

## Bis(2-cyanoacetamides): versatile precursors for bis(dihydropyridine-3,5-dicarbonitriles)

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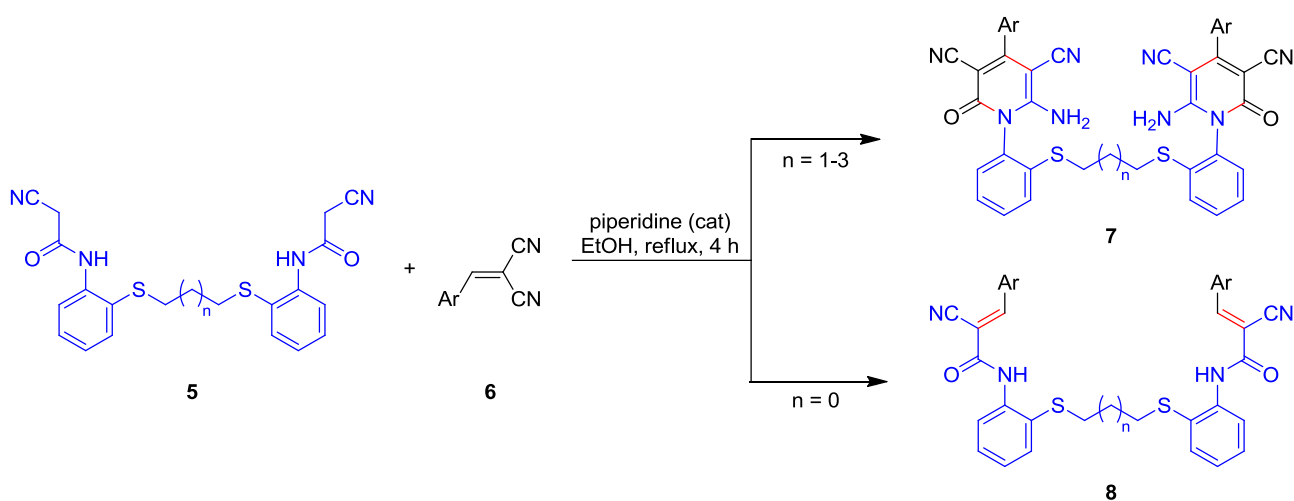
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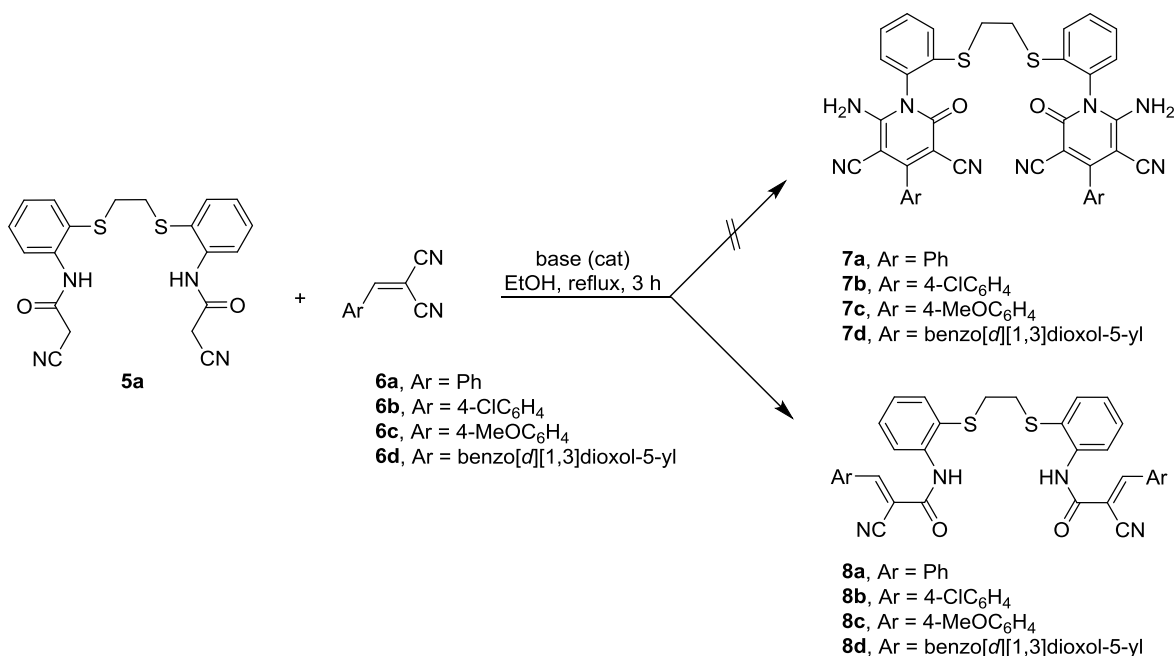
### Abstract

Bis(6-amino-1,2-dihydropyridine-3,5-dicarbonitriles) containing thioether linkages are prepared *via* the condensation of bis(cyanoacetamides) with  $\alpha$ -substituted cinnamionitriles in the presence of piperidine. The target compounds can also be obtained *via* a three-component reaction of bis(cyanoacetamides) with two equivalents of both aldehydes and malononitrile in ethanol containing piperidine as a base.



**Keywords:** Bis(cyanoacetamides), Michael addition, bis(dihydropyridine-3,5-dicarbonitrile), thioether linkage

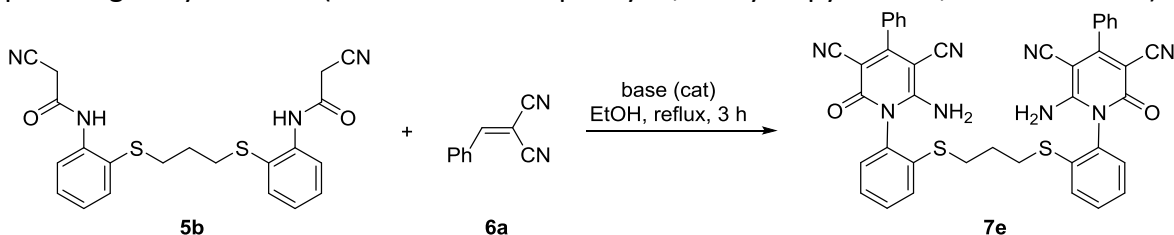




### Scheme 2. Unexpected formation of bis(2-cyano-3-phenylacrylamides) **8a-d**.

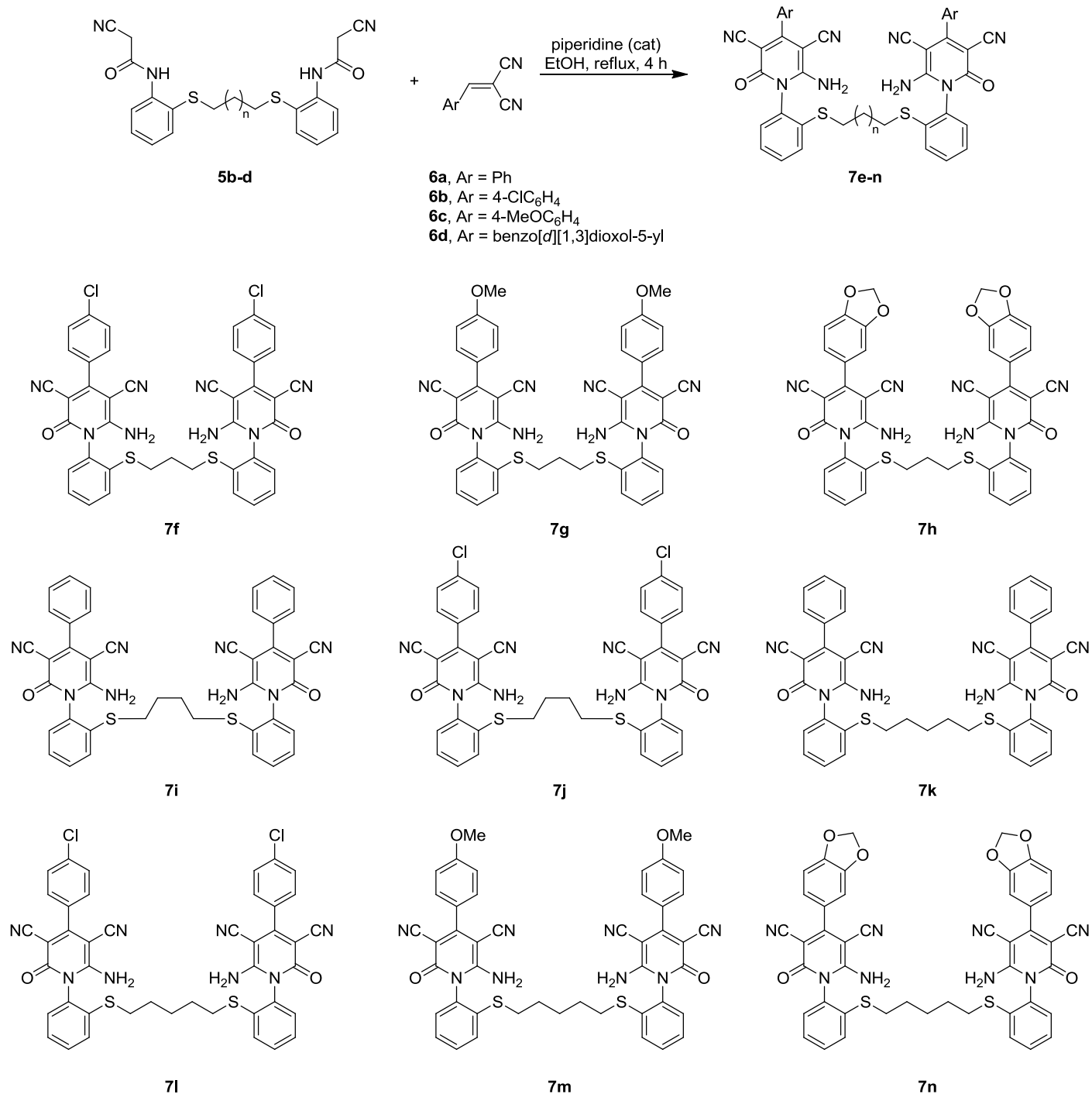
Fortunately, by increasing the number of methylene units between the two cyanoacetamide moieties, the desired products **7** could be obtained. Thus the reaction of bis(2-cyanoacetamide) **5b**, containing propyl linkage with benzylidenemalononitrile **6a** in refluxing ethanol in the presence of a variety of base catalysts including DBU, piperidine, DABCO, and triethylamine afforded the corresponding bis(6-amino-2-oxo-4-phenyl-1,2-dihydropyridine-3,5-dicarbonitrile) **7e** in good yield (Table 1).

**Table 1.** Optimizing the yield of bis(6-amino-2-oxo-4-phenyl-1,2-dihydropyridine-3,5-dicarbonitrile) **7e**



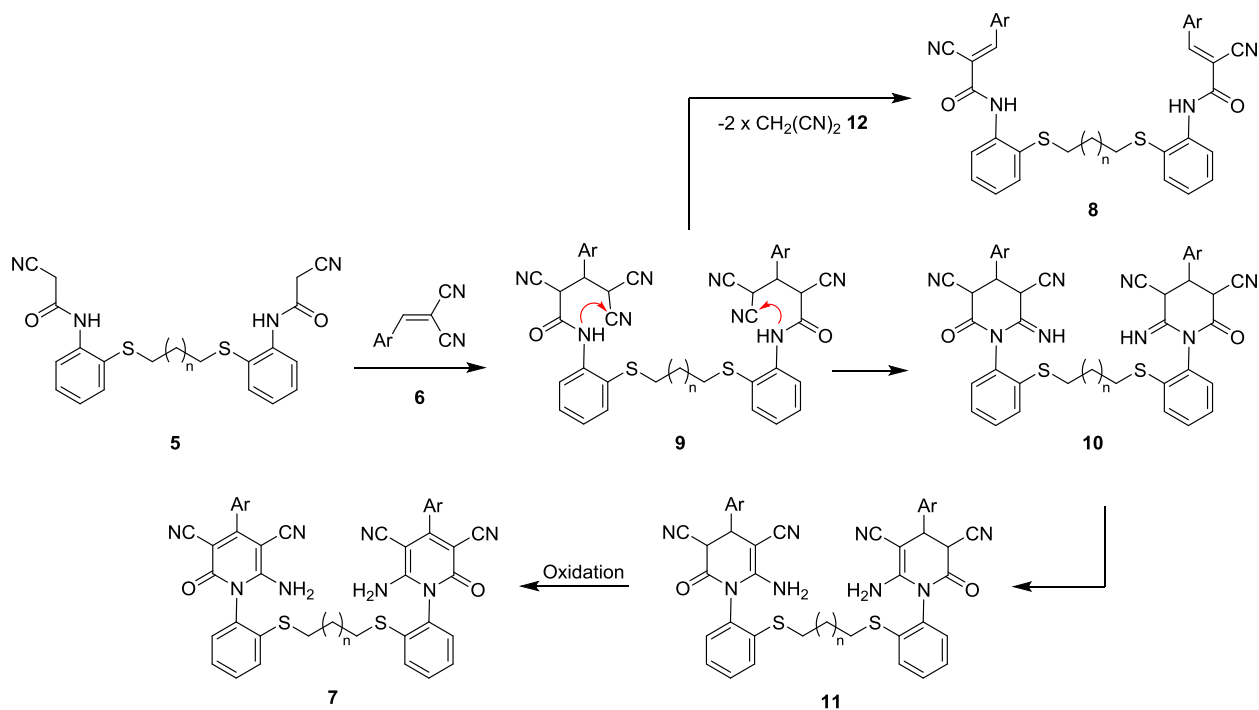
Entry	Base	Yield <b>7e</b> (%)
1	DBU	79
2	Piperidine	85
3	DABCO	82
4	Et <sub>3</sub> N	78

The use of piperidine in ethanol gave marginally better yields. With these conditions in hands, the scope of this reaction was investigated. A variety of bis(cyanoacetamides) containing thioether linkages **5b-d** underwent Michael-type addition reaction to the double bond of arylidene malononitriles **6a-d** in ethanol at reflux in the presence of piperidine leading to the formation of bis(pyridines) linked *via* thioethers **7** (Scheme 4).



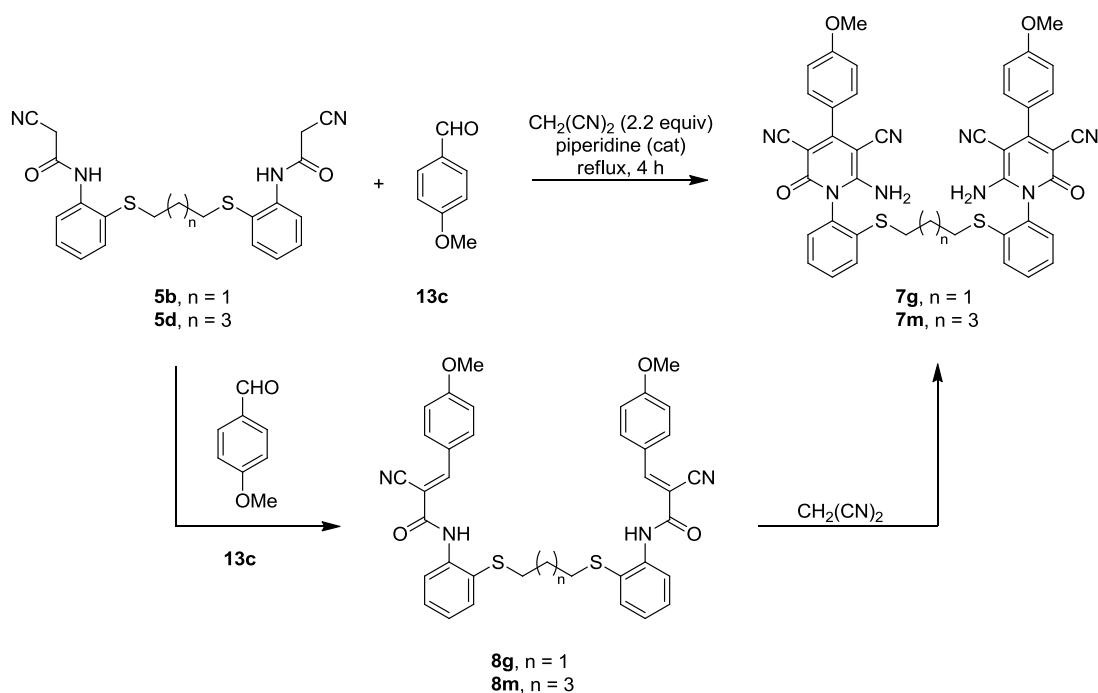
**Scheme 4.** Synthesis of bis(pyridine) derivatives **7f-n**.

The reaction proceeds most likely *via* initial Michael addition of the bis(cynomethylamide) **5** to the active C=C bond in arylidene malononitrile **6**, leading to the formation of adduct **9**. The cyclization involving NH and cyano group of the amide **9** leads to the formation of **10**. Isomerization of **10** to **11** and subsequent oxidation leads to the formation of the final isolable products **7** (Scheme 5). In few examples, especially those containing short thioether linkage, the adducts **9**, presumably for steric reasons, did not cyclize to give **7** but gave the bis(2-cyanoacrylamides) **8** *via* the loss of two molecules of malononitrile **12**.



**Scheme 5.** Proposed mechanism.

This pathway was confirmed by successful isolation of the bis(2-cyanoacrylamides) **8g** and **8m** through the direct reaction of bis(cyanoacetamides) **5b** and **5d** with 4-methoxybenzaldehyde **13c**. Subsequent reactions of **8g** and **8m** with malononitrile **12** gave compounds **7g** and **7m**, respectively. Moreover, the three-component reaction of 4-methoxybenzaldehyde **13c**, malononitrile **12** and bis(cyanoacetamides) **5b** and **5d** afforded the same products **7g** and **7m**, respectively, in good yield (Scheme 6).



**Scheme 6.** Synthesis of bis(pyridines) **7** through one pot three component reaction.

Elemental analyses as well as the spectroscopic data of the obtained products **7** support the proposed structures. The IR spectrum of **7f**, as a representative example, indicated the presence of the amino group at  $\bar{\nu}$  3437 and 3310  $\text{cm}^{-1}$ , C $\equiv$ N group at  $\bar{\nu}$  2216  $\text{cm}^{-1}$  and a characteristic band at  $\bar{\nu}$  1678  $\text{cm}^{-1}$ , which refers to the C=O group.  $^1\text{H}$  NMR spectrum displayed two broad singlets at  $\delta_{\text{H}}$  1.88 and 3.07 assigned to the propane linkage. In addition, it showed a broad singlet signal at  $\delta_{\text{H}}$  8.04 exchangeable with  $\text{D}_2\text{O}$  assignable to the  $\text{NH}_2$  protons. The aromatic protons appear at their expected positions in the region 7.40-7.68 ppm.

## Conclusions

An efficient synthesis of thioether-linked bis(cyanoacetamides) was developed. The compounds were investigated as building blocks for new bis(6-amino-1,2-dihydropyridine-3,5-dicarbonitriles) *via* Michael addition reactions with arylidenemalononitrile derivatives. The structural assignments of the new compounds were supported by spectroscopic data and elemental analyses. A rational mechanistic pathway for the formation of the products was proposed.

## Experimental Section

**General.** Melting points were measured with a Stuart melting point apparatus and are uncorrected. The IR spectra were recorded using a FTIR Bruker–vector 22 spectrophotometer as KBr pellets. The  $^1\text{H}$  NMR spectra were recorded in  $\text{DMSO}-d_6$  as solvent on Varian Gemini NMR spectrometer at 300 MHz using TMS as internal standard. Chemical shifts are reported as  $\delta$  values in ppm. Mass spectra were recorded with a Shimadzu GCMS–QP–1000 EX mass spectrometer in EI (70 eV) model. The elemental analyses were performed at the Micro analytical center, Cairo University.

**Synthesis of  $N,N'$ -{[alkane-1, $\omega$ -diylbis(sulfanediyl)]bis(2,1-phenylene)}bis(2-cyanoacetamide) (**5a-d**).** A solution of 1-cyanoacetyl-3,5-dimethylpyrazole **4** (0.2 mol) was added to a solution of bis(amines) **3a-d** (0.1 mol) in toluene (100 mL) and the mixture was refluxed for 5 h. After cooling, the deposited solid was collected and recrystallized from toluene, yielding **5a-d**, respectively.

**$N,N'$ -{[Ethane-1,2-diylbis(sulfanediyl)]bis(2,1-phenylene)}bis(2-cyanoacetamide) (**5a**).** Colorless crystals (390 mg, 95%), mp 192-194 °C (EtOH); IR ( $\bar{\nu}$   $\text{cm}^{-1}$ ): 3294 (NH), 2205 (CN), 1682 (CO);  $^1\text{H}$  NMR ( $\text{DMSO}-d_6$ ):  $\delta_{\text{H}}$  3.01 (s, 4H,  $\text{SCH}_2$ ), 3.94 (s, 4H,  $\text{CH}_2\text{CN}$ ), 7.16-7.55 (m, 8H, ArH's), 9.73 (s, 2H, 2 NH); Anal. For  $\text{C}_{20}\text{H}_{18}\text{N}_4\text{O}_2\text{S}_2$  (410.51) Calcd: C, 58.52; H, 4.42; N, 13.65. Found: C, 58.31; H, 4.63; N, 13.78%.

**$N,N'$ -{[Pentane-1,5-diylbis(sulfanediyl)]bis(2,1-phenylene)}bis(2-cyanoacetamide) (**5d**).** Colorless crystals (384 mg, 85%), mp 154-156 °C (EtOH); IR ( $\bar{\nu}$   $\text{cm}^{-1}$ ): 3447, 3306 ( $\text{NH}_2$ ), 2214 (CN), 1670 (CO);  $^1\text{H}$  NMR ( $\text{DMSO}-d_6$ ):  $\delta_{\text{H}}$  1.50-1.52 (m, 6H,  $\text{SCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{S}$ ), 2.85 (t, 4H,  $\text{SCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{S}$ ), 3.94 (s, 4H,  $\text{CH}_2\text{-CN}$ ), 7.18-7.50 (m, 8H, ArH's), 9.69 (br. s, 2H, 2 NH); Anal. for  $\text{C}_{23}\text{H}_{24}\text{N}_4\text{O}_2\text{S}_2$  (452.59) Calcd: C, 61.04; H, 5.35; N, 12.38. Found: C, 61.23; H, 5.47; N, 12.51%.

### General procedure for synthesis of compound **7e-n**

**Method A.** A mixture of bis(2-cyanoacetamides) **5a-d** (1 mmol) and activated cinnamionitriles **6a-d** (2.2 mmol) in absolute ethanol (15 mL) was heated at reflux in the presence of piperidine (0.2 mL) for 3 h. The crude solids were isolated and recrystallized from the proper solvent.

**Method B.** To a mixture of bis(2-cyanoacetamides) **5a-d**, aromatic aldehydes **13a-d** (2.2 mmol) and malononitrile **11** (2.2 mmol) in absolute ethanol (15 mL) piperidine (0.2 mL) was added. The mixture was heated at reflux for 3 h. The crude solids were isolated and recrystallized from the proper solvent.

**1,1'-[[Propane-1,3-diylbis(sulfanediyl)]bis(2,1-phenylene)]bis(6-amino-2-oxo-4-phenyl-1,2-dihydropyridine-3,5-dicarbonitrile) (7e).** Brown crystals (Method A. 618 mg, 85%), mp208-210 °C (Dioxane/EtOH, 25:75) IR ( $\bar{\nu}$  cm<sup>-1</sup>): 3441, 3311 (NH<sub>2</sub>), 2214 (CN), 1679 (CO); <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>):  $\delta_{\text{H}}$  1.86-1.90 (m, 2H, SCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>S), 3.07 (t, 4H, SCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>S), 7.25-7.64 (m, 18H, ArH's), 8.00 (s, br, 4H, 2 NH<sub>2</sub>); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>):  $\delta_{\text{C}}$  27.5, 29.7, 74.8, 115.4, 116.1, 127.4, 127.8, 128.6, 129.5, 130.3, 130.7, 132.0, 132.5, 134.4, 156.5, 158.7, 161.5; Anal. for C<sub>41</sub>H<sub>28</sub>N<sub>8</sub>O<sub>2</sub>S<sub>2</sub> (728.85) Calcd: C, 67.57; H, 3.87; N, 15.37. Found: C, 67.88; H, 4.12; N, 15.02%.

**1,1'-[[Propane-1,3-diylbis(sulfanediyl)]bis(2,1-phenylene)]bis[6-amino-4-(4-chlorophenyl)-2-oxo-1,2-dihydropyridine-3,5-dicarbonitrile] (7f).** Brown crystals (Method A: 438 mg, 55%), mp200-202 °C (Dioxane/EtOH, 25:75); IR ( $\bar{\nu}$  cm<sup>-1</sup>): 3437, 3310 (NH<sub>2</sub>), 2216 (CN), 1678 (CO); <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>):  $\delta_{\text{H}}$  1.85-1.92 (m, 2H, SCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>S), 3.07 (t, 4H, SCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>S), 7.40-7.68 (m, 16H, ArH's), 8.04 (s, br, 4H, 2 NH<sub>2</sub>); Anal. for C<sub>41</sub>H<sub>26</sub>Cl<sub>2</sub>N<sub>8</sub>O<sub>2</sub>S<sub>2</sub> (797.73) Calcd: C, 61.73; H, 3.29; N, 14.05. Found: C, 61.99; H, 3.50; N, 14.20%.

**1,1'-[[Propane-1,3-diylbis(sulfanediyl)]bis(2,1-phenylene)]bis[6-amino-4-(4-methoxyphenyl)-2-oxo-1,2-dihydropyridine-3,5-dicarbonitrile] (7g).** Pale yellow crystals (Method A, 551 mg, 70%; Method B, 592 mg, 75%), mp164-166 °C (EtOH); IR ( $\bar{\nu}$  cm<sup>-1</sup>): 3448, 3304 (NH<sub>2</sub>), 2215 (CN), 1669 (CO); <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>):  $\delta_{\text{H}}$  1.84-1.88 (m, 2H, SCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>S), 3.07 (t, 4H, SCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>S), 3.86 (s, 6H, 2 OCH<sub>3</sub>), 6.92-7.60 (m, 16H, ArH's), 8.03 (s, br, 4H, 2 NH<sub>2</sub>); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>):  $\delta_{\text{C}}$  27.8, 31.7, 55.2, 74.9, 113.9, 115.8, 116.4, 120.7, 126.4, 127.4, 129.5, 129.7, 130.5, 132.5, 135.7, 156.6, 158.9, 160.7, 161.0; Anal. for C<sub>43</sub>H<sub>32</sub>N<sub>8</sub>O<sub>4</sub>S<sub>2</sub> (788.90) Calcd: C, 65.47; H, 4.09; N, 14.20. Found: C, 65.19; H, 4.31; N, 14.32%.

**1,1'-[[Propane-1,3-diylbis(sulfanediyl)]bis(2,1-phenylene)]bis[6-amino-4-(benzo[d][1,3]dioxol-5-yl)-2-oxo-1,2-dihydropyridine-3,5-dicarbonitrile] (7h).** Pale yellow crystals (Method A, 587 mg, 72%), mp208-210 °C (Dioxane/EtOH, 25:75); IR ( $\bar{\nu}$  cm<sup>-1</sup>): 3442, 3326 (NH<sub>2</sub>), 2216 (CN), 1675 (CO); <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>):  $\delta_{\text{H}}$  1.84-1.88 (m, 2H, SCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>S), 3.09 (t, 4H, SCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>S), 6.16 (s, 4H, 2 OCH<sub>2</sub>O), 6.86-7.62 (m, 14H, ArH's), 7.95 (s, br, 4H, 2 NH<sub>2</sub>); Anal. for C<sub>43</sub>H<sub>28</sub>N<sub>8</sub>O<sub>6</sub>S<sub>2</sub> (816.87) Calcd: C, 63.23; H, 3.46; N, 13.72. Found: C, 63.00; H, 3.70; N, 13.99%.

**1,1'-[[Butane-1,4-diylbis(sulfanediyl)]bis(2,1-phenylene)]bis(6-amino-2-oxo-4-phenyl-1,2-dihydropyridine-3,5-dicarbonitrile) (7i).** Pale yellow crystals (Method A 504 mg, 68%), mp> 300 °C (Dioxane/EtOH, 25:75); IR ( $\bar{\nu}$  cm<sup>-1</sup>): 3443, 3315 (NH<sub>2</sub>), 2214 (CN), 1677 (CO); <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>):  $\delta_{\text{H}}$  1.69 (t, 4H, SCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>S), 2.98 (t, 4H, SCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>S), 7.40-7.57 (m, 18H, ArH's), 7.96 (s, br, 4H, 2 NH<sub>2</sub>); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>):  $\delta_{\text{C}}$  27.5, 31.2, 74.9, 115.5, 116.2, 120.7, 124.9, 127.5, 127.9, 128.6, 129.7, 130.3, 130.7, 132.3, 134.5, 135.6, 156.6, 158.8, 161.6; Anal. for C<sub>42</sub>H<sub>30</sub>N<sub>8</sub>O<sub>2</sub>S<sub>2</sub> (742.88) Calcd: C, 67.91; H, 4.07; N, 15.08. Found: C, 67.78; H, 4.24; N, 15.33%.

**1,1'-[[Butane-1,4-diylbis(sulfanediyl)]bis(2,1-phenylene)]bis[6-amino-4-(4-chlorophenyl)-2-oxo-1,2-dihydropyridine-3,5-dicarbonitrile] (7j).** Brown crystals (Method A: 405 mg, 50%), mp180-182 °C (Dioxane/EtOH, 25:75); IR ( $\bar{\nu}$  cm<sup>-1</sup>): 3439, 3308 (NH<sub>2</sub>), 2213 (CN), 1676 (CO); <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>):  $\delta_{\text{H}}$  1.68 (t, 4H, SCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>S), 2.97 (t, 4H, SCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>S), 7.22-7.67 (m, 16H, ArH's), 8.03 (s, br, 4H, 2 NH<sub>2</sub>); Anal. for C<sub>42</sub>H<sub>28</sub>Cl<sub>2</sub>N<sub>8</sub>O<sub>2</sub>S<sub>2</sub> (811.76) Calcd: C, 62.14; H, 3.48; N, 13.80. Found: C, 62.48; H, 3.66; N, 13.58%.

**1,1'-[[Pentane-1,5-diylbis(sulfanediyl)]bis(2,1-phenylene)]bis(6-amino-2-oxo-4-phenyl-1,2-dihydropyridine-3,5-dicarbonitrile) (7k).** Pale orange crystals (Method A: 522 mg, 69%), mp192-194 °C (Dioxane/EtOH, 25:75); IR ( $\bar{\nu}$  cm<sup>-1</sup>): 3440, 3314 (NH<sub>2</sub>), 2216 (CN), 1680 (CO); <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>):  $\delta_{\text{H}}$  1.55-1.58 (m, 6H, SCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>S), 2.95 (t, 4H, SCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>S), 7.23-7.57 (m, 18H, ArH's), 7.96 (s, br, 4H, 2 NH<sub>2</sub>); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>):  $\delta_{\text{C}}$  27.2, 27.9, 31.7, 74.8, 115.4, 115.9, 120.2, 126.3, 127.4, 127.8, 129.8, 130.2, 130.6, 132.3,

134.4, 135.6, 156.6, 158.7, and 161.5; Anal. for  $C_{43}H_{32}N_8O_2S_2$  (756.90) Calcd: C, 68.24; H, 4.26; N, 14.80. Found: C, 68.01; H, 4.10; N, 15.03%.

**1,1'-[[Pentane-1,5-diylbis(sulfanediyl)]bis(2,1-phenylene)]bis[6-amino-4-(4-chlorophenyl)-2-oxo-1,2-dihydropyridine-3,5-dicarbonitrile] (7l).** Pale yellow crystals (Method A. 487 mg, 59%), mp156-158 °C (EtOH); IR ( $\bar{\nu}$   $cm^{-1}$ ): 3440, 3316 (NH<sub>2</sub>), 2218 (CN), 1681 (CO); <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>):  $\delta_H$  1.55-1.57 (m, 6H, SCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>S), 2.91 (t, 4H, SCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>S), 7.23-7.68 (m, 16H, ArH's), 8.01 (s, br, 4H, 2 NH<sub>2</sub>); Anal. for  $C_{43}H_{30}Cl_2N_8O_2S_2$  (825.79) Calcd: C, 62.54; H, 3.66; N, 13.57. Found: C, 62.39; H, 3.28; N, 13.74%.

**1,1'-[[Pentane-1,5-diylbis(sulfanediyl)]bis(2,1-phenylene)]bis[6-amino-4-(4-methoxyphenyl)-2-oxo-1,2-dihydropyridine-3,5-dicarbonitrile] (7m).** Pale yellow crystals (Method A. 693 mg, 85%; Method B, 662 mg, 81%), mp314-316 °C (Dioxane); IR ( $\bar{\nu}$   $cm^{-1}$ ): 3447, 3306 (NH<sub>2</sub>), 2214 (CN), 1670 (CO); <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>):  $\delta_H$  1.55-1.58 (m, 6H, SCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>S), 2.94 (t, 4H, SCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>S), 3.85 (s, 6H, 2 OCH<sub>3</sub>), 7.10-7.61 (m, 16H, ArH's), 7.88 (s, br, 4H, 2 NH<sub>2</sub>); Anal. for  $C_{45}H_{36}N_8O_4S_2$  (816.96) Calcd: C, 66.16; H, 4.44; N, 13.72. Found: C, 66.35; H, 4.15; N, 13.98%.

**1,1'-[[Pentane-1,5-diylbis(sulfanediyl)]bis(2,1-phenylene)]bis[6-amino-4-(benzo[d][1,3]dioxol-5-yl)-2-oxo-1,2-dihydropyridine-3,5-dicarbonitrile] (7n).** Pale yellow crystals (Method A. 659 mg, 78%), mp186-188 °C (Dioxane/EtOH, 25:75); IR ( $\bar{\nu}$   $cm^{-1}$ ): 3444, 3327 (NH<sub>2</sub>), 2217 (CN), 1676 (CO); <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>):  $\delta_H$  1.54-1.56 (m, 6H, SCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>S), 2.94 (t, 4H, SCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>S), 6.16 (s, 4H, 2 OCH<sub>2</sub>O), 6.86-7.63 (m, 14H, ArH's), 7.91 (s, br, 4H, 2 NH<sub>2</sub>); Anal. for  $C_{45}H_{32}N_8O_6S_2$  (844.92) Calcd: C, 63.97; H, 3.82; N, 13.26. Found: C, 63.74; H, 3.99; N, 13.02%.

**General procedure for the preparation of compounds (8).** A mixture of substituted aldehydes **13** (2 mmol) and bis(2-cyanoacetamide) **5** (1 mmol) was refluxed in ethanol (20 mL) in the presence of piperidine (0.2 mL) for 3 h. The solid products so formed were recrystallized from dioxane or dioxane/EtOH (25:75).

**N,N'-[[Ethane-1,2-diylbis(sulfanediyl)]bis(2,1-phenylene)]bis[2-cyano-3-phenylacrylamide] (8a).** Colorless crystals (558 mg, 95%), mp220-222 °C (Dioxane/EtOH, 25:75); IR ( $\bar{\nu}$   $cm^{-1}$ ): 3294 (NH), 2205 (CN), 1682 (CO); <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>):  $\delta_H$  3.05 (s, 4H, SCH<sub>2</sub>), 7.22-8.00 (m, 18H, ArH's), 8.36 (s, 2H, 2 CH=C(CN)), and 9.93 (s, 2H, 2 NH); Anal. For  $C_{34}H_{26}N_4O_2S_2$  (586.73) Calcd: C, 69.60; H, 4.47; N, 9.55. Found: C, 69.25; H, 4.69; N, 9.77%.

**N,N'-[[Ethane-1,2-diylbis(sulfanediyl)]bis(2,1-phenylene)]bis[3-(4-chlorophenyl)-2-cyanoacrylamide] (8b).** Colorless crystals (590 mg, 90%), mp246-248 °C (Dioxane); IR ( $\bar{\nu}$   $cm^{-1}$ ): 3290 (NH), 2200 (CN), 1677 (CO); <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>):  $\delta_H$  3.02 (s, 4H, SCH<sub>2</sub>), 7.19-8.04 (m, 16H, ArH's), 8.33 (s, 2H, 2 CH=C(CN)), and 9.74 (s, 2H, 2 NH); Anal. for  $C_{34}H_{24}Cl_2N_4O_2S_2$  (655.61) Calcd: C, 62.29; H, 3.69; N, 8.55. Found: C, 62.02; H, 3.45; N, 8.78%.

**N,N'-[[Ethane-1,2-diylbis(sulfanediyl)]bis(2,1-phenylene)]bis[2-cyano-3-(4-methoxyphenyl)acrylamide] (8c).** Colorless crystals (563 mg, 87%), mp208-210 °C (Dioxane/EtOH, 25:75); IR ( $\bar{\nu}$   $cm^{-1}$ ): 3290 (NH), 2200 (CN), 1672 (CO); <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>):  $\delta_H$  3.28 (s, 4H, SCH<sub>2</sub>), 3.93 (s, 6H, OCH<sub>3</sub>) 7.10-8.28 (m, 18H, ArH's and CH=C(CN)), 9.72 (br. s, 2H, 2 NH); Anal. for  $C_{36}H_{30}N_4O_4S_2$  (646.78) Calcd: C, 66.85; H, 4.68; N, 8.66. Found: C, 66.72; H, 4.46; N, 8.87%.

**N,N'-[[Ethane-1,2-diylbis(sulfanediyl)]bis(2,1-phenylene)]bis[3-(benzo[d][1,3]dioxol-5-yl)-2-cyanoacrylamide] (8d).** Colorless crystals (560 mg, 83%), mp274-276 °C (Dioxane/EtOH, 25:75); IR ( $\bar{\nu}$   $cm^{-1}$ ): 3290 (NH), 2200 (CN), 1672 (CO); <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>):  $\delta_H$  3.02 (s, 4H, SCH<sub>2</sub>), 6.17 (s, 4H, 2 OCH<sub>2</sub>O), 7.09-7.86 (m, 14H, ArH's), 8.21 (s, 2H, CH=C(CN)), 9.72 (br. s, 2H, 2 NH); Anal. for  $C_{36}H_{26}N_4O_6S_2$  (674.75) Calcd: C, 64.08; H, 3.88; N, 8.30. Found: C, 64.19; H, 3.62; N, 8.45%.

**N,N'-[[Propane-1,3-diylbis(sulfanediyl)]bis(2,1-phenylene)]bis[2-cyano-3-(4-methoxyphenyl)acrylamide] (8g).** Pale yellow crystals (522 mg, 79%), mp202-204 °C (Dioxane/EtOH, 25:75); IR ( $\bar{\nu}$   $cm^{-1}$ ): 3448, 3304 (NH<sub>2</sub>), 2215 (CN), 1669 (CO); <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>):  $\delta_H$  1.741.77 (m, 2H, SCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>S), 2.97 (t, 4H, SCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>S), 3.87



(s, 6H, 2 OCH<sub>3</sub>), 7.12-7.99 (m, 16H, ArH's), 8.25 (s, 2H, CH=C(CN)), 9.66 (br. s, 2H, 2 NH); Anal. for C<sub>37</sub>H<sub>32</sub>N<sub>4</sub>O<sub>4</sub>S<sub>2</sub> (660.81) Calcd: C, 67.25; H, 4.88; N, 8.48. Found: C, 67.49; H, 4.99; N, 8.55%.

**N,N'-[Pentane-1,5-diylbis(sulfanediy)]bis(2,1-phenylene)]bis[2-cyano-3-(4-methoxyphenyl)acrylamide] (8m).** Pale yellow crystals (585 mg, 85%), mp134-136 °C (EtOH); IR ( $\bar{\nu}$  cm<sup>-1</sup>): 3447, 3306 (NH<sub>2</sub>), 2214 (CN), 1670 (CO); <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>):  $\delta$ <sub>H</sub> 1.49-1.50 (m, 6H, SCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>S), 2.85 (t, 4H, SCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>S), 3.87 (s, 6H, 2 OCH<sub>3</sub>), 7.13-8.04 (m, 16H, ArH's), 8.28 (s, 2H, CH=C(CN)), 9.70 (br. s, 2H, 2 NH); Anal. for C<sub>39</sub>H<sub>36</sub>N<sub>4</sub>O<sub>4</sub>S<sub>2</sub> (688.86) Calcd: C, 68.00; H, 5.27; N, 8.13. Found: C, 68.31; H, 5.41; N, 8.03%.

## Supplementary Material

Supplementary material for this article is available; copies of <sup>1</sup>H NMR spectra of compounds **5a**, **d**; **7f-i**; and **7k-n** and <sup>13</sup>C NMR spectra of compounds **7g**, **i**; **8a-d**; and **8g**, **m**. This material can be found *via* the "Supplementary Content" section of this article's webpage.

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