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A Synthesis of the Thiazolo[3,2-a]pyridine Ring System (1)

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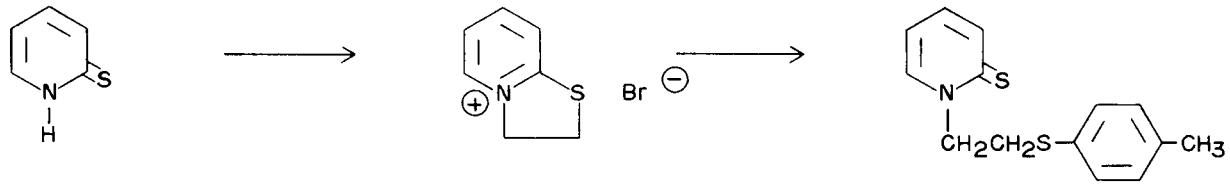
The recent publication of Bradsher and Lohr describing a synthesis of the thiazolo[3,2-a]pyridine ring system (2), prompted us to report our synthesis of this ring system and its susceptibility to a ring-opening reaction previously observed in the thiazolo-[2,3-i]purine ring system (3).

Treatment of 2-pyridinethiol (I) (4) with 1-bromo-2-chloroethane and potassium carbonate in N,N-dimethylformamide gave 2,3-dihydrothiazolo[3,2-a]-pyridinium bromide (II) in good yield. Reaction of II with *p*-toluenethiol and potassium carbonate in N,N-dimethylformamide resulted in attack at C-2 and opening of the dihydrothiazole ring to give 1-[2-(*p*-tolylthio)ethyl]pyridine-2(1H)-thione (III).



I II III

EXPERIMENTAL (5)

2,3-Dihydrothiazolo[3,2-a]pyridinium Bromide (II).

A mixture of 1-bromo-2-chloroethane (0.38 ml., 645 mg., 4.5 mmoles), 2-pyridinethiol (4) (500 mg., 4.5 mmoles) and potassium carbonate (625 mg., 4.5 mmoles) in 4 ml. of N,N-dimethylformamide was stirred at room temperature for 20 hr. The reaction mixture was thoroughly chilled and the precipitate, after filtration, was extracted with acetonitrile, giving a dark yellow solution. The solvent was removed *in vacuo* and the residue recrystallized from methanol; yield 620 mg. (63%), m.p. 240°. λ max in mμ (ε x 10^{-3}): *p*H 1-323 (5.78), 253 (8.25); *p*H 7-322 (5.72), 253 (8.23); *p*H 13-323 (5.70), 252 (8.00); CH_3OH-323 (5.78), 253 (8.27).

Anal. Calcd. for C_7H_8BrNS: C, 38.54; H, 3.70; Br, 36.64; S, 14.70. Found: C, 38.49; H, 3.71; Br, 36.59; S, 14.70.

1-[2-(*p*-Tolylthio)ethyl]pyridine-2(1H)-thione (III).

p-Toluenethiol (425 mg., 3.44 mmoles) was added to a stirred mixture of 2,3-dihydrothiazolo[3,2-a]pyridinium bromide (500 mg., 2.39 mmoles) and potassium carbonate (316 mg., 2.39 mmoles) in 5 ml. of dimethylformamide. After stirring for 3 hr. at 70-80°, the mixture was poured into 50 ml. of water. The brown solid that formed was collected by filtration and recrystallized from ethanol-water; yield 250 mg. (40%), m.p. 76°. λ max in mμ (ε x 10^{-3}): *p*H 1-347 (6.85), 247 (11.0), 254 (11.6); *p*H 7-347 (1.02), 274 (11.0), 254 (11.5); *p*H 13-347 (6.75), 274 (11.0), 253 (11.5); CH_3OH-363 (5.83), 286 (11.5), 252 (10.3).

Anal. Calcd. for $C_{14}H_{15}NS_2$: C, 64.36; H, 5.79; S, 24.50. Found: C, 64.21; H, 5.84; S, 24.75.

REFERENCES

(1) This work was supported by funds from the C. F. Kettering Foundation and from the Cancer Chemotherapy National Service Center, National Institutes of Health, Contract No. PH-43-64-51.

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(5) The melting points were determined on a Kofler Heizbank. The ultraviolet spectra were determined with a Cary Model 14 spectrophotometer.

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