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PHOSPHORUS ANALOGUES OF AMINO ACIDS AND PEPTIDES. PART III.[1] THE REACTION OF DIALKYL PHOSPHITES WITH AROMATIC ALDAZINES.

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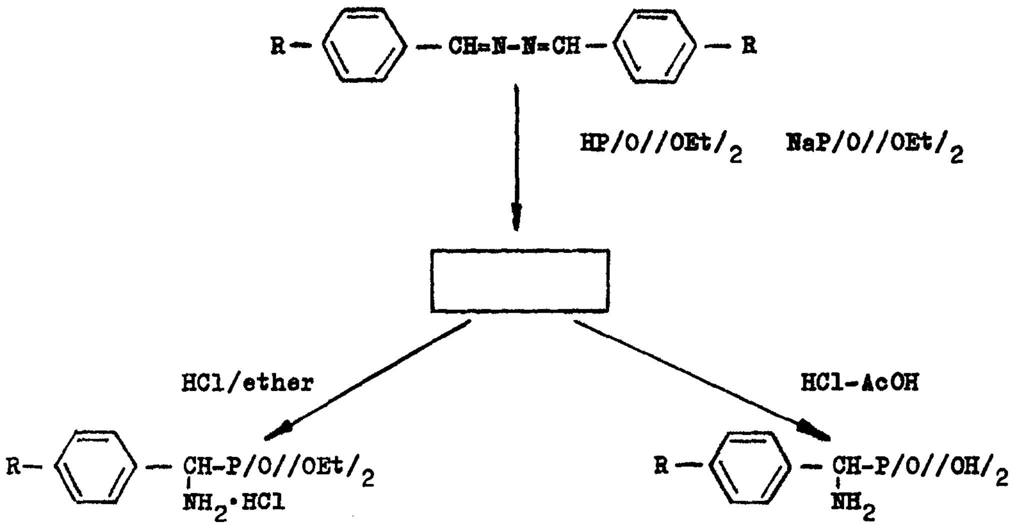
In our previous reports[2,3] we described aminobenzylphosphonic acid syntheses based on reactions of aromatic aldazines with dialkyl phosphites.

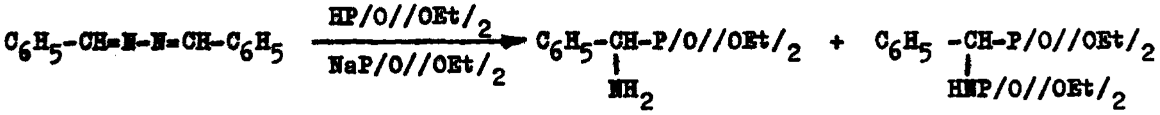
We applied the reaction conditions described in[2] to isolate α-aminobenzylphosphonic acid ester hydrochlorides with 50% yield, while to isolate free α-aminobenzylphosphonic acids with 70-90% yield[3] we subjected the reaction mixture to acid hydrolysis. In both cases one mole of aromatic aldazine was assumed to give always rise to two moles of amino acid ester or to two moles of free acid.



Yield ≈ 50%   Yield 80-90%

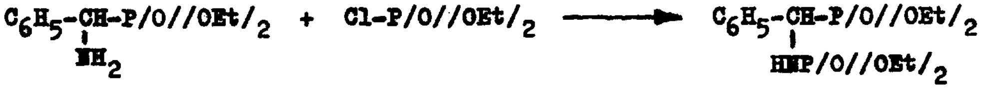
R: $-H$; $-CH_3$; $-OCH_3$; $-Br$

We studied that reaction on a model of benzaldazine and diethyl phosphite. We found that reaction to yield to α-aminobenzylphosphonic acid diethyl ester 2 and to the N-phosphorylated derivative of that ester 3. After hydrolysis each of the products 2 and 3 gives free α-aminobenzylphosphonic acid.



$$\underset{1}{C_6H_5\text{-}CH\text{=}N\text{-}N\text{=}CH\text{-}C_6H_5} \xrightarrow[NaP/O//OEt/_2]{HP/O//OEt/_2} \underset{2}{C_6H_5\text{-}\underset{NH_2}{CH}\text{-}P/O//OEt/_2} + \underset{3}{C_6H_5\text{-}\underset{HNP/O//OEt/_2}{CH}\text{-}P/O//OEt/_2}$$

The structure of the N-phosphorylated derivative 3, which was isolated from the reaction medium with satisfactory yield, was confirmed by elemental analysis and spectral methods /IR, H-NMR/. Moreover, we synthesized the derivative 3 by an independent procedure according to Zervas.[4/]



$$C_6H_5\text{-}\underset{NH_2}{CH}\text{-}P/O//OEt/_2 + Cl\text{-}P/O//OEt/_2 \longrightarrow C_6H_5\text{-}\underset{HNP/O//OEt/_2}{CH}\text{-}P/O//OEt/_2 \quad 3$$

The two products 3 /the one obtained by synthesis according to Zervas, and the one isolated from the reaction mixture of diethyl phosphite and benzaldazine/ had identical chemical and physical properties.

The products of the reaction of diethyl phosphite and benzaldazine 2 and 3 indicate that diethyl phosphite undergoes addition to the C=N bond in the benzaldazine molecule and reduces the N-N bond under simultaneous phosphorylation. The findings of further studies on the mechanism of the above reaction, which has to date not been described in the literature, are at present elaborated and will be published successively.

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