A New Method for the Synthesis of Fused 3-Amino-*s*-triazole Ring Systems

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Reaction of 2-methyl-2-thiopseudourea sulfate with 1-hydrazinophthalazine gave 3-amino-*s*-triazolo[3,4-*a*]phthalazine in good yield. 1-Amino-4-methyl-*s*-triazolo[4,3-*a*]quinoxaline and 1-amino-*s*-triazolo[4,3-*a*]quinoxalin-4(5*H*)one were similarly perpared.

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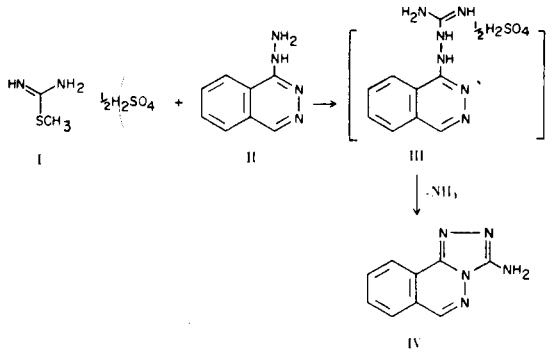
The use of cyanogen halide (1-2) for the synthesis of fused 3-amino-*s*-triazole ring systems is well described in the literature; for example, 3-amino-*s*-triazolo[3,4-*a*]-phthalazine (IV) was synthesized by reaction of 1-hydrazinophthalazine (II) with cyanogen bromide in 30% yield (2). The present work describes a new method for the synthesis of IV, and the general application of the method for the syntheses of 1-amino-4-methyl-*s*-triazolo-[4,3-*a*]quinoxaline (VI) and 1-amino-*s*-triazolo[4,3-*a*]-quinoxal in-4(5*H*)one (VIII).

Reaction of 2-methyl-2-thiopseudourea sulfate (I) with 1-hydrazinophthalazine (II) in water gave 3-amino-*s*-triazolo[3,4-*a*]phthalazine (IV) as yellow irregular prisms, m.p. 294-296°, in 51% yield. The structure assignment of IV rested upon the spectral and analytical data; for example, the mass spectrum showed the molecular ion (M^+) at m/e 185 and the pmr spectrum in deuterated dimethylfulfoxide showed three sets of signals at δ 6.44 (s, 2), 7.6-8.4 (m, 4) and 8.66 (s, 1). Furthermore, the

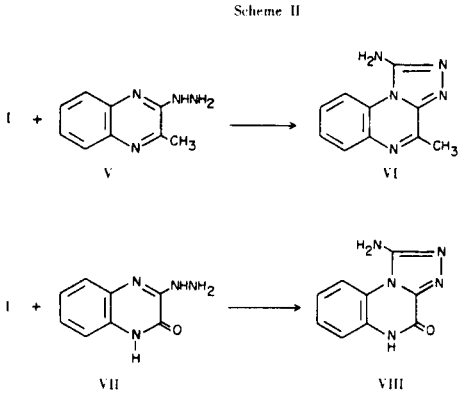
Scheme I



uv and ir spectra were essentially identical to those reported for IV in the literature (2). The reaction involved the initial formation of (1-phthalazinylamino)guanidine sulfate (III) which cyclized and eliminated ammonia (Scheme I). In a similar fashion, the reaction of 2-methyl-2-thiopseudourea sulfate (I) with 2-hydrazino-3-methylquinoxaline (V) or 3-hydrazino-2(1*H*)quinoxalinone (VII) gave, respectively, 1-amino-4-methyl-*s*-triazolo[4,3-*a*]quinoxaline (VI) in 46% yield or 1-amino-*s*-triazolo[4,3-*a*]quinoxalin-4(5*H*)one (VIII), in 65% yield (Scheme II).

This novel method for the synthesis of fused 3-amino-*s*-triazole ring systems provides a useful alternative to the existing one (1-2).

Scheme II



EXPERIMENTAL

All melting points were taken on a Mel-Temp apparatus. Pmr spectra were obtained on a Varian Model HA-100 spectrometer; chemical shifts (δ) are in ppm relative to internal tetramethylsilane. Ultraviolet spectra were taken on the Cary 14 instrument, using calibrated optically plane quartz cells. Mass spectra were recorded on A.E.I. MS 902. Infrared spectra were obtained on Perkin-Elmer Model 21.

3-Amino-*s*-triazolo[3,4-*a*]phthalazine (IV) (2).

A solution of 1-hydrazinophthalazine (1.0 g., 0.0062 mole) and 2-methyl-2-thiopseudourea sulfate (0.87 g., 0.0031 mole) in water (9.0 ml.) was refluxed for 4 hours. After cooling, the solution deposited 0.59 g. (51%) of IV as yellow crystals, m.p. 292-295°. Recrystallization from water gave 0.48 g. of yellow irregular prisms, m.p. 294-296° (Literature m.p. 291°); pmr (DMSO-d_6): δ 6.44 (s, NH_2, 2), 7.6-8.4 (m, ArH, 4), 8.66 (s, ArH, 1); uv max (methanol): 266 mμ (log ε 4.42), 258 (4.39), 209 (4.47); ir (potassium bromide): 3340, 3330, 3150, 1650, 1620, 1570, 1530, 1475, 1465, 1450, 1350, 1320, 1270, 1240, 1220, 1160, 980, 900, 750 cm^{-1}; M^+ at m/e 185 (calcd. for $C_9H_7N_5$, 185.19).

1-Amino-4-methyl-*s*-triazolo[4,3-*a*]quinoxaline (VI).

A solution of 2-hydrazino-3-methylquinoxaline (5.00 g., 0.0287 mole) and 2-methyl-2-thiopseudourea sulfate (4.00 g. 0.0144 mole) in a mixture of ethylene glycol (30 ml.) and water (20 ml.) was refluxed for 3 hours. After cooling, the solution deposited 2.6 g. (46%) of VI as peach crystals, m.p. 278-280°. Recrystallization from aqueous *p*-dioxane gave 2.0 g. of peach crystals, m.p. 279-281°; pmr (DMSO-d_6): δ 2.72 (s, CH_3, 3), 6.67 (s, NH_2, 2), 7.54 (m, ArH, 2), 7.83 (m, ArH, 1), 8.36 (m, ArH, 1).

Anal. Calcd. for $C_{10}H_9N_5$: C, 60.3; H, 4.55; N, 35.2. Found: C, 60.1; H, 4.53; N, 34.9.

1-Amino-*s*-triazolo[4,3-*a*]quinoxalin-4(5*H*)one (VIII).

A solution of 2-methyl-2-thiopseudourea (4.45 g., 0.016 mole)

and 3-hydrazino-2(1*H*)quinoxalinone (3) (5.29 g., 0.030 mole) in a mixture of *N,N*-dimethylformamide (60 ml.) and water (30 ml.) was refluxed for 5.5 hours. After cooling to room temperature the solution deposited 3.9 g. (65%) of compound VIII as yellow solid, m.p. $> 350°$. The product was purified by heating in 100 ml. of refluxing *N,N*-dimethylformamide and collecting the insolubles (1.89 g., m.p. $> 350°$).

Anal. Calcd. for $C_9H_7N_5O$: C, 53.7; H, 3.51; N, 34.8. Found: C, 53.8; H, 3.54; N, 34.5.

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