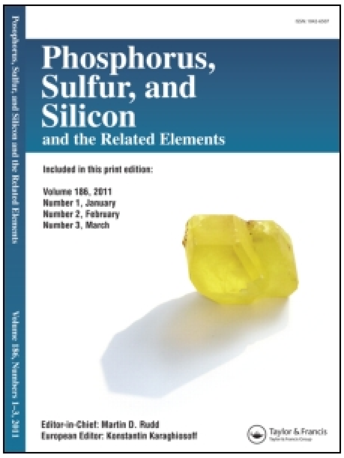

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# Phosphoric Anhydride in Organic Synthesis. Migration of the Dihydroxyphosphoryl Group in Amides

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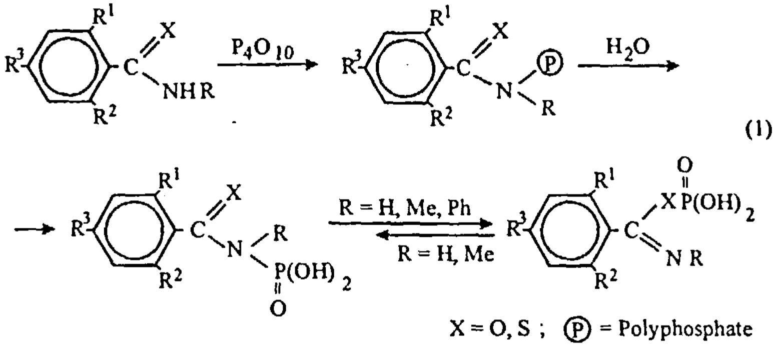
Acyclic and cyclic amides are phosphorylated by phosphoric anhydride. The phosphorylated acyclic amides exhibit a pronounced tendency to N-O reversible or irreversible phosphorotropy. In cyclic amides it is less specific. For hydrazide of benzoic acid there is determined 1 – 4 reversible phosphorotropy.

*Keywords:* phosphoric anhydride; amides; phosphorotropy; NMR spectrometry

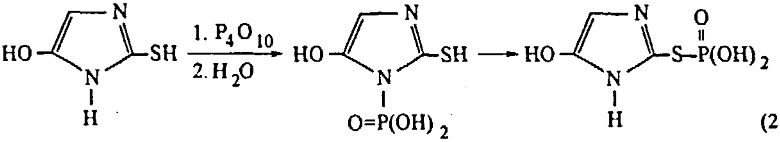
Phosphoric anhydride was found to be an active phosphorylating agent of a wide variety of nucleophilic reagents including amides. Generally the reactions of phosphoric anhydride with mono- and di-substituted acyclic amides such as benzoylamides, acetanilides or benzanilides are active and result in good yields of products[1 – 4] (Scheme 1).

Monitoring the processes by means of phosphorus-31 NMR reveals a distinctive similarities in the reactions pathways.



(1)

The attack by $P_4O_{10}$ is directed towards nitrogen as the most nucleophilic atom in the molecules. Under the influence of the N – H acid the tricyclic molecules of $P_4O_{10}$ brake down consecutively into dicyclic and monocyclic structures. The prevailing monocyclic structure in all cases is isotetrametaphosphoric rather than tetrametaphosphoric, the intermediate spectra possess an intensive singlet in the region between – 24 and – 28 ppm, assigned to trimetaphosphates. The latter species are formed by splitting the exocyclic P-O-P bond in isotetrametaphosphates. Triamidotrimetaphosphates are rather stable in the reaction mixture and on addition of the catalytic quantities of hydrochloric acid the signal flattens in 60 – 90 min. which is accompanied by gaining intensity of amidophosphates and symmetrical pyrophosphates signals. The latter undergo splitting into an amidophosphate which is registered by a signal between – 12 and – 13.5 ppm. Further on hydrochloric acid induces the process of the phosphoryl group N→O migration (phosphorotropy) monitored by the loss of intensity of the signal in the above region and sharp increase of the higher field signal or two signals assigned to the corresponding E and Z isomers of phosphates. In benzoylamides and acetanilides phosphorotropy is reversible whereas in benzanilides it proceeds up to entire formation of the O-phosphorylated isomer. Cyclic amides such as pyrrolidones were unreactive towards $P_4O_{10}$. Thiohydantoin can be phosphorylated by $P_4O_{10}$ with the moderate yield (Scheme 2).



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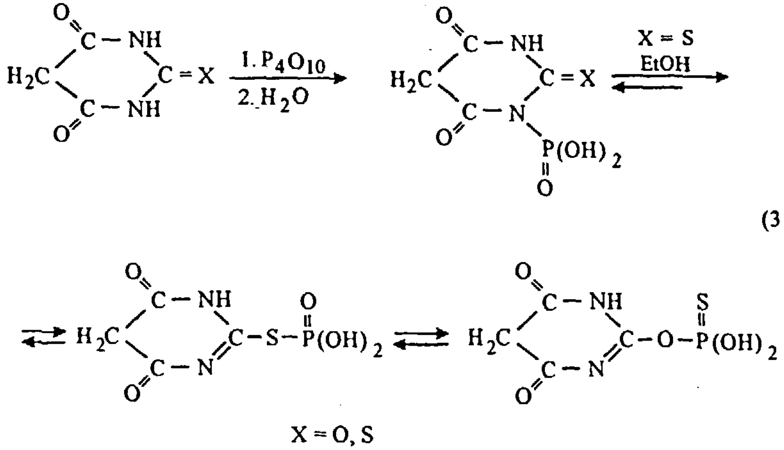
N-Phosphorylation is followed by N→S phosphorotropy (Scheme 2). Pyrimidinetriones react with $P_4O_{10}$ under mild conditions[1, 5] to give N-phosphorylated compounds (Scheme 3). The products are stable and exhibit no tendency to phosphorotropy.

Thiobarbituric acid and $P_4O_{10}$ form N-phosphorylated product (Scheme 3). Like phosphorylated thiohydantoin the product isomerizes reversibly into the S-phosphorylated form for which an equilibrium between the phosphothiol and phosphothione forms is determined (Scheme 3).

$P_4O_{10}$ Phosphorylates hydrazide of benzoic acid in the terminal $NH_2$ group (Scheme 4) and in the presence of moisture there is determined the 1 – 4 reversible shift[6] for the dihydroxyphosphoryl group.

The earlier determined 1–3 migration of the dialkoxy(aroxy)phosphoryl group in amides named by the authors[7] "phosphorotropy" consisted in the O→N shift of phosphorus. This underlines the specific character of the acidic dihydroxyphosphoryl group for which N→O migration is studied.



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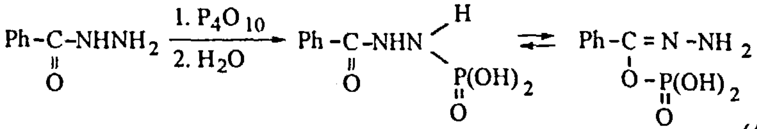

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