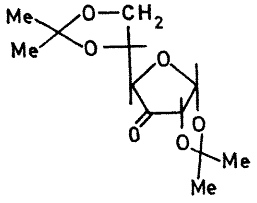
Carbohydrate C-Phosphonates

By (MRS.) L. EVELYN, L. D. HALL,* P. R. STEINER, and D. H. STOKES
(*Department of Chemistry, The University of British Columbia, Vancouver 8, B.C., Canada*)

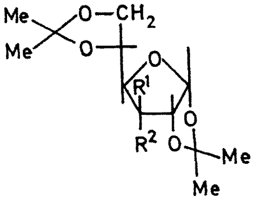
PROMPTED by the recent publication of Jones, Hamamura, and Moffatt,[1] we report the synthesis of *C*-phosphonate derivatives of carbohydrates, which have the phosphonate group bonded directly to a ring-carbon atom. Studies of such derivatives are relevant to the elucidation of the biochemical roles of carbohydrate phosphates and phosphonates; furthermore, detailed analyses of their n.m.r. spectra should extend our appreciation of the factors which control ^{31}P–^{1}H spin–spin coupling.

Coupling constants (Hz.) for the C-3 *epimers of dimethyl* (1,2;5,6-*di*-O-*isopropylidene*-α-D-*hexofuranose*) 3-C-*phosphonate*

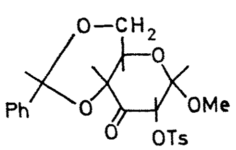
	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{5,6'}$	$J_{6,6'}$	$J_{P,2}$	$J_{P,4}$
(II)	3·8	—	—	4·8	6·5	5·9	−8·3	7·8	29·7
(III)	3·7	—	—	2·5	—	—	—	<0·5	7·5



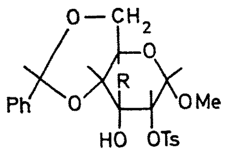
(I)



(II) R^1=PO·(OMe)$_2$; R^2=OH
(III) R^1=OH; R^2= PO·(OMe)$_2$



(IV)



(V) R =PO· (OMe)$_2$

Reaction of 1,2;5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuran-3-ulose[2] (I) with dimethyl phosphite and sodium methoxide in benzene solution, following the conditions of Abramov,[3] afforded a mixture of dimethyl (1,2;5,6-di-*O*-isopropylidene-α-D-allofuranose) 3-*C*-phosphonate (II), large prisms, m.p. 111—112°, $[\alpha]_D^{25}$ − 11·5° (*c* 5·3) and its 3-epimer, dimethyl (1,2;5,6-di-*O*-isopropylidene-α-D-glucofuranose) 3-*C*-phosphonate (III), fine needles, m.p. 85°, $[\alpha]_D^{25}$ − 41·7° (*c* 1·7). The relative yields of these isomers vary widely between different preparations; however, (II) always predominates. Although both isomers crystallise readily from ether–light petroleum (b.p. 30—60°), they can also be separated by column chromatography (Mallinckrodt Silicar CC-7, with graded elution by ether (5—100%)–benzene.

Assignment of the structures[†] of (II) and (III) followed directly from detailed analyses of their n.m.r. spectra; the coupling constants obtained by computer methods are listed in the Table. The *vicinal* ^{31}P–^{1}H couplings are in excellent agreement with the values expected on the basis of the known[4,5] angular dependence of *vicinal* ^{31}P–C–C–H coupling constants and on the assignment[6] of the $^{3}T_{2}$ conformation to both derivatives. Particularly noteworthy is the near-zero $J_{P,2}$ coupling for (III), which should[6] correspond to a dihedral angle of *ca.* 90° between the C-3–P and C-2–2-H bonds.

[†] All compounds had satisfactory elemental analyses. Optical rotations were determined for chloroform solutions. All n.m.r. spectra were measured with a modified Varian HA-100 spectrometer. In every instance the spectra indicated the presence of the required functional groups. All spectral assignments were checked, using appropriate computer programmes on an I.B.M. 7044 computer.

Pyranuloses also participate readily in the Abramov reaction. For example, reaction of the known[7] methyl 4,6-*O*-benzylidene-2-*O*-tosyl-α-D-*ribo*-hexopyran-3-uloside (IV) with dimethyl phosphite in benzene solution affords dimethyl (methyl 4,6-*O*-benzylidene-2-*O*-tosyl-α-D-allopyranoside) 3-*C*-phosphonate (V), fine needles, m.p. 178°, $[\alpha]_D^{25}$ + 22·4° (*c* 4·5), in 78% yield. The *allo*-configuration was assigned on the basis of the small magnitude of J_{P-2a-H} (*ca.* 4 Hz.).

Further studies of other members of this, and other classes of phosphonates, have confirmed the generality of the reactions outlined herein.

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