The Synthesis and Structure Proof of Pyrimido[4,5-*d*]pyridazines

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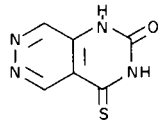
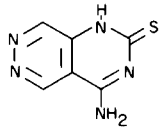
The synthesis of several pyrimido[4,5-*d*]pyridazines was reported by Kinoshita and Castle (3). In that publication two compounds (I and II) were proposed to have the structures shown. The structure of I was assigned

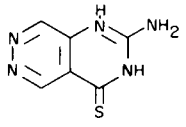


I

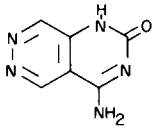


II

based upon analogy in the pyrimidine ring system (4). Likewise, the structure of II was based upon analogy with the pyrimidine series (5). We have now synthesized 2-aminopyrimido[4,5-*d*]pyridazine-4-thione (III) and 4-aminopyrimido[4,5-*d*]pyridazin-2-one (IV) and show the nonidentity of II and III by spectral means (see Experimental).

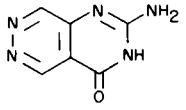


III



IV

From compound I prepared by the method of Kinoshita and Castle (3), IV was obtained by nucleophilic displacement of the sulfur atom with ammonia in ethanol under heat and pressure. The unequivocal synthesis of 2-aminopyrimido[4,5-*d*]pyridazin-4-one (V) reported by Kinoshita and Castle (3) was repeated and we now show the nonidentity of IV and V by spectral means thereby establishing the structure of I and IV.



V

EXPERIMENTAL

2-Aminopyrimido[4,5-*d*]pyridazine-4-thione (III).

A suspension of 0.3 g. (0.0018 mole) of 2-aminopyrimido-[4,5-*d*]pyridazin-4-one (V) (3) in 21 ml. of dry pyridine was heated under reflux in order to dissolve as much of V as possible. During a period of 5 minutes 0.81 g. (0.0036 mole) of phosphorus pentasulfide was added portionwise to the hot suspension and the reaction mixture was heated for one hour. The solvent was removed under reduced pressure and ice and water were added to the residue. The suspension was mixed and allowed to stand for ∿one half hour. The water was evaporated under reduced pressure and ice was again added to the residue and the mixture allowed to stand overnight at room temperature. The suspension was heated on a steam bath for one hour, cooled and removed by filtration. The solid was dissolved in 20 ml. of concentrated hydrochloric acid which was diluted with 40 ml. of water after solution. The solution was filtered and neutralized with solid sodium bicarbonate. The precipitate was collected by filtration and washed repeatedly with water, yield 0.16 g. (49%), m.p. $>360°$. Attempts to recrystallize the product from water or methanol were unsuccessful because of insolubility; infrared cm^{-1} (potassium bromide disc), 3290 (s), 3130 (s), 2780 (m), 2520 (m), 1880 (w), 1675 (s). 1625 (s), 1580 (s), 1555 (s), 1480 (s), 1425 (m), 1390 (m), 1310 (m), 1269 (s), 1211 (w), 1011 (w), 959 (m), 899 (m), 780 (w), 772 (w), 696 (m), 584 (m), 524 (m).

Anal. Calcd. for $C_6H_5N_5S$: C, 40.20; H, 2.81; N, 39.08. Found: C, 40.35; H, 3.03; N, 39.00.

4-Aminopyrimido[4,5-*d*]pyridazin-2-one (IV).

A mixture of 3.0 g. (0.017 mole) of pyrimido[4,5-*d*]pyridazin-2-one-4-thione (I) (3) and 300 ml. of absolute ethanol saturated cold with dry ammonia was heated at 130° for 5 hours in a stainless steel rocking autoclave. The cooled reaction mixture was filtered and the solid residue was dissolved in 30 ml. of concentrated hydrochloric acid. The acid solution was diluted with 60 ml. of water, filtered and neutralized with solid sodium bicarbonate. The precipitate was collected and suspended in 500 ml. of water and heated to boiling and the hot suspension was filtered. The solid residue was again suspended in 500 ml. of water, heated to boiling, filtered and dried, yield 1.3 g. (48%), m.p. $>360°$; infrared cm^{-1} (potassium bromide disc), 3220 (m), 3040 (s), 2890 (m), 2830 (m), 2750 (m), 1850 (w), 1730 (s), 1690 (s), 1615 (m), 1600 (m), 1515 (w), 1480 (s), 1350 (w), 1325 (s), 1311 (w), 1284 (s), 1225 (w), 1165 (m), 1146 (m), 985 (m), 963 (w), 917 (m), 869 (m), 793 (s), 759 (m), 720 (m), 676 (m), 630 (m), 589 (w), 540 (w), 516 (w), 495 (w), 479 (w), 456 (w).

Anal. Calcd. for $C_6H_5N_5O$: C, 44.17; H, 3.08; N, 42.93. Found: C, 44.30; H, 3.27; N, 42.84.

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