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# 2-Cyanopyridazin-3(2*H*)-ones: effective and chemoselective electrophilic cyanating agents

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**Abstract**—2-Cyanopyridazin-3(2*H*)-ones are novel, effective, selective and electrophilic cyanating agents. A variety of amino, thiol and carbon nucleophiles are chemoselectively *N*-, *S*- or *C*-cyanated in excellent yield using 2-cyanopyridanzin-3(2*H*)-ones in water or tetrahydrofuran.


## 1. Introduction

The introduction of a cyano group via carbon–carbon, carbon–nitrogen and carbon–sulfur forming reactions is a fundamental process in organic synthesis. Compounds containing the *N*-, *S*-, or *C*-cyano functional group are also found among many pharmaceuticals and their intermediates.[1,2] There are a limited number of reagents that can serve as a cyano cation ($CN^+$) equivalent or synthon, inter alia, tosyl cyanide,[3,4] 2-chlorobenzylthiocyanate,[5] cyanogen chloride,[6] 1-cyanobenzotriazole,[7,8] and 1-cyanoimidazole.[9] However, problems with poor solubility, lack of reactivity, cost, stability, corrosiveness, toxicity, complicated preparation, and/or availability have prompted the continuing search for a more effective, mild, and convenient class of electrophilic cyanating agents. Since, pyridazin-3(2*H*)-ones **1** readily form stable anions,[10] are good leaving groups, and have been used as a novel synthetic auxiliary.[11–14] Our attention focused upon their utility as electrophilic cyanating agents. Herein, we report the first synthesis and the application of the hitherto unknown 2-cyanopyridazin-3(2*H*)-ones **2** as electrophilic cyanating reagents toward various amines, sulfur, and carbon nucleophilies.

## 2. Results and discussion

A variety of 2-cyanopyridazin-3(2*H*)-ones **2** were readily prepared by treating the corresponding pyridazin-3(2*H*)-ones **1** with cyanogen bromide and triethylamine in tetrahydrofuran at room temperature (Table 1). Yields were good to excellent even in the presence of halide, phenolic, azide, and heteroatom substituents (Scheme 1).

**Table 1**. Preparation of 2-cyanopyridazin-3(2*H*)-ones (**2**)[a]

| Entry | **2** | Time (h) | Yield (%)[b] |
|---|---|---|---|
| 1 | **2a** | 1.2 | 92 |
| 2 | **2b** | 1.4 | 88 |
| 3 | **2c** | 1.0 | 85 |
| 4 | **2d** | 1.0 | 80 |
| 5 | **2e** | 1.2 | 80 |
| 6 | **2f** | 1.5 | 83 |
| 7 | **2g** | 1.3 | 85 |

[a] Compound **1** (1 equiv), BrCN (1 equiv) and $Et_3N$ (1 equiv), THF, at room temperature.
[b] Isolated yield.

Initially, the efficacy of **2a**–**g** for *N*-cyanation was evaluated using *N*-methylbenzylamine (**3a**) in water at 15–17 °C (Table 2, entries 1–7). Among seven *N*-cyanopyridazin-3(2*H*)-ones, **2a** and **2b** were the best *N*-cyanating agents. Consequently, **2a** and **2b** were further, studied in a variety of representative organic solvents (entries 8–17). Exclusive

*Keywords*: *N*-, *S*- *or C*-cyanation; Electrophilic cyanating agent; 2-Cyanopyridazin-3(2*H*)-ones.
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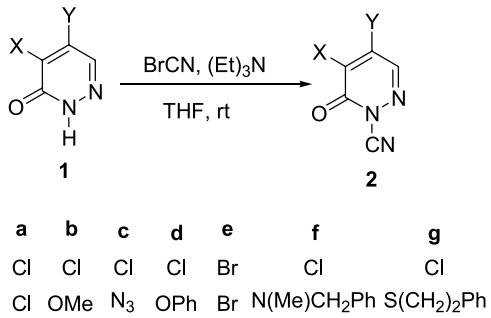



| 1,2 | a | b | c | d | e | f | g |
|---|---|---|---|---|---|---|---|
| X | Cl | Cl | Cl | Cl | Br | Cl | Cl |
| Y | Cl | OMe | $N_3$ | OPh | Br | $N(Me)CH_2Ph$ | $S(CH_2)_2Ph$ |

**Scheme 1.**

*N*-cyanation in good to excellent yields was obtained in acetonitrile, methanol, and toluene.

Cyanation of various nitrogen and sulfur nucleophiles **3b–h** with **2a–b** in water under neutral condition gave the corresponding *N*- or *S*-cyano derivatives **4b–h** in good to excellent yields (Table 3, entries 1–14).

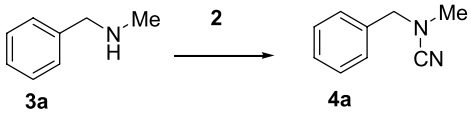
We also investigated the chemoselectivity in the cyanation of bifunctional nucleophiles such as 4-aminophenol, 4-aminobenzenethiol and 4-mercaptophenol. Firstly, compounds **3i–k** was treated with **2a–b** in water to give both 5-substituted-pyridazin-3(2*H*)-ones and cyanated **4i–k**. To enhance the chemoselectivity of the cyanation for bifunctional nucleophiles, we found that the best reaction condition requires the presence of 1 equiv of zinc chloride from preliminary experiments. Treatment of bifunctional nucleophiles **3i–k** with **2a**,**b** (entries 15–20) in the presence of zinc chloride in water chemoselectively afforded *N*- or *S*-cyano derivatives **4i–k** in good yields. In order to expand the applications of the α-cyanation for 1,3-dicarbonyl compounds, we examined the cyanation of **3l** and **3m**. Otherwise the cyanations of *N*- or *S*-nucleophile, the reactions of 1,3-dicarbonyl compounds in water, methanol, acetonitrile and toluene suffer from low yield, low selectivity, and long reaction time. Therefore, we chose tetrahydrofuran as solvent for the α-cyanation of 1,3-dicarbonyl compounds. Reaction of **2b** with β-diketone **3l** in tetrahydrofuran mediated by $ZnCl_2$ or NaH (entries 21 and 22, respectively) gave rise to deacetylated α-cyano ketone **4l** in excellent yields. A similar deacetylation has been reported.[15] On the other hand, deacetylation was not observed for **3m** under identical conditions. Reaction of **3m** with **2b** (2 equiv) in the presence of $ZnCl_2$ or NaH (entries 23 and 24, respectively) gave the corresponding α,α-dicyano derivative **4m** in excellent yields, whereas the use of just 1 equiv of **2b** under the same conditions afforded **4m** in 46–48% yields. In contrast to the behavior of **2b**, compound **2a** was not capable of cyanating the carbon nucleophiles and yielded 5-substituted-pyridazin-3(2*H*)-ones instead of **4l** or **4m**. Enhancement of the reactivity of cyano group at N-2 position for the cyanation of *N*-, *S*- or *C*-nucleophiles with **2** may be due to the chelation of **2** with zinc chloride (Fig. 1).

The different product selectivity between substrate **3l** and **3m** may be due to the different tautomerization of two substrates under our condition. In order to occur an intermolecular pyridazinone-mediated deacylation like Katritzky's mechanism,[15] the terminal acetyl group of **3l** and **3m** must be present as a keto-form. Under our reaction system, the structure (I) of **3l** may be more favorable than the structure (II), whereas the structure (IV) of **3m** may be more favorable than the structure (III) (Scheme 2).

## 3. Conclusion

In conclusion, 2-cyanopyridazin-3(2*H*)-ones such as **2a** and **2b** are novel and stable electrophilic cyanating agents. The methodology presented here, is an efficient, chemoselective, mild and/or eco-friendly procedure for cyanation of nitrogen, sulfur and carbon nucleophiles. The solvents

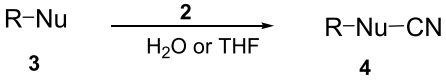
**Table 2**. Preparation of *N*-cyano-*N*-methylbenzylamine (**4a**) using **2** in various solvents

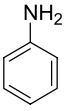
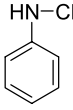
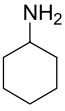
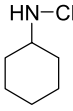
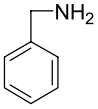
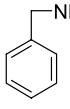
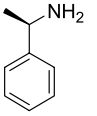
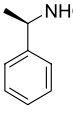
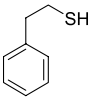
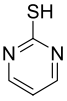
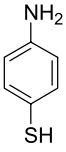
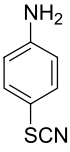
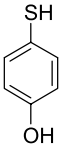
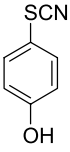
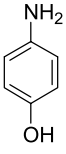
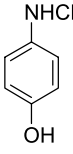
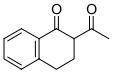
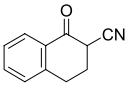
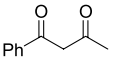
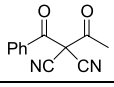



| Entry | 2 | Solvent | Temp (°C) | Time (h) | **4a** (%)[a] |
|---|---|---|---|---|---|
| 1 | **2a** | $H_2O$ | 15–17 | 0.5 | 95 |
| 2 | **2b** | $H_2O$ | 15–17 | 0.5 | 96 |
| 3 | **2c** | $H_2O$ | 15–17 | 1 | 88 |
| 4 | **2d** | $H_2O$ | 15–17 | 1 | 83 |
| 5 | **2e** | $H_2O$ | 15–17 | 1.2 | 82 |
| 6 | **2f** | $H_2O$ | 15–17 | 1.5 | 85 |
| 7 | **2g** | $H_2O$ | 15–17 | 1.3 | 84 |
| 8 | **2a** | $CH_2Cl_2$ | Reflux | 22 | 52 |
| 9 | **2b** | $CH_2Cl_2$ | Reflux | 28 | 41 |
| 10 | **2a** | THF | Reflux | 5 | —[b] |
| 11 | **2b** | THF | Reflux | 20 | 75 |
| 12 | **2a** | $CH_3CN$ | Reflux | 9 | 88 |
| 13 | **2b** | $CH_3CN$ | Reflux | 14 | 94 |
| 14 | **2a** | MeOH | Reflux | 6 | 91 |
| 15 | **2b** | MeOH | Reflux | 4 | 89 |
| 16 | **2a** | $C_6H_5CH_3$ | Reflux | 2 | 92 |
| 17 | **2b** | $C_6H_5CH_3$ | Reflux | 2 | 97 |

[a] Isolated yield. Compound **1** was isolated in good to excellent yields except for entries 1–4 and could be recycled.
[b] 5-(*N*-Methyl-*N*-benzylamino)-4-chloropyridazin-3(2*H*)-one was obtained in 80% yield.

**Table 3**. Cyanation of the substrates (**3**) with **2a–b** in water or THF




| Entry | 2 | Substrate (3) | | Temp (°C) | Solvent | Time (h) | 4 (%)[a] | |
|---|---|---|---|---|---|---|---|---|
| 1 | **2a** | **3b** |  | 15–17 | $H_2O$ | 1.5 |  | **4b** (91) |
| 2 | **2b** | | | 15–17 | $H_2O$ | 0.5 | | **4b** (92) |
| 3 | **2a** | **3c** |  | 15–17 | $H_2O$ | 1.0 |  | **4c** (89) |
| 4 | **2b** | | | 15–17 | $H_2O$ | 0.5 | | **4c** (93) |
| 5 | **2a** | **3d** |  | 15–17 | $H_2O$ | 1.2 |  | **4d** (84) |
| 6 | **2b** | | | 15–17 | $H_2O$ | 0.5 | | **4d** (86) |
| 7 | **2a** | **3e** | *n*-Bu–$NH_2$ | 15–17 | $H_2O$ | 1.0 | *n*-Bu–NHCN | **4e** (82) |
| 8 | **2b** | | | 15–17 | $H_2O$ | 0.8 | | **4e** (80) |
| 9 | **2a** | **3f** |  | 15–17 | $H_2O$ | 0.8 |  | **4f** (88) |
| 10 | **2b** | | | 15–17 | $H_2O$ | 0.8 | | **4f** (98) |
| 11 | **2a** | **3g** |  | 15–17 | $H_2O$ | 0.5 |  | **4g** (82) |
| 12 | **2b** | | | 15–17 | $H_2O$ | 0.8 | | **4g** (78) |
| 13 | **2a** | **3h** |  | 15–17 | $H_2O$ | 1.5 |  | **4h** (85) |
| 14 | **2b** | | | 15–17 | $H_2O$ | 1.2 | | **4h** (81) |
| 15 | **2a** | **3i** |  | 15–17 | $H_2O$ | 1.5 |  | **4i** (78)[b] |
| 16 | **2b** | | | 15–17 | $H_2O$ | 1.5 | | **4i** (85)[b] |
| 17 | **2a** | **3j** |  | 15–17 | $H_2O$ | 1.0 |  | **4j** (82)[b] |
| 18 | **2b** | | | 15–17 | $H_2O$ | 2.1 | | **4j** (85)[b] |
| 19 | **2a** | **3k** |  | 15–17 | $H_2O$ | 1.2 |  | **4k** (86)[b] |
| 20 | **2b** | | | 15–17 | $H_2O$ | 2.0 | | **4k** (85)[b] |
| 21 | **2b** | **3l** |  | Reflux | THF | 24 |  | **4l** (93)[c] |
| 22 | **2b** | | | 7–8 | THF | 9 | | **4l** (94)[d] |
| 23 | **2b** | **3m** |  | Reflux | THF | 14 |  | **4m** (97)[e] |
| 24 | **2b** | | | 7–8 | THF | 5 | | **4m** (95)[f] |

[a] Isolated yield. Compound **1** was isolated in good to excellent yield except for entry 12 and could be recycled.
[b] Using $ZnCl_2$ (30 mol%) as the catalyst.
[c] Using $ZnCl_2$ (1 equiv).
[d] Using NaH (60%, 1.2 equiv).
[e] Reaction conditions: **2b** (2 equiv), $ZnCl_2$ (1 equiv).
[f] Reaction conditions: **2b** (2 equiv), NaH (60%, 2.4 equiv).

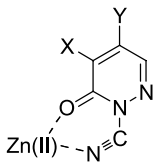
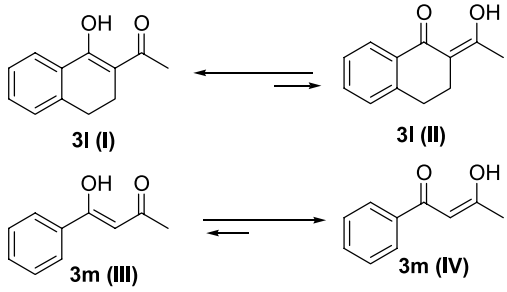



**Figure 1.** Chleation of **2** with Zn(II).




**Scheme 2.**

also affect the reactivity and the selectivity of these systems. Our investigation of the reactions of these new compounds is continuing and the results will be reported in due course.

## 4. Experimental

### 4.1. General

Melting points were determined with a capillary apparatus and uncorrected. $^1$H and $^{13}$C NMR spectra were recorded on a 300 MHz spectrometer with chemical shift values reported in units (ppm) relative to an internal standard (TMS). IR spectra were obtained on a IR spectrophotometer. Elemental analyses were performed with a Perkin Elmer 240C. Open-bed chromatography was carried out on silica gel (70–230 mesh, Merck) using gravity flow. The column was packed as slurries with the elution solvent. 4,5-Dichloropyridazin-3(2*H*)-one (**1a**) and 4,5-dibromopyridazin-3(2*H*)-one (**1e**) were prepared by the literature method.[16] 4-Chloro-5-substituted-pyridazin-3(2*H*)-ones **1b–d**, **1f** and **1g** were prepared from **1a** by the reported method.[17]

### 4.2. Synthesis of 2-cyanopyridazin-3(2*H*)-ones 2

Triethylamine (0.6 mL, 4.36 mmol) was added slowly to a stirred solution of **1** (1.1 g, 4.36 mmol) in THF (40 mL) at room temperature. After stirring 5 min, cyanogen bromide (4.36 mmol) was added. The reaction mixture was stirred at room temperature until **1** disappeared. After evaporating the solvent under reduced pressure, the resulting residue was applied to the top of an open-bed silica gel column (3.0× 5 cm). The column was eluted with methylene chloride. Fractions containing **2** were combined and evaporated under reduced pressure to give **2**.

**4.2.1. 2-Cyano-4,5-dichloropyridazin-3(2*H*)-one (2a).** Yield 92%. Mp 104–105 °C. $R_f$=0.56 (methylene chloride). IR (KBr) 3100, 3050, 2245, 1700, 1600, 1580, 1360, 1260, 1180, 1160, 960 cm$^{-1}$; $^1$H NMR ($CDCl_3$): $\delta$ 8.00 (s, 1H) ppm; $^{13}$C NMR ($CDCl_3$) $\delta$ 104.9, 134.9, 138.3, 141.2, 154.4 ppm. Elemental analysis calcd for $C_5HCl_2N_3O$: C, 34.52; H, 0.58; N, 24.15; found: C, 34.77; H, 0.53; N, 24.07.

**4.2.2. 2-Cyano-4-chloro-5-methoxypyridazin-3(2*H*)-one (2b).** Yield 88%. Mp 105–106 °C. $R_f$=0.61 (methylene chloride). IR (KBr) 3100, 3030, 2980, 2250, 1690, 1600, 1460, 1400, 1300, 1260, 1120, 960 cm$^{-1}$; $^1$H NMR ($CDCl_3$): $\delta$ 4.24 (s, 3H), 8.19 (s, 1H) ppm; $^{13}$C NMR ($CDCl_3$) $\delta$ 59.1, 105.6, 115.8, 133.8, 155.4, 156.9 ppm. Elemental analysis calcd for $C_6H_4ClN_3O_2$: C, 38.83; H, 2.17; N, 22.64; found: C, 38.87; H, 2.13; N, 23.46.

**4.2.3. 2-Cyano-4-chloro-5-azidopyridazin-3(2*H*)-one (2c).** Yield 85%. $R_f$=0.46 (methylene chloride). Mp 114–115 °C. $R_f$=0.67. IR (KBr) 3100, 3070, 2250, 2160, 2120, 1700, 1600, 1520, 1380, 1310, 1230, 1130, 1000, 860, 730, 700 cm$^{-1}$; $^1$H NMR ($CDCl_3$): $\delta$ 7.74 (s, 1H) ppm; $^{13}$C NMR ($CDCl_3$) $\delta$ 105.2, 122.0, 136.3, 140.5, 155.1 ppm. Elemental analysis calcd for $C_5HClN_6O$: C, 30.55; H, 0.51; N, 42.76; found: C, 30.77; H, 0.53; N, 42.37.

**4.2.4. 2-Cyano-4-chloro-5-phenoxypyridazin-3(2*H*)-one (2d).** Yield 80%. $R_f$=0.42 (methylene chloride). Mp 115–116 °C. IR (KBr) 3070, 2250, 1720, 1620, 1590, 1540, 1490, 1380, 1280, 1220, 1150, 860, 820, 780, 730, 690 cm$^{-1}$; $^1$H NMR ($CDCl_3$): $\delta$ 7.12–7.17 (m, 2H), 7.34–7.41 (m, 1H), 7.47–7.55 (m, 2H), 7.65 (s, 1H) ppm; $^{13}$C NMR ($CDCl_3$) $\delta$ 105.4, 118.8, 119.9, 127.2, 130.9, 135.3, 152.7, 153.7, 156.8 ppm. Elemental analysis calcd for $C_{11}H_6ClN_3O_2$: C, 53.35; H, 2.44; N, 16.97; found: C, 53.57; H, 2.33, N, 16.96.

**4.2.5. 2-Cyano-4,5-dibromopyridazin-3(2*H*)-one (2e).** Yield 80%. $R_f$=0.62 (methylene chloride). Mp 84–85 °C. $R_f$=0.67. IR (KBr) 3080, 3040, 2950, 2260, 1680, 1590, 1510, 1280, 1220, 1110, 960, 860, 720 cm$^{-1}$; $^1$H NMR ($CDCl_3$): $\delta$ 7.98 (s, 1H) ppm; $^{13}$C NMR ($CDCl_3$) $\delta$ 137.4, 138.2, 141.1, 142.4, 154.4 ppm. Elemental analysis calcd for $C_5HBr_2N_3O$: C, 21.53; H, 0.36; N, 15.07; found: C, 21.71; H, 0.33; N, 15.15.

**4.2.6. 2-Cyano-4-chloro-5-(benzylmethylamino)pyridazin-3(2*H*)-one (2f).** Yield 83%. $R_f$=0.49 (methylene chloride). Mp 105–106 °C. IR (KBr) 3050, 2980, 2950, 2260, 1690, 1625, 1560, 1500, 1460, 1420, 1360, 1310, 1260, 1240, 1200, 1140, 1100, 1060, 1030, 980, 900, 750, 730 cm$^{-1}$; $^1$H NMR (DMSO-$d_6$): $\delta$ 3.18 (s, 3H), 4.87 (s, 2H), 7.30 (dd, 3H, $J$=7.12 Hz, 7.39), 7.39 (dd, 2H, $J$=7.43 Hz, 7.51), 8.27 (s, 1H) ppm; $^{13}$C NMR (DMSO-$d_6$) $\delta$ 41.1, 56.8, 104.6, 107.6, 127.4, 127.9, 129.1, 136.9, 138.9, 147.5, 156.8 ppm. Elemental analysis calcd for $C_{13}H_{11}ClN_4O$: C, 56.84; H, 4.04; N, 20.40; found: C, 56.87; H, 4.13; N, 20.51.

**4.2.7. 2-Cyano-4-chloro-5-(phenethylsulfanyl)pyridazin-3(2*H*)-one (2g).** Yield 85%. $R_f$=0.51 (methylene chloride). Mp 141–143 °C. IR (KBr) 3080, 3000, 2950, 2270, 1700, 1590, 1500, 1460, 1440, 1380, 1310, 1290, 1230, 1120, 960, 860, 780, 740 cm$^{-1}$; $^1$H NMR ($CDCl_3$): $\delta$ 3.07 (t, 2H, $J$=7.34 Hz), 3.38 (t, 2H, $J$=7.34 Hz), 7.20–7.37 (m, 5H), 7.64 (s, 1H) ppm; $^{13}$C NMR ($CDCl_3$) $\delta$ 33.5, 35.7, 127.6, 128.7, 129.0, 136.9, 137.6, 143.9, 145.2, 152.3, 159.2 ppm. Elemental analysis calcd for $C_{13}H_{10}ClN_3OS$: C, 53.52; H, 3.45; N, 14.40; found: C, 53.63; H, 3.42; N, 14.50.

### 4.3. Typical cyanation of nucleophiles in water

Nucleophiles (1.2 equiv) was added slowly to a stirred solution of **2** (200 mg, 1.05 mmol) in water (20 mL) at 15–17 °C. The reaction mixture was stirred at room temperature until **2** disappeared. The product was extracted with $CH_2Cl_2$ (30 mL×2). The organic layer was dried over anhydrous magnesium sulfate and then the solvent evaporated under reduced pressure, the resulting residue was applied to the top of an open-bed silica gel column (3.0× 7 cm). The column was eluted with methylene chloride or methylene chloride: *n*-hexane=2:1 (v/v); methylene chloride/ether=10:1 (v/v). Fractions containing **4** were combined and evaporated under reduced pressure to give **4** in 78–98% yield.

### 4.4. Typical cyanation of 1,3-dicarbonyl compounds in presence of base or acid

NaH or $ZnCl_2$ (1.1 equiv) was added slowly to a stirred solution of active methylene (1.08 mmol) in dry-THF (20 mL) at 7–8 °C (for NaH) and at reflux temperature (for $ZnCl_2$). After stirring 5 min, **2** (200 mg, 1.08 mmol) was added. The reaction mixture was refluxed until carbanion or **2** disappeared. After evaporating the solvent under reduced pressure, the resulting residue was applied to the top of an open-bed silica gel column (3.0×10 cm). The column was eluted with methylene chloride: ether= 7:1 (v/v). Fractions containing **4l** or **4m** were combined and evaporated under reduced pressure to give **4l** or **4m** in 93–97% yield.

**4.4.1. *N*-Cyano-*N*-methylbenzylamine (4a).** Oil (colorless). $R_f$=0.70 (methylene chloride/*n*-hexane=2:1 (v/v)). IR (KBr) 3050, 2950, 2240, 1500, 1460, 1380, 1230, 1160, 1040, 740, 700 $cm^{-1}$. $^1H$ NMR ($CDCl_3$) $\delta$ 2.75 (s, 3H), 4.13 (s, 2H), 7.34 (m, 5H) ppm. $^{13}C$ NMR ($CDCl_3$) $\delta$ 37.7, 57.1, 118.8, 128.3, 128.5, 128.8, 134.3 ppm. Elemental analysis calcd for $C_9H_{10}N_2$: C, 73.94; H, 6.89; N, 19.16; found C, 73.98; H, 6.84; N, 19.21.

**4.4.2. *N*-Cyanoaniline (4b).** Oil (colorless). $R_f$=0.43 (methylene chloride/ether=10:1 (v/v)). IR (KBr) 3190, 3100, 3000, 2930, 2230, 1600, 1500, 1440, 1300, 1250, 750, 690, 490 $cm^{-1}$. $^1H$ NMR ($CDCl_3$) $\delta$ 6.19 (s, NH, $D_2O$ exchangable), 6.99 (d, 2H, $J$=8.65 Hz), 7.05 (m, 1H), 7.31 (m, 2H) ppm. $^{13}C$ NMR ($CDCl_3$) $\delta$ 111.7, 115.5, 123.5, 129.7, 137.4 ppm. Elemental analysis calcd for $C_7H_6N_2$: C, 71.17; H, 5.12; N, 23.71; found C, 71.21; H, 5.15; N, 23.73.

**4.4.3. *N*-Cyanocyclohexylamine (4c).** Oil (colorless). $R_f$= 0.36 (methylene chloride). IR (KBr) 3200, 2940, 2860, 2230, 1450, 1370, 1260, 1170, 1140, 950, 900 $cm^{-1}$. $^1H$ NMR ($CDCl_3$) $\delta$ 1.98–1.20 (m, 10H), 3.09 (m, 1H), 4.14 (s, NH, $D_2O$ exchangable) ppm. $^{13}C$ NMR ($CDCl_3$) $\delta$ 24.3, 25.1, 32.6, 54.4, 115.7 ppm. Elemental analysis calcd for $C_7H_{12}N_2$: C, 67.70; H, 9.74; N, 22.56; found C, 67.75; H, 9.75; N, 22.53.

**4.4.4. *N*-Cyanobenzylamine (4d).** Oil (colorless). $R_f$=0.32 (methylene chloride). IR (KBr) 3260, 3080, 3030, 2220, 1500, 1460, 1440, 1340, 1310, 1220, 1160, 750, 700 $cm^{-1}$. $^1H$ NMR ($CDCl_3$) $\delta$ 4.14 (d, 2H, $J$=5.57 Hz), 4.41 (bs, NH, $D_2O$ exchangable), 7.28–7.36 (m, 5H) ppm. $^{13}C$ NMR ($CDCl_3$) $\delta$ 50.1, 116.3, 127.8, 128.4, 128.9, 136.3 ppm. Elemental analysis calcd for $C_8H_8N_2$: C, 72.70; H, 6.10; N, 21.20; found C, 72.81; H, 6.15; N, 21.19.

**4.4.5. *N*-Cyano-*n*-butylamine (4e).** Oil (colorless). $R_f$= 0.48 (methylene chloride). IR (KBr) 3220, 2970, 2950, 2880, 2220, 1460, 1380, 1360, 1170 $cm^{-1}$. $^1H$ NMR ($CDCl_3$) $\delta$ 0.92–1.00 (t, 3H, $J$=3.36 Hz), 1.34–1.47 (m, 2H), 1.62–1.73 (m, 2H), 2.16 (m, 2H), 3.92 (bs, NH, $D_2O$ exchangable) ppm. $^{13}C$ NMR ($CDCl_3$) $\delta$ 13.8, 20.2, 28.8, 44.4, 147.2 ppm. Elemental analysis calcd for $C_5H_{10}N_2$: C, 61.19; H, 10.27; N, 28.54; found C, 61.22; H, 10.28; N, 28.49.

**4.4.6. (*R*)-*N*-Cyano-α-methylbenzylamine (4f).** Oil (colorless). $R_f$=0.29 (methylene chloride). IR (KBr) 3210, 3000, 2920, 2230, 1500, 1460, 1380, 1210, 1160, 760, 700 $cm^{-1}$. $^1H$ NMR ($CDCl_3$) $\delta$ 1.53 (d, 3H, $J$=6.80 Hz), 4.31 (bs, NH, $D_2O$ exchangable), 4.32–4.41 (m, 1H), 7.25–7.40 (m, 5H) ppm. $^{13}C$ NMR ($CDCl_3$) $\delta$ 22.0, 55.6, 115.3, 126.2, 128.3, 128.9, 141.5 ppm. Elemental analysis calcd for $C_9H_{10}N_2$: C, 73.94; H, 6.89; N, 19.16; found C, 73.88; H, 6.91; N, 19.19.

**4.4.7. 2-Phenylethyl thiocyanate (4g).** Oil (colorless). $R_f$= 0.50 (methylene chloride). IR (KBr) 3080, 3050, 2950, 2880, 2180, 1610, 1500, 1460, 1330, 1290, 1240, 1080, 1040, 760, 710 $cm^{-1}$. $^1H$ NMR ($CDCl_3$) $\delta$ 3.11 (m, 2H), 3.16 (m, 2H), 7.21 (d, 2H, $J$=7.00 Hz), 7.27 (dd, 1H, $J$= 7.50 Hz), 7.33 (dd, 2H, $J$=7.00, 7.50 Hz) ppm. $^{13}C$ NMR ($CDCl_3$) $\delta$ 34.0, 34.9, 110.8, 126.1, 127.5, 127.7, 136.5 ppm. Elemental analysis calcd for $C_9H_9NS$: C, 66.22; H, 5.56; N, 8.58; found C, 66.24; H, 5.60; N, 8.56.

**4.4.8. 2-Thiocyanatopyrimidine (4h).** Mp 112–113 °C (colorless). $R_f$=0.61 (methylene chloride). IR (KBr) 3100, 3000, 2180, 1570, 1390, 1280, 1180, 820, 770, 740, 700, 630 $cm^{-1}$. $^1H$ NMR ($CDCl_3$) $\delta$ 7.33 (dd, 1H, $J$=4.88 Hz), 8.72 (d, 2H, $J$=4.88 Hz) ppm. $^{13}C$ NMR ($CDCl_3$) $\delta$ 107.3, 119.7, 158.9, 164.2 ppm. Elemental analysis calcd for $C_5H_3N_3S$: C, 43.78; H, 2.20; N, 30.64; found C, 43.91; H, 2.30; N, 29.99.

**4.4.9. 4-Thiocyanatoaniline (4i).** Mp 55–56 °C (colorless). $R_f$=0.23 (methylene chloride). IR (KBr) 3430, 3350, 3250, 3060, 2970, 2930, 2150, 1640, 1600, 1500, 1440, 1300, 1180, 1080, 820, 670, 520 $cm^{-1}$. $^1H$ NMR ($CDCl_3$) $\delta$ 3.97 (bs, $NH_2$, $D_2O$ exchangeable), 6.64–6.68 (dd, 2H, $J$= 6.80 Hz), 7.32–7.36 (dd, 2H, $J$=6.86 Hz) ppm. $^{13}C$ NMR ($CDCl_3$) $\delta$ 109.6, 112.3, 116.1, 134.4, 148.9 ppm. Elemental analysis calcd for $C_7H_6N_2S$: C, 55.97; H, 4.03; N, 18.65; found C, 56.01; H, 4.06; N, 18.56.

**4.4.10. 4-Thiocyanatophenol (4j).** Mp 62–63 °C (colorless). $R_f$=0.38 (Ethyl acetate/*n*-hexane=1:3 (v/v)). IR (KBr) 3400, 2960, 2890, 2180, 1620, 1600, 1500, 1440, 1370, 1280, 1240, 1180, 840 $cm^{-1}$. $^1H$ NMR ($CDCl_3$) $\delta$ 6.00 (bs, OH, $D_2O$ exchangeable), 6.88 (dd, 2H, $J$= 6.50 Hz), 7.44 (dd, 2H, $J$=6.50 Hz) ppm. $^{13}C$ NMR ($CDCl_3$) $\delta$ 112.1, 113.4, 117.5, 134.2, 158.0 ppm. Elemental analysis calcd for $C_7H_5NOS$: C, 55.61; H, 3.33; N, 9.26; found C, 55.68; H, 3.36; N, 9.20.

**4.4.11. *N*-Cyano-4-hydroxyaniline (4k).** Mp 218–219 °C (colorless). $R_f$=0.41 (ethyl acetate/*n*-hexane=1:2 (v/v)). IR (KBr) 3200, 2990, 2930, 2230, 1620, 1510, 1440, 1360, 1280, 1260, 1220, 1110, 810, 620, 500 $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$) $\delta$ 6.77 (m, 4H), 9.17 (bs, NH, $D_2O$ exchangable), 9.62 (bs, OH, $D_2O$ exchangeable) ppm. $^{13}C$ NMR (DMSO-$d_6$) $\delta$ 111.9, 115.1, 115.2, 128.8, 151.8 ppm. Elemental analysis calcd for $C_7H_6N_2O$: C, 62.68; H, 4.51; N, 20.88; found C, 62.60; H, 4.66; N, 20.90.

**4.4.12. 2-Cyano-3,4-dihydro-1(2*H*)-naphthalenone (4l).** Mp 75–77 °C (colorless). $R_f$=0.76 (methylene chloride/*n*-hexane=2:1 (v/v)). IR (KBr) 3070, 2950, 2880, 2250, 1700, 1600, 1460, 1440, 1360, 1310, 1230, 1200, 920, 750 $cm^{-1}$. $^1H$ NMR ($CDCl_3$) $\delta$ 2.43–2.63 (m, 2H), 3.02–3.21 (m, 2H), 3.72–3.78 (dd, 1H, $J$=4.60, 4.61 Hz), 7.34–7.40 (dd, 1H, $J$=7.74, 7.44 Hz), 7.52–7.59 (m, 1H), 8.05–8.09 (dd, 1H, $J$=7.86, 7.89 Hz) ppm. $^{13}C$ NMR ($CDCl_3$) $\delta$ 27.7, 27.8, 40.8, 116.7, 127.5, 128.4, 129.0, 130.5, 134.8, 142.9, 187.8 ppm. Elemental analysis calcd for $C_{11}H_9NO$: C, 77.17; H, 5.30; N, 8.18; found C, 77.22; H, 5.32; N, 8.09.

**4.4.13. 2,2-Dicyano-1-benzoylacetone (4m).** Mp 68–69 °C (colorless). $R_f$=0.42 (methylene chloride). IR (KBr) 3070, 2930, 2220, 1735, 1690, 1600, 1550, 1440, 1400, 1360, 1290, 1180, 1020, 990, 860 $cm^{-1}$. $^1H$ NMR ($CDCl_3$) $\delta$ 2.54 (s, 3H), 7.48–7.54 (m, 2H), 7.59–7.65 (m, 1H), 8.01–8.05 (m, 2H) ppm. $^{13}C$ NMR ($CDCl_3$) $\delta$ 25.6, 88.2, 117.7, 128.6, 128.7, 128.8, 133.1, 133.8, 190.0, 200.2 ppm. Elemental analysis calcd for $C_{12}H_8N_2O_2$: C, 67.92; H, 3.80; N, 13.20; found C, 67.88; H, 3.78; N, 13.16.

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