VITAMIN B₆ ANALOGS

XIV.* 6-HALO DERIVATIVES OF PYRIDOXAL 5-PHOSPHATE

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6-Chloropyridoxal and 6-bromopyridoxal were synthesized by halogenation of pyridoxal ethyl-acetal with tert-butyl hypochlorite and dioxane dibromide, respectively. 6-Halo analogs of pyridoxal-5-phosphate were obtained by phosphorylation of the Schiff bases. The UV and PMR spectra were studied.

6-Chloro and 6-bromo analogs of pyridoxal-5-phosphate were synthesized to study some aspects of the mechanism of the action of pyridoxal phosphate-dependent enzymes. The synthesis was accomplished via the following scheme.

6-Bromopyridoxal (IIIb) was obtained in 80–83% yield by the bromination of pyridoxal ethylacetal (I) with dioxane dibromide with subsequent hydrolysis. The halogenation was carried out in the presence of triethylamine to eliminate the deactivating effect of the protonated nitrogen of the pyridine ring.

The reaction of I with tert-butyl hypochlorite in tert-butanol makes it possible to obtain 6-chloropyridoxal (IIIa) in good yields. The structures of the compounds obtained were proved by the UV and PMR spectra (Figs. 1 and 2).

An attempt to synthesize 6-halopyridoxamines by catalytic hydrogenation of 6-halopyridoxal oximes was unsuccessful, since the rate of hydrogenolysis of halogen is comparable to the rate of hydrogenation of the oxime group in the case of the 6-chloro derivative and appreciably exceeds that for the 6-bromo derivative.

A mixture of two compounds was obtained by phosphorylation of Schiff base IVb with polyphosphoric acid with subsequent separation on an ion-exchange resin. The PMR spectrum of the mixture (Fig. 3) contains 2-CH₃, 5-CH₂, and 4'-H signals but does not contain signals from the ring protons. All of the spectral lines are broad. The UV spectrum (Fig. 4) makes it possible to obtain important information. Characteristic for the mixture is the presence of two long-wave absorption maxima at 396 and 474 nm (Fig. 4, curve A). However, after separation by means of electrophoresis on paper, each of the two components has only

*See [6] for communication XIII.

Fig. 1. PMR spectrum of 6-bromopyridoxal (IIIb) in 2 N NaOD.

Fig. 2. PMR spectrum of 6-chloropyridoxal (IIIa) in 2 N NaOD.

Fig. 3. PMR spectrum of the mixture obtained by phosphorylation of 6-bromopyridoxylidene-p-anisidine in 2 N NaOD.

Fig. 4. UV spectra at pH 7: A) mixture obtained by phosphorylation of IVb; B) 6-bromopyridoxal phosphate (Vb); C) 6-hydroxypyridoxal phosphate (VI); D) 2-methyl-3-hydroxyl-4-formyl-5-methoxymethyl-6-bromopyridine (VII).