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SYNTHESIS OF *N,N*-DIALKYL-5(or 10)-OXOBENZO[*b*][1,8 or 1,7(or 1,6)]NAPHTHYRIDINE-10(5*H*)(or 5(10*H*))-CARBOTHIOAMIDES BASED ON THE REACTION OF THE RESPECTIVE (CHLOROPYRIDINYL)(2-ISOTHIOCYANATOPHENYL)METHANONES WITH SECONDARY AMINES

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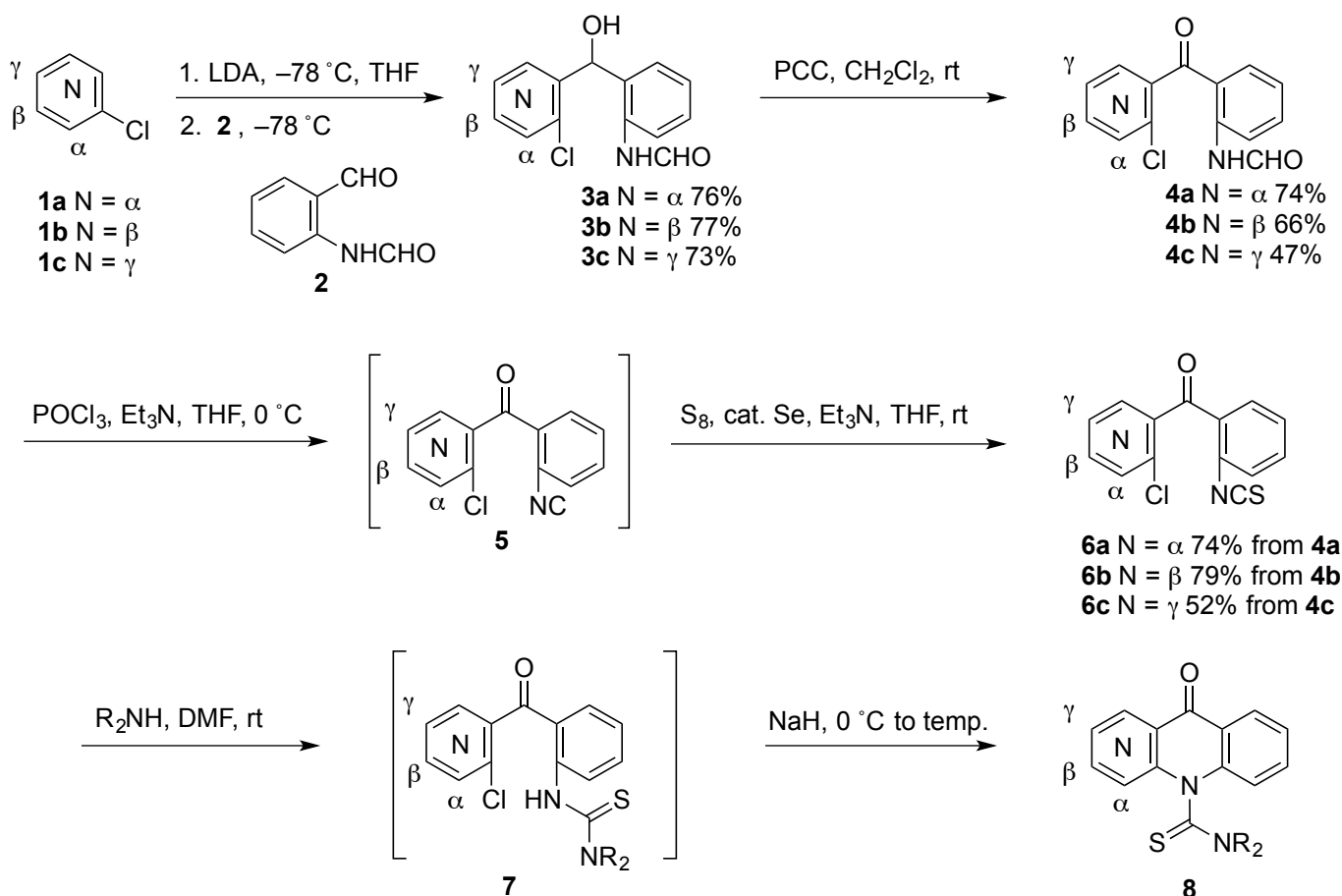
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Abstract – The addition of secondary amines to (2-chloropyridin-3-yl)(2-isothiocyanatophenyl)methanone, derived from 2-chloropyridine and *N*-(2-formylphenyl)formamide, followed by treatment of the resulting thiourea intermediates with sodium hydride has proven to provide a method for the synthesis of *N,N*-dialkyl-5-oxobenzo[*b*][1,8]naphthyridine-10(5*H*)-carbothioamides. Similarly, *N,N*-dialkyl-5-oxobenzo[*b*][1,7]naphthyridine-10(5*H*)-carbothioamides and *N,N*-dialkyl-10-oxobenzo[*b*][1,6]naphthyridine-5(10*H*)-carbothioamides can be prepared from the respective (chloropyridinyl)(2-isothiocyanatophenyl)methanones.

Previous work from our laboratory has established that the addition of secondary amines to (2-halophenyl)(2-isothiocyanatophenyl)methanones, followed by treatment of the resulting thiourea intermediates with sodium hydride, leads to a general approach to the synthesis of *N,N*-disubstituted 9-oxo-10*H*-acridine-10-carbothioamides.¹ We envisaged that a similar sequence using (chloropyridinyl)(2-isothiocyanatophenyl)methanones could provide access to aza-analogues of these derivatives. In this paper, we wish to describe the results of an extensive study of this methodology, which offer the first entry to *N,N*-dialkyl-5(or 10)-oxobenzo[*b*][1,8 or 1,7(or 1,6)]naphthyridine-10(5*H*) (or 5(10*H*))-carbothioamides. Several methods for the synthesis of benzo[*b*]naphthyridinone derivatives have been reported,² because they are interesting from a biological point of view.³ However, there have been so

far no reports on methods for the synthesis of these oxobenzo[*b*]naphthyridinecarbothioamide derivatives, which are of potential biological interest as well.

The synthesis of *N,N*-disubstituted oxobenzo[*b*]naphthyridinecarbothioamides (**8**) from chloropyridines (**1**) was conducted according to the sequence illustrated in Scheme 1. Thus, the reaction of lithiated chloropyridines⁴ with *N*-(2-formylphenyl)formamide, followed by the PCC oxidation of the resulting alcohols (**3**) led to the formation of *N*-{[2-(chloropyridinyl)carbonyl]phenyl}formamides (**4**). These formamides (**4**) were dehydrated with phosphorous oxychloride in the presence of triethylamine to afford the corresponding isocyanides (**5**), which, without any purification, were subjected to the treatment with sulfur in the presence of a catalytic amount of selenium under the Fujiwara's conditions⁵ to afford (chloropyridinyl)(2-isothiocyanatophenyl)methanones (**6**) in satisfactory yields from **4**. It should be noted that compounds (**4c**) and (**6c**), derived from 4-chloropyridine, were rather unstable. So, it must be used immediately after purification in the next steps.



Scheme 1

First, *N,N*-dialkyl-5-oxobenzo[*b*][1,8]naphthyridine-10(5*H*)-carbothioamides (**8a-c**) were prepared in one-pot from (2-chloropyridin-3-yl)(2-isothiocyanatophenyl)methanone (**6a**). Thus, **6a** was allowed to

react with secondary amines in DMF at room temperature to resulted in the immediate formation of the corresponding thiourea derivatives (**7**) (N = α position), which on treatment with sodium hydride at the same temperature underwent smooth ring closure to give the desired products in good yields (Table 1, Entries 1–3).

Table 1. Preparation of oxobenzo[*b*]naphthyridinecarbothioamides (**8**)

Entry	6	R ₂ NH	Temp	8	Yield/% ^a
1	6a (N = α)	Et ₂ NH	rt	8a	78
2	6a	pyrrolidine	rt	8b	83
3	6a	piperidine	rt	8c	85
4	6b (N = β)	Et ₂ NH	80 °C	8d	65
5	6b	pyrrolidine	80 °C	8e	62
6	6b	morpholine	100 °C	8f	58
7	6c (N = γ)	Et ₂ NH	rt	8g	49
8	6c	pyrrolidine	rt	8h	35
9	6c	morpholine	rt	8i	44

^a Yields of isolated products.

Next, *N,N*-dialkyl-5-oxobenzo[*b*][1,7]naphthyridine-10(5*H*)-carbothioamides (**8d-f**) could similarly be synthesized from (3-chloropyridin-4-yl)(2-isothiocyanatophenyl)methanone (**6b**). The addition of secondary amines to **6b** also completed immediately. However, the cyclization of the resulting thiourea intermediates (**7**) (N = β -position) with sodium hydride was very reluctant at room temperature and the higher temperatures (80 to 100 °C) were needed for satisfactory progress. Therefore, the yields of the desired products were somewhat lower than those of **8a-c** (Entries 4–6).

Subsequently, the successive treatment of (4-chloropyridin-3-yl)(2-isothiocyanatophenyl)methanone (**6c**) with secondary amines and sodium hydride was carried out to obtain the corresponding *N,N*-dialkyl-10-oxobenzo[*b*][1,6]naphthyridine-5(10*H*)-carbothioamides (**8g-i**). When **6c** was treated with secondary amines under the same conditions, a few spots, resulted from other than the expected thiourea derivative, were observed by TLC analyses in each case. After addition of sodium hydride, the intermediates were consumed smoothly at room temperature. However, these reactions resulted in the formation of rather complicated mixtures of products, from which only low-to-moderate yields of the desired products could be isolated (Entries 7–9). This may presumably be due to the instability of **6c** as stated above.

In conclusion, the method described here enables us to synthesize three types of oxobenzo[*b*] naphthyridinecarbothioamides from the respective chloropyridines by essentially same operations. As these derivatives are hard to prepare by previous methods and of potentially biological interest, the present method may be of value in organic synthesis.

EXPERIMENTAL

All melting points were obtained on a Laboratory Devices MEL-TEMP II melting apparatus and are uncorrected. IR spectra were recorded with a Perkin–Elmer Spectrum65 FTIR spectrophotometer. ^1H NMR spectra were recorded in CDCl_3 using TMS as an internal reference with a JEOL ECP500 FT NMR spectrometer operating at 500 MHz or a JEOL LA400FT NMR spectrometer operating at 400 MHz. ^{13}C NMR spectra were recorded in CDCl_3 using TMS as an internal reference with a JEOL ECP500 FT NMR spectrometer operating at 125 MHz. High-resolution MS spectra (DART, positive) were measured by a Thermo Scientific Exactive spectrometer. TLC was carried out on Merck Kieselgel 60 PF₂₅₄. Column chromatography was performed using WAKO GEL C-200E. All of the organic solvents used in this study were dried over appropriate drying agents and distilled prior to use.

Starting Materials. *n*-BuLi was supplied by Asia Lithium Corporation. All other chemicals used in this study were commercially available.

***N*-[2-(Hydroxymethyl)phenyl]formamide.** A solution of (2-aminophenyl)methanol (11 g, 86 mmol) in HCO_2Et (70 mL) was heated at reflux temperature for 45 h. After evaporation of excess HCO_2Et , the residue was purified by column chromatography on silica gel (AcOEt /hexane 1:2) to give the desired product (9.7 g, 75%); a white solid; mp 76–79 °C (hexane/ CH_2Cl_2) (lit.,⁶ 79–80 °C). Spectral (IR and ^1H NMR) data for this compound were identical to those reported previously.⁶

***N*-(2-Formylphenyl)formamide (2).** A mixture of the above alcohol (0.91 g, 6.0 mmol) and PCC (2.6 g, 12 mmol) in CH_2Cl_2 (65 mL) containing Celite 545 (12 g) was stirred at rt for 30 min. The mixture was filtered under reduced pressure, and the filtrate was concentrated by evaporation and subjected to purification by column chromatography on silica gel (THF/hexane 1:4) to give **2** (0.65 g, 73%); a white solid; mp 75–76 °C (hexane– CH_2Cl_2) (lit.,⁷ 75–77 °C). Spectral (IR and ^1H NMR) data for this compound were identical to those reported previously.⁷

Typical Procedure for the Preparation of *N*-{2-(Chloropyridinyl)hydroxymethyl}phenyl}formamides (3). ***N*-{2-(2-Chloropyridin-3-yl)hydroxymethyl}phenyl}formamide (3a).** To a stirred solution of LDA (5.0 mmol), generated by the standard conditions from *n*-BuLi and *i*-Pr₂NH, in THF (5 mL) at –78 °C was added a solution of 2-chloropyridine (0.23 g, 2.0 mmol) dropwise.⁴ After 1.5 h, a solution of **2** (0.15 g, 1.0 mmol) in THF (2 mL) was added and stirring was continued at the same temperature for an additional 15 min before saturated aqueous NH_4Cl (10 mL) was added. The mixture was warmed to rt and extracted with AcOEt (3 × 10 mL). The combined extracts were washed with brine (15 mL), dried (Na_2SO_4), and concentrated by evaporation. The residue was purified by column chromatography on silica gel to give **3a** (0.20 g, 76%); an orange oil; R_f 0.30 (AcOEt /hexane 1:4); IR (neat) 3320, 1677 cm^{-1} ; ^1H NMR (400 MHz) δ 2.23 and 2.73 (2s, combined 1H), 6.14 and 6.23 (combined 1H), 6.70–9.41 (m, 9H); ^{13}C NMR δ 69.38, 69.67, 121.26, 122.83, 124.39, 125.83, 126.03, 128.25, 128.79,

128.85, 129.35, 132.04, 132.51, 134.79, 135.61, 136.33, 136.40, 137.47, 137.53, 148.33, 148.33, 148.47, 149.16, 149.38, 160.56, 163.24. Anal. Calcd for C₁₃H₁₁ClN₂O₂: C, 59.44; H, 4.22; N, 10.66. Found: C, 59.39; H, 4.29; N, 10.37.

***N*-{[2-(3-Chloropyridin-4-yl)hydroxymethyl]phenyl}formamide (3b):** a yellow oil; *R_f* 0.36 (AcOEt/hexane 1:2); IR (neat) 3300, 1682 cm⁻¹; ¹H NMR (400 MHz) δ 3.81 and 4.19 (2d, *J* = 4.6 Hz each, combined 1H), 6.11 and 6.22 (2d, *J* = 4.6 Hz each, combined 1H), 6.92–8.79 (m, 9H). Anal. Calcd for C₁₃H₁₁ClN₂O₂: C, 59.44; H, 4.22; N, 10.66. Found: C, 59.30; H, 4.38; N, 10.64.

***N*-{[2-(4-Chloropyridin-3-yl)hydroxymethyl]phenyl}formamide (3c):** a yellow oil; *R_f* 0.23 (AcOEt/hexane 1:2); IR (neat) 3306, 1679 cm⁻¹; ¹H NMR (400 MHz) δ 3.9–4.5 (br, 1H), 6.22 and 6.30 (2s, combined 1H), 6.90–8.83 (m, 9H). Anal. Calcd for C₁₃H₁₁ClN₂O₂: C, 59.44; H, 4.22; N, 10.66. Found: C, 59.25; H, 4.20; N, 10.68.

Typical Procedure for the Preparation of *N*-{[2-(Chloropyridinyl)carbonyl]phenyl}formamides (4).

***N*-{[2-(2-Chloropyridin-3-yl)carbonyl]phenyl}formamide (4a).** Compound (3a) (0.15 g, 0.56 mmol) was oxidized with PCC (0.24 g, 1.1 mmol) in CH₂Cl₂ (6 mL) containing Celite 545 (1.1 g) as described for the preparation of 2 to give 4a (86 mg, 59%); a white solid; mp 149–151 °C (hexane/CH₂Cl₂); IR (KBr) 3277, 1695, 1638 cm⁻¹; ¹H NMR (500 MHz) δ 7.10–11.36 (m, 9H); ¹³C NMR δ 120.94, 121.61, 122.24, 123.10, 134.16, 134.85, 136.35, 137.34, 140.78, 147.19, 150.91, 159.86, 196.86. Anal. Calcd for C₁₃H₉ClN₂O₂: C, 59.90; H, 3.48; N, 10.75. Found: C, 59.70; H, 3.52; N, 10.43.

***N*-{[2-(3-Chloropyridin-4-yl)carbonyl]phenyl}formamide (4b):** a white solid; mp 146–147 °C (hexane/CH₂Cl₂); IR (KBr) 3288, 1694, 1644 cm⁻¹; ¹H NMR (500 MHz) δ 7.09–11.31 (m, 9H). Anal. Calcd for C₁₃H₉ClN₂O₂: C, 59.90; H, 3.48; N, 10.75. Found: C, 59.61; H, 3.53; N, 10.70.

***N*-{[2-(4-Chloropyridin-2-yl)carbonyl]phenyl}formamide (4c):** a white solid; mp 109–110 °C (hexane/CH₂Cl₂); IR (KBr) 3287, 1702, 1644, 1604 cm⁻¹; ¹H NMR (500 MHz) δ 7.10–11.32 (m, 9H). HR MS. Calcd for C₁₃H₁₀ClN₂O₂ (M+H): 261.0431. Found: *m/z* 261.0427.

Typical Procedure for the Preparation of (Chloropyridinyl)(2-isothiocyanatophenyl)methanones (6).

(2-Chloropyridin-3-yl)(2-isothiocyanatophenyl)methanone (6a). To a stirred solution of 4a (86 mg, 0.33 mmol) in THF (2 mL) containing Et₃N (0.23 g, 2.3 mmol) at 0 °C was added POCl₃ (76 mg, 0.50 mmol) dropwise.⁸ After 15 min, saturated aqueous NaHCO₃ (10 mL) was added and the mixture was extracted with AcOEt (3 × 10 mL). The combined extracts were washed with brine (15 mL), dried (Na₂SO₄), and concentrated by evaporation. The residual crude isocyanide (5a) was dissolved in THF (2 mL), and Et₃N (0.11 mL), S₈ (11 mg, 0.33 mmol), and Se (2.6 mg, 0.033 mmol) were added.⁵ The mixture was stirred overnight at rt and the precipitate was filtered off. The filtrate was concentrated by evaporation and the residue was purified by column chromatography on silica gel to give 6a (67 mg, 74%); a brown oil; *R_f* 0.33 (AcOEt/hexane 1:2); IR (neat) 2106, 1674 cm⁻¹; ¹H NMR (400 MHz) δ 7.36–7.40 (m, 2H), 7.44 (dd, *J* = 7.8,

4.9 Hz, 1H), 7.59 (t, $J = 7.8$ Hz, 1H), 7.66 (dd, $J = 7.8, 2.0$ Hz, 1H), 7.88 (dd, $J = 7.8, 2.0$ Hz, 1H), 8.56 (dd, $J = 4.9, 2.0$ Hz, 1H). Anal. Calcd for $C_{13}H_7ClN_2OS$: C, 56.83; H, 2.57; N, 10.20. Found: C, 56.75; H, 2.64; N, 10.05.

(3-Chloropyridin-4-yl)(2-isothiocyanatophenyl)methanone (6b): a brown oil; R_f 0.44 (AcOEt/hexane 1:2); IR (neat) 2106, 1678 cm^{-1} ; 1H NMR (400 MHz) δ 7.35 (d, $J = 4.6$ Hz, 1H), 7.37–7.41 (m, 2H), 7.61 (td, $J = 7.4, 1.1$ Hz, 1H), 7.67 (dd, $J = 7.4, 1.1$ Hz, 1H), 8.68 (d, $J = 4.6$ Hz, 1H), 8.74 (s, 1H). Anal. Calcd for $C_{13}H_7ClN_2OS$: C, 56.83; H, 2.57; N, 10.20. Found: C, 56.70; H, 2.43; N, 10.10.

(4-Chloropyridin-3-yl)(2-isothiocyanatophenyl)methanone (6c): a brown oil; R_f 0.26 (AcOEt/hexane 1:2); IR (neat) 2104, 1670 cm^{-1} ; 1H NMR (400 MHz) δ 7.35–7.40 (m, 2H), 7.45 (d, $J = 5.9$ Hz, 1H), 7.59 (td, $J = 7.8, 2.0$ Hz, 1H), 7.65 (d, $J = 7.8$ Hz, 1H), 8.64 (d, $J = 5.9$ Hz, 1H), 8.69 (s, 1H). HR MS. Calcd for $C_{13}H_8ClN_2OS$ (M+H): 275.0046. Found: m/z 275.0419.

Typical Procedure for the Preparation of *N,N*-Disubstituted Oxobenzonaphthyridine-carbothioamides (8). ***N,N*-Diethyl-5-oxobenzo[*b*][1,8]naphthyridine-10(5*H*)-carbothioamide (8a)**. To a stirred solution of **6a** (62 mg, 0.22 mmol) in DMF (2 mL) was added Et_2NH (16 mg, 0.22 mmol) dropwise. After 15 min, the mixture was cooled to 0 °C and NaH (60% in mineral oil; 9.0 mg, 0.22 mmol) was added. The mixture was warmed to rt and stirring was continued for 1 h before water (10 mL) was added. The resulting mixture was extracted with AcOEt (3 × 10 mL), and the combined extracts were washed with brine (15 mL) and dried (Na_2SO_4). After evaporation of the solvent, the residual solid was recrystallized from hexane/ Et_2O to give **8a** (0.47 g, 68%): a pale-yellow solid; mp 190–191 °C; IR (KBr) 1650, 1606, 1263 cm^{-1} ; 1H NMR (500 MHz) δ 1.04 (t, $J = 7.4$ Hz, 3H), 1.61 (t, $J = 7.4$ Hz, 3H), 3.33–3.38 (m, 2H), 4.15–4.22 (m, 1H), 4.33–4.40 (m, 1H), 7.31 (dd, $J = 8.0, 4.6$ Hz, 1H, 7-H), 7.38 (dd, $J = 8.0, 7.4$ Hz, 1H, 3-H), 7.49 (d, $J = 8.6$ Hz, 1H, 1-H), 7.74 (ddd, $J = 8.6, 7.4, 1.1$ Hz, 1H, 2-H), 8.50 (dd, $J = 8.0, 1.7$ Hz, 1H, 6-H), 8.75–8.78 (m, 2H, 4- and 8-H); ^{13}C NMR δ 10.50, 13.08, 47.16, 47.79, 116.62, 116.80, 118.77, 122.28, 123.09, 127.47, 134.45, 136.67, 139.49, 149.39, 153.98, 178.28, 180.35. HR MS. Calcd for $C_{17}H_{18}N_3OS$ (M+H): 312.1170. Found: m/z 312.1148. Anal. Calcd for $C_{17}H_{17}N_3OS$: C, 65.57; H, 5.50; N, 13.49. Found: C, 65.70; H, 5.57; N, 13.40.

10-(Pyrrolidin-1-ylcarbonothioyl)benzo[*b*][1,8]naphthyridin-5(10*H*)-one (8b): a yellow solid; mp 182–184 °C (hexane/ Et_2O); IR (KBr) 1645, 1607, 1265 cm^{-1} ; 1H NMR (500 MHz) δ 1.94–2.05 (m, 2H), 2.16–2.21 (m, 2H), 3.29–3.32 (m, 2H), 4.08–4.14 (m, 1H), 4.23–4.29 (m, 1H), 7.32 (dd, $J = 7.4, 4.6$ Hz, 1H), 7.39 (dd, $J = 8.0, 6.9$ Hz, 1H), 7.49 (d, $J = 8.0$ Hz, 1H), 7.75 (ddd, $J = 8.6, 6.9, 1.1$ Hz, 1H), 8.51 (dd, $J = 8.0, 1.1$ Hz, 1H), 8.76–8.79 (m, 2H); ^{13}C NMR δ 24.82, 25.84, 51.41, 53.74, 116.21, 116.78, 118.65, 122.24, 123.09, 127.56, 134.65, 136.83, 138.61, 148.79, 154.14, 177.56, 178.22. HR MS. Calcd for $C_{17}H_{16}N_3OS$ (M+H): 310.1014. Found: m/z 310.1000. Anal. Calcd for $C_{17}H_{15}N_3OS$: C, 66.00; H, 4.89; N, 13.58. Found: C, 65.90; H, 4.98; N, 13.28.

10-(Piperidin-1-ylcarbonothioyl)benzo[*b*][1,8]naphthyridin-5(10*H*)-one (8c): a yellow solid; mp 175–177 °C (hexane/CH₂Cl₂); IR (KBr) 1648, 1606, 1263 cm⁻¹; ¹H NMR (500 MHz) δ 1.39–1.45 (m, 1H), 1.58–1.65 (m, 1H), 1.67–1.79 (m, 2H), 1.88–1.96 (m, 1H), 2.03–2.09 (m, 1H), 3.31–3.36 (m, 1H), 3.43–3.47 (m, 1H), 4.33–4.38 (m, 1H), 4.69–4.74 (m, 1H), 7.32 (dd, *J* = 7.4, 4.6 Hz, 1H), 7.39 (d, *J* = 8.0, 7.4 Hz, 1H), 7.54 (d, *J* = 8.6 Hz, 1H), 7.75 (ddd, *J* = 8.6, 7.4, 1.1 Hz, 1H), 8.50 (dd, *J* = 8.0, 1.1 Hz, 1H), 8.76–8.79 (m, 2H); ¹³C NMR δ 23.76, 25.29, 26.25, 51.11, 51.81, 116.62, 116.67, 118.73, 122.20, 123.08, 127.43, 134.52, 136.71, 139.04, 149.10, 154.05, 178.19, 179.26. HR MS. Calcd for C₁₈H₁₈N₃OS (M+H): 324.1170. Found: *m/z* 324.1167. Anal. Calcd for C₁₈H₁₇N₃OS: C, 66.85; H, 5.30; N, 12.99. Found: C, 66.77; H, 5.19; N, 12.72.

***N,N*-Diethyl-5-oxobenzo[*b*][1,7]naphthyridine-10(5*H*)-carbothioamide (8d):** a yellow solid; mp 137–139 °C (hexane/CH₂Cl₂); IR (KBr) 1650, 1605, 1263 cm⁻¹; ¹H NMR (400 MHz) δ 1.02 (t, *J* = 7.8 Hz, 3H), 1.63 (t, *J* = 6.9 Hz, 3H), 3.33 (q, *J* = 6.9 Hz, 2H), 4.20–4.31 (m, 2H), 7.38–7.44 (m, 2H, 1- and 3-H), 7.76 (dd, *J* = 8.8, 6.9 Hz, 1H, 2-H), 8.26 (d, *J* = 4.9 Hz, 1H, 6-H), 8.51 (dd, *J* = 8.8, 2.0 Hz, 1H, 4-H), 8.59 (d, *J* = 4.9 Hz, 1H, 7-H), 8.95 (s, 1H, 9-H); ¹³C NMR δ 10.43, 13.59, 47.30, 47.99, 115.94, 118.69, 122.13, 123.31, 125.53, 127.62, 133.96, 134.93, 139.04, 139.98, 142.30, 177.20, 178.62. HR MS. Calcd for C₁₇H₁₈N₃OS (M+H): 312.1170. Found: *m/z* 312.1153. Anal. Calcd for C₁₇H₁₇N₃OS: C, 65.57; H, 5.50; N, 13.49. Found: C, 65.41; H, 5.48; N, 13.20.

10-(Pyrrolidin-1-ylcarbonothioyl)benzo[*b*][1,7]naphthyridin-5(10*H*)-one (8e): a yellow solid; mp 185–186 °C (hexane/CH₂Cl₂); IR (KBr) 1647, 1607, 1265 cm⁻¹; ¹H NMR (400 MHz) δ 1.98–2.03 (m, 2H), 2.17–2.23 (m, 2H), 3.26 (t, *J* = 6.9 Hz, 2H), 4.16 (t, *J* = 6.9 Hz, 2H), 7.39–7.42 (m, 2H), 7.78 (ddd, *J* = 8.6, 6.9, 1.7 Hz, 1H), 8.27 (d, *J* = 5.2 Hz, 1H), 8.52 (dd, *J* = 8.6, 1.7 Hz, 1H), 8.60 (d, *J* = 5.2 Hz, 1H), 8.94 (s, 1H); ¹³C NMR δ 24.77, 25.91, 51.39, 53.97, 115.44, 118.87, 122.16, 123.27, 125.60, 127.80, 133.17, 135.19, 138.23, 139.63, 142.33, 175.84, 177.18. HR MS. Calcd for C₁₇H₁₆N₃OS (M+H): 310.1014. Found: *m/z* 310.1006. Anal. Calcd for C₁₇H₁₅N₃OS: C, 66.00; H, 4.89; N, 13.58. Found: C, 65.94; H, 4.97; N, 13.54.

10-(Morpholin-4-ylcarbonothioyl)benzo[*b*][1,7]naphthyridin-5(10*H*)-one (8f): a yellow solid; mp 233–235 °C (hexane/CH₂Cl₂); IR (KBr) 1652, 1605, 1273 cm⁻¹; ¹H NMR (400 MHz) δ 3.38–3.41 (m, 2H), 3.56 (t, *J* = 4.9 Hz, 2H), 4.04 (t, *J* = 4.9 Hz, 2H), 4.50–4.63 (m, 2H), 7.41–7.44 (m, 2H), 7.80 (ddd, *J* = 8.7, 6.9, 2.0 Hz, 1H), 8.27 (d, *J* = 4.9 Hz, 1H), 8.52 (dd, *J* = 8.7, 2.0 Hz, 1H), 8.61 (d, *J* = 4.9 Hz, 1H), 8.97 (s, 1H); ¹³C NMR δ 50.11, 50.50, 66.05, 66.32, 115.58, 118.88, 122.52, 123.52, 125.60, 127.86, 133.61, 135.21, 138.65, 139.65, 142.58, 176.99, 178.51. HR MS. Calcd for C₁₇H₁₆N₃O₂S (M+H): 326.0963. Found: *m/z* 326.0949. Anal. Calcd for C₁₇H₁₅N₃O₂S: C, 62.75; H, 4.65; N, 12.91. Found: C, 62.71; H, 4.66; N, 12.70.

***N,N*-Diethyl-10-oxobenzo[*b*][1,6]naphthyridine-5(10*H*)-carbothioamide (8g):** a pale-yellow solid; mp 212–214 °C (hexane/CH₂Cl₂); IR (KBr) 1655, 1609, 1258 cm⁻¹; ¹H NMR (500 MHz) δ 1.01 (t, *J* = 7.4 Hz,

3H), 1.61 (t, $J = 7.4$ Hz, 3H), 3.25–3.34 (m, 2H), 4.19–4.27 (m, 2H), 7.22 (d, $J = 5.7$ Hz, 1H, 4-H), 7.39 (d, $J = 8.0$ Hz, 1H, 6-H), 7.42 (ddd, $J = 8.0, 7.4, 1.1$ Hz, 1H, 8-H), 7.75 (ddd, $J = 8.0, 7.4, 1.7$ Hz, 1H, 7-H), 8.53 (dd, $J = 8.0, 1.7$ Hz, 1H, 9-H), 8.69 (d, $J = 5.7$ Hz, 1H, 3-H), 9.63 (s, 1H, 1-H); ^{13}C NMR δ 10.38, 13.42, 47.28, 47.95, 109.64, 116.03, 116.59, 123.57, 123.80, 127.53, 134.71, 139.10, 143.55, 151.17, 152.11, 177.32, 178.35. HR MS. Calcd for $\text{C}_{17}\text{H}_{18}\text{N}_3\text{OS}$ (M+H): 312.1170. Found: m/z 312.1164. Anal. Calcd for $\text{C}_{17}\text{H}_{17}\text{N}_3\text{OS}$: C, 65.57; H, 5.50; N, 13.49. Found: C, 65.51; H, 5.56; N, 13.40.

5-(Pyrrolidin-1-ylcarbonothioyl)benzo[*b*][1,6]naphthyridin-10(5*H*)-one (8h): a white solid; mp 177–178 °C (hexane/ CH_2Cl_2); IR (KBr) 1652, 1607, 1262 cm^{-1} ; ^1H NMR (500 MHz) δ 1.97–2.02 (m, 2H), 2.16–2.22 (m, 2H), 3.20–3.23 (m, 2H), 4.13 (t, $J = 6.9$ Hz, 2H), 7.20 (d, $J = 5.7$ Hz, 1H), 7.37 (d, $J = 8.6$ Hz, 1H), 7.42 (t, $J = 7.4$ Hz, 1H), 7.75 (ddd, $J = 8.6, 7.4, 1.1$ Hz, 1H), 8.53 (dd, $J = 7.4, 1.1$ Hz, 1H), 8.70 (d, $J = 5.7$ Hz, 1H), 9.63 (s, 1H); ^{13}C NMR δ 24.74, 25.89, 51.34, 53.95, 109.21, 115.58, 116.66, 123.64, 123.76, 127.73, 134.95, 138.30, 142.80, 151.26, 152.33, 175.66, 177.29. HR MS. Calcd for $\text{C}_{17}\text{H}_{16}\text{N}_3\text{OS}$ (M+H): 310.1014. Found: m/z 310.0998. Anal. Calcd for $\text{C}_{17}\text{H}_{15}\text{N}_3\text{OS}$: C, 66.00; H, 4.89; N, 13.58. Found: C, 65.83; H, 5.07; N, 13.46.

5-(Morpholin-4-ylcarbonothioyl)benzo[*b*][1,6]naphthyridin-10(5*H*)-one (8i): a white solid; mp 231–232 °C (hexane/ CH_2Cl_2); IR (KBr) 1652, 1274 cm^{-1} ; ^1H NMR (500 MHz) δ 3.35 (t, $J = 4.9$ Hz, 2H), 3.54 (t, $J = 4.9$ Hz, 2H), 4.02 (t, $J = 4.9$ Hz, 2H), 4.54 (t, $J = 4.9$ Hz, 2H), 7.22 (d, $J = 5.7$ Hz, 1H), 7.39 (d, $J = 8.6$ Hz, 1H), 7.44 (dd, $J = 8.0, 7.4$ Hz, 1H), 7.78 (ddd, $J = 8.6, 7.4, 1.1$ Hz, 1H), 8.54 (dd, $J = 8.0, 1.1$ Hz, 1H), 8.72 (d, $J = 5.7$ Hz, 1H), 9.63 (s, 1H); ^{13}C NMR δ 50.07, 50.44, 66.00, 66.26, 109.30, 115.74, 116.56, 123.54, 123.98, 127.74, 134.94, 138.72, 143.19, 151.29, 152.41, 177.06, 178.27. HR MS. Calcd for $\text{C}_{17}\text{H}_{16}\text{N}_3\text{O}_2\text{S}$ (M+H): 326.0963. Found: m/z 326.0956. Anal. Calcd for $\text{C}_{17}\text{H}_{15}\text{N}_3\text{O}_2\text{S}$: C, 62.75; H, 4.65; N, 12.91. Found: C, 62.50; H, 4.63; N, 12.76.

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