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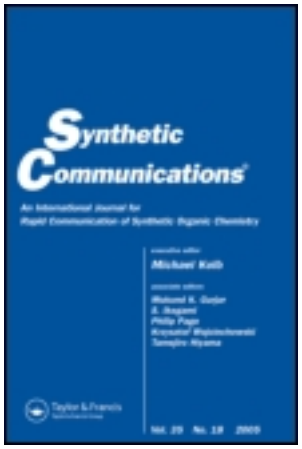


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# Facile Synthesis of 6-Aryl-3-cyanopyridine-2-(1H)-thiones from Aryl Ketones

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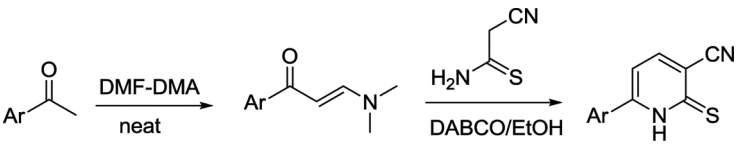
# FACILE SYNTHESIS OF 6-ARYL-3-CYANOPYRIDINE-2-(1*H*)-THIONES FROM ARYL KETONES

**Ren-Lin Zheng,[1] Xiu-Xiu Zeng,[1,2] Hai-Yun He,[1] Jun He,[2] Sheng-Yong Yang,[1] Luo-Ting Yu,[1] and Li Yang[1]**

[1]*State Key Laboratory of Biotherapy and Cancer Center, West China Hospital, West China Medical School, Sichuan University, Chengdu, China*
[2]*Department of Pharmaceutical and Bioengineering, School of Chemical Engineering, Sichuan University, Chengdu, China*

## GRAPHICAL ABSTRACT




**Stepwise** synthesis, 40-95% yield,13 examples
**One-pot** synthesis, 50-80% yield, 6 examples

**Abstract** *An improved synthesis of 6-aryl-3-cyanopyridine-2-(1*H*)-thiones utilizing enaminones as starting materials catalyzed by 1,4-diazabicyclo[2.2.2]octane (DABCO) was described. Moreover, a convenient one-pot conversion of aryl ketones to 6-aryl-3-cyanopyridine-2-(1*H*)-thiones was also developed in moderate to good yields (up to 80%).*

**Keywords** 6-Aryl-3-cyanopyridine-2-(1*H*)-thiones; DABCO; enaminones; one-pot synthesis

## INTRODUCTION

3-Cyanopyridine-2-(1*H*)-thiones are valuable compounds in organic synthesis not only because of their broad biological activities[1] but also because they serve as useful synthetic intermediates in the preparations of dyes, pesticides, and cannabinoid-1 receptor inverse agonists.[2] For example, in our recent search for Aurora-A kinase inhibitors,[3] compound **1** was prepared from 3-cyanopyridine-2-(1*H*)-thione **2** via Thorpe–Ziegler cyclization[4] (Scheme 1**)**.

Although a few procedures for accessing 6-aryl-3-cyanopyridine-2-(1*H*)-thiones **6** (Scheme 2) have been reported employing enaminones (**4** and **8**) or sodium

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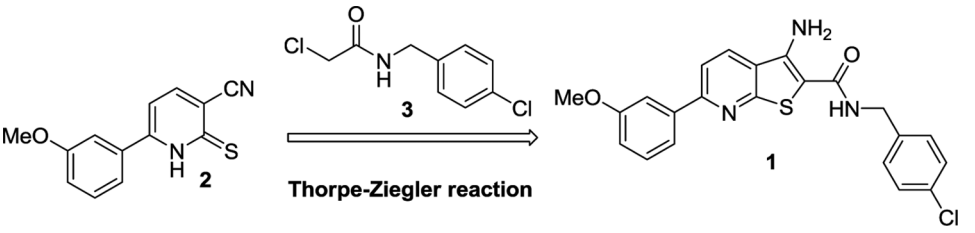


**Scheme 1.** Synthesis of compound **1**.

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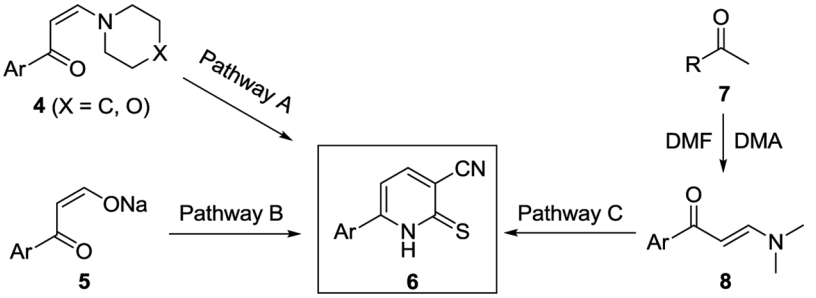
enolate (**5**),[5] these processes still have several limitations including the tedious synthesis of **4** in pathway A and the moisture-sensitive intermediate **5** in pathway B. Given the stability of **8** and the operational convenience of pathway C, we choose pathway C to prepare structurally diverse 6-aryl-3-cyanopyridine-2-(1*H*)-thiones **6.** Herein, we describe an improved synthesis of 6-aryl-3-cyanopyridine-2-(1*H*)-thiones **6** from enaminones **8** (pathway C) using 1,4-diazabicyclo[2.2.2]octane (DABCO) as the base as well as a convenient experimental protocol from aryl ketones **7** to **6** directly in one flask.

## RESULTS AND DISCUSSION

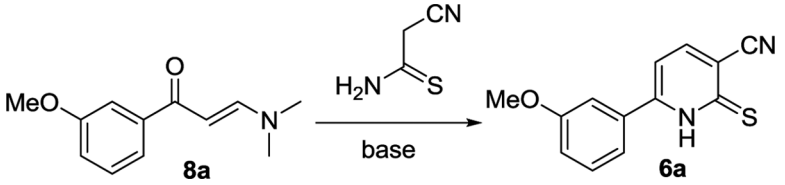
A series of enaminone **8** were readily prepared in 75–95% yield by the treatment of **7** with *N,N*-dimethylformamide dimethyl acetal (DMF-DMA) according to literature procedure[6] With enaminones **8** in hand, we set out to investigate the condensation conditions of **8a** with cyanothioacetamide under different basic conditions, and the results are shown in Table 1. Generally, inorganic basic conditions such as $KOH/H_2O$,[7] EtONa/EtOH,[8f] and *t*-BuOK/DMF[2b] (entries 1–3) gave only poor to moderate yields, while the $Et_3N$/EtOH system (entry 4) provided a much better result. Based on this observation, after screening of a range of organic bases (entries 4–9)[8a–c,8e,9] we were delighted to find that the yield could be improved to 79% using DABCO as base (entry 9). Finally, increasing the amount of cyanothioacetamide from 1.1 to 1.5 equiv. gave the best yield, 88%, as shown in entry 10.

To demonstrate the generality of this method, we next investigated the condensation of a variety of enaminones **8** with cyanothioacetamide under the optimized




**Scheme 2.** Reported and proposed routes toward **6**.

**Table 1.** Optimization of the cyclization of enaminone **8a** with cyanothioacetamide




| Entry | Solvent | Base | Temp. (°C) | Time (h) | Yield (%) |
|---|---|---|---|---|---|
| 1 | $H_2O$ | 10% KOH (aq.) | 40 (0.5 h), 60 (4 h) | 4.5 | 17 |
| 2 | DMF | *t*-BuOK | 55 | 9.5 | 38 |
| 3 | EtOH | EtONa | Reflux | 8 | 6 |
| 4 | EtOH | $Et_3N$ | Reflux | 4 | 60 |
| 5 | EtOH | Piperidine | Reflux | 7 | 48 |
| 6 | EtOH | DBU | Reflux | 2 | 47 |
| 7 | EtOH | Diisopropylamine | Reflux | 2.5 | 53 |
| 8 | EtOH | DIPEA | Reflux | 4 | 68 |
| 9 | EtOH | DABCO | Reflux | 4 | 79 |
| 10[a] | EtOH | DABCO | Reflux | 4 | 88 |

[a]The cyanothioacetamide amount used was 1.5 equiv.; the others were 1.1 equiv.

conditions (1.0 equiv. enaminone, 1.5 equiv. cyanothioacetamide, and 0.5 equiv. DABCO were refluxed in ethanol for 4 h).

As shown in Table 2, reactions of substrates containing electron-donating groups (entries 1–3) or electron-withdrawing groups (entries 5–8 and 10) on the phenyl ring gave comparably excellent yields with those of unsubstituted acetophenone (entry 4). Moreover, heteroaromatic ketones (entries 11, 12, and 13) could also undergo smooth condensation to generate 6-heterocyclic-3-cyanopyridine-2-(1*H*)-thiones **6k**, **6l**, and **6m** in moderate yields. However, substrate with strong electron-withdrawing ditrifluoromethyl substitute (Table 2, entry 9) gave only 40% yield.

To improve operational efficiency and yields, we speculated that the synthesis of 6-aryl-3-cyanopyridine-2-(1*H*)-thiones **6** might be achieved in one flask without isolation and purification of enaminones **8** by a simple evaporation of excess DMF-DMA in vacuo before condensation with cyanothioacetamide. This one-flask procedure proceeded successfully, and a variety of 6-aryl-3-cyanopyridine-2-(1*H*)-thiones were prepared from **7** directly in markedly greater overall yields (50–80%) than that of stepwise synthesis (Table 3, entries 1, 3, 4, and 6). It is noteworthy that the removal of excess DMF-DMA before the addition of cyanothioacetamide is essential.

In conclusion, an improved and efficient method for the synthesis of 6-aryl-3-cyanopyridine-2-(1*H*)-thiones has been developed. The approach features these advantages: (1) using DABCO as base improved the yields remarkably. (2) The convenient process allowed the two-step reaction to be done in a single reaction vessel without isolation and purification of the enaminones and only a simple evaporation in vacuo. The synthesis of antiproliferative thieno[2,3-*b*]pyridine derivatives employing these 6-aryl-3-cyanopyridine-2-(1*H*)-thiones is currently under investigation in our laboratory and will be reported in due course.

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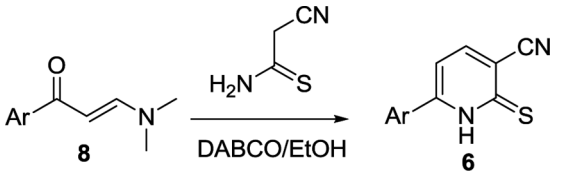
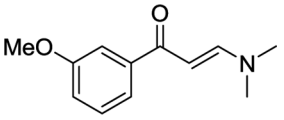
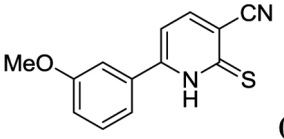
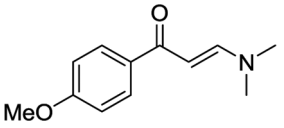
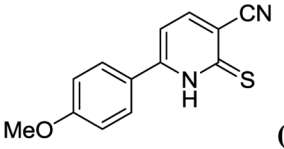
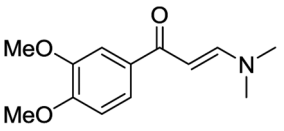
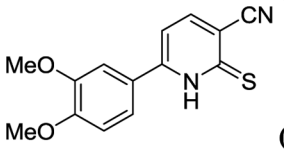
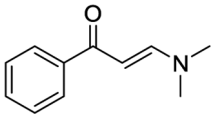
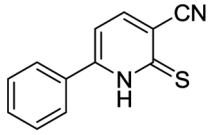
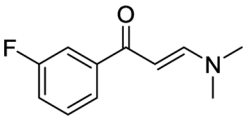
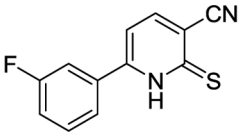
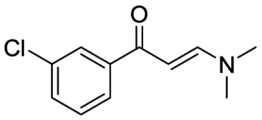
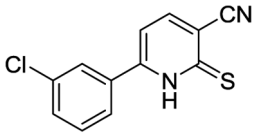
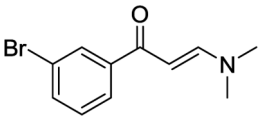
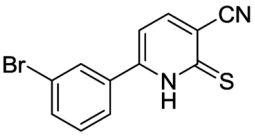
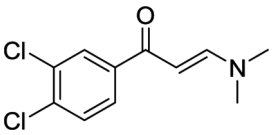
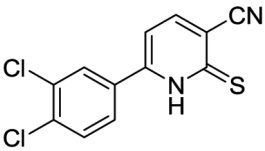
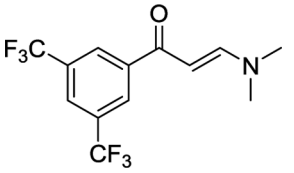
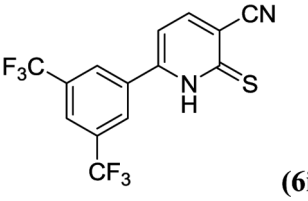
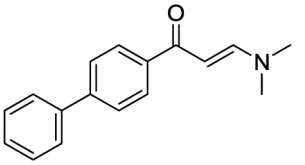
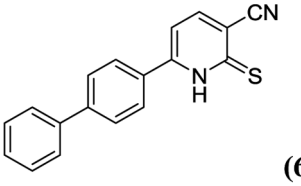
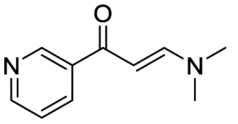
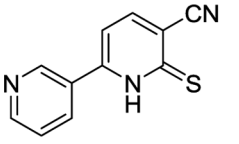
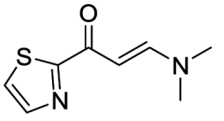
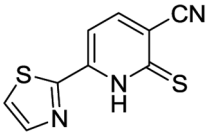
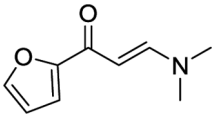
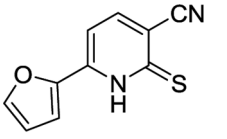
**Table 2.** Synthesis of compound **6**




| Entry | Starting materials | Product | Yield (%) |
|---|---|---|---|
| 1 |  |  **(6a)** | 90 |
| 2 |  |  **(6b)** | 88 |
| 3 |  |  **(6c)** | 81 |
| 4 |  |  **(6d)** | 93 |
| 5 |  |  **(6e)** | 88 |
| 6 |  |  **(6f)**[a] | 77 |
| 7 |  |  **(6g)**[a] | 79 |
| 8 |  |  **(6h)** | 97 |

(*Continued*)

**Table 2.** Continued

| Entry | Starting materials | Product | Yield (%) |
|---|---|---|---|
| 9 |  |  **(6i)**[a] | 40 |
| 10 |  |  **(6j)**[a] | 95 |
| 11 |  |  **(6k)** | 40 |
| 12 |  |  **(6l)**[a] | 68 |
| 13 |  |  **(6m)** | 62 |

[a]The product was a new compound.

## EXPERIMENTAL

All melting points were determined on an electric melting-point apparatus and were uncorrected. $^1$H NMR spectra were carried out on a Bruker Avance (Varian Unity Inova) 400-MHz spectrometer using tetramethylsilane (TMS) as internal reference chemical shift in δ (ppm). Low-resolution mass spectra (LRMS) were carried out on a Waters Quattro Premier XE triple quadrupole mass spectrometer. High-resolution mass spectra (HRMS) were recorded on a Waters Q-TOF Premier mass spectrometer.

### General Procedure for the Preparation of Enaminones 8

**Method A (stepwise procedure).** Aryl ketones (20 mmol) and *N,N*-dimethylformamide dimethyl acetal (DMF-DMA) (40 mmol) were refluxed until the starting materials were consumed, as determined by thin-layer chromatography

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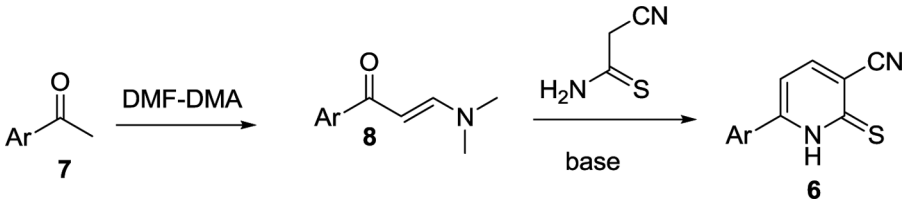
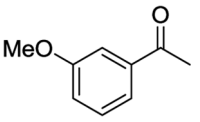
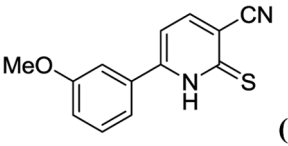
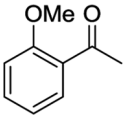
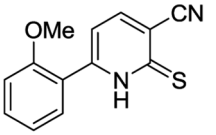
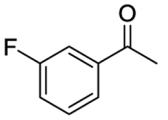
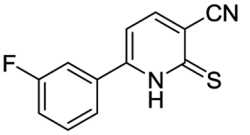
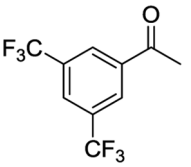
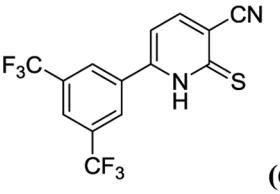
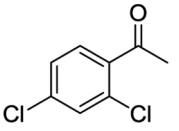
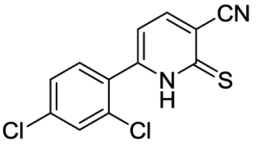
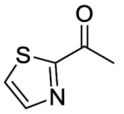
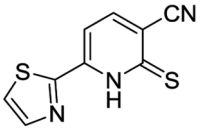
**Table 3.** One-pot synthesis of compound **6** from aromatic ketone **7**




| Entry | Starting material | Product | Yield (%) |
|---|---|---|---|
| 1 |  |  **(6a)** | 80/64[b] |
| 2 |  |  **(6n)**[a] | 75/—[c] |
| 3 |  |  **(6e)** | 65/52[b] |
| 4 |  |  **(6i)** | 50/15 |
| 5 |  |  **(6o)**[a] | 50/—[c] |
| 6 |  |  **(6l)** | 65/58[b] |

[a]The coressponding enaminones was oil.
[b]The overall yield from **7**.
[c]The experiment was not conducted.

(TLC), and then cooled to rt. The precipitate was filtered off and washed with cold petroleum followed by cold ethanol. The product was pure enough for the next step. Compounds **8b**, **8d–8i**, and **8k–8m** were prepared with stepwise procedures.

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**3-(Dimethylamino)-1-(3-methoxyphenyl) prop-2-en-1-one (8a).** Yield 75%, yellow solid, mp 43–44 °C. $^1$H NMR (400 MHz, $CDCl_3$): δ2.92 (s, 3H), 3.14 (s, 3H), 3.86 (s, 3H), 5.70 (d, $J = 12.4$ Hz, 1H), 6.99–7.02 (m, 1H), 7.29–7.33 (m, 1H), 7.45–7.47 (m, 2H), 7.80 (d, $J = 12.4$ Hz, 1H).

**Method B (one-pot procedure).** Aryl ketones (20 mmol) and DMF-DMA (40 mmol) were stirred under reflux until the starting materials was consumed as determined by TLC. Then the mixture was cooled to room temperature, the excess DMF-DMA was removed by evaporation in vacuum, and the residue was used directly for the second step. Compounds **8c** and **8j** were prepared with one-pot procedures.

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## General Procedure for the Preparation of 6-Aryl-3-cyanopyridine-2-(1*H*)-thiones (6a–6o)

Cyanothioacetamide (15 mmol) was added to a stirred suspension of the enaminone (**8a–m**) (10 mmol, prepared according to the procedure described previously) in ethanol (20 mL) in the presence of DABCO (5 mmol) at room temperature. The reaction mixture was stirred under reflux until complete conversion of the starting materials (2–4 h, monitored by TLC). The mixture was then cooled to room temperature and neutralized with diluted HCl solution to precipitate the crude products, which were washed with cold EtOH to give the products **6a–6o**. It is noteworthy that it is necessary to adjust the pH value of the reaction mixture to 7 with diluted HCl solution, especially for **6g**, **6h**, and **6l**. Other pH values of the reaction mixture might result in an upfield chemical shift of the NH of the 2-position pyridine in $^1$H NMR spectrum, together with a lowered yield.

**6-(3-Methoxyphenyl)-3-cyanopyridine-2-(1*H*)-thiones (6a).** Yield 90%, yellow solid, mp 204–206°C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 3.85 (s, 3H), 7.13–7.16 (m, 2H), 7.33–7.37 (m, 2H), 7.45 (t, $J = 8.0$ Hz, 1H), 8.15 (d, $J = 8.0$ Hz, 1H), 14.22 (br, 1H). HRMS (ESI): calcd. for $C_{13}H_{11}N_2OS$ $[M + H]^+$: 243.0587, found: 243.0589.

**6-(4-Methoxyphenyl)-3-cyanopyridine-2-(1*H*)-thiones (6b).** Yield 88%, yellow solid, mp 205–207°C (224–225°C).[5a] $^1$H NMR (400 MHz, DMSO-$d_6$): δ3.85 (s, 3H), 7.09 (dt, $J = 8.8$, 2.6 Hz, 3H), 7.77–7.81 (m, 2H), 8.09 (d, $J = 8.0$ Hz, 1H), 14.06 (br, 1H). HRMS (ESI): calcd. for $C_{13}H_{11}N_2OS$ $[M + H]^+$: 243.0587, found: 243.0591.

**6-(3,4-Dimethoxyphenyl)-3-cyanopyridine-2-(1*H*)-thiones (6c).** Yield 81%, yellow solid, mp > 230°C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ3.81 (t, $J = 8.4$ Hz, 3H), 3.88 (s, 3H), 7.11 (dd, $J = 8.4$, 3.6 Hz, 1H), 7.17 (d, $J = 8.4$ Hz, 1H), 7.40–7.44 (m, 2H), 8.10 (d, $J = 8.0$ Hz, 1H), 14.04 (br, 1H). $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 179.67, 156.85, 148.38, 147.49, 140.72, 133.43, 122.86, 120.97, 117.09, 110.37, 108.58, 102.32, 56.11 (2C). HRMS (ESI): calcd. for $C_{14}H_{11}N_2O_2S$ $[M - H]^-$: 271.0547, found: 271.0545.

**6-Phenyl-3-cyanopyridine-2-(1*H*)-thiones (6d).** Yield 93%, yellow solid, mp 222–224°C (254–255°C,[5a] 245–247[7d]). $^1$H NMR (400 MHz, DMSO-$d_6$): δ 7.10 (d, $J = 8.0$ Hz, 1H), 7.52–7.61 (m, 3H), 7.76–7.78 (m, 2H), 8.15 (d, $J = 8.0$ Hz, 1H),

14.25 (br, 1H). HRMS (ESI): calcd. for $C_{12}H_9N_2S$ $[M+H]^+$: 213.0481, found: 213.0485.

**6-(3-Fluorophenyl)-3-cyanopyridine-2-(1*H*)-thiones (6e).** Yield 88%, dark brown solid, mp 198–200°C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 7.14 (d, $J=7.6$ Hz, 1H), 7.45 (t, $J=7.8$ Hz, 1H), 7.56–7.63(m, 2H), 7.70 (d, $J=10.0$ Hz, 1H), 8.18 (d, $J=7.6$ Hz, 1H), 14.31 (br, 1H).$^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 112.26, 115.59, 115.82, 117.23, 118.42, 118.63, 124.85, 131.05, 131.13, 144.96, 152.26, 179.02. HRMS (ESI): calcd. for $C_{12}H_7FN_2NaS$ $[M+Na]^+$: 253.0206, found: 253.0211.

**6-(3-Chlorophenyl)-3-cyanopyridine-2-(1*H*)-thiones (6f).** Yield 77%, yellow solid, mp 168–170°C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 7.14 (d, $J=7.6$ Hz, 1H), 7.56 (t, $J=7.6$ Hz, 1H), 7.65 (d, $J=7.6$ Hz, 1H), 7.72 (d, $J=7.2$ Hz, 1H), 7.88 (s, 1H), 8.17 (d, $J=7.6$ Hz, 1H), 14.33 (br, 1H). $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 106.09, 117.99, 125.63, 127.55, 128.73, 131.09, 131.28, 133.87, 137.92, 142.94, 157.44, 179.03. HRMS (ESI): calcd. for $C_{12}H_8N_2S$ $[M+H]^+$: 247.0091, found: 247.0090.

**6-(3-Bromophenyl)-3-cyanopyridine-2-(1*H*)-thiones (6g).** Yield 79%, yellow solid, mp 164–166 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 7.10 (d, $J=8.0$ Hz, 1H), 7.42 (t, $J=7.8$ Hz, 1H), 7.54 (d, $J=8.0$ Hz, 1H), 7.61 (dd, $J=8.0$, 1.2 Hz, 1H), 7.96 (d, $J=8.0$ Hz, 1H), 8.21 (t, $J=1.8$ Hz, 1H), 13.85 (br, 1H). $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 108.98, 110.33, 120.69, 122.05, 125.69, 129.40, 130.68, 131.72, 140.18, 141.13, 154.81, 182.32. HRMS (ESI): calcd. for $C_{12}H_7BrN_2NaS$ $[M+Na]^+$: 312.9406, found: 312.9412.

**6-(3,4-Dichlorophenyl)-3-cyanopyridine-2-(1*H*)-thiones (6h).** Yield 97%, yellow solid, mp 178–180°C (220–221).[5a] $^1$H NMR (400 MHz, DMSO-$d_6$): δ7.14 (d, $J=8.0$ Hz, 1H), 7.53 (d, $J=7.6$ Hz, 1H), 7.71 (d, $J=8.8$ Hz, 1H), 7.98 (dd, $J=8.4$, 2.0 Hz, 1H), 8.25 (d, $J=2.0$ Hz, 1H), 14.05 (br, 1H). HRMS (ESI): calcd. for $C_{12}H_6Cl_2N_2NaS$ $[M+Na]^+$: 302.9521, found: 302.9529.

**6-(3,5-Ditrifluoromethylphenyl)-3-cyanopyridine-2-(1*H*)-thiones (6i).** Yield 40%, yellow solid, mp 190–192 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 7.34 (d, $J=7.6$ Hz, 1H), 8.24 (d, $J=8.0$ Hz, 1H), 8.34 (s, 1H), 8.50 (s, 2H), 14.61 (br, 1H). $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 179.32, 158.86, 141.75, 136.81, 131.87 (2C), 129.98 (2C), 124.71 (2C), 122.83, 121.75, 117.05, 101.78. HRMS (ESI): calcd. for $C_{14}H_7F_6N_2S$ $[M+H]^+$: 349.0229, found: 349.0236.

**6-(Biphenyl-4-yl)-3-cyanopyridine-2-(1*H*)-thiones (6j).** Yield 95%, yellow solid, mp>230°C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 7.18 (d, $J=7.6$ Hz, 1H), 7.44 (t, $J=7.8$ Hz, 1H), 7.52 (t, $J=7.6$ Hz, 2H), 7.77 (d, $J=7.2$ Hz, 2H), 7.88 (q, $J=19.2$ Hz, 4H), 8.17 (d, $J=8.0$ Hz, 1H), 14.28 (br, 1H). $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 178.98, 158.96, 141.78, 140.85, 139.47, 137.91, 129.2 (2C), 128.38 (4C), 127.81 (2C), 127.28 (2C), 122.81, 117.09. HRMS (ESI): calcd. for $C_{18}H_{13}N_2S$ $[M+H]^+$: 289.0794, found: 289.0798.

**6-(Pyridine-2-yl)-3-cyanopyridine-2-(1*H*)-thiones (6k).** Yield 40%, dark brown solid, mp 200–203°C (230–231.[5a]). $^1$H NMR (400 MHz, DMSO-$d_6$): δ 7.18 (d, $J=7.6$ Hz, 1H), 7.58 (q, $J=4.3$ Hz, 1H), 8.17–8.22 (m, 2H), 8.75 (dd, $J=4.8$,

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1.6 Hz, 1H), 8.93 (d, $J = 2.8$ Hz,1H), 14.44 (br, 1H). HRMS (ESI): calcd. for $C_{11}H_8N_3S$ $[M + H]^+$: 214.0433, found: 214.0430.

**6-(Thiazol-2-yl)-3-cyanopyridine-2-(1*H*)-thiones (6l).** Yield 68%, dark red solid, mp:221–222 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 7.48 (s, 1H), 8.13 (s, 2H), 14.02 (s, 1H). $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 180.01, 162.53, 161.79, 141.71, 123.92, 122.78, 117.21, 115.65, 101.85. HRMS(ESI): calcd. for $C_9H_4N_3S_2$ $[M - H]^-$:217.9852, found: 217.9855.

**6-(Furan-2-yl)-3-cyanopyridine-2-(1*H*)-thiones (6m).** Yield 62%, dark brown solid, mp 201 °C (221–222.[7f]). $^1$H NMR (400 MHz, DMSO-$d_6$): δ 6.81 (q, $J = 2.0$ Hz, 1H), 7.13 (d, $J = 8.0$ Hz, 1H), 7.89 (d, $J = 3.6$ Hz, 1H), 8.05–8.09 (m, 2H), 14.15 (br, 1H). HRMS (ESI): calcd. for $C_{10}H_7N_2OS$ $[M + H]^+$: 203.0274, found: 203.0278.

**6-(2-Methoxyphenyl)-3-cyanopyridine-2-(1*H*)-thiones (6n).** Yield 75% for two steps, yellow solid, mp 196–198 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 3.83 (s, 3H), 6.92 (d, $J = 8.0$ Hz, 1H), 7.05–7.11 (m, 1H), 7.17–7.20 (m, 1H), 7.43–7.48 (m, 1H), 7.52–7.56 (m, 1H), 8.13 (d, $J = 7.6$ Hz, 1H), 14.06 (br, 1H). $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ56.10, 112.10, 113.67, 115.05, 117.37, 120.84, 130.68, 133.10, 145.08, 151.88, 157.00, 157.13, 177.84. HRMS (ESI): calcd. for $C_{13}H_{11}N_2OS$ $[M + H]^+$: 243.0587, found: 243.0588.

**6-(2, 4-Dichlorophenyl) -3-cyanopyridine-2-(1*H*)-thiones (6o).** Yield 50% for two steps, yellow solid, mp 208–211 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 6.92 (d, $J = 7.2$ Hz, 1H), 7.61 (d, $J = 1.6$ Hz, 2H), 7.84–7.86 (m, 1H), 8.21 (d, $J = 8.0$ Hz, 1H), 14.51 (br, 1H). $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 114.08, 116.64, 117.00, 127.84, 129.46, 130.72, 132.84, 133.21, 136.37, 145.17, 150.42, 178.41. HRMS (ESI): calcd. for $C_{12}H_6Cl_2N_2NaS$ $[M + Na]^+$: 302.9521, found: 302.9527.

### One-Pot Synthesis of 6-Aryl-3-cyanopyridine-2-(1*H*)-thiones (6a)

3-Methoxyacetophenone (30 g, 200 mmol) and DMF-DMA (56 mL, 404 mmol) were stirred under reflux for 24 h. Then the reaction mixture was cooled to room temperature, and the excess DMF-DMA was removed by evaporation in vacuum.

The resulting residue in ethanol (400 mL) was added to cyanothioacetamide (30 g, 300 mmol) in the presence of DABCO (20 g, 100 mmol) at room temperature, and then the reaction mixture was stirred under reflux for 3 h. After it cooled to room temperature, the reaction mixture was neutralized with diluted HCl to precipitate the crude product, which was washed with cold EtOH to give a yellow product (38.7 g, 80% for two steps), mp 234–236 °C.

## ACKNOWLEDGMENTS

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