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Synthesis of Dihydrothiophenes or Spirocyclic Compounds by Domino Reactions of 1,3-Thiazolidinedione

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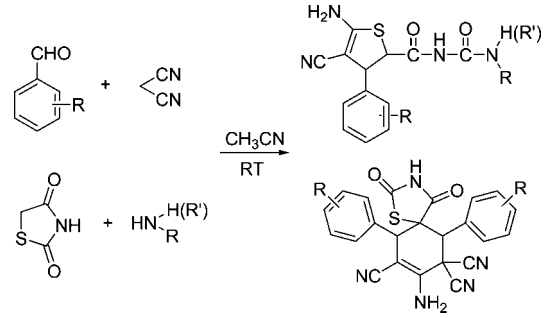

The domino reactions of 1,3-thiazolidinedione, malononitrile, and aromatic aldehydes in the presence of different organic amines were studied. Secondary amines such as pyrrolidine, piperidine, morpholine, and dimethylamine and primary amines such as benzylamine yield dihydrothiophene derivatives through a domino ring-opening/recyclization reaction of 1,3-thiazolidinedione. Bulky diethylamine, diisopropylamine, and 1,4-diazabicyclo[2.2.2]octane give spirocyclohexano-1,3-thiazole through a double Michael addition/spirocyclization reaction.

Introduction

Domino reactions have attracted particular attention over the past few decades because of their high efficiency in the construction of complex molecular frameworks.[1] Compared to stepwise reactions, this type of reaction minimizes waste since the amount of solvents, reagents, adsorbents, and energy is dramatically decreased.[2] Domino reactions are often accompanied by significant increases in molecular complexity and impressive selectivity.[3] Many of the reaction products have drug-like structures and might therefore exhibit interesting biological activities. They are also very useful in the drug discovery process and serve as powerful tools in the total synthesis of complex natural products.[4,5] In this regard, the development of new domino reaction methodologies is very important in the fields of organic and medicinal chemistry. We now report a novel domino reaction of 1,3-thiazolidinedione, malononitrile, aromatic aldehydes, and amines. This reaction is very unique because the ring-opening/recyclization or spirocyclization process occurs unexpectedly at the ring of 1,3-thiazolidinedione with different kinds of amines, and novel dihydrothiophene or spirocyclohexano[1,3]thiazole derivatives, which are normally difficult to prepare, are obtained in a very convenient manner.

Results and Discussion

It has been reported that when a mixture of arylidenemalononitrile, 1,3-thiazolidinedione, and piperidine was refluxed in ethanol, a cycloadduct pyrano[2,3-*d*][1,3]thiazole was produced in high yields.[6] Since arylidenemalononitrile can be conveniently prepared in situ from the Knovenogel condensation of aromatic aldehyde with malononitrile, we thought to develop a one-pot three-component reaction. A mixture of benzaldehyde,

(1) (a) Dömling, A. *Chem. Rev.* **2006**, *106*, 17–89. (b) Ramón, D. J.; Yus, M. *Angew. Chem., Int. Ed.* **2005**, *44*, 1602–1634. (c) Dömling, A.; Ugi, I. *Angew. Chem., Int. Ed.* **2000**, *39*, 3168–3210.

(2) (a) Zhu, J. P.; Bienaymé, H. *Multicomponent Reactions*; Wiley-VCH, 2004. (b) Tietze, L. F.; Brasche, G.; Gericke, K. *Domino Reactions in Organic Synthesis*; Wiley-VCH: Weinheim, 2006. (c) Tietze, L. F. *Chem. Rev.* **1996**, *96*, 115–136.

(3) (a) Fujioka, H.; Murai, K.; Kubo, O.; Ohba, Y.; Kita, Y. *Org. Lett.* **2007**, *9*, 1687–1690. (b) Yan, C. G.; Song, X. K.; Wang, Q. F.; Siemeling, U.; Bruhn, C. *Chem. Commun.* **2008**, 1440–1442.

(4) (a) Xue, D.; Chen, Y. C.; Wang, Q. W.; Cun, L. F.; Zhu, J.; Deng, J. G. *Org. Lett.* **2005**, *7*, 5293–5296. (b) Xue, D.; Li, J.; Zhang, Z. T.; Deng, J. G. *J. Org. Chem.* **2007**, *72*, 5443–5445.

(5) (a) Marchalin, S.; Baumlova, B.; Baran, P.; Oulyadi, H.; Daich, A. *J. Org. Chem.* **2006**, *71*, 9114–9127. (b) Inokuma, T.; Hoashi, Y.; Takemoto, Y. *J. Am. Chem. Soc.* **2006**, *128*, 9413–9419.

(6) (a) Abdelrazek, F. M.; Kandeel, Z. E.; Himly, K. M. H.; Elnagdi, M. H. *Synthesis* **1985**, 422–434. (b) Rao, V. S.; Grupta, S. V. S.; Giridhar, P.; Ganesh, N.; Jai, Reddy, B. S. *Indian J. Heterocycl. Chem.* **2000**, 247–250.

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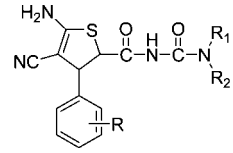
SCHEME 1. Synthetic Dihydrothiophenes 2a−2g, 3a−3j, 4a−4g, and 5a−5h



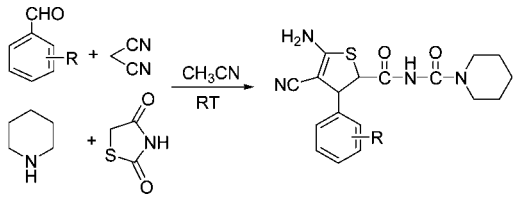
2a-2g: R_1, R_2 = CH_3, R = H, 4-CH_3, 4-OCH_3, 4-F, 4-Cl, 4-Br, 3-NO_2

3a-3j: R_1, R_2 = $(CH_2)_4$, R = H; 4-CH_3; 4-$CH(CH_3)_2$; 4-OCH_3; 4-OH; 4-OH-3-OCH_3; 4-F; 4-Cl; 4-Br; 3-NO_2

4a-4g: R_1, R_2 = $(CH_2CH_2)_2O$, R = H; 4-CH_3; 4-OCH_3; 4-F; 4-Cl; 4-Br; 3-NO_2

5a-5h: R_1 = H, R_2 = CH_2Ph; R = H; 4-CH_3; 4-$CH(CH_3)_2$; 4-OCH_3; 4-F; 4-Cl; 4-Br; 3-NO_2

TABLE 1. Results of One-Pot Four-Component Reactions



entry	compd	Ar	yield (%)
1	**1a**	Ph	41
2	**1b**	*p*-$CH_3C_6H_4$	31
3	**1c**	*p*-*i*-PrC_6H_4	45
4	**1d**	*p*-HOC_6H_4	32
5	**1e**	*p*-$CH_3OC_6H_4$	48
6	**1f**	4-HO-3-$CH_3OC_6H_4$	56
7	**1g**	*p*-FC_6H_4	43
8	**1h**	*p*-ClC_6H_4	35
9	**1i**	*p*-BrC_6H_4	49
10	**1j**	*p*-$NO_2C_6H_4$	27
11	**1k**	*m*-$NO_2C_6H_4$	46

malononitrile, 1,3-thiazolidinedione, and base catalyst piperidine in acetonitrile was stirred at room temperature for 2 days. In that time, yellow precipitates were observed forming at first, then disappearing and forming again. After filtration and analysis, it was surprising to find that the product is not the expected pyrano[2,3-*d*][1,3]thiazole.[6] All of the analytical data showed that a piperidine unit was introduced in the final product, and a novel polysubstituted 4,5-dihydrothiophene derivative **1a** was produced in 41% yield (Scheme 1). This surprising result is of value to us not only because we are interested in the design of the new domino reaction but also because we were unable to find examples of other methods allowing for such convenient synthesis in related literature. In this reaction piperidine behaves both as a base catalyst and as a nucleophile. To optimize the reaction condition, the influences of solvent and amount of piperidine were investigated by using the reaction of benzaldehyde as an example. An excess of piperidine (1.2, 1.5, or 2.0 times) did not increase the yield of the product. The reaction proceeds smoothly, and moderate yield of dihydrothiophene **1a** are produced in diethyl ether (18%), dioxane (34%), dimethylene dichloride (35%), methanol (33%), ethanol (38%), DMF (40%), and pyridine (24%).

Encouraged by the above interesting results, we utilized various aromatic aldehydes with different substituents under the same reaction conditions. The results are shown in Table 1. From these results, we could see that all of the reactions proceeded smoothly to afford the corresponding dihydrothiophenes in moderate yields (27−56%). Aromatic aldehydes carrying either electron-donating or electron-withdrawing substituents showed similar reactivity and reacted efficiently to yield the desired product. The structures of dihydrothiophenes were fully characterized by elemental analysis, ^{1}H and ^{13}C NMR, MS, and IR spectra and were further confirmed by single-crystal X-ray diffraction studies performed for one representative compound, **1e**. The 4,5-dihydrothiophene motif has been found in various natural products, biologically active compounds, and synthetic intermediates,[7,8] whose preparation often required lengthy steps and suffered from drawbacks, as well as lower yields.[9,10] The short reaction time and ease of handling should render this new domino reaction applicable to the synthesis of dihydrothiophene derivatives. As one of the typical heterocyclic compounds in the active methylene group, 1,3-thiazolidinedione and its derivatives perform interesting biological activities and take part in many condensation reactions[11−13] To the best of our knowledge, the ring cleavage of thiazolidinedione[14] and related heterocyclic compounds, such as 2-amino-1,3-thiazoline-5-ones and 2-thiohydantoins,[15,16] in the reactions was only apparent in a few cases.

In this reaction piperidine behaved both as a base catalyst and a nucleophile. In order to examine the substrate scope and

(7) (a) Martyres, D. H.; Baldwin, J. E.; Adlington, R. M.; Lee, V.; Probert, M. R.; Watkin, D. J. *Tetrahedron* **2001**, *57*, 4999–5007. (b) Dong, S.; Paquette, L. A. *J. Org. Chem.* **2005**, *70*, 1580–1596. (c) Zhu, W.; Chong, Y.; Choo, H.; Mathews, J.; Schinazi, R. F.; Chu, C. K. *J. Med. Chem.* **2004**, *47*, 1631–1640.

(8) (a) Tsuji, K.; Nakamura, K.; Ogino, T.; Konishi, N.; Tojo, T.; Ochi, T.; Seki, N.; Matsuo, M. *Chem. Pharm. Bull.* **1998**, *46*, 279. (b) Becker, F. F.; Mukhopadhyay, C.; Hackfeld, L.; Banik, I.; Banik, B. K. *Bioorg. Med. Chem.* **2000**, *8*, 2693–2698.

(9) (a) Sasaki, S.; Adachi, K.; Yoshifuji, M. *Org. Lett.* **2007**, *9*, 1729–1732. (b) Wilkinson, J. A.; Ardes-Guisot, N.; Ducki, S.; Leonard, J. *Tetrahedron* **2007**, *63*, 1065–1073.

(10) (a) Avalos, M.; Babiano, R.; Cintas, P.; Clemente, F. R.; Gordillo, R.; Jime'nez, J.; Palacios, J. C.; Raithby, P. R. *J. Org. Chem.* **2000**, *65*, 5089–5097. (b) Avalos, M.; Babiano, R.; Cabanillas, A.; Cintas, P.; Higes, F. J.; Jime'nez, J. L.; Palacios, J. C. *J. Org. Chem.* **1996**, *61*, 3738–3748.

(11) (a) Matiychuk, V. S.; Lesyk, R. B.; Obushak, M. O.; Gzella, A.; Atamanyuk, D. V.; Ostapiuk, Y. V.; Kryshchyshyn, A. P. *Tetrahedron Lett.* **2008**, *49*, 4648–4651. (b) Tietze, L. F.; Pfeiffer, T.; Schuffenhauer, A. *Eur. J. Org. Chem.* **1998**, *12*, 2733–2741.

(12) Sonawane, N. D.; Verkman, A. S. *Bioorg. Med. Chem.* **2008**, *16*, 8187–8195. (b) Verma, A.; Saraf, S. K. *Eur. J. Med. Chem.* **2008**, *43*, 897–905.

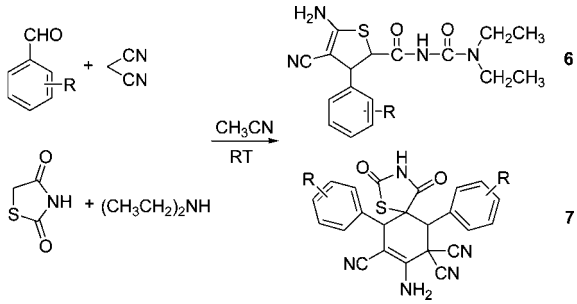
(13) Fábián, B.; Kudar, V.; Csámpai, A.; Nagy, T. Z.; Sohár, P. *J. Organomet. Chem.* **2007**, *692*, 5621–5632. (b) Maccari, M.; Ottanà, R.; Curinga, C.; Vigorita, M. G.; Rakowitz, D.; Steindl, T.; Langer, T. *Bioorg. Med. Chem.* **2005**, *13*, 2809–2823.

(14) (a) Arcadi, A.; Attanasi, O. A.; Giogi, G.; Filipone, P.; Rossi, E.; Santeusanio, S. *Tetrahedron Lett.* **2003**, *44*, 8391–8394. (b) kaupp, G.; Schmeyers, J. *Angew. Chem., Int. Eng. Engl.* **1993**, *32*, 1587–1589.

(15) Cook, A. H.; Harris, G.; Pollock, J. R. A.; Swan, J. M. *J. Chem. Soc.* **1950**, 1947–1954. (b) Schaumann, E.; Kausch, E.; Walter, W. *Chem. Ber.* **1977**, *110*, 820–832.

(16) (a) Ramachary, D. B.; Anebouselvy, K.; Chowdari, N. S.; Barbas, C. F., III. *J. Org. Chem.* **2004**, *69*, 5838–5849. (b) Ramachary, D. B.; Chowdari, N. S.; Barbas, C. F., III. *Angew. Chem., Int. Ed.* **2003**, *42*, 4233–4237. (c) Ramachary, D. B.; Barbas, C. F., III. *Chem.−Eur. J.* **2004**, *10*, 5323–5331.

TABLE 2. Results of the Four-Component Reactions with Et_2NH

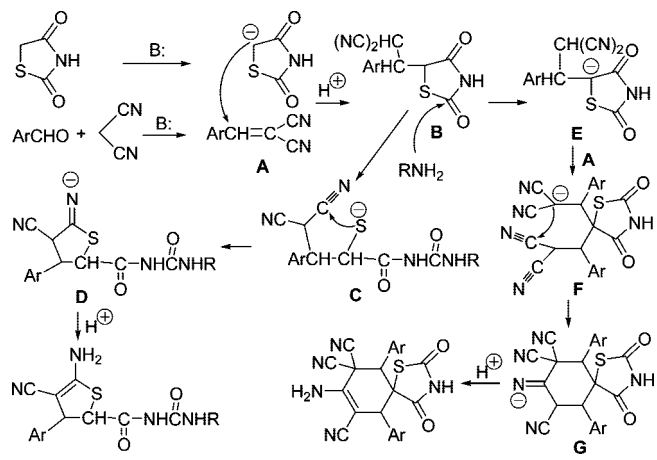


entry	Ar	compd	yield (%)	compd	yield (%)
1	Ph	**6a**	34	**7a**	
2	*p*-$CH_3C_6H_4$	**6b**	11	**7b**	30
3	*p*-*i*-PrC_6H_4	**6c**	10	**7c**	25
4	*p*-HOC_6H_4	**6d**	35	**7d**	
5	*p*-$CH_3OC_6H_4$	**6e**	49	**7e**	
6	4-HO-3-$CH_3OC_6H_4$	**6f**	41	**7f**	
7	*p*-FC_6H_4	**6g**	27	**7g**	
8	*m*-$NO_2C_6H_4$	**6h**	45	**7h**	
9	*p*-ClC_6H_4	**6i**		**7i**	14
10	*p*-BrC_6H_4	**6j**		**7j**	31

limitation of this novel domino reaction, a number of amines were tested under the above-mentioned reaction condition. Secondary amines such as dimethylamine, pyrrolidine, and morpholine and primary amines such as benzylamine reacted similarly, and new substituted dihydrothiophenes **2a**−**2g**, **3a**−**3j**, **4a**−**4g**, and **5a**−**5h** were obtained in moderate yields (Scheme 1). The structures of all of the dihydrothiophenes were fully characterized by elemental analysis, ^1H and ^{13}C NMR, MS, and IR spectra and further confirmed by single-crystal X-ray diffraction studies performed for **2a**, **2b**, **3b**, **3g**, **4d**, and **5f**. These results demonstrated that this reaction has great generality, and a library of dihydrothiophene ureidoformamides could be efficiently synthesized. The X-ray determinations of eight compounds all suggest that the two substituents at the 4,5-position of dihydrothiophene are in antiposition. With the ^1H NMR data we could concluded that dihydrothiophenes existed in *trans*-isomers, which might display that the stereochemical outcome of this reaction is thermodynamic control.

The reaction of diethylamine is a little more complicated. In addition to yielding dihydrothiophenes **6a**−**6h** (Table 2), in some cases a new type of spirocyclohexano-1,3-thiazoles **7** were also separated in low yields (Table 2). The reactions of *p*-chloro- and *p*-bromobenzaldehyde gave only spirocyclohexano-1,3-thiazoles **7i** and **7j**. The crystal structures of three spirocyclohexano-1,3-thiazoles, **7b**, **7c**, and **7i**, were determined. The formation of siprocyclic compounds **7** is also very interesting but not completely unreasonable. It can be observed that the spirocyclic compound comes from the double Michael addition reaction of thiazolidinedione with arylidenemalononitrile and the subsequent cyclization reaction, in which diethylamine acted as a base catalyst. This is a new example of the recently extensively studied domino Knoevenagel−Micheal reactions of 1,3-dicarbonyl compounds.[2a,16] On the basis of the above results, we thought that the steric property of amines played an important role in the reaction and determined the formation of the dihydrothiophene or spiroheterocyclic compound. The relatively bulky diethyl group decreases the nucleophilic property and hinders the formation of dihyrothiophene. Its basicity is not greatly decreased and it still acts as a base to catalyze the

SCHEME 2. Formation Mechanism for Dihydrothiophene and Spirocyclohexano-1,3-thiazole

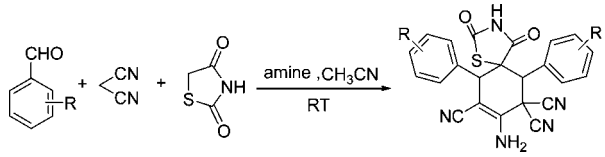


condensation reaction and subsequent cyclization to allow formation of the spirocyclohexano-1,3-thiazoles.

To explain the mechanism of this one-pot, multicomponent domino reaction and the formation of two kinds of products, we tentatively propose a plausible reaction mechanism, which is illustrated in Scheme 2. The first step is the formation of arylidenemalononitrile (**A**) derived from the Knoevenagel condensation of aromatic aldehyde with malononitrile catalyzed by amine. The second step is a Michael addition of the carbanion of 1,3-thiazolidinedione to arylidenemalononitrile (**A**) to yield adduct **B**. This intermediate (**B**) reacts further by two different paths that yield two different products. On the first reaction path, amine attacks the carbonyl group of thiazolidinedione to open its ring and cause the formation of a sulfide anion (**C**), which in turn intramolecularly attacks the one cyano group to form a sulfur-containing five-membered ring intermediate (**D**). Finally the 4,5-dihydrothiophene was produced through imine-enamine tautomerization. On the second path, amine can also attack a proton at the C-3 position of 1,3-thiazolidinedione to produce a new carbanion (**E**). This carbanion adds to the second arylidenemalononitrile (**A**) to form a double Michael adduct intermediate (**F**). Then the concomitant intramolecular addition of the cyano-stabilized carbanion to one of the cyano groups produces a six-membered carbon ring system (**G**). The spirocyclic compound was also produced through the imine-enamine tautomerization process. The relatively small amines have greater nucleophilic ability and favor the first reaction path. The bulky amines behave only as base catalysts and cause the formation of spirocyclic compounds.

To probe the credibility of our proposed mechanistic scheme and shed more light on the formation of two kinds of products, further experiments were carried out. First, in addition to the four-component procedure described above, we tested combinations containing plausible reaction intermediates. The reaction of previously prepared *p*-methoxybenzylidenemalononitrile with thiazolidinedione and piperidine in acetonitrile gives the desired dihydrothiophene **1e** in 36% yield. This result clearly shows that the intermediate arylidenemalononitrile (**A**), which is formed in situ, is the key intermediate of the reaction. The reactivity of some bulky amines, such as diisopropylamine and 1,4-diazabicyclic[2,2,2]octane (DABCO), in the reactions was also investigated. The results are listed in Table 3. We were very satisfied to find that only spirocyclic compounds were formed in moderate yields in these reactions, which strongly supported

TABLE 3. Amine-Catalyzed Formation of Spirocyclohexano-1,3-thiazole



entry	amine	Ar	compd	yield (%)
1	$(i\text{-Pr})_2$NH	Ph	**7a**	35
2	DABCO	Ph	**7a**	30
3	DABCO	p-$CH_3C_6H_4$	**7b**	29
4	$(i\text{-Pr})_2$NH	p-i-PrC_6H_4	**7c**	26
5	DABCO	p-i-PrC_6H_4	**7c**	30
6	$(i\text{-Pr})_2$NH	p-$CH_3OC_6H_4$	**7e**	39
7	DABCO	p-$CH_3OC_6H_4$	**7e**	42
8	DABCO	p-FC_6H_4	**7g**	28
9	$(i\text{-Pr})_2$NH	p-ClC_6H_4	**7i**	25
10	DABCO	p-ClC_6H_4	**7i**	48
11	$(i\text{-Pr})_2$NH	p-BrC_6H_4	**7j**	31
12	DABCO	p-BrC_6H_4	**7j**	55

the mechanism proposed in Scheme 2. DABCO usually gave better product yields than diisopropylamine. It should be pointed our that the proton signs of one molecular amine were observed in the ^{1}H and ^{13}C NMR spectra of all spirocyclic products, which means that one molecular amine coexisted with the product and could not be removed by crystallization. The X-ray determination of three spirocyclic compounds suggested the two aryl groups at the 6,10-positions are in antiposition, and the ^{1}H NMR data of compounds **7a**−**7j** all showed only one stereoisomer, which suggested that compounds **7a**−**7j** existed as anti diastereoisomers.

Conclusion

We have developed an interesting domino reaction of 1,3-thiazolidinedione, aromatic aldehydes, malononitrile, and amines in which the domino ring-opening and recyclization process was investigated. Furthermore, we established the scope and limitation of this reaction, which enabled further modification that led to molecular diversity. This reaction provides a convenient synthetic procedure for the preparation of dihydrothiophene and spirocyclohexano-1,3-thiazole derivatives, though the yield of the product is relatively lower. The potential uses of the reaction in synthetic and medicinal chemistry are quite significant.

Experimental Section

Typical Preparation Procedure of Dihydrothiophenes by One-Pot Four-Component Reaction of 1,3-Thiazolidinedione, Benzaldehyde, Malononitrile, and Piperidine. A mixture of benzaldehyde (4.0 mmol, 0.424 g), malononitrile (4.0 mmol, 0.264 g) and piperidine (4.0 mmol, 0.350 g) in acetonitrile (5.0 mL)was stirred at room temperature for 2 min. Then 1,3-thiazolidinedione (4.0mmol) was added, and the reaction was stirred at room temperature for additional 48 h. The resulting precipitate was collected by filtration and washed with acetonitrile. The crude product was recrystallized with a mixture of acetonitrile and *N*,*N*-dimthylforamide to give the pure product **1a**: white solid, 41%, mp 220−222 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 9.93 (s, 1H, NH), 7.38−7.36 (m, 2H, ArH), 7.30−7.28 (m, 3H, ArH), 7.07 (s, 2H, NH_2), 4.60 (d, J = 3 Hz, 1H, CH), 4.20 (s, 1H, CH), 3.33−3.29 (m, 4H, NCH_2), 1.57−1.51 (m, 2H, CH_2), 1.45−1.44 (m, 4H, CH_2). ^{13}C NMR (150 MHz, DMSO-d_6) δ: 161.8, 152.0, 142.2, 128.7, 127.4, 127.0, 118.4, 70.6, 55.6, 51.0, 25.4, 23.7. IR(KBr) v: 3667, 3399, 3306, 3194, 2942, 2855, 2195, 1686, 1654, 1587, 1491, 1449, 1246, 1137, 1025, 998, 751 cm^{-1}. MS (m/z): 355.53 ([M − 1]$^+$, 100%). Anal. Calcd for $C_{18}H_{20}N_4O_2S$: C 60.65, H 5.66, N 15.72. Found: C 60.83, H 5.38, N 15.54. The same reaction procedure was carried out by using other aromatic aldehydes and other amines to substitute piperidine to give products **1b**−**1k**, **2a**−**2g**, **3a**−**3j**, **4a**−**4g**, **5a**−**5h**.

Typical Preparation Procedure of Dihydrothiophene and Spirocyclohexano-1,3-thiazole by One-Pot Four-Component Reaction of 1,3-Thiazolidinedione, *p*-Methylbenzaldehyde, Malononitrile, and Diethylamine. A mixture of *p*-methylbenzaldehyde (8.0 mmol, 0.960 g), malononitrile (8.0 mmol, 0.528 g), and diethylamine (4.0 mmol, 0.292 g) in acetonitrile (5.0 mL) was stirred at room temperature for 2 min. Then 1,3-thiazolidinedione (4.0mmol) was added, and the reaction was stirred at room temperature for an additional 48 h. The resulting precipitate was collected by filtration and washed with acetonitrile. The crude product was refluxed in 50 mL of acetontrile for 2 h. After filtration the clean solution was cooled to give dihydrothiophene **6b**: light yellow solid, 11%, mp 176−178 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ: 9.77 (s, 1H, NH), 7.17 (s, 4H, ArH), 7.05 (s, 2H, NH_2), 4.58 (d, J = 3.0 Hz, 1H, CH), 4.45 (s, 1H, CH), 3.27−3.23 (m, 4H, CH_2), 2.29 (s, 3H, CH_3), 1.02 (t, J = 7.2 Hz, 6H, CH_3). ^{13}C NMR (150 MHz, DMSO-d_6) δ: 162.1, 152.6, 139.5, 137.1, 129.7, 127.3, 118.8, 71.2, 56.4, 51.2, 41.6, 21.0, 13.8. IR(KBr) v: 3408, 3325, 3228, 2977, 2932, 2180, 1672, 1579, 1481, 1353, 1259, 1201, 1152, 1093, 896, 815. MS (m/z): 358.62 ([M − 1]$^+$, 100%). Anal. Calcd for $C_{18}H_{22}N_4O_2S$: C 60.31, H 6.19, N 15.63. Found: C 60.48, H 6.57, N 15.84. The undisolved solid was filtrated out to give the spirocyclic product **7b**: white solid, 30%, mp 180−182 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ: 8.41−7.93 (brs, 1H, NH), 7.49 (d, J = 7.2 Hz,, 2H, ArH), 7.35 (s, 2H, NH_2), 7.13 (d, J = 7.8 Hz,, 2H, ArH), 7.10 (d, J = 7.8 Hz, 2H, ArH), 3.91 (s, 1H, CH), 3.89 (s, 1H, CH), 2.89 (brs, 4H, $2CH_2$), 2.50 (s, 6H, CH_3), 1.13 (t, J = 7.2 Hz,, 6H, $2CH_3$). ^{13}C NMR (150 MHz, DMSO-d_6) δ: 146.1, 138.7, 137.1, 135.1, 131.6, 130.6, 129.8, 129.0, 128.9, 118.6, 118.4, 114.2, 112.3, 80.4, 70.5, 57.2, 46.9, 42.8, 41.8, 21.1, 21.0, 11.4, 1.5. IR(KBr) v: 3413, 3342, 3228, 2987, 2791, 2496, 2255, 2208, 1706, 1625, 1515, 1454, 1366, 1317, 1206, 1120, 1047, 881, 825, 783. MS (m/z): 452.56 ([M − 1]$^+$, 100%). Anal. Calcd for $C_{25}H_{19}N_5O_2S.C_4H_{11}N$: C 66.14, H 5.74, N 15.96. Found: C 65.83, H 6.02, N 15.47. The same reaction procedure was carried out by using other aromatic aldehydes and other amine to substitute diethylamine to give products **6a**−**6h** and **7a**−**7j**.

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Supporting Information Available: Experimental details and spectroscopic data, including crystallographic data in CIF format of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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