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An Unprecedented Approach to the Single-Step Synthesis of 3,4-Fused Pyrimidin-2-one and Pyrimidin-2-thione Derivatives by a [3+2+1] Annulation

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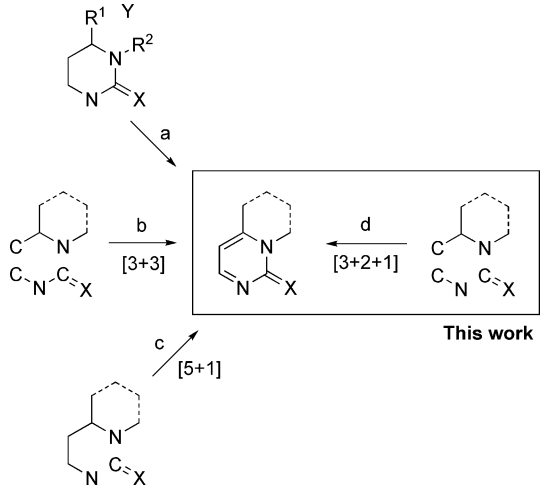
An unprecedented three-component coupling reaction was developed for the synthesis of 3,4-fused pyrimidin-2-one and pyrimidin-2-thione derivatives from an α-acidic imine compound, a nitrile, and triphosgene or carbon disulfide. This method can be used to easily prepare a variety of pyrimidines from commercially available reagents in a single step.

Introduction

3,4-Fused pyrimidin-2-one and pyrimidin-2-thione derivatives[1] are ubiquitous in natural products and biologically active substances[2] and are useful synthetic intermediates.[3] Currently, a number of methods for the efficient and practical synthesis of pyrimidine derivatives are available;[4,5] however, synthesis of the 3,4-fused pyrimidine skeleton is limited to the following general methods (Scheme 1): (i) intermolecular annulation and intramolecular cyclization of 3- or 4-substituted pyrimidine derivatives (route a);[6] (ii) [3+3] annulation of a C–C–N fragment, such as an α-acidic imine derivative, with a C–N–C fragment, such as an acyl heterocumulene derivative (route b);[7] and (iii) [5+1] annulation of an N–C–C–C–N fragment with a C-1 unit, such as a carbonyl compound or a heterocumulene (route c).[8]

Moreover, these methods often require the isolation of intermediates, the synthesis of starting materials, high reaction temperatures, and a prolonged reaction time, which decreases product yield. Hence, development of a novel procedure that allows for a facile, efficient, single-step synthesis of 3,4-fused pyrimidine derivatives using commercially available reagents is highly desirable.

We previously reported that intermolecular annulation of a 1-azaallylic anion,[9] which was generated from an α-acidic methylene compound and a nitrile in the presence of a base, and its synthetic equivalent, a functionalized enamine,[10] selectively produced a variety of nitrogen-containing heterocyclic compounds.[11] During our ongoing development of novel synthetic methods for multifunctionalized nitrogen-containing heterocycles using 1-azaallylic anions, we identified a practical three-component coupling reaction



Scheme 1. New approach to the synthesis of 3,4-fused pyrimidines.

using a picoline derivative, a nitrile, and triphosgene or carbon disulfide as a C-1 unit that produced 3,4-fused pyrimidin-2-one or pyrimidin-2-thione derivatives in a direct, one-pot synthesis. To the best of our knowledge, this approach to the synthesis of a 3,4-fused pyrimidine skeleton through a [3+2+1] annulation is rare (Scheme 1, route d). In this paper, we describe the preparation of pyrimidine derivatives using this unprecedented method.

Results and Discussion

On the basis of our previous studies, when the reaction mixture of 2-picoline (**1a**) and benzonitrile (**2a**) was initially treated with LDA in THF at –70 °C for 1 h, followed by the addition of triphosgene (**3**), the desired bicyclic pyrimidine derivative **4a** was obtained in 63% yield (Table 1, run 1). The structure of isolated pyrimidine **4a** was determined from spectroscopic data, elemental analysis, and X-ray crystallographic structural analysis. When triethylamine (Et_3N,

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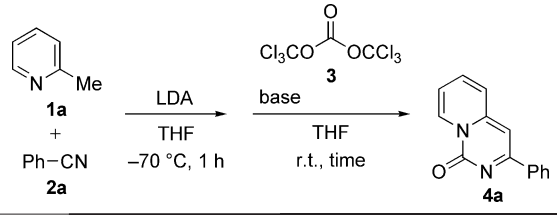
2 equiv.) was then added to the reaction mixture as a base, the yield increased to 83% yield (Table 1, run 2). Moreover, a prolongation of the reaction time to 2 h improved the yield of isolated product to nearly quantitative yield (Table 1, run 3). In contrast, reduction of the amount of added base to 1 equivalent resulted in a slight decrease in product yield compared with the addition of 2 equivalents (Table 1, run 4). Moreover, addition of pyridine did not enhance the product yield (Table 1, run 5). Thus, the reaction conditions used during run 3 (Table 1) were optimal for the three-component coupling reaction.

Table 1. Examination of the one-pot, three-component coupling reaction.



Run	Base (equiv.)	Time [h]	Yield [%][a]
1	none	0.5	63
2	Et_3N (2)	0.5	83
3	Et_3N (2)	2	(95)
4	Et_3N (1)	2	80
5	pyridine (2)	2	70

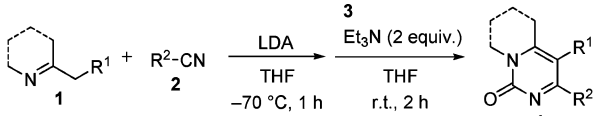
[a] NMR yield (Isolated yield).

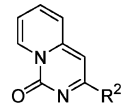
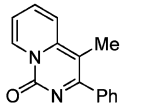
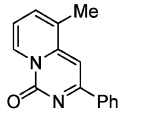
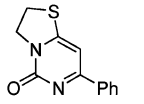
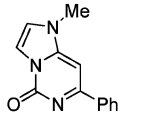
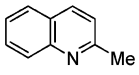
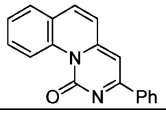
To extend the generality of the reaction, the annulation reaction was then conducted with the use of various picoline derivatives, related nitrogen-containing compounds, and nitriles. The results are summarized in Table 2. When nitriles **2b**,**c**, which had a methoxy group and a halogen group on the benzene ring, respectively, were treated with compounds **1a** and **3** under optimal reaction conditions, corresponding pyrimidine derivatives **4b**,**c** were obtained in excellent yields (Table 2, runs 2 and 3).

In addition, this method was successfully applied to the reaction with a nitrile, consisting of a heterocyclic ring or an aliphatic chain, producing expected products **4d**,**e** in moderate to good yields (Table 2, runs 4 and 5). When 2-ethylpyridine (**1b**) and 2,3-lutidine (**1c**) were then used instead of **1a**, the corresponding pyrimidine derivatives **4f**,**g** were produced, respectively, in good yields (Table 2, runs 6 and 7). Also, heterocycles containing more than one heteroatom, such as 2-methylthiazoline (**1d**) and 1,2-dimethylimidazole (**1e**), afforded the desired five-membered-ring-fused pyrimidines **4h**,**i** in good yields (Table 2, runs 8 and 9). Moreover, employment of 2-methylqunoline (**1f**) provided tricyclic pyrimidine derivatives **4j** in 91% yield (Table 2, run 10).

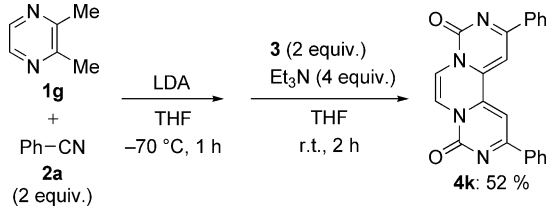
To further explore the scope of this chemistry, a double annulation reaction with the use of 2,3-dimethylpyrazine (**1g**), nitrile **2a**, and **3** was examined (Scheme 2). As expected, the desired reaction proceeded to produce polycyclic pyrimidine derivative **4k** in 52% yield.

Table 2. Single-step synthesis of pyrimidin-2-one derivatives **4**.



Run	Compound **1**	Nitrile **2**	Product **4**	Yield [%][a]
		R^2–CN		
1		**1a** **2a**	R^2 = Ph	**4a** 95
2		**1a** **2b**	R^2 = 4-MeO–C_6H_4–	**4b** 85
3		**1a** **2c**	R^2 = 4-Cl–C_6H_4–	**4c** 99
4		**1a** **2d**	R^2 = 4-Py	**4d** 73
5		**1a** **2e**	R^2 = $MeOCH_2$–	**4e** 53
6		**1b** **2a**		**4f** 93
7		**1c** **2a**		**4g** 76
8		**1d** **2a**		**4h** 83
9		**1e** **2a**		**4i** 77
10		**1f** **2a**		**4j** 91

[a] Isolated yield.

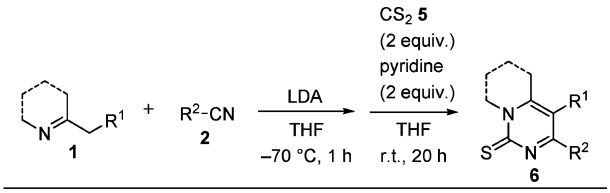


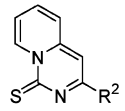
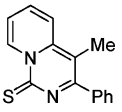
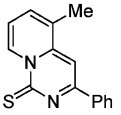
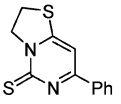
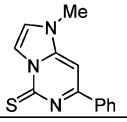
Scheme 2. Double annulation from 2,3-dimethylpyrazine.

We next attempted the synthesis of pyrimidin-2-thione derivatives by using carbon disulfide (CS_2) as a C-1 unit (Table 3). The desired annulation of compound **1a**, benzonitrile (**2a**), and carbon disulfide (**5**) gave expected product **6a** in 37% yield. However, addition of pyridine improved the yield to 70% (Table 3, run 1).

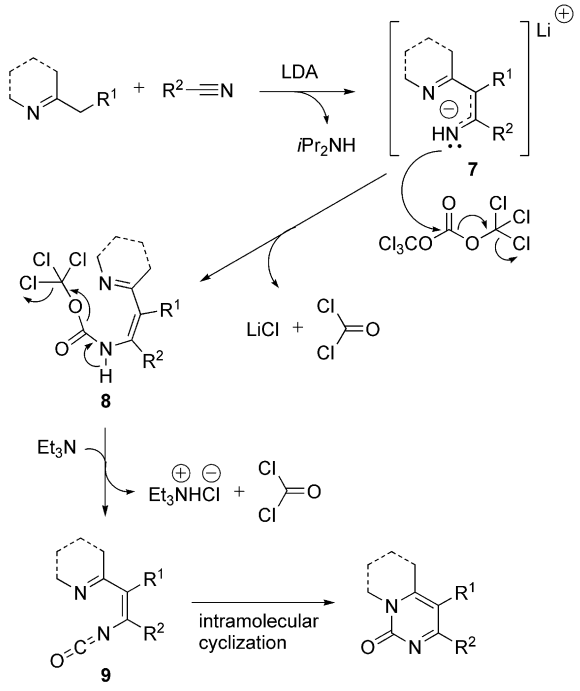
Thus, under these reaction conditions, we examined the preparation of pyrimidin-2-thione derivatives from heterocycle **1**, nitrile **2**, and CS_2. All reactions resulted in successful intermolecular annulation, producing the corresponding pyridine-2-thione derivatives **6a**–**g** in moderate to good yields (Table 3, runs 1–7).

Table 3. Single-step synthesis of pyrimidin-2-thione derivatives **6**.



Run	Compound **1**	Nitrile **2**	Product **6**		Yield [%][a]
		R^2–CN			
1	**1a**	**2a**	R^2 = Ph	**6a**	70
2	**1a**	**2b**	R^2 = 4-MeO–C_6H_4–	**6b**	41
3	**1a**	**2c**	R^2 = 4-Cl–C_6H_4–	**6c**	44
4	**1b**	**2a**		**6d**	80
5	**1c**	**2a**		**6e**	51
6	**1d**	**2a**		**6f**	51
7	**1e**	**2a**		**6g**	57

[a] Isolated yield.



Scheme 3. A plausible mechanism for the synthesis of pyrimidin-2-ones.

A plausible mechanism for the synthesis of pyrimidin-2-one derivatives using the novel method described in this study is shown in Scheme 3. First, azaallyl anion **7**, generated in situ from an α-acidic imine derivative and a nitrile in the presence of LDA, reacts with triphosgene to produce intermediate **8** with concurrent elimination of lithium chloride and phosgene. Then, intermediate **8** generates isocyanate **9** with liberation of hydrogen chloride and phosgene. Finally, intramolecular cyclization of intermediate **9** leads to the formation of the corresponding 3,4-fused pyrimidin-2-one derivative.

Conclusions

In conclusion, we demonstrated that our unprecedented [3+2+1] annulation protocol produces 3,4-fused pyrimidine derivatives by linking three common and commercially available reagents in a one-pot synthesis. We also found that the Et_3N-promoted reaction between 1-azaallylic anions, which were generated from α-acidic imines and nitriles, and triphosgene leads to 3,4-fused pyrimidin-2-one derivatives. Moreover, annulation of the anion with carbon disulfide in the presence of pyridine effectively produces a variety of bicyclic pyrimidin-2-thiones.

Experimental Section

General Methods: Column chromatography was performed by using NH silica gel. THF was distilled from sodium–benzophenone and dried with 5 Å MS. 2-Picoline, triethylamine, pyridine, diisopropylamine, and benzonitrile were distilled prior to use. Other materials were commercially available and were used without further purification. All reactions were carried out under a nitrogen atmosphere, unless otherwise noted. All melting points reported are uncorrected values. ^{1}H NMR spectra were measured at either 500 or 300 MHz by using tetramethylsilane as the internal standard. ^{13}C NMR spectra were measured at either 125 or 75 MHz by using the center peak of chloroform (δ = 77.0 ppm) as the internal standard. High-resolution mass spectra were measured by using NBA (3-nitrobenzyl alcohol) as the matrix. Elemental analyses were performed at Tokyo University of Science.

General Procedure for the Synthesis of Pyrimidin-2-ones 4a–j: To a THF (2 mL) solution of diisopropylamine (1.0 mmol) was added *n*BuLi (1.5 M in hexane, 1.1 mmol) at –70 °C, and then the mixture was stirred at the same temperature. After 30 min, α-acidic compound **1** (1.0 mmol) was added dropwise, and the mixture was stirred for 1 h at –70 °C. Nitrile **2** (1.0 mmol) was gradually added to the solution at –70 °C, and the mixture was stirred for 1 h at the same temperature. Triethylamine (2.0 mmol) was added to the reaction mixture at room temperature, followed by the addition of a THF (1 mL) solution of triphosgene (**3**, 1.0 mmol), and the reaction mixture was stirred for 2 h at the same temperature. To quench the reaction, a 2 M aqueous solution (5 mL) of KOH was added to the reaction mixture. The mixture was extracted several times with $CHCl_3$. The combined organic extract was then dried with Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by NH silica gel chromatography (hexane/AcOEt) to give pyrimidin-2-ones **4a**–**j**.

4a: Yield: 95% (211 mg); yellow solid (CH_2Cl_2/hexane); m.p. 155.1–156.3 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.98 (s, 1 H), 7.09 (t,

J = 7.0 Hz, 1 H), 7.67–7.68 (m, 3 H), 7.46 (d, *J* = 7.0 Hz, 1 H), 7.61 (t, *J* = 7.0 Hz, 1 H), 8.06–8.07 (m, 2 H), 9.03 (d, *J* = 7.0 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 96.4, 117.3, 124.4, 127.5, 128.4, 130.1, 130.8, 136.2, 136.8, 148.5, 151.8, 163.7 ppm. MS (FAB): *m*/*z* (%) = 223 (100) [M + H]. $C_{14}H_{10}N_2O$ (222.24): calcd. C 75.66, H 4.54, N 12.60; found C 75.98, H 4.94, N 12.71.

4b: Yield: 85% (214 mg); yellow solid (CH_2Cl_2/hexane); m.p. 200.8–201.2 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.80 (s, 1 H, O-*Me*), 6.90 (d, *J* = 8.0 Hz, 2 H), 6.93 (s, 1 H), 7.04 (t, *J* = 7.5 Hz, 1 H), 7.41 (d, *J* = 7.5 Hz, 1 H), 7.58 (t, *J* = 7.5 Hz, 1 H), 8.08 (d, *J* = 8.0 Hz, 2 H), 9.02 (d, *J* = 7.5 Hz, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 55.3, 95.5, 113.9, 116.7, 124.2, 129.2, 129.3, 130.2, 135.8, 148.5, 151.9, 162.1, 163.4 ppm. MS (FAB): *m*/*z* (%) = 253 (100) [M + H]. $C_{15}H_{12}N_2O_2$ (252.27): calcd. C 71.42, H 4.79, N 11.10; found C 71.45, H 4.83, N 11.33.

4c: Yield: 99% (254 mg); yellow solid (CH_2Cl_2/hexane); m.p. 216.7–217.5 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.98 (s, 1 H), 7.16 (t, *J* = 7.0 Hz, 1 H), 7.35 (d, *J* = 8.5 Hz, 2 H), 7.49 (d, *J* = 7.0 Hz, 1 H), 7.68 (t, *J* = 7.0 Hz, 1 H), 8.03 (d, *J* = 8.5 Hz, 2 H), 9.09 (d, *J* = 7.0 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 96.2, 117.6, 124.4, 128.8, 128.9, 130.4, 135.3, 136.5, 137.2, 148.7, 151.7, 162.5 ppm. MS (FAB): *m*/*z* (%) = 257 (100) [M + H]. $C_{14}H_9ClN_2O$ (256.69): calcd. C 65.51, H 3.53, N 10.91; found C 65.52, H 3.42, N 10.99.

4d: Yield: 73% (163 mg); yellow solid (CH_2Cl_2/hexane); m.p. 228.3–229.0 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.09 (s, 1 H) 7.27 (t, *J* = 7.5 Hz, 1 H), 7.60 (d, *J* = 7.5 Hz, 1 H), 7.77 (t, *J* = 7.5 Hz, 1 H), 7.91 (d, *J* = 6.0 Hz, 2 H) 8.65 (d, *J* = 6.0 Hz, 2 H) 9.15 (d, *J* = 7.5 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 96.9, 118.5, 121.2, 124.7, 130.7, 137.2, 144.2, 148.9, 150.3, 151.5, 161.1 ppm. MS (FAB): *m*/*z* (%) = 224 (100) [M + H]. $C_{13}H_9N_3O$ (223.23): calcd. C 69.95, H 4.06, N 18.82; found C 70.13, H 4.00, N 18.72.

4e: Yield: 53% (101 mg); yellow solid (CH_2Cl_2/hexane); m.p. 125.1–125.4 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.43 (s, 3 H, CH_2-O-*Me*), 4.37 (s, 2 H, *CH_2*-O-Me), 6.77 (s, 1 H), 7.18 (t, *J* = 8.0 Hz, 1 H), 7.44 (d, *J* = 8.0 Hz, 1 H), 7.68 (t, *J* = 8.0 Hz, 1 H), 9.06 (d, *J* = 8.0 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 59.0, 74.4, 96.2, 117.5, 124.0, 130.3, 136.5, 148.7, 151.3, 168.2 ppm. MS (FAB): *m*/*z* (%) = 191 (100) [M + H]. $C_{10}H_{10}N_2O_2$ (190.20): calcd. C 63.15, H 5.30, N 14.73; found C 65.50, H 5.09, N 14.77.

4f: Yield: 93% (220 mg); yellow solid (CH_2Cl_2/hexane); m.p. 182.5–183.3 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.20 (s, 3 H, Ar-*Me*), 7.16 (t, *J* = 7.5 Hz, 1 H), 7.27–7.30 (m, 3 H), 7.46–87.47 (m, 2 H), 7.62 (d, *J* = 7.5 Hz, 1 H), 7.73 (t, *J* = 7.5 Hz, 1 H), 9.12 (d, *J* = 7.5 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 13.8, 103.6, 117.1, 121.4, 127.6, 128.6, 129.0, 130.4, 136.4, 138.9, 147.3, 150.4, 165.3 ppm. MS (FAB): *m*/*z* (%) = 237 (100) [M + H]. $C_{15}H_{12}N_2O$ (236.27): calcd. C 76.25, H 5.12, N 11.86; found C 76.51, H 5.05, N 11.76.

4g: Yield: 76% (180 mg); yellow solid (CH_2Cl_2/hexane); m.p. 168.5–169.0 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.42 (s, 3 H, Ar-*Me*), 6.91 (s, 1 H), 6.97 (t, *J* = 6.5 Hz, 1 H), 7.35–7.64 (m, 3 H), 7.42 (d, *J* = 6.5 Hz, 1 H), 8.04–8.05 (m, 2 H), 8.93 (d, *J* = 6.5 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 18.3, 93.2, 116.4, 127.4, 128.3, 128.4, 130.7, 131.8, 135.6, 137.0, 148.4, 152.2, 163.3 ppm. MS (FAB): *m*/*z* (%) = 237 (100) [M + H]. $C_{15}H_{12}N_2O$ (236.27): calcd. C 76.25, H 5.12, N 11.86; found C 76.30, H 5.05, N 11.79.

4h: Yield: 83% (191 mg); colorless solid (CH_2Cl_2/hexane); m.p. 195.8–196.4 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.46 (t, *J* = 7.5 Hz, 2 H, N-CH_2-*CH_2*-S), 4.53 (t, *J* = 7.5 Hz, 2 H, N-*CH_2*-CH_2-S), 6.75 (s, 1 H), 7.40–7.48 (m, 3 H), 8.00–8.03 (m, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 27.5, 51.2, 95.9, 127.7, 128.5, 131.5, 135.9, 155.6, 161.9, 170.0 ppm. MS (FAB): *m*/*z* (%) = 231 (100) [M + H]. $C_{12}H_{10}N_2OS$ (230.29): calcd. C 62.59, H 4.38, N 12.16; found C 62.60, H 4.27, N 12.06.

4i: Yield: 77% (173 mg); colorless solid (CH_2Cl_2/hexane); m.p. 235.8–236.3 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.67 (s, 3 H, N-*Me*), 6.47 (s, 1 H), 6.90 (d, *J* = 2.0 Hz, 1 H), 7.35–7.36 (m, 3 H), 7.50 (d, *J* = 2.0 Hz, 1 H), 7.98–8.00 (m, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 33.0, 81.0, 110.4, 120.9, 127.3, 128.3, 130.1, 137.8, 146.1, 150.8, 162.3 ppm. MS (FAB): *m*/*z* (%) = 226 (100) [M + H]. $C_{13}H_{11}N_3O$ (225.25): calcd. C 69.32, H 4.92, N 18.66; found C 69.60, H 4.81, N 18.62.

4j: Yield: 91% (248 mg); yellow solid (CH_2Cl_2/hexane); m.p. 234.7–235.4 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.92 (s, 1 H), 7.11 (d, *J* = 8.7 Hz, 1 H), 7.43–7.48 (m, 4 H), 7.56–7.66 (m, 3 H), 8.14–8.17 (m, 2 H), 9.78 (d, *J* = 8.7 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 99.0, 121.8, 122.0, 126.2, 126.8, 127.8, 128.1, 128.7, 130.5, 131.5, 135.2, 135.6, 135.9, 149.5, 156.2, 165.5 ppm. MS (FAB): *m*/*z* (%) = 273 (100) [M + H]. $C_{18}H_{12}N_2O$ (272.30): calcd. C 79.39, H 4.44, N 10.29; found C 79.54, H 4.44, N 10.18.

Procedure for the Synthesis of Pyrimidin-2-one 4k: To a THF (4 mL) solution of diisopropylamine (2.0 mmol) was added *n*BuLi (1.5 M in hexane, 2.2 mmol) at –70 °C, and then the mixture was stirred at the same temperature. After 30 min, 2,3-dimethylpyrazine (**1g**, 1.0 mmol) was added dropwise, and the mixture was stirred for 1 h at –70 °C. Benzonitrile (**2a**, 2.0 mmol) was gradually added to the solution at –70 °C, and the mixture was stirred for 1 h at the same temperature. Triethylamine (4.0 mmol) was added at room temperature, followed by the addition of a THF (2 mL) solution of triphosgene (**3**, 2.0 mmol), and the reaction mixture was stirred for 2 h at the same temperature. To quench the reaction, a 2 M aqueous solution (10 mL) of KOH was added to the reaction mixture. The mixture was extracted several times with $CHCl_3$. The combined organic extract was then dried with Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by NH silica gel chromatography (hexane/AcOEt) to give pyrimidin-2-ones **4k** (52%, 191 mg) as a yellow solid (CH_2Cl_2/hexane). M.p. 382.9–383.6 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.55–7.63 (m, 8 H), 8.13 (s, 2 H), 8.21–8.23 (m, 4 H) ppm. ^{13}C NMR (75 MHz, [D_6]-DMSO): δ = 97.3, 114.0, 128.3, 129.0, 132.7, 135.6, 143.3, 151.4, 169.1 ppm. MS (FAB): *m*/*z* (%) = 367 (100) [M + H]. HRMS (FAB): calcd. for $C_{22}H_{14}N_4O_2$ [M + H] 367.1195; found 367.1205.

General Procedure for the Synthesis of Pyrimidin-2-thiones 6a–g: To a THF (2 mL) solution of diisopropylamine (1.0 mmol) was added *n*BuLi (1.5 M in hexane, 1.1 mmol) at –70 °C, and then the mixture was stirred at the same temperature. After 30 min, α-acidic compound **1** (1.0 mmol) was added dropwise, and the mixture was stirred for 1 h at –70 °C. Nitrile **2** (1.0 mmol) was gradually added to the solution at –70 °C, and the mixture was stirred for 1 h at the same temperature. Pyridine (2.0 mmol) was added to the reaction mixture at room temperature, followed by the addition of carbon disulfide (**5**, 2.0 mmol), and the reaction mixture was stirred for 20 h at the same temperature. To quench the reaction, a saturated aqueous solution (10 mL) of $NaHCO_3$ was added to the reaction mixture. The mixture was extracted several times with $CHCl_3$. The combined organic extract was then dried with Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by NH silica gel chromatography (hexane/AcOEt) to give pyrimidin-2-thiones **6a**–**g**.

6a: Yield: 70% (167 mg); yellow solid (CH_2Cl_2/hexane); m.p. 167.9–168.8 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.32 (t, *J* = 7.5 Hz, 1 H), 7.36–7.39 (m, 3 H), 7.41 (s, 1 H), 7.67 (d, *J* = 7.5 Hz, 1 H),

7.77 (t, J = 7.5 Hz, 1 H), 8.09–8.11 (m, 2 H), 10.34 (d, J = 7.5 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 102.7, 119.6, 125.7, 127.8, 128.6, 131.2, 135.1, 135.3, 136.6, 147.1, 156.6, 174.7 ppm. MS (FAB): m/z (%) = 239 (100) [M + H]. $C_{14}H_{10}N_2S$ (238.31): calcd. C 70.56, H 4.23, N 11.76; found C 70.39, H 4.54, N 11.65.

6b: Yield: 41% (110 mg); yellow solid (CH_2Cl_2/hexane); m.p. 269.6–270.4 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.87 (s, 3 H, O-*Me*), 6.98 (d, J = 9.5 Hz, 2 H), 7.35 (t, J = 7.0 Hz, 1 H), 7.38 (s, 1 H), 7.62 (d, J = 7.0 Hz, 1 H), 7.77 (t, J = 7.0 Hz, 1 H), 8.22 (d, J = 9.5 Hz, 2 H), 10.46 (d, J = 7.0 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 55.5, 101.6, 114.3, 118.9, 125.4, 128.0, 129.9, 135.6, 136.2, 147.3, 156.8, 162.7, 175.1 ppm. MS (FAB): m/z (%) = 269 (100) [M + H]. $C_{15}H_{12}N_2OS$ (268.33): calcd. C 67.14, H 4.51, N 10.44; found C 66.90, H 4.57, N 10.42.

6c: Yield: 44% (120 mg); brown solid (CH_2Cl_2/hexane); m.p. 239.3–240.1 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.42–7.45 (m, 4 H), 7.68 (d, J = 7.0 Hz, 1 H), 7.85 (t, J = 7.0 Hz, 1 H), 8.16 (d, J = 9.0 Hz, 2 H), 10.50 (d, J = 7.0 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 102.4, 119.9, 125.6, 129.1, 129.3, 134.0, 135.7, 136.9, 137.8, 147.3, 155.8, 175.2 ppm. MS (FAB): m/z (%) = 273 (100) [M + H]. $C_{14}H_9ClN_2S$ (272.75): calcd. C 61.65, H 3.33, N 10.27; found C 61.45, H 3.35, N 10.08.

6d: Yield: 80% (202 mg); yellow solid (CH_2Cl_2/hexane); m.p. 216.8–217.7 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.42 (s, 3 H, Ar-*Me*), 7.38–7.40 (m, 3 H), 7.48 (t, J = 7.0 Hz, 1 H), 7.57–7.59 (m, 2 H), 7.92 (d, J = 7.0 Hz, 1 H), 7.97 (t, J = 7.0 Hz, 1 H), 10.57 (d, J = 7.0 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.6, 111.0, 119.5, 122.4, 128.0, 129.3, 129.7, 136.0, 136.9, 137.9, 146.6, 158.8, 172.4 ppm. MS (FAB): m/z (%) = 253 (100) [M + H]. $C_{15}H_{12}N_2S$ (252.34): calcd. C 71.40, H 4.79, N 11.10; found C 71.02, H 4.78, N 11.08.

6e: Yield: 51% (129 mg); yellow solid (CH_2Cl_2/hexane); m.p. 243.5–244.3 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.63 (s, 3 H, Ar-*Me*), 7.28 (t, J = 7.0 Hz, 1 H), 7.46–7.48 (m, 4 H), 7.65 (d, J = 7.0 Hz, 1 H), 8.20–8.21 (m, 2 H), 10.42 (d, J = 7.0 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 18.8, 99.3, 118.5, 128.1, 128.8, 131.3, 133.0, 134.0, 136.0, 136.3, 147.3, 156.8, 176.1 ppm. MS (FAB): m/z (%) = 253 (100) [M + H]. $C_{15}H_{12}N_2S$ (252.34): calcd. C 71.40, H 4.79, N 11.10; found C 71.62, H 5.06, N 11.08.

6f: Yield: 51% (126 mg); yellow solid (CH_2Cl_2/hexane); m.p. 197.8–198.5 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.48 (t, J = 8.0 Hz, 2 H, N-CH_2-*CH_2*-S), 4.94 (t, J = 8.0 Hz, 2 H, N-*CH_2*-CH_2-S), 7.02 (s, 1 H), 7.43–7.45 (m, 2 H), 7.51 (t, J = 7.0 Hz, 1 H), 8.07 (m, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 26.1, 57.7, 100.9, 128.3, 128.8, 132.2, 135.0, 162.0, 163.9, 180.5 ppm. MS (FAB): m/z (%) = 247 (100) [M + H]. $C_{12}H_{10}N_2S_2$ (246.35): calcd. C 58.51, H 4.09, N 11.37; found C 58.59, H 4.28, N 11.54.

6g: Yield: 57% (138 mg); colorless solid (CH_2Cl_2/hexane); m.p. 295.7–296.5 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.85 (s, 3 H, N-*Me*), 7.00 (s, 1 H), 7.11 (d, J = 2.0 Hz, 1 H), 7.43–7.45 (m, 3 H), 8.13–8.14 (m, 2 H), 8.35 (d, J = 2.0 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, [D$_6$]DMSO): δ = 33.2, 88.9, 113.5, 124.0, 127.1, 128.6, 130.1, 136.8, 142.9, 154.2, 168.4 ppm. MS (FAB): m/z (%) = 242 (100) [M + H]. $C_{13}H_{11}N_3S$ (241.31): calcd. C 64.70, H 4.59, N 17.41; found C 64.47, H 4.74, N 17.28.

Supporting Information (see footnote on the first page of this article): Detailed experimental procedures and characterization data for novel compounds; ORTEP diagram of **4a**; copies of the ^{1}H and ^{13}C NMR spectra of novel products.

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