STEWART, R. F., DAVIDSON, E. R. & SIMPSON, W. T. (1965). *J. Chem. Phys.* **42**, 3175–3187.

STOUT, G. H. & JENSEN, L. H. (1968). *X-ray Structure Determination.* New York: Macmillan.

STROUD, R. M. (1973). *Acta Cryst.* **B29**, 690–696.

SUNDARALINGAM, M. (1965). *J. Amer. Chem. Soc.* **87**, 599–606.

SUNDARALINGAM, M. (1966). *Acta Cryst.* **21**, 495–506.

SUNDARALINGAM, M. (1972). In *The Jerusalem Symposia on Quantum Chemistry and Biochemistry.* Jerusalem: The Israel Academy of Sciences and Humanities. In the press.

WATSON, D. G., SUTOR, D. J. & TOLLIN, P. (1965). *Acta Cryst.* **19**, 111–124.

WILSON, A. J. C. (1942). *Nature, Lond.* **150**, 151–152.

Seven Basic Conformations of Nucleic Acid Structural Units

BY S.-H. KIM*

Department of Biology, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139, *U.S.A.*

HELEN M. BERMAN

The Institute for Cancer Research, Philadelphia, Pennsylvania 19111, *U.S.A.*

NADRIAN C. SEEMAN†

Department of Biological Science, Columbia University, New York, New York 10027, *U.S.A.*

AND MARSHALL D. NEWTON

Department of Chemistry, Brookhaven National Laboratory, Upton, New York 11973, *U.S.A.*

Seven basic conformations for dinucleoside phosphates are described. These conformations, derived by examination of the results of crystal structure determinations of dinucleoside phosphates and mononucleotides, conformation energy calculations, and *ab initio* molecular orbital calculations, can be considered as fundamental structural units of nucleic acids. Some possible nucleic-acid secondary structures are proposed from a consideration of these conformations.

Introduction

Studies of nucleotides and oligonucleotides can be very useful in describing and laying the groundwork for predicting possible secondary structures in nucleic acids. Structural information essential for nucleic acid model building can be obtained from (*a*) the crystal structures of nucleosides and mononucleotides (*e.g.* Arnott, 1970); (*b*) interpretation of diffraction patterns from nucleic acid fibers (*e.g.* Watson & Crick, 1953; Marvin, Spencer, Wilkins & Hamilton, 1961); (*c*) the crystal structures of dinucleoside phosphates (Seeman, Sussman, Berman & Kim, 1971; Rubin, Brennan & Sundaralingam, 1972) and oligonucleotides and (*d*) calculations of conformation energies (*e.g.* Olson & Flory, 1972). In the past, all model building of nucleic acids has been based on information from (*a*) and (*b*). We have extended this by adding information from (*c*) and (*d*) to allow us to present a comprehensive proposal of a basic set of building blocks for use in nucleic acid model building based on base sequences or low-resolution

electron density maps. We describe a set of seven basic building units, each of which is a dinucleoside phosphate of a particular conformation and which represents an overlapping building block. The derivation of the seven basic conformers and their polymers is given below.

The conformation of the nucleoside portion in nucleotides is the same

From surveys of the structures of 5'-mononucleotides and related compounds (Sundaralingam, 1969; Arnott, 1970), and from the results of the determination of the crystal structure of a dinucleoside phosphate, uridylyl-3',5'-adenosine phosphate (UpA), it was pointed out by Seeman *et al.* (1971) that all four major nucleosides have the same preferred conformations: the relationship between the base and the ribose sugar is the *anti* conformation (Donohue & Trueblood, 1960); the conformation of the ribose sugars is either C(3')-*endo* or C(2')-*endo*; there are CH$\cdots$O close contacts between O(5') of the sugar and the hydrogen bonded to either C(6) of the pyrimidine or C(8) of the purine. The latter interaction was also observed in n.m.r. studies of dinucleoside phosphates in aqueous solution (T'so,

---

* Present address: Dept. of Biochemistry, Duke University School of Medicine, Durham, North Carolina 27706, U.S.A.

† Present address: Dept. of Biology, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139, U.S.A.

Side view of bond being rotated.

View along the bond being rotated.
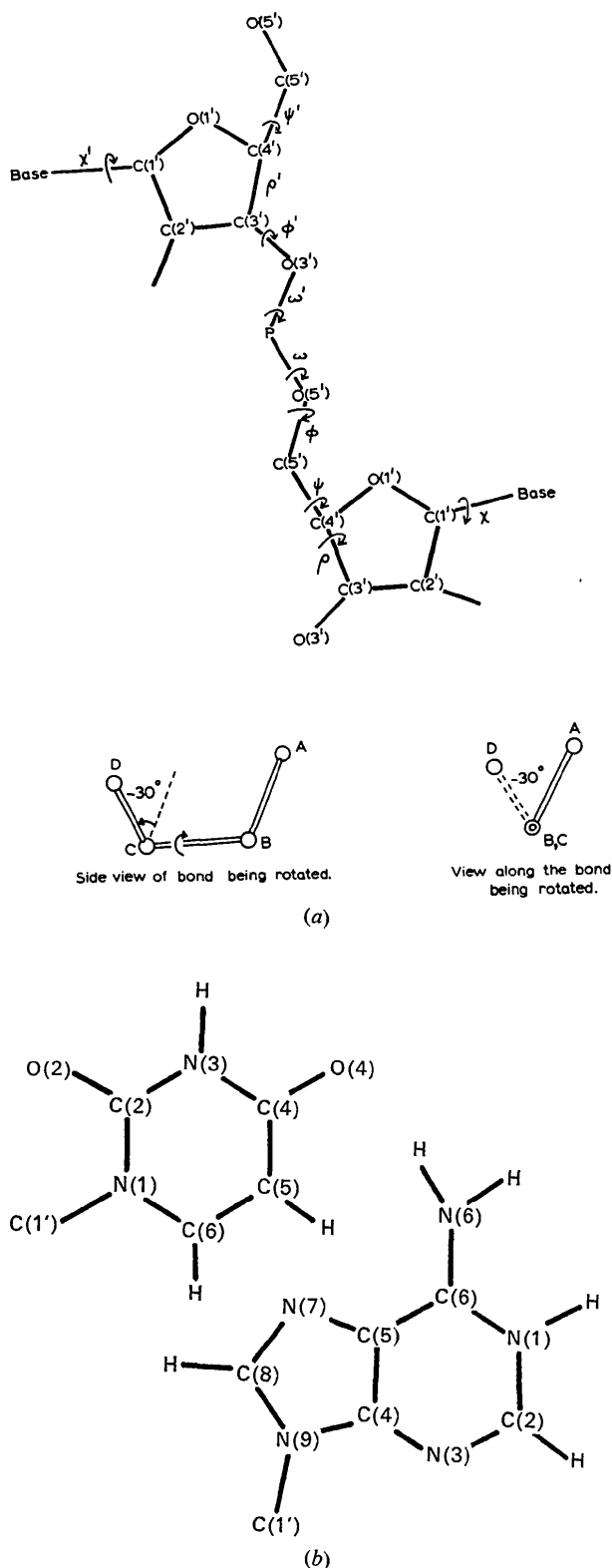
(a)

(b)

Fig. 1. (a) Schematic drawing of a dinucleoside phosphate showing the numbering system of atoms and the nomenclature for rotational bonds. (b) Numbering system used for uracil and adenine.

Kondo, Schweizer & Halles, 1969). The conformational rigidity of the nucleoside portion is obscured when one does not discriminate 5′-nucleotides from 3′-nucleotides and nucleosides.

From the survey, ψ and φ (Fig. 1) are found to be restricted to values near 55 and 200° respectively. This brings O(5′) into close proximity to the bases, and directs the lone-pair electrons of O(5′) toward H(C8) of the purine or H(C6) of the pyrimidine, thus facilitating the CH···O close contact. The angle φ' is also found to be restricted to a value near 215°. We shall, therefore, assign these values to the rigid nucleoside and examine the torsion angles (ω,ω') for the two phosphoester bonds alone to obtain the major conformations which can be found in a nucleic acid structure.

There are several principal conformations

The assumption of an ethane-type torsional barrier for the phosphoester bond would result in three favorable angles each, (60, 180, 300°), for ω and ω', giving 9 possible energy minima. This assumption is inappropriate for a dinucleoside phosphate (see below and Newton, 1973). To find the preferred conformations for dinucleoside phosphates, the following procedure was followed. (1) A rotation was performed around the P–O(5′) and P–O(3′) bonds of a UpA molecule whose torsion angles, except for ω and ω', are an average* of those found in the two independent molecules in the

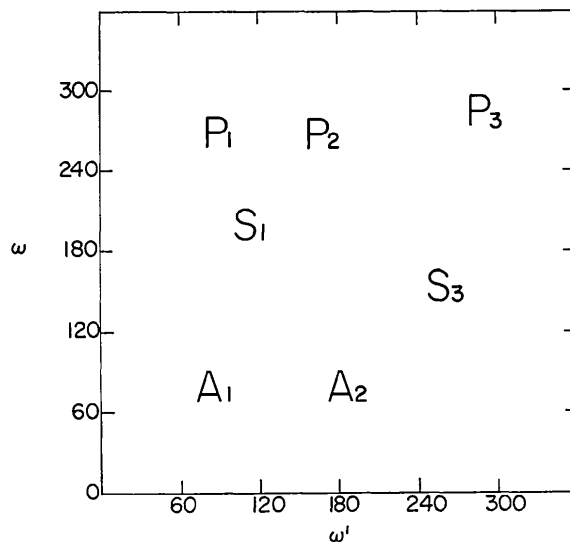* The maximum difference between the equivalent torsion angles in the two UpA molecules is 18° for φ'.

Fig. 2. ω/ω' Conformation map for the seven basic conformations. The symbol is placed on the representative value of ω/ω' for the particular conformer. Symbol P stands for parallel, S for skew and A for antiparallel with respect to the two sugar orientations in the dinucleoside phosphate. The number is ω' expressed as the nearest integral multiplier of 90°. The features of the map are similar for nucleotides with either 3′-endo or 2′-endo sugars.

crystal structure (Sussman, Seeman, Kim & Berman, 1972). Thus, several sterically acceptable regions were found. (2) The results of conformation energy calcula-
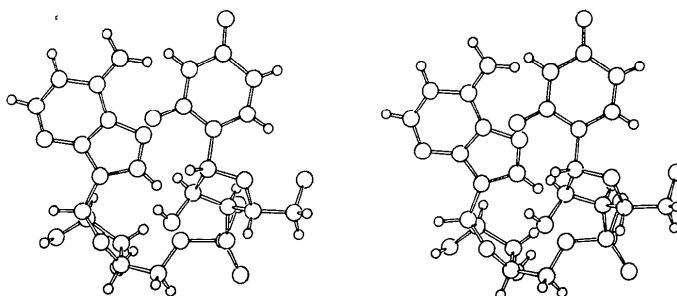
tions (Olson & Flory, 1972), were examined and some regions defined by (1) were eliminated, or reduced to better defined regions by excluding the area where the
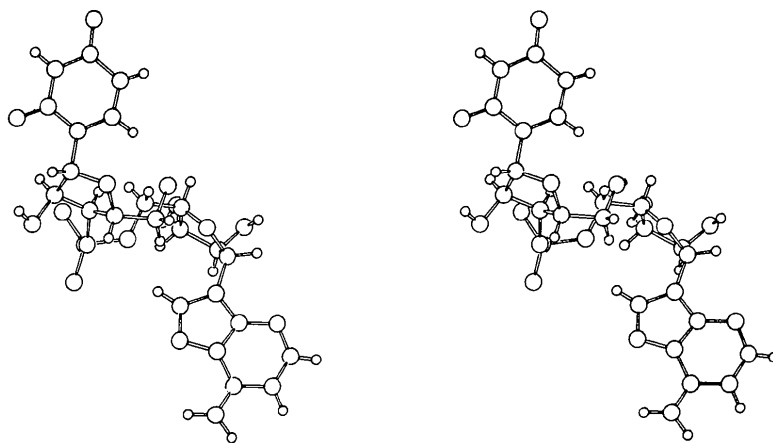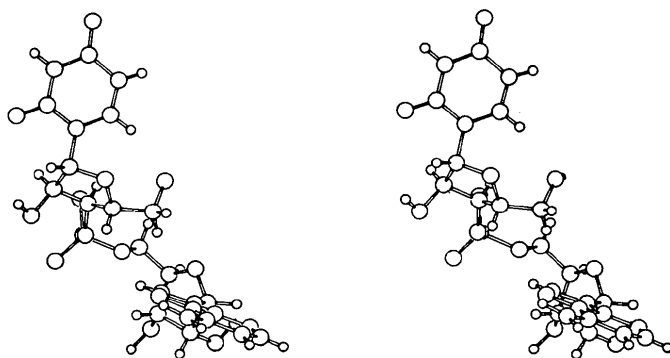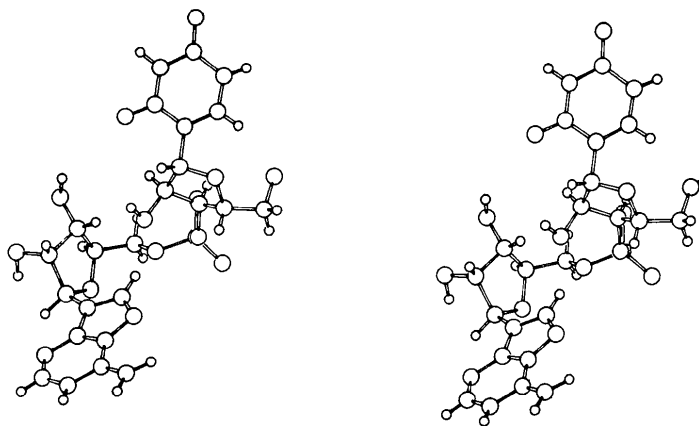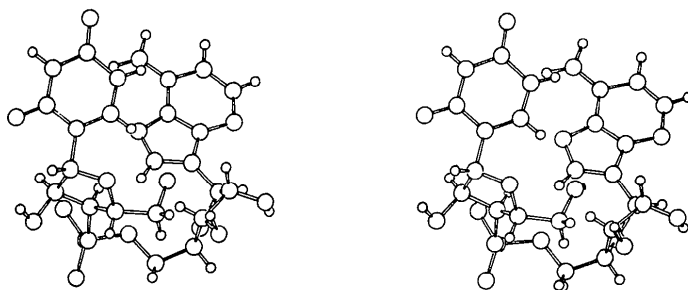

(a)
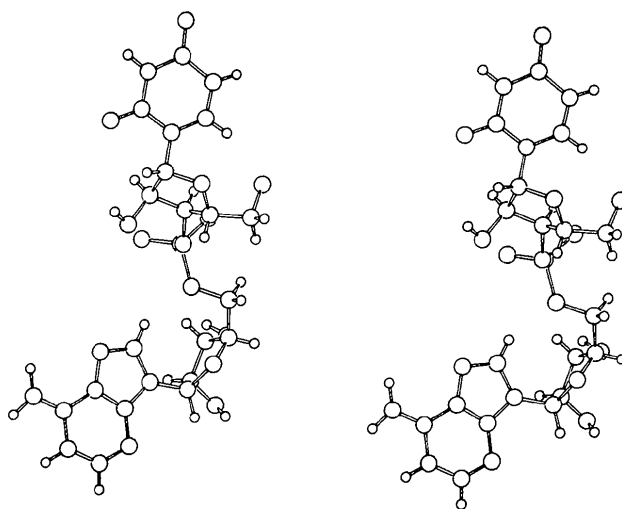
(b)

(c)

Fig. 3. Stereo-views of the seven basic conformations. Each dinucleoside phosphate is shown as viewed down the O(3′)–P bond. UpA is used as an example. (a) P_1, (b) P_2, (c) P_3.
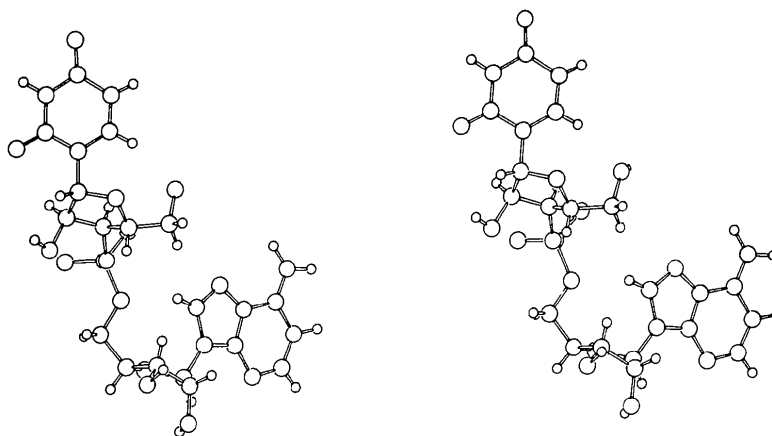
(d)

(e)

(f)

Fig. 3. (cont.) (d) S_1, (e) S_3, (f) A_1.

(g)

Fig. 3. (cont.) (g) A₂.

energy was calculated to be high, e.g. the region around $\omega/\omega' = 60°/300°$ was eliminated and the large region around $\omega/\omega' = 300°/60°$ was reduced to a smaller region around $\omega/\omega' = 270°/90°$. (3) The results from an *ab initio* molecular orbital calculation on dimethyl phosphate mono-anion (Newton, 1973) were used as in (2) to eliminate the region around $\omega/\omega' = 180°/180°$ where the energy was calculated to be about 7 kcal/mol higher than the global minimum. This high energy is due to the nature of the electronic interactions between lone-pair electrons and polar bonds on adjacent atoms. This is consistent with the fact that ω/ω' of $180°/180°$ has never been observed in the crystal structures of model compounds (Sundaralingam, 1969). (4) Two optimum conformations within previously derived regions, $\omega/\omega' = 80°/80°$ and $270°/170°$, were assumed because of their presence in the crystal structure of UpA.

By these processes of exclusion and optimization based on the UpA crystal structure, there remain only seven regions in the ω/ω' map. Each region defines a favorable conformation and is distinguished from others by an ω/ω' value which represents the center of a small angular range ($\pm 20°$) around the particular ω/ω' conformation angles. These seven conformations are idealized ones and are by no means rigid. The optimization of some desired property, such as the base stacking, may be accomplished by further small changes in χ, ψ, φ, and φ'.

In Fig. 2 we show the positions of the resulting seven possible conformers, of a model UpA with 3'-*endo* sugars, on a ω/ω' map; a map for a model UpA with C2'-*endo* sugars is very similar. The momenclature we have adopted is P_θ, A_θ, S_θ: P stands for those conformers whose ribose rings have parallel* orientation; A includes those conformers whose ribose rings are antiparallel; S includes those whose ribose rings are skew to one another; θ is ω' expressed as the nearest integral multiplier of 90°.

In Table 1 we examine the general structural features of the seven basic conformations from the point of view of base stacking, the relative orientations of the ribose sugars, the polymerizability of such a conformation, and, for the polymer, the relative orientation of

* By parallel, we mean that the vectors drawn from the center of the C(2') → C(3') bond to O(1') of each of the two ribose rings are approximately parallel.

Table 1. *The properties of the basic conformations*

	Sugar oxygen* orientation	Feasibility of base parallelism	Repeatability	ω/ω'	Relative position of base with respect to propagation axis
P_1	Same direction	yes	yes	270/90	away
P_2	Same direction	yes	yes	270/170	away
P_3	Same direction	yes	yes	280/290	toward
S_1	Skew direction	no	yes	200/110	away
S_3	Skew direction	no	yes	160/250	away
A_1	Opposite direction	yes	no	80/80	—
A_2	Opposite direction	yes	yes	80/180	away

* The orientation is defined by the vector C(3')–C(2') → O(1').

the bases with respect to the resultant propagation axis of the polymer. In Fig. 3 we show stereo views of the UpA molecule in each of the seven basic conformations.

The building blocks can be polymerized

With the exception of the A_1 conformation it is possible to polymerize each of the seven basic conformations. An A_1 polymer, that is a structure consisting of repeating overlapping A_1 dinucleoside phosphates, is sterically impossible. S_1 and S_3, while polymerizable, are unlikely to have parallel bases and are more likely to be found in loop or nonhelical sequences. Fig. 4 illustrates polymers of P_1, P_2, P_3 and A_2 conformers and the possible interaction among polymers of the same kind assuming only Watson–Crick base pairing. P_1 forms a polymer where the bases point away from the helix axis and has a pseudo-twofold screw axis. Two P_1 polymers can form an antiparallel ribbon-like structure [Fig. 4(a)] if alternating bases are complementary to each other; P_2 also forms a polymer with the bases pointing away from the helix axis and has a pseudo-fourfold screw axis [Fig. 4(b)]; four P_2 polymers can form an infinite base-paired array [Fig. 4(c)]; P_3 forms a polymer with the bases pointing towards the helix axis. Two complementary P_3 polymers can form a
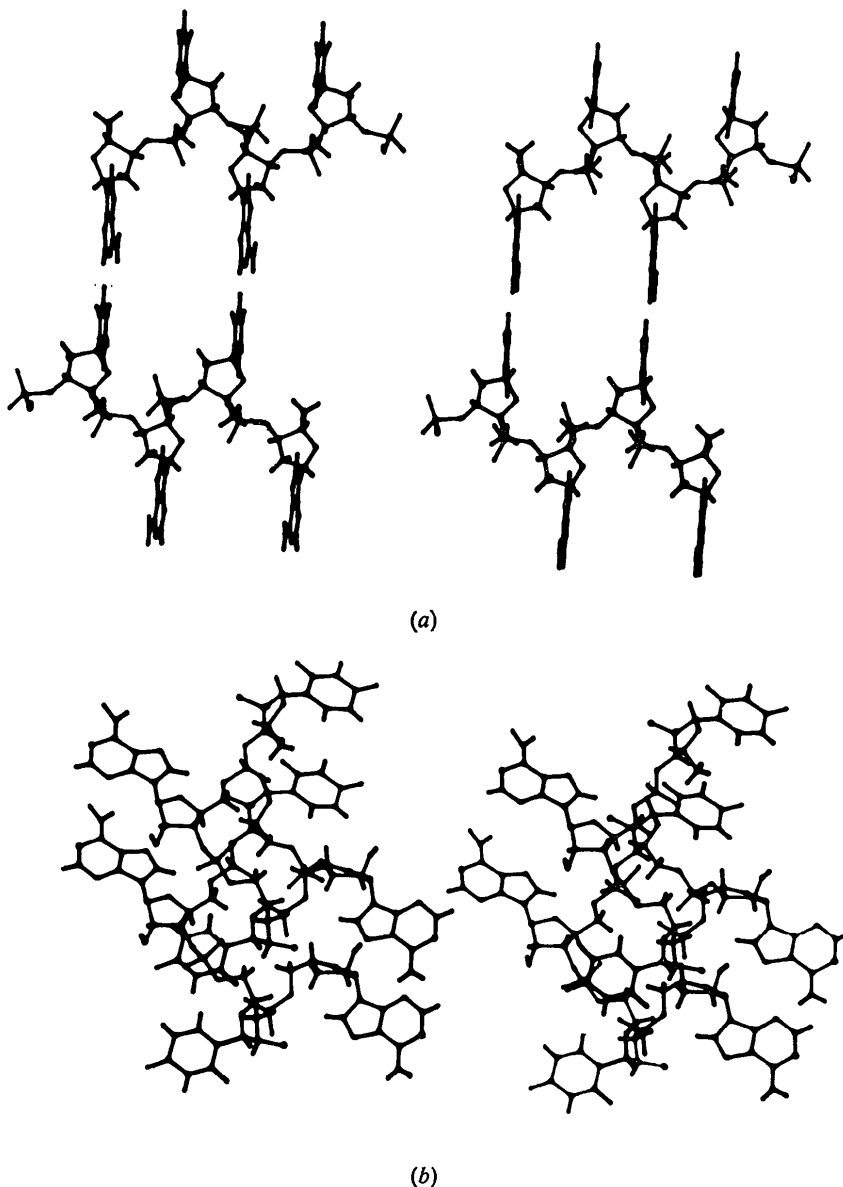

(a)

(b)

Fig. 4. Stereo-views of polymerized building blocks. (a) Two P_1 based paired polymers. P_1 forms a polymer where the bases point away from the helix axis. It has a pseudo-twofold screw axis. (b) One P_2 polymer. P_2 also forms a polymer with the bases pointing away from the helix axis and has a pseudo-fourfold screw axis.

(c)   (d)

(e)   (f)
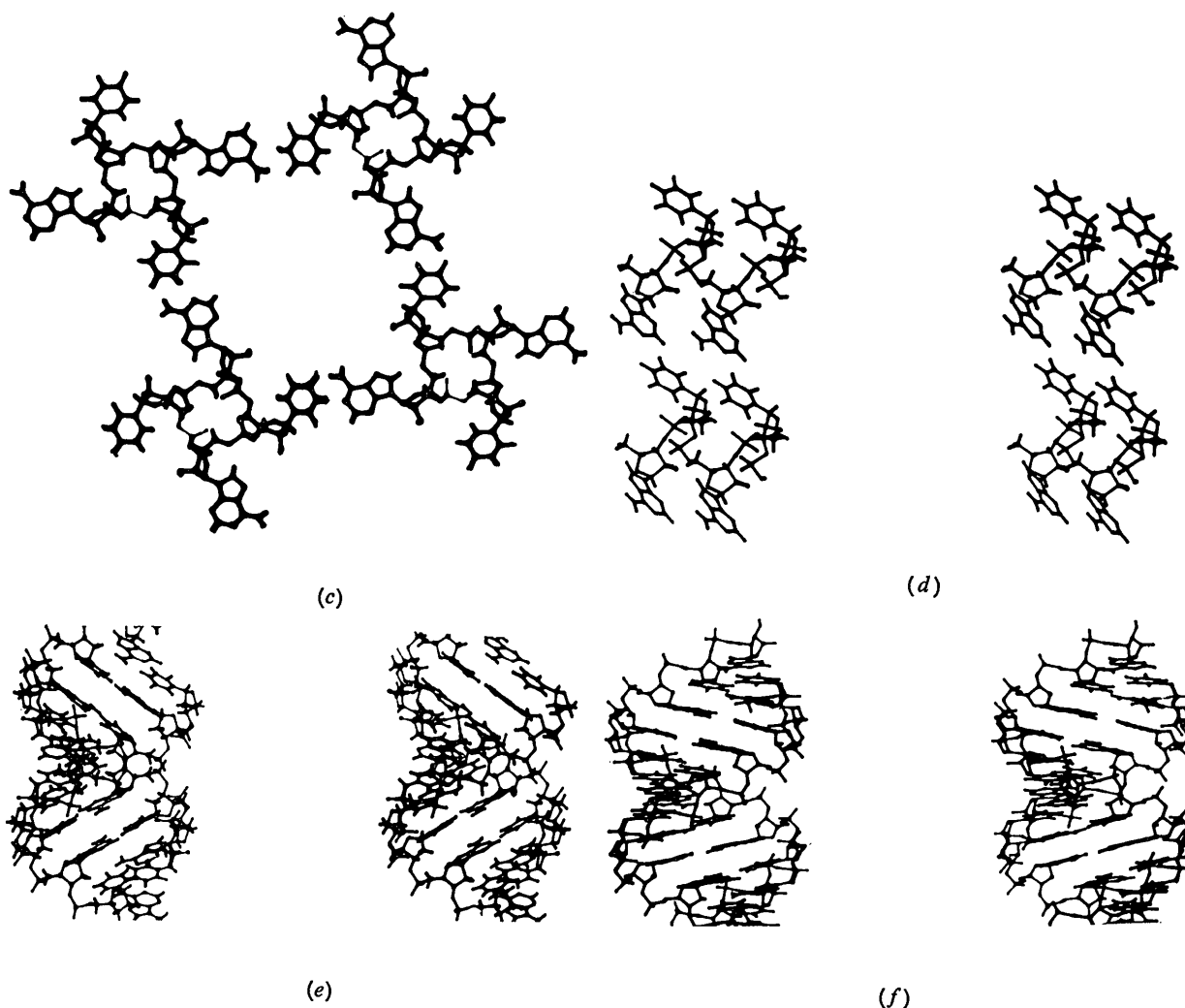
Fig. 4 (cont.) Stereo-views of polymerized building blocks. (c) Four P_2 polymers in a base paired array (not stereo). (d) Two base-paired A_2 polymers. A_2 forms a polymer with the bases pointing away from the helix axis. Each sugar orientation is antiparallel to its neighbors. (e) Two P_3 polymers. P_3 forms a polymer with the bases pointing towards the helix axis. Two complementary P_3 polymers can form a double helix similar to the ones observed. (f) RNA 11 which is composed of P_3 building blocks.

double helix similar to the ones which have been observed in fibrous DNA and RNA [Fig. 4(e), (f)]; A_2
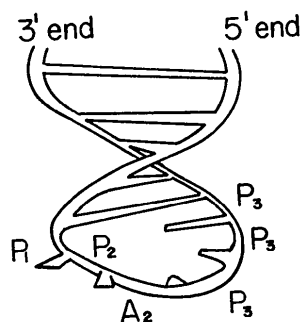

Fig. 5. Schematic drawing of a possible loop structure containing 5 nucleotides. Letters indicate conformation of particular phosphodiester linkage. Bar indicates base.

forms a polymer with the bases pointing away from the helix axis. Each sugar orientation is antiparallel to its neighbors and two A_2 polymers can form an antiparallel step-like structure [Fig. 4(d)] if the alternating bases are complementary to each other. With the exception of the P_3 polymers which can and do exist alone, the other polymers do not have 3·4 Å base stacking. They are therefore likely to exist in other favorable environments, for example as regions in larger structures of nucleic acids and in intercalated structures. S_1, S_3, A_1 and A_2 are the conformations likely to be found at the corners of RNA chain folding.

Different building blocks can be joined

By selecting the dinucleoside phosphate building blocks appropriately, small loop structures of nucleic

acids can be put together. A rule in so doing is that there must be either an odd number of A conformers or an even number of S conformers in a loop. This is because A conformers effect 180° turns in the direction of helix propagation and S conformers cause 90° turns. One example of a possible model for a five-nucleotide loop is shown in Fig. 5.

Discussion

These seven conformations can be considered as model basic conformations of nucleic acids. They are by no means rigid. Indeed, small changes in the sugar pucker and/or ψ, ψ', φ, φ', χ and χ' can give quite noticeable structural differences in a polymerized form. This is most clearly seen when one compares polyUpA [Fig. 4(e)] with RNA11 (Arnott, Dover & Wonacott, 1969) [Fig. 4(f)] which are both P_3 polymers. However, the gross features, as defined by Table 1, of both structures are similar, and differ quite markedly from those of the other six conformers. We hope that these conformers, as we have defined them, will be particularly useful in model fitting of low resolution Fourier maps of nucleic acids.

We wish to thank Alexander Rich, Jenny Glusker, Walter Hamilton and Joel Sussman for their encouragement and criticism and L. Katz, Director of the Graphics Facility for Interactive Displays for the use of the computer.

References

ARNOTT, S. (1970). Prog. Biophys. Molec. Biol. 21, 265–319.
ARNOTT, S., DOVER, S. D. & WONACOTT, A. J. (1969). Acta Cryst. B25, 2192–2206.
DONOHUE, J. & TRUEBLOOD, K. N. (1960). J. Mol. Biol. 2, 363–371.
MARVIN, D. A., SPENCER, M., WILKINS M. H. F. & HAMILTON, L. D. (1961). J. Mol. Biol. 3, 547–565.
NEWTON, M. (1973). J. Amer. Chem. Soc. In the press.
OLSON, W. & FLORY, P. (1972). Biopolymers, 11, 1–23, 25–56, 57–66.
RUBIN, J., BRENNAN, T. & SUNDARALINGAM, M. (1972). Biochemistry, 11, 3112–3128.
SEEMAN, N. C., SUSSMAN, J. L., BERMAN, H. M. & KIM, S.-H. (1971). Nature, New Biol. 233, 90–92.
SUNDARALINGAM, M. (1969). Biopolymers, 7, 821–860.
SUSSMAN, J. L., SEEMAN, N. C., KIM, S.-H. & BERMAN, H. M. (1972). J. Mol. Biol. 66, 403–421.
T'SO, P., KONDO, N., SCHWEIZER, M. & HALLES, D. (1969). Biochemistry, 8, 997–1028.
WATSON, J. D. & CRICK, F. M. C. (1953). Nature, Lond. 171, 737–738.

The Crystal and Molecular Structure of Octachloro-2,4-dihydropentalene

By GRETCHEN MANDEL AND JERRY DONOHUE

Department of Chemistry and Laboratory for Research on the Structure of Matter, University of Pennsylvania, Philadelphia, Pennsylvania 19104, U.S.A.

The unit cell of octachloro-2,4-dihydropentalene (ε-C_8Cl_8) is orthorhombic, space group $Pnma$ (D_{2h}^{16}), with lattice constants $a = 10\cdot170 \pm 0\cdot007$, $b = 7\cdot284 \pm 0\cdot006$, and $c = 17\cdot281 \pm 0\cdot010$ Å. With $Z = 4$, the calculated density is $1\cdot75$ g cm^{-3}. Three-dimensional data were collected at 21 °C on an automated diffractometer equipped with a graphite monochromator and Cu $K\alpha$ radiation by the θ–2θ scan technique. Direct phasing methods were used to obtain the trial structure. The final R value was 8·8%. The average carbon–chlorine bond distance is $1\cdot79 \pm 0\cdot01$ Å for aliphatic chlorine atoms and $1\cdot69 \pm 0\cdot02$ Å for vinyl chlorine atoms. The shortest intermolecular distance is a 3·51 Å chlorine–chlorine contact.

Introduction

The series of structures generated by dimerization and subsequent rearrangement of perchlorobutenyne has been studied by Roedig, Helm, West & Smith (1969). One of the reactions involves the thermal rearrangement at 180° of γ-C_8Cl_8 (m. p. 172°), (believed to be I on the basis of ultraviolet, infrared and n.q.r. spectra),

into δ-C_8Cl_8 (m. p. 86°) and ε-C_8Cl_8 (m. p. 111°). The δ-C_8Cl_8 was thought to be II and the structure of ε-C_8Cl_8 to be III or IV.