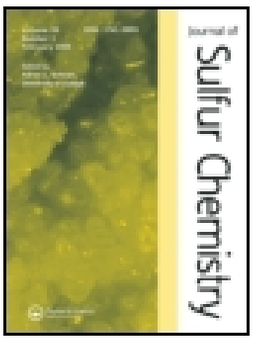

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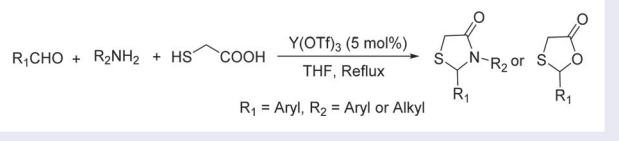
A facile and effective procedure for the synthesis of 4-thiazolidinone derivatives using $Y(OTf)_3$ as catalyst

Juan Luo, Zijun Zhong, Hongfu Ji, Jiayin Chen, Jun Zhao and Furen Zhang

Zhejiang Key Laboratory of Alternative Technologies for Fine Chemicals Process, School of Chemistry and Chemical Engineering, Shaoxing University, Shaoxing, People's Republic of China

ABSTRACT

A one-pot three-component reaction for the synthesis of 4-thiazolidinone derivatives has been established by reacting readily available and inexpensive starting materials of amines, aldehydes and thioglycolic acid using $Y(OTf)_3$ (5 mol%) as catalyst in tetrahydrofuran. This method is very efficient due to low catalyst loading and mild reaction conditions and provides an efficient and promising synthetic strategy for the construction of the thiazolidinone skeleton.



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Three-component reaction; 4-thiazolidinones; thioglycolic acid; 1,3-oxathiolan-5-ones; yttrium triflate

1. Introduction

4-Thiazolidinone derivatives are an important family of organic compounds because they have broad range of biological and medicinal properties such as anticancer,[1–3] anti-HIV,[4–6] antimalarial,[7] antihistaminic,[8] antibacterial,[9] anti-inflammatory[10] and antiarrhythmic.[11] In view of the biological significance of 4-thiazolidinone derivatives, the synthesis of such compounds has attracted considerable attention. Recently, many synthetic methods for preparing 4-thiazolidinone derivatives have been reported.[12–28] Each of these methods not only has its own advantages, but also suffers from one or more disadvantages such as complex experimental and work-up procedures, the requirement of special catalysts (such as protic acid,[26] molecular iodine in [bmim][BF_4][29] and [bmim][PF_6][22]) or special apparatus (such as microwave),[15,17,26] low yields and limited tolerance of functional groups. Therefore, the development of a facile approach to synthesize these compounds with structural and bioactive diversity is highly desirable and valuable for biological chemistry and drug discovery.

CONTACT Furen Zhang frzhang@usx.edu.cn Zhejiang Key Laboratory of Alternative Technologies for Fine Chemicals Process, School of Chemistry and Chemical Engineering, Shaoxing University, Shaoxing, Zhejiang Province 312000, People's Republic of China

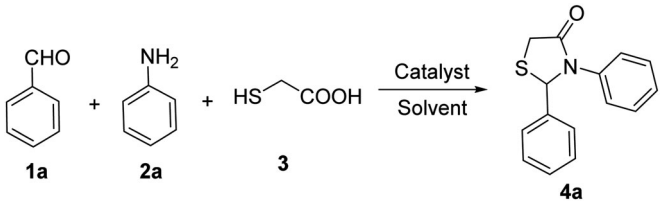
Lewis acid-catalyzed reactions are of great interest in view of their unique reactivities and selectivities and mild reaction conditions used.[30,31] Owing to their unique catalytic advantages, a wide variety of synthetic reactions catalyzed by Lewis acid have been developed.[30,31] However, conventional Lewis acids such as $AlCl_3$, $TiCl_4$, etc., are moisture sensitive and easily decomposed or deactivated in the presence of even a small amount of water. Since the first report of water-compatible lanthanide triflates,[32] new type of Lewis acids [33–35] has become literature-known catalysts for organic synthesis. Moreover, in almost all cases, the triflates are still active in the coexistence of many Lewis bases containing nitrogen, oxygen, phosphorus and sulfur atoms, and reuse of the triflates is possible and metal triflate catalysts are clean and regarded as environmentally friendly catalysts.

In the past several years, our group has developed a series of multi-component reactions that provide easy access to multi-functionalized heterocyclic structures of chemical and biological interest.[36–40] In view of the prominent merits of lanthanide triflates and biological and medical activities of heterocycles, we have great interest in the synthesis of heterocycles using lanthanide triflates as catalysts. As a continuous effort, we report a facile and efficient synthesis of 4-thiazolidinone derivatives catalyzed by yttrium triflate between amines, aldehydes and thioglycolic acid under mild reaction conditions.

2. Results and discussion

In order to optimize the reaction conditions, we selected benzaldehyde (**1a**), aniline (**2a**) and thioglycolic acid (**3**) as a model starting material to examine their behavior under different conditions (Scheme 1); different types and loadings of catalysts, a variety of solvents (including tetrahydrofuran (THF), methanol, ethanol and toluene) and various reaction temperatures were screened in the model reaction. The results are shown in Table 1. It is noteworthy to mention that in the absence of a catalyst, no product was found even after 24 h (Table 1, Entry 1). Inorganic acid (H_2SO_4) and organic acid (AcOH, TfOH and TFA) exhibit low activity and only give low yields (11–39%) of goal products (Table 1, Entries 2–5). However, metal triflate catalysts exhibited a remarkably high activity for the formation of 2,3-diphenylthiazolidin-4-one (**4a**) (Table 1, Entries 6–8). Yttrium triflate showed a superior advantage and gave the best yield of 86% (Table 1, Entry 6). Then, the effect of catalyst loading on the reaction was evaluated. The results showed decreasing the amount of yttrium triflate from 10 to 5 mol% only led to a trace decrease in the yields from 86% to 85% (Table 1, Entries 6, 9), but a further decrease to 3 mol% did reduce the yield significantly (Table 1, Entries 6,10). However, no significant increase in the yield of product **4a** was obtained as when the amount of yttrium triflate was increased from 10 to 20 mol% (Table 1, Entries 6, 11). Therefore, yttrium triflate (5 mol%) was chosen as the catalyst for all further reactions.

To further optimize reaction conditions, screening of solvents was carried out, and the results are also presented in Table 1. It was observed that 2,3-diphenylthiazolidin-4-one (**4a**) could be obtained using all the above solvents. When the reaction was carried out in alcohol (MeOH or EtOH), the product was generated in good to excellent yields (Table 1, Entries 12–13). Whereas when chloroform was used as solvent, only 70% yield product was obtained (Table 1, Entry 14), and when toluene was used as solvent, only trace goal product **4a** was obtained (Table 1, Entry 15). Additionally, the addition of a small amount



Scheme 1. The optimization of the model reaction.

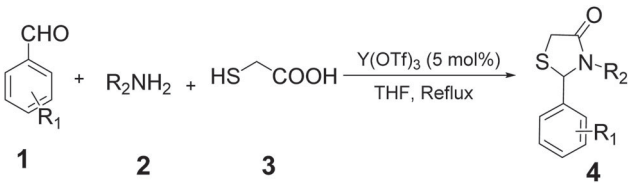
Table 1. Optimization of reaction conditions for synthesis of 2,3-diphenylthiazolidin-4-one **4a**.[a]

Entry	Catalyst (mol%)	Solvent	T (°C)	Time(h)	Yield(%)[b]
1	–	THF	Reflux	24	0
2	H_2SO_4 (10)	THF	Reflux	5	22
3	HOAc (10)	THF	Reflux	5	11
4	TfOH (10)	THF	Reflux	5	34
5	TFA (10)	THF	Reflux	5	39
6	$Y(OTf)_3$ (10)	THF	Reflux	5	86
7	$Yb(OTf)_3$ (10)	THF	Reflux	5	80
8	$Sc(OTf)_3$ (10)	THF	Reflux	5	83
9	$Y(OTf)_3$ (5)	THF	Reflux	5	85
10	$Y(OTf)_3$ (3)	THF	Reflux	5	72
11	$Y(OTf)_3$ (20)	THF	Reflux	5	87
12	$Y(OTf)_3$ (10)	MeOH	Reflux	5	77
13	$Y(OTf)_3$ (10)	C_2H_5OH	80	5	76
14	$Y(OTf)_3$ (10)	$CHCl_3$	Reflux	5	70
15	$Y(OTf)_3$ (10)	PhMe	70	5	22
16	$Y(OTf)_3$ (10)	THF/H_2O[c]	65	5	83
17	$Y(OTf)_3$(10)	THF	20	24	0
18	$Y(OTf)_3$(10)	THF	40	5	47
19	$Y(OTf)_3$(10)	THF	60	5	77
20	$Y(OTf)_3$ (10)	THF	80[d]	5	85

[a]Reaction conditions: **1a** (1.0 mmol), **2a** (1.0 mmol), **3a** (1.0 mmol), Catalyst (5 mol%) and THF (3.0 mL).
[b]Isolated yields.
[c]V_{THF}/V_{H2O} = 3.0 mL/0.5 mL.
[d]The reaction was carried out in sealed tube.

of water did not reduce the yield of the goal product, obviously (Table 1, Entry 16). Subsequently, the same reaction was carried out in THF at temperatures ranging from 20°C to 80°C (Table 1, Entries 17–20), with an increment of 20°C. As shown in Table 1, the results showed that reflux temperature (65°C) is enough to push the reaction successfully; thus, the reflux temperature was chosen as the reaction temperature for all further reactions.

Under optimal conditions, reactions of different aldehydes and amines were performed and afforded 2,3-diaryl-4-thiazolidinone derivatives with good to excellent yields (Scheme 2, Table 2). As shown in Table 2, at the beginning, we made a search for the aldehydes substrate scope using aniline and thioglycolic acid as model substrates (Table 2, Entries 1–4). The results indicate that aromatic aldehydes bearing both electron-donating and withdrawing functional groups, such as methyl, fluoro or chloro, were able to give the corresponding compound **4** with good yields (72–85%) in six hours. To further expand the scope of the reaction, different amines were used as substrates with aldehydes and thioglycolic acid. It is worth noting that amines bearing electron-donating groups such as methyl



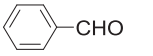
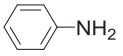
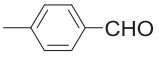
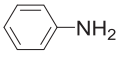
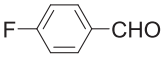
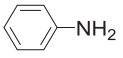
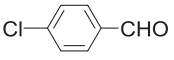
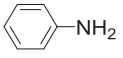
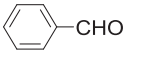
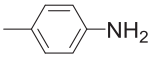
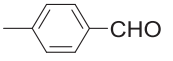
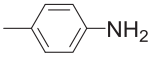
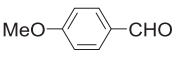
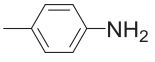
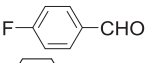
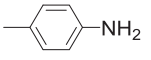
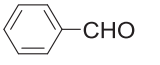
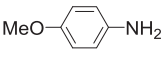
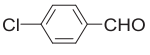
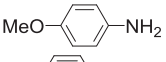
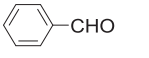
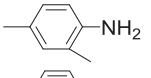
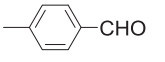
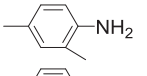
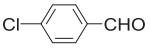
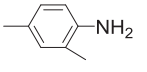
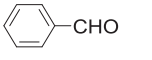
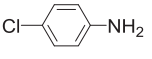
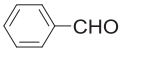
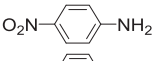
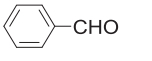
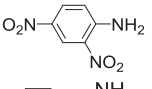
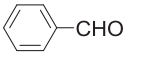
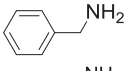
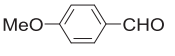
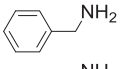
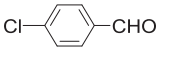
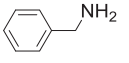
Scheme 2. The synthesis of 1,3-oxathiolan-5-one derivatives **4**.

or methoxy can give the corresponding 2,3-diaryl-4-thiazolidinones with excellent yields of 93–94% (Table 2, Entries 5–13). However, amines bearing electron-withdrawing functional groups such as nitro or chloro could not display reactivity under standard conditions even under prolonged reaction times (Table 2, Entries 14–16). To further examine the efficiency and applicability of this three-component reaction, benzylamine was employed to react with aromatic aldehydes and thioglycolic acid. To our delight, under the above optimized conditions, these reactions proceeded smoothly to give 4-thiazolidinone derivatives with excellent yields of 92–94% (Table 2, Entries 17–19). In comparison with the similar reaction type reported previously, which was conducted either under special reaction conditions or with limited aldehyde substrates, and thereby suffered from narrow substrate scope, long reaction time and unsatisfactory conversion in some cases, this approach offers a global and efficient shortcut to prepare 4-thiazolidinones containing a wider substrate scope, higher catalytic efficiency of yttrium triflate, mild reaction conditions and higher yields.

It is worth noting that aside from the expected products **4**, several undesired products **5** were generated when using different substrates **1** (Scheme 3). When the reaction was performed with aromatic aldehydes bearing strong electron-withdrawing functional groups, such as 2-nitro, 3-nitro or 4-nitro, as substrates to react with amines, none of the expected 2,3-diaryl-4-thiazolidinones (**4**) was obtained, but the corresponding 1,3-oxathiolan-5-one derivatives (**5**) were obtained with good yields (82–89%).[41] The aromatic amines could not display reactivity under similar reaction conditions; we attributed such results to the higher reactivity of nitrobenzaldehydes, in which the existence of a strong electron-withdrawing group reduced the stability of C = N bond of Schiff base intermediates obviously.

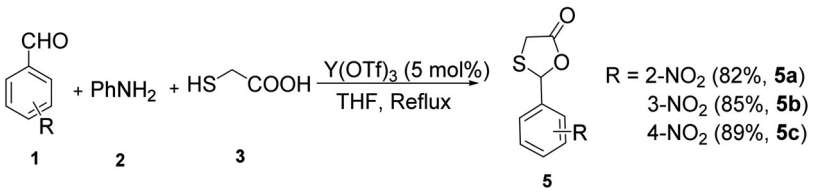
Additionally, aside from the products **4** and **5**, several unexpected products **6** and **7** also were obtained when ethanol was used as solvent (Scheme 4). We found that the products are not the expected cyclization products **4** and **5**. Instead, we found that ethoxy group was introduced in the final product with ethanol as the substrate. Moreover, ethanol could be introduced in different positions by different types of reactions. When the reaction was performed with aromatic aldehydes bearing weak electron-withdrawing functional groups, such as chloro, as substrates to react with amines, diethyl 2,2′-(((4-chlorophenyl)methylene)bis(sulfanediyl)) diacetate (**6**) was obtained with good yield (86%). When the reaction was performed with aromatic aldehydes bearing strong electron-withdrawing functional groups, such as nitro, as substrates to react with amines, ethyl 2-((ethoxy(aryl)methyl)thio)acetate (**7**) were obtained with good yields (82–88%). The results indicate that aromatic aldehydes bearing different electron-withdrawing functional groups were able to affect the types of goal products. Moreover, thioglycolic acid still

Table 2. Synthesis of 4-thiazolidinone derivatives by $Y(OTf)_3$ catalyst.[a]

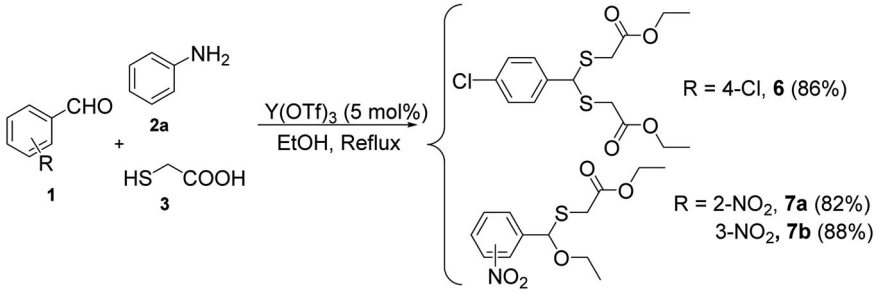
Entry	Aldehyde	Amine	Product	Time (h)	Yield(%)[b]	Ref.
1			**4a**	6	85	27
2			**4b**	6	75	27
3			**4c**	6	72	27
4			**4d**	6	76	27
5			**4e**	5	86	27
6			**4f**	5	88	27
7			**4g**	5	85	22
8			**4h**	5	89	22
9			**4i**	5	83	27
10			**4j**	5	87	15
11			**4k**	5	92	–
12			**4l**	5	93	–
13			**4m**	5	89	–
14			**4n**	6	0	–
15			**4o**	6	0	–
16			**4p**	6	0	–
17			**4q**	4	93	27
18			**4r**	4	94	27
19			**4s**	4	92	19

[a]Reaction conditions: **1** (1.0 mmol), **2** (1.0 mmol), **3** (1.0 mmol), $Y(OTf)_3$ (5 mol%) and THF (3.0 mL) at reflux.
[b]Isolated yields.

displayed high reactivity under standard conditions. We attributed the formation of compounds **6** and **7** to the high reaction activity of ethanol, which prevented the cycloaddition reaction. Note that this result is significant because there is no literature precedent for the synthesis of ethyl 2-((ethoxy(aryl)methyl)thio)acetate derivatives (**7**).



Scheme 3. The synthesis of 1,3-oxathiolan-5-one derivatives **5**.



Scheme 4. The synthesis of undesired products **6** and **7**.

3. Conclusion

In summary, we have reported a one-pot three-component reaction (benzaldehydes, amines and thioglycolic acid) as an approach to the annulations of 2,3-diaryl-4-thiazolidinones and 1,3-oxathiolan-5-ones. Particularly, valuable features of this method included the structural diversity of products, mild reaction conditions and higher catalytic efficiency of yttrium triflate, as well as short reaction times. Therefore, this work not only provides plenty of novel 2,3-diaryl-4-thiazolidinone and 1,3-oxathiolan-5-one derivatives, but also enriches the research contents of rare earth metals.

4. Experimental

4.1. General

All reagents were commercial products without further purification, unless otherwise stated. Analytical thin layer chromatography (TLC) was performed using Merck silica gel GF254 plates. Column chromatography was carried out with silica gel (Silica Gel 200–300 mesh, pH 6.0–7.0 for 10% suspension). Melting points were measured on an X-4 melting point apparatus. ^{1}HNMR spectra were recorded on a 400 MHz instrument (Bruker Avance 400 Spectrometer). Chemical shifts (δ) are given in ppm relative to TMS as the internal reference, with coupling constants (J) in Hz. ^{13}C NMR spectra were recorded at 100 MHz. Chemical shifts were reported in ppm with the internal chloroform signal at 77.0 ppm as a standard. Elemental analysis was carried out on EuroEA elemental analyzer.

4.2. General procedure for synthesis of 2,3-diaryl-4-thiazolidinones 4

In a 10-mL reaction vial, benzaldehyde (1.0 mmol), amine (1.0 mmol), thioglycolic acid (1.0 mmol) and THF (3.0 mL) were mixed. The mixture was stirred in THF at reflux temperature. Upon completion as shown by TLC monitoring, the reaction mixture was cooled to room temperature and extracted with ethyl acetate (5.0 mL × 3). The combined organic layer was dried over Na_2SO_4, and concentrated in vacuum. The resulting residue was purified by column chromatography on silica gel with the eluent (ethyl acetate/petroleum ether = 1:10–1:2) to give the pure products.

4.2.1. 2,3-Diphenylthiazolidin-4-one (4a) [27]

Yellow solid, mp 127–128°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.23–7.34 (m, 9H, ArH), 7.10–7.13 (m, 1H, ArH), 6.01 (s, 1H, CH), 3.89 (d, 1H, J = 15.6 Hz, CH_2), 3.78 (d, 1H, J = 16.4 Hz, CH_2) ppm.

4.2.2. 3-Phenyl-2-(p-tolyl)thiazolidin-4-one (4b) [27]

Yellow solid, mp 115–116°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.23–7.27 (m, 2H, ArH), 7.14–7.21 (m, 5H, ArH), 7.08–7.10 (d, 2H, J = 7.6 Hz, ArH), 6.03 (s, 1H, CH), 4.00 (d, 1H, J = 15.6 Hz, CH_2), 3.94 (d, 1H, J = 16.0 Hz, CH_2), 2.28 (s, 3H, CH_3) ppm.

4.2.3. 2-(4-Fluorophenyl)-3-phenylthiazolidin-4-one (4c) [27]

Brown solid, mp 127–128°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.24–7.28 (m, 4H, ArH), 7.12–7.20 (m, 3H, ArH), 6.95–7.00 (m, 2H, ArH), 6.08 (s, 1H, CH), 3.96 (dd, 1H, J = 15.6, 1.2 Hz, CH_2), 3.88 (dd, 1H, J = 15.6, 0.8 Hz, CH_2) ppm.

4.2.4. 2-(4-Chlorophenyl)-3-phenylthiazolidin-4-one (4d) [27]

Brown solid, mp 128–130°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.09–7.48 (m, 9H, ArH), 6.08 (s, 1H, CH), 3.99 (dd, 1H, J = 15.6, 1.2 Hz, CH_2), 3.89 (d, 1H, J = 15.6 Hz, CH_2) ppm.

4.2.5. 2-Phenyl-3-(p-tolyl)thiazolidin-4-one (4e) [27]

Yellow solid, mp 116–118°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.33 (d, 2H, J = 8.0 Hz, ArH), 7.23–7.27 (m, 3H, ArH), 7.19 (d, 2H, J = 8.4 Hz, ArH), 7.09 (d, 2H, J = 8.0 Hz, ArH), 6.05 (s, 1H, CH), 3.99 (dd, 1H, J = 16.0, 1.2 Hz, CH_2), 3.90 (d, 1H, J = 15.6 Hz, CH_2), 2.30 (s, 3H, CH_3) ppm.

4.2.6. 2,3-Di-p-tolylthiazolidin-4-one (4f) [27]

Yellow solid, mp 129–130°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.19 (d, 2H, J = 8.0 Hz, ArH), 7.10 (d, 2H, J = 7.2 Hz, ArH), 6.98 (d, 2H, J = 8.0 Hz, ArH), 6.30 (d, 2H, J = 8.4 Hz, ArH), 6.04 (s, 1H, CH), 3.99 (dd, 1H, J = 16.0, 1.2 Hz, CH_2), 3.87 (d, 1H, J = 15.6 Hz, CH_2), 2.31 (s, 3H, CH_3), 2.26 (s, 3H, CH_3) ppm.

4.2.7. 2-(4-Methoxyphenyl)-3-(p-tolyl)thiazolidin-4-one (4g) [22]

Yellow solid, mp 145–146°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.23 (d, 2H, J = 8.4 Hz, ArH), 7.08 (d, 2H, J = 8.4 Hz, ArH), 7.00 (d, 2H, J = 8.4 Hz, ArH), 6.81 (d, 2H, J = 8.4 Hz, ArH), 6.03 (s, 1H, CH), 3.98 (dd, 1H, J = 16.0, 1.2 Hz, CH_2), 3.88 (d, 1H, J = 15.6 Hz, CH_2), 3.77 (s, 3H, OMe), 2.26 (s, 3H, CH_3) ppm.

4.2.8. 2-(4-Fluorophenyl)-3-(p-tolyl)thiazolidin-4-one (4h) [22]

Pale yellow solid, mp 172–174°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.30–7.31 (m, 2H, ArH), 7.09 (d, 2H, J = 8.0 Hz, ArH), 6.99 (d, 4H, J = 9.2 Hz, ArH), 6.05 (s, 1H, CH), 3.98 (dd, 1H, J = 16.0, 1.6 Hz, CH_2), 3.89 (d, 1H, J = 15.6 Hz, CH_2), 2.27 (s, 3H, CH_3) ppm.

4.2.9. 3-(4-Methoxyphenyl)-2-phenylthiazolidin-4-one (4i) [27]

Yellow solid, mp 60–62°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.30 (s, 5H, ArH), 7.03 (d, 2H, J = 9.2 Hz, ArH), 6.79 (d, 2H, J = 8.8 Hz, ArH), 5.99 (s, 1H, CH), 4.01 (dd, 1H, J = 15.6, 1.6 Hz, CH_2), 3.73 (d, 1H, J = 15.6 Hz, CH_2) ppm.

4.2.10. 2-(4-Chlorophenyl)-3-(4-methoxyphenyl)thiazolidin-4-one (4j) [15]

Yellow solid, mp 166–168°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40 (d, 2H, J = 8.4 Hz, ArH), 7.33 (d, 2H, J = 8.8 Hz, ArH), 7.17 (d, 2H, J = 8.8 Hz, ArH), 6.84 (d, 2H, J = 8.4 Hz, ArH), 6.40 (s, 1H, CH), 4.02 (dd, 1H, J = 15.2, 2.0 Hz, CH_2), 3.86 (d, 1H, J = 15.2 Hz, CH_2), 3.68 (s, 3H, OMe) ppm.

4.2.11. 3-(2,4-Dimethylphenyl)-2-phenylthiazolidin-4-one (4k)

Yellow solid, mp 220–222°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.48–7.52 (m, 3H, ArH), 7.35–7.42 (m, 3H, ArH), 6.99 (s, 1H, ArH), 6.63 (s, 1H, ArH), 5.64 (s, 1H, CH), 3.25 (d, 1H, J = 12.0 Hz, CH_2), 2.99 (d, 1H, J = 11.6 Hz, CH_2), 2.27 (s, 3H, CH_3), 2.22 (s, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.0, 143.5, 139.0, 135.6, 131.3, 128.7, 128.4, 127.5, 127.3, 126.3, 126.0, 121.0, 70.3, 32.8, 21.0, 19.8 ppm; Anal. Calcd for $C_{17}H_{17}NOS$: C, 72.05; H, 6.05; N, 4.94. Found: C, 71.88; H, 5.87; N, 5.23.

4.2.12. 3-(2,4-Dimethylphenyl)-2-(p-tolyl)thiazolidin-4-one (4l)

Yellow solid, mp 166–168°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37 (d, 2H, J = 8.0 Hz, ArH), 7.21 (d, 3H, J = 8.0 Hz, ArH), 6.98 (s, 1H, ArH), 6.65 (s, 1H, ArH), 5.62 (s, 1H, CH), 3.25 (d, 1H, J = 12.0 Hz, CH_2), 2.97 (dd, 1H, J = 12.0, 1.6 Hz, CH_2), 2.38 (s, 3H, CH_3), 2.26 (s, 3H, CH_3), 2.20 (s, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.5, 143.4, 139.1, 135.7, 131.1, 128.6, 128.2, 127.4, 127.3, 126.2, 126.0, 121.1, 70.6, 32.3, 21.5, 21.2, 19.9 ppm; Anal. Calcd for $C_{18}H_{19}NOS$: C, 72.69; H, 6.44; N, 4.71. Found: C, 72.78; H, 6.10; N, 5.02.

4.2.13. 2-(4-Chlorophenyl)-3-(2,4-dimethylphenyl)thiazolidin-4-one (4m)

Pale yellow solid, mp 228–230°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.50 (s, 1H, ArH), 7.43 (d, 2H, J = 8.4 Hz, ArH), 7.36 (d, 2H, J = 8.4 Hz, ArH), 7.00 (s, 1H, ArH), 6.61 (s, 1H, ArH), 5.57 (s, 1H, CH), 3.22 (d, 1H, J = 12.0 Hz, CH_2), 2.99 (d, 1H, J = 12.0 Hz, CH_2), 2.26 (s, 3H, CH_3), 2.24 (s, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.9, 143.2, 138.9, 135.5, 131.3, 128.5, 128.1, 127.3, 127.1, 126.5, 126.0, 121.1, 70.4, 32.1, 20.1, 19.9 ppm; Anal. Calcd for $C_{17}H_{16}ClNOS$: C, 64.24; H, 5.07; N, 4.41. Found: C, 64.39; H, 4.88; N, 4.20.

4.2.14. 3-Benzyl-2-phenylthiazolidin-4-one (4q) [27]

White solid, mp 156–158°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.20–7.40 (m, 8H, ArH), 7.07–7.13 (m, 2H, ArH), 5.36 (s, 1H, CH), 5.16 (d, 1H, J = 14.8 Hz, CH_2), 3.90 (d, 1H, J = 15.6 Hz, CH_2), 3.76 (d, 1H, J = 15.6 Hz, CH_2), 3.53 (d, 1H, J = 14.8 Hz, CH_2) ppm.

4.2.15. 3-Benzyl-2-(4-methoxy)thiazolidin-4-one (4r) [27]

Yellow solid, mp 144–146°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.88–7.28 (m, 9H, ArH), 5.35 (s, 1H, CH), 5.11 (d, 1H, J = 14.8 Hz, CH_2), 3.87 (d, 1H, J = 15.6 Hz, CH_2), 3.81 (s, 3H, OMe), 3.74 (d, 1H, J = 15.6 Hz, CH_2), 3.52 (d, 1H, J = 14.8 Hz, CH_2) ppm.

4.2.16. 3-Benzyl-2-(4-chlorophenyl)thiazolidin-4-one (4s) [19]

White solid, mp 208–210°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37 (d, 2H, J = 8.4 Hz, ArH), 7.31–7.32 (m, 3H, ArH), 7.17 (d, 2H, J = 8.4 Hz, ArH), 7.08–7.10 (m, 2H, ArH), 5.36 (s, 1H, CH), 5.16 (d, 1H, J = 14.8 Hz, CH_2), 3.91 (d, 1H, J = 15.6 Hz, CH_2), 3.78 (d, 1H, J = 15.6 Hz, CH_2), 3.53 (d, 1H, J = 14.8 Hz, CH_2) ppm.

4.3. General procedure for synthesis of 2,3-diaryl-4-thiazolidinones 5

In a 10-mL reaction vial, nitrobenzaldehyde (1.0 mmol), amine (1.0 mmol), thioglycolic acid (1.0 mmol) and THF (3.0 mL) were mixed. The mixture was stirred at reflux temperature. Upon completion as shown by TLC monitoring, the reaction mixture was cooled to room temperature and extracted with ethyl acetate (5.0 mL × 3). The combined organic layer was dried over Na_2SO_4, and concentrated in vacuum. The resulting residue was purified by column chromatography on silica gel with the eluent (ethyl acetate/petroleum ether = 1:10–1:6) to give the pure products.

4.3.1. 2-(2-Nitrophenyl)-1,3-oxathiolan-5-one (5a) [41]

Pale yellow solid, mp 64–66°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.25 (d, 1H, J = 8.4 Hz, ArH), 7.76 (t, 1H, J = 6.8 Hz, ArH), 7.69 (d, 1H, J = 7.2 Hz, ArH), 7.60 (t, 1H, J = 8.4 Hz, ArH), 7.13 (s, 1H, CH), 3.77 (d, 1H, J = 16.8 Hz, CH_2), 3.66 (d, 1H, J = 16.8 Hz, CH_2) ppm; Anal. Calcd for $C_9H_7NO_4S$: C, 48.00; H, 3.13; N, 6.22. Found: C, 47.81; H, 2.76; N, 6.51.

4.3.2. 2-(3-Nitrophenyl)-1,3-oxathiolan-5-one (5b) [41]

Pale yellow solid, mp 70–72°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.51 (d, 1H, J = 8.4 Hz, ArH), 8.25 (d, 1H, J = 7.69 Hz, ArH), 7.77 (d, 1H, J = 8.0 Hz, ArH), 7.64 (t, 1H, J = 8.0 Hz, ArH), 6.55 (s, 1H, CH), 3.93 (d, 1H, J = 16.4 Hz, CH_2), 3.82 (d, 1H, J = 16.4 Hz, CH_2) ppm; Anal. Calcd for $C_9H_7NO_4S$: C, 48.00; H, 3.13; N, 6.22. Found: C, 48.15; H, 2.81; N, 6.00.

4.3.3. 2-(4-Nitrophenyl)-1,3-oxathiolan-5-one (5c) [41]

Pale yellow solid, mp 82–84°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.30 (d, 2H, J = 8.8 Hz, ArH), 7.65 (d, 2H, J = 8.8 Hz, ArH), 6.56 (s, 1H, CH), 3.92 (d, 1H, J = 16.8 Hz, CH_2), 3.80 (d, 1H, J = 16.8 Hz, CH_2) ppm; Anal. Calcd for $C_9H_7NO_4S$: C, 48.00; H, 3.13; N, 6.22. Found: C, 48.31; H, 3.38; N, 6.31.

4.4. General procedure for synthesis of 2,3-diaryl-4-thiazolidinones 6 and 7

In a 10-mL reaction vial, aromatic aldehyde (1.0 mmol), amine (1.0 mmol), thioglycolic acid (1.0 mmol) and EtOH (3.0 mL) were mixed. The mixture was stirred at 80°C. Upon

completion as shown by TLC monitoring, the reaction mixture was cooled to room temperature and extracted with ethyl acetate (5.0 mL × 3). The combined organic layer was dried over Na_2SO_4, and concentrated in vacuum. The resulting residue was purified by column chromatography on silica gel with the eluent (ethyl acetate/petroleum ether = 1:10–1:4) to give the pure products.

4.4.1. Diethyl 2,2′-(((4-chlorophenyl)methylene)bis(sulfanediyl))diacetate (6) [42]

Brown oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.41 (d, 2H, J = 8.4 Hz, ArH), 7.32 (d, 2H, J = 8.4 Hz, ArH), 5.34 (s, 1H, CH), 4.12–4.18 (m, 4H, CH_2), 3.42 (d, 2H, J = 15.2 Hz, CH_2), 3.16 (d, 2H, J = 14.8 Hz, CH_2), 1.27 (t, 6H, J = 7.2 Hz, CH_3) ppm.

4.4.2. Ethyl 2-((ethoxy(2-nitrophenyl)methyl)thio)acetate (7a)

Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.96 (d, 1H, J = 8.0 Hz, ArH), 7.87 (d, 1H, J = 7.6 Hz, ArH), 7.63 (t, 1H, J = 7.6 Hz, ArH), 7.45 (t, 1H, J = 7.6 Hz, ArH), 6.42 (s, 1H, CH), 4.06–4.11 (m, 2H, CH_2), 3.86–3.94 (m, 1H, CH_2), 3.50–3.58 (m, 1H, CH_2), 3.22 (d, 1H, J = 15.2 Hz, CH_2), 3.10 (d, 1H, J = 15.2 Hz, CH_2), 1.22–1.29 (m, 6H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.0, 146.6, 134.9, 133.1, 128.7, 128.1, 125.0, 80.2, 65.1, 61.5, 30.7, 14.8, 14.0 ppm; Anal. Calcd for $C_{13}H_{17}NO_5S$: C, 52.16; H, 5.72; N, 4.68. Found: C, 52.00; H, 5.43; N, 4.31.

4.4.3. Ethyl 2-((ethoxy(3-nitrophenyl)methyl)thio)acetate (7b)

Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.36 (s, 1H, ArH), 8.16 (d, 1H, J = 8.4 Hz, ArH), 7.82 (d, 1H, J = 7.6 Hz, ArH), 7.55 (t, 1H, J = 8.0 Hz, ArH), 5.77 (s, 1H, CH), 4.08–4.16 (m, 2H, CH_2), 3.89–3.97 (m, 1H, CH_2), 3.53–3.59 (m, 1H, CH_2), 3.23 (d, 1H, J = 15.2 Hz, CH_2), 3.08 (d, 1H, J = 14.8 Hz, CH_2), 1.31 (t, 3H, J = 7.2 Hz, CH_3), 1.26 (t, 3H, J = 7.2 Hz, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.0, 148.2, 141.7, 132.6, 129.2, 123.0, 121.6, 84.0, 65.0, 61.5, 30.3, 14.8, 14.1 ppm; Anal. Calcd for $C_{13}H_{17}NO_5S$: C, 52.16; H, 5.72; N, 4.68. Found: C, 51.88; H, 5.39; N, 4.89.

Disclosure statement

No potential conflict of interest was reported by the authors.

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