

**h) Orientation  $\gamma$  about the C4'–C5' bond**

The rotation about the C4'–C5' bond allows atom O5' to assume different positions relative to the furanose. Three main conformations with all substituents staggered are possible (Fig. 9).

These conformations can be denoted either by the torsion angle  $\gamma$ , or, still frequently in use, by the two torsion angles  $\phi_{OO} = \text{O5'–C5'–C4'–O4'}$  and  $\phi_{OC} = \text{O5'–C5'–C4'–C3'} = \gamma$ . The  $\pm$  *gauche*, *trans* notation is used most commonly.

Table 4. Definitions for orientation about the C4'–C5' bond.

$\gamma$	$\phi_{OO}, \phi_{OC}$
+sc	<i>gauche</i> , <i>gauche</i> ; gg; (+) <i>gauche</i> ; +g
–sc	<i>trans</i> , <i>gauche</i> ; tg; <i>trans</i> ; t
ap	<i>gauche</i> , <i>trans</i> ; gt; (–) <i>gauche</i> ; –g

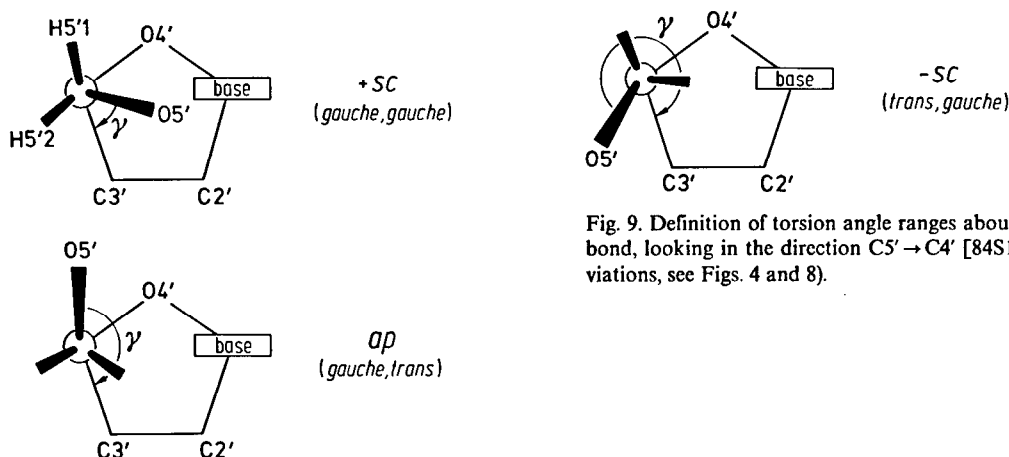


Fig. 9. Definition of torsion angle ranges about the C4'–C5' bond, looking in the direction C5'  $\rightarrow$  C4' [84S1] (for abbreviations, see Figs. 4 and 8).

### 1.3 Geometry of helices

The nucleic acids preferentially form the well-known Watson-Crick double helix but there are also single, triple and quadruple helices which are found with e.g. poly(A), poly(A)·2 poly(U), [poly(G)]<sub>4</sub>.

**a) Helical parameters**

The parameters used to define the geometry of a helix are (Fig. 10):

$n$  = number of residues (nucleotides) per helix turn

$h$  = unit height (translation per residue along the helix axis)

$t = 360^\circ/n$  = unit twist (angle of rotation per residue about the helix axis)

$P$  = pitch height of helix (the identical repeat) =  $n \cdot h$ .

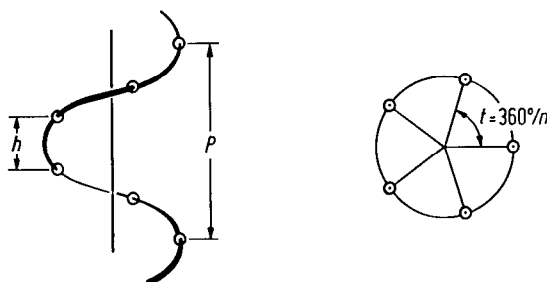


Fig. 10. Definition of helical parameters: pitch  $P$ , axial rise per residue  $h$ , and unit twist  $t$ , shown for a right-handed helix with  $n=5$  residues per turn [84S1].

**b) Cylindrical coordinates**

Atomic coordinates of a helical molecule are given in cylindrical notation  $r, \phi, z$  (Fig. 11) where

- $r_i$  = radial distance of atom  $i$  from helix axis  
 $\phi_i$  = rotation angle for atom  $i$  from a given origin  
 $z_i$  = axial rise of atom  $i$  from a given origin.

In double helices, origin points  $\phi_i = 0^\circ$  and  $z_i = 0$  are generally defined by a (pseudo)-twofold axis.

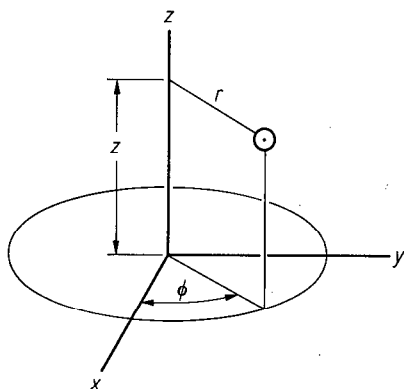


Fig. 11. Definition of cylindrical coordinates  $r, \phi, z$  [84S1].

**c) The complementary Watson-Crick base pairs**

In a nucleic acid double helix, the geometrical features are determined by the conditions imposed by the Watson-Crick base pairs. These (and the two opposing polynucleotide strands) are said to be complementary because they are linked by specific hydrogen bonds:

adenine { with thymine (in DNA)  
           { with uracil (in RNA)  
 guanine with cytosine.

The base pair geometry illustrated in Fig. 12a exhibits some characteristic features:

- 1) in A:T(U) and G:C base pairs the distances between C1' atoms are nearly the same,  $\approx 10.6 \text{ \AA}$
- 2) the angles formed by glycosyl C1'-N bonds and the line connecting C1'-----C1' are nearly the same,  $\approx 56^\circ$
- 3) a pseudo-dyad located perpendicular to and on the center of the C1'-----C1' line relates one base to the other in a base pair, Fig. 12b.

**d) Other base pairs are possible: Hoogsteen base pair and reversed configurations**

For purely geometrical reasons, nucleic acids can form 26 base pairs between like (homo) and different (hetero) bases, which all have two or three hydrogen bonds [84S1]. The Hoogsteen A:U base pair and the reversed Watson-Crick and Hoogsteen base pair configurations (Fig. 13a...c) are of some biological importance. The G:C Hoogsteen base pair is only possible if C is protonated at N3.

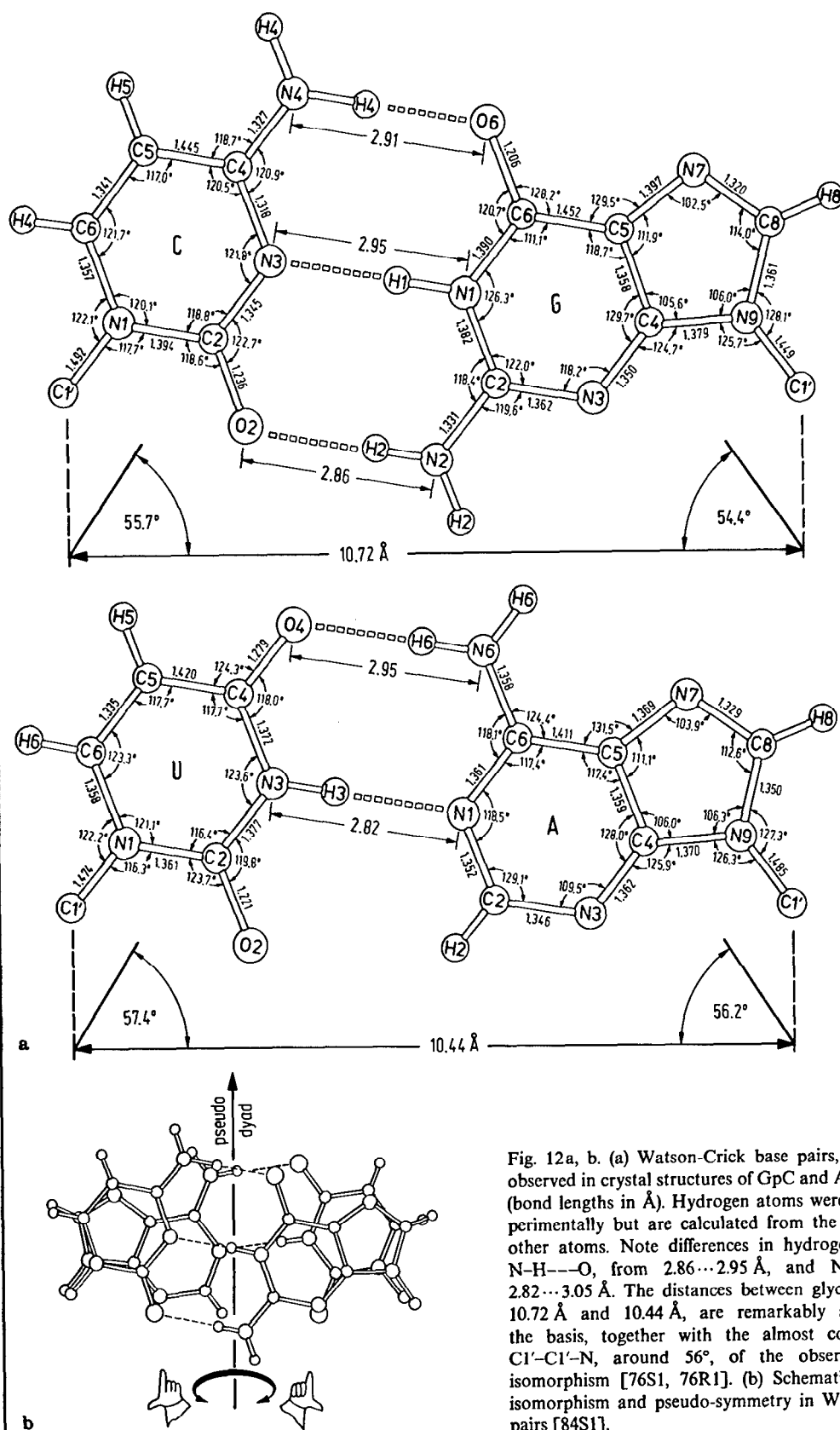


Fig. 12a, b. (a) Watson-Crick base pairs, C:G and U:A, observed in crystal structures of GpC and ApU, respectively (bond lengths in Å). Hydrogen atoms were not located experimentally but are calculated from the positions of the other atoms. Note differences in hydrogen bond lengths N-H...O, from 2.86...2.95 Å, and N-H...N, from 2.82...3.05 Å. The distances between glycosyl C1' atoms, 10.72 Å and 10.44 Å, are remarkably similar and are the basis, together with the almost coinciding angles, C1'-C1'-N, around 56°, of the observed geometrical isomorphism [76S1, 76R1]. (b) Schematic description of isomorphism and pseudo-symmetry in Watson-Crick base pairs [84S1].

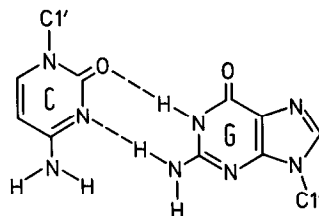


Fig. 13a–c. Base pair configurations other than Watson-Crick. (a) Hoogsteen A:U base pair in schematic illustration (top) and in the neutron diffraction crystal structure of 1-methylthymine:9-methyladenine (bond lengths in Å) (bottom), taken from [73F1, 84S1]. (b) Reversed Hoogsteen A:U base pair. (c) Reversed Watson-Crick A:U and G:C base pairs.

**e) Consequences of Watson-Crick base pair geometry for double helix geometry**

Features 1), 2) and 3) in the previous paragraph c) indicate that:

- i) base pairs are nearly isomorphous, no matter whether we have A:T(U), T(U):A, G:C or C:G. They can therefore substitute each other without disturbing the geometry of the double helix
- ii) the pseudo-dyad symmetry axis requires that the direction of the sugar-phosphate backbone attached to the C1' of one base is opposite to that attached to the C1' of the other base. This implies that the two strands of a double helix are antiparallel, and that they are related by (pseudo)-dyad symmetry axes located within each base pair and also (for geometrical reasons) between all base pairs
- iii) because the glycosyl bonds are positioned on the same side of the base pair, the sugars are closer together on the (purine N3, pyrimidine O2) side than on the (purine O6/N6, pyrimidine N4/O4) side. This gives rise to a *minor groove* and a *major groove* which determine macroscopically the picture of a double helix (Fig. 14). The dimensions of the grooves can be given in Å units, as defined in chapter 2.2.

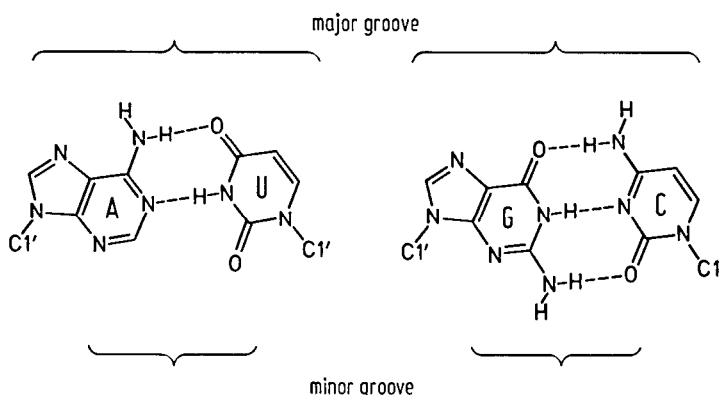


Fig. 14. Schematic description for A:U(T) and G:C base pairs occurring in RNA (DNA). Hydrogen bonds N-H---N and N-H---O indicated by dashed lines. Minor and major groove sides of base pairs are defined [84S1].

**f) Base pair propeller, twist, roll, tilt, dislocation, slide**

The geometry of a base pair and its position in a double helix and relative to the helix axis is characterized by several parameters. These are all defined in chapter 2.2 and therefore not described here.

**1.4 Geometry of bases, sugars, and phosphate groups**

The binding geometry of a molecule is defined by bond angles and bond distances. These parameters were averaged for the base, sugar and phosphate moieties in the four common nucleosides. They are given in Fig. 15a...c, with details indicated in the respective legends. For the phosphate group, Fig. 15c, data are given for (i) deprotonated monophosphate group, (ii) protonated monophosphate group, (iii) phosphodiester group, (iv) protonated pyrophosphate ester group as it occurs in ADP etc. Figs. 15a...c were taken from [84S1].