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Synthesis of 2-(5-Substituted-1,3,4-thiadiazolo-2-ylimino)-4-t under Microwave Irradiation

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Synthesis of 2-(5-Substituted-1,3,4-thiadiazolo-2-ylimino)-4-thiazolidinones under Microwave Irradiation

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Abstract: Fifteen 2-(5-substituted-1,3,4-thiadiazolo-2-ylimino)-4-thiazolidinones were efficiently synthesized from the reaction of ammonium thiocyanate with 2-chloro-*N*-(5-substutited-1,3,4-thiadiazolo-2-yl)acetamides under microwave irradiation. The target compounds were obtained in better yields (75–98%) and shorter time (5 min) than with conventional heating.

Keywords: microwave irradiation, synthesis, 1,3,4-thiadiazoles, 4-thiazolidinones

INTRODUCTION

The 1,3,4-thiadiazole derivatives have attracted continued interest over the years because of their varied biological activities.[1,2] In particular, a large number of 4-thiazolidinone derivatives possess antituberculosis, anticancer, antibacterial, antifungal, and anticonvulsant activities.[3–9] Therefore, 1,3,4-thiadiazole and 4-thiazolidone moieties are prospective scaffolds for the design of drugs. There have some reports for the synthesis of 3-nonsubstituted 4-thiazolidinones.[10,11] However, these reactions suffered from drawbacks such as long reaction times, the use of high boiling solvents, low yields,

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and use of reactants with high toxicity, which limit their use for the synthesis of complex molecules. A simple and efficient approach for the synthesis of functionalized 4-thiazolidinone is our interest.

Moreover, microwave (MW) irradiation is currently used to carry out a wide range of reactions.[12] Compared with the traditional reactions under refluxing, the MW reaction technique is often rapid and most convenient, occurs in high yields, and has stereoselective, environmental, and economic advantages.

Given this background, we have designed and synthesized a series of new compounds containing the 1,3,4-thiadiazole ring and 4-thiazolidinone moiety under MW irradiation.

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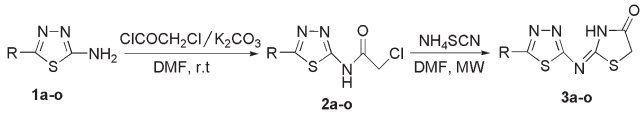
RESULTS AND DISCUSSION

As described in Scheme 1, the starting material 2-amino-5-aryloxymethylene/aryl-1,3,4-thiadiazoles (**1a**–**o**) were synthesized as in our previous work.[13] 2-Chloro-*N*-(5-aryloxymethylene/aryl-1,3,4-thiadiazolo-2-yl)acetamides (**2a**–**o**) were obtained from the reaction of **1a**–**o** and chloroacetyl chloride in the presence of anhydrous potassium carbonate. Compounds (**2a**–**o**) were treated with ammonium thiocyanate in *N*,*N*-dimethylformamide (DMF) under MW irradiation to provide 2-(5-aryloxymethylene/aryl-1,3,4-thiadiazolo-2-ylimino)thiazolidin-4-one (**3a**–**o**).

Preliminary experiments to examine the reaction time, the solvent, and irradiation power were performed using **2a** (1.0 mmol) and ammonium thiocyanate (1.5 mmol) as a model system to synthesize the compound **3a** (Table 1). First, various reaction times and irradiation power were tested using DMF (4 mL) as a solvent (Table 1, entries 1–5). All comparative reactions were conducted under optimized conditions, and compound **3a** was obtained under MW irradiation. The best yield of **3a** (92%) was obtained by carrying out the reaction in DMF under MW irradiation (350 W) for 5 min. Second, other solvents were tested including ethanol (EtOH), acetonitrile (MeCN), dimethyl sulfoxide (DMSO), and tetrahydrofuran (THF) (Table 1, entries 6–9). In general, the use of DMF and DMSO resulted in a faster reaction with a higher yield, in contrast to a reaction in



Scheme 1. R = $C_6H_5OCH_2$ (**a**), 2-$ClC_6H_4OCH_2$ (**b**), 2-$CH_3C_6H_4OCH_2$ (**c**), 4-$CH_3C_6H_4OCH_2$ (**d**), 4-$ClC_6H_4OCH_2$ (**e**), 4-$CH_3OC_6H_4OCH_2$ (**f**), 2-$CH_3OC_6H_4$-OCH_2 (**g**), 3-$CH_3C_6H_4OCH_2$ (**h**), 3-$NO_2C_6H_4OCH_2$ (**i**), 4-$NO_2C_6H_4OCH_2$ (**j**), 2,4-Cl_2-$C_6H_3OCH_2$ (**k**), C_6H_5 (**l**), 2-ClC_6H_4 (**m**), 3-$CH_3C_6H_4$ (**n**), and 3-$NO_2C_6H_4$ (**o**).

Table 1. Synthesis of **3a** (MW = microwave irradiation; Δ^a = conventional heating)

Entry	Solvent	Mode of activation	Time	Power/ temp.	Yield (%)[b]
1	DMF	MW	3 min	350 W	56
2	DMF	MW	5 min	350 W	92
3	DMF	MW	7 min	350 W	92
4	DMF	MW	5 min	210 W	71
5	DMF	MW	5 min	490 W	63
6	EtOH	MW	5 min	350 W	<10
7	MeCN	MW	5 min	350 W	Trace
8	DMSO	MW	5 min	350 W	82
9	THF	MW	5 min	350 W	0
10	DMF	Δ	8 h	80°C	82
11	DMSO	Δ	8 h	80°C	80

[a]The reaction was conducted with **2a** (1.0 mmol) and ammonium thiocyanate (1.5 mmol) at 80°C.

All the products were investigated thoroughly by ^{1}H NMR, ^{13}C NMR, IR, and element analysis.

[b]Isolated yields.

less polar THF. Third, the reaction was also carried out with conventional heating (Table 1, entries 10 and 11) but requires extended heating time (8 h), providing the product in a lower yield (80–82%).

The IR spectrum of **2a–o** displayed bands at 3201–3163 and 1713–1702 cm^{-1} due to -NH- and -C═O stretching frequencies, respectively. The ^{1}H NMR spectrum of **2a** displayed a singlet at δ 11.62, which accounts for the NH proton, and a multiplet appeared at δ 7.35–6.99, which accounts for five aromatic protons of the phenyl ring. Two singlets appeared at δ 5.52 and 4.54 due to two methylene protons each on the OCH_2 and $ClCH_2$ protons. The mass spectrum of **2a** gave a molecular ion peak at m/z 283 (16.5%), and protonated molecular ion peak at m/z 285 (6.5%), which are in agreement with its molecular formula $C_{11}H_{10}ClN_3O_2S$. Other prominent fragment ions appeared at m/z 192 (23%), 190 (61%), 114 (100%), and 94 (25%).

The formation of 2-(5-aryloxymethylene/aryl)-1,3,4-thiadiazolo-2-ylimino)thiazolidin-4-one (**3a–o**) was confirmed by recording ^{1}H NMR, ^{13}C NMR, and mass spectra. The IR spectrum of **3a–o** displayed bands at 3168–3102 and 1737–1721 cm^{-1} due to -NH- and -C═O stretching frequencies, respectively. The ^{1}H NMR spectrum of **3a** exhibited two singlets at δ 4.10 and 5.48, which account for two methylene protons each on the SCH_2 and OCH_2 protons. Aromatic protons resonated as a multiplet at δ 6.99–7.35, and a singlet appeared at δ 12.37, which accounts for the NH proton. The ^{13}C NMR displayed peaks at 35.80 (CH_2), 64.50 (CH_2), 115.10 (2C), 121.85, 129.85 (2C), 157.42, 163.35, 166.37, 171.55, and 174.17 (C═O), which account for all the carbon atoms in the molecule. The mass spectrum

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of **3a** exhibited a molecular ion peak at m/z 306 (5%) in accordance with its molecular formula $C_{12}H_{10}N_4O_2S_2$. Other prominent peaks appeared at m/z 214 (11%), 213 (100%), 159 (26%), 131 (9%), 127 (25%), and 94 (6%).

In conclusion, we have described a fast, easy, and efficient protocol for the preparation of 2-(5-aryloxymethylene/aryl-1,3,4-thiadiazolo-2-ylimino)-4-thiazolidinones under MW irradiation. The ease of the reaction procedure and workup, high yields, and very short reaction times make this procedure a useful and attractive alternative to the currently available methods.

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EXPERIMENTAL

All reagents were obtained commercially and used without further purification. Melting points were determined on an XT-4 electrothermal micromelting-point apparatus and are uncorrected. IR spectra were recorded using KBr pellets on Nicolet Avatar 36 fourier transform infrared (FT-IR) spectrophotometer. NMR spectra were recorded at 400 (^{1}H) and 100 (^{13}C) MHz, respectively, on a Varian Mercury plus-400 instrument using DMSO as solvent and TMS as internal standard. Mass spectroscopy (MS) spectra were recorded on a Trace DSQ mass spectrometer. Elemental analyses were performed on a Carlo-Erba 1106 Elemental Analysis instrument. MW experiments were carried out in a domestic oven operating at a frequency of 2450 MHz.

General Synthetic Procedure for Compounds 2a–o

Chloroacetyl chloride (0.57 g, 5.0 mmol) was added dropwise to a solution of compound (**1a–o**) (5.0 mmol) and anhydrous potassium carbonate (0.69 g, 5.0 mmol) in dry DMF (20 mL). The mixture was stirred for 4 h at room temperature, then poured onto ice water. The obtained precipitate was filtered off, washed with water (3 × 5 mL), and recrystallized from EtOH–DMF to give the products.

Data

Compound **2a**. Yield: 89%. White crystals. Mp: 182–183°C (158°C [14]). ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 11.62 (s, 1H, NH), 7.35–6.99 (m, 5H, ArH), 5.52 (s, 2H, OCH_2), 4.54 (s, 2H, $ClCH_2$). IR (KBr) ν: 3178, 1707, 1591 cm^{-1}. Anal. calcd. for $C_{11}H_{10}ClN_3O_2S$: C, 46.56; H, 3.55; N, 14.81. Found: C, 46.77; H, 3.56; N, 14.74.

Compound **2b**. Yield: 91%. White crystals. Mp: 196–197°C (166°C [14]). ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 11.61 (s, 1H, NH), 7.37–7.01 (m, 4H, ArH), 5.51 (s, 2H, OCH_2), 4.53 (s, 2H, $ClCH_2$). IR (KBr) ν: 3198, 1708,

1583 cm^{-1}. Anal. calcd. for $C_{11}H_9Cl_2N_3O_2S$: C, 41.52; H, 2.85; N, 13.21. Found: C, 41.35; H, 2.86; N, 13.27.

Compound **2c**. Yield: 90%. White crystals. Mp: 225–227°C (152°C [14]). ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 11.60 (s, 1H, NH), 7.10–6.99 (m, 4H, ArH), 5.51 (s, 2H, OCH_2), 4.52 (s, 2H, $ClCH_2$), 2.24 (s, 3H, CH_3); IR (KBr) ν: 3192, 1705, 1583 cm^{-1}. Anal. calcd. for $C_{12}H_{12}ClN_3O_2S$: C, 48.40; H, 4.06; N, 14.11. Found: C, 48.60; H, 4.07; N, 14.04.

Compound **2d**. Yield: 91%. White crystals. Mp: 185–186°C (138°C [14]). ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 11.60 (s, 1H, NH), 7.00 (d, $J = 8.0$ Hz, 2H, ArH), 7.15 (d, $J = 8.0$ Hz, 2H, ArH), 5.53 (s, 2H, OCH_2), 4.52 (s, 2H, $ClCH_2$), 2.23 (s, 3H, CH_3). IR (KBr) ν: 3193, 1706, 1582 cm^{-1}. Anal. calcd. for $C_{12}H_{12}ClN_3O_2S$: C, 48.40; H, 4.06; N, 14.11. Found: C, 48.61; H, 4.08; N, 14.05.

Compound **2e**. Yield: 86%. White crystals. Mp: 178–180°C (160°C [14]). ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 11.61 (s, 1H, NH), 7.21 (d, $J = 8.4$ Hz, 2H, ArH), 7.44 (d, $J = 8.4$ Hz, 2H, ArH), 5.53 (s, 2H, OCH_2), 4.51 (s, 2H, $ClCH_2$); IR (KBr) ν: 3195, 1707, 1585 cm^{-1}. Anal. calcd. for $C_{11}H_9Cl_2N_3O_2S$: C, 41.52; H, 2.85; N, 13.21. Found: C, 41.70; H, 2.86; N, 13.27.

Compound **2f**. Yield: 87%. White crystals. Mp: 179–180°C. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 11.60 (s, 1H, NH), 7.00 (d, $J = 8$ Hz, 2H, ArH), 6.87 (d, $J = 8$ Hz, 2H, ArH), 5.52 (s, 2H, OCH_2), 4.51 (s, 2H, $ClCH_2$), 3.71 (s, 3H, CH_3). IR (KBr) ν: 3179, 1705, 1581 cm^{-1}. Anal. calcd. for $C_{12}H_{12}ClN_3O_3S$: C, 45.94; H, 3.85; N, 13.39. Found: C, 46.13; H, 3.86; N, 13.34.

Compound **2g**. Yield: 85%. White crystals. Mp: 201–202°C. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 11.59 (s, 1H, NH), 6.90–6.83 (m, 4H, ArH), 5.50 (s, 2H, OCH_2), 4.51 (s, 2H, $ClCH_2$), 3.70 (s, 3H, CH_3). IR (KBr) ν: 3181, 1706, 1583 cm^{-1}. Anal. calcd. for $C_{12}H_{12}ClN_3O_3S$: C, 45.94; H, 3.85; N, 13.39. Found: C, 46.16; H, 3.84; N, 13.45.

Compound **2h**. Yield: 85%. White crystals. Mp: 174–176°C. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 11.61 (s, 1H, NH), 7.11–6.80 (m, 4H, ArH), 5.51 (s, 2H, OCH_2), 4.53 (s, 2H, $ClCH_2$), 2.21 (s, 3H, CH_3). IR (KBr) ν: 3190, 1708, 1580 cm^{-1}. Anal. calcd. for $C_{12}H_{12}ClN_3O_2S$: C, 48.40; H, 4.06; N, 14.11. Found: C, 48.19; H, 4.07; N, 14.17.

Compound **2i**. Yield: 80%. White crystals. Mp: 200–202°C. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 11.65 (s, 1H, NH), 7.35–6.99 (m, 4H, ArH), 5.54 (s, 2H, OCH_2), 4.56 (s, 2H, $ClCH_2$). IR (KBr) ν: 3163, 1703,

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1616 cm^{-1}. Anal. calcd. for $C_{11}H_9ClN_4O_4S$: C, 40.19; H, 2.76; N, 17.04. Found: C, 40.38; H, 2.77; N, 17.12.

Compound **2j**. Yield: 81%. White crystals. Mp: 182–184°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 11.64 (s, 1H, NH), 8.25 (d, $J = 8$ Hz, 2H, ArH), 7.30 (d, $J = 8$ Hz, 2H, ArH), 5.60 (s, 2H, OCH_2), 4.53 (s, 2H, $ClCH_2$). IR (KBr) ν: 3167, 1704, 1610 cm^{-1}. Anal. calcd. for $C_{11}H_9ClN_4O_4S$: C, 40.19; H, 2.76; N, 17.04. Found: C, 40.00; H, 2.77; N, 17.11.

Compound **2k**. Yield: 85%. White crystals. Mp: 200–202°C (148°C [14]). ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 11.61 (s, 1H, NH), 7.45–7.06 (m, 3H, ArH), 5.51 (s, 2H, OCH_2), 4.55 (s, 2H, $ClCH_2$). IR (KBr) ν: 3166, 1704, 1605, cm^{-1}. Anal. calcd. for $C_{11}H_8Cl_3N_3O_2S$: C, 37.47; H, 2.29; N, 11.92. Found: C, 37.65; H, 2.30; N, 11.88.

Compound **2l**. Yield: 86%. Yellow crystals. Mp: 198–200°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 11.64 (s, 1H, NH), 7.94–7.55 (m, 5H, ArH), 4.58 (s, 2H, $ClCH_2$). IR (KBr) ν: 3184, 1705, 1571 cm^{-1}. Anal. calcd. for $C_{10}H_8ClN_3OS$: C, 47.34; H, 3.18; N, 16.56. Found: C, 47.13; H, 3.19; N, 16.49.

Compound **2m**. Yield: 81%. White crystals. Mp: 210–211°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 11.63 (s, 1H, NH), 7.47–7.19 (m, 4H, ArH), 4.57 (s, 2H, $ClCH_2$). IR (KBr) ν: 3181, 1703, 1578 cm^{-1}. Anal. calcd. for $C_{10}H_7Cl_2N_3OS$: C, 41.68; H, 2.45; N, 14.58. Found: C, 41.86; H, 2.46; N, 14.65.

Compound **2n**. Yield: 91%. Yellow crystals. Mp: 206–208°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 11.62 (s, 1H, NH), 7.24–7.00 (m, 4H, ArH), 4.56 (s, 2H, $ClCH_2$), 2.31 (s, 3H, CH_3). IR (KBr) ν: 3201, 1702, 1575 cm^{-1}. Anal. calcd. for $C_{11}H_{10}ClN_3OS$: C, 49.35; H, 3.76; N, 15.69. Found: C, 49.58; H, 3.75; N, 15.76.

Compound **2o**. Yield: 74%. White crystals. Mp: 225–227°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 11.67 (s, 1H, NH), 8.44–7.62 (m, 4H, ArH), 4.61 (s, 2H, $ClCH_2$). IR (KBr) ν: 3176, 1713, 1585 cm^{-1}. Anal. calcd. for $C_{10}H_7ClN_4O_3S$: C, 40.21; H, 2.36; N, 18.76. Found: C, 40.38; H, 2.37; 18.84.

General Synthetic Procedure for Compounds 3a–o

The mixture of compound (**2a–o**) (1.0 mmol) and ammonium thiocyanate (0.11 g, 1.5 mmol) in DMF (4 mL) was placed into a Pyrex® open vessel and irradiated in a domestic microwave oven at 350 W for 5 min (max. temp 155°C). Progress of the reaction was monitored by thin-layer chromatography (TLC). After completion of the reaction, the reaction mixture was left

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to cool and poured onto ice water. The resulting precipitate was collected by filtration and recrystallized from EtOH–DMF to obtain **3a–o**.

Data

Compound **3a**. Yield: 92%. Yellow crystals. Mp: 226–228°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 12.37 (s, 1H, NH), 7.35–6.99 (m, 5H, ArH), 5.48 (s, 2H, OCH_2), 4.10 (s, 2H, SCH_2). ^{13}C NMR (100 MHz, DMSO-d_6) δ: 174.16, 171.55, 166.37, 163.35, 157.42, 129.85, 121.85, 115.10, 64.50, 35.08. MS: m/z 306 (5%, M^+), 213 (100%). IR (KBr) ν: 3165, 1728, 1595 cm^{-1}. Anal. calcd. for $C_{12}H_{10}N_4O_2S_2$: C, 47.04; H, 3.29; N, 18.29. Found: C, 47.24; H, 3.30; N, 18.21.

Compound **3b**. Yield: 98%. Yellow crystals. Mp: 241–242°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 12.38 (s, 1H, NH), 7.39–7.02 (m, 4H, ArH), 5.59 (s, 2H, OCH_2), 4.10 (s, 2H, SCH_2). ^{13}C NMR (100 MHz, DMSO-d_6) δ: 174.11, 171.46, 166.30, 163.46, 151.86, 130.12, 128.40, 123.45, 123.32, 116.59, 65.02, 35.76. MS: m/z 340 (16.5%, M^+), 213 (100%). IR (KBr) ν: 3121, 1726, 1603 cm^{-1}. Anal. calcd. for $C_{12}H_9ClN_4O_2S_2$: C, 42.29; H, 2.66; N, 16.44. Found: C, 42.09; H, 2.67; N, 16.52.

Compound **3c**. Yield: 92%. Yellow crystals. Mp: 246–248°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 12.35 (s, 1H, NH), 7.13–6.97 (m, 4H, ArH), 5.40 (s, 2H, OCH_2), 4.11 (s, 2H, SCH_2), 2.33 (s, 3H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6) δ: 174.09, 171.44, 166.27, 163.54, 155.83, 130.47, 127.29, 125.72, 121.84, 115.03, 65.15, 35.74, 14.52. MS: m/z 320 (7%, M^+), 213 (100%). IR (KBr) ν: 3167, 1728, 1600 cm^{-1}. Anal. calcd. for $C_{13}H_{12}N_4O_2S_2$: C, 48.73; H, 3.78; N, 17.49. Found: C, 48.92; H, 3.77; N, 17.56.

Compound **3d**. Yield: 92%. Yellow crystals. Mp: 242–244°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 12.36 (s, 1H, NH), 7.02 (d, $J = 8$ Hz, 2H, ArH), 7.18 (d, $J = 8$ Hz, 2H, ArH), 5.41 (s, 2H, OCH_2), 4.11 (s, 2H, SCH_2), 2.34 (s, 3H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6) δ: 174.10, 171.47, 166.31, 163.52, 155.46, 131.87, 131.01, 114.76, 65.13, 35.75, 24.49. MS: m/z 320 (8%, M^+), 213 (100%). IR (KBr) ν: 3168, 1731, 1598 cm^{-1}. Anal. calcd. for $C_{13}H_{12}N_4O_2S_2$: C, 48.73; H, 3.78; N, 17.49. Found: C, 48.54; H, 3.79; N, 17.42.

Compound **3e**. Yield: 97%. Yellow crystals. Mp: 247–248°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 12.39 (s, 1H, NH), 7.23 (d, $J = 8.4$ Hz, 2H, ArH), 7.43 (d, $J = 8.4$ Hz, 2H, ArH), 5.55 (s, 2H, OCH_2), 4.10 (s, 2H, SCH_2). ^{13}C NMR (100 MHz, DMSO-d_6) δ: 174.13, 171.49, 166.32, 163.42, 155.59, 129.95, 127.38, 116.52, 64.95, 35.78. MS: m/z 340 (18%, M^+), 213 (100%). IR (KBr) ν: 3125, 1721, 1602 cm^{-1}. Anal. calcd. for $C_{12}H_9ClN_4O_2S_2$: C, 42.29; H, 2.66; N, 16.44. Found: C, 42.48; H, 2.67; N, 16.51.

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Compound **3f**. Yield: 91%. Grey crystals. Mp: 207–208°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 12.35 (s, 1H, NH), 6.99 (d, $J = 8$ Hz, 2H, ArH), 6.88 (d, $J = 8$ Hz, 2H, ArH), 5.41 (s, 2H, OCH_2), 4.10 (s, 2H, SCH_2), 3.70 (s, 3H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6) δ: 174.07, 171.43, 166.24, 163.61, 154.26, 151.31, 116.32, 114.81, 65.22, 55.47, 35.73. MS: m/z 336 (13%, M^+), 213 (100%). IR (KBr) ν: 3117, 1726, 1606 cm^{-1}. Anal. calcd. for $C_{13}H_{12}N_4O_3S_2$: C, 46.42; H, 3.60; N, 16.66. Found: C, 46.28; H, 3.61; N, 16.73.

Compound **3g**. Yield: 92%. Yellow crystals. Mp: 202–203°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 12.34 (s, 1H, NH), 6.91–6.83 (m, 4H, ArH), 5.38 (s, 2H, OCH_2), 4.10 (s, 2H, SCH_2), 3.72 (s, 3H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6) δ: 174.05, 171.39, 166.20, 163.64, 147.15, 147.07, 121.81, 114.28, 65.24, 55.82, 35.72. MS: m/z 336 (10%, M^+), 213 (100%). IR (KBr) ν: 3120, 1724, 1605 cm^{-1}. Anal. calcd. for $C_{13}H_{12}N_4O_3S_2$: C, 46.42; H, 3.60; N, 16.66. Found: C, 46.61; 3.59; N, 16.73.

Compound **3h**. Yield: 88%. Yellow crystals. Mp: 217–218°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 12.37 (s, 1H, NH), 7.13–6.81 (m, 4H, ArH), 5.45 (s, 2H, OCH_2), 4.10 (s, 2H, SCH_2), 2.30 (s, 3H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6) δ: 174.11, 171.49, 163.49, 166.33, 157.74, 140.13, 129.80, 122.08, 113.95, 112.12, 64.98, 35.77, 25.15. MS: m/z 320 (8%, M^+), 213 (100%). IR (KBr) ν: 3164, 1729, 1597 cm^{-1}. Anal. calcd. for $C_{13}H_{12}N_4O_2S_2$: C, 48.73; H, 3.78; N, 17.49. Found: C, 48.96; H, 3.79; N, 17.41.

Compound **3i**. Yield: 75%. Brown crystals. Mp: 252–254°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 12.40 (s, 1H, NH), 7.35–6.99 (m, 4H, ArH), 5.60 (s, 2H, OCH_2), 4.11 (s, 2H, SCH_2). ^{13}C NMR (100 MHz, DMSO-d_6) δ: 174.18, 171.72, 166.48, 162.52, 157.83, 150.42, 130.92, 121.35, 114.28, 110.54, 65.00, 35.80. MS: m/z 351 (12%, M^+), 213 (100%). IR (KBr) ν: 3134, 1735, 1577 cm^{-1}. Anal. calcd. for $C_{12}H_9N_5O_4S_2$: C, 41.02; H, 2.58; N, 19.93. Found: C, 41.19; H, 2.57; N, 20.02.

Compound **3j**. Yield: 79%. Grey crystals. Mp: 253–255°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 12.39 (s, 1H, NH), 8.25 (d, $J = 8$ Hz, 2H, ArH), 7.30 (d, $J = 8$ Hz, 2H, ArH), 5.66 (s, 2H, OCH_2), 4.11 (s, 2H, SCH_2). ^{13}C NMR (100 MHz, DMSO-d_6) δ: 174.18, 171.85, 166.60, 162.61, 161.84, 141.73, 126.07, 115.71, 65.08, 35.80. MS: m/z 351 (15%, M^+), 213 (100%). IR (KBr) ν: 3130, 1733, 1581 cm^{-1}. Anal. calcd. for $C_{12}H_9N_5O_4S_2$: C, 41.02; H, 2.58; N, 19.93. Found: C, 41.20; H, 2.59; N, 20.01.

Compound **3k**. Yield: 82%. Yellow crystals. Mp: 224–226°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 12.36 (s, 1H, NH), 7.47–7.04 (m, 3H, ArH),

5.56 (s, 2H, OCH_2), 4.10 (s, 2H, SCH_2). ^{13}C NMR (100 MHz, DMSO-d_6) δ: 174.10, 171.44, 166.30, 163.49, 150.05, 132.24, 128.58, 128.52, 124.76, 117.82, 65.19, 35.75. MS: m/z 375 (21%, M^+), 213 (100%). IR (KBr) ν: 3129, 1734, 1586 cm^{-1}. Anal. calcd. for $C_{12}H_8Cl_2N_4O_2S_2$: C, 38.41; H, 2.15; N, 14.93. Found: C, 38.58; H, 2.16; N, 14.86.

Compound **3l**. Yield: 87%. Yellow crystals. Mp: 242–243°C. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 12.38 (s, 1H, NH), 7.95–7.54 (m, 5H, ArH), 4.13 (s, 2H, SCH_2). ^{13}C NMR (100 MHz, DMSO-d_6) δ: 185.53, 177.09, 174.13, 165.78, 131.21, 130.18, 129.57, 127.24, 35.86. MS: m/z 276 (31%, M^+), 199 (100%). IR (KBr) ν: 3111, 1726, 1583 cm^{-1}. Anal. calcd. for $C_{11}H_8N_4OS_2$: C, 47.81; H, 2.92; N, 20.27. Found: C, 48.03; H, 2.93; N, 20.36.

Compound **3m**. Yield: 87%. Yellow crystals. Mp: 222–224°C. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 12.37 (s, 1H, NH), 7.45–7.18 (m, 4H, ArH), 4.12 (s, 2H, SCH_2). ^{13}C NMR (100 MHz, DMSO-d_6) δ: 185.49, 177.05, 174.07, 165.90, 134.65, 132.94, 131.27, 130.12, 129.70, 127.56, 35.83. MS: m/z 310 (24%, M^+), 199 (100%). IR (KBr) ν: 3113, 1725, 1580 cm^{-1}. Anal. calcd. for $C_{11}H_7ClN_4OS_2$: C, 42.51; H, 2.27; N, 18.03. Found: C, 42.31; H, 2.28; N, 18.11.

Compound **3n**. Yield: 96%. Green crystals. Mp: 217–218°C. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 12.36 (s, 1H, NH), 7.25–6.98 (m, 4H, ArH), 4.12 (s, 2H, SCH_2), 2.30 (s, 3H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6) δ: 185.45, 177.02, 174.05, 165.96, 139.63, 131.37, 131.14, 130.07, 129.92, 124.25, 35.81, 25.10. MS: m/z 290 (45%, M^+), 199 (100%). IR (KBr) ν: 3120, 1722, 1572 cm^{-1}. Anal. calcd. for $C_{12}H_{10}N_4OS_2$: C, 49.64; H, 3.47; N, 19.30. Found: C, 49.86; H, 3.48; N, 19.22.

Compound **3o**. Yield: 78%. Grey crystals. Mp: 255–257°C. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 12.37 (s, 1H, NH), 8.45–7.60 (m, 4H, ArH), 4.14 (s, 2H, SCH_2). ^{13}C NMR (100 MHz, DMSO-d_6) δ: 185.78, 177.40, 174.15, 166.01, 149.56, 133.15, 131.16, 131.14, 121.90, 121.82, 35.89. MS: m/z 321 (56%, M^+), 199 (100%). IR (KBr) ν: 3102, 1737, 1651 cm^{-1}. Anal. calcd. for $C_{11}H_7N_5O_3S_2$: C, 41.12; H, 2.20; N, 21.79. Found: C, 41.31; H, 2.19; N, 21.88.

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