. Therefore, it can be considered that **B** quickly undergoes isomerization to **C,** which, in turn, undergoes an intramolecular six-member ring cyclization and deprotonation to afford **D**. Then, the nucleophilic attack of thionamide on carbonyl produces the five-member ring intermediate **E**. Next, C–N bond cleavage of **E** generates 5-unsubstituted rhodanine **4** and intermediate **F**. Protonation and isomerization of **F** forms carbamate **5**.
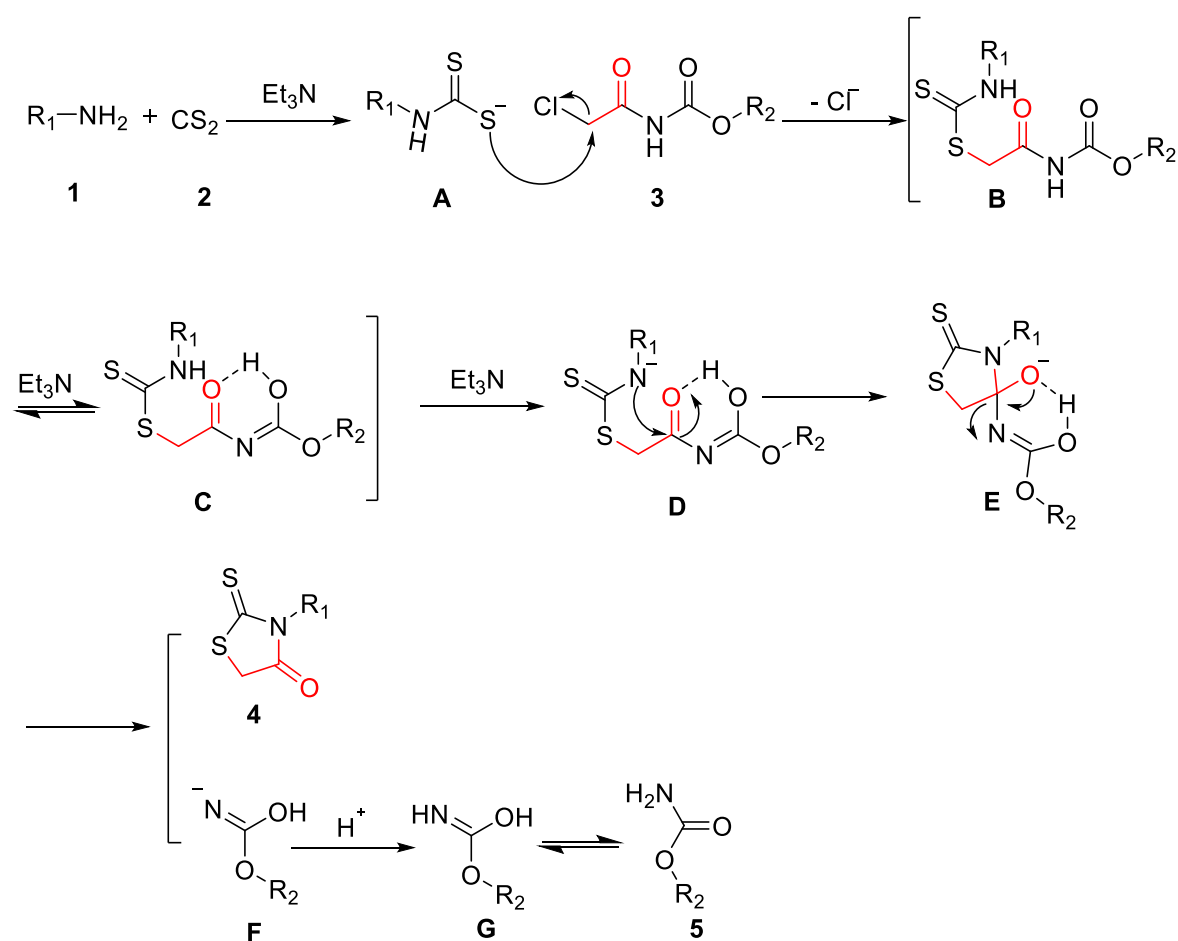
Scheme 5. Plausible mechanism.

3. Materials and Methods

3.1. General Information

All starting materials were commercially available and used without further purification unless otherwise stated. TLC analysis was performed using pre-coated glass plates. Column chromatography was performed using silica gel (200–300 mesh) for separation and purification. ^{1}H NMR and ^{19}F NMR spectra were recorded on Varian Mercury Plus400 spectrometers, and ^{13}C NMR spectra was recorded on Bruker AVANCE600 spectrometer, with CDCl$_3$ or DMSO-d_6 as solvents. Resonances (δ) are given in parts per million relatives to tetramethylsilane or a residual solvent peak (CDCl$_3$: ^{1}H: δ = 7.26 ppm, ^{13}C: δ = 77.00 ppm; DMSO-d_6: ^{1}H: δ = 2.50 ppm, ^{13}C: δ = 39.50 ppm). Data are reported as follows: chemical shift; multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet); coupling constants (Hz); and integration. HRMS were obtained on an AB Sciex Triple TOF® 5600$^+$. The X-ray crystal-structure determinations of **4af**, **4al**, and **5a** were obtained on a d8 venture system. Melting points were measured using a WRX-4 apparatus. Optical rotations were determined on a Rudolph Autopol IV polarimeter.

3.2. General Procedure A: Synthesis of 3a–3j

To a solution of 2-chloroacetamide (1.70 g, 18.2 mmol) in anhydrous 1,2-dichloroethane (20 mL) was added oxalyl chloride (2 mL) at 0 °C, then refluxed in an oil bath at 90 °C for 4 h. The reaction mixture was then cooled to 0 °C, and alcohol or amine (18.2 mmol) was added into the reaction mixture. The reaction mixture was stirred for another 5 min. Upon completion, the solid was filtrated and washed with 1,2-dichloroethane to give **3a–3j** [39].

4-Methoxyphenyl (2-chloroacetyl)carbamate (3a): 4-Methoxyphenol (2.26 g, 18.2 mmol) was used in general procedure A. The crude product was purified from the culture filtrate providing **3a** as a yellow solid in 78% yield (3.46 g, 14.2 mmol). M.p. 149.5–151.3 °C; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 11.45 (s, 1H), 7.20–7.08 (m, 2H), 7.02–6.92 (m, 2H), 4.55 (s, 2H), 3.75 (s, 3H) ppm; ^{13}C NMR (150 MHz, DMSO-d_6) δ 166.9, 157.1, 150.5, 143.1, 122.6 (2C), 114.5, 114.5, 55.4, 44.3 ppm; HRMS (ESI): *m/z* [M+H]$^+$ calcd for $C_{10}H_{10}ClNO_4$: 244.0371, found: 244.0370.

p-Tolyl (2-chloroacetyl)carbamate (3b): *p*-Cresol (1.97 g, 18.2 mmol) was used in general procedure A. The crude product was purified from the culture filtrate providing **3b** as a yellow solid in 91% yield (3.77 g, 16.6 mmol). M.p. 162.8–164.2 °C; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 11.46 (s, 1H), 7.30–7.16 (m, 2H), 7.13–7.00 (m, 2H), 4.55 (s, 2H), 2.31 (s, 3H) ppm; ^{13}C NMR (150 MHz, DMSO-d_6) δ 166.9, 150.2, 147.5, 135.4, 129.9 (2C), 121.4 (2C), 44.3, 20.4 ppm; HRMS (ESI): *m/z* [M+H]$^+$ calcd for $C_{10}H_{10}ClNO_3$: 228.0422, found: 228.0423.

Phenyl (2-chloroacetyl)carbamate (3c): Phenol (1.71 g, 18.2 mmol) was used in general procedure A. The crude product was purified from the culture filtrate providing **3c** as a white solid in 88% yield (3.42 g, 16.0 mmol). M.p. 130.1–132.0 °C; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 11.51 (s, 1H), 7.49–7.40 (m, 2H), 7.33–7.26 (m, 1H), 7.25–7.18 (m, 2H), 4.56 (s, 2H) ppm; ^{13}C NMR (150 MHz, DMSO-d_6) δ 166.9, 150.1, 149.7, 129.6 (2C), 126.1, 121.7 (2C), 44.3 ppm; HRMS (ESI): *m/z* [M+H]$^+$ calcd for $C_9H_8ClNO_3$: 214.0265, found: 214.0266. NMR and HRMS data are consistent with those previously reported [40].

2-Bromobenzyl (2-chloroacetyl)carbamate (3d): (2-Bromophenyl)methanol (3.40 g, 18.2 mmol) was used in general procedure A. The crude product was purified from the culture filtrate providing **3d** as a white solid in 90% yield (5.02 g, 16.4 mmol). M.p. 154.7–156.3 °C; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 11.18 (s, 1H), 7.74–7.62 (m, 1H), 7.60–7.51 (m, 1H), 7.49–7.39 (m, 1H), 7.37–7.26 (m, 1H), 5.20 (s, 2H), 4.49 (s, 2H) ppm; ^{13}C NMR (150 MHz, DMSO-d_6) δ 166.6, 151.2, 134.6, 132.6, 130.5, 130.4, 128.0, 122.8, 66.3, 44.2 ppm; HRMS (ESI): *m/z* [M-H]$^-$ calcd for $C_{10}H_9BrClNO_3$: 305.9360, found: 305.9350.

2-Chloro-N-(phenylcarbamoyl)acetamide (3e): Aniline (1.69 g, 18.2 mmol) was used in general procedure A. The crude product was purified from the culture filtrate providing **3e** as a white solid in 73% yield (2.83 g, 13.3 mmol). M.p. 150.4–152.1 °C; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 10.92 (s, 1H), 10.17 (s, 1H), 7.62–7.45 (m, 2H), 7.40–7.32 (m, 2H), 7.18–7.04 (m, 1H), 4.40 (s, 2H) ppm; ^{13}C NMR (150 MHz, DMSO-d_6) δ 168.6, 150.2, 137.4, 128.9 (2C), 123.8, 119.7 (2C), 43.2 ppm; HRMS (ESI): *m/z* [M+H]$^+$ calcd for $C_9H_9ClN_2O_2$: 213.0425, found: 213.0425. NMR and HRMS data are consistent with those previously reported [39].

2-Chloro-N-(p-tolylcarbamoyl)acetamide (3f): *p*-Toluidine (1.95 g, 18.2 mmol) was used in general procedure A. The crude product was purified from the culture filtrate providing **3f** as a white solid in 71% yield (2.93 g, 12.9 mmol). M.p. 183.5–185.1 °C; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 10.89 (s, 1H), 10.10 (s, 1H), 7.46–7.38 (m, 2H), 7.17–7.09 (m, 2H), 4.39 (s, 2H), 2.26 (s, 3H) ppm; ^{13}C NMR (150 MHz, DMSO-d_6) δ 168.6, 150.2, 134.9, 132.9, 129.3 (2C), 119.7 (2C), 43.2, 20.4 ppm; HRMS (ESI): *m/z* [M-H]$^-$ calcd for $C_{10}H_{11}ClN_2O_2$: 225.0436, found: 225.0426. NMR and HRMS data are consistent with those previously reported [41].

2-Chloro-N-((4-methoxyphenyl)carbamoyl)acetamide (3g): 4-Methoxyaniline (2.24 g, 18.2 mmol) was used in general procedure A. The crude product was purified from the culture filtrate providing **3g** as a white solid in 70% yield (3.09 g, 12.7 mmol). M.p. 170.7–172.4 °C; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 10.87 (s, 1H), 10.01 (s, 1H), 7.46–7.40 (m, 2H), 6.95–6.87 (m, 2H), 4.38 (s, 2H), 3.73 (s, 3H) ppm; ^{13}C NMR (150 MHz, DMSO-d_6) δ 168.5, 155.8, 150.2, 130.3, 121.6 (2C), 114.1 (2C), 55.2, 43.1 ppm; HRMS (ESI): *m/z* [M-H]$^-$ calcd for $C_{10}H_{11}ClN_2O_3$: 241.0385, found: 241.0381. NMR and HRMS data are consistent with those previously reported [41].

2-Chloro-N-((5-chloro-2-nitrophenyl)carbamoyl)acetamide (3h): 5-Chloro-2-nitroaniline (3.14 g, 18.2 mmol) was used in general procedure A. The crude product was purified from the culture filtrate providing **3h** as a yellow solid in 42% yield (2.23 g, 7.6 mmol). M.p. 226.8–228.4 °C; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 11.97 (s, 1H), 11.36 (s, 1H),8.61–8.53 (m, 1H), 8.25–8.17 (m, 1H), 7.42–7.35 (m, 1H), 4.41 (s,

2H) ppm; ^{13}C NMR (150 MHz, DMSO-d_6) δ 168.5, 150.4, 139.6, 136.6, 134.3, 127.5, 123.7, 122.1, 43.1 ppm; HRMS (ESI): *m/z* [M-H]$^-$ calcd for C$_9$H$_7$Cl$_2$N$_3$O$_4$: 289.9741, found: 289.9740.

Methyl (2-chloroacetyl)carbamate (3i): Methanol (0.58 g, 18.2 mmol) was used in general procedure A. The crude product was purified from the culture filtrate providing **3i** as a white solid in 95% yield (2.62 g, 17.3 mmol). M.p. 143.6–145.4 °C; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 10.99 (s, 1H), 4.50 (s, 2H), 3.66 (s, 3H) ppm; ^{13}C NMR (150 MHz, DMSO-d_6) δ 166.7, 152.2, 52.5, 44.3 ppm; HRMS (ESI): *m/z* [M+H]$^+$ calcd for C$_4$H$_6$ClNO$_3$:152.0109, found: 152.0109. NMR and HRMS data are consistent with those previously reported [42].

Ethyl (2-chloroacetyl)carbamate (3j): Ethanol (0.84 g, 18.2 mmol) was used in general procedure A. The crude product was purified from the culture filtrate providing **3j** as a white solid in 95% yield (2.86 g, 17.3 mmol). M.p. 45.1–46.2 °C; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 10.94 (s, 1H), 4.48 (s, 2H), 4.12 (q, *J* = 6.7 Hz, 2H), 1.21 (t, *J* = 7.0 Hz, 3H) ppm; ^{13}C NMR (150 MHz, DMSO-d_6) δ 166.7, 151.6, 61.4, 44.3, 14.1 ppm; HRMS (ESI): *m/z* [M+H]$^+$ calcd for C$_5$H$_8$ClNO$_3$: 166.0265, found: 166.0264.

3.3. General Procedure B: Synthesis of 4a-4al

A mixture of amine (0.5 mmol) or diamine (0.25 mmol), carbon disulfide (38 mg, 0.5 mmol), methyl (2-chloroacetyl)carbamate (76 mg, 0.5 mmol), and triethylamine (61 mg, 0.6 mmol) in MeCN (3 mL) was stirred at room temperature for 10 min. After disappearance of the reactant (monitored by TLC), added 50 mL water to the mixture, then extracted with ethyl acetate 3 times (3 × 50 mL). The extract was dried over anhydrous Na$_2$SO$_4$ and evaporated. The residue was purified by column chromatography on silica gel to give **4a–4al**.

3-(4-Methylbenzyl)-2-thioxothiazolidin-4-one (4a): Amine **1a** (61 mg, 0.5 mmol) was used in general procedure B. The crude product was purified by flash chromatography on silica gel providing **4a** as a red solid in 96% yield (114 mg, 0.48 mmol). TLC R_f = 0.24 (petroleum ether/ethyl acetate, 10:1); M.p. 71.2–72.7 °C; ^{1}H-NMR (400 MHz, CDCl$_3$) δ 7.37–7.31 (m, 2H), 7.15–7.09 (m, 2H), 5.15 (s, 2H), 3.96 (s, 2H), 2.32 (s, 3H) ppm; ^{13}C NMR (150 MHz, CDCl$_3$) δ 201.0, 173.9, 138.0, 131.7, 129.2 (2C), 129.1 (2C), 47.4, 35.4, 21.2 ppm; HRMS (ESI): *m/z* [M-H]$^-$ calcd for C$_{11}$H$_{11}$NOS$_2$: 236.0209, found: 236.0208. NMR and HRMS data are consistent with those previously reported [33].

3-(4-Methoxybenzyl)-2-thioxothiazolidin-4-one (4b): Amine **1b** (69 mg, 0.5 mmol) was used in general procedure B. The crude product was purified by flash chromatography on silica gel providing **4b** as a red solid in 91% yield (115 mg, 0.46 mmol). TLC R_f = 0.23 (petroleum ether/ethyl acetate, 10:1); M.p. 98.1–99.3 °C; ^{1}H-NMR (400 MHz, CDCl$_3$) δ 7.47–7.38 (m, 2H), 6.87–6.79 (m, 2H), 5.12 (s, 2H), 3.95 (s, 2H), 3.78 (s, 3H) ppm; ^{13}C NMR (150 MHz, CDCl$_3$) δ 201.1, 173.9, 159.5, 130.8 (2C), 127.0, 113.8 (2C), 55.3, 47.1, 35.4 ppm; HRMS (ESI): *m/z* [M-H]$^-$ calcd for C$_{11}$H$_{11}$NO$_2$S$_2$: 252.0158, found: 252.0158. NMR and HRMS data are consistent with those previously reported [33].

3-(4-Butylbenzyl)-2-thioxothiazolidin-4-one (4c): Amine **1c** (82 mg, 0.5 mmol) was used in general procedure B. The crude product was purified by flash chromatography on silica gel providing **4c** as a red oil in 72% yield (101 mg, 0.36 mmol). TLC R_f = 0.24 (petroleum ether/ethyl acetate, 10:1); ^{1}H-NMR (400 MHz, CDCl$_3$) δ 7.41–7.33 (m, 2H), 7.16–7.08 (m, 2H), 5.15 (d, *J* = 2.5 Hz, 2H), 3.97 (d, *J* = 2.9 Hz, 2H), 2.59–2.55 (m, 2H), 1.63–1.51 (m, 2H), 1.38–1.29 (m, 2H), 0.97–0.88 (m, 3H) ppm; ^{13}C NMR (150 MHz, CDCl$_3$) δ 201.1, 173.9, 143.1, 131.9, 129.1 (2C), 128.6 (2C), 47.4, 35.4, 35.3, 33.5, 22.3, 13.9 ppm; HRMS (ESI): *m/z* [M-H]$^-$ calcd for C$_{14}$H$_{17}$NOS$_2$: 278.0679, found: 278.0675.

3-([1,1′-Biphenyl]-4-ylmethyl)-2-thioxothiazolidin-4-one (4d): Amine **1d** (92 mg, 0.5 mmol) was used in general procedure B. The crude product was purified by flash chromatography on silica gel providing **4d** as a white solid in 94% yield (141 mg, 0.47 mmol). TLC R_f = 0.21 (petroleum ether/ethyl acetate, 10:1); M.p. 130.2–131.9 °C; ^{1}H-NMR (400 MHz, CDCl$_3$) δ 7.61–7.49 (m, 6H), 7.47–7.41 (m, 2H), 7.39–7.32 (m, 1H), 5.23 (s, 2H), 4.00 (s, 2H) ppm; ^{13}C NMR (150 MHz, CDCl$_3$) δ 201.0, 173.9, 141.2, 140.6, 133.7, 129.6 (2C), 128.8 (2C), 127.5, 127.3 (2C), 127.1 (2C), 47.3, 35.4 ppm; HRMS (ESI): *m/z* [M-H]$^-$ calcd for C$_{16}$H$_{13}$NOS$_2$: 298.0366, found: 298.0367.

3-(4-Fluorobenzyl)-2-thioxothiazolidin-4-one (4e): Amine **1e** (63 mg, 0.5 mmol) was used in general procedure B. The crude product was purified by flash chromatography on silica gel providing **4e** as a brown oil in 92% yield (111 mg, 0.46 mmol). TLC R_f = 0.29 (petroleum ether/ethyl acetate, 10:1); ^{1}H-NMR (400 MHz, CDCl$_3$) δ 7.61–7.52 (m, 4H), 5.23 (s, 2H), 4.02 (s, 2H) ppm; ^{13}C NMR (150 MHz, CDCl$_3$) δ 200.8, 173.7, 138.4, 129.3 (3C), 125.6, 125.6, 47.0, 35.4 ppm; ^{19}F NMR (376 MHz, CDCl$_3$) δ −113.6 ppm; HRMS (ESI): *m/z* [M-H]$^-$ calcd for C$_{10}$H$_8$FNOS$_2$: 239.9959, found: 239.9958. NMR and HRMS data are consistent with those previously reported [34].

2-Thioxo-3-(4-(trifluoromethyl)benzyl)thiazolidin-4-one (4f): Amine **1f** (88 mg, 0.5 mmol) was used in general procedure B. The crude product was purified by flash chromatography on silica gel providing **4f** as a brown solid in 90% yield (131 mg, 0.45 mmol). TLC R_f = 0.31 (petroleum ether/ethyl acetate, 10:1); M.p. 124.0–125.5 °C; ^{1}H-NMR (400 MHz, CDCl$_3$) δ 7.49–7.42 (m, 2H), 7.03–6.95 (m, 2H), 5.14 (s, 2H), 3.98 (s, 2H) ppm; ^{13}C NMR (150 MHz, CDCl$_3$) δ 200.9, 173.8, 163.3, 161.7, 131.2, 131.1, 130.5, 115.5, 115.3, 46.8, 35.4 ppm; ^{19}F NMR (376 MHz, CDCl$_3$) δ −62.9 ppm; HRMS (ESI): *m/z* [M-H]$^-$ calcd for C$_{11}$H$_8$F$_3$NOS$_2$: 289.9927, found: 289.9928. NMR and HRMS data are consistent with those previously reported [43].

2-Thioxo-3-(4-(trifluoromethoxy)benzyl)thiazolidin-4-one (4g): Amine **1g** (96 mg, 0.5 mmol) was used in general procedure B. The crude product was purified by flash chromatography on silica gel providing **4g** as a brown oil in 90% yield (138 mg, 0.45 mmol). TLC R_f = 0.24 (petroleum ether/ethyl acetate, 10:1); ^{1}H-NMR (400 MHz, CDCl$_3$) δ 7.57–7.46 (m, 2H), 7.20–7.12 (m, 2H), 5.17 (s, 2H), 4.00 (s, 2H) ppm; ^{13}C NMR (150 MHz, CDCl$_3$) δ 200.9, 173.8, 149.1, 133.3, 130.8 (2C), 121.0 (2C), 119.5, 46.8, 35.4 ppm; ^{19}F NMR (376 MHz, CDCl$_3$) δ −58.0 ppm; HRMS (ESI): *m/z* [M-H]$^-$ calcd for C$_{11}$H$_8$F$_3$NO$_2$S$_2$: 305.9876, found: 305.9875.

4-((4-Oxo-2-thioxothiazolidin-3-yl)methyl)benzonitrile (4h): Amine **1h** (66 mg, 0.5 mmol) was used in general procedure B. The crude product was purified by flash chromatography on silica gel providing **4h** as a yellow solid in 84% yield (104 mg, 0.42 mmol). TLC R_f = 0.29 (petroleum ether/ethyl acetate, 6:1); M.p. 158.0–159.8 °C; ^{1}H-NMR (400 MHz, CDCl$_3$) δ 7.53–7.47 (m, 2H), 7.19–7.13 (m, 2H), 5.21 (s, 2H), 4.04 (s, 2H) ppm; ^{13}C NMR (150 MHz, CDCl$_3$) δ 200.7, 173.7, 139.7, 132.4 (2C), 129.6 (2C), 118.4, 112.1, 47.0, 35.5 ppm; HRMS (ESI): *m/z* [M-H]$^-$ calcd for C$_{11}$H$_8$N$_2$OS$_2$: 247.0005, found: 247.0007. NMR and HRMS data are consistent with those previously reported [44].

3-([1,1′-Biphenyl]-3-ylmethyl)-2-thioxothiazolidin-4-one (4i): Amine **1i** (92 mg, 0.5 mmol) was used in general procedure B. The crude product was purified by flash chromatography on silica gel providing **4i** as a red oil in 81% yield (121 mg, 0.41 mmol). TLC R_f = 0.30 (petroleum ether/ethyl acetate, 10:1); ^{1}H-NMR (400 MHz, CDCl$_3$) δ 7.71–7.67 (m, 1H), 7.60–7.51 (m, 3H), 7.50–7.32 (m, 5H), 5.25 (s, 2H), 3.98 (s, 2H) ppm; ^{13}C NMR (150 MHz, CDCl$_3$) δ 201.0, 173.9, 141.6, 140.6, 135.2, 129.0, 128.8 (2C), 128.0 (2C), 127.5, 127.2 (2C), 127.0, 47.6, 35.4 ppm; HRMS (ESI): *m/z* [M-H]$^-$ calcd for C$_{16}$H$_{13}$NOS$_2$: 298.0366, found: 298.0368.

3-(3-Aminobenzyl)-2-thioxothiazolidin-4-one (4j): Amine **1j** (61 mg, 0.5 mmol) was used in general procedure B. The crude product was purified by flash chromatography on silica gel providing **4j** as a yellow oil in 91% yield (108 mg, 0.46 mmol). TLC R_f = 0.21 (petroleum ether/ethyl acetate, 3:1); ^{1}H-NMR (400 MHz, CDCl$_3$) δ 7.14–7.05 (m, 1H), 6.85–6.79 (m, 1H), 6.75 (s, 1H), 6.64–6.57 (m, 1H), 5.09 (s, 2H), 3.97 (s, 2H), 3.30 (s, 2H) ppm; ^{13}C NMR (150 MHz, CDCl$_3$) δ 201.1, 173.9, 146.6, 135.8, 129.5, 119.2, 115.3, 114.9, 47.6, 35.4 ppm; HRMS (ESI): *m/z* [M-H]$^-$ calcd for C$_{10}$H$_{10}$N$_2$OS$_2$: 237.0162, found: 237.0156.

3-(3-Chlorobenzyl)-2-thioxothiazolidin-4-one (4k): Amine **1k** (71 mg, 0.5 mmol) was used in general procedure B. The crude product was purified by flash chromatography on silica gel providing **4k** as a brown oil in 89% yield (115 mg, 0.45 mmol). TLC R_f = 0.30 (petroleum ether/ethyl acetate, 10:1); ^{1}H-NMR (400 MHz, CDCl$_3$) δ 7.41 (s, 1H), 7.36–7.30 (m, 1H), 7.29–7.22 (m, 2H), 5.14 (s, 2H), 4.01 (s, 2H) ppm; ^{13}C NMR (150 MHz, CDCl$_3$) δ 200.8, 173.7, 136.5, 134.4, 129.8, 129.0, 128.4, 127.3, 47.0, 35.4 ppm; HRMS (ESI): *m/z* [M-H]$^-$ calcd for C$_{10}$H$_8$ClNOS$_2$: 255.9663, found: 255.9663.

3-(2-Chlorobenzyl)-2-thioxothiazolidin-4-one (4l): Amine **1l** (71 mg, 0.5 mmol) was used in general procedure B. The crude product was purified by flash chromatography on silica gel providing

4l as a yellow solid in 94% yield (121 mg, 0.47 mmol). TLC R_f = 0.25 (petroleum ether/ethyl acetate, 8:1); M.p. 73.4–74.6 °C; ^{1}H-NMR (400 MHz, CDCl$_3$) δ 7.41–7.36 (m, 1H), 7.25–7.15 (m, 2H), 6.95-6.87 (m, 1H), 5.29 (s, 2H), 4.10 (s, 2H) ppm; ^{13}C NMR (150 MHz, CDCl$_3$) δ 200.5, 173.5, 132.9, 131.6, 129.8, 128.8, 126.9, 126.9, 45.4, 35.5 ppm; HRMS (ESI): *m/z* [M-H]$^-$ calcd for C$_{10}$H$_8$ClNOS$_2$: 255.9663, found: 255.9663. NMR and HRMS data are consistent with those previously reported [33].

3-(2-Methylbenzyl)-2-thioxothiazolidin-4-one (4m): Amine **1m** (61 mg, 0.5 mmol) was used in general procedure B. The crude product was purified by flash chromatography on silica gel providing **4m** as a white solid in 96% yield (114 mg, 0.48 mmol). TLC R_f = 0.31 (petroleum ether/ethyl acetate, 8:1); M.p. 107.0–108.4 °C; ^{1}H-NMR (400 MHz, CDCl$_3$) δ 7.21–7.15 (m, 2H), 7.15–7.06 (m, 1H), 6.95–6.87 (m, 1H), 5.17 (s, 2H), 4.06 (s, 2H), 2.43 (s, 3H) ppm; ^{13}C NMR (150 MHz, CDCl$_3$) δ 200.9, 173.8, 135.7, 132.2, 130.5, 127.6, 126.1, 125.5, 45.2, 35.5, 19.5 ppm; HRMS (ESI): *m/z* [M-H]$^-$ calcd for C$_{11}$H$_{11}$NOS$_2$: 236.0209, found: 236.0208.

3-((1*H*-Indol-5-yl)methyl)-2-thioxothiazolidin-4-one (4n): Amine **1n** (73 mg, 0.5 mmol) was used in general procedure B. The crude product was purified by flash chromatography on silica gel providing **4n** as a white solid in 91% yield (119 mg, 0.46 mmol). TLC R_f = 0.22 (petroleum ether/ethyl acetate, 3:1); M.p. 157.8–159.2 °C; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 11.11 (s, 1H), 7.54–7.46 (m, 1H), 7.39–7.29 (m, 2H), 7.15–7.06 (m, 1H), 6.43–6.35 (m, 1H), 5.13 (s, 2H), 4.34 (s, 2H) ppm; ^{13}C NMR (150 MHz, DMSO-d_6) δ 203.2, 174.6, 135.3, 127.4, 125.9, 125.4, 121.4, 119.8, 111.2, 101.0, 47.5, 35.9 ppm; HRMS (ESI): *m/z* [M-H]$^-$ calcd for C$_{12}$H$_{10}$N$_2$OS$_2$: 261.0162, found: 261.0161.

3-(Naphthalen-1-ylmethyl)-2-thioxothiazolidin-4-one (4o): Amine **1o** (79 mg, 0.5 mmol) was used in general procedure B. The crude product was purified by flash chromatography on silica gel providing **4o** as a yellow oil in 91% yield (124 mg, 0.46 mmol). TLC R_f = 0.29 (petroleum ether/ethyl acetate, 10:1); ^{1}H-NMR (400 MHz, CDCl$_3$) δ 8.15–8.08 (m, 1H), 7.91–7.84 (m, 1H), 7.81–7.74 (m, 1H), 7.63–7.47 (m, 2H), 7.42–7.33 (m, 1H), 7.17–7.09 (m, 1H), 5.66 (s, 2H), 4.05 (s, 2H) ppm; ^{13}C NMR (150 MHz, CDCl$_3$) δ 200.9, 173.7, 133.7, 130.8, 129.2, 128.9, 128.4, 126.5, 125.9, 125.1, 123.9, 122.9, 45.4, 35.4 ppm; HRMS (ESI): *m/z* [M-H]$^-$ calcd for C$_{14}$H$_{11}$NOS$_2$: 272.0209, found: 272.0206.

3-(Furan-2-ylmethyl)-2-thioxothiazolidin-4-one (4p): Amine **1p** (49 mg, 0.5 mmol) was used in general procedure B. The crude product was purified by flash chromatography on silica gel providing **4p** as a red oil in 89% yield (95 mg, 0.45 mmol). TLC R_f = 0.28 (petroleum ether/ethyl acetate, 10:1); ^{1}H-NMR (400 MHz, CDCl$_3$) δ 7.41–7.31 (m, 1H), 6.48–6.38 (m, 1H), 6.36–7.26 (m, 1H), 5.19 (s, 2H), 4.01 (s, 2H) ppm; ^{13}C NMR (150 MHz, CDCl$_3$) δ 200.3, 173.4, 147.7, 142.6, 110.5, 110.5, 40.4, 35.3 ppm; HRMS (ESI): *m/z* [M-H]$^-$ calcd for C$_8$H$_7$NO$_2$S$_2$: 211.9845, found: 211.9845. NMR and HRMS data are consistent with those previously reported [45].

3-(Thiophen-2-ylmethyl)-2-thioxothiazolidin-4-one (4q): Amine **1q** (57 mg, 0.5 mmol) was used in general procedure B. The crude product was purified by flash chromatography on silica gel providing **4q** as a red solid in 91% yield (104 mg, 0.46 mmol). TLC R_f = 0.22 (petroleum ether/ethyl acetate, 10:1); M.p. 93.7–95.4 °C; ^{1}H-NMR (400 MHz, CDCl$_3$) δ 7.34–7.17 (m, 2H), 7.03–6.89 (m, 1H), 5.33 (s, 2H), 3.97 (s, 2H) ppm; ^{13}C NMR (150 MHz, CDCl$_3$) δ 200.2, 173.3, 135.8, 129.2, 126.6, 126.4, 41.9, 35.4 ppm; HRMS (ESI): *m/z* [M-H]$^-$ calcd for C$_8$H$_7$NOS$_3$: 227.9617, found: 227.9619. NMR and HRMS data are consistent with those previously reported [45].

(*S*)-3-(1-Phenylethyl)-2-thioxothiazolidin-4-one (4r): Amine **1r** (61 mg, 0.5 mmol) was used in general procedure B. The crude product was purified by flash chromatography on silica gel providing **4r** as a brown oil in 81% yield (96 mg, 0.41 mmol). TLC R_f = 0.30 (petroleum ether/ethyl acetate, 10:1); [α]$_D^{25}$ = 26.2 (*c* 1.00, CH$_3$OH); ^{1}H-NMR (400 MHz, CDCl$_3$) δ 7.38–7.27 (m, 2H), 7.50–7.40 (m, 3H), 6.39 (q, *J* = 7.2 Hz, 1H), 3.79 (q, 2H), 1.86 (d, 3H) ppm; ^{13}C NMR (150 MHz, CDCl$_3$) δ 202.1, 173.4, 138.0, 128.3 (2C), 127.9, 127.6 (2C), 55.2, 34.1, 15.0 ppm; HRMS (ESI): *m/z* [M-H]$^-$ calcd for C$_{11}$H$_{11}$NOS$_2$: 236.0209, found: 236.0207. NMR and HRMS data are consistent with those previously reported [46].

3-Phenethyl-2-thioxothiazolidin-4-one (4s): Amine **1s** (61 mg, 0.5 mmol) was used in general procedure B. The crude product was purified by flash chromatography on silica gel providing **4s** as a red solid in 92% yield (109 mg, 0.46 mmol). TLC R_f = 0.24 (petroleum ether/ethyl acetate, 10:1);

M.p. 111.3–112.7 °C; ^{1}H-NMR (400 MHz, CDCl$_3$) δ 7.45–7.15 (m, 5H), 4.25–4.15 (m, 2H), 3.93 (s, 2H), 3.03–2.89 (m, 2H) ppm; ^{13}C NMR (150 MHz, CDCl$_3$) δ 200.9, 173.5, 137.3, 128.9 (2C), 128.6 (2C), 126.8, 45.7, 35.2, 32.6 ppm; HRMS (ESI): *m/z* [M-H]$^-$ calcd for C$_{11}$H$_{11}$NOS$_2$: 236.0209, found: 236.0211. NMR and HRMS data are consistent with those previously reported [34].

3-(Cyclobutylmethyl)-2-thioxothiazolidin-4-one (4t): Amine **1t** (43 mg, 0.5 mmol) was used in general procedure B. The crude product was purified by flash chromatography on silica gel providing **4t** as a yellow oil in 93% yield (94 mg, 0.47 mmol). TLC R_f = 0.21 (petroleum ether/ethyl acetate, 10:1); ^{1}H-NMR (400 MHz, CDCl$_3$) δ4.06 (dd, *J* = 7.3, 1.6 Hz, 2H), 3.97 (d, *J* = 1.7 Hz, 2H), 2.80 (dd, *J* = 14.7, 7.3 Hz, 1H), 2.09–1.92 (m, 2H), 1.75–1.91 (m, 4H) ppm; ^{13}C NMR (150 MHz, CDCl$_3$) δ201.6, 174.2, 49.4, 35.3, 33.4, 26.2 (2C), 18.3 ppm; HRMS (ESI): *m/z* [M-H]$^-$ calcd for C$_8$H$_{11}$NOS$_2$: 200.0209, found: 200.0208.

3-(2-(Thiophen-2-yl)ethyl)-2-thioxothiazolidin-4-one (4u): Amine **1u** (64 mg, 0.5 mmol) was used in general procedure B. The crude product was purified by flash chromatography on silica gel providing **4u** as a brown solid in 92% yield (112 mg, 0.46 mmol). TLC R_f = 0.30 (petroleum ether/ethyl acetate, 10:1); M.p. 125.5–127.3 °C; ^{1}H-NMR (400 MHz, CDCl$_3$) δ 7.24–7.13 (m, 1H), 7.00–6.90 (m, 1H), 6.91–6.82 (m, 1H), 4.24 (dd, *J* = 10.6, 4.6 Hz, 2H), 3.95 (d, *J* = 1.7 Hz, 2H), 3.18 (t, *J* = 6.7 Hz 2H) ppm; ^{13}C NMR (150 MHz, CDCl$_3$) δ 200.8, 173.5, 139.2, 127.0, 125.9, 124.3, 45.5, 35.3, 26.6 ppm; HRMS (ESI): *m/z* [M-H]$^-$ calcd for C$_9$H$_9$NOS$_3$: 241.9774, found: 241.9773.

3-(2-(1*H*-Indol-3-yl)ethyl)-2-thioxothiazolidin-4-one (4v): Amine **1v** (80 mg, 0.5 mmol) was used in general procedure B. The crude product was purified by flash chromatography on silica gel providing **4v** as a yellow solid in 91% yield (126 mg, 0.46 mmol). TLC R_f = 0.26 (petroleum ether/ethyl acetate, 4:1); M.p. 178.0–179.4 °C; ^{1}H-NMR (400 MHz, CDCl$_3$) δ 8.04 (s, 1H), 7.83-7.71 (m, 1H), 7.40–7.30 (m, 1H), 7.24–7.13 (m, 2H), 7.12–7.06 (m, 1H), 4.34–4.21 (m, 2H), 3.87 (s, 2H), 3.11 (dd, *J* = 9.1, 6.7 Hz, 2H) ppm; ^{13}C NMR (150 MHz, CDCl$_3$) δ 201.3, 173.7, 136.2, 127.4, 122.4, 122.2, 119.7, 118.8, 111.9, 111.2, 45.4, 35.4, 22.6 ppm; HRMS (ESI): *m/z* [M-H]$^-$ calcd for C$_{13}$H$_{12}$N$_2$OS$_2$: 275.0318, found: 275.0316.

4-(2-(4-Oxo-2-thioxothiazolidin-3-yl)ethyl)benzenesulfonamide (4w): Amine **1w** (100 mg, 0.5 mmol) was used in general procedure B. The crude product was purified by flash chromatography on silica gel providing **4w** as a yellow solid in 89% yield (141 mg, 0.45 mmol). TLC R_f = 0.24 (petroleum ether/ethyl acetate, 1:1); M.p. 197.6-199.0 °C; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 7.81–7.71 (m, 2H), 7.47–7.37 (m, 2H), 7.34 (s, 2H), 4.25 (s, 2H), 4.07 (t, *J* =7.5 Hz, 2H), 2.92 (t, *J* = 7.4 Hz, 2H) ppm; ^{13}C NMR (150 MHz, DMSO-d_6) δ 203.0, 174.1, 142.5, 141.8, 129.2 (2C), 125.9 (2C), 44.6, 35.8, 31.8 ppm; HRMS (ESI): *m/z* [M-H]$^-$ calcd for C$_{11}$H$_{12}$N$_2$O$_3$S$_3$: 314.9937, found: 314.9934.

3-Methyl-2-thioxothiazolidin-4-one (4x): Amine **1x** (16 mg, 0.5 mmol) was used in general procedure B. The crude product was purified by flash chromatography on silica gel providing **4x** as a yellow solid in 96% yield (71 mg, 0.48 mmol). TLC R_f = 0.29 (petroleum ether/ethyl acetate, 10:1); M.p. 259.4–261.0 °C; ^{1}H-NMR (400 MHz, CDCl$_3$) δ 4.02 (s, 2H), 3.39 (s, 3H) ppm; ^{13}C NMR (150 MHz, CDCl$_3$) δ 201.3, 173.8, 35.7, 31.3 ppm; HRMS (ESI): *m/z* [M-H]$^-$ calcd for C$_4$H$_5$NOS$_2$: 145.9740, found: 145.9735. NMR and HRMS data are consistent with those previously reported [34].

3-Butyl-2-thioxothiazolidin-4-one (4y): Amine **1y** (37 mg, 0.5 mmol) was used in general procedure B. The crude product was purified by flash chromatography on silica gel providing **4y** as a yellow oil in 94% yield (89 mg, 0.47 mmol). TLC R_f = 0.21 (petroleum ether/ethyl acetate, 10:1); ^{1}H-NMR (400 MHz, CDCl$_3$) δ 4.03–3.92 (m, 4H), 1.69–1.56 (m, 2H), 1.46–1.25 (m, 2H), 1.01–0.89 (m, 3H) ppm; ^{13}C NMR (150 MHz, CDCl$_3$) δ 201.2, 173.9, 44.6, 35.3, 28.8, 20.0, 13.7 ppm; HRMS (ESI): *m/z* [M-H]$^-$ calcd for C$_7$H$_{11}$NOS$_2$: 188.0209, found: 188.0200. NMR and HRMS data are consistent with those previously reported [34].

3-Hexyl-2-thioxothiazolidin-4-one (4z): Amine **1z** (51 mg, 0.5 mmol) was used in general procedure B. The crude product was purified by flash chromatography on silica gel providing **4z** as a yellow oil in 94% yield (102 mg, 0.47 mmol). TLC R_f = 0.28 (petroleum ether/ethyl acetate, 10:1); ^{1}H-NMR (400 MHz, CDCl$_3$) δ 4.07–3.89 (m, 4H), 1.71–1.55 (m, 2H), 1.37–1.28 (m, 6H), 0.95–0.83 (m, 3H) ppm; ^{13}C NMR (150 MHz, CDCl$_3$) δ 201.2, 173.9, 44.8, 35.4, 31.3, 26.7, 26.4, 22.5, 14.0 ppm; HRMS (ESI):

m/z [M-H]⁻ calcd for $C_9H_{15}NOS_2$: 216.0522, found: 216.0512. NMR and HRMS data are consistent with those previously reported [47].

3-Decyl-2-thioxothiazolidin-4-one (4aa): Amine **1aa** (79 mg, 0.5 mmol) was used in general procedure B. The crude product was purified by flash chromatography on silica gel providing **4aa** as a yellow oil in 92% yield (126 mg, 0.46 mmol). TLC R_f = 0.29 (petroleum ether/ethyl acetate, 10:1); ¹H-NMR (400 MHz, CDCl₃) δ 4.08–3.82 (m, 4H), 1.70–1.55 (m, 2H), 1.38–1.02 (m, 14H), 0.98–0.76 (m, 3H) ppm; ¹³C NMR (150 MHz, CDCl₃) δ 201.2, 173.9, 44.8, 35.3, 31.9, 29.5, 29.4, 29.3, 29.1, 26.8, 26.7, 22.7, 14.1 ppm; HRMS (ESI): *m/z* [M-H]⁻ calcd for $C_{13}H_{23}NOS_2$: 272.1148, found: 272.1150.

3-Dodecyl-2-thioxothiazolidin-4-one (4ab): Amine **1ab** (93 mg, 0.5 mmol) was used in general procedure B. The crude product was purified by flash chromatography on silica gel providing **4ab** as a yellow oil in 88% yield (133 mg, 0.44 mmol). TLC R_f = 0.25 (petroleum ether/ethyl acetate, 10:1); ¹H-NMR (400 MHz, CDCl₃) δ 4.10–3.82 (m, 4H), 1.72–1.54 (m, 2H), 1.44–1.08 (m, 18H), 0.95–0.78 (m, 3H) ppm; ¹³C NMR (150 MHz, CDCl₃) δ 201.2, 173.9, 44.8, 35.3, 31.9, 29.6 (2C), 29.5, 29.5, 29.3, 29.1, 26.8, 26.7, 22.7, 14.1 ppm; HRMS (ESI): *m/z* [M-H]⁻ calcd for $C_{15}H_{27}NOS_2$: 300.1461, found: 300.1464.

3-Allyl-2-thioxothiazolidin-4-one (4ac): Amine **1ac** (29 mg, 0.5 mmol) was used in general procedure B. The crude product was purified by flash chromatography on silica gel providing **4ac** as a red oil in 91% yield (79 mg, 0.46 mmol). TLC R_f = 0.30 (petroleum ether/ethyl acetate, 10:1); ¹H-NMR (400 MHz, CDCl₃) δ 5.90–5.73 (m, 1H), 5.27 (t, *J* = 14.6 Hz, 2H), 4.61 (d, *J* = 5.9 Hz, 2H), 4.00 (s, 2H) ppm; ¹³C NMR (150 MHz, CDCl₃) δ 200.7, 173.5, 129.4, 119.6, 46.5, 35.4 ppm; HRMS (ESI): *m/z* [M-H]⁻ calcd for $C_6H_7NOS_2$: 171.9896, found: 171.9895. NMR and HRMS data are consistent with those previously reported [34].

3-(4-((6-Methoxyquinolin-8-yl)amino)pentyl)-2-thioxothiazolidin-4-one (4ad): Amine **1ad** (130 mg, 0.5 mmol) was used in general procedure B. The crude product was purified by flash chromatography on silica gel providing **4ad** as a yellow oil in 88% yield (165 mg, 0.44 mmol). TLC R_f = 0.29 (petroleum ether/ethyl acetate, 8:1); ¹H-NMR (400 MHz, CDCl₃) δ 8.64-8.44 (m, 1H), 7.93 (d, *J* = 8.2 Hz, 1H), 7.36–7.27 (m, 1H), 6.36 (s, 1H), 6.28 (s, 1H), 6.00 (d, *J* = 7.8 Hz, 1H), 3.89 (s, 3H), 3.67 (dd, *J* = 16.3, 9.9 Hz, 1H), 3.59–3.45 (m, 2H), 1.96–1.69 (m, 5H), 1.42–1.21 (m, 4H) ppm; ¹³C NMR (150 MHz, CDCl₃) δ 159.4, 144.7, 144.3, 135.2, 134.9, 130.0, 129.9, 121.9 (2C), 96.9, 91.9 (2C), 55.2, 47.5, 45.1, 33.6, 26.7, 20.7 ppm; HRMS (ESI): *m/z* [M-H]⁻ calcd for $C_{18}H_{21}N_3O_2S_2$: 374.1002, found: 374.1007.

3,3′-(1,4-Phenylenebis(methylene))bis(2-thioxothiazolidin-4-one) (4ae): Diamine **1ae** (34 mg, 0.25 mmol) was used in general procedure B. The crude product was purified by flash chromatography on silica gel providing **4ae** as a yellow solid in 88% yield (81 mg, 0.22 mmol). TLC R_f = 0.24 (petroleum ether/ethyl acetate, 4:1); M.p. 266.5–268.3 °C; ¹H-NMR (400 MHz, DMSO-*d₆*) δ 7.24 (s, 4H), 5.03 (s, 4H), 4.34 (s, 4H) ppm; ¹³C NMR (150 MHz, DMSO-*d₆*) δ 203.3 (2C), 174.5 (2C), 134.4 (2C), 127.7 (4C), 46.5 (2C), 36.0 (2C) ppm; HRMS (ESI): *m/z* [M-H]⁻ calcd for $C_{14}H_{12}N_2O_2S_4$: 366.9709, found: 366.9705.

3,3′-(Propane-1,3-diyl)bis(2-thioxothiazolidin-4-one) (4af): Diamine **1af** (19 mg, 0.25 mmol) was used in general procedure B. The crude product was purified by flash chromatography on silica gel providing **4af** as a yellow solid in 89% yield (68 mg, 0.22 mmol). TLC R_f = 0.29 (petroleum ether/ethyl acetate, 3:1); M.p. 122.8–124.5 °C; ¹H-NMR (400 MHz, CDCl₃) δ 4.08-4.01 (m, 4H), 4.00 (s, 4H), 2.13–2.00 (m, 2H) ppm; ¹³C NMR (150 MHz, CDCl₃) δ 201.2 (2C), 173.9 (2C), 41.8 (2C), 35.4 (2C), 24.8 ppm; HRMS (ESI): *m/z* [M-H]⁻ calcd for $C_9H_{10}N_2O_2S_4$: 304.9552, found: 304.9549. NMR and HRMS data are consistent with those previously reported [48].

3,3′-((Ethane-1,2-diylbis(oxy))bis(ethane-2,1-diyl))bis(2-thioxothiazolidin-4-one) (4ag): Diamine **1ag** (37 mg, 0.25 mmol) was used in general procedure B. The crude product was purified by flash chromatography on silica gel providing **4ag** as a yellow oil in 76% yield (72 mg, 0.19 mmol). TLC R_f = 0.29 (petroleum ether/ethyl acetate, 3:1); ¹H-NMR (400 MHz, CDCl₃) δ 7.10-6.99 (m, 4H), 6.91–6.81 (m, 4H), 5.41–4.71 (m, 4H), 3.81–3.75 (m, 4H) ppm; ¹³C NMR (150 MHz, CDCl₃) δ 157.2 (2C), 155.6 (2C), 144.3 (2C), 122.5 (2C), 114.4 (2C), 55.6 (2C) ppm; HRMS (ESI): *m/z* [M-H]⁻ calcd for $C_{12}H_{16}N_2O_4S_4$: 378.9920, found: 378.9917.

Ethyl (*S*)-2-(4-oxo-2-thioxothiazolidin-3-yl)-4-phenylbutanoate (4ah): Amine **1ah** (104 mg, 0.5 mmol) was used in general procedure B. The crude product was purified by flash chromatography on silica gel providing **4ah** as a yellow oil in 81% yield (131 mg, 0.41 mmol). TLC R_f = 0.23 (petroleum ether/ethyl acetate, 8:1); $[\alpha]_D^{25}$ = 23.6 (*c* 1.00, CH$_3$OH); ^{1}H-NMR (400 MHz, CDCl$_3$) δ 7.29–7.24 (m, 2H), 7.21–7.12 (m, 3H), 5.59 (d, *J* = 8.6 Hz, 1H), 4.27–4.08 (m, 2H), 3.72 (d, *J* = 18.1 Hz, 1H), 3.55 (d, *J* = 18.2 Hz, 1H), 2.82 (dd, *J* = 13.1, 6.8 Hz, 1H), 2.74–2.50 (m, 3H), 1.28–1.20 (m, 3H) ppm; ^{13}C NMR (150 MHz, CDCl$_3$) δ 201.2, 173.3, 167.9, 140.2, 128.5 (2C), 128.2 (2C), 126.2, 62.0, 57.7, 34.3, 32.5, 28.2, 14.1 ppm; HRMS (ESI): *m/z* [M-H]$^-$ calcd for C$_{15}$H$_{17}$NO$_3$S$_2$: 322.0577, found: 322.0568.

3-Cyclohexyl-2-thioxothiazolidin-4-one (4ai): Amine **1ai** (50 mg, 0.5 mmol) was used in general procedure B. The crude product was purified by flash chromatography on silica gel providing **4ai** as a yellow solid in 91% yield (98 mg, 0.46 mmol). TLC R_f = 0.22 (petroleum ether/ethyl acetate, 10:1); M.p. 120.3–122.1 °C; ^{1}H-NMR (400 MHz, CDCl$_3$) δ 4.86 (t, *J* = 10.9 Hz, 1H), 3.82 (s, 2H), 2.45-2.15 (m, 2H), 1.94–1.76 (m, 2H), 1.60–1.51 (m, 2H), 1.44–1.31 (m, 2H), 1.32–1.16 (m, 2H) ppm; ^{13}C NMR (150 MHz, CDCl$_3$) δ 202.4, 174.3, 58.5, 33.9, 27.5 (2C), 26.0 (2C), 25.0 ppm; HRMS (ESI): *m/z* [M-H]$^-$ calcd for C$_9$H$_{13}$NOS$_2$: 214.0366, found: 214.0365. NMR and HRMS data are consistent with those previously reported [49].

3-(Tetrahydro-2*H*-pyran-4-yl)-2-thioxothiazolidin-4-one (4aj): Amine **1aj** (51 mg, 0.5 mmol) was used in general procedure B. The crude product was purified by flash chromatography on silica gel providing **4aj** as a white solid in 92% yield (100 mg, 0.46 mmol). TLC R_f = 0.27 (petroleum ether/ethyl acetate, 4:1); M.p. 160.7–162.1 °C; ^{1}H-NMR (400 MHz, CDCl$_3$) δ 5.13 (t, *J* = 12.2 Hz, 1H), 4.08 (d, *J* = 11.3 Hz, 2H), 3.86 (s, 2H), 3.46 (t, *J* = 11.9 Hz, 2H), 2.78–2.61 (m, 2H), 1.60–1.49 (m, 2H) ppm; ^{13}C NMR (150 MHz, CDCl$_3$) δ 202.1, 174.0, 67.6 (2C), 55.3, 33.9, 27.7 (2C) ppm; HRMS (ESI): *m/z* [M-H]$^-$ calcd for C$_8$H$_{11}$NO$_2$S$_2$: 216.0158, found: 216.0160. NMR and HRMS data are consistent with those previously reported [49].

3-(3-Oxocyclobutyl)-2-thioxothiazolidin-4-one (4ak): Amine **1ak** (43 mg, 0.5 mmol) was used in general procedure B. The crude product was purified by flash chromatography on silica gel providing **4ak** as a yellow solid in 88% yield (89 mg, 0.44 mmol). TLC R_f = 0.28 (petroleum ether/ethyl acetate, 4:1); M.p. 166.0–167.6 °C; ^{1}H-NMR (400 MHz, CDCl$_3$) δ 5.85–5.65 (m, 1H), 4.00–3.91 (m, 4H), 3.45–3.34 (m, 2H) ppm; ^{13}C NMR (150 MHz, CDCl$_3$) δ 201.8, 201.4, 174.2, 51.0 (2C), 41.9, 34.3 ppm; HRMS (ESI): *m/z* [M-H]$^-$ calcd for C$_7$H$_7$NO$_2$S$_2$: 199.9845, found: 199.9847.

3-(1-methyl-2-oxo-5-phenyl-2,3-dihydro-1*H*-benzo[e][1,4]diazepin-3-yl)-2-thioxothiazolidin-4 -one (4al): Amine **1al** (133 mg, 0.5 mmol) was used in general procedure B. The crude product was purified by flash chromatography on silica gel providing **4al** as a white solid in 92% yield (176 mg, 0.46 mmol). TLC R_f = 0.30 (petroleum ether/ethyl acetate, 4:1); M.p. 178.5-180.1 °C; ^{1}H-NMR (400 MHz, CDCl$_3$) δ 7.68–7.58 (m, 3H), 7.50–7.31 (m, 5H), 7.28 (s, 1H), 6.75 (s, 1H), 4.10 (s, 2H), 3.46 (s, 3H) ppm; ^{13}C NMR (150 MHz, CDCl$_3$) δ 202.1, 172.0, 168.0, 166.8, 143.0, 137.9, 132.2, 130.8, 130.7, 130.0 (2C), 128.3, 128.2 (2C), 124.4, 121.4, 74.8, 35.8, 34.3 ppm; HRMS (ESI): *m/z* [M+H]$^+$ calcd for C$_{19}$H$_{15}$N$_3$O$_2$S$_2$: 382.0678, found: 382.0681.

3.4. General Procedure for the Synthesis of 4-Methoxyphenyl Carbamate (5a)

A mixture of *p*-tolylmethanamine (61 mg, 0.5 mmol), carbon disulfide (38 mg, 0.5 mmol), 4-methoxyphenyl (2-chloroacetyl)carbamate (122 mg, 0.5 mmol), and triethylamine (61 mg, 0.6 mmol) in MeCN (3 mL) was stirred at room temperature for 10 min. After disappearance of the reactant (monitored by TLC), added 50 mL water to the mixture, and then extracted with ethyl acetate 3 times (3 × 50 mL). The extract was dried over anhydrous Na$_2$SO$_4$ and evaporated. The residue was purified by column chromatography on silica gel to afford the product **4a** (TLC R_f = 0.24, petroleum ether/ethyl acetate = 10:1) as a red solid in 94% yield (112 mg, 0.47 mmol) and **5a** (TLC R_f = 0.30, petroleum ether/ethyl acetate = 3:1) as a white solid in 80% yield (67 mg, 0.40 mmol). M.p. 127.3–129.0 °C; ^{1}H-NMR (400 MHz, CDCl$_3$) δ 7.15–7.00 (m, 2H), 6.95–6.83 (m, 2H), 5.05 (s, 2H), 3.80 (s, 3H); ^{13}C NMR

(150 MHz, CDCl$_3$) δ 157.2, 155.5, 144.3, 122.5 (2C), 114.4 (2C), 55.6; HRMS (ESI): *m/z* [M+H]$^+$ calcd for C$_8$H$_9$NO$_3$: 168.0655, found: 168.0654.

CCDC 1970414 (**4af**), CCDC 1970415 (**4al**), and CCDC 1970413 (**5a**) contain the Supplementary Crystallographic Data for this paper. These data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: +44 1223 336033; E-mail: deposit@ccdc.cam.ac.uk).

4. Conclusions

In summary, we established an efficient approach for the synthesis of *N*-substituted rhodanines via a base-assisted one-pot coupling and continuous cyclization of a primary amine, carbon disulphide, and methyl (2-chloroacetyl)carbamate. A series of substituted alkyl- and benzylamines were successively obtained, providing structurally diverse *N*-substituted rhodanines in outstanding yield. Further application of this promising method in pharmaceutical synthesis is in progress in our laboratory.

Supplementary Materials: The following are available online. Supporting information including the spectrums of ^{1}H, ^{13}C-NMR, ^{19}F-NMR, and X-ray Crystallography.

Author Contributions: X.S. directed this project, Y.L. carried out the experiments, M.-L.T. checked and analyzed the data, and Z.H. and C.Z. revised the paper. All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest: The authors declare no conflicts of interest.

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Sample Availability: Samples of the compounds are available from the authors.