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# Reactions of 4-substituted 5*H*-1,2,3-dithiazoles with primary and secondary amines: fast and convenient synthesis of 1,2,5-thiadiazoles, 2-iminothioacetamides and 2-oxoacetamides

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ABSTRACT

The treatment of 5*H*-1,2,3-dithiazole-5-thiones **1** in chloroform under reflux and 5*H*-1,2,3-dithiazol-5-ones **2** in THF at room temperature with primary aliphatic amines and benzylamine afforded 1,2,5-thiadiazole-3(2*H*)-thiones **3** and 1,2,5-thiadiazol-3(2*H*)-ones **6**, respectively. The structure of dithiazolone **3f** was confirmed by X-ray diffraction analysis. The reaction of dithiazolone **2e** bearing an electron-donating methyl group in the 4-position gave 2-oxoacetamide **7e** in high yield. The reaction of thiones **1** with secondary aliphatic amines in DMSO yielded 2-iminothioacetamides **8** in moderate yields together with elemental sulfur. Interestingly, the treatment of dithiazolones **2** with secondary amines under the same conditions afforded 2-oxoacetamides **9**—the products of the hydrolysis of corresponding imino derivatives **10**, which was isolated as **10b**. A general mechanism was proposed for the formation of the products.



## 1. Introduction

The exploration of the synthetic utility of 1,2,3-dithiazoles[1] has been focused on the chemistry of 4-chloro-5*H*-1,2,3-dithiazol-5-ones, 5-thiones, 5-arylimines, and 5-ylidenes, which can be easily prepared from 4,5-dichloro-5*H*-1,2,3-dithiazolium chloride (Appel salt).[2] The best studied are reactions of 1,2,3-dithiazoles with primary and secondary alkylamines. The nucleophilic attack occurs at the C-2 carbon of the ring yielding diatomic sulfur, $S_2$, a chloride anion, and various functionalized derivatives such as *N*′-aryl-*N*-alkylcyanoformamidines,[3] *N*-alkyl- and *N*,*N*-dialkylcyanothioformamides,[4] *N*,*N*′-disubstituted ureas,[5] and (alkylamino)cyanomethylidenes.[6] Reactivity of these compounds toward nucleophiles may be in part attributed to the presence of the chlorine atom at the C-4 position that can be easily removed as a chloride anion to generate a cyano group. Other 1,2,3-dithiazoles, except for 4-chloro-1,2,3-dithiazoles, are not readily available.[7] Meanwhile, one might expect 1,2,3-dithiazoles with weaker leaving groups in the 4-position to have reactivity different from 4-chloro derivatives. Recently we have found that 4-substituted 1,2,3-dithiazoles 5-ones and 5-thiones, which can be selectively obtained in a one pot reaction of various ethanoneoximes,[8] undergo a new transformation to 1,2,5-thiadiazole-3(2*H*)-thiones and -ones, respectively, upon treatment with primary amines.[9] We undertook a systematic study of the reactions of 1,2,3-dithiazoles **1** and **2** with primary and secondary amines to understand how the starting amine and the reaction conditions affect the final product. Here, we report the conditions for the selective synthesis of each class of compounds, the mechanisms proposed on the basis of the reaction pathways, and the results of the X-ray diffraction analysis for one compound of the class.

## 2. Results and discussion

### 2.1. Reactions with primary amines

4-Substituted 1,2,3-dithiazole-5-thiones **1** and 1,2,3-dithiazol-5-ones **2** were found to be inert toward primary aromatic amines. Aniline did not react in various solvents such as benzene, acetonitrile, or dimethylformamide, and 1,2,3 dithiazoles were isolated from the reaction mixtures in quantitative yields.

The treatment of 4-phenyl-5*H*-1,2,3-dithiazole 5-thione **1a** with more basic benzylamine afforded, in various solvents (chloroform,

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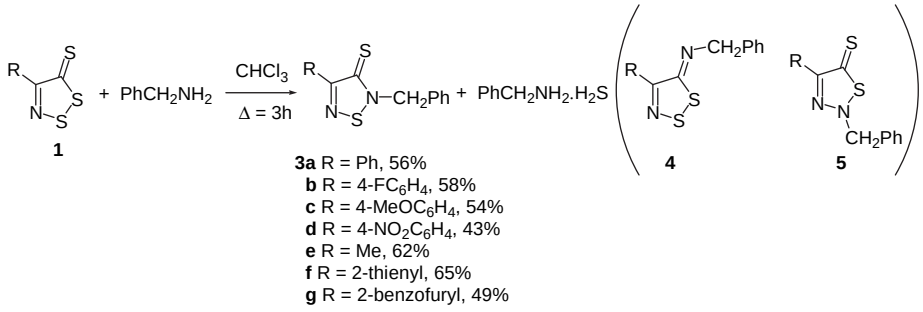
THF, and acetonitrile), novel compound **3a**, a yellow solid $C_{15}H_{12}N_2S_2$. According to the mass spectra, elemental analysis, and $^1H$ and $^{13}C$ NMR data, it is formally a product of benzylamine addition and $H_2S$ elimination, whose formation was confirmed by isolation of benzylammonium hydrogen sulfide from the reaction mixture in practically quantitative yield (Scheme 1).

4-Phenyl-5*H*-1,2,3-dithiazole 5-thione **1a** reacted in the same way with other primary amines, viz. allylamine and *iso*-butylamine, to give the corresponding 2,4-disubstituted 1,2,5-thiadiazole-5-thiones (Scheme 2).

To the best of our knowledge, 1,2,5-thiadiazole-5-thiones are practically unknown; there is no reliable data on their synthesis.

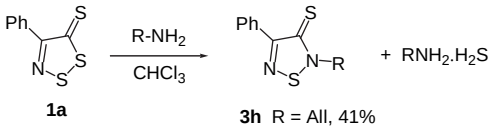



**3a** R = Ph, 56%
**b** R = 4-$FC_6H_4$, 58%
**c** R = 4-$MeOC_6H_4$, 54%
**d** R = 4-$NO_2C_6H_4$, 43%
**e** R = Me, 62%
**f** R = 2-thienyl, 65%
**g** R = 2-benzofuryl, 49%

**Scheme 1.** Reaction of 5*H*-1,2,3-dithiazole-5-thiones **1** with benzylamine.

Three isomeric structures can be proposed for this product: 1,2,5-thiadiazolone **3a**, imino-1,2,3-dithiazole **4**, and 1,2,3-thiadiazole **5**. The analysis of the spectroscopic data and the NMR spectra calculated for these structures did not allow the best choice. Structure **3a** was finally proved by the X-ray analysis of closely related analogue **3f** (see below).

We extended the reaction with benzylamine to other 1,2,3-dithiazole-5-thiones **1**. 1,2,5-Thiadiazolothiones **3** were obtained in all reactions in moderate yields (Scheme 1).




**3h** R = All, 41%
**3i** R = *i*-Bu, 54%

**Scheme 2.** Reaction of 4-phenyl-5*H*-1,2,3-dithiazole-5-thione **1a** with aliphatic amines.

The structure of thieno derivative **3f** was confirmed by X-ray diffraction analysis (Fig. 1). The thiadiazole ring bond lengths and

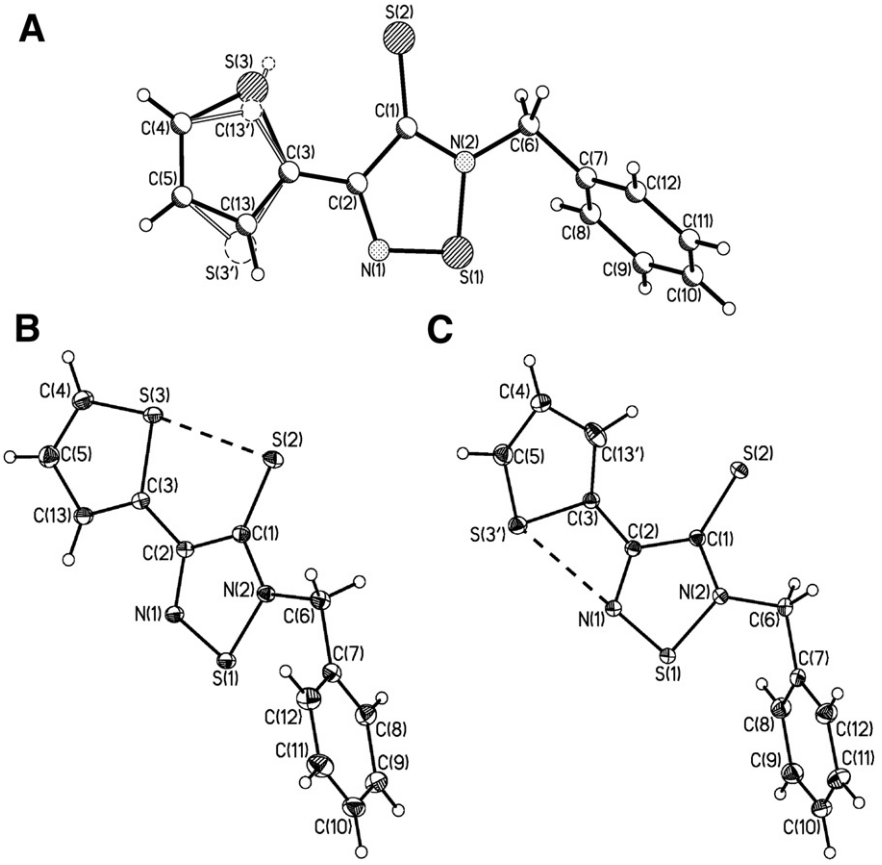


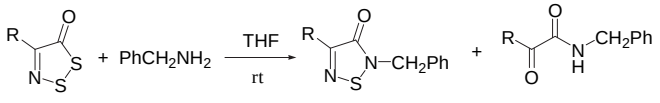

**Figure 1.** General view of compound **3f** (A), which is a superposition of two isomers *cis*-**3f** (B) and *trans*-**3f** (C) in a ratio 4:1, with representation of atoms via thermal ellipsoids at 50% probability level. Selected bond lengths (Å): C(1)–S(2) 1.6799(7), S(1)–N(1) 1.6222(6), S(1)–N(2) 1.6887(6), N(1)–C(2) 1.3228(9), C(1)–C(2) 1.4614(10), C(1)–N(2) 1.3526(9), C(2)–C(3) 1.4521(10), N(2)–C(6) 1.4675(9); selected bond angles (°): C(2)–C(1)–N(2) 106.73(6), C(1)–C(2)–N(1) 114.65(6), C(2)–N(1)–S(1) 112.07(5), N(1)–S(1)–N(2) 93.14(3), C(1)–N(2)–S(1) 113.36(5), C(1)–C(2)–C(3) 126.23(6).

angles, except for S(1)–N(1) and N(1)–C(2) bonds, fall in the range typical for such type of heterocyclic compounds. A close investigation of the molecular geometry of **3f** revealed the significant contribution of the betaine-like resonance form with formal single N(1)–C(2) and double N(1)–S(1) bonds. Moreover, when the standard dataset with $2\theta$ below 60° was used, an unexpected elongation (up to 1.543(4) Å) of the presumably double C(3)–C(13) bond was observed in the **3f** crystal. The addition of high-angle data ($2\theta$<90°) resulted in the superposition (80:20) of two isomers with *cisoid* and *transoid* dispositions of S(2) and S(3) atoms in **3f** (Fig. 1). The cis form (*cis*-**3f**) appears to be stabilized by the extremely short intermolecular contact between sulfur of the C=S group and sulfur of the thiophene ring (S···S 3.1812(7) Å, C(4)S(3)S(2) 171.33(6)°) accompanied by a charge transfer from the lone pair (Lp) of the S(2) atom to the σ* orbital of the C–S bond. In turn, S(3′) of the minor component (*trans*-**3f**) presumably binds to the N(1) thiadiazole atom (S···N 2.9342(8) Å, S(1)N(1)S(4) 175.95(6)°) through the charge transfer from one of the sulfur Lps to the S(1)–N(1) bond σ* orbital.

Quantum chemical calculations (B3LYP/6–311+G*) and a subsequent topological analysis of theoretical electron density functions[10] for two isomers showed that the *cisoid*-form was stabilized by the S···S interaction that contributed 2.9 kcal/mol, as estimated by Espinosa's correlation scheme.[11,12] In the second isomer a weaker (1.8 kcal/mole) C(13′)–H···S(2) binding was observed instead of the S···N–C interaction. On the other hand, *trans*-**3f** was found to be a little more stable (0.63 kcal/mol) than *cis*-**3f**, apparently, owing to a conjugation between the thiadiazole and thiophene cycles that was more pronounced in the *transoid*-form.

The N(1) atom of both isomers participates in the formation of the N···S–N interaction (S···N 2.9045(8) Å, N(1′)S(1)N(2) 168.56(7)°) with the charge being transferred from nitrogen Lp to the σ* orbital of the latter bond that leads to the dimerization of the neighboring molecules. These supramolecular associates are assembled into the 3D framework by a few weak S···H, π···π, and S···S contacts.

It was envisaged that, upon the reaction with primary amines, 1,2,3-dithiazol-5-ones **2** should give ketone **6**. We checked this possibility by the treatment of dithiazolone **2a** with benzylamine, yet it appeared that the formation of 1,2,5-dithiazolone **6a** was complicated by a side reaction yielding *N*-substituted 2-oxoacetamide **7a** (Scheme 3).




**2**

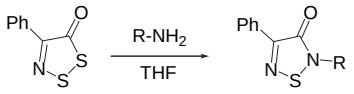
**6a** R = Ph, 94%
**b** R = 4-$FC_6H_4$, 100%
**c** R = 4-$MeOC_6H_4$, 100%
**d** R = 4-$NO_2C_6H_4$, 90%
**f** R = 2-thienyl, 95%
**g** R = 2-benzofuryl, 96%

**7e** R = Me, 87%

**Scheme 3.** Reaction of 5*H*-1,2,3-dithiazol-5-ones **2** with benzylamine.

To obtain thiadiazolone **6a** selectively, the reaction between **2a** (R=Ph) and benzylamine was investigated in detail; the nature of the solvent appeared crucial for reaction to occur. If the reaction was carried out in an inert solvent such as chloroform, the starting dithiazolone **2a** was isolated in a practically quantitative yield. Attempts to employ strong aprotic dipolar solvents such as DMF or acetonitrile at room temperature led to formation of the mixtures **6**/**7** in a ratio of 1:1 and 1:2, respectively. The treatment of benzylamine with **2a** in absolute THF gave selectively 1,2,5-thiadiazolone **6a** in 94% yield. We then applied these conditions to other ketones **2**. 1,2,5-Thiadiazolones **6** were obtained in high yield in practically all reactions. The treatment of dithiazolone **2e** bearing the electron-donating methyl group in position-4 with benzylamine in THF gave 2-oxoacetamide **7e** in high yield; no traces of thiadiazolone **6e** were detected (Scheme 3).

Dithiazolone **2a** reacted with other primary amines in a similar way to afford the corresponding 1,2,5-thiadiazol-5-ones **6h–j** in high yields (Scheme 4).




**2a**

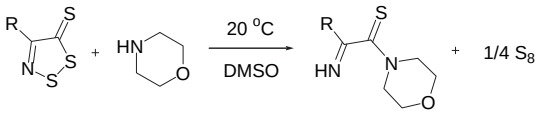
**6h** R = All, 89%
**6i** R = *n*-Bu, 97%
**6j** R = *i*-Pr, 93%

**Scheme 4.** Reaction of 4-phenyl-5*H*-1,2,3-dithiazol-5-one **2a** with aliphatic amines.

Up to date, a few papers[13–16] have reported syntheses of 1,2,5-thiadiazol-3-ones, but we have developed a general and very simple method for their preparation that allows high yields.

## 2.2. Reactions with secondary amines

Thione **1a** did not react with morpholine in chloroform, acetonitrile, or THF even under harsh conditions (refluxing for 5 h); starting thione **1a** was isolated from the reaction mixtures in practically quantitative yields. The treatment of thione **1a** with 2 equiv of morpholine in DMSO gave new product **8a** along with elemental sulfur (Scheme 5). Compound **8a** (75%), a colorless solid $C_{12}H_{14}N_2OS$, according to its mass spectrum, elemental analysis, and $^1H$ and $^{13}C$ NMR data has the structure of 2-iminothioacetamide. The $^1H$ NMR spectrum of **8a** showed the NH group (9.5 ppm), and the IR spectrum showed an intensive NH absorption at 3190–3240 $cm^{-1}$.

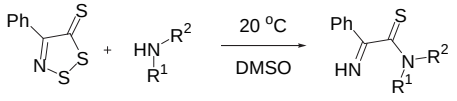



**1**

**8a** R = Ph, 75%
**8b** R = 4-$FC_6H_4$, 69%
**8c** R = 4-$MeOC_6H_4$, 77%
**8d** R = 4-$NO_2C_6H_4$, 72%
**8e** R = 2-thienyl, 66%
**8f** R = 2-benzofuryl, 69%

**Scheme 5.** Reaction of 5*H*-1,2,3-dithiazole-5-thiones **1** with morpholine.

Dithiazole **1a** reacted in the same way with other secondary amines—diethylamine, piperidine, and pyrrolidine—to give the corresponding imines **8g**,**h**,**i** (Scheme 6).

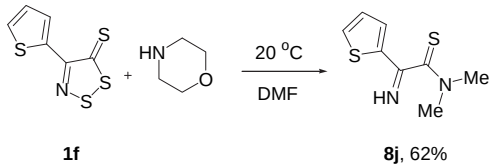



**1a**

**8g** $R^1 = R^2$ = Et, 78%
**8h** $R^1;R^2$ = -$(CH_2)_5$-, 84%
**8i** $R^1;R^2$ = -$(CH_2)_4$-, 35%

**Scheme 6.** Reaction of 4-phenyl-5*H*-1,2,3-dithiazole-5-thione **1a** with secondary amines.

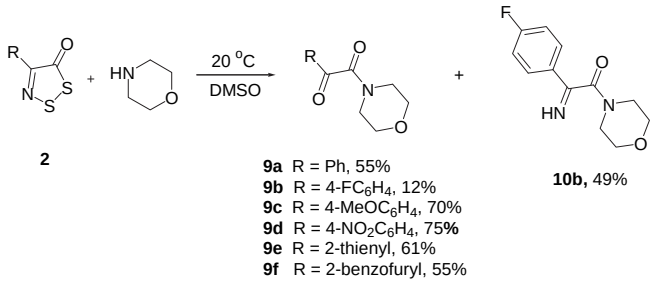
If the reaction of dithiazole **1f** with morpholine was carried out in DMF, dimethylamino derivative **8j** was formed instead of morpholine **8e** (Scheme 7). Apparently, the initially formed **8e** further reacts with dimethylamine (from DMF) to substitute the morpholino group.




**Scheme 7.** Reaction of 5*H*-1,2,3-dithiazole-5-thione **1f** with morpholine in DMF.

Only one example of a 4-substituted 2-iminothioacetamide is known.[17] It was prepared by catalytic amination of the corresponding oxo derivative with ammonia. They may be useful precursors in the preparation of various heterocyclic compounds, as was shown for *N*′-arylthiocarbamoyl-*N*,*N*-dialkylamidines.[18]

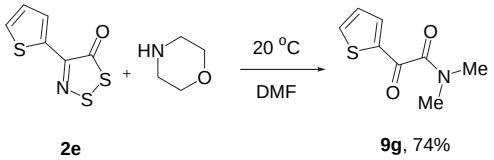
The treatment of 5*H*-1,2,3-dithiazol 5-ones **2** with 2 equiv of morpholine in DMSO at room temperature afforded new products, though these were 2-morpholin-4-yl-2-oxoethanones **9** rather than imino derivatives, as could be expected by analogy with thiones **1** (Scheme 8). Elemental sulfur was also isolated in 80–85% yield (calculated to $S_2$).




**Scheme 8.** Reaction of 5*H*-1,2,3-dithiazol-5-ones **2** with morpholine.

Apparently 2-iminoacetamides **10** can be considered as the most probable intermediates in the formation of 2-oxoethanones **9**. However only in one case we did manage to isolate stable **10b** (49%) that was easily transformed to oxo derivative **9b** by a further reaction with morpholine in DMSO. Low yield of **9b** is explained by the side generation of **10b**.

The treatment of ketone **2e** with morpholine in DMF gave derivative **9e**, instead of the expected morpholino, leading to dimethylamine **9g** (Scheme 9).

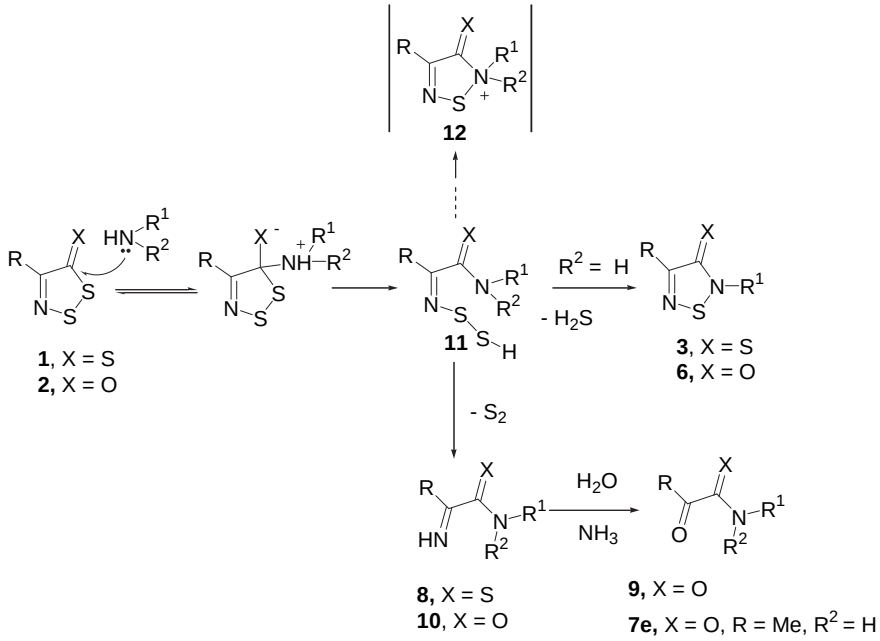



**Scheme 9.** Reaction of 5*H*-1,2,3-dithiazole-5-one **2e** with morpholine in DMF.

2-Oxoacetamides **9** are well known compounds possessing various biological activity, including inhibition of enzymes,[19] antiviral action,[20] inhibition of HIV-1 infection,[21] etc.

## 2.3. Reaction mechanisms

A plausible mechanism for all the described transformations could be as follows: a nucleophilic attack of the amine onto the C-5 position of the dithiazole ring followed by the heterocyclic ring opening to form key intermediate **11**. In the case of primary amines, the 1,2,5-thiadiazole cycle is probably formed through an intramolecular attack of amide (thioamide) nitrogen onto the S-2 sulfur atom with hydrogen sulfide elimination. In the reaction with secondary aliphatic amines, the ring closure that gives salt **12** is unlikely or reversible. The formation of imines **8** or **10** could occur via elimination of $S_2$ and oxamides **9** and **7e** through the further hydrolysis of **8** and **10** with $NH_3$ elimination (Scheme 10).




**Scheme 10.** A plausible mechanism for the reaction of 5*H*-1,2,3-dithiazoles with primary and secondary amines.

## 3. Conclusion

In summary, 5*H*-1,2,3-dithiazole-5-thiones **1** and 5*H*-1,2,3-dithiazol-5-ones **2** are found to be convenient precursors for previously unknown 1,2,5-thiadiazole-3(2*H*)-thiones **3** and 1,2,5-thiadiazol-3(2*H*)-ones **6** in the reactions with primary amines. The reactions of secondary amines led to the heterocyclic ring opening to form 2-oxoacetamides and 2-iminothioacetamides, which are promising compounds for the preparation of various heterocyclic systems. Finally, 4-substituted 5*H*-1,2,3-dithiazoles gave different products from 4-chloro derivatives since the chlorine atom was readily expelled as a chloride anion and the cyano group was generated.

## 4. Experimental

### 4.1. General

Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. IR spectra were recorded on a Specord M-80 instrument in KBr pellets. $^1$H NMR were recorded on a Bruker WM 250 spectrometer (250 MHz) and $^{13}$C NMR spectra were recorded on a Bruker AM 300 (75.5 MHz) in $CDCl_3$ or $D_2O$ solutions. *J* values are given in hertz. Mass spectra were recorded on a Finnigan MAT INCOS 50 instrument using electron impact ionization. Elemental analyses were performed on Perkin Elmer 2400 Elemental Analyser.

5*H*-1,2,3-Dithiazole-5-thiones **1** and 5*H*-1,2,3-dithiazol-5-ones **2** were prepared as previously reported.[8]

DFT calculations of the isolated *cis*-**2f** and *trans*-**2f** were performed with the Gaussian03[22] program package using the B3LYP functional. Full optimization of the molecules was carried out with the 6-311+G* basis set starting from the X-ray structural data. As convergence criteria, the standard threshold limits of $4.5\times10^{-4}$ and $1.8\times10^{-3}$ au were applied for the maximum force and displacement, respectively. The topological analysis of computed electron densities was performed using the AIM2000 program packages.[23]

### 4.2. Reaction of 5*H*-1,2,3-dithiazole-5-thiones 1 and 5*H*-1,2,3-dithiazol-5-ones 2 with primary amines

*General procedure.* Primary amine (1 mmol) was added to a solution of the appropriate 1,2,3-dithiazole **1** or **2** (0.5 mmol) in THF (4 mL) at room temperature. The reaction mixture was stirred for 2–3 h at room temperature, the alkylammonium hydrogen sulfide filtered off, and the solvent evaporated under reduced pressure. The residue was purified by column chromatography (Silica gel Merck 60, light petroleum, and then light petroleum/$CH_2Cl_2$ mixtures).

*4.2.1. 2-Benzyl-4-phenyl-1,2,5-thiadiazole-3(2H)-thione (**3a**).* Yield 56%. Yellow crystalline solid, mp 95–97 °C; $R_f$=0.49 (hexane/$CH_2Cl_2$=4:1). Anal. Calcd for $C_{15}H_{12}N_2S_2$: C, 63.35; H, 4.25; N, 9.85; S, 22.55. Found: C, 63.45; H, 4.39; N, 10.05; S, 22.68. $^1$H NMR (250 MHz, $CDCl_3$) $\delta$: 5.31 (2H, s, $CH_2$), 7.49 (8H, m, Ar), 8.42 (2H, m, Ar). $^{13}$C NMR (75.5 MHz, $CDCl_3$) $\delta$: 53.8 ($CH_2$), 128.1, 129.1, 129.5, 129.9, 129.9, and 130.5 (10CH, Ar), 133.0, 133.2, and 160.5 (three sp$^2$ tertiary C), 177.4 (C=S). MS (EI, 70 eV), *m*/*z* (%): ($M^+$, 25), 251 (13). IR (KBr): $\nu$=3064, 2928 (C–H), 2852, 1496, 1456, 1428, 1344, 1332, 1292, 1208, 1028, 848, 772, 756, 708, 696 cm$^{-1}$.

*4.2.2. 2-Benzyl-4-(4-fluorophenyl)-1,2,5-thiadiazole-3(2H)-thione (**3b**).* Yield 58%. Yellow crystalline solid, mp 140–143 °C; $R_f$=0.48 (hexane/$CH_2Cl_2$=1:1). Anal. Calcd for $C_{15}H_{11}FN_2S_2$: C, 59.58; H, 3.67; N, 9.26. Found: C, 59.70; H, 3.92; N, 9.32. $^1$H NMR (250 MHz, $CDCl_3$) $\delta$: 5.30 (2H, s, $CH_2$), 7.17 (2H, d, *J* 8.8, Ar), 7.48 (5H, s, Ar), 8.49 (2H, m, Ar). $^{13}$C NMR (75.5 MHz, $CDCl_3$) $\delta$: 53.8 ($CH_2$), 115.2, 129.6, 130.0, 131.2, and 131.3 (9CH), 129.2, 133.0, 160.9, and 165.7 (four sp$^2$ tertiary C), 177.2 (C=S). MS (EI, 70 eV), *m*/*z* (%): 302 ($M^+$, 17), 269 (7), 121 (22). IR (KBr): $\nu$=3032, 1600, 1520, 1460, 1440, 1336, 1296, 1224, 1204, 1160, 968, 820, 804, 756, 736, 700 cm$^{-1}$.

*4.2.3. 2-Benzyl-4-(4-methoxyphenyl)-1,2,5-thiadiazole-3(2H)-thione (**3c**).* Yield 54%. Yellow crystalline solid, mp 86–88 °C; $R_f$=0.61 (hexane/$CH_2Cl_2$=1:1). Anal. Calcd for $C_{16}H_{14}N_2OS_2$: C, 61.12; H, 4.49; N, 8.91. Found: C, 61.20; H, 4.63; N, 8.97. $^1$H NMR (250 MHz, $CDCl_3$) $\delta$: 3.87 (3H, s, $CH_3$), 5,29 (2H, s, $CH_2$), 6.97 (2H, d, *J* 8.8, Ar), 7.46 (5H, m, Ar), 8.48 (2H, d, *J* 8.8, Ar). $^{13}$C NMR (75.5 MHz, $CDCl_3$) $\delta$: 53.6 ($CH_2$), 55.4 ($CH_3$), 113.4, 129.4, 129.8, 129.9, and 130.7 (9CH); 125.8, 133.2, 159.9, and 161.3 (four sp$^2$ tertiary C), 177.2 (C=S). MS (EI, 70 eV), *m*/*z* (%): 314 ($M^+$, 8), 133 (15). IR (KBr): $\nu$=3028, 3008, 2956 (C–H), 2832, 1612, 1520, 1456, 1420, 1340, 1328, 1300, 1256, 1208, 1168, 1028, 832, 764, 700 cm$^{-1}$.

*4.2.4. 2-Benzyl-4-(4-nitrophenyl)-1,2,5-thiadiazole-3(2H)-thione (**3d**).* Yield 43%. Yellow crystalline solid, mp 148 °C; $R_f$=0.40 (hexane/$CH_2Cl_2$=1:1). Anal. Calcd for $C_{15}H_{11}N_3O_2S_2$: C, 54.69; H, 3.37; N, 12.76. Found: C, 54.82; H, 3.69; N, 12.83. $^1$H NMR (250 MHz, $CDCl_3$) $\delta$: 5.30 (2H, s, $CH_2$), 7.51 (5H, m, Ar), 8.34 (2H, d, *J* 8.8, Ar), 8.73 (2H, d, *J* 8.8, Ar). $^{13}$C NMR (75.5 MHz, $CDCl_3$) $\delta$: 54.0 ($CH_2$), 123.3, 129.7, 130.0, 130.0, and 130.2 (9CH), 132.8, 138.4, 145.3, and 168.2 (four sp$^2$ tertiary C), 177.2 (C=S). MS (EI, 70 eV), *m*/*z* (%): 329 ($M^+$, 15), 297 (7), 149 (12). IR (KBr): $\nu$=2960, 2924 (C–H), 2851, 1732, 1596, 1512, 1482, 1456, 1444, 1340, 1316, 1284, 1204, 1068, 860, 844, 760, 716, 704 cm$^{-1}$.

*4.2.5. 2-Benzyl-4-methyl-1,2,5-thiadiazole-3(2H)-thione (**3e**).* Yield 62%. Yellow crystalline solid, mp 84–85 °C; $R_f$=0.62 (hexane/$CH_2Cl_2$=4:1). Anal. Calcd for $C_{10}H_{10}N_2S_2$: C, 54.02; H, 4.53; N, 12.60. Found: C, 54.08; H, 4.72; N, 12.53. $^1$H NMR (250 MHz, $CDCl_3$) $\delta$: 2.58 (3H, s, $CH_3$), 5.26 (2H, s, $CH_2$), 7.44 (5H, m, Ar). $^{13}$C NMR (75.5 MHz, $CDCl_3$) $\delta$: 19.2 ($CH_3$), 53.35 ($CH_2$), 129.2 (2CH), 129.49 (2CH), 129.52 (1CH), 133.2, and 163.2 (two sp$^2$ tertiary C), 179.1 (C=S). MS (EI, 70 eV), *m*/*z* (%): 222 ($M^+$, 32), 189 (22). IR (KBr): $\nu$=3032, 2924 (C–H), 2852, 1496, 1456, 1376, 1348, 1336, 1208, 1180, 1012, 816, 760, 700, 628 cm$^{-1}$.

*4.2.6. 2-Benzyl-4-(thien-2-yl)-1,2,5-thiadiazole-3(2H)-thione (**3f**).* Yield 65%. Yellow crystalline solid, mp 146–147 °C; $R_f$=0.53 (hexane/$CH_2Cl_2$=4:1). Anal. Calcd for $C_{13}H_{10}N_2S_3$: C, 53.76; H, 3.47; N, 9.65. Found: C, 53.56; H, 3.67; N, 9.45. $^1$H NMR (250 MHz, $CDCl_3$) $\delta$: 5.32 (2H, s, $CH_2$), 7.16 (1H, dd, *J* 3.7, 5.1, Ar), 7.46 (5H, m, Ar), 7.52 (1H, d, *J* 5.1, Ar), 8.57 (1H, d, *J* 2.9, Ar). $^{13}$C NMR (75.5 MHz, $CDCl_3$) $\delta$: 53.5 ($CH_2$), 127.2, 129.5, 129.8, 129.9, 130.1, and 130.6 (8C–H), 133.2. 135.3, and 155.4 (three sp$^2$ tertiary C), 175.9 (C=S). MS (EI, 70 eV), *m*/*z* (%): 290 ($M^+$, 70), 257 (36), 148 (22). IR (KBr): $\nu$=2920 (C-H), 1516, 1456, 1412, 1380, 1316, 1288, 1200, 816, 752, 724, 696 cm$^{-1}$.

*4.2.7. 2-Benzyl-4-(1-benzofuran-2-yl)-1,2,5-thiadiazole-3(2H)-thione (**3g**).* Yield 49%. Yellow crystalline solid, mp 188–191 °C; $R_f$=0.31 (hexane/$CH_2Cl_2$=1:1). Anal. Calcd for $C_{17}H_{12}N_2OS_2$: C, 62.94; H, 3.73; N, 8.63. Found: C, 62.64; H, 3.97; N, 8.54. $^1$H NMR (250 MHz, $CDCl_3$) $\delta$: 5.30 (2H, s, $CH_2$), 7.29 (1H, t, Ar), 7.39 (1H, m, Ar), 7.47 (5H, m, Ar), 7.57 (1H, d, *J* 8.1, Ar), 7.73 (1H, d, *J* 8.1, Ar), 8.80 (1H, s, Ar). $^{13}$C NMR (75.5 MHz, $CDCl_3$) $\delta$: 53.6 ($CH_2$), 111.4, 111.6, 123.1, 123.6, 126.9, 129.6, 129.9, and 130.1 (10CH), 127.8, 132.9, 148.5, 151.5, and 155.2 (five sp$^2$ tertiary C), 175.8 (C=S). MS (EI, 70 eV), *m*/*z* (%): 324 ($M^+$, 10), 260 (5), 143 (14). IR (KBr): $\nu$=2928 (C–H), 1576, 1456, 1376, 1304, 1188, 1156, 1140, 1060, 972, 836, 756, 700 cm$^{-1}$.

*Benzylammonium hydrogen sulfide*. Colorless crystalline solid. Anal. Calcd for $C_7H_{11}NS$: C, 59.53; H, 7.85; N, 9.92. Found: C, 59.68; H, 7.97; N, 9.70. $^1$H NMR (250 MHz, $D_2O$) $\delta$: 3.96 (2H, s, $CH_2$), 6.86 (4H, m, $NH_2$, $H_2S$), 7.60 (5H, m, Ar). MS (EI, 70 eV), *m*/*z* (%): 107 ($M^+$−34, 30), 91 (25).

*4.2.8. 2-Allyl-4-phenyl-1,2,5-thiadiazole-3(2H)-thione (**3h**).* Yield 41%. Yellow crystalline solid, mp 92–94 °C; $R_f$=0.40 (hexane/$CH_2Cl_2$=5:1). Anal. Calcd for $C_{11}H_{10}N_2S_2$: C, 56.38; H, 4.30; N, 11.95. Found: C, 56.58; H, 4.47; N, 11.70. $^1$H NMR (250 MHz, $CDCl_3$) $\delta$: 4.85 (2H, d, *J* 6.6, $CH_2$), 5.56 (2H, m, $CH_2$), 6.13 (1H, m, CH); 7.50 (3H, m, Ar), 8.41 (2H, m, Ar). $^{13}$C NMR (75.5 MHz, $CDCl_3$) $\delta$: 51.7 ($CH_2$), 123.9 ($CH_2$), 129.5 (CH), 128.1 (2CH, Ar), 129.0 (2CH, Ar), 130.5 (1CH, Ar), 133.0, and 160.7 (two sp$^2$ tertiary C), 177.2 (C=S). MS (EI, 70 eV), *m*/*z* (%): 234 ($M^+$, 47), 193 (8), 135 (33), 104 (53). IR (KBr): $\nu$=3072, 2924 (C–H), 2852, 1424, 1344, 1336, 1304, 1204, 1152, 1028, 952, 848, 780, 712, 692 cm$^{-1}$.

*4.2.9. 2-Isobutyl-4-phenyl-1,2,5-thiadiazole-3(2H)-thione (**3i**).* Yield 54%. Yellow crystalline solid, mp 106–109 °C; $R_f$=0.54 (hexane/$CH_2Cl_2$=5:1). Anal. Calcd for $C_{12}H_{14}N_2S_2$: C, 57.56; H, 5.64; N, 11.19. Found: C, 57.68; H, 5.72; N, 11.40. $^1$H NMR (250 MHz, $CDCl_3$) $\delta$: 1.07 (6H, d, *J* 6.6, $2CH_3$), 2.45 (1H, m, CH), 4.15 (2H, m, $CH_2$), 7.51 (3H, m, Ar), 8.40 (2H, m, Ar). $^{13}$C NMR (75.5 MHz, $CDCl_3$) $\delta$: 20.2 ($2CH_3$), 27.5 (CH), 56.2 ($CH_2$), 128.1 (2CH, Ar), 129.1 (2CH, Ar), 130.5 (1CH, Ar), 133.2, and 178.1 (two sp$^2$ tertiary C), 178.9 (C=S). MS (EI, 70 eV), *m*/*z* (%): 250 ($M^+$, 28), 193 (70), 135 (78), 103 (48). IR (KBr): $\nu$=2960, 2928 (C–H), 2856, 1728, 1504, 1468, 1444, 1368, 1336, 1296, 1264, 1200, 1148, 1124, 1080, 940, 832, 692 cm$^{-1}$.

*4.2.10. 2-Benzyl-4-phenyl-1,2,5-thiadiazol-3(2H)-one (**6a**).* Yield 94%. Colorless crystalline solid, mp 87–90 °C; $R_f$=0.40 (hexane/$CH_2Cl_2$=5:1). Anal. Calcd for $C_{15}H_{12}N_2OS$: C, 67.14; H, 4.51; N, 10.44. Found: C, 67.28; H, 4.39; N, 10.50. $^1$H NMR (250 MHz, $CDCl_3$) $\delta$: 5.05 (2H, s, $CH_2$), 7.40 (5H, s, Ar), 7.48 (3H, m, Ar), 8.48 (2H, m, Ar). $^{13}$C NMR (75.5 MHz, $CDCl_3$) $\delta$: 47.9 ($CH_2$), 126.9, 128.0, 128.6, 128.7, 129.22, and 130.5 (10CH, Ar), 128.8, 137.2, and 149.6 (three sp$^2$ tertiary C), 161.3 (C=O). MS (EI, 70 eV), *m*/*z* (%): 268 ($M^+$, 12), 135 (10). IR (KBr): $\nu$=3268, 3048, 2920 (C–H), 1648 (C=O), 1456, 1444, 1264, 1072, 824, 784, 756, 740, 700, 688, 620 cm$^{-1}$.

*4.2.11. 2-Benzyl-4-(4-fluorophenyl)-1,2,5-thiadiazol-3(2H)-one (**6b**).* Yield 100%. Colorless crystalline solid, mp 72–74 °C; $R_f$=0.42 (hexane/$CH_2Cl_2$=1:1). Anal. Calcd for $C_{15}H_{11}FN_2OS$: C, 62.92; H, 3.87; N, 9.78. Found: C, 63.08; H, 3.92; N, 9.55. $^1$H NMR (250 MHz, $CDCl_3$) $\delta$: 5.03 (2H, s, $CH_2$), 6.99 (2H, m, Ar), 7.39 (5H, m, Ar), 8.46 (2H, m, Ar). $^{13}$C NMR (75.5 MHz, $CDCl_3$) $\delta$: 47.8 ($CH_2$), 115.4, 115.72, 126.7, 128.7, 129.0, and 129.2 (9CH, Ar), 125.8, 134.7, 148.4, and 161.1 (four sp$^2$ tertiary C), 164.1 (C=O). MS (EI, 70 eV), *m*/*z* (%): 286 ($M^+$, 100), 153 (5), 121 (87). IR (KBr): $\nu$=3052, 2924 (C–H), 2852, 1648 (C=O), 1596, 1512, 1444, 1268, 1236, 1156, 1076, 840, 824, 752, 700, 620 cm$^{-1}$.

*4.2.12. 2-Benzyl-4-(4-methoxyphenyl)-1,2,5-thiadiazol-3(2H)-one (**6c**).* Yield 100%. Colorless crystalline solid, mp 68–72 °C; $R_f$=0.35 (hexane/$CH_2Cl_2$=1:1). Anal. Calcd for $C_{16}H_{14}N_2O_2S$: C, 64.41, H, 4.73, N, 9.39. Found: C, 64.65; H, 4.92; N, 9.55. $^1$H NMR (250 MHz, $CDCl_3$) $\delta$: 3.87 (3H, s, $CH_3$), 5,03 (2H, s, $CH_2$), 7.14 (2H, d, *J* 9.5, Ar), 7.39 (5H, m, Ar), 8.49 (2H, m, Ar). $^{13}$C NMR (75.5 MHz, $CDCl_3$) $\delta$: 47.9 ($CH_2$), 53.4 ($OCH_3$), 113.9, 128.6, 128.7, 128.9, and 129.2 (9CH, Ar), 125.2, 134.9, 149.2, and 161.3 (four sp$^2$ tertiary C), 161.4 (C=O). MS (EI, 70 eV), *m*/*z* (%): 298 ($M^+$, 43), 256 (12), 160 (5), 133 (45). IR (KBr): $\nu$=3028, 2938 (C–H), 2852, 1644 (C=O), 1600, 1520, 1456, 1308, 1252, 1172, 1076, 1024, 848, 756, 696, 620 cm$^{-1}$.

*4.2.13. 2-Benzyl-4-(4-nitrophenyl)-1,2,5-thiadiazol-3(2H)-one (**6d**).* Yield 94%. Colorless crystalline solid, mp 157–158 °C; $R_f$=0.33 (hexane/$CH_2Cl_2$=1:1). Anal. Calcd for $C_{15}H_{11}N_3O_3S$: C, 57.50; H, 3.54; N, 13.41. Found: C, 57.39; H, 3.69; N, 13.54. $^1$H NMR (250 MHz, $CDCl_3$) $\delta$: 5.06 (2H, s, $CH_2$); 7.42 (5H, m, Ar); 8.30 (2H, d, *J* 8.8, Ar), 8.80 (2H, d, *J* 8.8, Ar). $^{13}$C NMR (75.5 MHz, $CDCl_3$) $\delta$: 48.2 ($CH_2$), 123.8, 127.6, 128.8, 129.3, and 129.4 (9CH), 134.3, 137.1, 147.1, and 148.5 (four sp$^2$ tertiary C), 161.0 (C=O). MS (EI, 70 eV), *m*/*z* (%): 313 ($M^+$, 38), 180 (55), 149 (18). IR (KBr): $\nu$=3084, 2924 (C-H), 2852, 1656 (C=O), 1596, 1512, 1496, 1452, 1348, 1320, 1256, 1072, 820, 756, 700 cm$^{-1}$.

*4.2.14. 2-Benzyl-4-(2-thienyl)-1,2,5-thiadiazol-3(2H)-one (**6f**).* Yield 95%. Colorless crystalline solid, mp 101–102 °C; $R_f$=0.45 (hexane/$CH_2Cl_2$=5:1). Anal. Calcd for $C_{13}H_{10}N_2OS_2$: C, 56.91; H, 3.67; N, 10.21. Found: C, 57.08; H, 3.89; N, 10.40. $^1$H NMR (250 MHz, $CDCl_3$) $\delta$: 5,05 (2H, s, $CH_2$), 7.17 (1H, dd, *J* 2.9, 5.1, Ar), 7.40 (5H, m, Ar), 7.52 (1H, d, *J* 5.1, Ar), 8.25 (1H, d, *J* 2.9, Ar). $^{13}$C NMR (75.5 MHz, $CDCl_3$) $\delta$: 48.1 ($CH_2$), 127.9, 128.5, 128.8, 129.1, 129.3 and 129.4 (8CH), 134.6, 134.9, and 146.2 (three sp$^2$ tertiary C), 160.2 (C=O). MS (EI, 70 eV), *m*/*z* (%): 274 ($M^+$, 43), 135 (23), 109 (40). IR (KBr): $\nu$=3110, 3100, 3032, 2936, 1644, 1496, 1456, 1436, 1424, 1416, 1236, 1220, 1056, 1020, 844, 828, 756, 712, 700 cm$^{-1}$.

*4.2.15. 2-Benzyl-4-(1-benzofuran-2-yl)-1,2,5-thiadiazol-3(2H)-one (**6g**).* Yield 96%. Colorless crystalline solid, mp 156 °C; $R_f$=0.27 (hexane/$CH_2Cl_2$=4:1). Anal. Calcd for $C_{17}H_{12}N_2O_2S$: C, 66.22; H, 3.92; N, 9.08. Found: C, 66.40; H, 4.12; N, 9.40. $^1$H NMR (250 MHz, $CDCl_3$) $\delta$: 5.07 (2H, s, $CH_2$), 7.29 (1H, m, Ar), 7.41 (6H, m, Ar), 7.60 (1H, d, *J* 8.1, Ar), 7.72 (1H, d, *J* 7.3, Ar), 8.04 (1H, s, Ar). $^{13}$C NMR (75.5 MHz, $CDCl_3$) $\delta$: 48.0 ($CH_2$), 109.4, 111.7, 122.8, 123.7, 126.8, 128.8, 129.2, and 129.3 (10CH), 127.8, 134.4, 142.2, 148.3, and 155.4 (five sp$^2$ tertiary C), 160.0 (C=O). MS (EI, 70 eV), *m*/*z* (%): 308 ($M^+$, 38), 175 (7), 143 (35). IR (KBr): $\nu$=1640 (C=O), 1576, 1452, 1300, 1248, 1156, 1140, 1072, 836, 812, 772, 756, 770, 612 cm$^{-1}$.

*4.2.16. 2-Allyl-4-phenyl-1,2,5-thiadiazol-3(2H)-one (**6h**).* Yield 89%. Colorless oil; $R_f$=0.52 (hexane/$CH_2Cl_2$=5:1). Anal. Calcd for $C_{11}H_{10}N_2OS$: C, 60.53; H, 4.62; N, 12.83. Found: C, 60.68; H, 4.67; N, 12.70. $^1$H NMR (250 MHz, $CDCl_3$) $\delta$: 4.52 (2H, d, *J* 6.6, $CH_2$), 5.42 (2H, m, $CH_2$), 5.99 (1H, m, CH All), 7.49 (3H, m, Ar), 8.46 (2H, m, Ar). $^{13}$C NMR (75.5 MHz, $CDCl_3$) $\delta$: 44.6 ($CH_2$), 120.9 ($CH_2$), 126.8, 128.5, and 130.5 (5CH), 149.7 (CH, All), 131.1, and 132.0 (two sp$^2$ tertiary C), 161.0 (C=O). MS (EI, 70 eV), *m*/*z* (%): 218 ($M^+$, 30), 178 (3), 135 (25), 104 (25). IR (KBr): $\nu$=3068, 2924 (C–H), 2852, 1660 (C=O), 1444, 1424, 1296, 1240, 1180, 1084, 1068, 1028, 788, 744, 692 cm$^{-1}$.

*4.2.17. 2-Butyl-4-phenyl-1,2,5-thiadiazol-3(2H)-one (**6i**).* Yield 97%. Colorless oil; $R_f$=0.43 (hexane/$CH_2Cl_2$=5:1). Anal. Calcd for $C_{12}H_{14}N_2OS$: C, 61.51; H, 6.02; N, 11.96. Found: C, 61.68; H, 6.20; N, 12.14. $^1$H NMR (250 MHz, $CDCl_3$) $\delta$: 0.99 (3H, t, *J* 7.3, $CH_3$), 1.45 (2H, sext, *J* 7.3, $CH_2$), 1.78 (2H, q, *J* 7.3, $CH_2$), 3.93 (2H, t, *J* 7.3, $CH_2$), 7.47 (3H, m, *J* 6.6, Ar), 8.46 (2H, m, Ar). $^{13}$C NMR (75.5 MHz, $CDCl_3$) $\delta$: 13.6 ($CH_3$), 20.00 ($CH_2$), 31.5 ($CH_2$), 43.8 ($CH_2$), 126.9, 128.5, and 130.4 (5CH, Ar), 132.1, and 149.7 (two sp$^2$ tertiary C), 161.3 (C=O). MS (EI, 70 eV), *m*/*z* (%): 234 ($M^+$, 32), 178 (72), 149 (46), 135 (50), 104 (100). IR (KBr): $\nu$=2960, 2928 (C–H), 2852, 1660 (C=O), 1468, 1444, 1260, 1236, 1156, 1088, 1072, 1032, 824, 788, 744, 692, 652 cm$^{-1}$.

*4.2.18. 2-Isopropyl-4-phenyl-1,2,5-thiadiazol-3(2H)-one (**6j**).* Yield 93%. Colorless oil; $R_f$=0.15 (hexane/$CH_2Cl_2$=5:1). Anal. Calcd for $C_{11}H_{12}N_2OS$: C, 59.97; H, 5.49; N, 12.72. Found: C, 60.08; H, 5.42; N, 12.90. $^1$H NMR (250 MHz, $CDCl_3$) $\delta$: 1.50 (6H, d, *J* 6.6, $2CH_3$), 4.75 (1H, sept, *J* 6.6, CH); 7.47 (3H, m, Ar), 8.46 (2H, t, *J* 3.7, Ar). $^{13}$C NMR (75.5 MHz, $CDCl_3$) $\delta$: 22.4 ($2CH_3$), 48.2 (CH, *i*-Pr), 127.0, 128.5, and 130.4 (5CH), 132.2, and 150.4 (two sp$^2$ tertiary C), 160.9 (C=O). MS (EI, 70 eV), *m*/*z* (%): 220 ($M^+$, 32), 178 (73), 135 (22), 104 (100). IR (KBr): $\nu$=3068, 2968, 2924, 2852, 1732, 1664, 1464, 1444, 1392, 1300, 1240, 1180, 1152, 1132, 788, 744, 692, 768, 756, 688, 688, 632 cm$^{-1}$.

*4.2.19. N-Benzyl-2-oxopropanamide (**7e**).* Yield 87%. Colorless crystalline solid, mp 45–46 °C, lit.[24] colorless oil; $R_f$=0.56

($CH_2Cl_2$). Anal. Calcd for $C_{10}H_{11}NO_2$: C, 67.78; H, 6.26; N, 7.90. Found: C, 68.06; H, 6.48; N, 8.01. $^1$H NMR (250 MHz, $CDCl_3$) $\delta$: 2.47 (3H, s, $CH_3$), 4.45 (2H, s, $CH_2$); 7.27 (6H, m, Ar, NH). $^{13}$C NMR (75.5 MHz, $CDCl_3$) $\delta$: 24.4 ($CH_3$), 43.3 ($CH_2$), 127.7, 127.8, and 128.7 (5CH), 137.1 (one $sp^2$ tertiary C), 160.0 and 197.0 (2C=O). MS (EI, 70 eV), $m/z$ (%): 177 ($M^+$, 28), 106 (68), 65 (51), 43 (100). IR (KBr): $\nu$=3300 (NH), 3050 and 2930 (CH), 1724 and 1672 (C=O), 1524, 1436, 1360, 1212, 1172, 1080, 944, 748, 704, 612 cm$^{-1}$.

### 4.3. Reaction of 5*H*-1,2,3-dithiazole-5-thiones 1 and 5*H*-1,2,3-dithiazol-5-ones 2 with secondary amines

*General procedure*. Secondary amine (1 mmol) was added to a solution of the appropriate 1,2,3-dithiazole **1** or **2** (0.5 mmol) in DMSO (2 mL) at room temperature. The reaction mixture was stirred for 2–3 h at room temperature, filtered from elemental sulfur. $CH_2Cl_2$ (20 mL) was added to the filtrate, which was then washed with $H_2O$, dried $MgSO_4$ and the solvent was evaporated under reduced pressure. The residue was separated by column chromatography (Silica gel Merck 60, $CH_2Cl_2$, and then $CH_2Cl_2$/acetone mixtures).

*4.3.1. 2-Morpholin-4-yl-1-phenyl-2-thioxoethanimine (**8a**).* Yield 75%. Colorless crystalline solid, mp 112–115 °C; $R_f$=0.65 ($CH_2Cl_2$/acetone=10:1). Anal. Calcd for $C_{12}H_{14}N_2OS$: C, 61.51; H, 6.02; N, 11.96. Found: C, 61.73; H, 6.12; N, 12.10. $^1$H NMR (250 MHz, $CDCl_3$) $\delta$: 3.57 (4H, m, 2$OCH_2$), 3.85 (2H, t, *J* 5.1, $NCH_2$), 4.33 (2H, t, *J* 5.1, $NCH_2$), 7.45 (3H, m, Ar), 7.84 (2H, d, *J* 6.6, Ar), 9.56 (1H, s, NH). $^{13}$C NMR (75.5 MHz, $CDCl_3$) $\delta$: 47.6 and 51.9 (2$NCH_2$), 66.4, and 66.5 (2$OCH_2$), 127.4 (2CH, Ar), 129.1 (1CH, Ar), 131.9 (2CH, Ar), 134.0, and 174.6 (two $sp^2$ tertiary C), 196.6 (C=S). MS (EI, 70 eV), $m/z$ (%): 234 ($M^+$, 9), 176 (55), 149 (67), 131 (14), 104 (100). IR (KBr): $\nu$=3244 (N–H), 2976, 2916 (C–H), 2852, 1604, 1576, 1480, 1368, 1296, 1272, 1236, 1188, 1172, 1104, 1028, 932, 848, 684, 660 cm$^{-1}$.

*4.3.2. 2-Morpholin-4-yl-1-(4-fluorophenyl)-2-thioxoethanimine (**8b**).* Yield 69%. Colorless crystalline solid, mp 137–138 °C; $R_f$=0.52 ($CH_2Cl_2$/acetone=5:1). Anal. Calcd for $C_{12}H_{13}FN_2OS$: C, 57.12; H, 5.19; N, 11.10. Found: C, 57.13; H, 5.32; N, 11.23. $^1$H NMR (250 MHz, $CDCl_3$) $\delta$: 3.58 (4H, m, 2$OCH_2$), 3.86 (2H, m, $NCH_2$), 4.33 (2H, m, $NCH_2$), 7.08 (2H, d, *J* 8.8, Ar), 7.88 (2H, m, Ar), 9.40 (1H, s, NH). $^{13}$C NMR (75.5 MHz, $CDCl_3$) $\delta$: 47.6 and 52.0 (2$NCH_2$), 66.4, and 66.5 (2$OCH_2$), 116.1 (2CH, Ar, d, *J* 28.5), 129.9 (2CH, Ar), 130.4, 165.0 (d, *J* 251.0), and 173.3 (three $sp^2$ tertiary C), 196.3 (C=S). MS (EI, 70 eV), $m/z$ (%): 252 ($M^+$, 25), 194 (63), 167 (73), 122 (100). IR (KBr): $\nu$=3240 (N–H), 2976, 2920 (C–H), 2852, 1604, 1508, 1488, 1272, 1236, 1184, 1152, 1104, 1060, 1032, 936, 832, 840, 728, 624 cm$^{-1}$.

*4.3.3. 2-Morpholin-4-yl-1-(4-methoxyphenyl)-2-thioxoethanimine (**8c**).* Yield 77%. Colorless crystalline solid, mp 115–117 °C; $R_f$=0.61 ($CH_2Cl_2$/acetone=5:1). Anal. Calcd for $C_{13}H_{16}N_2O_2S$: C, 59.07; H, 6.10; N, 10.60. Found: C, 58.83; H, 6.03; N, 10.71. $^1$H NMR (250 MHz, $CDCl_3$) $\delta$: 3.47 (4H, m, 2$OCH_2$), 3.74 (3H, s, $OCH_3$), 4.23 (4H, m, $NCH_2$), 6.82 (2H, d, *J* 8.1, Ar), 7.69 (2H, d, *J* 8.1, Ar), 9.06 (1H, s, NH). $^{13}$C NMR (75.5 MHz, $CDCl_3$) $\delta$: 47.5, and 51.8 (2$NCH_2$), 55.4 ($OCH_3$), 66.3 and 66.4 (2$OCH_2$), 114.1 (2CH, Ar), 129.2 (2CH, Ar), 126.4, 162.5, and 173.7 (three $sp^2$ tertiary C), 196.8 (C=S). MS (EI, 70 eV), $m/z$ (%): 264 ($M^+$, 52), 206 (54), 179 (64), 134 (100), 130 (50). IR (KBr): $\nu$=3248 (N–H), 2920 (C–H), 2828, 1604, 1600, 1512, 1484, 1436, 1272, 1236, 1168, 1108, 1028, 932, 916, 884, 852, 732, 664 cm$^{-1}$.

*4.3.4. 2-Morpholin-4-yl-1-(4-nitrophenyl)-2-thioxoethanimine (**8d**).* Yield 72%. Colorless crystalline solid, mp 203–204 °C; $R_f$=0.29 ($CH_2Cl_2$/acetone=5:1). Anal. Calcd for $C_{12}H_{13}N_3O_3S$: C, 51.60; H, 4.69; N, 15.04. Found: C, 51.83; H, 4.72; N, 15.10. $^1$H NMR (250 MHz, $CDCl_3$) $\delta$: 3.58 (4H, m, 2$OCH_2$), 3.89 (2H, m, $NCH_2$), 4.34 (2H, m, $NCH_2$), 8.12 (2H, d, *J* 9.1, Ar), 8.30 (2H, d, *J* 8.2, Ar), 9.81 (1H, s, NH). $^{13}$C NMR (75.5 MHz, $CDCl_3$) $\delta$: 47.5, and 51.9 (2$NCH_2$), 66.3 (2$OCH_2$), 123.9, and 128.7 (4CH, Ar), 130.7, 139.7, and 172.3 (three $sp^2$ tertiary C), 195.1 (C=S). MS (EI, 70 eV), $m/z$ (%): 279 ($M^+$, 69), 221 (100), 194 (88), 149 (72), 130 (81). IR (KBr): $\nu$=3232, 2924 (C–H), 2852, 1588, 1516, 1488, 1444, 1348, 1340, 1272, 1240, 1104, 1032, 856 cm$^{-1}$.

*4.3.5. 2-Morpholin-4-yl-1-(2-thienyl)-2-thioxoethanimine (**8e**).* Yield 66%. Colorless crystalline solid, mp 138–141 °C; $R_f$=0.47 ($CH_2Cl_2$/acetone=10:1). Anal. Calcd for $C_{10}H_{12}N_2OS_2$: C, 49.97; H, 5.03; N, 11.66. Found: C, 49.99; H, 5.25; N, 11.43. $^1$H NMR (250 MHz, $CDCl_3$) $\delta$: 3.64 (4H, m, $OCH_2$), 3.87 (2H, t, *J* 5.1, $NCH_2$), 4.32 (2H, m, $NCH_2$), 7.09 (1H, d, *J* 5.1, Ar), 7.39 (1H, m, Ar), 7.52 (1H, d, *J* 5.1, Ar), 10.27 (1H, s, NH). $^{13}$C NMR (75.5 MHz, $CDCl_3$) $\delta$: 48.5, and 51.8 (2$NCH_2$), 66.3, and 66.4 (2$OCH_2$), 127.2, 130.7, and 131.7 (3CH), 133.9, and 164.0 (two $sp^2$ tertiary C), 195.6 (C=S). MS (EI, 70 eV), $m/z$ (%): 240 ($M^+$, 36), 182 (66), 155 (84), 110 (100). IR (KBr): $\nu$=3260 (N–H), 3080 and 2930 (C–H), 1650, 1580, 1500, 1420, 1270, 1160, 1100, 1050, 860, 830, 730 cm$^{-1}$.

*4.3.6. 1-(1-Benzofuran-2-yl)-2-morpholin-4-yl-2-thioxoethanimine (**8f**).* Yield 69%. Colorless crystalline solid, mp 140–141 °C; $R_f$=0.63 ($CH_2Cl_2$/acetone=5:1). Anal. Calcd for $C_{14}H_{14}N_2O_2S$: C, 61.29; H, 5.14; N, 10.21. Found: C, 61.02; H, 5.18; N, 10.06. $^1$H NMR (250 MHz, $CDCl_3$) $\delta$: 3.72 (4H, m, $OCH_2$), 3.91 (2H, t, *J* 5.1, $NCH_2$), 4.39 (2H, m, $NCH_2$), 7.18 (1H, s, CH, Ar), 7.31 (1H, m, CH, Ar), 7.45 (1H, m, Ar), 7.56 (1H, d, *J* 5.1, Ar), 7.64 (1H, d, *J* 5.1, Ar), 10.40 (1H, s, NH). $^{13}$C NMR (75.5 MHz, $CDCl_3$) $\delta$: 48.0, and 52.1 (2$NCH_2$), 66.4, and 66.7 (2$OCH_2$), 110.7, 111.9, 122.9, 124.0, and 127.5 (5CH), 127.7, 140.8, 147.6, and 155.8 (four $sp^2$ tertiary C), 193.5 (C=S). MS (EI, 70 eV), $m/z$ (%): 274 ($M^+$, 26), 216 (50), 189 (100). IR (KBr): $\nu$=3240 (N–H), 2920 and 2860 (C–H), 1650, 1590, 1490, 1440, 1240, 1160, 1100, 1030, 960, 850, 760 cm$^{-1}$.

*4.3.7. N,N-Diethyl-2-imino-2-phenylethanethioamide (**8g**).* Yield 78%. Colorless crystalline oil; $R_f$=0.66 ($CH_2Cl_2$/acetone=5:1). Anal. Calcd for $C_{12}H_{16}N_2S$: C, 65.41; H, 7.32; N, 12.71. Found: C, 65.53; H, 7.52; N, 12.73. $^1$H NMR (250 MHz, $CDCl_3$) $\delta$: 1.16 (3H, t, *J* 7.3, $CH_3$), 1.35 (3H, t, *J* 7.3, $CH_3$), 3.52 (2H, m, $CH_2$), 4.07 (2H, m, $CH_2$), 7.45 (3H, m, Ar), 7.92 (2H, m, Ar), 9.84 (1H, s, NH). $^{13}$C NMR (75.5 MHz, $CDCl_3$) $\delta$: 10.9, and 13.5 (2$CH_3$), 44.8, and 48.3 (2$NCH_2$), 114.3 (2CH, Ar), 128.1 (1CH, Ar), 129.0 (2CH, Ar), 131.7, and 139.6 (two $sp^2$ tertiary C), 196.9 (C=S). MS (EI, 70 eV), $m/z$ (%): 220 ($M^+$, 62), 205 (100), 149 (100), 116 (22), 104 (42). IR (KBr): $\nu$=3200 (N–H), 2980, 2932 (C–H), 2852, 1596, 1572, 1507, 1444, 1352, 1276, 1224, 1100, 1076, 760, 700, 664 cm$^{-1}$.

*4.3.8. 1-Phenyl-2-piperidin-1-yl-2-thioxoethanimine (**8h**).* Yield 84%. Colorless crystalline solid, mp 147–149 °C; $R_f$=0.81 ($CH_2Cl_2$/acetone=10:1). Anal. Calcd for $C_{13}H_{16}N_2S$: C, 67.20; H, 6.94; N, 12.06. Found: C, 67.33; H, 6.93; N, 11.91. $^1$H NMR (250 MHz, $CDCl_3$) $\delta$: 1.54 (2H, m, $CH_2$), 1.75 (4H, m, 2$CH_2$), 3.51 (2H, t, *J* 5.9, $NCH_2$), 4.26 (2H, t, *J* 5.9, $NCH_2$), 7.46 (3H, m, Ar), 7.86 (2H, d, *J* 6.6, Ar), 8.48 (1H, s, NH). $^{13}$C NMR (75.5 MHz, $CDCl_3$) $\delta$: 6.4, 25.3, and 26.4 (3$CH_2$), 48.5, and 52.9 (2-$NCH_2$), 127.4 (2CH), 128.7 (1CH), 131.6 (2CH), 134.1, and 174.9 (two $sp^2$ tertiary C), 195.1 (C=S). MS (EI, 70 eV), $m/z$ (%): 232 ($M^+$, 52), 176 (36), 149 (90), 128 (20), 104 (88). IR (KBr): $\nu$=3192 (N–H), 2988, 2944 (C–H), 2860, 1600, 1572, 1508, 1444, 1352, 1284, 1252, 1184, 1136, 1012, 892, 908, 844, 696, 660 cm$^{-1}$.

*4.3.9. 1-Phenyl-2-pyrrolidin-1-yl-2-thioxoethanimine (**8i**).* Yield 35%. Colorless crystalline oil. Yield 35%. Colorless oil; $R_f$=0.61 ($CH_2Cl_2$/acetone=5:1). Anal. Calcd for $C_{12}H_{14}N_2OS$: C, 66.02; H, 6.46; N, 12.83. Found: C, 66.13; H, 6.52; N, 12.73. $^1$H NMR (250 MHz, $CDCl_3$) $\delta$: 2.00 (4H, m, 2$CH_2$), 3.41 (2H, t, *J* 5.9, N–$CH_2$), 3.90 (2H, t, *J* 6.6, $CH_2$), 7.44 (3H, m, Ar), 7.84 (2H, d, *J* 6.6, Ar), 9.50 (1H, s, NH). $^{13}$C NMR (75.5 MHz, $CDCl_3$) $\delta$: 24.3, and 26.4 (2$CH_2$), 51.9, and 52.3 (2$NCH_2$), 114.3 (2CH), 128.1 (1CH), 129.0

(2CH), 131.6, and 135.2 (two $sp^2$ tertiary C), 194.1 (C=S). MS (EI, 70 eV), *m*/*z* (%): 218 ($M^+$, 32), 149 (63), 114(44), 104 (95). IR (KBr): $\nu$=3200 (N–H), 2972, 2924 (C–H), 2872, 1604, 1572, 1496, 1448, 1340, 1256, 1200, 1036, 944, 876, 692 $cm^{-1}$.

*4.3.10. 2-Imino-N,N-dimethyl-2-(2-thienyl)ethanethioamide (**8j**).* Yield 62%. Colorless crystalline solid, mp 68–70 °C; $R_f$=0.63 ($CH_2Cl_2$/acetone=5:1). Anal. Calcd for $C_8H_{10}N_2S_2$: C, 48.45; H, 5.08; N, 14.13. Found: C, 48.65; H, 5.38; N, 14.03. $^1$H NMR (250 MHz, $CDCl_3$) $\delta$: 3.25 (3H, s, $CH_3$), 3.54 (3H, s, $CH_3$), 7.08 (1H, dd, *J* 3.7, 5.1, Ar), 7.35 (1H, d, *J* 3.7, Ar), 7.51 (1H, d, *J* 5.1, Ar), 9.04 (1H, s, NH). $^{13}$C NMR (75.5 MHz, $CDCl_3$) $\delta$: 24.3, and 26.4 ($2NCH_3$), 127.2, 130.7, and 131.7 (3CH), 133.9, and 164.0 (two $sp^2$ tertiary C), 195.6 (C=S). MS (EI, 70 eV), *m*/*z* (%): 198 ($M^+$, 32), 120 (63), 83 (44). IR (KBr): $\nu$=3200 (N–H), 2972, 2924 (C–H), 2872, 1604, 1572, 1496, 1448, 1340, 1256, 1200, 1036, 944, 876, 692 $cm^{-1}$.

*4.3.11. 2-Morpholin-4-yl-2-oxo-1-phenylethanone (**9a**).* Yield 55%. Colorless crystalline solid, mp 51–53 °C; $R_f$=0.49 ($CH_2Cl_2$/acetone=10:1), lit.[25] mp 50–51 °C.

*4.3.12. 1-(4-Fluorophenyl)-2-morpholin-4-yl-2-oxoethanone (**9b**).* Yield 12%. Colorless crystalline solid, mp 76–78 °C; $R_f$=0.44 ($CH_2Cl_2$/acetone=10:1). Anal. Calcd for $C_{12}H_{12}FNO_3$: C, 60.76; H, 5.10; N, 5.90. Found: C, 60.83; H, 5.32; N, 6.03. $^1$H NMR (250 MHz, $CDCl_3$) $\delta$: 3.39 (2H, t, *J* 5.1, $NCH_2$), 3.66 (2H, t, *J* 5.1, $NCH_2$), 3.80 (4H, m, $2OCH_2$), 7.19 (2H, d, *J* 8.8, Ar), 7.98 (2H, m, Ar). $^{13}$C NMR (75.5 MHz, $CDCl_3$) $\delta$: 41.8, and 46.4 ($2NCH_2$), 66.7, and 66.8 ($2OCH_2$), 116.5 (2CH, d, *J* 23.0), 132.6 (2CH, d, *J* 9.8), 129.7, and 131.2 (two $sp^2$ tertiary C), 166.9, and 189.4 (2C=O). MS (EI, 70 eV), *m*/*z* (%): 237 ($M^+$, 9), 123 (100), 114 (17). IR (KBr): $\nu$=3068, 2924 (C–H), 2864, 1768 (C=O), 1672 (C=O), 1632, 1596, 1508, 1444, 1272, 1232, 1160, 1112, 984, 852, 764, 612 $cm^{-1}$.

*4.3.13. 1-(4-Methoxyphenyl)-2-morpholin-4-yl-2-oxoethanone (**9c**).* Yield 12%. Colorless crystalline solid, mp 108–110 °C; $R_f$=0.36 ($CH_2Cl_2$/acetone=3:1). Anal. Calcd for $C_{13}H_{15}NO_4$: C, 62.64; H, 6.07; N, 5.62. Found: C, 62.63; H, 6.17; N, 5.76. $^1$H NMR (250 MHz, $CDCl_3$) $\delta$: 3.35 (2H, m, $NCH_2$), 3.61 (2H, m, $NCH_2$), 3.74 (4H, m, $2OCH_2$), 3.85 (3H, s, $OCH_3$), 6.95 (2H, d, *J* 7.3, Ar), 7.88 (2H, d, *J* 7.3, Ar). $^{13}$C NMR (75.5 MHz, $CDCl_3$) $\delta$: 41.3, and 45.3 ($2NCH_2$), 55.7 ($OCH_3$), 66.7, and 66.8 ($2OCH_2$), 114.4 (2CH, Ar), 132.1 (2CH, Ar), 126.1, and 165.2 (two $sp^2$ tertiary C), 165.8, and 189.8 (2C=O). MS (EI, 70 eV), *m*/*z* (%): 249 ($M^+$, 7), 135 (100), 114 (6). IR (KBr): $\nu$=2980, 2940 (C–H), 2916 (C–H), 2884, 1664 (C=O), 1628, 1600, 1576, 1424, 1256, 1192, 1176, 1112, 1024, 984, 848, 764 $cm^{-1}$.

*4.3.14. 2-Morpholin-4-yl-1-(4-nitrophenyl)-2-oxoethanone (**9d**).* Yield 75%. Colorless crystalline solid, mp 141–143 °C; $R_f$=0.60 ($CH_2Cl_2$/acetone=3:1). Anal. Calcd for $C_{12}H_{12}N_2O_5$: C, 54.55; H, 4.58; N, 10.60. Found: C, 54.73; H, 4.72; N, 10.72. $^1$H NMR (250 MHz, $CDCl_3$) $\delta$: 3.41 (2H, t, *J* 5.1, $NCH_2$), 3.81 (4H, m, $2OCH_2$), 3.89 (2H, t, *J* 5.1, $NCH_2$), 8.16 (2H, d, *J* 8.8, Ar), 8.35 (2H, d, *J* 8.1, Ar). $^{13}$C NMR (75.5 MHz, $CDCl_3$) $\delta$: 42.0, and 46.4 ($2NCH_2$), 66.7, and 66.8 ($2OCH_2$), 124.2 (2CH, Ar), 130.9 (2CH, Ar), 137.6, and 151.2 (two $sp^2$ tertiary C), 164.1, and 188.7 (2C=O). MS (EI, 70 eV), *m*/*z* (%): 264 ($M^+$, 4), 234 (14), 150 (32), 114 (100). IR (KBr): $\nu$=3104, 3072, 2928 (C–H), 2868, 1684 (C=O), 1602, 1636, 1524, 1384, 1268, 1212, 1112, 984, 852, 728, 712 $cm^{-1}$.

*4.3.15. 2-Morpholin-4-yl-2-oxo-1-(2-thienyl)ethanone (**9e**).* Yield 61%. Colorless crystalline solid, mp 101–103 °C; $R_f$=0.39 ($CH_2Cl_2$/acetone=10:1). Anal. Calcd for $C_{10}H_{11}NO_3S$: C, 53.32; H, 4.92; N, 6.22. Found: C, 52.99; H, 4.89; N, 6.17. $^1$H NMR (250 MHz, $CDCl_3$) $\delta$: 3.49 (2H, t, *J* 5.1, $NCH_2$), 3.67 (2H, t, *J* 5.1, $NCH_2$), 3.76 (4H, m, $2OCH_2$), 7.18 (1H, d, *J* 5.1, Ar), 7.81 (1H, m, Ar), 7.84 (1H, d, *J* 5.1, Ar). $^{13}$C NMR (75.5 MHz, $CDCl_3$) $\delta$: 42.0, and 46.5 ($NCH_2$), 66.6, and 66.8 ($2OCH_2$), 128.7, 136.3 and 136.8 (3CH), 140.3 (one $sp^2$ tertiary C), 164.4, and 182.8 (2C=O). MS (EI, 70 eV), *m*/*z* (%): 225 ($M^+$, 6), 114 (46), 111 (100). IR (KBr): $\nu$=3070, 2920 and 2860 (CH), 1640 (C=O), 1520, 1410, 1360, 1300, 1270, 1230, 1120, 1040, 960, 830, 750 $cm^{-1}$.

*4.3.16. 1-(1-Benzofuran-2-yl)-2-morpholin-4-yl-2-oxoethanone (**9f**).* Yield 55%. Colorless oil; $R_f$=0.69 ($CH_2Cl_2$/acetone=5:1). Anal. Calcd for $C_{14}H_{13}NO_4$: C, 64.86; H, 5.05; N, 5.40. Found: C, 64.46; H, 5.35; N, 5.27. $^1$H NMR (250 MHz, $CDCl_3$) $\delta$: 3.62 (2H, m, $2NCH_2$), 3.64 (2H, m, $NCH_2$), 3.78 (4H, m, $2OCH_2$), 7.12 (1H, s, Ar), 7.26 (1H, m, Ar), 7.40 (1H, m, Ar), 7.51 (1H, d, *J* 8.1, Ar), 7.26 (1H, d, *J* 7.3, Ar). $^{13}$C NMR (75.5 MHz, $CDCl_3$) $\delta$: 42.1, and 47.1 ($2NCH_2$), 66.7, and 66.9 ($2OCH_2$), 111.7, 112.1, 123.1, 124.0, and 127.6 (5CH), 128.2, 156.5, and 161.3 (three $sp^2$ tertiary C), 164.6, and 179.8 (2C=O). MS (EI, 70 eV), *m*/*z* (%): 259 ($M^+$, 7), 173 (10), 144 (100).

*4.3.17. N,N-Dimethyl-2-oxo-2-(2-thienyl)acetamide (**9g**).* Yield 74%. Colorless oil; $R_f$=0.43 ($CH_2Cl_2$/acetone=5:1). IR and mass spectra are similar to the literature data.[26]

### 4.4. Crystallographic data

Crystals of **3f** ($C_{13}H_{10}N_2S_3$, *M*=290.41) are monoclinic, space group $P2_1/c$, at 100 K: *a*=12.6684(3), *b*=13.9186(7), *c*=7.4243(5) Å, $\beta$=104.972(5)°, *V*=1264.66(11) $Å^3$, *Z*=4 (*Z*′=1), $d_{calcd}$=1.525 g $cm^{-3}$, $\mu$(Mo K$\alpha$)=5.66 $cm^{-1}$, *F*(000)=600. Intensities of 50,901 reflections were measured with a Bruker SMART APEX2 CCD diffractometer [$\lambda$(Mo K$\alpha$)=0.71072 Å, $\omega$-scans, $2\theta$<90°] and 10,363 independent reflections [$R_{int}$=0.0458] were used in further refinement. The structure was solved by direct method and refined by the full-matrix least-squares technique against $F^2$ in the anisotropic–isotropic approximation. The positions of hydrogen atoms were calculated, and they were refined in isotropic approximation in riding model. The molecule is disordered by two positions with the 80:20 ratio. For **3f** the refinement converged to *wR*2=0.0927 and GOF=1.003 for all independent reflections (*R*1=0.0355 was calculated against *F* for 7426 observed reflections with $I>2\sigma(I)$). All calculations were performed using SHELXTL PLUS 5.0.

CCDC 723464 contains the supplementary crystallographic data for compound **3f**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.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## References and notes


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