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Nucleic-Acid Constituents. VIII.* The Crystal and Molecular Structure of Sodium Uridine-5′-*O*-methylphosphate–Methanol

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Sodium uridine-5′-*O*-methylphosphate–methanol, $C_{10}H_{14}N_2O_9PNa.CH_3OH$ ($mpU.CH_3OH$), crystallizes with two molecules in a monoclinic unit cell in space group $P2_1$: $a = 7{\cdot}904$ (4), $b = 14{\cdot}903$ (7), $c = 7{\cdot}271$ (4) Å, $\beta = 103{\cdot}74$ (4)° at 20°C. Diffractometer data (1197 significant reflexions, Mo $K\alpha$ radiation) were collected at room temperature. The structure was solved by Patterson methods and refined by least squares ($R_w = 2{\cdot}5\%$). The uracil base has the *anti* orientation ($\chi = 79{\cdot}1°$) with respect to the sugar. The ribose ring has an *S*-type [C(2′)-*endo*] conformation with a pseudorotation phase angle $P = 166{\cdot}4°$ and $\varphi_{\max} = 36{\cdot}9°$. The orientation of the methyl ester phosphate group is g^+ (*gauche–gauche*) with respect to O(1′) and C(3′). Base stacking is absent; nevertheless, the backbone assumes a right-handed helical arrangement. A detailed description of the phosphodiester geometry is given.

Introduction

This paper is part of a project on the synthesis, and NMR, ORD and X-ray investigations of nucleic-acid constituents. Sodium uridine-5′-*O*-methylphosphate (mpU) may serve as a reference compound for physical measurements of di- and oligonucleotides. The methyl group simulates the role of the next nucleoside in the phosphate backbone and was introduced in order to determine its influence, if any, on the conformation of the backbone chain (Altona *et al.*, unpublished). The chemical synthesis will be described elsewhere (Oltshoorn, Altona & van Boom, 1978). The chemical formula and numbering of the atoms are depicted in Fig. 1(*a*).

Experimental

Crystals of mpU were obtained from a mixture of water and methanol as colourless monoclinic needles. The lattice constants at 20°C were determined with a three-circle diffractometer using Cu $K\alpha$ radiation ($\lambda = 1{\cdot}54178$ Å): $a = 7{\cdot}904$ (4), $b = 14{\cdot}903$ (7), $c = 7{\cdot}271$ (4) Å, $\beta = 103{\cdot}74$ (4)°. The absence of reflexions $0k0$ for k odd indicates space group $P2_1$. The assumption of two molecules per unit cell ($Z = 2$) gives $d_c = 1{\cdot}518$ g cm^{-3}. The unit cell was later found to contain two additional molecules of methanol, resulting in $d_c = 1{\cdot}566$ g cm^{-3}. The reflexion intensities (1197 independent observed reflexions and 324 non-significant reflexions with intensities $<2\sigma$) were recorded at 20°C on a three-circle diffractometer using graphite-monochromatized Mo $K\alpha$ radiation ($\lambda = 0{\cdot}71069$ Å). The ω scan was used between $\theta_{\min} = 4$ and $\theta_{\max} = 25°$.

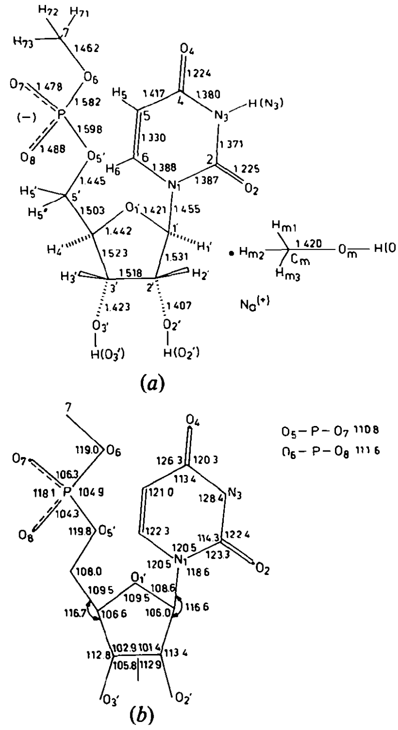

Fig. 1. (*a*) The numbering of the atoms and bond distances (Å) in sodium uridine-5′-*O*-methylphosphate–methanol. (*b*) Valency angles (°).

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[*] Part VII: de Kok, Romers, de Leeuw, Altona & van Boom (1977).

Repeated measurements of standard reflexions indicated a crystal decay of 17%. Since the linear absorption coefficient for Mo *Kα* radiation is only 2·569 cm^{-1}, the correction for absorption was omitted.

Refinement

The structure was solved by a vector-shift method using the readily located Na and P positions. In this way the phosphate group, the uracil base and the sugar ring, except C(1′), were located. C(1′) and an extra atom were found in a difference Fourier map. Initially the extra atom was interpreted as a water molecule, but further refinement revealed the presence of one molecule of methanol per nucleotide unit. With the exception of six methyl H atoms and H(O2′) all remaining H atoms were located in difference Fourier maps.

The heavy atoms were refined (block-diagonal approximation) anisotropically and the H atoms located from Fourier maps isotropically. The methyl H atoms and H(O2′) were introduced at calculated positions with fixed isotropic temperature factors. The scattering factors of the heavy atoms were taken from *International Tables for X-ray Crystallography* (1974) and those of H from Stewart, Davidson & Simpson (1965). The anisotropic temperature factors are defined as $\exp(-2\pi^2 \sum_{i,j} a_i^* a_j^* h_i h_j U_{ij})$ $(i, j = 1, 2, 3)$, and the unweighted and the weighted reliability indices as $R = \sum ||F_o| - |F_c|| / \sum |F_o|$ and $R_w = [\sum w(|F_o| - |F_c|)^2 / |wF_o^2|]^{1/2}$. The final unweighted and weighted reliability indices are $R = 0{\cdot}040$ and $R_w = 0{\cdot}025$.† The positional parameters of the heavy atoms are in Table 1.

Table 1. *Fractional coordinates* (×10^4) *of the heavy atoms*

E.s.d.'s referring to the last digit are given in parentheses.

	x	*y*	*z*
Na	−189 (2)	6270 (1)	−139 (2)
P	8460 (2)	4976 (0)	6326 (2)
C(1′)	2590 (6)	4168 (3)	2586 (7)
C(2′)	2768 (6)	5175 (3)	3007 (7)
C(3′)	3802 (6)	5479 (3)	1608 (7)
C(4′)	5000 (6)	4685 (3)	1550 (7)
C(5′)	6826 (6)	4752 (4)	2753 (7)
C(2)	1340 (6)	2821 (3)	3647 (8)
C(4)	2122 (6)	2406 (3)	7042 (7)
C(5)	3157 (7)	3193 (3)	7374 (8)
C(6)	3235 (7)	3750 (4)	5967 (7)
C(7)	8100 (8)	3316 (4)	7378 (11)
C(*m*)	4565 (9)	6849 (5)	6946 (12)
N(1)	2327 (5)	3594 (3)	4112 (5)
N(3)	1309 (6)	2278 (3)	5160 (6)
O(1′)	4157 (4)	3906 (2)	2102 (4)
O(2′)	1159 (4)	5619 (2)	2761 (5)
O(3′)	2558 (5)	5616 (3)	−135 (5)
O(5′)	6726 (4)	4965 (2)	4663 (4)
O(2)	605 (4)	2620 (2)	2020 (5)
O(4)	1940 (5)	1857 (2)	8234 (5)
O(6)	9088 (4)	3965 (2)	6545 (4)
O(7)	9854 (4)	5488 (2)	5757 (4)
O(8)	7869 (4)	5290 (2)	8018 (4)
O(*m*)	4599 (5)	5931 (2)	7475 (5)

Discussion of the structure

The bond lengths and valency angles involving the heavy atoms are given in Fig. 1. If a 40% underestimation due to the block-diagonal refinement is assumed, the e.s.d.'s are about 0·009 Å for the bonds involving C, N and O and 0·005 Å for the P—O bonds. The e.s.d.'s of the valency and torsion angles are about 0·5 and 0·6°.

The bond lengths and valency angles display the expected features. With the exception of the angle C(2)—N(1)—C(6), comparison with the mean values of nine uracil moieties given in Table 5 of de Graaff, Admiraal, Koen & Romers (1977) shows no important differences at a significance level of 99%. At this same level the difference in length between the bonds P—O(5′) and P—O(6) (0·016 Å) is significant. This difference is a recurring feature in phosphodiesters. On the other hand, the differences in length between P—O(7) and P—O(8) (0·013 Å) and between O(1′)—C(1′) and O(1′)—C(4′) (0·021 Å) must be considered as not significant. Nevertheless, the latter difference is consistent with values quoted elsewhere (*cf.* de Kok, Romers, de Leeuw, Altona & van Boom, 1977). Furthermore, we note that the C(4′)—C(5′) bond length (1·503 Å) is significantly smaller than the commonly observed value of 1·533 Å (*Tables of Interatomic Distances and Configuration in Molecules and Ions*, 1965). This feature, as well as the observed difference in length between C(2′)—O(2′) and C(3′)—O(3′) (0·016 Å), has been noted earlier by Sundaralingam (1965) in his survey of mononucleosides.

A number of torsion angles are listed in Table 2. It can be seen that the ribose ring has the *S*-type [C(2′)-*endo*] conformation with C(2′) as the flap of an (approximate) envelope. According to the characterization proposed by Altona & Sundaralingam (1972) the ribose ring has a phase angle of pseudorotation $P = 166{\cdot}4°$, well within the usual range, and a puckering angle $\varphi_{\max} = 36{\cdot}9°$. The uracil base has an *anti* orientation with respect to the sugar. The value of the orientation angle O(1′)—C(1′)—N(1)—C(6) is, however, quite large ($\chi = 79{\cdot}1°$) in comparison with the normal

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† Lists of structure factors, thermal parameters and H atom positional parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 33510 (7 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 2. *Selected torsion angles* (°) *of* mpU

Notation*	Designation	Angle	Mean values		Conformation
			†	‡	
τ_0	C(4')–O(1')–C(1')–C(2')	−19·8			*S*-type
τ_1	O(1')–C(1')–C(2')–C(3')	34·3			C(2')-*endo*
τ_2	C(1')–C(2')–C(3')–C(4')	−34·9			
τ_3	C(2')–C(3')–C(4')–O(1')	24·6			$P = 166{\cdot}4°$
τ_4	C(3')–C(4')–O(1')–C(1')	−3·0			$\varphi_{\max} = 36{\cdot}9°$
ψ'	O(3')–C(3')–C(4')–C(5')	148·2 (*S*)	82 (*N*)	148 (*S*)	
ψ	C(3')–C(4')–C(5')–O(5')	52·8	54	57	g^+ (*gauche–gauche*)
φ	C(4')–C(5')–O(5')–P	173·4	174	167	*t*
ω	C(5')–O(5')–P–O(6)	293·1	290		g^-
ω'	O(5')–P–O(6)–C(7)	288·3	289		g^-
	O(1')–C(4')–C(5')–O(5')	291·5			
χ	O(1')–C(1')–N(1)–C(6)	79·1			*anti*
	C(5')–O(5')–P–O(8)	175·6			
	C(5')–O(5')–P–O(7)	47·6			

* Notation as proposed by Sundaralingam (1973).

† The mean values of dinucleotides in the stacked state are derived from GpC–Ca (four observations) (Hingerty, Subramanian, Stellman, Sato, Broyde & Langridge, 1976); GpC–Na (Rosenberg, Seeman, Day & Rich, 1976); ApU1 and ApU2 (Seeman, Rosenberg, Suddath, Kim & Rich, 1976) and the ApA$^+$ part of Ap$^+$Ap$^+$A (Suck, Manor & Saenger, 1976).

‡ The mean values of *S*-type mononucleotides are taken from 5'-AMP (Neidle, Kühlbrandt & Achari, 1976); Na$_2$ATP, molecule *B* (Kennard, Isaacs, Motherwell, Coppola, Wampler, Larson & Watson, 1971); Rb(5'-ADP) (Viswamitra & Hosur, 1976); Na(5'-IMP) (Rao & Sundaralingam, 1969); Rb(5'-AMP) (Suck & Saenger, 1972) and Ba(5'-UMP) (Shefter & Trueblood, 1965).

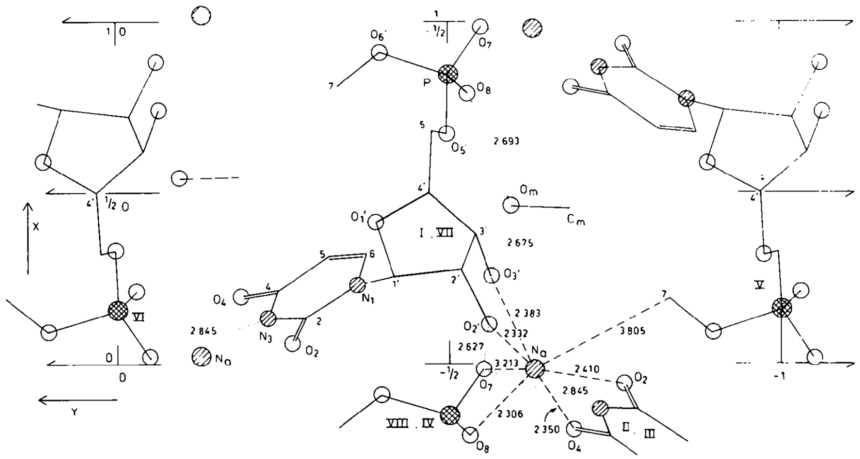

Fig. 2. Projection of the structure of mpU along [001].

value of 50°. The observed difference can be interpreted as a packing effect (see next section). The methyl ester phosphate group has a *gauche–gauche* (g^+) orientation with respect to O(1') and C(3').

Inspection of the projection of the structure along [001] (Fig. 2) indicates the absence of base–base stacking and the presence of a folded backbone. Comparison of the backbone torsion angles of the title compound with the corresponding mean values for a number of dinucleotides in the stacked state (Table 2) reveals a striking similarity in the folding pattern, suggesting that the backbone of mpU in the solid state has preserved the ability to form the right-handed helical state that is typical for polynucleotides. There is, however, a major difference at the part of the chain defined by the sugar conformation. All structures quoted (see Table 2) consist of ribonucleotides with A-RNA-type helical conformations and consequently an *N*-type ribose conformation (Altona & Sundaralingam, 1973) characterized by $\psi' = 82°$ (mean value). In contrast, mpU displays an *S*-type ribose conformation with an associated backbone torsion angle $\psi' = 148{\cdot}2°$. The *S*-type ribose form is characteristic for the B-DNA family. No structural data for stacked dinucleotides in which one or both sugar moieties adopt the *S* conformation are as yet available. Examination of data for six 5'-mononucleotides with similar *S*-type riboses allows us to compare the backbone torsion angles of the fragments C(5')–O–P–O–H(CH$_3$) and C(5')–O–P–O–P with that present in mpU (see column 5, Table 2). As expected, three backbone angles (ψ', ψ and φ) of mpU fall within preferred ranges. Interestingly, the phosphodiester angle ω in Rb(5'-ADP) and Na$_2$ATP [293 and 309° respectively; C(3') replaced by P] also agrees with those occurring in mpU but the former cannot be regarded *a priori* as candidates for building blocks of B-DNA. Therefore the structure of mpU may be considered as a model for the B-DNA family of helical polynucleotide structures for which no molecular details other than those based on fibre diffraction studies are as yet available.

This facilitates the interpretation of NMR parameters for oligonucleotides in solution in terms of equilibrating *N* and *S* forms of the sugar ring with a built-in preference for a helical backbone. Comparison of the NMR data of mpU and other mononucleotide methyl esters with those of (unstacked) dinucleotides will be published elsewhere (Altona *et al.*, to be published). It should be mentioned that the backbones of a number of unstacked dinucleotides assume different conformations about one or both of the ω,ω' angles [*cf.* the $^{+}$Ap^{+}A part of Ap^{+}Ap^{+}A (Suck, Manor & Saenger, 1976), UpA1 and UpA2 (Sussman, Seeman, Kim & Berman, 1972) and pTpT (Camerman, Fawcett & Camerman, 1976)]. Next to the sugar conformation, the two backbone torsion angles mentioned are thought to play an important role in the architecture of a polynucleotide chain.

Packing

The packing is illustrated in a projection along [001] in Fig. 2. Base–base stacking is obviously absent. The Na atom is surrounded by five O atoms in an irregular way at distances varying between 2·306 and 2·410 Å (see also Table 3): O(2′) and O(3′) of the reference molecule (I) at x,y,z; O(2,II) at $-x$, $-\frac{1}{2}+y$, $-z$; O(4,III) at $-x$, $-\frac{1}{2}+y$, $1-z$ and O(8,IV) at $-1+x, y, -1+z$. The coordination is completed by O(7,IV) (3·213 Å) and C(7,V) (3·805 Å) at $1-x$, $-\frac{1}{2}+y$, $1-z$. The simultaneous contacts of Na with O(2) and O(4) can only be achieved by giving the uracil base an extra twist of ~30° about the bond C(1′)—N(1), explaining why the glucosidic torsion angle has the large value of 79°.

Table 3. *Intermolecular distances* (Å) *with e.s.d.'s in parentheses*

	Operation			Distance	Molecule
Contacts with sodium					
Na···O(2)	$-x$,	$-\frac{1}{2}+y$,	$-z$	2·410 (5)	(II)
Na···O(4)	$-x$,	$-\frac{1}{2}+y$,	$1-z$	2·350 (5)	(III)
Na···O(8)	$-1+x$,	y,	$-1+z$	2·306 (5)	(IV)
Na···O(2′)	x,	y,	z	2·332 (5)	(I)
Na···O(3′)	x,	y,	z	2·383 (5)	(I)
Na···O(7)	$-1+x$,	y,	$-1+z$	3·213 (5)	(IV)
Na···C(7)	$1-x$,	$-\frac{1}{2}+y$,	$1-z$	3·805 (10)	(V)
Hydrogen bridges					
N(3)—H···O(7)	$1-x$,	$\frac{1}{2}+y$,	$1-z$	2·845 (8)	(VI)
O(3′)—H···O(*m*)	x,	y,	z	2·675 (7)	(I)
O(*m*)—H···O(8)	x,	y,	$-1+z$	2·693 (7)	(VII)
O(2′)—H···O(7)	$-1+x$,	y,	z	2·627 (7)	(VIII)
Hydrogen–hydrogen contacts					
H(4′)···H(5)	x,	y,	$-1+z$	2·29	(VII)
H(O3′)···H(O*m*)	x,	y,	$-1+z$	2·36	(VII)
H(4′)···H(O*m*)	x,	y,	$-1+z$	2·48	(VII)
H(71)···H(O2′)	$1-x$,	$-\frac{1}{2}+y$,	$1-z$	2·72	(V)

Hydrogen bonds N(3)—H···O(7) (2·845 Å) connect molecules (I) and (VI) at $1-x$, $\frac{1}{2}+y$, $1-z$. The methanol molecule connects (I) and (VII) at x, y, $-1+z$ by means of two hydrogen bridges: O(3′,I)—H···O(*m*I) (2·675 Å) and O(*m*I)—H···O(8,VII) (2·693 Å). Finally, O(2′) donates a H atom to O(7,VIII) at $-1+x$, y, z. The corresponding distance O(2′)—H···O(7,VIII) is 2·627 Å.

The packing is completed by three H—H contacts between molecules (I) and (VII) and one between (I) and (V) (see Table 3). In this way mpU is packed rather tightly and surrounded by 14 neighbouring molecules.

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The Crystal Structure of Hexakis(isopropylammonium) Dihydrogenoctamolybdate(6−) Dihydrate, $(C_3H_{10}N)_6[H_2Mo_8O_{28}].2H_2O$

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$(C_3H_{10}N)_6[H_2Mo_8O_{28}].2H_2O$ crystallizes in the triclinic space group $P\bar{1}$ with a = 10·66 (1), b = 12·29 (1), c = 9·65 (2) Å, α = 104·6 (2), β = 82·1 (5), γ = 96·5 (2)° and Z = 1. The structure was determined by the heavy-atom method and refined by the least-squares method to R = 0·033 for 4511 observed reflexions. The unit cell contains a $[H_2Mo_8O_{28}]^{6-}$ complex anion, six $(C_3H_{10}N)^+$ cations and two water molecules. The $[H_2Mo_8O_{28}]^{6-}$ anion is composed of MoO_6 octahedra sharing edges (with two protons at two apices of octahedra) and belongs to a new structural family of octamolybdate isopolyanions.

Introduction

Crystals of the title compound, obtained from an aqueous solution of isopropylamine and ammonium heptamolybdate, are colourless and transparent, but turn reddish violet on exposure to ultraviolet rays; they are bleached again on heating. ESR measurements suggested that a reduction of some of the Mo^{VI} ions to Mo^{V} is responsible for the induction of a colour centre (Yamase, Hayashi & Ikawa, 1974). In order to obtain a clue to the reduction mechanism, the structure determination of this substance has been undertaken.

Experimental

The symmetry and approximate cell dimensions of the crystals were determined from oscillation and Weissenberg photographs. The more accurate cell dimensions were obtained by least-squares calculations based on the 2θ values of 19 reflexions measured on a Philips automated four-circle diffractometer (Mo $K\alpha$ radiation). The crystal data are in Table 1.

Intensities were measured with a crystal of dimensions 0·1 × 0·1 × 0·1 mm on the Philips four-circle diffractometer in the ω–2θ mode (with graphite-monochromated Mo $K\alpha$ radiation). Of the 5814 reflexions

Table 1. *Crystal data*

$(C_3H_{10}N)_6[H_2Mo_8O_{28}].2H_2O$		a	10·66 (1) Å
FW	806·2	b	12·29 (1)
Crystal system	Triclinic	c	9·65 (2)
Space group	$P\bar{1}$	α	104·6 (2)°
Z	1	β	82·1 (5)
D_x	2·22 g cm^{-3}	γ	96·5 (2)
μ(Mo $K\alpha$)	20·6 cm^{-1}	V	1207 (2) Å^3

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