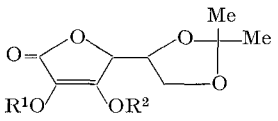
SPECIALIA

The Oxidative Dephosphorylation of Phosphoryl Esters Derived from L-Ascorbic Acid

We wish to report the synthesis and oxidative dephos phorylation of the 2- and 3-phenylphosphoryl esters [I: R^1=P(O)(OH)(OPh), R^2=H] and [I: R^1=H, R^2=P(O)(OH)(OPh)] of 5,6-isopropylidene L-ascorbic acid.



(I)

Previous work[1] on the phosphorylation of isopropylidene L-ascorbic acid [I: R^1=R^2=H][2] using phosphorus oxychloride gave, in low yield, a phosphate ester of unknown structure. In our hands, treatment of [I: R^1 = R^2 = H] with dicyclohexyl carbodiimide and monophenyl phosphoric acid in anhydrous pyridine gave a mixture of products, electrophoresis of which, at pH 5.5, indicated the presence of two phosphorus-containing compounds: each was enolic (ferric chloride/ferricyanide spray)[3].

Chromatography on DEAE cellulose, using gradient elution with triethylammonium acetate at pH 5.5, gave two compounds, A and B, the former being isolated as its barium salt (in 50% yield), and the latter as its cyclohexylammonium salt (in 25% yield). Treatment of each with diazomethane, followed by comparison of (a) proton NMR spectra and (b) the products of ozonolysis with those from [I: R^1 = R^2 = Me] and [I: R^1 = H, R^2 = Me][4], indicated that A was the 2-isomer [I: R^1 = P(O)(OPh)(OH), R^2 = H] and B was the corresponding 3-isomer of 5,6-isopropylidene L-ascorbic acid.

Since ene-diols bear a vinylogous relationship to catechols and hydroquinones, comparison with the behaviour of *ortho*- and *para*-hydroxyphenyl phosphate esters[5,6] leads one to expect that phosphate esters of ene-diols should undergo oxidative dephosphorylation. Treatment of both A and B with aqueous iodine or bromine led to a rapid liberation of monophenyl phosphoric acid. With a tenfold excess of bromine in ethanol, both A and B acted as sources for phosphoryl transfer, phenyl ethyl phosphate being produced.

The recent report[7] of analogous behaviour using the corresponding sulphate ester [I: R^1 = H, R^2 = SO_3H] is entirely in accord with our observations[8].

Zusammenfassung. Die 2- und 3-Phenylphosphorylester von 5,6-Isopropyliden L-ascorbinsäure wurden synthetisiert. Nach Oxydierung in Wasser oder Äthanol übertragen diese Ester ihre Phosphorylgruppe auf das Lösungsmittel.

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University Chemical Laboratory, Cambridge (England), April 13, 1966.

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[8] We wish to thank the Jane Coffin Childs Memorial Fund for a Fellowship (to J.W.B.H.), the University of Cambridge for the award of an I.C.I. Fellowship (to D.W.H.) and Roche Products Limited (Welwyn) for the gift of the L-ascorbic acid.
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Synthesis of Phyllokinin, a Natural Bradykinin Analogue

We report the synthesis of a peptide of the formula H-Arg-Pro-Pro-Gly-Phe-Ser-Pro-Phe-Arg-Ile-Tyr(OSO_3H)-OH according to the Scheme. The product was found to be identical with phyllokinin[1,2]. Condensation of O-acetyl-serine with *p*-nitrophenyl-*ter*-butylcarbonate in DMF with one equivalent of TEA afforded N-CTB-O-acetyl-serine (50% yield; DCEA salt: m.p. 154–155°; $[\alpha]_D^{20}$ + 13°, c 1, DMF. *Anal.* Calcd. for $C_{22}H_{40}N_2O_6$: C 61.6; H 9.4; N 6.5; Found C 61.6; H 9.4; N 6.0) that, by treatment with *p*-nitrophenol and DCCI in AcOEt, afforded *p*-nitrophenyl N-CTB-O-acetyl-serinate (75% yield; m.p. 90°; $[\alpha]_D^{20}$ – 51°, c 1, DMF. *Anal.* Calcd. for $C_{16}H_{20}N_2O_8$: C 52.2; H 5.5; N 7.6; Found C 52.3; H 5.6;

[1] A. Anastasi, V. Erspamer, and J. M. Cei, Symposium on Hypotensive Peptides, Florence, Italy, October 1965.
[2] All the amino acids have the L-configuration. The following abbreviations are used throughout this paper: CBO = carbobenzyloxy; CTB = carbo-*ter*-butyloxy; TEA = triethylamine; E^a = electrophoretic mobility of a sample pre-treated with HCl/AcOH; DMF = dimethylformamide; THF = tetrahydrofurane; DCEA = dicyclohexylamine; DCCI = dicyclohexylcarbodiimide; NHS = N-hydroxy-succinimide.