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The synthesis of the parent ring system and some of the derivatives of 1*H*-pyrazolo[3,4-*d*]thieno[2,3-*b*]pyridine are described.

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Previously we had communicated the synthesis of 3-amino-1*H*-pyrazolo[3,4-*d*]thieno[2,3-*b*]pyridine (Ia) and 3-hydroxy-1*H*-pyrazolo[3,4-*d*]thieno[2,3-*b*]pyridine (Ib) in a preliminary form (2), now we would like to report the synthesis of the parent ring system Id and some of its derivatives.

4-Chloro-5-cyanothieno[2,3-*b*]pyridine (IIa) (3) when treated with hydrazine, methylhydrazine, and phenylhydrazine gave Ia, Ic, and III, respectively. The structures Ic and III for the cyclized products were ascribed due to the first nucleophilic attack of the more basic nitrogen of the hydrazine on the four position of IIa followed by cyclization involving the cyano group at the five position. This seems to be in agreement with the results of some related reactions earlier reported in the literature (4). A deamination reaction of Ia could lead to the parent system in fact when Ia was subjected to the aprotic diazotization with *t*-butyl nitrite in tetrahydrofuran (5), the parent ring system was obtained in 89% yield. The structure of the parent ring system (Id) was confirmed by its elemental analysis, infrared spectrum (disappearance of the absorption due to the NH<sub>2</sub> and appearance of a broad NH ab-

sorption band between 2500 and 3500 cm<sup>-1</sup>), pmr spectrum (appearance of a singlet at δ 9.00 due to the proton at C-3), and its mass spectrum (*m/e*, 175 (M<sup>+</sup>)).

Further aprotic diazotizations were carried out on Ia using bromoform and chloroform as the solvents and substrates. When treated with *t*-butyl nitrite in the presence of bromoform, Ia gave the bromo compound (Id) in 86% yield. A similar treatment of Ia in wet chloroform led to the formation of Ib, *albeit*, in poor yield. This Id was identical with the product earlier prepared from the reaction of hydrazine on Iib (2). When dry chloroform was used in this reaction a small amount of a compound was isolated. This was identified from its mass spectrum (*m/e*, 348 (M<sup>+</sup>)) as a dimeric compound (IV).

On acylation Ia gave a diacylated product which on the basis of its pmr spectrum has been assigned the tentative structure V. The second acyl group is believed to have entered N-1 rather than at N-5. This is based on the analogy drawn from the diacetylation of 3-amino-1,2,4-triazole (6) where it was found that in the 1-acetyl-3-acetyl-amino-1,2,4-triazole the H-5 of the triazole ring suffers a deshielding of 1.41 ppm. In the present work H-4 suffers a downfield shift of only 0.22 ppm and this could not be ascribed as to the acylation of N-5.

## EXPERIMENTAL

The pmr spectra were taken on a 60 MHz Hitachi Perkin-Elmer model R-20B using tetramethylsilane as an internal reference. Infrared absorption spectra were examined as potassium bromide pellets. The melting points were observed on a Fisher-Johns apparatus and are uncorrected.

### 3-Amino-1*H*-pyrazolo[3,4-*d*]thieno[2,3-*b*]pyridine (Ia).

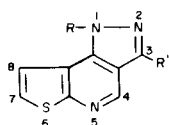
A mixture of 3 g of 4-chloro-5-cyanothieno[2,3-*b*]pyridine (IIa) (3) in 25 ml of hydrazine hydrate was heated under reflux for 7 hours. The precipitate was filtered, washed with water and dried to give 2.2 g (75%) of Ia.

In an alternate method a mixture of 3 g of IIa, 1.5 ml of hydrazine hydrate in 25 ml of ethanol was heated under reflux for 7 hours. The precipitate was filtered, washed with water and dried to give 2 g (70%) of Ia, which was crystallized from a mixture of dimethyl sulfoxide and water, mp > 300°; pmr (DMSO-*d*<sub>6</sub>): δ 8.92 (s, 1H, H-4), 7.75 (d, 1H, J = 6 Hz, H-7), and 7.55 (d, 1H, J = 6 Hz, H-8); ir: 3350-3100 cm<sup>-1</sup> (NH<sub>2</sub> and NH).

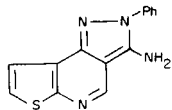
*Anal.* Calcd. for C<sub>8</sub>H<sub>6</sub>N<sub>4</sub>S: C, 50.52; H, 3.15; N, 16.84. Found: C, 50.64; H, 3.20; N, 16.79.

### 3-Hydroxy-1*H*-pyrazolo[3,4-*d*]thieno[2,3-*b*]pyridine (Ib).

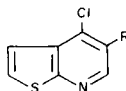
A mixture of 0.5 g of ethyl 4-chlorothieno[2,3-*b*]pyridine-5-carboxylate



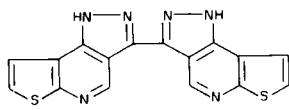
- Ia, R = H, R' = NH<sub>2</sub>  
 Ib, R = H, R' = OH  
 Ic, R = Me, R' = NH<sub>2</sub>  
 Id, R = R' = H  
 Ie, R = H, R' = Br



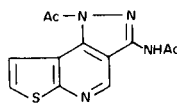
III



- IIa, R = CN  
 Iib, R = CO<sub>2</sub>Et



IV



V

(IIb) (3) and 20 ml of hydrazine hydrate was heated under reflux for 7 hours. The precipitate was filtered, washed with water, and crystallized from a mixture of dimethyl sulfoxide and water to give 0.4 g (80%) of Ib, mp  $>300^\circ$ ; pmr (DMSO- $d_6$ ):  $\delta$  8.86 (s, 1H, H-4), 7.81 (d, 1H, J = 6 Hz, H-7), 7.62 (d, 1H, J = 6 Hz, H-8), 8.26 (s, exchangeable hydrogen); ir: 3350-2980  $\text{cm}^{-1}$  ( $\text{NH}_2$  and OH).

*Anal.* Calcd. for  $\text{C}_9\text{H}_5\text{N}_3\text{OS}$ : C, 50.26; H, 2.61; N, 21.99. Found: C, 50.43; H, 2.80; N, 21.84.

#### 3-Amino-1-methyl-1H-pyrazolo[3,4-d]thieno[2,3-b]pyridine (Ic).

On heating a mixture of 0.5 g IIa, 2.5 ml of methylhydrazine, and 15 ml of ethanol for 7 hours, the precipitate obtained was filtered and crystallized from dimethyl sulfoxide to give 0.36 g (68%) of Ic, mp 248-249°; pmr (TFA):  $\delta$  9.69 (s, 1H, H-4), 8.15 (d, 1H, J = 6 Hz, H-7), 8.00 (d, 1H, J = 6 Hz, H-8), and 4.47 (s, 3H,  $\text{CH}_3$ ); ir: 3460 and 3310  $\text{cm}^{-1}$  ( $\text{NH}_2$ ).

*Anal.* Calcd. for  $\text{C}_9\text{H}_8\text{N}_4\text{S}$ : C, 52.92; H, 3.95; N, 27.43. Found: C, 52.86; H, 4.08; N, 27.24.

#### 1H-Pyrazolo[3,4-d]thieno[2,3-b]pyridine (Id).

A mixture of 10 ml of dry tetrahydrofuran and 1.5 ml of *t*-butyl nitrite protected by a calcium chloride drying tube was heated under reflux on a water bath and to the mixture 0.5 g of Ia was added in portions. After a two hours heating tetrahydrofuran and other volatile materials evaporated under reduced pressure leaving 0.41 g (89%) of crude Id which was crystallized from a mixture of dimethyl sulfoxide and water, mp 175°; pmr (TFA):  $\delta$  9.59 (s, 1H, H-4), 9.00 (s, 1H, H-3), 8.25 (d, 1H, J = 6 Hz, H-7), 8.04 (d, 1H, J = 6 Hz, H-8); ir: 3500-3100  $\text{cm}^{-1}$  (br NH); ms: *m/e* 175 ( $\text{M}^+$ ).

*Anal.* Calcd. for  $\text{C}_8\text{H}_5\text{N}_3\text{S}$ : C, 54.86; H, 2.86; N, 24.00. Found: C, 55.18; H, 2.62; N, 23.74.

#### 3-Bromo-1H-pyrazolo[3,4-d]thieno[2,3-b]pyridine (Ie).

The method for obtaining Id above was used but instead of tetrahydrofuran bromoform was used in the reaction. From 0.5 g of Ia, 0.58 g (86%) of Ie, mp 258-259° was obtained which was crystallized from a mixture of dimethyl sulfoxide and water; pmr (DMSO- $d_6$ ):  $\delta$  8.82 (s, 1H, H-4), 8.00 (d, J = 6 Hz, H-7), 7.70 (d, 1H, J = 6 Hz, H-8); ir: 3500-3300  $\text{cm}^{-1}$  (br NH).

*Anal.* Calcd. for  $\text{C}_8\text{H}_4\text{BrN}_3\text{S}$ : C, 37.81; H, 1.59; N, 16.54. Found: C, 37.60; H, 1.65; N, 16.30.

#### 3-Amino-2-phenyl-2H-pyrazolo[3,4-d]thieno[2,3-b]pyridine (III).

A mixture of 0.6 g of IIa and 1.5 ml of phenylhydrazine in 15 ml of ethanol was heated under reflux for 6 hours. The precipitate was filtered and crystallized from a mixture of dimethyl sulfoxide and water to give 0.44 g (53%) of III as dark brownish solid which was further purified by sublimation of 270°/28 mm to give white crystals mp  $>300^\circ$ ; pmr (DMSO- $d_6$ ):  $\delta$  8.98 (s, 1H, H-4), 7.18 (s, 2H, H-7 and H-8), 7.60 (s, 5H,  $\text{C}_6\text{H}_5$ ); ir: 3500 and 3300  $\text{cm}^{-1}$  ( $\text{NH}_2$ ).

*Anal.* Calcd. for  $\text{C}_{14}\text{H}_{10}\text{N}_4\text{S}$ : C, 63.14; H, 3.78; N, 21.04. Found: C, 63.34; H, 3.88; N, 21.25.

#### 1-Acetyl-3-acetylamino-2H-pyrazolo[3,4-d]thieno[2,3-b]pyridine (V).

The mixture from 0.5 g of Ia, 2.5 g of anhydrous sodium acetate, and 6 ml of acetic anhydride was heated on a water bath for half an hour and then poured over crushed ice. The cream colored precipitate was filtered off and crystallized from ethanol. Further purification was carried out by sublimation at 230°/28 mm to afford white crystals of V, mp 263-264°; yield, 0.72 g (99%); pmr (DMSO- $d_6$ ):  $\delta$  9.14 (s, 1H, H-4), 8.25 (d, 1H, J = 7 Hz, H-7), 7.90 (d, 1H, J = 7 Hz, H-8), 2.74 and 2.23 (2s, 6H,  $2\text{CH}_3$ ); ir: 3300-3100  $\text{cm}^{-1}$  (NH), 1750 and 1660 ( $\text{amide C=O}$ ).

*Anal.* Calcd. for  $\text{C}_{12}\text{H}_{10}\text{N}_4\text{O}_2\text{S}$ : C, 52.54; H, 3.67; N, 20.43. Found: C, 52.60; H, 3.71; N, 20.28.

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