Synthesis of 2-Substituted 3-Oxoisothiazolo[5,4-*b*]pyridines

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Starting with 2-chloro-3-pyridinecarboxylic acid **1**, three different routes to prepare 3-oxoisothiazolo-[4,5-*b*]pyridines **10** were studied.

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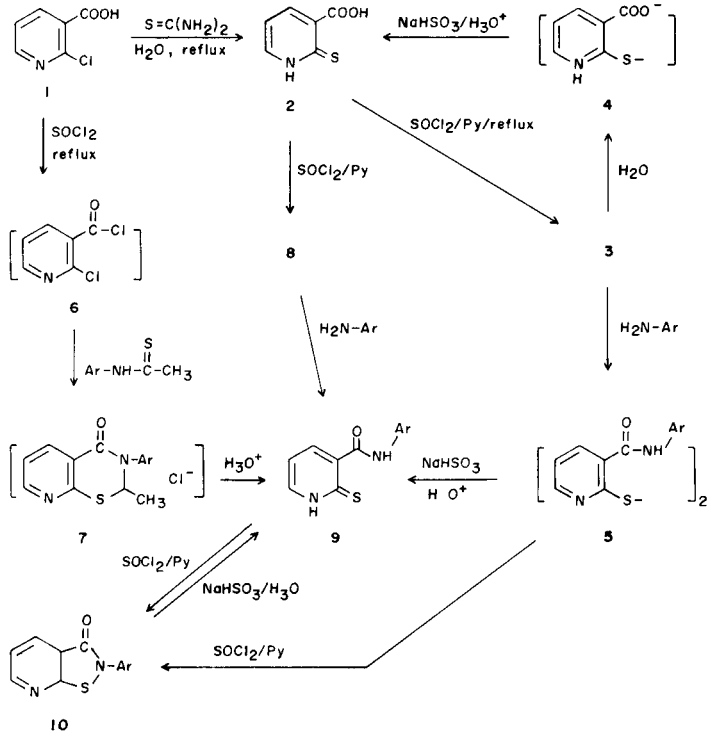
Although numerous 3-oxo-1,2-benzoisothiazoles have been known for more than 60 years [1,2] and some biological activities have been reported for them [1], examples of isothiazole-3-ones fused with heterocyclic rings are relatively unknown in the literature. All three 3-oxoisothiazole 1,1-dioxides have been reported as sweetening agents related to saccharin [3,4]. 4,5,6,7-Tetrahydro-3-oxoisothiazolo[4,5-*c*]pyridines, its [5,4-*c*]analog and 5,6,7,8-tetrahydro-3-oxo-4*H*-isothiazolo[4,5-*d*]azepines have been recently described and studied [5] as agonists of γ-aminobutyric acid (GABA). Some 3-oxoisothiazolo[5,4-*b*]pyridines have been reported in several patents [6,7,8] and described as fungicides, bactericides and other similar biological activities [6], inhibitors of blood platelet aggregation [7] and antiacne agents [8].

Two recent papers [9,10] report the preparation of some 3-oxoisothiazolo[5,4-*b*]pyridines substituted in the pyridine ring [9] and several 2-substituted derivatives of all four isomeric 3-oxoisothiazolopyridines [10]: -[5,4-*b*]-, [5,4-*c*]-, -[4,5-*c*]- and -[4,5-*b*]-. The three first types of these compounds are described as active inhibitors of blood platelet aggregation [7,10].

We are interested in the study of different classes of organic compounds as inhibitors of tromboxane A_2 synthetase as potential blood platelet antiaggregants [11] and with this objective in mind we report in this paper new methods for the synthesis of 2-substituted 3-oxoisothiazolo-[5,4-*b*]pyridines.

Starting with 2-chloro-3-pyridinecarboxylic acid **2**, three different new routes to prepare **10** were studied (see Scheme).



5, 7, 9, 10	Ar
5 a	C_6H_5-
5 b	p-Cl-C_6H_4-
5 c	p-CH_3-C_6H_4-
5 d	p-CH_3-O-C_6H_4
e	
f	
g	

When **1** was treated with thiourea in boiling water, the previously known **2** [12,13] was obtained in good yield (85%). This compound reacted with boiling thionyl chloride to give **3**. Compound **3** was not directly analyzed, however, its hydrolysis with diluted hydrochloric acid gave **4**, which was characterized by elemental analysis, ir, ^{1}H-nmr and mass spectra. On the other hand, the reduction of **4** with sodium bisulfite in acid medium gave the starting compound **2**.

When crude compound **3** was treated with different aryl amines in toluene, the respective new *N*-arylamides **5** were obtained. Compounds **5** were characterized by analytical and spectral data. The ir spectra show bands about 3270-3280 cm^{-1} (NH) and 1645 cm^{-1} (C=O); the ^{1}H-nmr spectra show signals at about δ 7.2-7.4 (c, H-5, 1H), 8.12-8.17 (dd, H-4, 1H, $J_{4,5}$ = 7.5 Hz), 8.43-8.53 (dd, H-6, 1H, $J_{6,5}$ = 5 Hz) in DMSO-d_6 solution.

Reduction of **5** with sodium bisulfate in diluted hydrochloric acid gave (about 90%) the respective *N*-substituted 1,2-dihydro-2-thioxo-3-pyridinecarboxamides **9**. Surprisingly only a small number of these compounds have been reported in the literature [7,10] by different methods to those described in this paper.

Compounds **9** were also prepared by two other different methods. Compound **2** treated with thionyl chloride in methylene chloride/pyridine at about 0° gave **8**. This compound was not isolated but the crude product reacted with different arylamines to give **9** (44-73% for **9a-9g**). With the other procedure the acyl chloride **6** was prepared from **1** and thionyl chloride. Compound **6** was not isolated but the crude product reacted with *N*-arylthioacetamides to give the intermediate **7**, which was hydrolyzed with dilute hydrochloric acid to give **9** (25-39% for **9a-9d**). The attempted use of *N*-arylthiobenzamides in these reactions under similar conditions was unsuccessful.

Compounds **9** were characterized by elemental analysis and spectral data. The ir spectra show signals about 3200-2700 cm^{-1} (NH) and 1645-1680 cm^{-1} (C=O); the ^{1}H-nmr shows signals at δ 7.05-7.15 (c, H-5, 1H), 7.85-8.10 (dd, H-6, 1H, $J_{6,5}$ = 7.5 Hz), 8.50-8.70 (dd, H-4, 1H, $J_{4,5}$ = 7.5 Hz), 13.0-14.8 (s, NH, 1H) and 14.0-15.1 (bs, NH, 1H) in DMSO-d_6 solution.

Compounds **5** and **9** were very easily oxidized with thionyl chloride in pyridine/chloroform at room temperature to give **10** (about 77-92% of yield). This type of oxidation has been reported using halogens (chlorine, bromine or iodine) [1,7,10,15,16,17] or sulfuryl chloride [14,15]. However, we have found that thionyl chloride at room temperature was very efficient.

Compounds **10** were characterized by elemental analysis and spectral data. The ir spectra show a characteristic band at about 1670-1705 (C=O); the ^{1}H-nmr spectra show the expected signals at δ 7.3-7.5 (c, H-5, 1H), 8.1-8.4 (dd, H-4, 1H, $J_{4,5}$ = 7.5 Hz), 8.60-8.85 (dd, H-6, 1H, $J_{6,5}$ = 4.5 Hz), in deuteriochloroform solution.

Compound **10** was easily reduced with sodium bisulfite in diluted hydrochloric acid to give **9** in about 90% yield.

EXPERIMENTAL

Melting points were determined on a Kofler melting point apparatus and they are uncorrected. Elemental analysis were obtained from vacuum dried samples (over phosphorus pentoxide at 3-4 mm Hg, 2-3 hours, at about 60-70°). The ir spectra were recorded on a Perkin-Elmer 687 apparatus using potassium bromide pellets for solid products and placing the products between sodium chloride plates for liquid compounds. The frequencies are expressed in cm^{-1}. The nmr spectra were obtained on a Perkin-Elmer R-32 (90 MHz) instrument with TMS as the internal reference at a concentration of about 0.1 g/ml and with solvents as indicated. The chemical shifts are reported in ppm from TMS as internal reference and are given in δ units.

The thin-layer chromatography (tlc) was carried out on silicagel (DSF-5 Cammag, 0.3 mm thickness) with benzene:dioxane:acetic acid (90:25:4 v/v), as the solvent. The plates were scanned under ultraviolet light λ = 254 and 366 nm.

1,2-Dihydro-2-thioxo-3-pyridinecarboxylic Acid (**2**).

A suspension of 16.0 g (0.21 mole) of **1** and 16.0 g (0.21 mole) of thiourea in 200 ml of water was boiled with vigorous stirring for 4 hours. The solid changed progressively to a yellow colour. The cold suspension was filtered and the solid was dissolved in 400 ml of water by the addition of sodium hydroxide solution to reach *p*H 6. After filtering, the solution was brought to about *p*H 2-3 by the addition of hydrochloric acid. The yellow pricipitate was collected by filtration and recrystallized, mp 244-266°, from methanol/DMF, yield 26.8 g (85%), (reported [12] mp 270°); ir: 2600-3180, 2100-2400, 1680; nmr (DMSO-d_6): 7.15 (c, H-5, 1H), 8.15 (dd, H-6, 1H, $J_{6,5}$ = 5 Hz), 8.50 (dd, H-4, 1H, $J_{4,5}$ = 7.5 Hz), 14.5 (bs, -COOH, 1H).

Anal. Calcd. for $C_6H_5NO_2S$: C, 46.45; H, 3.22; N, 9.03. Found: C, 46.39; H, 3.42; N, 9.12.

2,2'-Dithiobis(3-pyridinecarboxylic Acid) (**4**).

A mixture of 1.0 g (6.45 mmoles) of **2** in 5 ml of thionyl chloride, 0.5 ml of pyridine and 5 ml of chloroform was boiled for 1 hour. Solvent was removed in vacuum, the residual material treated with toluene and solvent removed again in vacuum. This operation was repeated until all the thionyl chloride was removed. The crude solid compound **3** was boiled with diluted hydrochloric acid for 1 hour. After cooling the solution, a solid **4** was collected and recrystallized, mp 218-220°, from ethanol/DMF (0.8 g, 80%); ir: 3490, 2750-3300, 2450-2650, 1690; nmr (DMSO-d_6): 5.50 (bs, NH$^+$, 1H), 7.28 (c, H-5, 1H), 8.25 (dd, H-4, 1H, $J_{4,5}$ = 7.5 Hz), 8.50 (dd, H-6, 1H, $J_{6,5}$ = 5 Hz); ms: 155 (M$^+$-153, 86), 153 (M$^+$-155, 100), 111 (M$^+$-197, 63), 109 (M$^+$-199, 40).

Anal. Calcd. for $C_{12}H_8N_2O_4S_2$: C, 46.74; H, 2.62; N, 9.09. Found: C, 46.18; H, 3.01; N, 9.27.

2,2'-Dithiobis(3-pyridinecarboxamides) (**5**).

To a stirred suspension of **3** (see above) in 5 ml of toluene, 6.45 mmoles of the corresponding amine in 10 ml of toluene was added. The mixture was boiled for 1.5 hours. The solvent was removed in vacuum, the solid residue recrystallized from solvent as indicated.

2,2'-Dithiobis[*N*-(phenyl)-3-pyridinecarboxamide] (**5a**).

Compound **5a** was obtained from aniline, mp 190-192°, recrystallized from methanol, yield 65%; ir: 3270, 1645; nmr (DMSO-d_6): 7.0-7.8 (m, 6H), 8.12 (dd, H-4, 1H, $J_{4,5}$ = 7.5 Hz), 8.42 (dd, H-6, 1H, $J_{6,5}$ = 5 Hz), 10.7 (s, NH, 1H).

Anal. Calcd. for $C_{24}H_{18}N_4O_2S_2$: C, 62.88; H, 3.93; N, 12.23. Found: C, 62.52; H, 3.95; N, 11.98.

2,2$_9$-Dithiobis[*N*-(4-chlorophenyl)-3-pyridinecarboxamide] (**5b**).

Compound **5b** was obtained from *p*-chloroaniline, mp 200-202° dec, recrystallized from methanol, yield 69%; ir: 3270, 1645; nmr (DMSO-d_6): 7.30-7.50 (m, H-5, H-3', H-5', 3H), 7.65-7.90 (m, H-2', H-6', 2H), 8.17 (dd, H-4, 1H, $J_{4,5}$ = 7.5 Hz), 8.53 (dd, H-6, 1H, $J_{6,5}$ = 5 Hz), 10.75 (s, NH, 1H); ms: 264 (M^+-262, 26), 262 (M^+-264, 6), 138 (M^+-388, 100), 127 (M^+-399, 77).

Anal. Calcd. for $C_{24}H_{16}Cl_2N_4O_2S_2$: C, 54.64; H, 3.06; N, 10.62. Found: C, 54.25; H, 3.09; N, 10.51.

2,2'-Dithiobis[*N*-(4-methylphenyl)-3-pyridinecarboxamide] (**5c**).

Compound **5c** was obtained from *p*-toluidine, mp 200-202°, recrystallized from methanol, yield 69%; ir: 3280, 1645; nmr (DMSO-d_6): 2.30 (s, CH_3, 3H), 7.00-7.40 (m, H-5, H-3', H-5', 3H), 7.50-7.75 (m, H-2', H-6, 2H), 8.15 (dd, H-4, 1H, $J_{4,5}$ = 7.5 Hz), 8.48 (dd, H-6, 1H, $J_{6,5}$ = 5 Hz), 10.70 (s, NH, 1H).

Anal. Calcd. for $C_{22}H_{22}Cl_2N_4O_2$: C, 64.19; H, 4.52; N, 11.52. Found: C, 64.25; H, 4.60; N, 11.50.

2,2$_9$-Dithiobis[*N*-(4-methoxyphenyl)-3-pyridinecarboxamide] (**5d**).

Compound **5d** was obtained from *p*-anisidine, mp 206-208°, recrystallized from 2-propanol, yield 63%; ir: 3280, 1645; nmr (DMSO-d_6): 3.8 (s, CH_3O, 3H), 6.85-7.10 (m, H-3', H-5', 2H), 7.27-7.42 (c, H-5, 1H), 7.5-7.75 (m, H-2', H-6', 2H), 8.15 (dd, H-4, 1H, $J_{4,5}$ = 7.5 Hz), 8.50 (dd, H-6, 1H, $J_{6,5}$ = 4.5 Hz), 10.7 (s, NH, 1H).

Anal. Calcd. for $C_{26}H_{22}N_4O_4S_2$: C, 60.23; H, 4.25; N, 10.81. Found: C, 59.95; H, 4.23; N, 10.61.

1,2-Dihydro-2-thioxo-3-pyridinecarboxamides (**9**).

Method A.

A mixture of **1** (6.3 mmoles) and thionyl chloride (5 ml) was boiled for 1.5 hours. The excess of reagent was removed in vacuum. Toluene was added to the residual material and solvent evaporated in vacuum again. This last operation was repeated until all the thionyl chloride was removed. The crystalline residue of **6** was dissolved in dried dioxane (10 ml) and then the corresponding *N*-arylthioacetamide (6.3 mmoles) was added to the reaction mixture. After boiling the mixture for 1 hour, solvent was removed in vacuum and the residual material hydrolyzed with diluted hydrochloric acid (100 ml, 1*M*) for 12 hours at room temperature with stirring. The reaction mixture was neutralized with diluted sodium hydroxide and the solid collected and recrystallized.

Method B.

To an ice-cold suspension of **2** (6.3 mmoles) in pyridine (3 ml) and methylene chloride (8 ml) a solution of thionyl chloride (2 ml) in methylene chloride (8 ml) was added and the ice-cold mixture was stirred for 1 hour. Solvent was removed in vacuum to a temperature below 40°. Toluene was added to the residual material and the solvent was again evaporated in vacuum. This operation was repeated until the odor of thionyl chloride was not apparent. The residual yellow solid **8** was dissolved in chloroform (8 ml) and pyridine (2 ml) and then a solution of the corresponding amine (6.3 mmoles) in chloroform (8 ml) was added to the reaction mixture at 0°. The mixture was stirred at room temperature for 3 hours and then the solvent removed in vacuum. The solid residue was suspended in water (100 ml) and the suspension neutralized. The solid was collected and recrystallized as indicated.

Method C.

To a stirred suspension of the corresponding compound **5** (2 mmoles) in 1*M* hydrochloric acid (10 ml), sodium bisulfite (1.0 g) was slowly added. The mixture was stirred at room temperature for 1 hour and then the solid material collected by filtration and recrystallized.

Method D.

This method is similar to method C, but starting with the corresponding compound **10**.

N-(Phenyl)-1,2-dihydro-2-thioxo-3-pyridinecarboxamide (**9a**).

Compound **9a** was obtained from aniline, mp 205-207°, recrystallized from methanol/acetone, yields, method A, 30%; method B, 51%; methods C and D, 90%; ir: 3200-2800, 1645; nmr (DMSO-d_6): 7.0-7.2 (m, 2H), 7.30-7.50 (m, 2H), 7.60-7.80 (m, 2H), 8.0 (dd, H-6, 1H, $J_{6,5}$ [5] 4.5 Hz), 8.55 (dd, H-4, 1H, $J_{4,5}$ [5] 7.5 Hz), 12.95 (s, NH, 1H), 14.10 (bs, NH, 1H).

Anal. Calcd. for $C_{12}H_{10}N_2OS$: C, 62.61; H, 4.34; N, 12.17. Found: C, 62.26; H, 4.52; N, 11.98.

N-(4-Chlorophenyl)-1,2-dihydro-2-thioxo-3-pyridinecarboxamide (**9b**).

Compound **9b** was obtained from *p*-chloroaniline, mp 266-228°, recrystallized from acetone/methanol, yields, method A, 27%; method B, 73%; methods C and D, 90-92%; ir: 3200-2800, 1645; nmr (DMSO-d_6): 7.10 (c, H-5, 1H), 7.30-7.50 (m, H-3', H-5', 2H), 7.55-7.75 (d, H-2', H-6', 2H), 8.05 (dd, H-6, 1H, $J_{6,5}$ = 4.5 Hz), 8.53 (dd, H-4, 1H, $J_{4,5}$ = 7.5 Hz), 13.0 (s, NH, 1H), 14.2 (bs, NH, 1H).

Anal. Calcd. for $C_{12}H_9ClN_2OS$: C, 54.44; H, 3.40; N, 10.58. Found: C, 54.11; H, 3.69; N, 10.68.

N-(4-Methylphenyl)-1,2-dihydro-2-thioxo-3-pyridinecarboxamide (**9c**).

Compound **9c** was obtained from *p*-toluidine, mp 204-206°, recrystallized from acetone/methanol, yields, method A, 39%; method B, 68%; methods C and D, 85-90%; ir: 3200-2800, 1645; nmr (DMSO-d_6): 2.30 (s, CH_3, 3H), 7.0-7.3 (m, H-5, H-3', H-5', 3H), 7.65 (d, H-2, H-6', 2H), 7.85 (dd, H-6, 1H, $J_{6,5}$ = 4.5 Hz), 8.70 (dd, H-4, 1H, $J_{4,5}$ = 7.5 Hz), 13.20 (s, NH, 1H), 14.0 (bs, NH, 1H).

Anal. Calcd. for $C_{13}H_{12}N_2OS$: C, 63.93; H, 4.92; N, 11.47. Found: C, 63.75; H, 5.06; N, 11.50.

N-(4-Methoxyphenyl)-1,2-dihydro-2-thioxo-3-pyridinecarboxamide (**9d**).

Compound **9d** was obtained from *p*-anisidine, mp 204-206°, recrystallized from acetone/methanol, yields, method A, 25%; method B, 60%; methods C and D, 90%; ir: 3200-2880, 1645; nmr (DMSO-d_6): 3.80 (s, CH_3, 3H), 6.80-7.15 (m, H-5, H-3', H-5', 3H), 7.55-7.70 (d, H-2', H-6', 2H), 7.85 (dd, H-6, 1H, $J_{6,5}$ = 4.5 Hz), 8.67 (dd, H-4, 1H, $J_{4,5}$ = 7.5 Hz), 13.3 (s, NH, 1H), 14.1 (bs, NH, 1H).

N-(2-Pyridyl)-1,2-dihydro-2-thioxo-3-pyridinecarboxamide (**9e**).

Compound **9e** was obtained from 2-aminopyridine, mp 201-203° dec; recrystallized from acetone/chloroform, yields, method B, 44%; ir: 3200-2800, 1665; nmr (DMSO-d_6): 7.05-7.25 (m, H-5, H-5', 2H), 7.75-7.95 (m, H-4', 1H), 8.05 (dd, H-6, 1H, $J_{6,5}$ = 4.5 Hz), 8.2-8.45 (m, H-3', H-6', 2H), 8.65 (dd, H-4, 1H, $J_{4,5}$ = 7.5 Hz), 13.5 (s, NH, 1H).

Anal. Calcd. for $C_{11}H_9N_3OS$: C, 57.14; H, 3.89; N, 18.18. Found: C, 56.92; H, 4.01; N, 17.97.

N-(2-Pyrimidyl)-1,2-dihydro-2-thioxo-3-pyridinecarboxamide (**9f**).

Compound **9f** was obtained from 2-aminopyridine, mp 240° dec; recrystallized from acetone/chloroform, yields, method B, 44%; ir: 3200-2750, 1680, 1665; nmr (DMSO-d_6): 7.05-7.35 (m, H-5, H-5', 2H), 8.1 (dd, H-6, 1H, $J_{6,5}$ = 4.5 Hz), 8.80-8.50 (m, H-4, H-4', H-6', 3H), 13.5 (s, NH, 1H).

Anal. Calcd. for $C_{10}H_8N_4OS$: C, 51.72; H, 3.45; N, 24.14. Found: C, 51.58; H, 3.51; N, 24.01.

N-(2-Thiazolyl)-1,2-dihydro-2-thioxo-3-pyridinecarboxamide (**9g**).

Compound **9g** was obtained from 2-aminothiazole, mp 245° dec; recrystallized from acetone/chloroform, yields, method B, 72%; ir: 3100, 3080, 2700, 1660; nmr (DMSO-d_6): 7.15 (c, H-5, 1H), 7.32 (d, H-5', 1H), 7.55 (d, H-4', 1H), 8.10 (dd, H-6, 1H, $J_{6,5}$ = 4.5 Hz), 8.63 (dd, H-4, 1H, $J_{4,5}$ = 7.5 Hz), 14.8 (bs, NH, 1H), 15.1 (bs, NH, 1H).

Anal. Calcd. for $C_9H_6N_3OS_2$: C, 45.57; H, 2.95; N, 17.72. Found: C, 45.89; H, 2.72; N, 17.55.

3-Oxoisothiazolo[5,4-*b*]pyridines (**10**).

To a solution of the corresponding compound or **9** (2 mmoles) in chloroform (5 ml) and pyridine (3 ml), thionyl chloride (1 ml) was added and the mixture stirred for 10 minutes. Solvents were removed in vacuum and the residue treated with toluene (7 ml) and the solvent evapo-

rated in vacuum again. This last operation was repeated until no odor of thionyl chloride remained. The solid residue was washed with dilute ammonium hydroxide and the solid material collected by filtration and recrystallized as indicated.

2-(Phenyl)-3-oxoisothiazolo[5,4-*b*]pyridine (**10a**).

Compound **10a** was obtained from **5a** or **9a**, mp 134-136°, recrystallized from methanol, yield 87%; ir: 3060, 1670; nmr (deuteriochloroform): 7.20-7.80 (m, H-5, C_6H_5-, 6H), 8.28 (dd, H-4, 1H, $J_{4,5}$ 7.5 Hz), 8.75 (dd, H-6, 1H, $J_{6,5}$ 4.5 Hz).

Anal. Calcd. for $C_{12}H_8N_2OS$: C, 63.16; H, 3.51; N, 12.28. Found: C, 62.80; H, 3.41; N, 12.17.

2-(4-Chlorophenyl)-3-oxoisothiazolo[5,4-*b*]pyridine (**10b**).

Compound **10b** was obtained from **5b** or **9b**, mp 197-199°, recrystallized from methanol/acetone, yield 90%; ir: 3060, 1675; nmr (deuteriochloroform): 7.20-7.85 (m, H-5, *p*-ClC_6H_4-, 5H), 8.37 (dd, H-4, 1H, $J_{4,5}$ 7.6 Hz), 8.85 (dd, H-6, 1H, $J_{6,5}$ 4.5 Hz).

Anal. Calcd. for $C_{12}H_7ClN_2OS$: C, 54.86; H, 2.67; N, 10.67. Found: C, 54.66; H, 2.59; N, 10.58.

2-(4-Methylphenyl)-3-oxoisothiazolo[5,4-*b*]pyridine (**10c**).

Compound **10c** was obtained from **9c**, mp 141-143°, recrystallized from methanol/acetone, yield 92%; ir: 3040, 1675; nmr (deuteriochloroform): 7.40 (s, CH_3, 3H), 7.20-7.60 (m, H-5, *p*-$CH_3C_6H_4$-, 5H), 8.37 (dd, H-4, 1H, $J_{4,5}$ 7.5 Hz), 8.75 (dd, H-6, 1H, $J_{6,5}$ 4.6 Hz).

Anal. Calcd. for $C_{13}H_{10}N_2OS$: C, 64.46; H, 4.13; N, 11.57. Found: C, 64.19; H, 4.15; N, 11.47.

2-(4-Methylphenyl)-3-oxoisothiazolo[5,4-*b*]pyridine (**10d**).

Compound **10d** was obtained from **5d**, mp 164-166°, recrystallized from methanol, yield 88%; ir: 3060, 1675; nmr (deuteriochloroform): 3.90 (s, CH_3, 3H), 7.12 (d, H-3', H-5', 2H), 7.52 (d, H-2', H-6', 2H), 8.12 (m, H-5, 1H), 9.05-9.20 (m, H-4, H-6, 2H).

Anal. Calcd. for $C_{13}H_{10}N_2O_2S$: C, 60.46; H, 3.87; N, 10.85. Found: C, 60.10; H, 3.81; N, 10.77.

2-(2-Pyridyl)-3-oxoisothiazolo[5,4-*b*]pyridine (**10e**).

Compound **10e** was obtained from **9e**, mp 222-224°, recrystallized from chloroform/methanol, yield 70%; ir: 3060, 1685; nmr (DMSO-d_6): 7.25-7.60 (m, H-5, H-5', 2H), 7.9-8.1 (m, H-4, 1H), 8.25-8.60 (m, H-4, H-3', H-6', 3H), 8.85 (dd, H-6, 1H, $J_{6,5}$ = 4.5 Hz).

Anal. Calcd. for $C_{11}H_7N_3OS$: C, 57.64; H, 3.05; N, 18.34. Found: C, 57.50; H, 2.97; N, 18.10.

2-(2-Pyrimidyl)-3-oxoisothiazolo[5,4-*b*]pyridine (**10f**).

Compound **10f** was obtained from **9f**, mp 180-182° dec, recrystallized from chloroform/methanol, yield 77%; ir: 3060, 3040, 1705; nmr (deuteriochloroform): 7.17 (t, H-5', 1H), 7.35 (c, H-5, 1H), 8.33 (dd, H-4, 1H, $J_{4,5}$ = 7.5 Hz), 8.70-8.85 (m, H-6, H-4', H-6', 3H).

Anal. Calcd. for $C_{10}H_6N_4OS$: C, 52.17; H, 2.61; N, 24.35. Found: C, 51.99; H, 2.51; N, 24.27.

2-(2-Thiazolyl)-3-oxoisothiazolo[5,4-*b*]pyridine (**10g**).

Compound **10g** was obtained from **9g**, mp 198-200°dec, recrystallized from DMF/acetone, yield 75%; ir: 3070, 1675; nmr (trifluoroacetic acid): 7.57 (d, H-5', 1H), 7.75-8.10 (m, H-5, H-4', 2H), 8.75-9.00 (m, H-4, H-6, 2H).

Anal. Calcd. for $C_9H_5N_3OS_2$: C, 45.96; H, 2.13; N, 17.87. Found: C, 46.01; H, 2.08; N, 17.78.

1,2-Dihydro-2-thioxo-3-pyridinecarboxylic Acid **2** from **4**.

Compound **4** was treated as described above for the preparation of **9** from **5** (method C) and **2** (90%) was obtained (see above mp, ir, nmr).

REFERENCES AND NOTES

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