Alkaline Hydrolysis of 1,2,5-Thiadiazole-3,4-dicarboxylic Acid Bishydrazide

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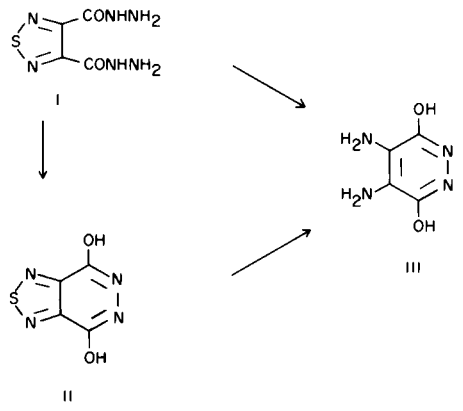
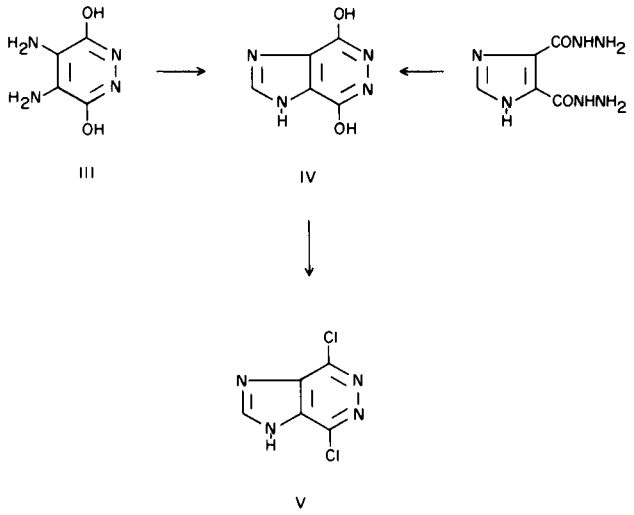
In the course of our study of antitubercular compounds we found that when 1,2,5-thiadiazole-3,4-dicarboxylic acid bishydrazide (I) was hydrolyzed with 10% hydrochloric acid splitting off one mole of hydrazine, facile ring closure occurred to give, 4.7-dihydroxy-1,2,5-thiadiazolo[3,4-*d*]pyridazine (II). On the contrary, alkaline hydrolysis of the acid bishydrazide (I), although one mole of hydrazine was similarly split off, did not produce the thiadiazolo[3,4-*d*]pyridazine derivative (II). Instead the thiadiazole ring was cleaved to give a new compound (III), which contained no sulfur atom (1). Furthermore, this substance (III) was also obtained by the alkaline hydrolysis of dihydroxy thiadiazolo[3,4-*d*]pyridazine (II). The structure of this new compound (III) was suggested by the infrared and NMR spectral studies.



In order to confirm the structure of III, the following experiment was performed. Condensation of III with formic acid by the usual procedure for the formation of imidazoles from *o*-diamines, gave compound IV, $C_5H_4N_4O_2$, which could not be identified directly (melting point >360°). In order to identify this compound it was treated with phosphorous oxychloride in the presence of dimethylaniline to give compound V, $C_5H_2Cl_2N_4$. This product was identical with the compound obtained earlier from 4,7-dihydroxyimidazo[4,5-*d*]-pyridazine by Castle *et. al.* (2).



EXPERIMENTAL (3)

Alkaline hydrolysis of 1,2,5-thiadiazole-3,4-dicarboxylic acid bishydrazide (I).

Three grams of 1,2,5-thiadiazole-3,4-dicarboxylic acid bishydrazide (I) was added to 50 ml. of 5% aqueous sodium hydroxide. The reaction mixture was refluxed for 2 hours during which time the colour of the solution turned dark red and then pale yellow. This yellow solution was acidified with acetic acid giving a precipitate which was collected by filtration. The product was dissolved in 5% aqueous sodium hydroxide and reprecipitated with acetic acid giving 1.2 g. of III as a white powder, m.p. 332° dec; infrared spectra (nujol mull), cm^{-1}, -NH_2 at 3367, 3289, 3225 and -CO-NH- at 1645, 1623; NMR (10% in DMSO with tetramethylsilane as internal standard), 4.5-5.5 (-NH_2, broad peak).

Anal. Calcd. for $C_4H_6N_4O_2$: C, 33.80; H, 4.26. Found: C, 33.83; H, 4.49.

Alkaline hydrolysis of 4,7-dihydroxy-1,2,5-thiadiazolo[3,4-*d*]-pyridazine (II).

One gram of 4,7-dihydroxy-1,2,5-thiadiazolo[3,4-*d*]pyridazine (II) and 5 ml. of 10% aqueous sodium hydroxide were treated in the same manner as described above. The product was identified as III by infrared spectral comparison.

Condensation of 4,5-diamino-3,6-dihydroxy pyridazine (III) with formic acid.

4,5-Diamino-3,6-hydroxypyridazine (III) (1.2 g.) was added to 20 ml. of 80% formic acid. The mixture was heated under reflux for 5 hours. After the first ten minutes of heating, the compound dissolved and then a white precipitate appeared. After cooling, the precipitate was filtered, dissolved in 5% aqueous sodium hydroxide and reprecipitated with acetic acid to give 1.1 g. of IV as a white powder, m.p. $>360^{\circ}$.

Anal. Calcd. for $C_5H_4N_4O_2$: C, 39.48; H, 2.65. Found: C, 39.61; H, 2.85.

Chlorination of 4,7-dihydroxyimidazo[4,5-*d*]pyridazine (IV).

The chlorination of IV was carried out according to the procedure of Castle and coworkers (2). The crude product was recrystallized from ethanol to give 0.3 g. of white needles (V), m.p. 240-241° dec.

Anal. Calcd. for $C_5H_2Cl_2N_4$: C, 31.78; N, 1.07. Found: C, 31.60; H, 1.36.

Acknowledgment.

The author wishes to express his gratitude to Professor S. Kakimoto for his kind encouragement and advice.

REFERENCES

(1) I. Sekikawa, *Bull. Chem. Soc., Japan*, 32, 1229 (1960).

(2) N. R. Patel, W. M. Rich and R. N. Castle, *J. Heterocyclic Chem.*, 5, 13 (1968).

(3) All melting points were taken in capillaries and are uncorrected. The NMR spectra were obtained with a Nippon Denshi 3 H 60 spectrometer using tetramethylsilane as the internal standard. Chemical shifts are recorded as δ values. The infrared spectra was recorded with a Shimazu IR-27B spectrophotometer.

Received November 7, 1968 Sapporo, Japan