Received: 2 May 2019 | Revised: 31 August 2019 | Accepted: 12 September 2019

DOI: 10.1002/jhet.3761

WILEY

ARTICLE

Synthesis of pyrazine-2,3-dicarbonitriles via the one-pot three-component reaction of 4-benzoyl-5-phenylamino-2,3-dihydrothiophene-2,3-dione, diaminomaleonitrile, and functionalized alcohols in acetonitrile

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Abstract

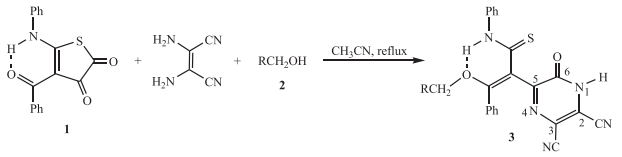
An efficient one-pot three-component reaction of 4-benzoyl-5-phenylamino-2,-3-dihydrothiophene-2,3-dione, diaminomaleonitrile, and alcohols with hetero-atom substituents or several hydroxyl groups in acetonitrile solvent under reflux led to the formation of 5-(2-substituted ethoxy or propoxy-2-phenyl-1-*N*-phenylthiocarbamoylethenyl)-6-oxo-1,6-dihydropyrazine-2,3-dicarbonitrile derivatives in good yields.

1 | INTRODUCTION

Heterocycles are considered as the largest category in organic chemistry and have a special biological and industrial significance. Pyrazines are important flavor components in food[1] and show interesting anticancer[1–4] and antituberculosis activities[1,5–8] and apply in microbial metabolism[9] and also as μ-opioid receptor antagonists.[10] Diaminomaleonitrile (DAMN) is an important pioneer for the synthesis of heterocyclic compounds.[11–13] Pyrazine-2,3-dicarbonitrile derivatives are usually synthesized through DAMN condensation, which usually have been synthesized through condensation of DAMN with α-diketones,[14–16] glyoxal, α-keto aldehydes, α-keto oximes,[11] α-keto thioester,[17] α-keto esters,[18,19] and 4-acylfuran-2,3-diones.[20] 2,3-Dicyanopyrazines are very powerful electron acceptors and are especially suitable building blocks for the functional dyes and nonlinear optical materials (NLOs).[21–23] In particular, 2,3-dicyanopyrazines can be used as a convenient precursor for fluorescent dyes and can be applied as an emitter for electro luminescence devices.[24–28] Pyrazine-2,3-dicarbonitriles may be used as precursors for tetrapyrazinoporphyrazines (TPyzPzs), the heterocyclic aza analogs of the phthalocyanines (AzaPcs).[29–33] Furthermore, pyrazine-2,3-dicarbonitrile derivatives exhibit varying degrees of biological activity[34] such as fungicidal[35] and herbicidal activities.[36] Earlier, we found that the reactions of 4-benzoyl-5-phenylamino-2,3-dihydrothiophene-2,3-dione (**1**) with DAMN in the presence of alcohols as reactant and solvent at room temperature provided 1,6-dihydropyrazine-2,3-dicarbonitrile derivatives that have *N*-phenylthiocarbamoyl group.[17] In part of our studies on 2,3-dihydrothiophene-2,3-dione **1** associated with the synthesis of the corresponding 1,6-dihydro pyrazine-2,3-dicarbonitrile derivatives, we have now achieved the one-pot three-component reaction of 2,3-dihydrothiophene-2,3-dione **1**, DAMN, and functionalized alcohols **2** with high boiling point or expensive just as a reactant in acetonitrile solvent under reflux has led to 1,6-dihydropyrazine-2,3-dicarbonitriles **3** (Schemes **1**).

2 | RESULTS AND DISCUSSION

The aim of this study was to introduce acetonitrile as a convenient solvent for one-pot three-component reaction of 4-benzoyl-5-phenylamino-2,3-dihydrothiophene-2,3-dione (**1**), DAMN, and functionalized alcohols **2** under reflux conditions (Scheme 1). In order to further optimize



SCHEME 1 One-pot three-component reaction of 4-benzoyl-5-phenylamino-2,3-dihydrothiophene-2,3-dione (**1**), diaminomaleonitrile and functionalized alcohols **2**

the reaction conditions, the model reaction was carried out using 2,3-dihydrothiophene-2,3-dione **1**, DAMN, and 2,2,2-trifluoroethanol (**2a**) under various conditions (Table 1). The reaction conditions were optimized based on the solvent and temperature used for the synthesis of the corresponding 1,6-dihydropyrazine-2,3-dicarbonitrile **3a**.

To identify the best solvent and temperature in this reaction, the model reaction was performed with different solvents such as n-hexane, CH_3Cl, THF, acetone, CH_3CN, DMF, and solvent-free under room temperature and reflux conditions (Table 1). Acetonitrile under reflux condition exhibited the best performance in the reaction (84% yield). The yield gradually increased as we shifted from less polar to more polar solvents. The refluxing plays a main role in product yield and reaction time.

To show the generality of this new method, the reactions were performed using 4-benzoyl-5-phenylamino-2,-3-dihydrothiophene-2,3-dione (**1**), DAMN, and functionalized alcohols **2** in acetonitrile solvent under reflux conditions for 2 to 3 hours in good yields (Table 2).

Compounds **3a-g** are explained by elemental analyses, IR, ^{1}H NMR, ^{13}C NMR spectroscopy, and mass spectrometry. The mass spectra of some products exhibited fairly weak molecular ion peaks. Structural comparison of **3a-g** can easily be seen through the IR and ^{13}C NMR spectra. The IR spectra of **3a-g** showed the characteristic absorption bands of C≡N, amide C—O, thioamide C—N, NH, C—S, and ether C—O—C (asy and sy) groups at 2250 to 2240, 1747 to 1728, 1545 to 1538, 1375 to 1359, 1184 to 1164, 1219 to 1207, and 1125 to 1078 cm^{-1}, respectively. Their ^{13}C NMR spectra also showed signals at δ 59.62 to 74.33, 118.72 to 122.91, 146.81 to 147.23, 162.63 to 163.25, and 188.00 to 188.24 ppm due to the carbons of the ether C—O, 2C≡N, C_5—N, amide C—O, and thioamide C—S. In the ^{1}H NMR spectra of **3a-g**, we have two sets of multiplet signals for aliphatic and aromatic protons and two broad singlets at δ 12.08 to 12.14 and 13.77 to 13.89 ppm for the amidic and thioamidic NH protons, respectively. The high deshilding of the thioamidic NH proton is probably the result of the amino group participation in the intramolecular hydrogen bonding with the oxygen of ether fragment.

Carbon atoms C-2, C-3, and C-5 in compound **1** are electrophilic sites that can display different reactivities depending on the structures of the nucleophiles and reaction conditions.[37] DAMN cyclizes by nucleophilic attack on the α-ketothioesteric fragment (C-2 and C-3) of **1**, then

TABLE 1 Optimization of one-pot three-component reaction conditions for the synthesis of 5-(2-(2′,2′,2′-trifluoroethoxy)-2-phenyl-1-*N*-phenylthiocarbamoylethenyl)-6-oxo-1,6-dihydropyrazine-2,3-dicarbonitrile (**3a**)[a]

Entry	Solvent	Time (h)	T (°C)	Yield (%)[b]
1	n-hexane	4	r.t.	11
2	n-hexane	3	Reflux	18
3	$CHCl_3$	4	r.t.	29
4	$CHCl_3$	3	Reflux	40
5	THF	4	r.t.	34
6	THF	3	Reflux	46
7	Acetone	4	r.t.	45
8	Acetone	3	Reflux	57
9	CH_3CN	3	r.t.	72
10	**CH_3CN**	**2**	**Reflux**	**84**
11	DMF	3	r.t.	70
12	DMF	2	Reflux	79
13	Solvent free	4	r.t.	31
14	Solvent free	3	50	46
15	Solvent free	3	60	42

[a]Reaction conditions: 2,3-dihydrothiophene-2,3-dione 1 (1.0 mmol), diaminomaleonitrile (1.0 mmol), 2,2,2-trifluoroethanol (2a, 1.0 mmol) and solvent (10 mL).
[b]Isolated yields.

TABLE 2 Synthesis of 5-(2-substituted ethoxy or propoxy-2-phenyl-1-*N*-phenylthiocarbamoylethenyl)-6-oxo-1,6-dihydropyrazine-2,3-dicarbonitrile derivatives (**3a-g**)[a]

Entry	R	Product	Time (h)	Yield (%)[b]
1	CF_3	3a	2	84
2	CCl_3	3b	2	80
3	$MeOCH_2$	3c	3	75
4	$HSCH_2$	3d	3	74
5	$HOCH_2CH_2SCH_2$	3e	3	77
6	$HOCH_2$	3f	3	78
7	$HOCH_2CH(oh)$	3 g	2	81

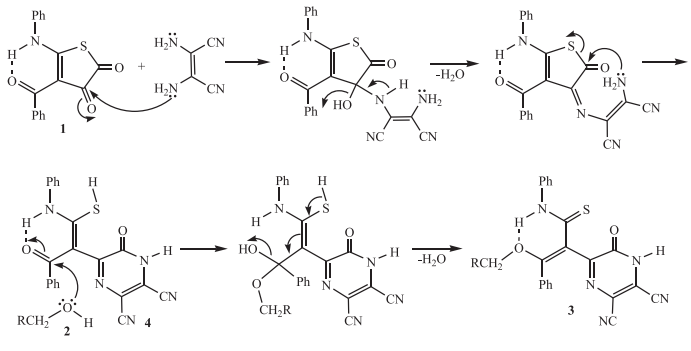
[a]Reaction conditions: 2,3-dihydrothiophene-2,3-dione **1** (1.0 mmol), diaminomaleonitrile (1.0 mmol), functionalized alcohol **2** (1.0 mmol) and acetonitrile (10 mL).
[b]Isolated yields.

the nucleophilic attack of the alcohols on the ketonic carbonyl group of intermediate **4** form 1,6-dihydropyrazine-2,3-dicarbonitrile derivatives **3** (Scheme 2).[17] In the case of phenol in order to attack the intermediate **4**, the electrons of the phenol oxygen atom are involved in the resonance with aromatic ring and to some extent they have sp^2 properties, thus phenol is not suitable as a nucleophile and does not participate in the reaction.

The significant degree of selectivity that occurs in electrophile-nucleophile interactions is predicted by Pearson's hard and soft acids and bases (HSAB) theory.[38] Therefore, compound **3d** shows that nucleophilic attack of 2-mercaptoethanol from the hydroxy group (OH) as hard nucleophile occur at ketonic carbonyl group as hard electrophile of intermediate **4** and the thiol group (SH) as soft nucleophile does not take part in the nucleophilic attack.

3 | CONCLUSIONS

An proficient method and one-pot three-component coupling for the synthesis of 5-(2-substituted ethoxy or propoxy-2-phenyl-1-*N*-phenylthiocarbamoylethenyl)-6-oxo-1,6-dihydropyrazine-2,3-dicarbonitriles (**3a-g**) is reported from the reaction of 4-benzoyl-5-phenylamino-2,3-dihydrothiophene-2,3-dione (**1**), DAMN, and functionalized alcohols **2a-g** in acetonitrile solvent under reflux conditions. This procedure provides multiple advantages over previous report,[17] such as simpler evaporation of acetonitrile than evaporation of alcohols with high boiling point, low cost of acetonitrile than some functionalized alcohols, and good isolated yields.



SCHEME 2 Proposed mechanism for the one-pot three-component synthesis of 1,6-dihydropyrazine-2,3-dicarbonitrile **3**

4 | EXPERIMENTAL

4.1 | General

The chemicals were purchased from Merck in high purity and used without further purification. All melting points are uncorrected and were determined in capillary tube on Electrothermal 9100 apparatus. The elemental analyses (C, H, and N) were obtained from a Heraeus CHN-O-Rapid analyzer. These results agree favorably with the calculated values. FT-IR spectra were recorded from KBr disk using a Thermo Nicolet 8700 spectrometer and frequencies were reported in cm^{-1}.

^1H NMR and ^{13}C NMR spectra were obtained on a Bruker DRX-300 AVANCE at 300 and 75 MHz instrument with DMSO-d_6 as solvent and using TMS as an internal standard. Chemical shifts and coupling constants were reported in ppm and Hz, respectively. Thin-layer chromatography was carried out on silica gel 254 analytical sheets obtained from Fluka. Mass spectra were recorded on an Agilent HP 5973 mass spectrometer operating at an ionization potential of 70 eV.

4.2 | Material

Ethyl 2,4-dioxo-4-phenylbutanoate was prepared from diethyl oxalate (6.0 mmol) and acetophenone (4.0 mmol) in the presence of sodium ethoxide (8.4 mmol) in absolute ethanol (30 mL) under N_2 atmosphere.[39] 4-Benzoyl-5-phenylamino-2,3-dihydrothiophene-2,3-dione (**1**) was obtained by careful addition of phenyl isothiocyanate (10 mmol) to ethyl 2,4-dioxo-4-phenylbutanoate (10 mmol) in KOH (10 mmol) and DMF (20 mL) with stirring for 24 hours at room temperature.[37]

4.3 | General procedure for the synthesis of 1,6-dihydropyrazine-2,3-dicarbonitriles (3a-g)

A mixture of 4-benzoyl-5-phenylamino-2,-3-dihydrothiophene-2,3-dione (**1**, 0.309 g, 1.0 mmol), DAMN (0.108 g, 1.0 mmol), and functionalized alcohols **2a-g** (1.0 mmol) in the acetonitrile (10 mL) was refluxed for 2 to 3 hours. The progress of the reaction was monitored by TLC (eluent AcOEt/hexane 4:1). The solvent was evaporated, the residue was recrystallized from ethanol for **3a**, **3c-e**, and methanol:hexane (9:1) for **3b**. For derivatives **3f**,**g**, the solution was poured into H_2O (10 mL), a precipitate formed, which was filtered and crystallized from ethanol: H_2O (4:1).

4.4 | 5-(2-(2′,2′,2′-Trifluoroethoxy)-2-phenyl-1-*N*-phenylthiocarbamoylethenyl)-6-oxo-1,6-dihydropyrazine-2,3-dicarbonitrile (3a)

Orange powder; yield: 0.40 g (84%); mp 218 to 22°C. IR (KBr):$^{-}\nu$ 3257 (NH), 3034 (CH, aromatic), 2248 (CN), 1740 (C—O, amide), 1603 (C—C), 1573 (NH), 1540, 1362, 1179 (C—N, NH, C—S, thioamide), 1269 (C—F), 1216, 1122 (C—O—C) cm^{-1}; ^1H NMR (DMSO-d_6): δ 5.11 (2H, q, $^3J_{HF}$ 9.0 Hz, CH_2O), 7.28 (1H, t, ^3J 7.6 Hz, CH_{para} of Ph-NH), 7.44 (2H, t, ^3J 7.6 Hz, $2CH_{meta}$ of Ph-NH), 7.49 to 7.95 (7H, m, 2Ph), 12.10, 13.86 (2H, 2br s, 2NH); ^{13}C NMR (DMSO-d_6): δ 60.46, 60.93, 61.40, 61.92 (q, $^2J_{CF}$ 36.4 Hz, CH_2O), 117.86, 121.62, 125.38, 129.14 (q, $^1J_{CF}$ 282 Hz, CF_3), 114.27 (—C), 118.83, 122.91 (2CN), 123.04, 126.46, 127.22, 128.71, 128.82, 129.21 (10C, 2Ph), 130.75 (C_{ipso} of Ph—C—C), 139.47 (C_{ipso} of Ph—NH), 147.07 (C_5), 147.52 (C_3), 149.92 (C_2), 161.27 (O—C—), 162.83 (C—O, amide), 188.08 (C—S) ppm. EI-MS: *m/z* (%) 480 ($M^+ - 1$, 16), 448 (26), 426 (30), 394 (32), 352 (8), 322 (6), 295 (8), 261 (6), 244 (15), 177 (24), 165 (16), 145 (10), 109 (15), 93 (36), 77 (100), 51 (29). Anal. Calcd for $C_{23}H_{14}F_3N_5O_2S$ (481.45): C, 57.38%; H, 2.93%; N, 14.55%; found: C, 57.60%; H, 3.18%; N, 14.76%.

4.5 | 5-(2-(2′,2′,2′-Trichloroethoxy)-2-phenyl-1-*N*-phenylthiocarbamoylethenyl)-6-oxo-1,6-dihydropyrazine-2,3-dicarbonitrile (3b)

Brown powder; yield: 0.43 g (80%); mp 248 to 250°C. IR (KBr):$^{-}\nu$ 3255 (NH), 3036 (CH, aromatic), 2249 (CN), 1747 (C—O, amide), 1601 (C—C), 1560 (NH), 1541, 1361, 1164 (C—N, NH, C—S, thioamide), 1210, 1118 (C—O—C) cm^{-1}; ^1H NMR (DMSO-d_6): δ 5.26 (2H, s, CH_2O), 7.28 (1H, t, ^3J 7.5 Hz, CH_{para} of Ph-NH), 7.44 (2H, t, ^3J 7.5 Hz, $2CH_{meta}$ of Ph—NH), 7.49–7.95 (7H, m, 2Ph), 12.13, 13.87 (2H, 2br s, 2NH); ^{13}C NMR (DMSO-d_6): δ 74.33 (CH_2O), 95.03 (CCl_3), 114.29 (—C), 118.79, 121.66 (2CN), 123.09, 126.41, 126.97, 128.68, 128.79, 129.23 (10C, 2Ph), 130.71 (C_{ipso} of Ph—C—C), 139.43 (C_{ipso} of Ph-NH), 147.23 (C_5), 148.38 (C_3), 149.90 (C_2), 161.26 (O—C—), 163.25 (C—O, amide), 188.06 (C—S) ppm. EI-MS: *m/z* (%) 534 (M^++4, 1), 532 (M^++2, 9), 530 (M^+, 26), 496 (23), 396 (5), 352 (15), 321 (12), 295 (15), 261 (10), 244 (22), 177 (16), 165 (17), 145 (13), 109 (23), 93 (81), 77 (100), 51 (36). Anal. Calcd for $C_{23}H_{14}Cl_3N_5O_2S$ (530.81): C, 52.04%; H, 2.66%; N, 13.19%; found: C, 52.23%; H, 2.84%; N, 12.95%.

4.6 | 5-(2-(2′-Methoxyethoxy)-2-phenyl-1-*N*-phenylthiocarbamoylethenyl)-6-oxo-1,6-dihydropyrazine-2,3-dicarbonitrile (3c)

Brown powder; yield: 0.34 g (75%); mp 178 to 18°C. IR (KBr):$^{-}\nu$ 3297 (NH), 2240 (CN), 1742 (C—O, amide), 1613 (C—C), 1567 (NH), 1538, 1359, 1172 (C—N, NH, C—S, thioamide), 1207, 1117, 1098 (C—O—C) cm^{-1}; ^1H NMR (DMSO-d_6): δ 3.29 (3H, s, CH_3O), 3.68, 4.49 (4H, 2br t, $2CH_2O$), 7.28 (1H, t, ^3J 7.5 Hz, CH_{para} of Ph—NH), 7.45 (2H, t, ^3J 7.5 Hz, $2CH_{meta}$ of Ph—NH), 7.52 to 7.93 (7H, m, 2Ph), 12.14, 13.77 (2H, 2br s, 2NH); ^{13}C NMR (DMSO-d_6): δ 58.13 (CH_3O), 64.91, 69.60 ($2CH_2O$), 114.26 (—C), 118.73, 121.46 (2CN), 122.91, 126.35, 126.98, 128.67, 128.75, 129.15 (10C, 2Ph), 130.62 (C_{ipso} of Ph—C—C), 139.46 (C_{ipso} of Ph-NH), 147.17 (C_5), 148.43 (C_3), 149.86 (C_2), 161.66 (O—C—), 162.78 (C—O, amide), 188.17 (C—S) ppm. EI-MS: *m/z* (%) 457 (M^+, 27), 424 (33), 354 (8), 322 (5), 295 (12), 261 (5), 244 (11), 220 (20), 165 (13), 135 (25), 109 (13), 93 (100), 77 (79), 45 (80). Anal. Calcd for $C_{24}H_{19}N_5O_3S$ (457.50): C, 63.01%; H, 4.19%; N, 15.31%; found: C, 62.84%; H, 3.98%; N, 15.09%.

4.7 | 5-(2-(2′-Mercaptoethoxy)-2-phenyl-1-*N*-phenylthiocarbamoylethenyl)-6-oxo-1,6-dihydropyrazine-2,3-dicarbonitrile (3d)

Green powder; yield: 0.34 g (74%); mp 201 to 203°C. IR (KBr):$^{-}\nu$ 3263 (NH), 3140 (CH, aromatic), 2925 (CH, aliphatic), 2249 (CN), 1736 (C—O, amide), 1545, 1375, 1182 (C—N, NH, C?S, thioamide), 1215, 1012 (C—O—C) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 1.22 (1H, br s, SH), 3.11 (2H, t, ^{3}J 6.5 Hz, CH_2SH), 3.59 (2H, t, ^{3}J 6.5 Hz, CH_2O), 7.29 (1H, t, ^{3}J 7.6 Hz, CH_{para} of Ph—NH), 7.45 (2H, t, ^{3}J 7.6 Hz, $2CH_{meta}$ of Ph-NH), 7.52 to 7.94 (7H, m, 2Ph), 12.08, 13.89 (2H, 2br s, 2NH); ^{13}C NMR (DMSO-d_6): δ 31.69 (CH_2SH), 59.62 (CH_2O), 114.21 (—C), 118.99, 121.31 (2CN), 123.03, 126.41, 127.28, 128.71, 128.81, 129.16 (10C, 2Ph), 130.75 (C_{ipso} of Ph—C—C), 139.43 (C_{ipso} of Ph—NH), 147.16 (C_5), 149.69 (C_3), 151.34 (C_2), 162.16 (O—C—), 164.609 (C—O, amide), 188.00 (C?S) ppm. EI-MS: *m/z* (%) 459 (M^+, 5), 426 (23), 388 (3), 354 (7), 322 (27), 246 (6), 165 (14), 109 (27), 93 (100), 77 (93), 51 (70). Anal. Calcd for $C_{23}H_{17}N_5O_2S_2$ (459.54): C, 60.11%; H, 3.73%; N, 15.24%; found: C, 60.27%; H, 3.53%; N, 15.02%.

4.8 | 5-(2-(2′-(2″-Hydroxyethylthio) ethoxy)-2-phenyl-1-*N*-phenylthiocarbamoylethenyl)-6-oxo-1,6-dihydropyrazine-2,3-dicarbonitrile (3e)

Olive powder; yield: 0.39 g (77%); mp 208 to 210°C. IR (KBr):$^{-}\nu$ 3511 (NH), 3112 (CH, aromatic), 2243 (CN), 1728 (C—O, amide), 1602 (C—C), 1574 (NH), 1544, 1364, 1183 (C—N, NH, C—S, thioamide), 1219, 1125 (C—O—C) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 2.68 (2H, t, ^{3}J 6.6 Hz, CH_2S), 2.92 (2H, t, ^{3}J 6.8 Hz, CH_2S), 3.56 (2H, t, ^{3}J 6.6 Hz, CH_2OH), 4.50 (2H, t, ^{3}J 6.8 Hz, CH_2O), 7.28 (1H, t, ^{3}J 7.5 Hz, CH_{para} of Ph—NH), 7.45 (2H, t, ^{3}J 7.5 Hz, $2CH_{meta}$ of Ph—NH), 7.50 to 7.94 (7H, m, 2Ph), 12.12, 13.82 (2H, 2br s, 2NH), OH proton is missing in spectrum; ^{13}C NMR (DMSO-d_6): δ 29.77, 34.31 ($2CH_2S$), 60.94 (CH_2OH), 65.21 (CH_2O), 114.28 (—C), 118.84, 121.49 (2CN), 122.94, 126.42, 126.99, 128.73, 128.83, 129.14 (10C, 2Ph), 130.69 (C_{ipso} of Ph—C—C), 139.47 (C_{ipso} of Ph—NH), 146.90 (C_5), 148.36 (C_3), 149.93 (C_2), 160.01 (O—C—), 162.63 (C—O, amide), 188.24 (C—S) ppm. EI-MS: *m/z* (%) 503 (M^+, 1), 460 (2), 426 (38), 394 (38), 352 (7), 322 (16), 295 (10), 244 (12), 220 (30), 165 (19), 109 (20), 93 (100), 77 (85), 44 (29). Anal. Calcd for $C_{25}H_{21}N_5O_3S_2$ (503.60): C, 59.62%; H, 4.20%; N, 13.91%; found: C, 59.46%; H, 4.41%; N, 14.13%.

4.9 | 5-(2-(2′-Hydroxyethoxy)-2-phenyl-1-*N*-phenylthiocarbamoylethenyl)-6-oxo-1,6-dihydropyrazine-2,3-dicarbonitrile (3f)

Orange crystals; yield: 0.35 g (78%); mp 258 to 260°C (Moloudi et al[17] yield: 0.30 g (68%); mp 257–259°C). IR (KBr):$^{-}\nu$ 3450 (NH), 3250 (OH), 2965 (CH, aliphatic), 2240 (CN), 1740 (C—O, amide), 1607 (C—C), 1573 (NH), 1542, 1363, 1184 (C—N, NH, C—S, thioamide), 1218, 1078 (C—O—C), 1032 (C—OH) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 3.73 (2H, br t, ^{3}J 4.9 Hz, CH_2OH), 4.38 (2H, t, ^{3}J 4.9 Hz, CH_2-O), 4.95 (1H, br t, OH), 7.28 (1H, t, ^{3}J 7.6 Hz, CH_{para} of Ph-NH), 7.44 (2H, t, ^{3}J 7.6 Hz, $2CH_{meta}$ of Ph-NH), 7.56 to 7.93 (7H, m, 2Ph), 12.13, 13.81 (2H, 2br s, 2NH); ^{13}C NMR (DMSO-d_6): δ 62.65 (CH_2OH), 67.50 (CH_2O), 114.23 (—C), 118.73, 121.39 (2CN), 122.95, 126.33, 126.79, 128.62, 128.74, 129.11 (10C, 2Ph), 130.64 (C_{ipso} of Ph-C—C), 139.41 (C_{ipso} of Ph—NH), 146.86 (C_5), 148.70 (C_3), 149.82 (C_2), 160.32 (O—C—), 162.89 (C—O, amide), 188.16 (C—S) ppm. EI-MS: *m/z* (%) 443 (M+, 1), 322 (6), 220 (15), 165 (9), 93 (93), 77 (51), 44 (100). Anal. Calcd for $C_{23}H_{17}N_5O_3S$ (443.48): C, 62.29%; H, 3.86%; N, 15.79%; found: C, 62.05%; H, 4.08%; N, 15.48%.

4.10 | 5-(2-(2′,3′-Dihydroxypropoxy)-2-phenyl-1-*N*-phenylthiocarbamoylethenyl)-6-oxo-1,6-dihydropyrazine-2,3-dicarbonitrile (3 g)

Dark red crystals; yield: 0.38 g (81%); mp 192 to 194°C. IR (KBr):$^{-}\nu$ 3243 (NH), 3055 (CH, aromatic), 2250 (CN), 1734 (C—O, amide), 1599 (C—C), 1559 (NH), 1540, 1363, 1176 (C—N, NH, C?S, thioamide), 1213, 1119 (C—O—C) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 3.45, 3.66, 3.84 (3H, m, CH_2OH, CHOH), 4.28, 4.41 (2H, m, CH_2O), 7.28 (1H, t, ^{3}J 7.6 Hz, CH_{para} of Ph—NH), 7.45 (2H, t, ^{3}J 7.6 Hz, $2CH_{meta}$ of Ph—NH), 7.52 to 7.94 (7H, m, 2Ph), 12.12, 13.81 (2H, 2br s, 2NH), 2OH protons are missing in spectrum; ^{13}C NMR (DMSO-d_6): δ 62.64 (CH_2OH), 67.46 (CHOH), 69.23 (CH_2O), 114.22 (—C), 118.72, 121.38 (2CN), 122.96, 126.34, 126.80, 128.67, 128.75, 129.11 (10C, 2Ph), 130.62 (C_{ipso} of Ph—C—C), 139.40 (C_{ipso} of Ph—NH), 146.87 (C_5), 148.71 (C_3), 149.81 (C_2), 160.31 (O—C—), 162.88 (C—O, amide), 188.16 (C—S) ppm. EI-MS: *m/z* (%) 473 (M^+, 1), 388 (2), 373 (38), 354 (38), 322 (16), 295 (10), 220 (12), 195 (30), 165 (19), 135 (0), 93 (100), 77 (85), 44 (29). Anal. Calcd for $C_{24}H_{19}N_5O_4S$ (473.50): C, 60.88%; H, 4.04%; N, 14.79%; found: C, 60.59%; H, 3.86%; N, 15.03%.

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SUPPORTING INFORMATION

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How to cite this article: Shahnaei R, Kabirifard H, Fathololoomi P. Synthesis of pyrazine-2,3-dicarbonitriles via the one-pot three-component reaction of 4-benzoyl-5-phenylamino-2,3-dihydrothiophene-2,3-dione, diaminomaleonitrile, and functionalized alcohols in acetonitrile. *J Heterocyclic Chem*. 2019;1–6. https://doi.org/10.1002/jhet.3761