SYNTHESIS OF 3-HYDROXYPYRIDINE PHOSPHATES

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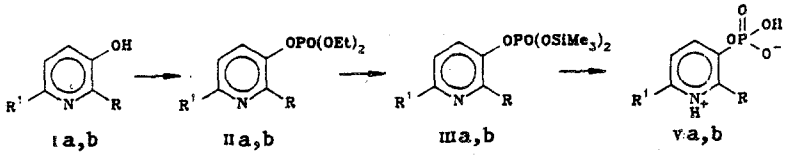
3-Hydroxypyridines are known to possess biological activity. In this regard, a series of studies have appeared recently concerning their chemical modification. Since the metabolism of various pharmaceutical agents involved a phosphorylation stage [1], it was of interest to us to study 3-hydroxypyridine phosphates.

We propose herein simple and efficient methods for the synthesis of internal and acidic phosphates derived from 3-hydroxypyridine and its derivatives.

The internal esters II were prepared by Todd–Atherton [2, 3], by reaction of the appropriate 3-hydroxypyridine with diethylphosphite and carbon tetrachloride in the presence of a trialkylamine. In order to drive the phosphorylation reaction to completion the reaction mixture was heated at 60°C for 30 min, and the products were then purified by distillation at severe vacuum ($1.33 \cdot 10^{-2}$ Pa).



Ia,b IIa,b IIIa,b Va,b

I–Va R=R¹=H; b R=C_6H_5, R¹=H etc.

Disilylphosphates III were prepared by treatment of esters II with trimethylchlorosilane and sodium iodide, at a reagent mole ratio of 1:5:2, for 5 h. The compounds are listed with; yield, %: bp, °C; ^{31}P-NMR spectrum (δ, ppm in CCl_4 relative to 85% H_3PO_4 as external standard); R_f (Silufol UV-254; benzene–dioxane, 3:2); n_D^{20}: IIa, 81; −6.0; 0.5; 1.4755; IIb; 68; 110; −6.5; 0.6; 1.4655; IIIa; 95; IIIb; 71; 130; −22.5. In the case of the synthesis of the monosilylphosphate IV the reagent ratio was 1:1:1.

After evaporation of excess trimethylchlorosilane the resulting oily compounds III were subjected to methanolysis. The resulting crystalline precipitates corresponded to the structures V based on their spectral characteristics and results of elemental analysis. The compounds are listed; yield, % (calculated relative to esters III); mp, °C (from aqueous ethanol); ^{31}P-NMR spectrum (δ, ppm); R_f: Va: 85; 167; −4.4; 0.3; Vb; 43; 276; −4.5; 0.3. The results of elemental analyses of these compounds agreed with their calculated values.

The reaction sequence proposed herein constitutes an accessible approach to the synthesis of important heterocycles containing phosphate fragments.

LITERATURE CITED

1. V. P. Zherdev, Ad. K. Sariev, T. A. Voronina, L. D. Smirnov, and N. A. Klyuev, Farmakol. Toksikol., No. 6, (1987).
2. D. Purdela and R. Vilchanu, Chemistry of Organic Phosphorus Compounds [in Russian], Khimiya, Moscow (1972), p. 381.
3. F. R. Atherton, H. F. Howard, and A. R. Todd, J. Chem. Soc., No. 8, 1106 (1948).

V. I. Lenin Moscow State Pedagogical Institute, Moscow 119021. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 1, pp. 132-133, January, 1988. Original article submitted January 23, 1987.

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