UDC 547.822.5

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Methods for the preparation of 3,5-dibromo- and 2,3,5,6-tetrabromo-4-hydroxypyridines and pentabromopyridine were modified. The structure of 2,3,5,6-tetrabromo-4-hydroxypyridine, which exists in the enol form, was established by means of its IR and PMR spectra.

In contrast to pentafluoro- and pentachloropyridine, up until now pentabromopyridine was a compound that was difficult to obtain, and little study had consequently been devoted to it.

A multistep method for the preparation of pentabromopyridine in 57% [2] overall yield was described in [1]; the method consists of successive introduction of bromine atoms in 4-hydroxypyridine and subsequent replacement of the hydroxyl group by bromine by the action of phosphorus pentabromide.

We have substantially modified this method for the preparation of pentabromopyridine. We used 4-hydroxypyridine as the starting compound. It was converted immediately to 2,3,5,6-tetrabromo-4-hydroxypyridine (I) in 70% yield by treatment with bromine in 80% oleum. Bromination under the same conditions of 3,5dibromo-4-hydroxypyridine (II), obtained in quantitative yield by the action of bromine in hydrobromic acid on 4-hydroxypyridine, raised the yield of I to 90%.

It is known that pyridines that contain a hydroxyl group in the 2 or 4 position exist in the oxo form [3]. The accumulation of halogen atoms in 2-pyridones or 4-pyridones leads to shifting of the tautomeric equilibrium to favor the enol form [4, 5]. According to the data in [2], 3,5-dibromo-4-hydroxypyridine exists in the pyridone form [ $\nu_{\text{max}}$  2580-3180 (NH) and 1616 cm<sup>-1</sup> (CO)]. The introduction of an additional two bromine atoms in II leads to the disappearance in the IR spectrum of the band characteristic for the carbonyl group and to the appearance of a broad band at 3100-3150 cm<sup>-1</sup>, which is characteristic for the vibrations of an associated hydroxyl group. Thus 2,3,5,6-tetrabromo-4-hydroxypyridine, like its fluoro [4] and chloro [5] analogs, exists in the enol form. The difference in the structures of II and I is explained by the different basicities of the nitrogen heteroatom – the less basic compound exists in the hydroxy form. In view of the limited solubility of I in nonpolar aprotic solvents, we recorded the PMR spectrum of its methyl derivative [6] in the noncrystallized form. The presence of one singlet at  $\delta$  3.07 ppm additionally confirms that I exists exclusively in the hydroxy form.

The hydroxyl group in I was replaced by bromine by means of phosphorus oxybromide, which, in contrast to phosphorus pentabromide, eliminates the need to use an autoclave and substantially raises the yield of pentabromopyridine.



Three absorption bands are observed in the UV spectrum of an n-hexane solution of pentabromopyridine. The first two bands ( $\lambda_{\max}$  224 and 244 nm) are related to the  $\pi - \pi^*$  transitions characteristic for an aromatic system. The third band corresponds to an  $n - \pi^*$  transition associated with migration of the electron density of

Institute of Organic Chemistry, Academy of Sciences of the Ukrainian SSR, Kiev 252660. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 1, pp. 70-71, January, 1978. Original article submitted February 8, 1977.

the unshared pair of electrons of the nitrogen atom to the  $\pi^*$  orbital of the ring. A vibrational structure appears in this band, as a consequence of which there are two absorption maxima at 297 and 305 nm. When hexane is replaced by acetonitrile, a small hypsochromic shift is observed for the third band ( $\lambda_{max}$  295 and 303 nm); this is in agreement with the character of the shift for an  $n-\pi^*$  transition.

When the ratios of the peak intensities of all three bands of pentachloropyridine [7] and pentabromopyridine are compared, one may note that the intensity of the  $n-\pi^*$  band of the latter compound is higher; this is evidently associated with an increase in the s character of the orbital of the unshared pair of electrons of the nitrogen atom [8].

## EXPERIMENTAL

The PMR spectrum of a benzene solution of pentabromopyridine was recorded at room temperature with a Tesla BS-487-B spectrometer (80 MHz) with hexamethyldisiloxane as the external standard. The IR spectra of the KBr pellets of the compounds were recorded with a UR-20 spectrometer. The UV spectra were recorded with a Specord UV-vis spectrophotometer. The solvents were purified, and their purity was verified prior to the spectral measurements.

<u>3.5-Dibromo-4-hydroxypyridine (II)</u>. A 1.9-g (0.02 mole) sample of 4-hydroxypyridine was dissolved in 25 ml of 48% hydrobromic acid, 4 ml (0.08 mole) of bromine was added, and the mixture was refluxed for 1.5 h. The entire reaction mixture began to crystallize when the mixture was cooled. Ice water was added, and the solid material was removed by filtration. The product was purified by dissolving in aqueous alkali and acidification of the solution with hydrochloric acid. The yield of product with mp 350-351°C (mp 370°C [9]) was 4.65 g (92%). Found: Br 63.1; N 5.4%.  $C_5H_3Br_2NO$ . Calculated: Br 63.2; N 5.5%.

2,3,5,6-Tetrabromo-4-hydroxypyridine (I). A) A total of 1000 ml of 85% oleum was added to a mixture prepared at  $-10^{\circ}$ C from 40 g (0.421 mole) of 4-hydroxypyridine and 50 ml of H<sub>2</sub>SO<sub>4</sub> (sp. gr. 1.84), and the mixture was stirred (the stirrer was equipped with a Teflon seal) at 80°C for 85 h. Dry bromine [80 ml (1.6 mole)] was added in 20-ml portions in the first 20 h, and 50 ml (1 mole) of bromine was added in 10-ml portions in the next 40 h, after which the excess bromine was separated, and the mixture was poured over ice. Workup gave 129.8 g (75%) of a product with mp 256-257°C (from acetic acid) (mp 257-258°C [1]).

B) A total of 45 ml (0.9 mole) of bromine was added with stirring at 80°C in the course of 20 h to a mixture of 101.2 g (0.4 mole) of II in 1100 ml of 80% oleum, after which 30 ml (0.6 mole) of bromine was added in the course of 30 h. The mixture was then heated at 80°C for another 20 h, after which the excess bromine was separated, and the mixture was poured over ice. Workup gave 147.5 g (90%) of a product with mp 257-258°C.

Pentabromopyridine. A mixture of 15 g (0.05 mole) of phosphorus oxybromide and 20.5 g (0.05 mole) of I was heated at 150°C for 2 h, after which it was cooled and treated with 100 ml of ice water. Workup gave 23.4 g (99%) of a product with mp 207-208°C (from benzene) (mp 208-209°C [1]). IR spectrum: 508 w, 560 m, 718 w, 750 s, 730 w, 1038 m, 1150 w, 1210 w, 1250 m, 1280 s, 1310 m, 1380 w, and 1480 s cm<sup>-1</sup>.

## LITERATURE CITED

- 1. H. Pfanz and H. Dorn, Arch. Pharm., <u>289</u>, 651 (1956).
- 2. I. Collins and H. Suschitzky, J. Chem. Soc. (C), 1523 (1970).
- 3. A. R. Katritzky and J. M. Lagowski, Adv. Heterocycl. Chem., 1, 339 (1963).
- 4. R. D. Chambers, J. Hutchinson, and W. K. R. Musgrave, J. Chem. Soc., 5634 (1964).
- 5. A. R. Katritzky, J. D. Rowe, and S. K. Roy, J. Chem. Soc. (B), 758 (1967).
- 6. D. J. Berry, B. J. Wakefield, and J. D. Cook, J. Chem. Soc. (C), 1227 (1971).
- 7. T. Y. Giacobbe, S. D. McGregor, and F. L. Beman, J. Heterocycl. Chem., <u>11</u>, 889 (1974).
- 8. S. F. Mason, J. Chem. Soc., 1240 (1959).
- 9. E. Ochiai, T. Ito, and S. Okuda, J. Pharm. Soc. Jpn., 71, 591 (1951).