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α-DEOXY-α-HYDROXYAMINO SUGAR PHOSPHONATES AND THE CORRESPONDING NITROXIDE FREE-RADICALS*

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ABSTRACT

Treatment of sugar aldonitrones with dialkyl phosphites gave sugar α-deoxy-α-(*N*-hydroxy-*N*-methylamino)phosphonates, often highly stereoselectively. Repeated nucleophilic addition to a nitrone followed by oxidation of the resulting hydroxylamine allows the "first generation" nitrone, 1,2-*O*-isopropylidene-α-D-*xylo*-pentodialdo-1,4-furanose 5-(*N*-methyloxime), to be converted into the "third generation" cyclic nitrone, [(4*R*)-4-diethoxyphosphoryl-5*H*,6*H*-1,3-oxazino][6,5-*c*](1,2-*O*-isopropylidene-α-D-*xylo*-tetrofuranose) *N*-oxide. The configurational and conformational assignments for all the new compounds prepared were based on short and long-range H,H, H,P, and P,C couplings, and new empirical rules regarding long-range H,P couplings are proposed. The sugar α-deoxy-α-hydroxyaminophosphonates spontaneously oxidised in the air to give the corresponding nitroxide free-radicals, which afforded good e.s.r. spectra that allowed epimers at the α-carbon atom to be discriminated.

INTRODUCTION

Although *N*-hydroxyglycosylamines have been known for decades[3], pure deoxyhydroxyamino sugars have been described only recently[1,4]. Most of these compounds were more stable than expected and many were slowly and spontaneously oxidised to nitroxides in the air, in such a way as to afford a solution in which the standing concentration of free radicals was high enough to enable the recording of good e.s.r. spectra but still too low to degrade the resolution of the n.m.r. spectra of their hydroxylamine counterpart. Under these conditions, the couple

*Sugar Free-Radicals, Part VI (for Part V, see ref. 1); and Phosphorus-bearing Sugars, Part VIII (for Part VII, see ref. 2).
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GlycNHOH ⇄ GlycNHO· is promising as a biological probe.

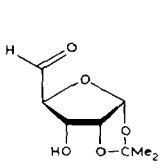
We now report on the synthesis and structure of α-deoxy-α-hydroxyamino sugar phosphonates, which are potential biological analogues of sugar phosphates and sugar amino acids. This work has been the subject of preliminary communications[1,5].

RESULTS AND DISCUSSION

Reaction of the dialdose derivative **1**[6] with *N*-methylhydroxylamine gave the sugar nitrone **2**. Nitrones **2**, **4**[8], and **3**[7], when subjected to nucleophilic attack by dialkyl phosphites, afforded the expected α-deoxy-α-(*N*-hydroxy-*N*-methylamino) sugar phosphonates, **5**, **6**, **7**, **8**, and **10** either as pure isomers or as mixtures of epimers.

The ^{1}H-n.m.r. spectra of solutions of the nitrones **2**–**4** in chloroform revealed $J_{4,5}$ values (3.7, 4.0, and 5.0 Hz, respectively) which indicated small or zero contributions from conformers where the H-4/H-5 dihedral angle was either 0° or 180°. The Garbish equation[9] predicts couplings of 4.85 and 3.60 Hz for dihedral angles of 120° and 60°, respectively. These values are close to those found for **2**–**4** and, as the conformations in which the double bond eclipses a C-4 substituent other than hydrogen are sterically forbidden, the only feasible classical conformers would be **17** and/or **18**. When the spectra of solutions of **2** or **3** in chloroform–methyl sulfoxide with increasing concentrations of methyl sulfoxide were recorded, the $J_{4,5}$ value increased to a maximum of 5.5 Hz. N.O.e. experiments for solutions in chloroform and chloroform–methyl sulfoxide indicated H-5 and *N*-Me to be *cis*, thus confirming the *Z* configuration of these nitrones, but did not show any interaction between H-5 and H-3, thus ruling out the synclinal conformation **17**. Thus, for solutions in chloroform, **2** and **3** each possesses a hydrogen bond between the nitrone oxygen and the hydroxyl group, imposing a conformation (**19**, ~110°) slightly distorted from the antiperiplanar conformation **18**. Addition of methyl sulfoxide breaks the hydrogen bond, and **2** and **3** then adopt a conformation similar to that of **4** (mostly **18**). As a consequence of this conformational equilibrium, the nitrone group presents its *re* face (at C-5) in intermolecular nucleophilic attack.

Treatment of **4** with dimethyl or diethyl phosphite gave **5** and **6**, respectively, as mixtures of epimers in which the (5*R*)-isomer preponderated. On the other hand, the nitrones **3** and **2**, with HO-3 unsubstituted, afforded only the (5*R*)-epimer of the phosphonates **7**, **8**, and **10**. Analysis of the product mixture containing (5*R*)-**7** revealed no (5*S*)-**7** but the oxaphospholane (5*S*)-**9** (~3%) and two epimers (~4%) at the phosphorus atom of the (5*R*)-isomer, namely, (5*R*)-**9** and (5*R*)-**9′**. The abundant isomer is formed by nucleophilic attack at the more accessible face of the nitrone group in the most stable ground-state conformation, but the most important steric factor seems to be the establishment of a (most probably hydrogen) bond between the nitrone oxygen and HO-3. The present results do not indicate whether this phenomenon plays a more prominent role in the ground state or at the transition state.



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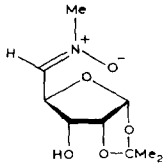

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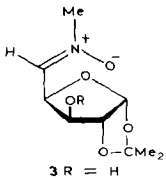

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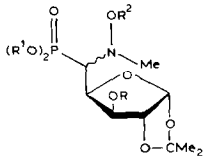
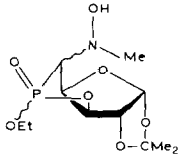
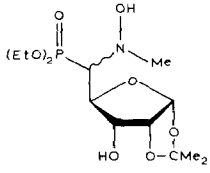
4 R = Me



5 R = R^1 = Me, R^2 = H
6 R = Me, R^1 = Et, R^2 = H
7 R = R^2 = H, R^1 = Et
8 R = R^2 = H, R^1 = Me
11 R = Me, R^1 = Et, R^2 = Ac
[12 R = R^2 = Ac, R^1 = Et]



9 and 9'



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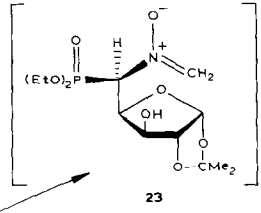

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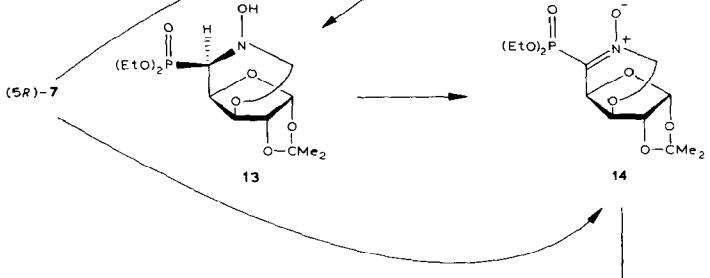
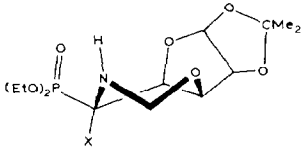
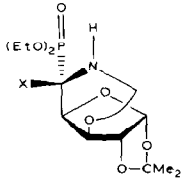


(5R)-7

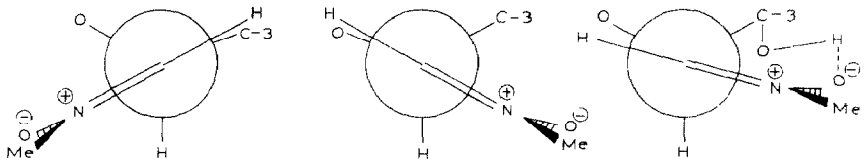
13

14





15 X = H
16 X = D

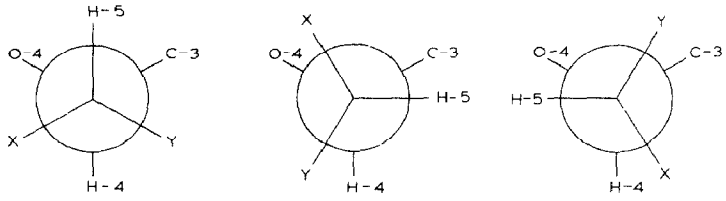


17 18 19

The configurations of all the new compounds were established from their n.m.r. data which are collected in Tables I and II.

From the values of $J_{4,5}$ (Table II), it is apparent that the 3-*O*-methyl-*xylo*-derivatives **5** and **6** exist in conformation **20**. This is not the case for their 3-hydroxy analogs **7** and **8**, because of the hydrogen bond between the two hydroxyl groups. In order to force **7** and **8** to adopt conformation **20**, methyl sulfoxide-d_6 was used as solvent and the diacetate (**12**) of **7** was prepared. A monoacetate (**11**) of **6** was also prepared.

For these compounds in conformation **20**, there exists an unambiguous relationship between the configuration at C-5 and the relative topographical distribution of C-3 and the phosphorus atom [antiperiplanar for the (5*R*)-isomer, gauche for the (5*S*)-isomer]. The existence of a "Karplus-type" relationship for $^3J_{PCCC}$ *versus* $\theta_{P,C}$ is well established[10–16], even if the presence of electronegative substituents on the coupling path have been shown to decrease the J values[12–16]. This latter rule is confirmed by the present results: the (5*R*)-compounds with $J_{4,5}$ values >10.5 Hz are good models of a $\theta_{P,C-3}$ of 180°, and the maximum value noted for $J_{P,C-3}$ is 9.4 Hz. This value is smaller than those reported in the literature (21.1[15], 17[14], and 13.3 Hz[16] for compounds bearing two oxygen substituents on the coupling path). Thus, an extra nitrogen substituent decreases $J_{P,C-3}$ by a few Hz.



20 21 22

(5*R*)-isomer X = $P(O)(OR^1)_2$, Y = $NMeOR^2$
(5*S*)-isomer X = $NMeOR^2$, Y = $P(O)(OR^1)_2$

Whereas the configuration of the *xylo* compounds **5–8** can be deduced unambiguously from the $J_{P,C-3}$ value for conformation **20** [~0 Hz for the (5*S*)-compounds, and >7 Hz for their (5*R*)-epimers], the problem was more difficult for the *ribo* compound **10**, which could not be made to adopt conformation **20**. A study of the other coupling constants for the model compounds **5–12** proved to be helpful.

TABLE I

CHEMICAL SHIFTS (δ) FOR COMPOUNDS **5–15**

Compounds	^1H						^{13}C						*P*
	H-1	*H-2*	*H-3*	*H-4*	*H-5*	NCH_3 (NCH_2)	*C-1*	*C-2*	*C-3*	*C-4*	*C-5*	NCH_3 (NCH_2)	
(5*R*)-**5**	5.93	4.59	3.92	4.47	3.61	2.97	105.00	80.80	83.70	77.70	63.20	46.95	
(5*S*)-**5**	5.94	4.58	3.86	4.67	3.77	3.00	104.70	80.90	84.00	77.30	62.90	45.90	
(5*R*)-**6**	5.92	4.60	3.95	4.50	3.62	3.00	105.00	80.90	83.80	77.80	63.30	46.86	−25.10
(5*S*)-**6**	5.95	4.60	3.90	4.70	3.77	3.02	104.50	80.80	84.00	77.10	63.20	45.70	
(5*R*)-**7**	5.98	4.55	4.38	4.62	3.77	2.90	104.70	84.90	76.00	77.00	65.30	46.00	−23.60
(5*R*)-**7**[a]	6.00	4.59	4.31	4.57	3.48	2.95	104.50	84.03	73.69	78.32	63.00	46.50	
(5*R*)-**8**	5.98	4.58	4.34	4.62	3.71	2.89	104.40	84.57	75.27	76.73	64.64	45.56	−26.00
(5*R*)-**8**[a]	5.81	4.39	4.12	4.32	3.31	2.75	104.60	84.04	73.66	78.33	62.95	46.67	
(5*R*)-**11**	5.93	4.51	4.06	4.34	3.59	3.07	105.40	80.80	84.00	78.10	62.30	45.30	
(5*R*)-**12**	5.90	4.49	5.39	4.52	3.57	2.97	104.80	82.22	77.00	75.90	62.30	44.68	
(5*R*)-**9**	6.10	4.70	4.55	4.74	3.30	2.85	106.30	82.69	80.74	78.72	67.78	47.40	
(5*R*)-**9′**	6.01	4.69	4.67	4.90	3.40	2.82	106.45	83.18	80.87	79.73	67.46	48.17	
(5*S*)-**9**	5.90	4.73	4.86	5.10	3.30	2.91	105.20	83.68	83.49	80.57	65.98	46.77	−43.00
(5*R*)-**10**	5.79	4.60	4.29	4.33	3.43	2.90	103.50	78.80	72.65	76.60	66.90	46.50	
(5*R*)-**10**[a]	5.63	4.46	4.20	4.38	3.53	2.60	103.50	78.75	75.30	72.50	67.50	45.00	
(5*R*)-**13**	5.98	4.59	4.33	4.33	4.06	4.66 4.97	104.09	83.71	82.00	71.74	59.50	76.45	−17.75
14	6.02	4.70	4.29	4.90	—	4.96 5.07	104.80	82.55	85.87	78.02	131.30	70.91	
(5*S*)-**15**	6.00	4.42	4.07	4.13	3.48	4.20 4.57	105.72	83.17	78.10	70.55	51.90	77.35	−21.74

[a]In methyl sulfoxide.

TABLE II

COUPLING CONSTANTS FOR COMPOUNDS **5–15**

Compounds	$J_{1,2}$	$J_{3,4}$	$J_{4,5}$	$J_{P,1}$	$J_{P,2}$	$J_{P,4}$	$J_{P,5}$	$J_{P,C-3}$	$J_{P,C-4}$	$J_{P,C-5}$	J_{PCNC}	*Other data*	
(5*R*)-**5**	4.0	3.0	10.0	0.0	2.0	6.5	14.0	7.6	2.5	134	2.8		
(5*S*)-**5**	4.0	3.0	11.0	0.5	0.0	5.0	17.0	0.0	6.8	146	6.6		
(5*R*)-**6**	4.0	3.0	10.0	0.0	2.0	6.2	14.0	8.5	4.6	134	2.4		
(5*S*)-**6**	4.0	3.1	11.0	0.5	0.0	5.0	19.5	0.0	7.5	146	7.0		
(5*R*)-**7**	4.0	3.0	6.0	0.0	0.5	11.0	18.0	5.8	4.1	142	5.1		
(5*R*)-**7**[a]	4.0	2.0	10.0	0.2	1.0	7.0	14.0	8.6	2.4	140	0.0		
(5*R*)-**8**	3.7	2.8	5.2	0.0	0.5	13.0	18.0	6.0	2.2	143	4.6		
(5*R*)-**8**[a]	3.7	2.0	10.0	0.0	1.5	8.0	14.3	9.1	1.8	136	0.0		
(5*R*)-**11**	4.0	3.0	10.5	0.0	2.0	7.0	15.0	9.4	2.7	139	0.0		
(5*R*)-**12**	4.0	3.0	11.0	0.0	2.5	8.0	17.0	9.0	2.3	146	0.0		
(5*R*)-**9**	3.8	2.8	4.7	0.0	0.0	34.0	10.3	6.2	0.0	147	14.4	$J_{P,C-2}$ 7.0	$J_{P,3}$ 4.5
(5*R*)-**9**′	3.5	3.5	4.5	0.0	0.0	32.0	12.0	5.2	0.0	137	5.2	$J_{P,C-2}$ 5.9	$J_{P,3}$ 3.0
(5*S*)-**9**	4.0	3.0	0.0	0.0	0.0	25.0	10.0	7.8	14.5	136	13.4	$J_{P,C-2}$ 8.4	$J_{P,3}$ 2.0
(5*R*)-**10**	4.0	9.0	4.0	0.0	0.5	17.0	20.0	4.6	0.0	145	3.2	$J_{2,3}$ 4.0	
(5*R*)-**10**[a]	3.0	9.0	0.0	0.0	0.0	26.0	23.0	0.0	0.0	150	0.0		
(5*R*)-**13**	4.0	?	1.0	1.0	0.0	?	27.0	0.0	14.5	154	0.0	$J_{HA^b,5}$ 2.0	$J_{HA^b,P}$ 0.5
14	4.0	2.5	—	0.0	1.7	5.0	—	6.7	5.5	206	6.8	$J_{HA^b,4}$ 0.2	$J_{HA^b,P}$ 1.0
(5*S*)-**15**	4.0	2.0	3.0	0.0	2.5	2.5	24.5	9.5	4.5	163	15.9	$J_{3,P}$ 2.0	$J_{HB^c,P}$ 4.0
												$J_{3,NH}$ 4.0	$J_{NH,5}$ 13.3

[a]In methyl sulfoxide. [b]H-*pro-S*-3 of the oxazine ring. [c]Probably H-*pro-R*-5 of the oxazine ring.

For example, the $^3J_{P,4}$ value confirmed the conformational assignments made using the $J_{4,5}$ coupling. The $^3J_{P,4}$ couplings follow a "Karplus-type" rule which, as usual, depends on the substitution pattern at the phosphorus atom and also on the nature of the substituents along the coupling path. For compounds (5*S*)-**5** and (5*S*)-**6**, which exist almost exclusively in conformation **20**, the $^3J_{P,4}$ value (5.0 Hz) corresponds to a dihedral angle of 60°. This is in better agreement with that (4.5 Hz) calculated using the classical Benezra equation[17] than with our revised value[16] (1.2 Hz), thus confirming the influence of factors other than dihedral angle on the coupling constants involving a phosphorus atom. The long-range couplings $^5J_{P,1}$ and $^5J_{P,2}$ are indicative[18] of the position of a phosphorus atom at C-5 ($^5J_{P,1}$ >0.5, $^5J_{P,2}$ 0 Hz for P and O-4 antiperiplanar, $^5J_{P,2}$ >0.5, $^5J_{P,1}$ 0 Hz for P and C-3 antiperiplanar). On the other hand, the values of $J_{P,4}$ and $J_{P,C-3}$ obtained for solutions of **7** and **8** in chloroform prove that the hydrogen bond involves HO-3 and NOH (and not HO-3 and P=O).

In solution in methyl sulfoxide, the *ribo* compound **10** had $J_{4,5}$ 0, and $J_{P,4}$ 26 Hz. From the $J_{4,5}$ value, a $\theta_{P,4}$ of either ~150° or ~30° could be deduced but, owing to the extremely large difference[16,17] between $^3J_{H,P}$ (0°) and $^3J_{H,P}$ (180°), any coupling constant of >18 Hz can be assigned to a dihedral angle of >90°, in this instance, ~150°. This conclusion is confirmed by the zero value of $J_{P,C-3}$. Under these conditions, the four possibilities represented by conformers **21** and **22** are reduced to two, namely, (5*R*)-**21** and (5*S*)-**22**. Molecular models indicated that **22** is sterically not feasible, which establishes the 5*R* configuration of **10**. Confirmation is afforded by the n.m.r. spectrum for a solution in chloroform, where the hydrogen bond between NOH and HO-3 results in a contribution to the conformational equilibrium of some of a conformer somewhat similar to **20**, the values of $J_{P,C-3}$ and $J_{P,2}$ indicating its 5*R* configuration.

The $J_{P,5}$, $J_{P,C-4}$, $J_{P,C-5}$, and J_{PCNC} values depend mostly on the conformation around C–N or C–P bonds; to a large extent, they are correlated with the configuration at C-5 but, owing to the mobility of the groups involved, they are generally not readily interpretable in detail. Nevertheless, they reflect the difference in steric hindrance around C-5 between the two half-spaces separated by the H-4–C-4–C-5 plane. For example, for conformation **20**, J_{PCNC} is >6.5 Hz for the (5*S*)-isomers and <3 Hz for the (5*R*)-isomers. This coupling is very sensitive to hydrogen bonding, which increases the value measured for the (5*R*)-isomers to ~5 Hz, the *N*-methyl group being restricted to a position almost antiperiplanar to the phosphorus atom. For conformation **20**, $J_{P,C-4}$ is always smaller for the (5*R*)-compounds (<2.8 Hz) than for (5*S*)-isomers (>6.8 Hz).

Oxidation of (5*R*)-**7** with 1,4-benzoquinone gave 33% of **13** which was oxidised further to **14**. It was impossible to avoid the over-oxidation to give **14**. Oxidation of **7** with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) gave 67% of **14**. From previous studies[1] of the isolation of "methylenic nitrones", it is clear that **7** is first oxidised to **23** which immediately cyclises to give **13**. The stereochemistry at C-5 was not affected by the oxidation, as shown by the n.m.r. spectra

of **13**. A ^4J coupling of 2.0 Hz between H-5 and one of the methylene protons of the perhydro-oxazine ring (H*pro-S*) indicated a planar-W coupling path and established the conformation of this ring to be close to $^{O\text{-}3}C_{C\text{-}5}$ but flattened around the C-3–C-4 bond, approaching an $^{O,N}F$ flattened chair[19] ($^{1,3}F$ using the numbering of the oxazine ring). The 5*R* configuration was established by the zero values of $^3J_{P,C\text{-}3}$ and $^5J_{P,2}$, and by the existence of a $^5J_{P,1}$ coupling.

As shown by the n.m.r. data, particularly the values of $J_{P,4}$ and $J_{P,2}$, the dihydro-oxazine ring of **14** adopts an approximately planar conformation with the oxygen atom pointing towards the *endo* face of the bicyclic system. Not unexpectedly, the reduction of **14** proceeded from the *exo* face, leading to the (5*S*)-isomer of **15**, the configuration of which was clearly indicated by the n.m.r. data. The two large $^3J_{P,C}$ couplings with C-3 and the perhydro-oxazine methylene group indicate a double antiperiplanar orientation. This and the small value of $J_{4,5}$ are only compatible with the diethoxyphosphoryl substituent being equatorial in the same flattened chair as noted for **13**, but for a compound of the 5*S* configuration. This view was confirmed by the large $J_{H\textit{pro-S},P}$ and $^5J_{P,2}$ values and the small value of $^3J_{P,4}$. The axial disposition of H-5 is confirmed by the very large $J_{H,NH}$ coupling, which proves that the NH bond is also axial.

All these reactions constitute a "cascade" of regio- and/or stereo-selective transformations. For example, the "first generation" nitrone **3**, on nucleophilic attack, gave stereoselectively the "first generation" hydroxylamine **7** whose regioselective oxidation (on the *N*-methyl group) gave the "second generation" nitrone **23**, which cyclised to the "second generation" hydroxylamine **13** whose regioselective oxidation (only on the methine group) afforded the "third generation" nitrone **14**, which was stereoselectively reduced to **15**.

The deoxyhydroxyamino sugars **5–10** and **13** gave good e.s.r. spectra after storage in the air or on bubbling air into their solutions. In some instances, better resolved spectra were obtained by increasing the temperature to 70–80°. The e.s.r. data are collected in Table III and examples are given in Figs. 1 and 2. The angular dependance of e.s.r. hyperfine coupling constants of hydrogen atoms is well established[20] and, for simple nitroxides, is expressed by $a_H = 26 \cos^2\theta$. This relationship holds[5,21] for sugar derivatives where both protons of a methylene group are coupled to a nitroxide. The examples of e.s.r. spectra of nitroxides bearing α-phosphorus substituents are few but, from carbon analogues[22], it is possible to propose, for phosphonates, the relationship $a_P = 148 \cos^2\theta$, where θ represents the dihedral angle between the *p* orbital of the nitroxide nitrogen and the Cα-P bond. Compound **13** is a good model to check the validity of this relationship since two pairs of geminal nuclei coupled to the nitroxide are present. The computed values of θ were 45°, 64°, and 70° for the hydrogens and 56° for the phosphorus. For a pair of geminal nuclei (H,H or H,P), the corresponding θ values (θ and θ') could be related by one of the three following equations, depending on the angular relationship between the *p* orbital of the nitrogen atom and the angle H–Cα–H or H–Cα–P:

$$\theta + \theta' = 120°;\ \theta + \theta' = 60°;\ \theta - \theta' = 60°.$$

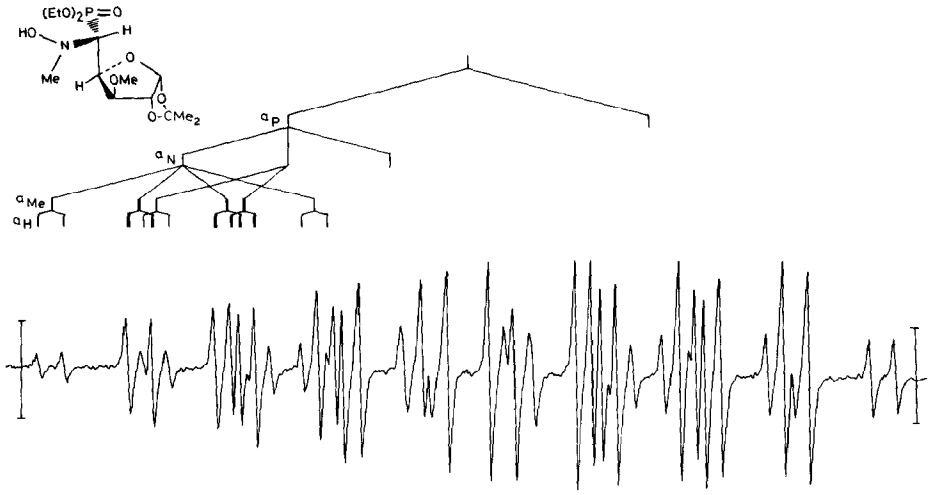


Fig. 1. E.s.r. spectrum of (5*R*)-**6**.

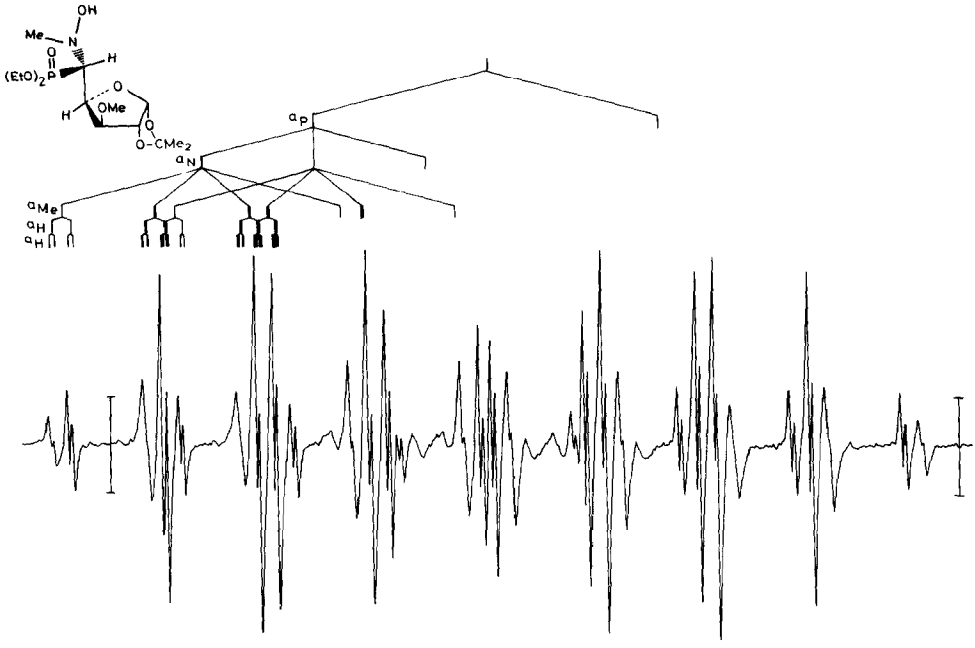


Fig. 2. E.s.r. spectrum of (5*S*)-**6**.

TABLE III

E.S.R. DATA FOR THE NITROXIDE FREE-RADICALS FORMED ON OXIDATION OF DEOXYHYDROXYAMINO SUGARS

Starting compound	g	a_P	a_N	a_{CH_1}	a_{CH_2}	a_{Ha}	a_{Hb}
(5*R*)-**5**	2.0060	50.2	14.4	12.1	—	3.4	0.3
(5*S*)-**5**	2.0060	44.8	14.4	12.2	—	2.4	0.8
(5*R*)-**6**	2.0060	50.2	14.3	12.2	—	3.6	—
(5*R*)-**6**[a]	2.0060	49.4	14.4	12.5	—	2.7	—
(5*S*)-**6**	2.0063	44.8	14.4	12.2	—	2.4	0.8
(5*R*)-**7**	2.0060	41.2	14.6	12.3	—	3.6	—
(5*R*)-**7**[a]	2.0062	50.0	14.5	13.0	—	2.5	—
(5*R*)-**8**	2.0061	47.0	14.3	12.1	—	2.8	—
(5*R*)-**8**[a]	2.0062	49.3	14.6	12.5	—	2.5	—
(5*S*)-**9**	2.0060	54.8	15.1	12.1	—	5.5	—
(5*R*)-**10**	2.0062	36.6	14.3	12.2	—	3.2	—
(5*R*)-**10**[a]	2.0060	40.0	14.5	12.4	—	3.4	—
(5*R*)-**13**	2.0063	46.3	14.1	—	13 and 3.1	5.0	—

[a]In methyl sulfoxide.

A good agreement with the first equation can be found by associating the angular values of 56° (a_P = 40.3 G) and 64° (a_H = 5 G) on one hand, and 45° (a_H = 13 G) and 70° (a_H = 3.1 G) on the other. The first equation implies that the *p* orbital of the nitrogen atom should project along the N–C bond inside the H–Cα–X angle and that both θ and θ' should be <90°. This situation obtains in the "sofa" conformer where all atoms but the nitrogen of the perhydro-oxazine ring are co-planar with the nitrogen pointing toward the *endo* face. Molecular models show this conformer to be quite strained, but they do not take into account a possible rehybridisation of C-3 and C-4 of the furanoid ring (due to their position at the junction of the two rings) which could alleviate some of this strain.

For most of the open-chain sugar nitroxides previously studied[1,4,5,21], only eclipsed conformers were present at conformational equilibrium. It is not the case here, where the set of equations describing this situation admits no solution. Using the above equations related to the hyperconjugation model, θ (relative to H) and θ' (relative to P) values were computed as well as the sum ($\theta + \theta'$) for each nitroxide. This sum was always close to 120° (range 115–129°). If this corresponds to a pure conformer, its average θ and θ' values would be 65° and 55°, respectively.

Some general observations can be made. For nitroxides whose associated hydroxylamine exists in conformation **20**, there is a good correlation between a_P and the configuration [a_P >49 G for (5*R*)-compounds, a_P <45 G for (5*S*)-compounds]. Some correlation with $J_{P,C\text{-}4}$ and J_{PCNC} indicates that the same general steric factors control the rotamer population about the C–P and C–N bonds for the hydroxylamines and the corresponding nitroxides. The solvent has a negligible

effect on the a_P hyperfine coupling [see the data relative to (5*R*)-**6** in Table III] except when a hydrogen bond can be broken, *cf.* (5*R*)-**7**. In e.s.r., as in n.m.r., spectroscopy, particularly when a phosphorus nucleus is involved, the pertinent dihedral angle is the most important single factor responsible for the value of the coupling constant, but others are also operative, such as the relative orientation of the P=O bond and the plane of the nitroxide. For example, if there is a good agreement between the hyperfine coupling constants and the assumed corresponding dihedral angles (sum of θ and θ' close to 120°), there is also a correlation between the value of that sum and $J_{P,C\text{-}5}$, which in turn depends on the orientation of the phosphoryl group[16].

The work described here provides the first examples of usable e.s.r. spectra obtained from pairs of pure isolated epimers and demonstrates the chiral discriminating power of this method. In the examples described here, the presence of a phosphorus atom in a strategic position made easy the configurational assignments of the diamagnetic precursors. In the general case (the absence of a phosphorus nucleus), the e.s.r. spectra can be more discriminating than n.m.r. spectra.

EXPERIMENTAL

General methods. — Solutions were concentrated under diminished pressure at <40°. Melting points are uncorrected and were obtained with a Mettler FP 52 melting-point microscope. T.l.c. was performed on silica gel HF_{254} (Merck) with detection by u.v. light or with phosphomolybdic–sulfuric acid[23]. Dry-column chromatography[24] was conducted with silica gel 60 F_{254} (Merck). I.r. spectra were recorded with a Perkin–Elmer Model 357 or Beckman AccuLab 5 spectrophotometer, and u.v. spectra with a Unicam SP 800 spectrophotometer. N.m.r. spectra were recorded at 35 or 20° for solutions in $CDCl_3$ (internal Me_4Si) with a Perkin–Elmer R32 (90 MHz), Bruker WP 200 Sy, or Bruker WH 360 spectrometer. Optical rotations were measured on solutions in chloroform with a Schmidt–Haensch polarimeter. E.s.r. spectra were recorded on a Varian E-9 spectrometer (X-band, 100 kHz modulation) equipped with a variable temperature device. The *g* values were measured by using a DPPH sample and the magnetic field was calibrated with an n.m.r. marker. All the hyperfine coupling constants were checked by simulating the corresponding e.s.r. spectra with a 9830 Hewlett–Packard desk computer.

*1,2-O-Isopropylidene-α-*D-ribo-*pentodialdo-1,4-furanose 5-(N-methyloxime)* (**2**). — To a solution of 1,2-*O*-isopropylidene-α-D-*ribo*-pentodialdo-1,4-furanose[6] (**1**; 2 g, 10.6 mmol) in water (16 mL) were added *N*-methylhydroxylamine hydrochloride (1.37 g, 16.5 mmol) and sodium acetate (1.35 g, 16.5 mmol). After stirring for 2 h at room temperature, the solution was extracted with chloroform, and the extract was dried ($MgSO_4$) and concentrated. The residue was recrystallised from ether–hexane to give **2** (1.25 g, 54%), m.p. 162.6–164.8°, $[\alpha]_D^{20}$ +65° (*c* 1.1); ν_{max}^{KBr} 3230 (OH), 1600 (C=N), 1380 and 1385 (CMe_2), 1195 cm^{-1} (N^+–O^-); λ_{max}^{EtOH} 238 nm (ε 11791). ^{1}H-N.m.r. data ($CDCl_3$): δ 1.40, 1.64 (2 s, 6 H, CMe_2),

3.73 (s, 3 H, NMe), 6.95 (d, 1 H, H-5), 4.16 (dd, 1 H, $J_{2,3}$ 4.5, $J_{3,4}$ 9.5 Hz, H-3), 4.70 (t, 1 H, $J_{1,2}$ 3.5 Hz, H-2), 5.14 (bd, 1 H, $J_{4,5}$ 3.7 Hz, H-4), 5.80 (d, 1 H, H-1), 5.97 (bs, 1 H, OH), 6.95 (d, 1 H, H-5). Mass spectrum: *m/z* 88 (100), 100 (78), 89 (75), 85 (42), 84 (39), 59 (36), 55 (28), 202 (24, $M^+ - Me$), 120 (23), 217 (14, M^+).

Anal. Calc. for $C_9H_{15}NO_5$ (217.1): C, 49.76; H, 6.96; N, 6.45. Found: C, 49.68; H, 7.05; N, 6.38.

*(5R)- and (5S)-5-Deoxy-5-dimethoxyphosphoryl-5-(*N*-hydroxy-*N*-methyl amino)-1,2-O-isopropylidene-3-O-methyl-α-*D*-xylo-1,4-pentofuranose* (**5**). — To a stirred solution of 1,2-*O*-isopropylidene-3-*O*-methyl-α-D-*xylo*-pentodialdo-1,4-furanose 5-(*N*-methyloxime) (**4**; 300 mg, 1.3 mmol) in dimethyl phosphite (10 mL) was added a trace of sodium methoxide. After 24 h, the solvent was removed under reduced pressure. Column chromatography of the resulting syrup, using ether–methanol–hexane (30:3:1), afforded (5*R*)-**5** (240 mg, 54%) and a mixture (90 mg, 20%) of (5*R*)-**5** and (5*S*)-**5**. T.l.c. of this mixture, using ether–methanol (10:1), afforded the (5*S*)-isomer (15 mg, 3.4%).

Compound (5*R*)-**5** had m.p. 131–133.5°, $[\alpha]_D^{20}$ −42° (*c* 1.6); ν_{max}^{KBr} 3290 (OH), 1365 (CMe_2), 1210 (P=O), 1180 cm^{-1} (P–O–C). Mass spectrum: *m/z* 168 (100), 174 (75), 232 (43), 142 (35), 153 (33), 152 (22), 87 (22), 216 (19), 113 (15), 88 (15), 341 (7, M^+), 326 (2, $M^+ - Me$).

Anal. Calc. for $C_{12}H_{24}NO_8P$ (341.30): C, 42.23; H, 7.09; N, 4.10; P, 9.08. Found: C, 42.30; H, 6.98; N, 4.33; P, 9.42.

See the Tables for some spectroscopic data for (5*S*)-**5**.

*(5R)- and (5S)-5-Deoxy-5-diethoxyphosphoryl-5-(*N*-hydroxy-*N*-methyl amino)-1,2-O-isopropylidene-3-O-methyl-α-*D*-xylo-1,4-pentofuranose* (**6**). — To a stirred solution of **4** (380 mg, 1.65 mmol) in diethyl phosphite (15 mL) was added a trace of sodium ethoxide. After 24 h, the solvent was removed under reduced pressure. Column chromatography of the resulting syrup, using ether–methanol–hexane (30:3:1), afforded (5*R*)-**6** (170 mg, 28%) and a mixture of (5*R*)-**6** and (5*S*)-**6** (250 mg, 41%). Column chromatography of this mixture, using ether–methanol (10:1), gave (5*S*)-**6** (90 mg, 15%).

Compound (5*R*)-**6** had m.p. 131–133°, $[\alpha]_D^{20}$ −46° (*c* 1.3); ν_{max}^{KBr} 3310 (OH), 1370 (CMe_2), 1235 (P=O), 1170 cm^{-1} (P–O–C). Mass spectrum: *m/z* 196 (100), 232 (71), 174 (52), 369 (48, M^+), 181 (22), 142 (16), 216 (12), 87 (12), 370 (8, $M^+ + 1$), 233 (8), 354 (7, $M^+ - Me$).

Anal. Calc. for $C_{14}H_{28}NO_8P$ (369.35): C, 45.53; H, 7.64; N, 3.79; P, 8.39. Found: C, 45.34; H, 7.89; N, 3.77; P, 8.49.

Compound (5*S*)-**6** was a syrup, $[\alpha]_D^{20}$ −20° (*c* 1.1); ν_{max}^{film} 3320 (OH), 1370 (CMe_2), 1215 (P=O), 1160 (P–O–C). Mass spectrum: *m/z* 113 (100), 84 (80), 85 (74), 100 (61), 87 (60), 232 (50), 59 (48), 196 (48), 174 (42), 83 (37), 369 (9, M^+), 254 (3, $M^+ - Me$).

Anal. Found: C, 45.80; H, 7.80; N, 3.57; P, 8.15.

*(5R)-5-Deoxy-5-diethoxyphosphoryl-5-(*N*-hydroxy-*N*-methylamino)-1,2-O-isopropylidene-α-*D*-xylo-1,4-pentofuranose* (**7**). — To a stirred solution of the

nitrone **3**[7] (900 mg, 4.15 mmol) in diethyl phosphite (45 mL) was added a trace of sodium ethoxide. After 48 h, the solvent was removed under reduced pressure. Column chromatography of the resulting syrup, using ether–methanol–hexane (30:3:1), afforded a syrupy mixture (1.03 g, 70%) of (5*R*)-**7** (~90%), (5*R*)-**9** (5%), (5*S*)-**9** (4%), and (5*R*)-**9′** (~1%) (n.m.r. data). Upon storage, **7** crystallised; m.p. 85–86.5°, $[\alpha]_D^{20}$ −24° (*c* 4.2); ν_{max}^{KBr} 3320 (OH), 1370 (CMe_2), 1210 (P=O), 1160 cm^{-1} (P–O–C). Mass spectrum: *m/z* 196 (100), 160 (87), 181 (54), 218 (34), 355 (28, M^+), 180 (20), 202 (17), 168 (13), 309 (13), 340 (12, M^+ − Me).

Anal. Calc. for $C_{13}H_{26}NO_8P$ (355.33): C, 43.94; H, 7.38; N, 3.94; P, 8.72. Found: C, 44.21; H, 7.63; N, 3.83; P, 8.91.

*(5*R*)-5-Deoxy-5-dimethoxyphosphoryl-5-(*N*-hydroxy-*N*-methylamino)-1,2-O-isopropylidene-α-*D*-xylo-1,4-pentofuranose* (**8**). — To a stirred solution of **3** (3 g, 13.8 mmol) in dimethyl phosphite (38 mL) was added a trace of sodium ethoxide. After 48 h, the solvent was removed. Column chromatography of the resulting syrup, using isopropyl ether–methanol (5:1), afforded **8** (1.88 g, 45%), m.p. 111.7–112.2°, $[\alpha]_D^{25}$ −21° (*c* 1.1); ν_{max}^{KBr} 3380 (OH), 1390 and 1380 (CMe_2), 1210 (P=O), 1170 (P–O–C). Mass spectrum: *m/z* 160 (100), 168 (96), 153 (88), 59 (77), 88 (46), 73 (33), 100 (32), 79 (31), 85 (31), 142 (30), 312 (5, M^+ − Me), 327 (5, M^+).

Anal. Calc. for $C_{11}H_{22}NO_8P$ (327.27): C, 40.37; H, 6.78; N, 4.28; P, 9.46. Found: C, 40.22; H, 6.97; N, 4.36; P, 9.58.

*(5*S*)-5-Deoxy-3,5-*O*,C-ethoxyphosphoryl-5-(*N*-hydroxy-*N*-methylamino)-1,2-O-isopropylidene-α-*D*-xylo-1,4-pentofuranose* [*(5*S*)-**9**]. — This compound was obtained in a very low yield after repeated column chromatography of the product in the mother liquors of the crystallisation of (5*R*)-**7**. It had m.p. 138.5–140.7°, $[\alpha]_D^{20}$ −6° (*c* 1); ν_{max}^{KBr} 3280 (OH), 1375 (CMe_2), 1245 (P=O), 1165 cm^{-1} (P–O–C). Mass spectrum: *m/z* 57 (100), 168 (84), 113 (74), 71 (71), 85 (43), 99 (35), 122 (13), 142 (12), 249 (7), 294 (5, M^+ − Me), 309 (2, M^+).

Anal. Calc. for $C_{11}H_{20}NO_7P$ (309.26): C, 42.72; H, 6.52; N, 4.53; P, 10.02. Found: C, 42.57; H, 6.40; N, 4.58; P, 9.85.

*(5*R*,P_R)- and (5*R*,P_S)-5-Deoxy-3,5-*O*,C-ethoxyphosphoryl-5-(*N*-hydroxy-*N*-methylamino)-1,2-O-isopropylidene-α-*D*-xylo-1,4-pentofuranose* [*(5*R*)-**9** and (5*R*)-**9′**]. — These compounds were obtained from the mother liquors of (5*R*)-**7**. They could also be prepared from (5*R*)-**7** by treatment with silica gel in benzene or with triethylamine–tetrahydrofuran. Their n.m.r. data are collected in Tables I and II.

*(5*R*)-5-Deoxy-5-diethoxyphosphoryl-5-(*N*-hydroxy-*N*-methylamino)-1,2-O-isopropylidene-α-*D*-ribo-1,4-pentofuranose* (**10**). — To a stirred solution of **2** (1 g, 4.6 mmol) in diethyl phosphite (45 mL) was added a trace of sodium ethoxide. After 48 h, the solvent was removed under reduced pressure. Dry-column chromatography of the resulting syrup, using ether–methanol–hexane (30:3:1), afforded **10** (940 mg, 57%) as a syrup (there was no trace of the 5*S* isomer); $[\alpha]_D^{22}$ +4° (*c* 1.3); ν_{max}^{film} 3320 (OH), 1360 and 1380 (CMe_2), 1220 (P=O), 1170 cm^{-1} (P–O–C). Mass spectrum: *m/z* 83 (100), 85 (74), 234 (11), 111 (5), 118 (5), 120 (4), 163 (4), 160 (3), 297 (3), 235 (3), 340 (1, M^+ − Me).

Anal. Calc. for $C_{13}H_{26}NO_8P$ (355.33): C, 43.94; H, 7.38; N, 3.94; P, 8.72. Found: C, 44.20; H, 7.69; N, 3.84; P, 8.50.

(5R)-5-(N-Acetoxy-N-methylamino)-5-deoxy-5-diethoxyphosphoryl-1,2-O-isopropylidene-3-O-methyl-α-D-xylo-1,4-pentofuranose (**11**). — Compound **6** (90 mg, 0.24 mmol) was stirred overnight with a solution of acetic anhydride (2.5 mL) and pyrdine (5 mL). The mixture was then worked-up in the usual manner and gave **11** (70 mg, 70%), as a syrup, $[\alpha]_D^{22}$ −17° (*c* 1.2); ν_{max}^{KBr} 1760 (C=O), 1375 (CMe_2), 1250 (P=O), 1170 cm^{-1} (P–O–C). Mass spectrum: *m/z* 101 (100), 73 (51), 83 (41), 111 (26), 85 (25), 196 (10), 65 (9), 232 (9), 369 (9, M^+ − Ac), 205 (9), 396 (0.5, M^+ − Me), 411 (0.3, M^+).

Anal. Calc. for $C_{16}H_{30}NO_9P$ (411.39): C, 46.71; H, 7.35; N, 3.40; P, 7.53. Found: C, 46.82; H, 7.54; N, 3.39; P, 7.45.

(5R)-5-(N-Acetoxy-N-methylamino)-3-O-acetyl-5-deoxy-5-diethoxyphosphoryl-1,2-O-isopropylidene-α-D-xylo-1,4-pentofuranose (**12**). — A solution of **7** (400 mg, 1.13 mmol) in acetic anhydride (2.5 mL) and pyridine (5 mL) was stirred overnight and the mixture was then worked-up in the usual manner. Column chromatography of the product, using ether–methanol–hexane (30:3:1), afforded **12** (310 mg, 63%), $[\alpha]_D^{20}$ −19° (*c* 1.5); ν_{max}^{film} 1775 (O–C=O), 1755 (N–O–C=O), 1375 (CMe_2), 1220 (P=O), 1165 cm^{-1} (P–O–C). Mass spectrum: *m/z* 84 (100), 111 (64), 149 (62), 397 (32), 260 (29), 178 (22), 142 (19), 93 (16), 163 (15), 143 (15), 424 (4, M^+ − Me), 439 (0.6, M^+).

This compound could not be obtained in a state sufficiently pure to give a satisfactory elemental analysis.

[(4R)-4-Diethoxyphosphoryl-3-hydroxy-5H,6H-1,3-oxazino][6,5-c](1,2-O-isopropylidene-α-D-xylo-tetrofuranose) (**13**). — To a stirred solution of (5*R*)-**7** (290 mg, 0.82 mmol) in CH_2Cl_2 (20 mL) at −10° under N_2 was added dropwise a solution of 1,4-benzoquinone (81 mg, 0.75 mmol) in CH_2Cl_2 (5 mL). After 1 h, the mixture was washed several times with aqueous 10% NaOH, dried ($MgSO_4$), and concentrated. Column chromatography of the syrupy residue, using ether–methanol–hexane (30:3:1), gave a product that was recrystallised from ether–hexane to give **13** (95 mg, 33%), m.p. 109.6–114.3°, $[\alpha]_D^{23}$ −52° (*c* 1); ν_{max}^{KBr} 3320 (OH), 1390 and 1375 (CMe_2), 1230 (P=O), 1175 cm^{-1} (P–O–C). Mass spectrum: *m/z* 353 (100, M^+), 216 (75), 336 (30), 338 (21, M^+ − Me), 182 (20), 181 (17), 113 (17), 354 (15, M^+ + 1), 155 (13), 236 (13).

Anal. Calc. for $C_{13}H_{24}NO_8P$ (353.31): C, 44.19; H, 6.86; N, 3.96; P, 8.76. Found: C, 44.00; H, 7.09; N, 3.85; P, 8.48.

[(4R)-4-Diethoxyphosphoryl-5H,6H-1,3-oxazino][6,5-c](1,2-O-isopropylidene-α-D-xylo-tetrofuranose) N-oxide (**14**). — To a stirred solution of (5*R*)-**7** (300 mg, 0.85 mmol) in $CHCl_3$ (20 mL) at 0° under N_2 was added dropwise a solution of DDQ (767 mg, 3.4 mmol) in $CHCl_3$. The mixture was then washed several times with aqueous 10% NaOH, dried ($MgSO_4$), and concentrated. Recrystallisation of the product gave **14** (200 mg, 67%), m.p. 110.3–112°, $[\alpha]_D^{19}$ +38° (*c* 2.1); ν_{max}^{KBr} 1550 (C=N), 1385 and 1370 (CMe_2), 1260 (P=O), 1155 cm^{-1} (P–O–C); λ_{max}^{EtOH} 260 nm (ε

14192). Mass spectrum: *m/z* 113 (100), 336 (83, $M^+ - Me$), 292 (74), 195 (74), 109 (70), 180 (61), 234 (61), 236 (42), 194 (39), 81 (37), 351 (31, M^+).

Anal. Calc. for $C_{13}H_{22}NO_8P$ (351.30): C, 44.45; H, 6.31; N, 3.99; P, 8.82. Found: C, 44.23; H, 6.47; N, 3.93; P, 8.91.

*[(4S)-4-Diethoxyphosphorylperhydro-1,3-oxazino][6,5-c](1,2-O-isopropylidene-α-*D*-xylo-tetrofuranose)* (**15**). — To a solution of **14** (500 mg, 1.42 mmol) in ethanol (10 mL) at 0° was added water (5 mL) and then, dropwise with stirring, a solution of sodium borohydride (53 mg, 1.42 mmol) in ethanol (5 mL). After 1 h at 20°, the solution was concentrated, a solution of the residue in saturated aqueous ammonium chloride was extracted with CH_2Cl_2, and the extract was dried ($MgSO_4$) and then concentrated. Recrystallisation of the residue from ether–hexane yielded **15** (280 mg, 58%), m.p. 102.4–105.6°, $[\alpha]_D^{22}$ −11° (*c* 1); ν_{max}^{KBr} 3170 (NH), 1385 and 1375 (CMe_2), 1255 (P=O), 1170 cm^{-1} (P–O–C). Mass spectrum: *m/z* 163 (100), 194 (37), 113 (12), 200 (12), 164 (11), 205 (10), 135 (9), 138 (9), 149 (8), 201 (7), 322 (2, $M^+ - Me$), 337 (1, M^+).

Anal. Calc. for $C_{13}H_{24}NO_7P$ (337.31): C, 46.29; H, 7.17; N, 4.15; P, 9.18. Found: C, 46.19; H, 7.37; N, 4.31; P, 9.32.

The deuterated analogue **16** of **15** was obtained by using sodium borodeuteride.

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REFERENCES

1 J. M. J. Tronchet, D. Schwarzenbach, E. Winter-Mihaly, C. Diamantides, U. Likic', G. Galland-Barrera, C. Jorand, K. D. Pallie, J. Ojha-Poncet, J. Rupp, and G. Moret, *Helv. Chim. Acta*, 65 (1982) 1404–1411.
2 J. R. Neeser, J. M. J. Tronchet, and E. J. Charollais, *Can. J. Chem.*, 61 (1983) 2112–2120.
3 P. Richsbieth, *Ber.*, 20 (1887) 2673–2674.
4 J. M. J. Tronchet, E. Winter-Mihaly, F. Habashi, D. Schwarzenbach, U. Likic', and M. Geoffroy, *Helv. Chim. Acta*, 64 (1981) 610–616.
5 J. M. J. Tronchet, M. Geoffroy, F. Habashi, D. Schwarzenbach, E. Winter-Mihaly, U. Likic', J. Ojha, and C. Jorand, *Int. Carbohydr. Symp., XIth, Vancouver, Canada*, 1982, Abstr. I-77.
6 J. Kiss, R. D'Souza, J. A. van Koeveringe, and W. Arnold, *Helv. Chim. Acta*, 65 (1982) 1522–1537.
7 H. Paulsen and M. Budzis, *Chem. Ber.*, 107 (1974) 1998–2008.
8 J. M. J. Tronchet and E. Winter-Mihaly, *Helv. Chim. Acta*, 55 (1972) 1266–1271; *Carbohydr. Res.*, 31 (1973) 159–172.
9 E. W. Garbish, Jr., *J. Am. Chem. Soc.*, 86 (1964) 5561–5564.
10 R. B. Wetzel and G. L. Kenyon, *J. Am. Chem. Soc.*, 96 (1974) 5189–5198.
11 C. A. Kingsbury and D. Thoennes, *Tetrahedron Lett.*, (1976) 3037–3040.
12 G. W. Buchanan and C. Benezra, *Can. J. Chem.*, 54 (1976) 231–237.

13 G. W. BUCHANAN AND F. G. MORIN, *Can. J. Chem.*, 55 (1977) 2885–2892.
14 J. THIEM AND B. MEYER, *Org. Magn. Reson.*, 11 (1978) 50–51.
15 L. D. QUIN, M. J GALLAGHER, C. T. CUNKLE, AND D. B. CHESTNUT, *J. Am. Chem. Soc.*, 102 (1980) 3136–3143.
16 J.-R. NEESER, J. M. J. TRONCHET, AND E J. CHAROLLAIS, *Can. J Chem.*, 61 (1983) 2112–2120.
17 C. BENEZRA, *J. Am. Chem. Soc* , 95 (1973) 6890–6902.
18 J. M. J. TRONCHET AND K. D PALLIE, unpublished results; K. D PALLIE, Ph.D. Thesis No. 2030, University of Geneva, 1982
19 J. M. J. TRONCHET, F. BARBALAT-REY, AND J. M. CHALET, *Carbohydr. Res* , 30 (1973) 229–238.
20 C. HELLER AND M. M. MCCONNEL, *J. Chem. Phys.*, 32 (1960) 1535.
21 J. M. J. TRONCHET, F. HABASHI, U LIKIC', AND M. GEOFFROY, unpublished results; F. HABASHI, Ph D. Thesis No. 2058, University of Geneva, 1983.
22 W. DAMERAU, G. LASSMAN, AND K. LOHS, *J. Magn. Reson.*, 5 (1971) 408–415
23 W. MEYER ZU RECKENDORF, *Chem. Ber.*, 96 (1963) 2019–2023
24 W. LOEW AND M. M. GOODMAN, *Chem. Ind (London)*, (1967) 2026–2032.