

AN EFFICIENT AND NOVEL SYNTHESIS OF FUSED THIAZOL-2(3H)-ONES

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Abstract - Reaction of *o*-bromo aromatic amines (2, 4, 7, 10, 15) with ethyl potassium xanthate gave the corresponding fused thiazol-2(3H)-thiones (16, 19, 22) which in turn were first alkylated with methyl iodide and then treated with sodium methoxide to produce fused thiazol-2(3H)-ones (18, 21, 24). Treatment of 4-(4-pyridinyl)benzenamine dihydrobromide (1) with DMSO gave 2-bromo-4-(4-pyridinyl)benzenamine (2). Reduction of 4-(4-bromo-3-nitrophenyl)pyridine (3) with stannous chloride gave 2-bromo-5-(4-pyridinyl)benzenamine (4). Treatment of 5-bromo-2-methyl[3,4'-bipyridin]-6(1H)-one (5) with phosphorous oxychloride and ammonia sequentially yielded amino compound (7). Hofmann reaction of 2-chloro-6-methyl[3,4'-bipyridine]-3-carboxamide resulted in amino compound (10). 5-Acyl-6-methylpyridin-2(1H)-ones (11) were converted to 3-bromo-1,6-naphthyridin-2-amines (15) via a four-step sequence.

Recently, there has been considerable interest in 2(3H)-benzothiazolones as herbicides,² pesticides,³ fungicides,⁴ and pharmaceutical agents.⁵ We have also been interested in 6-(4-pyridyl)-2(3H)-benzothiazolone (18a) and its analogs for its cAMP PDE III activity. The most common method⁵ for the preparation of 2(3H)-benzothiazolones involves the reaction of phosgene with *o*-aminothiophenols which in turn are prepared by the Herz reaction⁶ of anilines. However, the Herz reaction of 4-(4-pyridyl)aniline (1) gave impure 2-amino-5-(4-

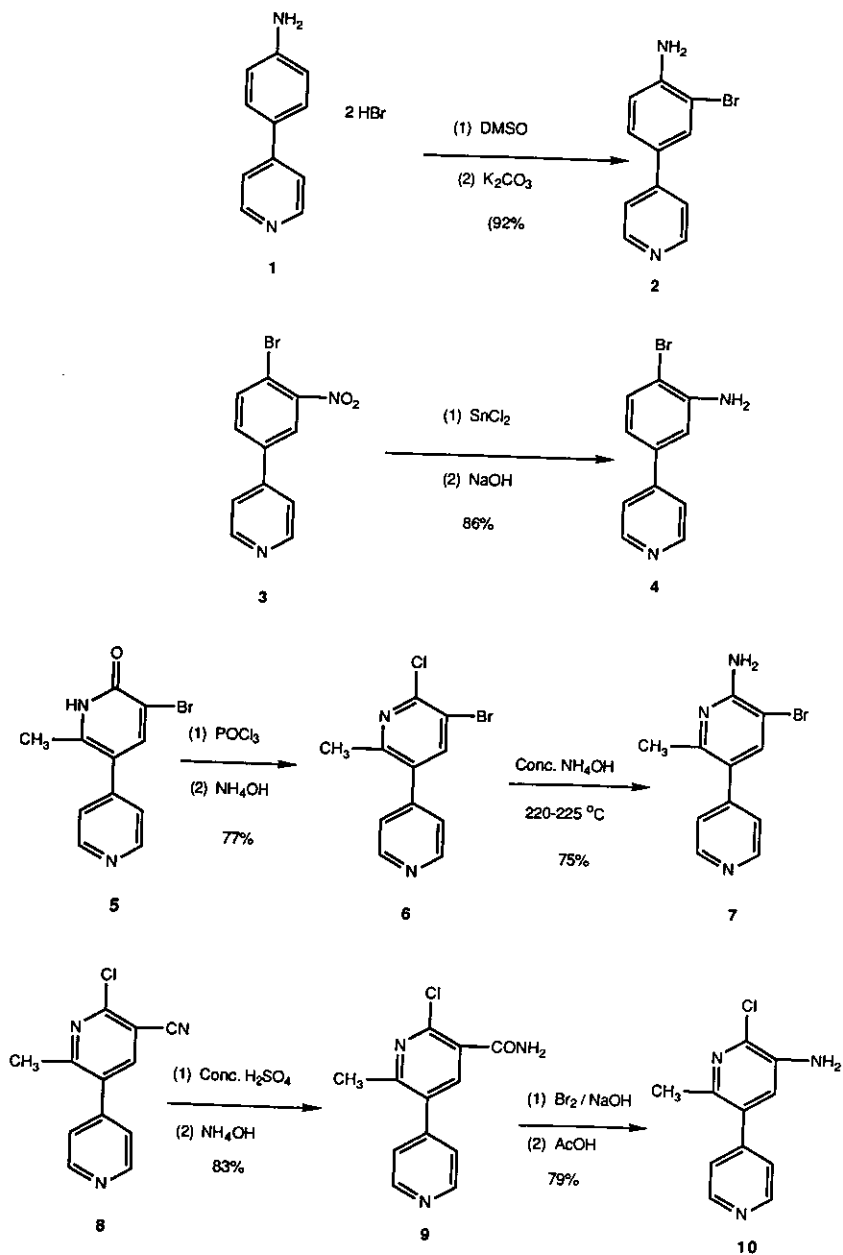
pyridyl)thiophenol in a low yield from which only a small quantity of 18a was prepared. Since multigram quantities of 18a were needed, we looked for an alternate approach to 18a. We wish to report here a novel synthesis of 18a and its analogs.

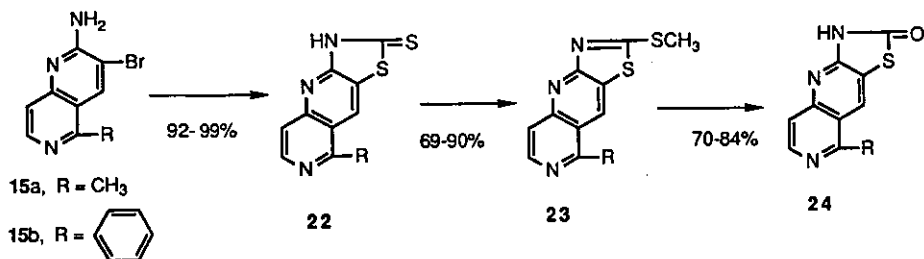
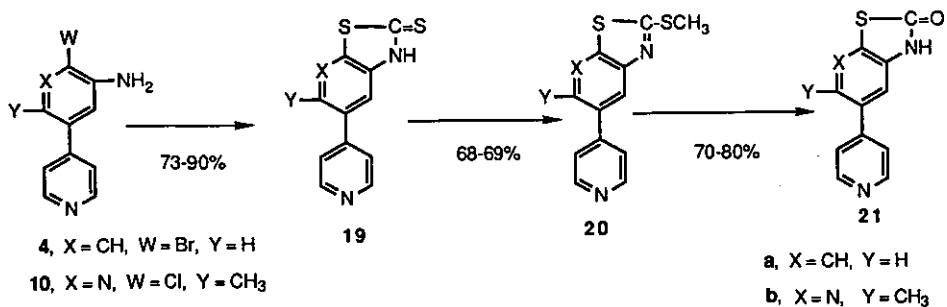
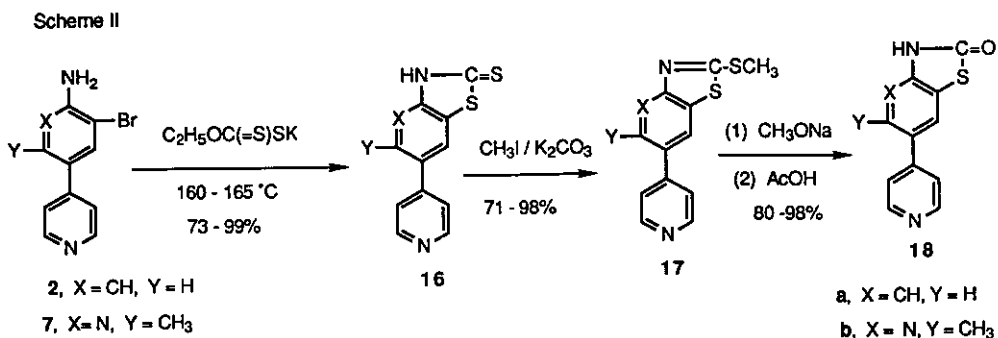
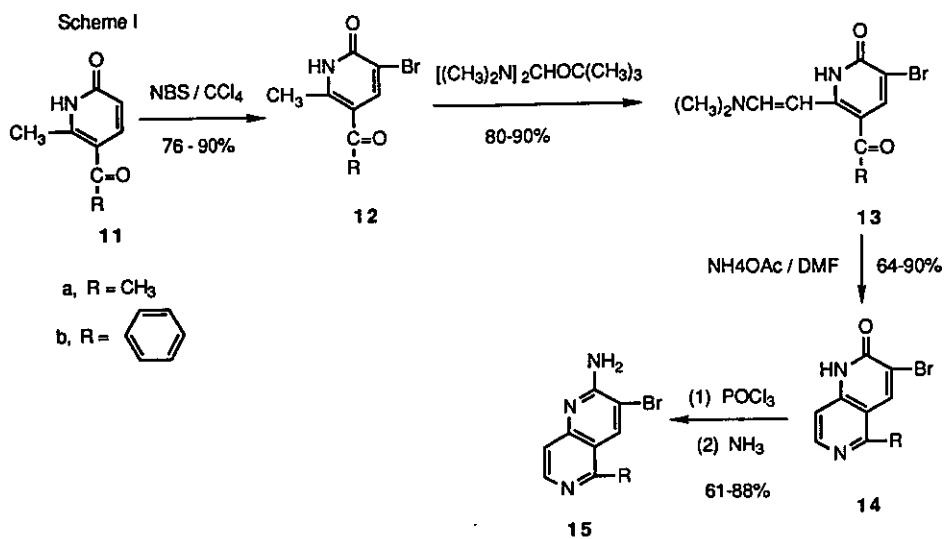
In 1980, French workers⁷ reported the preparation of naphtho[2,3-d]thiazol-2(3H)-thione by the condensation of 3-bromo-2-naphthylamine with carbon disulfide in the presence of sodium in 2-methoxyethanol at 180°C in 30% yield. However, the reaction of 2-bromo-4-(pyridyl)aniline (2) was unsuccessful under these conditions. After further investigation, we have found that the reaction of ethyl potassium xanthate with 2 in 1-methyl-2-pyrrolidinone (NMP) at 160-165 °C leads to the formation of 6-(4-pyridyl)-2(3H)-benzothiazolthione (16a) in almost quantitative yield (Scheme II). To our knowledge, ethyl potassium xanthate has not been used before in this type of reaction. Unfortunately, the conversion of 16a to 18a by the widely used oxidative procedure⁸ was unsuccessful. On the other hand, the treatment of 2-methylthiobenzothiazole derivative (17a) with sodium methoxide followed by quenching with acetic acid gave 18a in 98% yield. This type of transformation ($>-S-CH_3 \rightarrow >-O$) is unprecedented in the literature. We believe this reaction probably involves the displacement of the methylthio group by a methoxy group, and the resulting methyl ether is cleaved by the sodium mercaptide⁹ generated *in situ*. We have extended this procedure to the synthesis of thiazolo[4,5-b]pyridin-2(3H)-ones (18b, 21b) and thiazolo[4,5-b][1,6]naphthyridin-2(3H)-ones (24a, 24b) which were also obtained in high yield (Scheme II).

The starting *o*-bromo aromatic amines were prepared as follows. Treatment of 4-(4-pyridyl)aniline dihydrobromide¹⁰ with hot dimethyl sulfoxide¹¹ gave 2. Reduction of 2-bromo-5-(4-pyridinyl)nitrobenzene (3)¹² with stannous chloride gave the amino compound (4). Treatment of 5-bromo-2-methyl[3,4'-bipyridin]-6(1H)-one (5)¹³ with phosphorous oxychloride and ammonia sequentially yielded aminobipyridine (7). Hofmann reaction of carboxamide (9) prepared from nitrile (8)¹⁴ provided aminobipyridine (10). The preparation of 3-bromo-1,6-naphthyridin-2-amines (15) is depicted in Scheme 1. Bromination of 5-acyl-6-methylpyridin-2(1H)-ones (11)¹⁵ with *N*-bromosuccinimide gave 3-bromopyridones (12) which were reacted with Brederick's reagent to produce 6-(2-(dimethylamino)ethenyl)pyridones (13). Treatment of 13

with ammonium acetate gave 1,6-naphthyridinones (14) which were treated with phosphorous oxychloride followed by ammonia to give 15.

In conclusion, the method described here affords fused thiazol-2(3H)-ones in high yields from readily available *o*-bromo aromatic amines and will be useful in the preparation of related compounds.





EXPERIMENTAL

The melting points were determined in open capillaries in an oil bath and are uncorrected. The ^1H nmr spectra were recorded on a Varian HA-100 spectrometer, and all the spectra are reported in parts per million relative to Me_4Si (δ). Compounds (12b-15b) were prepared by following the procedure for the preparation of 12a-15a, respectively.

2-Bromo-4-(4-pyridinyl)benzenamine (2): A stirred mixture of 4-(4-pyridinyl)benzenamine dihydrobromide (1)¹⁰ (158 g, 0.48 mol) and DMSO (750 ml) was heated on a steam bath for 1.5 h and then poured into ice cold water (1 l). The resulting mixture was neutralized by treating with solid potassium carbonate. The resulting tan precipitate was collected, washed with water, and recrystallized from isopropanol-hexanes to give 109.8 g (92%) of an off-white solid: mp 158-160°C; ^1H nmr (CDCl_3) δ 8.50 (d, $J = 5.8$ Hz, 2H, 2'-H, 6'-H), 7.87 (s, 1H, 3-H), 7.62 (m, 3H), 6.90 (d, $J_o = 7.5$ Hz, 1H), 5.68 (br s, 2H, NH_2). Anal. Calcd for $\text{C}_{11}\text{H}_9\text{N}_2\text{Br}$: C, 53.04; H, 3.64; N, 11.25. Found: C, 52.92; H, 3.78; N, 11.58.

2-Bromo-5-(4-pyridinyl)benzenamine (4): To a stirred solution of $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$ (34 g, 0.15 mol), water (90 ml) and conc. HCl (180 ml) was added 4-(4-bromo-3-nitrophenyl)pyridine (3)¹² (14 g, 0.05 mol) and the resulting mixture was stirred at ambient temperature for 45 min, heated on a steam bath for 4 h, and then concentrated under reduced pressure. The residue was treated with 10% aqueous NaOH until strongly basic. The insoluble orange product was collected, washed with water, and recrystallized from isopropanol-hexanes after treatment with charcoal to give 10.1 g (86%) of 4 as light orange flakes: mp 141-144°C; ^1H nmr (CDCl_3) δ 8.66, 7.54 (A_2B_2 , $J = 5.7$ Hz, 4H, $\text{C}_5\text{H}_4\text{N}$), 7.51 (d, $J_o = 7.4$ Hz, 1H, 3-H), 7.00 (d, $J_m = 1.1$ Hz, 1H, 6-H), 6.87 (dd, $J_o = 7.4$ Hz, $J_m = 1.1$ Hz, 4-H). Anal. Calcd for $\text{C}_{11}\text{H}_9\text{N}_2\text{Br}$: C, 53.04; H, 3.64; N, 11.25. Found: C, 53.13; H, 3.91; N, 11.08.

5-Bromo-6-chloro-2-methyl-3,4'-bipyridine (6): A stirred mixture of 5-bromo-6-methyl[3,4'-bipyridin]-6(1H)-one (5)¹³ (265 g, 1 mol) and phosphorous oxychloride (1 l, 10.7 mol) was heated under reflux for 9 h and then most of the unreacted phosphorous oxychloride was removed under reduced pressure. The oily residue was poured into a vigorously stirred mixture of water, ice, and conc. aqueous ammonia. More ice and conc. aqueous ammonia were added during the quenching process to keep the temperature $<5^\circ\text{C}$ and the pH on the basic side. The brown solid product was collected, washed with water, dried, and recrystallized from

isopropanol-hexanes after treatment with charcoal to give 200.4 g (71%) of light orange crystals of **6**: mp 106-107°C. Anal. Calcd for $C_{11}H_8N_2BrCl$: C, 46.60; H, 2.84; N, 9.88. Found: C, 46.72; H, 2.88; N, 9.89.

3-Bromo-6-methyl[3,4'-bipyridin]-2-amine (7): A mixture of **6** (28 g, 0.1 mol) and concentrated aqueous ammonia (375 ml) was heated in an autoclave at 220-225°C for 24 h and then cooled to room temperature. The tan solid was collected, washed with water, and recrystallized from isopropanol to give 19.7 g (75%) of tan crystals: mp 169-170°C; 1H nmr (DMSO- d_6) δ 8.62, 7.42 (A_2B_2 , $J = 5.9$ Hz, 4H, C_5H_4N), 6.67 (s, 1H, 4-H), 6.44 (br s, 2H, NH_2), 2.30 (s, 3H, CH_3). Anal. Calcd for $C_{11}H_8N_2BrCl$: C, 46.60; H, 2.84; N, 9.88. Found: C, 46.72; H, 2.73; N, 9.84.

6-Chloro-2-methyl[3,4'-bipyridine]-5-carboxamide (9): To stirred conc. H_2SO_4 (250 ml) cooled in ice bath was added 6-chloro-2-methyl[3,4'-bipyridine]-5-carbonitrile (**8**)¹⁴ (50 g, 0.22 mol) over 30 min. The resulting mixture was stirred until all the compound dissolved (4 h). The resulting dark red solution was left at room temperature for 72 h and then poured into a vigorously stirred mixture of ice, water, and aqueous ammonia. The light orange solid precipitate was collected, washed with water, and recrystallized from isopropanol to give 44.6 g (83%) of **9**: mp 205-206°C. Anal. Calcd for $C_{12}H_{10}N_3OCl$: C, 58.19; H, 4.07; N, 16.97. Found: C, 50.32; H, 4.09; N, 16.85.

6-Chloro-2-methyl[3,4'-bipyridin]-5-amine (10): To a stirred mixture of **9** (33.7 g, 0.14 mol), 35% aqueous NaOH (80 ml), and water (250 ml) cooled in ice-salt bath was added bromine (8.6 ml, 0.16 mol) over 20 min. The resulting light orange solution was stirred for 1 h and then the ice bath was removed, left at room temperature overnight and finally heated on a steam bath for 1 h. After this, the reaction mixture was acidified with acetic acid. The resulting brown precipitate was collected, washed with water, and recrystallized from isopropanol-ether to afford 23.7 g (79%) of **10**: mp 180-181°C; 1H nmr ($CDCl_3$) δ 8.66, 7.23 (A_2B_2 , $J = 4.8$ Hz, 4H, C_5H_4N), 6.90 (s, 1H, 4-H), 2.35 (s, 3H, CH_3). Anal. Calcd for $C_{11}H_{10}N_3Cl$: C, 60.14; H, 4.59; N, 19.13. Found: C, 59.78; H, 4.66; N, 18.93.

5-Acetyl-3-bromo-6-methylpyridin-2(1H)-one (12a): A stirred mixture of 5-acetyl-6-methylpyridin-2(1H)-one (**11a**)¹⁵ (15.1 g, 0.1 mol), *N*-bromosuccinimide (20.8 g, 0.11 mol), benzoyl peroxide (100 mg, 0.4 mmol), and carbon tetrachloride (250 ml) was heated under

reflux for 8 h and then concentrated on a rotary evaporator. The residual light orange solid was slurried in water (300 ml) and collected. Recrystallization from ethanol gave 17.1 g (74%) of a white granular solid: mp 228-230°C. Anal. Calcd for $C_8H_8NO_2Br$: C, 41.77; H, 3.50; N, 6.09. Found: C, 41.92; H, 3.60; N, 6.11.

5-Benzoyl-3-bromo-6-methylpyridin-2(1H)-one (12b): yield 90%; mp 228-230°C (ethanol). Anal. Calcd for $C_{13}H_{10}NO_2Br$: C, 53.45; H, 3.45; N, 4.79. Found: C, 53.75; H, 3.66; N, 4.88.

5-Acetyl-3-bromo-6-[(2-(dimethylamino)ethenyl)pyridin-2(1H)-one (13a): To a stirred mixture of 12a (23.4 g, 0.1 mol) and *p*-dioxane (200 ml) was added Bredereck's reagent (23 ml, 0.11 mol). The resulting mixture was heated on a steam bath for 5 h and then the insoluble yellow product was collected and dried to afford 25.6 g (90%) of 13a: mp 228-230°C. Anal. Calcd for $C_{11}H_{13}N_2OBr$: C, 46.34; H, 4.60; N, 9.82. Found: C, 46.54; H, 4.51; N, 10.16.

5-Benzoyl-3-bromo-6-[(2-(dimethylamino)ethenyl)pyridin-2(1H)-one (13b): yield 80%; mp 242-244°C. Anal. Calcd for $C_{16}H_{13}N_2O_2Br$: C, 55.35; H, 4.35; N, 8.07. Found: C, 55.37; H, 4.38; N, 8.21.

3-Bromo-5-methyl-1,6-naphthyridin-2(1H)-one (14a): A stirred mixture of 13a (22 g, 0.08 mol), ammonium acetate (14.8 g, 0.2 mol) and DMF (150 ml) was heated on a steam bath for 5 h and then concentrated under reduced pressure. The tan solid residue was slurried in water (200 ml) and collected. Recrystallization from ethanol gave 12.4 g (64%) of tan crystals: mp 245-247°C; 1H nmr (CF_3CO_2D) δ 8.76 (s, 1H, 4-H), 8.52 (d, $J = 7.0$ Hz, 1H, 7-H), 7.82 (d, $J = 7.0$ Hz, 1H, 8-H), 3.12 (s, 3H, CH_3). Anal. Calcd for $C_9H_7N_2OBr$: C, 45.22; H, 2.95; N, 11.72. Found: C, 45.21; H, 2.95; N, 11.38.

3-Bromo-5-phenyl-1,6-naphthyridin-2(1H)-one (14b): yield 97%; mp >300°C (DMF); 1H nmr (CF_3CO_2D) δ 8.73 (d, $J = 7.0$ Hz, 1H, 7-H), 8.63 (s, 1H, 4-H), 7.97 (d, $J = 7.0$ Hz, 1H, 8-H), 7.82 (m, 5H, C_6H_5). Anal. Calcd for $C_{14}H_9N_2OBr$: C, 55.84; H, 3.01; N, 9.30. Found: C, 55.81; H, 3.10; N, 9.39.

3-Bromo-5-methyl-1,6-naphthyridin-2-amine (15a): A mixture of 14a (58 g, 0.24 mol) and phosphorous oxychloride (500 ml, 5.4 mol) was heated under reflux with stirring for 16 h and then concentrated under reduced pressure. The viscous oily residue was dissolved in chloroform (300 ml) and poured into a vigorously stirred mixture of ice and conc. aqueous ammonia. The resulting mixture was extracted with chloroform (3 x 500 ml). Removal of the

chloroform gave a red solid which was added to ethanol saturated with ammonia (500 ml), and heated in an autoclave at 100-105°C for 16 h and then cooled to room temperature. The mixture was concentrated under reduced pressure. The residue was slurried in 10% aqueous potassium carbonate (100 ml). The yellow solid product was collected, washed with water, and recrystallized from ethanol to afford 29.4 g (61%) of pale yellow crystals: mp 208-210°C; ^1H nmr ($\text{CF}_3\text{CO}_2\text{D}$) δ 9.00 (s, 1H, 4-H), 8.66 (d, $J = 7.0$ Hz, 1H, 7-H), 8.12 (d, $J = 7.0$ Hz, 1H, 8-H), 3.20 (s, 3H, CH_3). Anal. Calcd for $\text{C}_9\text{H}_8\text{N}_3\text{Br}$: C, 45.40; H, 3.39; N, 17.65. Found: C, 45.22; H, 3.22; N, 17.55.

3-Bromo-5-phenyl-1,6-naphthyridin-2-amine (15b): yield 88%; mp 218-221°C (ethanol); ^1H nmr ($\text{CF}_3\text{CO}_2\text{D}$) δ 8.86 (d, $J = 6.4$ Hz, 1H, 7-H), 8.80 (s, 1H, 4-H), 8.25 (d, $J = 6.4$ Hz, 1H, 8-H), 7.80 (m, 5H, C_6H_5). Anal. Calcd for $\text{C}_{14}\text{H}_{10}\text{N}_3\text{Br}$: C, 56.02; H, 3.36; N, 14.00. Found: C, 56.10; H, 3.45; N, 13.96.

General Procedure. Preparation of 6-(4-pyridinyl)benzothiazol-2(3H)-thione (16a). A stirred mixture of **2** (24.8 g, 0.1 mol), $\text{C}_2\text{H}_5\text{OC}(=\text{S})\text{SK}$ (30.2 g, 0.2 mol), and NMP (200 ml) was heated in an oil bath at 160-170°C for 7 h, and then dissolved in hot water and filtered. The filtrate was acidified with acetic acid and the resulting tan crystals were collected, washed with water, and dried to yield 22.4 g (92%): mp >300°C; ^1H nmr ($\text{CF}_3\text{CO}_2\text{D}$) δ 8.88, 8.41 (A_2B_2 , $J = 6.8$ Hz, 4H, $\text{C}_5\text{H}_4\text{N}$), 8.17 (d, $J_m = 1.1$ Hz, 1H, 7-H), 8.04 (dd, $J_o = 8.6$ Hz, $J_m = 1.1$ Hz, 5-H), 7.77 (d, $J_o = 8.6$ Hz, 1H, 4-H). Anal. Calcd for $\text{C}_{12}\text{H}_8\text{N}_2\text{S}_2$: C, 58.99; H, 3.30; N, 11.47. Found: C, 58.59; H, 3.32; N, 11.18.

5-Methyl-6-(4-pyridinyl)thiazolo[4,5-b]pyridin-2(3H)-thione (16b): yield 73%; mp 295-297°C; ^1H nmr ($\text{DMSO}-d_6$) δ 8.69, 7.46 (A_2B_2 , $J = 6.0$ Hz, 4H, $\text{C}_5\text{H}_4\text{N}$), 8.03 (s, 1H, 7-H), 2.47 (s, 3H, CH_3). Anal. Calcd for $\text{C}_{12}\text{H}_9\text{N}_3\text{S}_2$: C, 55.58; H, 3.50; N, 16.20. Found: C, 55.28; H, 3.48; N, 16.29.

5-(4-Pyridinyl)benzothiazol-2(3H)-thione (19a): yield 90%; mp >265°C (decomp.) (methanol/chloroform); ^1H nmr ($\text{CF}_3\text{CO}_2\text{D}$) δ 9.04, 8.53 (A_2B_2 , $J = 4.1$ Hz, 4H, $\text{C}_5\text{H}_4\text{N}$), 8.28 (s, 1H, 4-H), 8.04 (s, 2H, 6-H, 7-H). Anal. Calcd for $\text{C}_{12}\text{H}_8\text{N}_2\text{S}_2$: C, 58.99; H, 3.30; N, 11.30. Found: C, 58.74; H, 3.34; N, 11.32.

6-Methyl-5-(4-pyridinyl)thiazolo[5,4-b]pyridin-2(3H)-thione (19b): yield 73%; mp 285-287°C (methanol); ^1H nmr ($\text{CF}_3\text{CO}_2\text{D}$) δ 9.12, 8.34 (A_2B_2 , $J = 5.5$ Hz, 4H, $\text{C}_5\text{H}_4\text{N}$), 8.24 (s, 1H, 4-H),

2.85 (s, 3H, CH₃). Anal. Calcd for C₁₂H₉N₃S₂: C, 55.58; H, 3.50; N, 16.20. Found: C, 55.57; H, 3.57; N, 16.06.

8-Methylthiazolo[4,5-b][1,6]naphthyridin-2(3H)-thione (22a): yield 99%; mp >300°C; ¹H nmr (CF₃CO₂D) δ 8.85 (s, 1H, 9-H), 8.53 (d, J = 7.0 Hz, 1H, 6-H), 8.20 (d, J = 7.0 Hz, 1H, 5-H), 3.27 (s, 3H, CH₃). Anal. Calcd for C₁₀H₇N₃S₂: C, 51.48; H, 3.02; N, 18.01. Found: C, 51.50; H, 3.00; N, 17.87.

8-Phenylthiazolo[4,5-b][1,6]naphthyridin-2(3H)-thione (22b): yield 92%; mp >300°C; ¹H nmr (CF₃CO₂D) δ 8.76 (d, J = 6.8 Hz, 1H, 6-H), 8.72 (s, 1H, 9-H), 8.37 (d, J = 6.8 Hz, 1H, 5-H), 7.88 (m, 5H, C₆H₅). Anal. Calcd for C₁₅H₉N₃S₂: C, 61.00; H, 3.07; N, 14.23. Found: C, 60.57; H, 2.96; N, 14.10.

General Procedure. Preparation of 2-Methylthio-6-(4-pyridinyl)benzothiazole (17a): A stirred mixture of 16a (24.4 g, 0.1 mol), anhydrous milled K₂CO₃ (16.6 g, 0.12 mol), and DMF (200 ml) was stirred at ambient temperature for 30 min and then treated with methyl iodide (14.2 g, 0.1 mol) dissolved in DMF (10 ml) over a period of 20 min. After further stirring for 30 min, most of the DMF was removed under reduced pressure. The residue was washed with water, and recrystallized from isopropanol-ether to give 18.1 g (71%) of 17a: mp 100-102°C; ¹H nmr (CDCl₃) δ 8.67, 7.53 (A₂B₂, J = 5.7 Hz, 4H, C₅H₄N), 8.61 (s, 1H, 7-H), 7.94 (d, J_o = 8.5 Hz, 1H, 4-H), 7.67 (dd, J_o = 8.5 Hz, J_m = 1.3 Hz, 5-H), 2.82 (s, 3H, CH₃). Anal. Calcd for C₁₃H₁₀N₂S₂: C, 60.44; H, 3.90; N, 10.84. Found: C, 60.81; H, 3.81; N, 10.70.

6-Methyl-2-methylthio-6-(4-pyridinyl)thiazolo[4,5-b]pyridine (17b): yield 99%; mp 173-175°C (isopropanol); ¹H nmr (CDCl₃) δ 8.25, 7.33 (A₂B₂, J = 6.0 Hz, 4H, C₅H₄N), 7.93 (s, 1H, 7-H), 2.92 (s, 3H, CH₃), 2.64 (s, 3H, CH₃). Anal. Calcd for C₁₃H₁₁N₃S₂: C, 57.12; H, 4.06; N, 15.37. Found: C, 57.17; H, 4.04; N, 15.18.

2-Methylthio-5-(4-pyridinyl)benzothiazole (20a): yield 68%; mp 99-100°C (isopropanol-hexanes); ¹H nmr (CDCl₃) δ 8.68 (d, J = 6.0 Hz, 2H, 2'-H, 6'-H), 8.13 (d, J_m = 1.1 Hz, 1H, 4-H), 7.83 (d, J_o = 8.4 Hz, 1H, 7-H), 7.55 (m, 3H, 6-H, 3'-H, 5'-H), 2.82 (s, 3H, SCH₃). Anal. Calcd for C₁₃H₁₀N₂S₂: C, 60.44; H, 3.90; N, 10.84. Found: C, 60.48; H, 4.08; N, 10.73.

6-Methyl-2-methylthio-5-(4-pyridinyl)thiazolo[5,4-b]pyridine (20b): yield 69%; mp 169-171°C (ethanol); ¹H nmr (CDCl₃) δ 8.72, 7.31 (A₂B₂, J = 5.8 Hz, 4H, C₅H₄N), 7.88 (s, 1H, 4-H), 2.80

(s, 3H, CH₃), 2.57 (s, 3H, CH₃). Anal. Calcd for C₁₃H₁₁N₃S₂: C, 57.13; H, 4.06; N, 15.37. Found: C, 57.14; H, 4.02; N, 15.29.

8-Methyl-2-methylthiothiazolo[4,5-b][1,6]naphthyridine (23a): yield 69%; mp 204-206°C (ethanol); ¹H nmr (CF₃CO₂D) δ 9.78 (s, 1H, 9-H), 8.84 (d, J = 7.0 Hz, 1H, 6-H), 8.58 (d, J = 7.0 Hz, 1H, 5-H), 3.45 (s, 3H, CH₃), 3.11 (s, 3H, CH₃). Anal. Calcd for C₁₁H₉N₃S₂: C, 53.42; H, 3.69; N, 16.99. Found: C, 53.34; H, 3.57; N, 16.88.

2-Methylthio-8-phenylthiazolo[4,5-b][1,6]naphthyridine (23b): yield 90%; mp 198-200°C (methanol); ¹H nmr (CF₃CO₂D) δ 9.52 (s, 1H, 9-H), 8.99 (d, J = 7.1 Hz, 1H, 6-H), 8.66 (d, J = 7.1 Hz, 1H, 5-H), 7.83 (m, 5H, C₆H₅), 3.09 (s, 3H, CH₃). Anal. Calcd for C₁₆H₁₁N₃S₂: C, 62.11; H, 3.58; N, 13.58. Found: C, 62.11; H, 3.76; N, 13.53.

General Procedure. Preparation of 6-(4-Pyridinyl)benzothiazol-2(3H)-one (18a): A mixture of 17a (25.8 g, 0.1 mol), CH₃ONa (10.8 g, 0.2 mol), and DMF (100 ml) was stirred at room temperature for 7 h and then concentrated under reduced pressure. The residue was dissolved in water and acidified with acetic acid. The resulting precipitate was collected and recrystallized from ethanol to give 23.3 g (98%) of tan crystals of 18a: mp 300-302°C; ¹H nmr (CF₃CO₂D) δ 8.83, 8.35 (A₂B₂, J = 7.0 Hz, 4H, C₅H₄N), 8.12 (d, J_m = 1.8 Hz, 1H, 7-H), 7.96 (dd, J_o = 8.5 Hz, J_m = 1.8 Hz, 1H, 5-H), 7.68 (d, J_o = 8.5 Hz, 1H, 4-H). Anal. Calcd for C₁₂H₈N₂OS: C, 63.14; H, 3.53; N, 12.27. Found: C, 62.94; H, 3.52; N, 12.10.

5-Methyl-6-(4-pyridinyl)thiazolo[4,5-b]pyridin-2(3H)-one (18b): yield 80%; mp >300°C (methanol); ¹H nmr (DMSO-d₆) δ 7.93 (s, 1H, 7-H), 8.67, 7.46 (A₂B₂, J = 6.8 Hz, 4H, C₅H₄N), 2.44 (s, 3H, CH₃). Anal. Calcd for C₁₆H₁₁N₃S₂: C, 62.11; H, 3.58; N, 13.58. Found: C, 62.11; H, 3.76; N, 13.53.

5-(4-Pyridinyl)benzothiazol-2(3H)-one (21a): yield 70%; mp >275°C (decomp.) (methanol/chloroform); ¹H nmr (CF₃CO₂D) δ 8.87, 8.41 (A₂B₂, J = 6.6 Hz, 4H, C₅H₄N), 8.08 (s, 1H, 4-H), 7.87 (m, 2H, 6-H, 7-H). Anal. Calcd for C₁₂H₈N₂OS: C, 63.14; H, 3.53; N, 12.27. Found: C, 63.04; H, 3.49; N, 12.24.

6-Methyl-5-(4-pyridinyl)thiazolo[5,4-b]pyridin-2(3H)-one (21b): yield 84%; mp 252-254°C (isopropanol); ¹H nmr (CF₃CO₂D) δ 9.07, 8.24 (A₂B₂, J = 6.5 Hz, 4H, C₅H₄N), 8.35 (s, 1H, 4-H), 2.84 (s, 3H, CH₃). Anal. Calcd for C₁₂H₉N₃OS: C, 59.24; H, 3.73; N, 17.27. Found: C, 59.29; H, 3.77; N, 17.11.

8-Methylthiazolo[4,5-*b*][1,6]naphthyridin-2(3*H*)-one (24a): yield 84%; mp >300°C (methanol); ¹H nmr (CF₃CO₂D) δ 8.90 (s, 1H, 9-H), 8.46 (d, J = 7.0 Hz, 1H, 6-H), 8.14 (d, J = 7.0 Hz, 1H, 5-H), 3.20 (s, 3H, CH₃). Anal. Calcd for C₁₀H₇N₃OS: C, 55.29; H, 3.25; N, 19.34. Found: C, 54.89; H, 3.36; N, 19.20.

8-Phenylthiazolo[4,5-*b*]naphthyridin-2(3*H*)-one (24b): yield 70%; mp >300°C (ethanol); ¹H nmr (CF₃CO₂D) δ 8.79 (s, 1H, 9-H), 8.73 (d, J = 7.0 Hz, 1H, 6-H), 8.33 (d, J = 7.0 Hz, 1H, 5-H), 7.73 (m, 5H, C₆H₅). Anal. Calcd for C₁₅H₉N₃OS: C, 64.50; H, 3.25; N, 15.04. Found: C, 64.35; H, 3.30; N, 14.97.

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