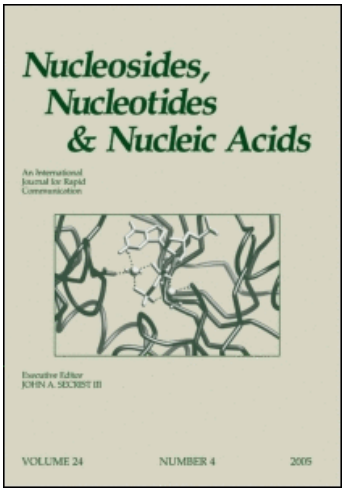

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The Effect of Exocyclic Substituents on Base-Pair Propeller Twist

C. C. Wilson[a]
[a] Neutron Science Division, ISIS Facility, Rutherford Appleton Laboratory, Oxon, UK

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THE EFFECT OF EXOCYCLIC SUBSTITUENTS ON BASE-PAIR PROPELLER TWIST

C C Wilson

Neutron Science Division, ISIS Facility,
Rutherford Appleton Laboratory, Chilton, Didcot, Oxon OX11 0QX, UK.

Abstract

Base-pair propeller twists for a series of small nucleic acid fragments calculated excluding the exocyclic base atoms are found to be slightly reduced on average. This reduction is more pronounced for pyrimidine than for the more aromatic purine bases. However, the magnitude of twist for base-pairs without exocyclic atoms included in the mean planes remains very significant, showing this to be an intrinsic property.

Introduction

There has been much recent interest in the extensive local variation in helix twist angles exhibited in single crystal structures of oligonucleotides. Earlier fibre studies had led to the determination of average conformational parameters and the elucidation of average sequence-dependent changes, thus leading to models of regular A and B DNA helices. However there is evidence that biological activity can be closely correlated with variations in local helical twist and thus the quantification of such sequence-dependent parameters in the single crystal studies can be of crucial importance in trying to understand the mechanisms by which such activity manifests itself. Structural[1,2] and elastic beam mechanical[3] explanations for these variations have been given. These explain these parameters in terms of steric hindrance or clash between purines on opposite strands of the helix at adjacent base-pairs.

One of these parameters, base-pair propeller twist, is defined[4] as the angle between the two base planes in a hydrogen bonded base-pair viewed along the axis joining them (Figure 1). The agreement between the sequence-derived sum function relating to propeller twist (Σ_4) and the actual measured propeller twist variation shows the weakest correlation of the parameters considered in these analyses. Coupled with the fact that propeller twist in fact worsens the cross-chain steric clash between purines in double helices, the existence of significant propeller twist values in oligonucleotides points strongly at the intrinsic nature of the phenomenon.

One of the most instructive ways of investigating effects such as these is to extract as much geometric and conformational information as possible from studies of mononucleoside and

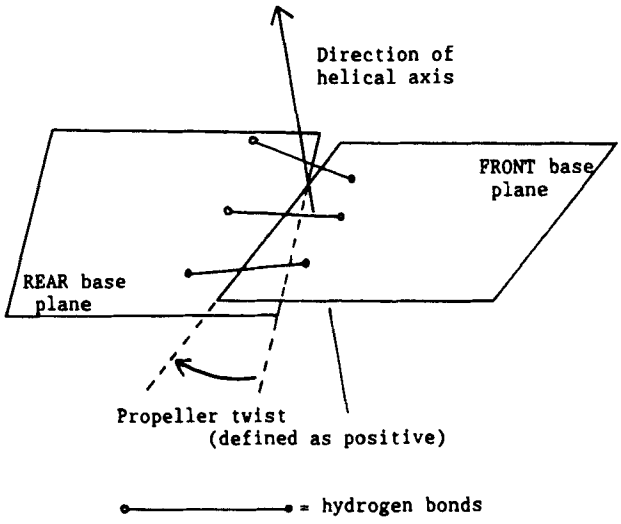

FIGURE 1 - Schematic view of propeller twisting in a base-pair

mononucleotide structures, which can serve to give important information on the disposition of base-pairs and indicate how much of the local geometry is intrinsic to a base-pair and how much is due to the duplex structure. Among the data available in this type of small molecule study are propeller twist θ_p, buckle, C1'-C1' separation and the detailed hydrogen bonding parameters.

Recently the presence of significant magnitudes of propeller twist has been demonstrated in several classes of nucleic acid fragments, among them single crystals of nucleosides and nucleotides[5,6] and co-crystal complexes of nucleic acid bases[5,7]. In these materials there were found to be average twist magnitudes of 14.7° and 4.4° respectively. As discussed earlier[5] these calculations of propeller twist magnitude were performed assuming that the exocyclic atoms on the two component bases were an integral part of the base-pair system. This would appear reasonable since the hydrogen bonding system holding the pair together tends to intimately involve these exocyclic atoms.

The obvious question following from this is the extent to which including these exocyclic atoms distorts the base-pair from the geometry which would be adopted were only the planar heterocyclic components of the bases to be considered. If the propeller twist in these compounds results primarily from distortions of these exocyclic atoms then it may be that a base-pair can be regarded as truly planar, a result which would be of great significance in our understanding of base-pair geometry. To this end the earlier analyses were extended to include the case of exclusion of exocyclic atoms.

Classification of base-pairs

There are several convenient groupings into which base-pair types can be placed. Wilson and Tollin[5] use the following :

WT(I)	Pyrimidine-Pyrimidine (Y-Y) Watson-Crick:	Y(pyr)..Y(pyr), Y(pyr)..Y(pyr).
WT(II)	Purine-Pyrimidine (R-Y) Watson-Crick:	R(pyr)..Y(pyr), R(pyr)..Y(pyr).
WT(III)	Purine-Purine (R-R) Watson-Crick:	R(pyr)..R(pyr), R(pyr)..R(pyr).
WT(IV)	Purine-Pyrimidine (R-Y) Hoogsteen:	R(pyr)..Y(pyr), R(imidazole)..Y(pyr).
WT(V)	Purine-Purine (R-R) Hoogsteen:	R(pyr)..R(pyr), R(pyr)..R(imidazole).
WT(VI)	Purine-Purine (R-R) : "double Hoogsteen"	R(pyr)..R(imidazole), R(imidazole)..R(pyr).

where **(pyr)** represents an atom on the six-membered part of the base and **(imidazole)** represent an atom on the five-membered ring (only for purine bases).

In the Hobsza and Sandorfy classification[6] the base-pairs are divided into 29 types, as summarised below :

Type	**Base 1 - Base 2**	**H bonds (B1..B2)**
HS(GG I)	*Guanosine-Guanosine*	: N1..O6, O6..N1.
HS(GG CC)	Cytosine-Cytosine	: N3..N4, N4..N3.
HS(GG III)	Guanosine-Guanosine	: N1..N7, N2..O6.
HS(GG IV)	Guanosine-Guanosine	: N2..N3, N3..N2.
HS(AA I)	Adenosine-Adenosine	: N1..N6, N6..N1.
HS(GG II)	Guanosine-Guanosine	: N1..O6, N2..N7.
HS(AA II)	Adenosine-Adenosine	: N1..N6, N6..N7.
HS(TT III)	Thymidine-Thymidine	: O2..N3, N3..O2.
HS(TT II)	Thymidine-Thymidine	: N3..O4, O4..N3.
HS(AA III)	Adenosine-Adenosine	: N6..N7, N7..N6.
HS(TT I)	Thymidine-Thymidine	: N3..O2, O4..N3.
HS(GC WC)	Guanine-Cytosine	: O6..N4, N1..N3, N2..O2.
HS(GC II)	Guanine-Cytosine	: N1..O2, N2..N3.
HS(AC I)	Adenine-Cytosine	: N6..N3, N1..N4.
HS(GA I)	Guanine-Adenine	: O6..N6, N1..N1.
HS(GT I)	Guanine-Thymine	: O6..N3, N1..O4.
HS(GC I)	Guanine-Cytosine	: N3..N4, N2..N3.
HS(TA RWC)	Thymine-Adenine	: N3..N1, O2..N6.
HS(GT II)	Guanine-Thymine	: O6..N3, N1..O2.
HS(TA RH)	Thymine-Adenine	: N3..N7, O2..N2.
HS(TA WC)	Thymine-Adenine	: O4..N6, N3..N1.
HS(TA H)	Thymine-Adenine	: O4..N6, N3..N7.
HS(GA II)	Guanine-Adenine	: N3..N6, N2..N7.
HS(GA III)	Guanine-Adenine	: O6..N6, N1..N7.
HS(GA IV)	Guanine-Adenine	: N3..N6, N2..N1.
HS(TC I)	Thymine-Cytosine	: N3..N3, O2..N4.
HS(TC II)	Thymine-Cytosine	: O4..N4, N3..N3.
HS(AC II)	Adenine-Cytosine	: N6..N3, N7..N4.

Finally, the most obvious classifications by base-type have been examined. These are division into purine (Pur) and pyrimidine (Pyr) structures and into e.g. adenine (A), thymine (T) etc. bases. The equivalence of all the classifications used is shown below.

Wilson-Tollin	Hobsza-Sandorfy	Base names	Base types
WT(I)	HS(CC)	C-C	Y-Y Homo
	HS(TT I)	T-T	Y-Y Homo
	HS(TT II)	T-T	Y-Y Homo
	HS(TT III)	T-T	Y-Y Homo
	HS(TC I)	T-C	Y-Y Het
	HS(TC II)	T-C	Y-Y Het
WT(II)	HS(GC WC)	G-C	R-Y Het
	HS(GC II)	G-C	R-Y Het
	HS(AC I)	A-C	R-Y Het
	HS(GA I)	G-A	R-R Het
	HS(GT I)	G-T	R-Y Het
	HS(GC I)	G-C	R-Y Het
	HS(TA RWC)	T-A	Y-R Het
	HS(GT II)	G-T	R-Y Het
	HS(TA WC)	T-A	Y-R Het
	HS(GA IV)	G-A	R-R Het
WT(III)	HS(GG I)	G-G	R-R Homo
	HS(GG IV)	G-G	R-R Homo
	HS(AA I)	A-A	R-R Homo
WT(IV)	HS(TA RH)	T-A	Y-R Het
	HS(GA II)	G-A	R-R Het
	HS(GA III)	G-A	R-R Het
	HS(AC II)	A-C	R-Y Het
WT(V)	HS(GG II)	G-G	R-R Homo
	HS(GG III)	G-G	R-R Homo
	HS(AA II)	A-A	R-R Homo
WT(VI)	HS(AA III)	A-A	R-R Homo

Calculations

The data were extracted from the Cambridge Structural Database and analysed as described earlier[6] using the programs CSSR[9], PHELIX[10], HELIX[11] and ROLL[12]. The 54 base-pairs from Ref. 6 and the 37 from Ref. 7 (Table 1) were analysed for propeller twist excluding the exocyclic atoms from the base system. The results of the analysis are summarised in Table 2 which shows the average values of propeller twist for the various classifications of base-pair.

Possible systematic effects on the calculations due to different crystallographic refinement procedures have been ignored, since the general trends found in the calculations should not be dependent on these unless a particular class of compounds has been treated in a unique way. This is unlikely, since for single crystal studies of molecules as small as nucleosides and nucleic acid bases, all atomic positional parameters tend to be refined independently. If one were to study larger molecules such as oligonucleotides and attempt to draw conclusions from the removal of one or two exocyclic atoms in these, then the results would be less likely to be valid, since often bases may be constrained as a rigid unit in refinements of such large structures.

Results

The most noticeable feature of the data presented in Table 2 is the very small but systematic reduction of the average propeller twist value in the base-pairs analysed when exocyclic atoms are removed from the base-pair system. This implies that although the exocyclic atoms tend on average to be fairly close to coplanarity with the mean base plane, a reasonable conclusion since these are often involved in delocalised electronic systems with the ring atoms, these exocyclic atoms do tend to deviate more than the others from the mean plane - again a not unreasonable conclusion. The overall reduction in twist is slight and the average propeller twist magnitudes for base-pairs, even with exocyclic atoms excluded, remain very significant, in agreement with the earlier work[5,6,7]. The more sophisticated analysis presented here does, however, contradict the earlier result[5] which appeared to indicate a marginal *increase* in average propeller twist value when exocyclic atoms were excluded from the calculation.

Of particular interest is the fact that the average propeller twist decreases *more* on exclusion of exocyclic atoms for the least aromatic bases (pyrimidines) than for the more aromatic purines. The average reduction for pyrimidines is some 13(3)% (maximum of 22(2)% for U..U) whereas that for purines is only 4(1)% (maximum of 6(2)% for A..A). This result again agrees with the conclusion that exocyclic atoms show an additional deviation from the plane of the base to which they are attached. In addition it seems that this deviation is on average further out of the plane of the base-*pair*, as opposed to just the plane of the parent base. If this exocyclic atom deviation were solely related to single base geometry, it might be expected that such deviations of exocyclic atoms from a base plane might reduce the calculated propeller twist in as many cases as they would increase it. On average this does not happen - the propeller twist increase due to these exocyclic atoms is systematic - perhaps reflecting the effect the formation of a base-pair has on the structures of the component bases, probably via both steric and electronic mechanisms.

Discussion

The existence of propeller twist within duplex structures appears to be crucial to the stability and function of such molecules. In single crystal oligonucleotide studies the twist tends to have a magnitude in the range 10-20°. The results from earlier work on single crystals of mononucleosides[5,6,7], suggest that a non-zero propeller twist is often an intrinsic property of a base-pair in such monomeric structures. We have seen here that while this twist is to a small extent magnified by deviations from coplanarity of the exocyclic atoms in the bases, even when these are excluded the intrinsic propeller twist remains of significant size (Figure 2).

The evidence in the current work seems to reinforce earlier conclusions that base-pairs are intrinsically distinctly non-planar units. In terms of the original ladder analogy of DNA structure, the rungs are twisted about their long axes, and the degree of twist is only held reasonably constant by the forces introduced by the sugar-phosphate backbone and by cross-chain interactions.

Analysing nucleic acid fragment geometry reinforces the possibility that non-coplanarity of bases in base-pairs is the most naturally adopted conformation. This calls into question the common assumption that isolated base-pairs should be coplanar and that propeller twist is introduced solely as a response to purine base stacking along a single strand of a double helix. The

TABLE 1 - Bibliographic details for structures analysed.

3018 BRADOM 8-BROMO-2',3'-O-ISOPROPYLIDENE-ADENOSINE MONOHYDRATE : S.FUJII,T.FUJIWARA,K.TOMITA 3 1985 (1976) NUCLEIC ACIDS RES.
3099 BRINOS10 8-BROMOINOSINE : H.STERNGLANZ,J.M.THOMAS,C.E.BUGG 33 2097 (1977) ACTA CRYST.,SECT.B
8445 DXCYTD 2'-DEOXYCYTIDINE : D.W.YOUNG,H.R.WILSON 31 961 (1975) ACTA CRYST.,SECT.B
10256 GUANSH10 GUANOSINE DIHYDRATE : U.THEWALT,C.E.BUGG,R.E.MARSH 26 1089 (1970) ACTA CRYST.,SECT.B
12378 LEUAUR10 5-(N-(L-LEUCYL)AMINO)URIDINE HYDRATE : P.NARAYANAN,H.M.BERMAN 33 2047 (1977) ACTA CRYST.,SECT.B
12652 MADENS10 2'-O-METHYLADENOSINE : P.PRUSINER,M.SUNDARALINGAM 32 161 (1976) ACTA CRYST.,SECT.B
20558 TGUANS10 6-THIOGUANOSINE MONOHYDRATE : U.THEWALT,C.E.BUGG 94 8892 (1972) J.AM.CHEM.SOC.
21061 TMSADS10 5'-METHYLTHIO-ADENOSINE : N.BORKAKOTI,R.A.PALMER 34 867 (1978) ACTA CRYST.,SECT.B
21650 TPTAMP CHLORO(TERPYRIDYL) PLATINUM(II) ADENOSINE-5'-MONOPHOSPHATE HYDRATE : Y.WONG,S.J.LIPPARD 824 (1977) J.CHEM.SOC.,CHEM.COMM.
22834 IPADOS 2',3'-O-ISOPROPYLIDENE-ADENOSINE : S.SPRANG,D.C.ROHRER,M.SUNDARALINGAM 34 2803 (1978) ACTA CRYST.,SECT.B
23154 ADMOPM ADENOSINE-5'-O-METHYLPHOSPHATE METHANOL SOLVATE : J.D.HOOGENDORP,G.C.VERSCHOOR,C.ROMERS 34 3662 (1978) ACTA CRYST.,SECT.B
24352 CYADOT 8,2'-CYCLOADENOSINE TRIHYDRATE : S.NEIDLE,G.L.TAYLOR,P.C.COWLING 35 708 (1979) ACTA CRYST.,SECT.B
24383 DMURID 5-DIMETHYLAMINO-URIDINE : E.EGERT,H.J.LINDNER,W.HILLEN,H.G.GASSEN 35 920 (1979) ACTA CRYST.,SECT.B
24812 ZADENH10 2-AZA-ADENOSINE HEMIHYDRATE : P.SINGH,D.J.HODGSON 35 973 (1979) ACTA CRYST.,SECT.B
28133 ARFUAE 9ALPHA-D-ARABINOFURANOSYL-ADENINE : S.J.CLINE,D.J.HODGSON 563 540 (1979) BIOCH.BIOPH.ACTA
29458 AMOADB 3'-CYCLOBUTYLAMINO-3'-DEOXYADENOSINE METHANOL SOLVATE : W.S.SHELDRICK,M.MORR 36 2328 (1980) ACTA CRYST.,SECT.B
29459 AMOADC 3'-(N-BENZYL-N-METHYLAMINO)-3'-DEOXYADENOSINE : W.S.SHELDRICK,M.MORR 36 2328 (1980) ACTA CRYST.,SECT.B
29794 CORDCP 3'-DEOXY-ADENOSINE (CORDYCEPIN) : M.M.RADWAN,H.R.WILSON 36 2185 (1980) ACTA CRYST.,SECT.B
31814 THPSUR 4-THIO-PSEUDOURIDINE: C.L.BARNES,S.W.HAWKINSON,P.W.WIGLER 36 2299 (1980) ACTA CRYST.,SECT.B
33789 BADPEB (S)-ADENOSYL-(L)-HOMOCYSTEINE HYDRATE (FORM II) : T.ISHIDA,H.MORIMOTO,M.INOUE,T.FUJIWARA, K.-I.TOMITA 671 (1981) J.CHEM.SOC.,CHEM.COMM.
35768 BAYKER 2',3'-O-ISOPROPYLIDENE-5'-DEOXY-6(R),5'-CYCLO-5,6-DIHYDROURIDINE : Y.YAMAGATA,S.FUJII, T.FUJIWARA,K.-I.TOMITA,T.UEDA 654 242 (1981) BIOCHIM.BIOPHYS.ACTA
39181 NAAMPH10 SODIUM ADENOSINE-(3'-5')-CYCLIC-MONOPHOSPHATE TETRAHYDRATE (MONOCLINIC FORM) : K.I.VARUGHESE,C.T.LU,G.KARTHA 104 3398 (1982) J.AM.CHEM.SOC.
39226 SAHCYA10 S-ADENOSYL-L-HOMOCYSTEINE HYDRATE : H.-S.SHIEH,H.M.BERMAN 38 1513 (1982) ACTA CRYST.,SECT.B
39293 BADPEB10 S-ADENOSYL-L-HOMOCYSTEINE HYDRATE (FORM II) : T.ISHIDA,A.TANAKA,M.INOUE,T.FUJIWARA, K.-I.TOMITA 104 7239 (1982) J.AM.CHEM.SOC.
39594 BIVVIL 2',3'-O-(TETRAISOPROPYL-1,3-DISILOXANEDIYL)-CYTIDINE (AT 97 DEG.K) : J.D.HOOGENDORP,C.ROMERS 38 2738 (1982) ACTA CRYSTALLOGR.,SECT.B
40769 BONTAZ PENTA-AQUA-PENTAKIS(MU-2—GUANOSINE-3'-MONOPHOSPHATE)-TRI-COPPER(II) HEPTAHYDRATE : W.S.SHELDRICK 38 16 (1983) Z.NATURFORSCH.,TEIL B
41337 SAHCYB10 S-8-AZA-ADENOSYL-L-HOMOCYSTEINE MONOHYDRATE : V.B.PETT,H.-S.SHIEH,H.M.BERMAN 38 2611 (1982) ACTA CRYST.,SECT.B
42685 BUKYAH 8,5'-ANHYDRO-8-HYDROXY-9BETA-D-RIBOFURANOSYL-ADENINE MONOHYDRATE : S.SUGIO,H.MIZUNO, K.KITAMURA,K.HAMADA,M.IKEHARA,K.-I.TOMITA 39 745 (1983) ACTA CRYST.,C (CR.STR.COMM.)
42702 BULDER 3',5'-BIS(O-ACETYL)-5-BROMO-2'-DEOXYURIDINE : J.N.LOW 39 796 (1983) ACTA CRYST.,C
43305 BUVPOX (C1'-R,C3'-R,C4'-R)-2'-DEOXY-3'-S-ETHYL-3'-THIOADENOSINE (ABSOLUTE CONFIGURATION) : B.DIMKE,E.SCHLIMME,V.ZABEL,W.SAENGER 1409 (1983) JUSTUS LIEBIGS ANN.CHEM.
44306 ZZZAOV01 5'-DEOXY-5',6-EPITHIO-5,6-DIHYDRO-2',3'-O-ISOPROPYLIDENE-URIDINE (TRICLINIC FORM) : N.GAUTHAM,T.P.SESHADRI,M.A.VISWAMITRA,S.A.SALISBURY,D.M.BROWN 39 1389 (1983) ACTA CRYST.,C
44534 CALDEY 5-BROMO-2'-DEOXYCYTIDINE : J.N.LOW,P.TOLLIN,D.W.YOUNG 10 1369 (1981) CRYST.STRUCT.COMMUN.
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45745 BUKYAH10 8,5'-ANHYDRO-8-HYDROXY-9-BETA-D-RIBOFURANOSYLADENINE MONOHYDRATE : S.SUGIO,H.MIZUNO, K.KITAMURA,K.HAMADA,M.IKEHARA,K.-I.TOMITA 40 712 (1984) ACTA CRYST.,C
49309 CABSUT01 3',5'-DI-O-ACETYLTHYMIDINE (3',5'-DIACETYL-5-METHYL-2'-DEOXYURIDINE) : C.C.WILSON,J.N.LOW,P.TOLLIN,H.R.WILSON 40 1712 (1984) ACTA CRYST.,C
49564 CIYTOT ETHYLENEDIAMINE-(1,10-PHENANTHROLINE)-PLATINUM(II) TETRAKIS(CYTIDINE-3'-MONOPHOSPHATE) DOTRIACONTAHYDRATE : S.VIJAY-KUMAR,T.D.SAKORE,H.M.SOBELL 12 3649 (1984) NUCLEIC ACIDS RES.

TABLE 1 ctd

53945 DAHMII 2',3',5'-TRI-O-ACETYLGUANOSINE : C.C.WILSON,J.N.LOW,P.TOLLIN 41 1123 (1985) ACTA CRYST.,C
55540 DECDIY HEXA-AQUA-MAGNESIUM BIS((2-PYRIDINIUMYL)-(2-PYRIDYL)-AMINE) BIS(ADENOSINE-5'-TRIPHOSPHORIC ACID-O,O',O'')-MAGNESIUM(II) DODECAHYDRATE : R.CINI,M.C.BURLA,A.NUNZI,G.P.POLIDORI,P.F.ZANAZZI 2467 (1984) J.CHEM.SOC.,DALTON
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56273 DEMXEY 8-METHYLGUANOSINE TRIHYDRATE : K.HAMADA,I.HONDA,S.FUJII,T.FUJIWARA,K.-I.TOMITA 41 1486 (1985) ACTA CRYST.,C
57361 CICRAH10 BIS(ADENOSINE 5'-TRIPHOSPHATO)-MANGANESE HEXA-AQUA-MANGANESE BIS(2,2'-DIPYRIDYLAMINE) DODECAHYDRATE : M.SABAT,R.CINI,T.HAROMY,M.SUNDARALINGAM 24 7827 (1985) BIOCHEMISTRY
58479 DIVPIH DIPOTASSIUM 2'-METHOXY-GRISEOLIC ACID TRIHYDRATE : S.TAKAHASHI,F.NAKAGAWA,K.KAWAZOE,Y.FURUKAWA,S.SATO,C.TAMURA,A.NAITO 38 830 (1985) J.ANTIBIOT.
59676 DOGYED CIS-THYMIDINE-(3'-5')-CYCLIC-N,N-DIMETHYLPHOSPHORAMIDATE ACETONE SOLVATE : W.G.BENTRUDE,A.E.SOPCHIK,W.N.SETZER,R.B.BATES,R.B.ORTEGA 42 584 (1986) ACTA CRYST.,C
59740 DOHSIC TETRAKIS(ADENOSINIUM) DIHYDRO-DECAVANADATE(V) UNDECAHYDRATE : M.V.CAPPARELLI,D.M.L.GOODGAME,P.B.HAYMAN,A.C.SKAPSKI 776 (1986) J.CHEM.SOC.,CHEM.COMM.

3393 BURBAD 1-METHYL-5-BROMOURACIL-9-ETHYL-8-BROMO-ADENINE COMPLEX : S.S.TAVALE,T.D.SAKORE,H.M.SOBELL 43 375 (1969) J.MOL.BIOL.
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TABLE 2 - Comparison of average propeller twist values for systems including and excluding exocyclic atoms.

Nucleosides and Nucleotides				Nucleic Acid Bases			
Class	Number of base-pairs	Propeller twist (°) With exo atoms	Propeller twist (°) Without exo atoms	Class	Number of base-pairs	Propeller twist (°) With exo atoms	Propeller twist (°) Without exo atoms
All	54	14.7	14.0	All	37	4.4	4.3
R-R	38	15.7	15.4	Homo	12	1.6	1.3
Y-Y	16	12.1	10.5	Hetero	25	5.8	5.7
A	31	16.8	16.4	AU	8	7.1	7.2
G	6	11.6	11.5	PU	5	6.0	5.6
I	1	8.2	9.3	PT	3	4.7	4.9
C	6	7.1	6.9	GC	4	4.4	4.4
U	8	14.9	11.9	AT	2	5.5	5.4
T	2	16.0	15.9	AH	1	5.1	4.6
				CU	2	5.0	5.0
WT							
I	16	12.1	10.5	R-R Het	1	5.1	4.6
III	4	22.9	23.5	Y-Y Het	2	5.0	5.0
V	26	14.7	14.6	R-Y Het	22	5.9	5.8
VI	8	15.5	14.0				
				AA	5	1.3	0.9
HS				GG	3	1.6	1.5
AAI	2	23.3	23.5	PP	1	3.7	3.2
AAII	21	16.6	16.6	UU	2	0.7	0.5
AAIII	8	15.5	14.0	CC	1	2.9	2.3
GGI	2	22.4	23.5				
GGIII	5	6.6	6.3	R-R Homo	9	1.6	1.4
CC	4	8.7	9.2	Y-Y Homo	3	1.4	1.1
TTII	3	22.8	18.0				
TTIII	4	16.9	15.0	WT			
				I	5	2.9	2.7
				II	12	5.3	5.3
				III	7	1.7	1.5
				IV	11	6.4	6.4
				V	1	1.7	1.6
				VI	1	1.0	0.0
				HS			
				GCWC	4	4.4	4.4
				TARWC	2	10.8	11.2
				TAH	6	9.9	8.0
				TARH	4	4.1	4.4
				TAWC	1	4.6	5.2
				GAIII	1	5.1	4.6
				AAI	3	1.2	1.0
				AAII	1	1.7	1.6
				AAIII	1	1.0	0.0
				GGIV	4	2.1	1.9
				TTII	2	0.7	0.5

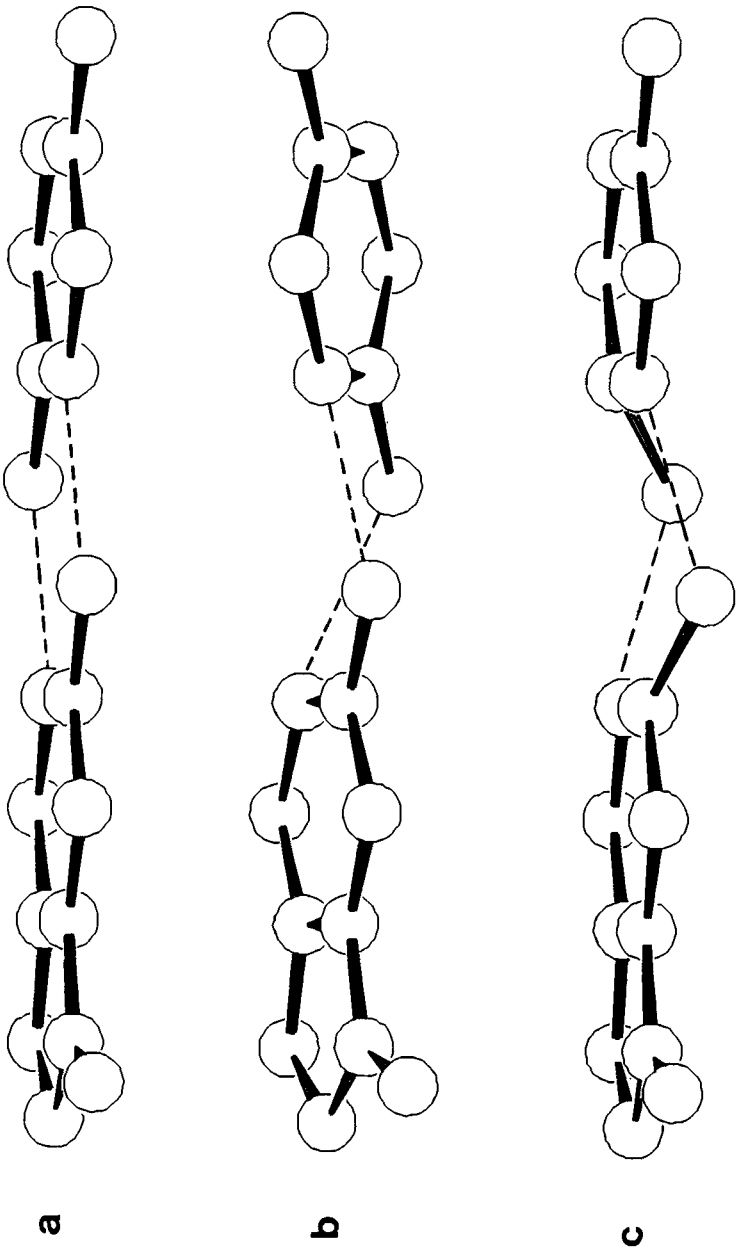

FIGURE 2 – The twisting of a base-pair from coplanarity (a) tends to be manifest as a twist of the entire base planes (b) rather than be dominated by deviations of the exocyclic atoms (c). The present results show that the effect illustrated in (c) does tend to occur, but in a much less exaggerated way and with only a slight effect on the size of the twist. Drawn using SCHAKAL[15].

intrinsic problems of this viewpoint mentioned above - the cross-chain clash introduced by the twist and the poor agreement of propeller twist variation along an oligonucleotide chain with the predictions of Calladine's mechanical analysis - are thus partly mitigated by postulating the natural adoption of propeller twist by base-pairs. The double helical framework is thus seen to modulate rather than create this twist.

For theoretical work on isolated DNA fragments this lack of coplanarity of bases within a base-pair has serious implications. Calculations of base-pair geometry have normally been made on the assumption that a base-pair is a planar entity[8] and it seems that in many cases this assumption is invalid. Most theoretical calculations concentrate on the optimisation of the electronic structure of the planar base-pair, and the models tend not to allow for a three-dimensional character of the pair. It is important that calculations, whether non-empirical or semi-empirical, take this into account in order to give results which are valid for the discussion of base-pair geometry in real systems.

On a similar note, it is found that the propeller twists exhibited by nucleic acid bases tend to be considerably smaller than those in nucleosides. While in earlier work there was found to be no correlation between propeller twist in oligonucleotides and the degree of base-base stacking present[13], there is the possibility that the smaller twist found in nucleic acid bases is related to planar group stacking. This possibility is under investigation[14]. The alternative to stacking effects is that the electronic properties of the bases in a nucleoside structure are significantly affected by the presence of the N1/N9 sugar group. It is conceivable that this change in electronic properties could affect the coplanarity or otherwise of the base-pair. Such considerations are, however, beyond the scope of the present work on structural geometry.

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