The Photo-initiated Hydrolysis of 3,5-Dimethoxybenzyl Phosphates

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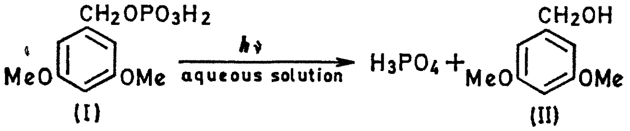
Summary 3,5-Dimethoxybenzyl phosphate undergoes photo-initiated hydrolysis in aqueous solution and the corresponding acetate can be used to photo-activate phosphoryl transfer by a phospho-mono-ester dissolved in acetonitrile.

3,5-DIMETHOXYBENZYL ACETATE readily undergoes photo-initiated hydrolysis in 50% aqueous dioxan,[1] and the 3,5-dimethoxybenzyloxycarbonyl group has been used as a photosensitive *N*-protecting group in peptide synthesis.[2] We report that 3,5-dimethoxybenzyl phosphate is photolabile, an observation which may be of use in the synthesis of phosphate esters.

3,5-Dimethoxybenzylphosphoric acid (I) was prepared[3] as its dicyclohexylammonium salt[†] (λ_{max} 275—277·5 nm, log ϵ 3·25) and mM-aqueous solutions of it were irradiated with a 62·5 w medium pressure water-cooled lamp in a quartz apparatus. Samples removed after different time intervals were examined by paper chromatography using propan-2-ol : ammonia : water (7 : 1 : 2). The results indicated that the photo-initiated hydrolysis to orthophosphate[4] and the parent alcohol (II) (isolable in 60—80% yield) proceeded most readily in neutral or acidic solution. Chromatographic analysis using acid developing solvents failed to reveal the presence of polyphosphates. In the absence of u.v. light, aqueous solutions of (I) under comparable pH conditions were stable over prolonged periods.



[†] Satisfactory spectra and elemental analyses were obtained for all new compounds.

Previous calculations have indicated that *m*-methoxy-groups stabilise the potential benzylic carbonium ion in the first excited state of 3,5-dimethoxybenzyl systems, and in accordance with this view, irradiation of the acetate of (II) leads to heterolytic C–O cleavage.[1] Photolysis of (I) in 50% aqueous ethanol produced no ethyl phosphate implying that exclusive C–O bond fission also occurs in this case. By contrast, 3,5-dinitrophenyl phosphate, which is photolabile in alkaline solution, breaks down with almost complete P–O bond fission.[5]

% *Of total phosphate appearing as orthophosphate after irradiation*[4]

	Irradiation time 15 min.	 30 min.
0·1N-KOH	Not analysed	19%
Glycine buffer pH 10.. ..	13%	24%
Water pH 8	81%	94%
Acetate buffer pH 4	100%	
0·1N-HCl	100%	

Irradiation of a 10^{-3}M-aqueous solution of the monophenyl ester of (I) for 45 min. gave orthophosphate (6%), monophenyl phosphate (61%), and unchanged diester (33%). The photo-initiated hydrolysis was again pH sensitive, complete decomposition of the diester in 10^{-2}N-HCl occurring within 15 min. The products, orthophosphate (16%) and monophenyl phosphate (84%), indicate that monophenyl phosphate itself may also undergo some photo-hydrolysis. The diester was stable over a considerable period in the absence of u.v. light.

The probable formation of carbonium ions during the photolysis of 3,5-dimethoxybenzyl esters led us to investigate the possibility of a photo-initiated phosphoryl transfer. A solution of 3,5-dimethoxybenzyl acetate (4 mM) and phenyl dihydrogen phosphate (4 mM) in dry acetonitrile was irradiated for 4 hr. Chromatographic analysis revealed the presence of orthophosphate (5%), unchanged monophenyl phosphate (71%), and P^1P^2-diphenylpyrophosphate (24%). A control reaction from which the acetate was omitted showed that no pyrophosphate was formed under comparable conditions.

The reaction probably proceeds *via* the attack of a carbonium ion on acetonitrile to form a nitrilium salt. This then reacts with phenyl phosphate to give an imidoyl phosphate, which in turn leads to the pyrophosphate.[6]

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