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Nelson N. H. Teng, Martin S. Itzkowitz, and Ignacio Tinoco, Jr.

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Calculation of the Rotational Strengths of Mononucleosides[1]

Nelson N. H. Teng,[2] Martin S. Itzkowitz, and Ignacio Tinoco, Jr.

Contribution from the Department of Chemistry and the Laboratory of Chemical Biodynamics, Lawrence Radiation Laboratory, University of California, Berkeley, California 94720.

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Abstract: The rotational strengths of the two longer wavelength transitions B_{2U}, B_{1U}, of four mononucleosides (adenosine, guanosine, uridine and cytidine) as a function of the glycosidic rotational angles have been investigated theoretically. The transition in each base is characterized by transition monopoles; the sugar is treated as a sum of bond polarizabilities. The interaction among these polarizabilities is also considered. Rotational strengths were calculated using three different sets of transition monopoles and many combinations of bond polarizabilities. We conclude that adenosine, uridine and cytidine may have primarily one conformation, but that in guanosine the base is not definitely fixed with respect to the ribose. Calculation on different anomeric nucleosides of adenosine and uridine shows that the configuration at the anomeric carbon (C1') determines the sign of the optical rotation. The configuration at C2' influences the glycosidic angular dependence of rotational strength more profoundly than that at C3' and C5'. These results are in good agreement with experiments. The signs and magnitude of the calculated rotational strengths are in good agreement with experiment for the anti conformation of all the isomers of adenosine. As the conformation of the nucleosides in B-form

DNA is quite different from the anti form, we calculate that the rotational strengths of the nucleosides in the polynucleotide are very different from those in solution.

Introduction

Many workers have measured the circular dichroism (CD) and optical rotatory dispersion (ORD) of polynucleotides, and have shown that optical activity is an important tool for conformational assignments. Theories have been developed to facilitate the interpretation of the spectra of polynucleotides.[3,4] However, in the theories, the CD and ORD of the monomer units themselves have been ignored. Recently, experimental and theoretical studies of the optical activity and conformation of nucleosides have appeared.[5-7] In particular, an extended series of articles by D. W. Miles et al.[8] have investigated this problem in detail.

In the present communication we have used an improved version of Kirkwood polarizability theory to include the presence of a classical polarizability near a quantum system. The rotational strengths of mononucleosides are calculated using transition monopoles on the bases interacting with polarizable bonds of the sugars. We try to examine the calculations critically. Three different sets of transition monopoles have been employed with various degrees of success. The effect of different values of bond polarizability and variation of the positions of furanosyl OH groups has also been examined. The calculated rotational strengths as a function of the glycosidic angle are in qualitative agreement with calculations of Miles et al., using bond transition dipoles on the bases.

In the next section a detailed description of the theoretical method is given; in section III we discuss the numerical methods and the data used, and in section IV we demonstrate the application of the theory to the four mononucleosides found in nucleic acids and to various anomeric isomers of adenosine and uridine.

II. Theory

Rosenfeld[9] characterized the optical rotation by the rotational strength for the optical transition from 0 to A, $R_{0A} = \mathrm{Im}(\underset{\sim}{\mu}_{0A} \cdot \underset{\sim}{m}_{A0})$. Im denotes the imaginary part of a complex number. $\underset{\sim}{\mu}_{0A}$ is the electric dipole transition moment vector and $\underset{\sim}{m}_{A0}$ is the magnetic dipole transition moment vector defined as follows:

$$\underset{\sim}{\mu}_{0A} = \sum_j \langle 0|\underset{\sim}{\mu}_j| A\rangle \tag{1}$$

$$\underset{\sim}{m}_{A0} = \frac{e}{2mc} \sum_j \underset{\sim}{R}_j \times \langle A |\underset{\sim}{P}_j| 0\rangle + \sum_j \langle A |\underset{\sim}{m}_j'| 0\rangle. \tag{2}$$

where $\underset{\sim}{R}_j$ is the vector distance from an arbitrary origin to the origin of group j; $\underset{\sim}{\mu}_j$ is the electric dipole moment operator of group j; $\underset{\sim}{P}_j$ is the linear momentum operator of group j; $\underset{\sim}{m}_j$ is the magnetic moment operator of group j relative to the origin in group j. The origin is usually selected to minimize the contribution of $\underset{\sim}{m}_j'$ to rotational strength. c, e, m are the usual notations for speed of light, electronic charge and electronic mass. The molecular wavefunctions for states 0 and A are $|0\rangle$ and $|A\rangle$. Therefore, for an electrically allowed, magnetically forbidden transition ($\langle A |\underset{\sim}{m}_j'| 0\rangle = 0$) the expression for rotational strength is

$$R_{0A} = (-\pi\nu_{0A}/2c) \sum_{i\neq j} \underset{\sim}{R}_{ij} \langle 0 |\underset{\sim}{\mu}_i| A\rangle \times \langle A |\underset{\sim}{\mu}_j| 0\rangle \tag{3}$$

where ν_{0A} is the frequency of the transition and $\underset{\sim}{R}_{ij} = \underset{\sim}{R}_j - \underset{\sim}{R}_i$.

It can be seen that the optical activity originates from the interaction between electric transition dipoles located asymmetrically with respect to one another. In equation (3) we have resolved R_{0A} into groups. The obvious separation into groups for mononucleosides would be to treat the base as the major chromophore and the furanose as an asymmetric substituent. The furanoise is further subdivided into bonds. For a particular transition $0 \rightarrow A$ of the base, which is far removed in energy from any transitions in the furanose, it is a good approximation to replace the transition dipole from the bonds of the furanose by the dipole that would be induced in a classical polarizability placed within the transition field of the base.

$$\underset{\sim}{\mu}_{jA0} = \underset{\sim}{\alpha}_j \cdot \underset{\sim}{E}_j^{eff} \tag{4}$$

where $\underset{\sim}{\alpha}_j$ is the polarizability tensor of the j^{th} furanose bond and $\underset{\sim}{E}_j^{eff}$ is the effective field at the jth bond due to the transition $0 \rightarrow A$.

To evaluate the effective field $\underset{\sim}{E}_j^{eff}$, one expands the molecular wavefunctions in a linear combination of atomic orbitals,

$$|0\rangle = \sum_s C_{0s} |s\rangle$$

$$|A\rangle = \sum_s C_{As} |s\rangle$$

We obtain

$$\underset{\sim}{E}_j^{eff} = -\nabla_j \langle A|\frac{1}{r_j}|0\rangle$$

$$= -\nabla_j \sum_{s,t} C_{As}^* C_{0t} \cdot \langle s|\frac{1}{r_j}|t\rangle \tag{5}$$

The standard point monopole approximation sets

$$\langle s|\frac{1}{r_j}|t\rangle = \delta_{st} \cdot \frac{1}{r_{sj}} \tag{6}$$

where δ_{st} is the Kronecker δ.

Alternatively, one may treat $\psi_0|\psi_A$ as a charge distribution and do a multipole expansion ($\sum_j \underset{\sim}{E}_j^{eff}$) about the center of the charge. The practical limit in terms of computer programming on the CDC 6600 computer used for our calculations is the octupole term, and convergence is poor. We abandoned this method in favor of the use of equation (6). In the hopes of increased accuracy we calculated the integrals $\langle s|\frac{1}{r_i}|s\rangle$ in terms of Slater $2p\pi$ orbitals to obtain $\underset{\sim}{E}_j^{eff}$. This was found to make a negligible correction to rotational strengths; we therefore used for a zero order $\underset{\sim}{E}_j^{eff}$:

$$\underset{\sim}{E}_j^{eff} = \sum_s \rho_s \frac{\underset{\sim}{r}_{js}}{|r_{js}|^3} \qquad (7)$$

where $\rho_s \equiv C_{As}\, C_{Os}$ is the monopole charge of atom s due to the base transition $0 \rightarrow A$. $\underset{\sim}{r}_{js}$ is a position vector from the j^{th} group to the s^{th} monpole. By combining equations (3), (4) and (7), we have an expression for the rotational strength of transition $0 \rightarrow A$ in the base of a nucleoside. The base is represented by transition monopoles on each atom and the furanose is approximated by bond polarizabilities.

$$R_{0A} = \left(-\frac{\pi\, \nu_{0A}}{2c}\right) \sum_{i \neq j} \sum_s \rho_s \underset{\sim}{R}_{ij} \cdot (\underset{\sim}{\mu}_{iA0} \times \underset{\sim}{\alpha}_j \cdot r_{js})/|r_{js}|^3 \qquad (8)$$

where $\underset{\sim}{R}_{ij}$ is the distance from the base transition dipole ($\underset{\sim}{\mu}_{iA0}$) to bond j in the furanose. This is the most commonly used expression for calculating optical activity under conditions mentioned above. However, this expression has only considered the monopole field caused by the base and has ignored the interaction among the furanose bonds. This approximation may be good in situations where the asymmetric perturbation is an aliphatic chain.[10] But in the furanose ring, for the most

(10)

part, the sugar bonds are much closer to each other than to the base, so each bond will feel the effect of the induced dipoles in all other bonds. To include this effect we replace $\underset{\sim}{E}_j^{eff}$ by a more complete expression

$$\underset{\sim}{\mu}_{jA0} = \underset{\sim}{\alpha}_j \cdot \underset{\sim}{E}_j^{eff} = \underset{\sim}{\alpha}_j \cdot \left[\sum_s \rho_s \frac{\underset{\sim}{r}_{js}}{|r_{js}|^3} - \sum_k \underset{\sim}{T}_{jk} \cdot \underset{\sim}{\mu}_{kA0}\right] \tag{9}$$

where $\underset{\sim}{T}_{jk} = (\underset{\sim}{1} - 3\,\underset{\sim}{r}_{jk}\,\underset{\sim}{r}_{jk}/\,r_{jk}^{\,2})(\frac{1}{r_{jk}^3})$ the dipole interaction tensor between points j and k.

These coupled linear equations can be solved for $\underset{\sim}{\mu}_{jA0}$.

$$\underset{\sim}{\mu}_{jA0} = \sum_k (\underset{\sim}{1} + \underset{\sim}{\alpha}\underset{\sim}{T})^{-1}_{jk} \cdot \underset{\sim}{\alpha}_k \cdot \sum_s \rho_s \frac{\underset{\sim}{r}_{js}}{|r_{js}|^3} \tag{10}$$

Substituting equation (10) in (3), we have the final expression for the rotational strength with the furanose interaction treated self consistently.

$$R_{0A} = (-\frac{\pi\,\nu_{0A}}{2c}) \sum_{i\neq j} \sum_k \sum_s \rho_s\, \underset{\sim}{R}_{ij} \cdot \underset{\sim}{\mu}_{iA0} \times (\underset{\sim}{1} + \underset{\sim}{\alpha}\underset{\sim}{T})^{-1}_{jk} \cdot \underset{\sim}{\alpha}_k \cdot \underset{\sim}{r}_{ks}/|r_{ks}|^3 \tag{11}$$

For all calculations R_{0A} was evaluated using transition monopoles only as in equation (8) and also self consistently including the sugar bond-bond induced dipole coupling as in equation (11).

III. Calculation

We consider each base to have two $\pi \rightarrow \pi^*$ transitions with maxima between 240 $m\mu$ and 280 $m\mu$. The transition frequency ν_{0A} is taken as the location of the major experimental UV absorption maximum.[4]

Coordinates. The coordinates used in the computation are taken from Spencer[11] for the bases (Table I) and Sundaralingam and Jensen[12] for the 2'endo ribose and 3'endo ribose. The coordinates for the α anomers were obtained by reflection from that of β nucleosides about the plane of C1', C2' and O' of the furanose. The numbering system and the nomenclature for the pentofuranoses is shown in Fig. 1.

TABLE I (11) ATOMIC COORDINATES OF PURINE AND PYRIMIDINE BASES

Adenine			Cytosine		
Atom	X(Å)	Y(Å)	Atom	X(Å)	Y(Å)
N_1	-2.791	4.407	N_1	0.000	1.470
C_2	-3.201	3.134	C_2	-1.207	2.139
N_3	-2.391	2.078	N_3	-1.231	3.489
C_4	-1.079	2.298	C_4	-0.070	4.132
C_5	-0.604	3.583	C_5	1.157	3.504
C_6	-1.500	4.633	C_6	1.181	2.125
N_7	0.763	3.598	O_2	-2.253	1.511
C_8	1.055	2.280	N_4	-0.094	5.472
N_9	0.000	1.470			
N_6	-1.041	5.892			

Guanine			Uracil		
N_1	-2.799	4.348	N_1	0.000	1.470
C_2	-3.205	3.051	C_2	-1.207	2.139
N_3	-2.378	2.010	N_3	-1.159	3.518
C_4	-1.079	2.298	C_4	0.010	4.251
C_5	-0.604	3.583	C_5	1.205	3.504
C_6	-1.462	4.702	C_6	1.181	2.125
N_7	0.763	3.598	O_2	-2.269	1.538
C_8	1.055	2.280	O_4	0.010	5.471
N_9	0.000	1.470			
N_2	-4.523	2.807			
O_6	-1.045	5.848			

The conformation of the furanose has been subject of debate.[12-15] We have used 2'endo conformation, consistent with the majority of crystal structures of nucleosides, for most of the calculations. The 2'endo ribose and 3'endo deoxyribose coordinates are given in Table II. Coordinates of the other sugars were obtained by interchanging H and OH atoms and changing bond lengths. In solution, the positions of the hydroxyl groups of the furanose are not precisely known. In an effort to determine the influence of OH position on R_{0A}, we have rotated the OH groups about their individual CO axes for both adenosine and uridine. The effect on the calculated R_{0A} is small; the shape of the curve when R_{0A} is plotted vs. the glycosidic angle (ϕ_{CN}) is not significantly altered. Slight variation in magnitude of R_{0A} is found when the OH at the C'2 position is rotated; however, no noteiceable change is observed in the case of C'3 and C'5. This finding is consistent with our conclusion (Section IV) about the importance of configuration at C'2 position.

Glycosidic rotation. We have chosen the definition of glycosidic rotation by Donohue and Trueblood.[16] The sugar-base torsion angle ϕ_{CN} is defined as the angle formed by the plane of the base and C_1'-O_1' bond of the furanose ring when viewed along the C_1'-N bond. ϕ_{CN} is taken as zero when C_2 of the base is anti-planar to O_1'. Positive rotation is clockwise rotation of C_1'-O_1' when one looks from C_1' to N. Donohue and Trueblood define "anti" conformation for ϕ_{CN} equal to $-30° \pm 45°$ and "syn" for ϕ_{CN} equal to $+150° \pm 45°$.

Transition monopoles and dipoles. Three sets of monopoles for the various transitions of the four bases were used in the computation. We

Table II. Coordinates of 2'endo ribose and 3' endo deoxy ribose[12]

Atoms	2'endo ribose x	y	z
C1	0.00	0.00	0.00
H1	-0.51	-0.16	0.74
O1	1.35	-0.43	0.00
C2	-0.62	-0.58	-1.25
H2	-0.26	0.08	-1.89
O2	-2.02	-0.57	-1.26
OH2	-2.60	-1.09	-0.59
C3	0.08	-1.94	-1.31
H3	0.02	-2.33	-2.02
O3	-0.53	-2.80	-0.34
OH3	-0.48	-3.80	-0.42
C4	1.51	-1.59	-0.86
H4	1.81	-2.46	-0.38
C5	2.48	-1.28	-1.97
H5	3.37	-0.73	-1.40
H5'	2.98	-2.14	-2.36
O5	1.95	-0.44	-3.00
OH5	1.88	-1.15	-3.69

Atoms	3'endo decxyribose x	y	z
C1	0.00	0.00	0.00
H1	-0.40	-0.53	0.96
O1	1.37	-0.43	0.00
C2	-0.68	-0.65	-1.21
H2	-1.28	-1.47	-1.11
H2'	-1.35	-0.16	-1.86
C3	0.52	-1.08	-2.10
H3	0.87	-0.28	-2.80
O3	-0.24	-2.16	-2.96
OH3	0.06	-3.00	-2.40
C4	1.57	-1.37	-1.08
H4	1.20	-2.36	-0.70
C5	3.02	-1.26	-1.52
H5	3.71	-1.64	-0.80
H5'	3.28	-1.80	-2.39
O5	3.27	0.09	-2.04
OH5	4.06	0.23	-2.73

used monopoles described by Bush[17] and those calculated from self-consistent field with and without configuration interaction.[18] The monopoles obtained from Bush were calculated by an SCF-LCAO-CI method done by H. De Voe of National Institutes of Health. His method was that of Viellard and Pullman (1963) extended to the excited states. The monopoles selected by Bush were not just the lowest energy transitions but were chosen so that the transition moment directions were consistent with experimental directions, or what were inferred to be the most likely directions. Bush's procedure assumes the order of the excited state in energy may be incorrect. The magnitudes of all the monopoles were scaled to give the measured transition moment magnitudes. The scaled monopoles for the B_{2U} and B_{1U} transitions are given in Table III.

The base transition dipoles were calculated from the transition monopoles placed on each nucleus of the base. The point transition dipole is assumed to be at the center of transition charge of the base (Table IV).

The effect of different transition monopoles and the use of a self consistent treatment of the furanose bond interactions is shown in Fig. 2. One sees that the self consistent theory for induced dipoles in the sugar [Equation (11)] gives very different results from Equation (8). We use Equation (11) for all the calculations discussed in this paper.

Polarizabilities. Bond polarizabilities have always been the subject of controversy. The merits of different measurements of polarizability have frequently been discussed, especially by users wanting to evaluate optical activity.[4,8,22] Because of the uncertainties in the bond polarizabilities, the agreement between experiment and the result of any calculation

Table III.[a,b] Monopoles for the B_{2U} and B_{1U} transitions

	Trans. B_{2U}			Trans. B_{1U}		
Atom	SCF/CI[20]	SCF[19]	Push/DeVoe[17]	SCF/CI	SCF	Push/DeVoe
Adenine						
N1	-0.178	0.035	-0.030	0.023	-0.064	
C2	0.091	-0.072	-0.037	-0.063	-0.050	
N3	-0.129	0.140	-0.107	0.087	-0.014	
C4	-0.063	0.018	-0.291	-0.089	-0.051	
C5	-0.018	0.032	0.126	0.088	0.060	
C6	0.156	-0.114	0.232	-0.033	0.031	
N7	0.046	-0.085	0.055	-0.020	0.009	
C8	-0.180	0.134	-0.105	0.050	0.026	
N9	0.069	0.031	0.112	0.034	0.023	
N6	0.206	-0.117	0.046	-0.078	0.030	
Guanine						
N1	0.051	0.041	-0.032	0.116	0.039	-0.044
C2	0.100	0.101	0.030	-0.060	-0.013	-0.165
N3	-0.101	-0.080	-0.050	0.097	0.081	0.076
C4	0.090	0.060	-0.104	0.108	0.125	-0.181
C5	-0.112	-0.083	-0.034	-0.045	-0.079	0.105
C6	-0.013	-0.000	0.035	-0.008	0.007	0.003
N7	0.009	0.003	0.043	-0.039	-0.063	-0.042
C8	-0.060	-0.067	-0.291	0.207	0.099	0.127
N9	-0.009	-0.010	0.249	-0.088	0.000	0.028
O6	-0.003	-0.002	0.166	-0.243	-0.191	0.054
N2	0.049	0.039	-0.008	-0.046	-0.005	-0.049
Cytosine						
N1	-0.202	-0.135	-0.097	0.129	0.095	-0.007
C2	-0.006	-0.029	0.005	0.011	0.004	0.012
N3	0.311	0.256	-0.135	0.187	0.105	-0.043
C4	-0.121	-0.112	0.070	-0.043	-0.043	0.039
C5	0.167	0.079	0.044	0.021	0.175	-0.061
C6	-0.156	-0.118	-0.032	0.000	0.047	-0.078
N4	-0.117	-0.083	0.155	-0.215	-0.136	0.014
O2	0.123	0.142	-0.011	-0.089	-0.011	-0.111
Uracil						
N1	0.104	0.080	-0.090	-0.017	-0.085	0.008
C2	-0.006	-0.001	-0.003	0.000	0.004	0.001
N3	0.024	0.017	-0.006	0.151	0.292	-0.062
C4	-0.017	0.030	-0.008	0.054	0.129	-0.021
C5	-0.286	-0.185	0.202	0.012	0.132	0.001
C6	0.237	0.179	0.235	0.008	-0.013	-0.017
O4	-0.063	-0.136	0.086	-0.178	-0.365	-0.001
O2	0.005	0.016	-0.005	-0.029	-0.124	0.091

a The numbering system of the bases is given in Figure 1.
b The monopoles are scaled to experiments.

Table IV. Data for transition moments

Base	Monopoles	Trans. energy (ev) Theory	Trans. energy (ev) Exptl.[a]	Exptl. trans. moment magnitude[a] eÅ	Exptl. trans. moment magnitude[a] Debye	Calculated trans. vector[b]	Calculated trans. (eÅ)	Transition center[c] (Å) X	Transition center[c] (Å) Y
Adenine		B_{2U}							
	SCF/CI	4.8	4.77	0.813	3.90	+0.02 $\tilde{i}$ + 0.81 $\tilde{j}$		1.24	3.65
	SCF	5.2				-0.14 $\tilde{i}$ - 0.8 $\tilde{j}$		1.02	3.47
	Bush/DeVoe	5.6				-0.22 $\tilde{i}$ + 0.78 $\tilde{j}$		0.96	3.10
		B_{1U}							
	SCF/CI	5.0	5.17	0.35	1.68	-0.14 $\tilde{i}$ - 0.32 $\tilde{j}$		1.21	3.26
	SCF	5.5				-0.34 $\tilde{i}$ + 0.08 $\tilde{j}$		1.41	3.47
	Bush/DeVoe								
Guanine		B_{2U}							
	SCF/CI	4.3	4.47	0.514	2.46	+0.51 $\tilde{i}$ + 0.07 $\tilde{j}$		1.74	2.92
	SCF	4.4				+0.50 $\tilde{i}$ + 0.10 $\tilde{j}$		1.73	2.85
	Bush/DeVoe	5.8				+0.22 $\tilde{i}$ + 0.45 $\tilde{j}$		0.34	2.92
		B_{1U}							
	SCF/CI	5.1	4.94	0.806	3.87	-0.21 $\tilde{i}$ - 0.78 $\tilde{j}$		1.06	3.44
	SCF	5.4				+0.08 $\tilde{i}$ - 0.80 $\tilde{j}$		0.86	3.65
	Bush/DeVoe	4.2				-0.80 $\tilde{i}$ + 0.07 $\tilde{j}$		1.33	3.04
Uracil		B_{2U}							
	SCF/CI	4.8	4.72	0.685	3.29	-0.09 $\tilde{i}$ - 0.68 $\tilde{j}$		0.76	2.94
	SCF	5.1				-0.06 $\tilde{i}$ - 0.68 $\tilde{j}$		0.57	3.27
	Bush/DeVoe	5.2				+0.05 $\tilde{i}$ + 0.68 $\tilde{j}$		0.80	3.01
		B_{1U}							
	SCF/CI	5.4	5.17	0.241	1.16	-0.08 $\tilde{i}$ - 0.23 $\tilde{j}$		-0.50	4.14
	SCF	5.5				+0.04 $\tilde{i}$ - 0.24 $\tilde{j}$		-0.43	3.79
	Bush/DeVoe	6.3				-0.15 $\tilde{i}$ - 0.18 $\tilde{j}$		-1.29	2.52
Cytosine		B_{2U}							
	SCF/CI	4.1	4.57	0.632	3.04	-0.62 $\tilde{i}$ + 0.09 $\tilde{j}$		-0.25	3.02
	SCF	4.2				-0.63 $\tilde{i}$ - 0.04 $\tilde{j}$		-0.47	2.95
	Bush/DeVoe	5.4				+0.18 $\tilde{i}$ + 0.60 $\tilde{j}$		-0.22	3.64
		B_{1U}							
	SCF/CI	5.1	5.17	0.549	2.63	-0.00 $\tilde{i}$ - 0.55 $\tilde{j}$		-0.62	3.49
	SCF	5.3				-0.11 $\tilde{i}$ - 0.54 $\tilde{j}$		-0.09	3.52
	Bush/DeVoe	6.8				+0.40 $\tilde{i}$ + 0.38 $\tilde{j}$		0.06	2.85

(a) Resolved from spectra of Pabst Laboratories.[21]
(b) Transition moment vectors are scaled to experimental magnitude. i, j are unit directional vectors referring to X,Y axes defined in Table I.
(c) Coordinates are defined in Table I.

which is sensitive to the values of bond polarizability should be examined critically.

Different sets of values of bond polarizabilities have been published (Table V). These values include those which have been proven satisfactory for other workers,[10] and those existing in the current literature. The rotational strength of uridine resulting from different combinations of possible values of bond polarizabilities, using the SCF/CI monopoles, is shown in Fig. 3. The calculated R_{0A} is more sensitive to C-O and O-H bond polarizabilities than C-C and C-H bonds. The same conclusion is obtained with the other two sets of monopoles. This is unfortunate because the bond polarizabilities for C-O and O-H bonds are the least well known. For all the computations, unless otherwise stated, we have used Le Fevre's (1955) bond polarizabilities (set II in Table V) and treated carbon and oxygen equivalently (curve 6 in Fig. 3).

IV. Results and Discussion

Results of the calculations are given in Tables VI, VII, VIII, and Fig. 4. The rotational strengths of the B_{2U} and B_{1U} transitions were calculated using equation (11) for each of the four nucleosides (Table VI). The effect of the 2'endo and 3'endo furanose conformation is also included. From the results, it can be seen that the rotational strength calculation depends critically on the choice of wavefunctions. However, the rotational strengths from the SCF/CI and SCF monopoles nearly always agree in sign and magnitude with each other. Quantitative comparison with experiment is difficult, because of the uncertainty in assignment and resolution of the CD spectrum into bands. In Table VI the experimental rotational strengths are given to one significant figure, or the

Table V. Bond Polarizabilities ($Å^3$)

	Bond	α_{33}(a)	α_{11}(a)
I.[22]			
	C-H	0.46	0.77
	C-C	0.99	0.27
	C-O	1.23	0.27
II.[23]			
	C-H	0.8	0.6
	C-C	1.85	0.02
III.[24]			
	C-H	0.64	0.64
	C-C	0.99	0.27
	C-O	0.89	0.46
IV.[25]			
	C-H	0.77	0.59
	C-C	1.35	0.23

(a) α_{33} is along the bond and α_{11} is perpendicular to the bond.

Table VI. Calculated rotational strengths for different monopoles and furanose configurations and conformations. The four ribonucleosides are in the 2'endo conformation.

Compound	Expl. R_{0A} x 10^{40}e.s.u.	Monopoles	Theoretical R_{0A} x 10^{40}e.s.u. B_{2U} Anti	B_{2U} Syn	B_{1U} Anti	B_{1U} Syn
Adenosine	$-2(B_{2U}+B_{1U})$	SCF/CI	-2	+3	+0	+0
		SCF	-2	+3	+2	-4
		Bush-DeVoe	+8	-8		
Guanosine	$-0(B_{2U})$	SCF/CI	+2	-4	-2	+3
	$-1(B_{1U})$	SCF	+2	-4	-2	+2
		Bush-DeVoe	-7	+7	+8	-16
Uridine	$+9(B_{2U})$	SCF/CI	+1	+0	+0	-0
	$-4(B_{1U})$	SCF	+1	+0	-2	+2
		Bush-DeVoe	+2	-1	+0	-1
Cytidine	$+12(B_{2U})$	SCF/CI	+27	-31	-7	+7
	$-6(B_{1U})$	SCF	+19	-24	-5	+5
		Bush-DeVoe	-6	+6	-2	+0
2'deoxy A	$-1(B_{2U}+B_{1U})$					
2' endo		SCF/CI	-2	+4		
3' endo		SCF/CI	-7	+0		
2'deoxy G	$-0(B_{2U})$					
	$-0(B_{1U})$					
2' endo		SCF/CI	+1	-5		
3' endo		SCF/CI	+5	-0		
2'deoxy U						
	$+3(B_{2U})$					
2' endo		SCF/CI	+5	+2		
3' endo		SCF/CI	+3	+1		
2'deoxy C	$+ (B_{2U})$					
	$- (B_{1U})$					
2' endo		SCF/CI	+24	-34		
3' endo		SCF/CI	+35	+0		

Table VII. Comparison of calculated and experimental rotational strengths for different anomeric adenosines

Compound	λ_{max} (mμ)	Exptl. Maximum molar ellipticities[a]	$R_{0A}(B_{2U}) \times 10^{+40}$ e.s.u. Expt.[a,b]	Theory[d] anti	syn
α-Lyx	260	3750	2.7 (c)	3	-7
β-Lyx	256	-3560	-2.7	-2	6
α-Ribo	256	5410	4.4	3	-6
β-Ribo	265	-2970	-2.5 (c)	-2	3
α-Ara	258	3570	2.8	1	-6
β-Ara	258	-5380	-4.1	-2	4
α-Xyl	258	6960	6.0	5	-7
β-Xyl	259	-2450	-2.0	-3	5

(a) The experimental results from Ingwall[28]. Molar ellipticities are in units of deg ℓ/mole cm.

(b) The rotational strengths are evaluated by fitting the spectrum by Gaussian curves on a duPont curve resolver and computed using the formula, $R_i = 1.23 \times 10^{-42} (\theta_i \Delta_i/\lambda_i)$ where Δ_i is the half width of the resolved Gaussian.

(c) Single Gaussian is not possible. Composite Gaussian curves are used. See Ref. 24.

(d) SCF/CI monopoles used.

Table VIII. Calculated $R_{OA}(B_{2U})$ of nucleosides[a] with glycosidic angle ϕ_{CN} present in polynucleotides

Base	$R_{OA}(B_{2U}) \times 10^{+40}$ e.s.u.		
	ϕ_{CN}[b] = -11° (RNA-11)	-14° (DNA-A)	-86° (DNA-B)
A	-3	-3	+5
G	+1	+1	-1
U (T)	+2	+6	+1
C	+31	+32	-25

(a) SCF/CI monopoles and 2'endo conformation for ribose and deoxyribose were used.

(b) ϕ_{CN}'s are from Ref. (26).

sign is simply given. The calculated values are shown for two conformations: anti (ϕ_{CN} = -30°) and syn (ϕ_{CN} = +150°). The experimental value, of course, represents an average value over the conformations actually present in solution. With SCF/CI or SCF monopoles the signs of the calculated rotational strengths for the first two transitions are consistent with three of the four mononucleosides in the anti conformation. Calculations for guanosine are not consistent with experiment for either syn or anti conformations.

Fig. 4 shows what values of the glycosidic angle give correct results for the calculated signs of the B_{2U} and B_{1U} rotational strengths. For uridine and cytidine about half the possible range of angles (+150° $\geq \phi_{CN} \geq$ -30°) give the correct sign for both B_{2U} and B_{1U}. For adenosine only the anti range (-10° $\geq \phi_{CN} \geq$ -90°) is consistent with the signs of the rotational strengths. For guanosine a very small overlap occurs ($\phi_{CN} \approx$ -100°) between values of ϕ_{CN} which give the correct sign for both B_{2U} and B_{1U} rotational strengths. This probably indicates that guanosine does not exist mainly in one conformation, but instead, includes a wide range of conformations. There is some evidence that the conformation of guanosine depends on pH, as might be expected for a conformationally mobile molecule.

One way of testing this idea further is to calculate an average rotational strength by weighting each calculated rotational strength at angle ϕ_{CN} by the probability of finding the molecule with this value of ϕ_{CN}. We used a probability distribution for the glycosidic bond (ϕ_{CN}), which we had estimated earlier,[27] to obtain an average rotational strength for the B_{2U} transitions for each mononucleoside. Although

magnitudes were changed, no signs changes, so a positive B_{2U} rotational strength was still obtained for guanosine in disagreement with experiment.

The temperature dependence of the rotational strengths was also calculated. This gives an increase in rotational strengths with decreasing temperature as expected. It also gives the correct order of magnitude change[13] as the temperature is lowered from +90°C to -70°C. For cytidine there is a calculated 3% increase, for adenosine a calculated 30% increase.

In Table VII the results for the anomeric cis-trans isomers of adenosine are given. The calculated results for the anti conformation agree well with experiment. The agreement between theory and experiment is excellent when one considers the α and β pairs of the different isomers. The calculation gives not only the correct sign for each one of the pairs, but also provides the correct relative magnitudes. We see that experimentally the sign of the CD for the anomeric adenosine depends on the configuration at carbon C1': α gives a positive CD at high wavelength, β gives a negative CD. The good agreement with the calculated rotational strenghts is strong evidence that all eight of these molecules are primarily in anti conformation.

We also carried out calculations on uracil with different sugars. Experimentally,[29] it was found the rotational strengths of β-D-ara-U and β-D-lyx-U were similar and approximately twice that of β-D-rib-U. The R_{OA} calculated for these compounds are $+10 \times 10^{-40}$, $+11 \times 10^{-40}$, and $+2 \times 10^{-40}$ for ara, lyx and rib U respectively. The Bush/DeVoe monopoles were used and anti conformation was assumed.

We have found that a configuration change at the C2' position of the furanose alters the glycosidic angular dependence of R_{OA} more significantly

than that at the C3' position. The calculated R_{0A} vs. ϕ_{CN} for ribo and xyl compounds are similar in curve shape, positions of maximum, minimum and zero crossing, whereas the same holds for ara and lyx compounds. Experimentally, it was found that the configuration at C2' profoundly affects the magnitude of the Cotton effect.[8,28,29] It was reported previously[30] that a cis-oriented hydroxyl group at C2' interacts with the base and that cis-nucleosides gave a Cotton effect larger in magnitude than the trans anomers. It was found that[29] the amplitudes of the Cotton effect of α-D-rib-U, α-D-UMP are larger than their β-anomers; however, the magnitudes of α-lyx nucleosides give smaller Cotton effects compared to their β-anomers. Examination of molecular model suggests that the C1'-C2' trans configuration allows the base to rotate more freely about the glycosidic bond. By inspection of the R_{0A} vs. ϕ_{CN} curve, it can be seen that a range of allowed values of ϕ_{CN} always results in decreasing the amplitude of a trans compound.

The main reason for beginning this study was to estimate the contribution of base-sugar interactions to the CD of polynucleotides. Table VIII shows the calculated B_{2U} rotational strengths for nucleosides with the glycosidic angle found in different double-stranded nucleic acids: A-form DNA,[31] B-form DNA[32] and RNA-II.[33] One sees that in B-form DNA the calculated rotational strengths are very different from those of A-DNA, RNA, or anti mononucleosides. This means one cannot ignore base-sugar interactions in understanding the CD of double-stranded nucleic acids. The CD of the mononucleoside in solution may be very different from its contribution to the CD of the nucleic acid.

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FIGURE CAPTIONS

Figure 1. Nomenclatures and configurations of the nucleic acid bases and the pentafuranoses.

Figure 2. The effect of different transition monopoles and the self-consistent treatment of furanose bonds on $R_{B(2U)}$ vs. ϕ_{CN} of uridine. The top three curves are self-consistently treated as in equation (11). The bottom three curves are without the self-consistent furanoise treatment [equation (8)].

Figure 3. Calculated rotational strengths of B_{2U} transitions of uridine as a function of ϕ_{CN} using different values of polarizabilities. The various sets of polarizabilities are given in Table V.

(1) Set I, treating OH equivalent to CH;

(2) set III, treating OH equivalent to CH;

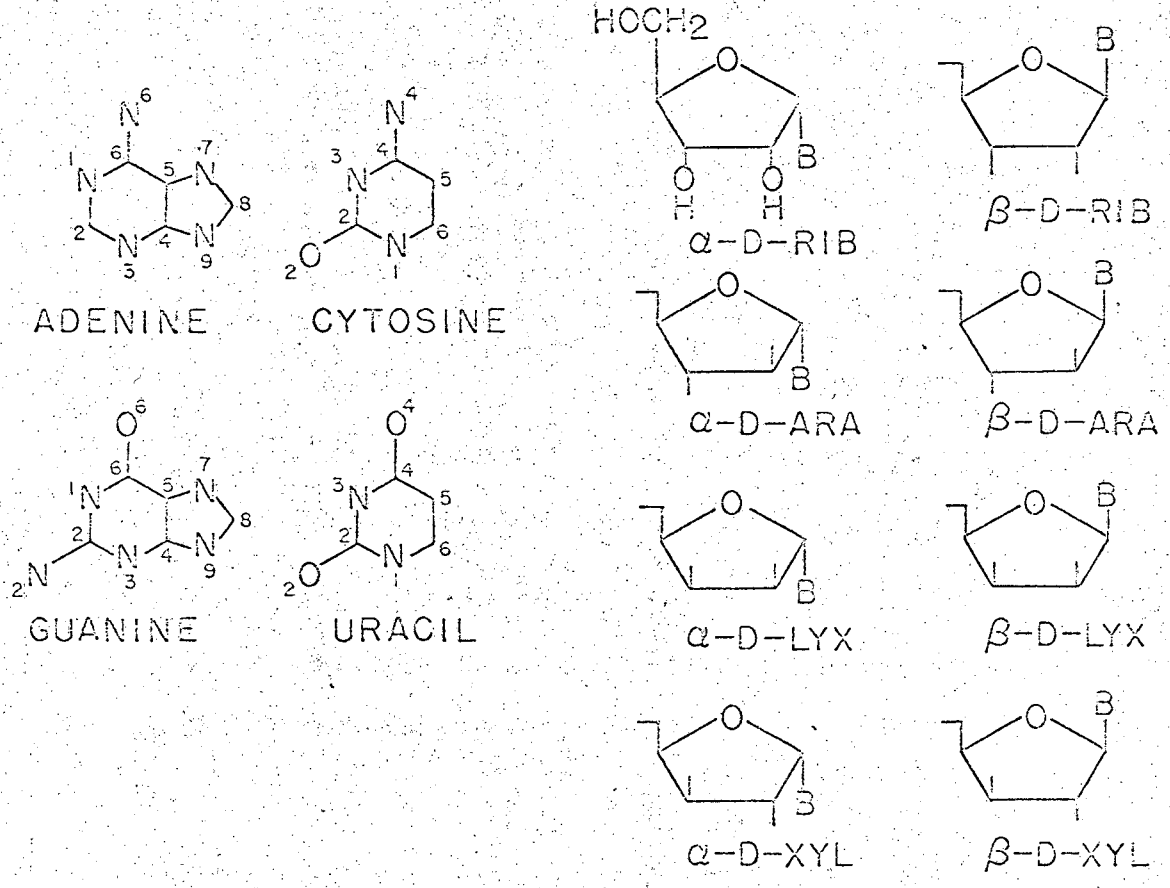
(3) set II, approximating OH by α_{33}=0.8, α_{11}=0.6;

(4) set IV, treating OH equivalent to CH and CO equivalent to CC;

(5) set I, approximating OH by 0.8, 0.6;

(6) set II, treating OH equivalent to CH and CO equivalent to CC.

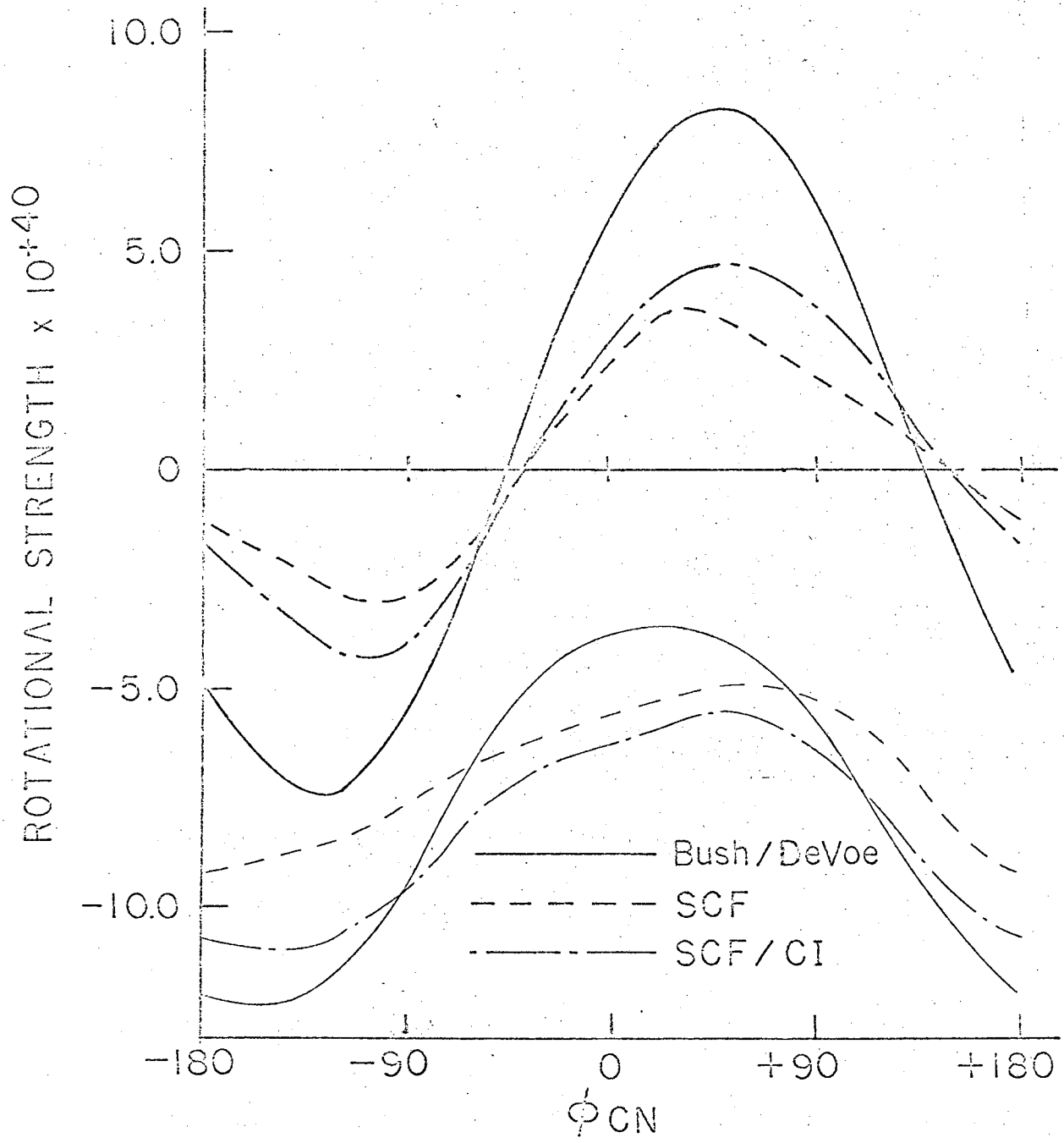
Figure 4. Glycosidic angle (ϕ_{CN}) and calculated sign of the rotational strength. The range of angles labeled α,β-purines and pyrimidines shown are those found in crystals by X-ray scattering (Ref. 26). The rotational strengths were calculated with SCF/CI monopoles. (a) Purines, the measured signs of the rotational strengths are minus for both B_{2U} and B_{1U} transitions of adenosine and guanosine; (b) pyrimidines, the measured signs are plus for the B_{2U} transitions and minus for the B_{1U} transitions of uridine and cytidine.



CONFIGURATION OF THE NUCLEIC ACID BASES AND THE PENTOFURANOSES

XBL709-5401

Figure 1


10.0
5.0
0
-5.0
-10.0
ROTATIONAL STRENGTH x 10⁺⁴⁰
Bush / DeVoe
SCF
SCF / CI
-180
-90
0
+90
+180
φ CN

XBL709-5404

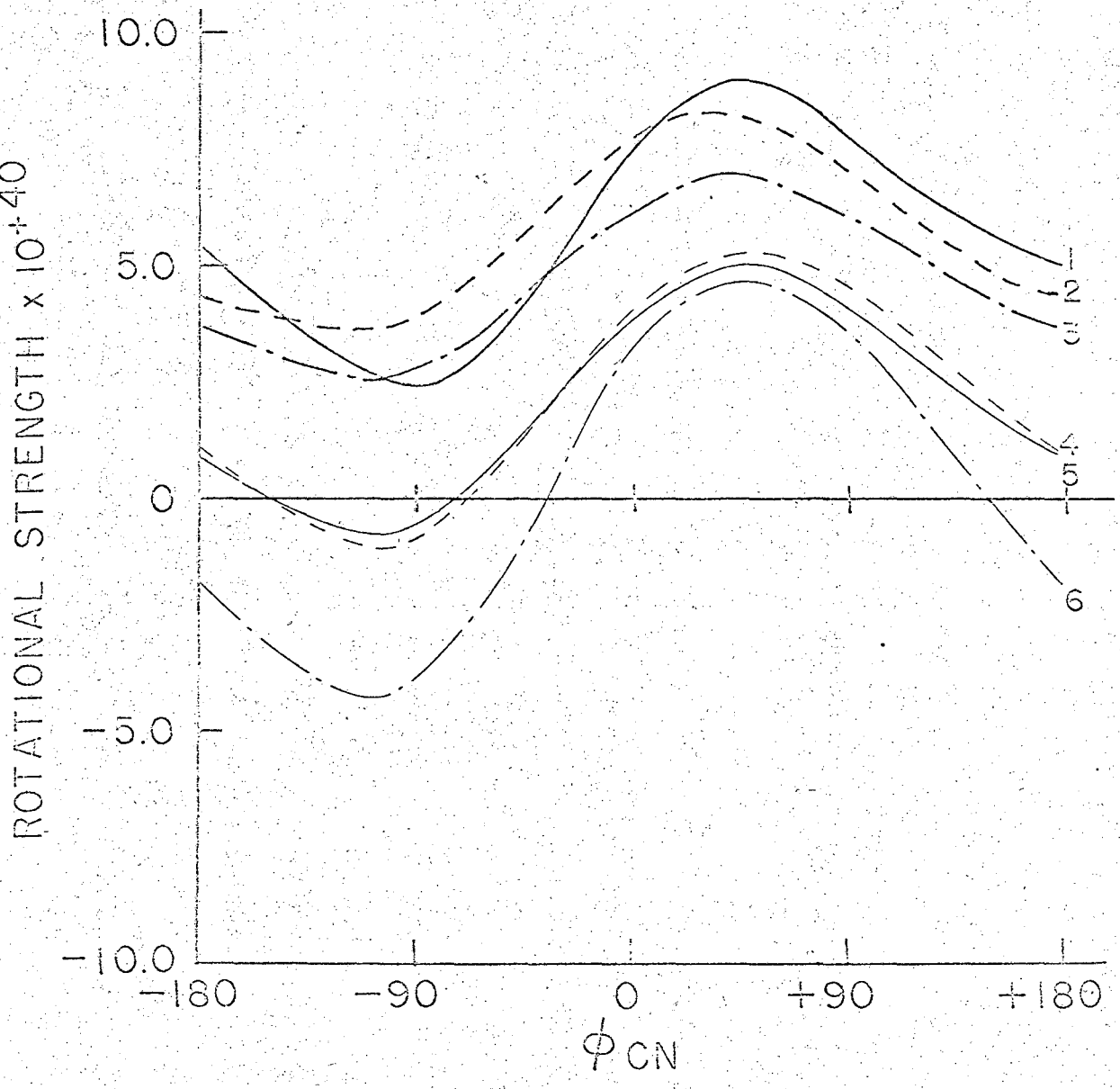


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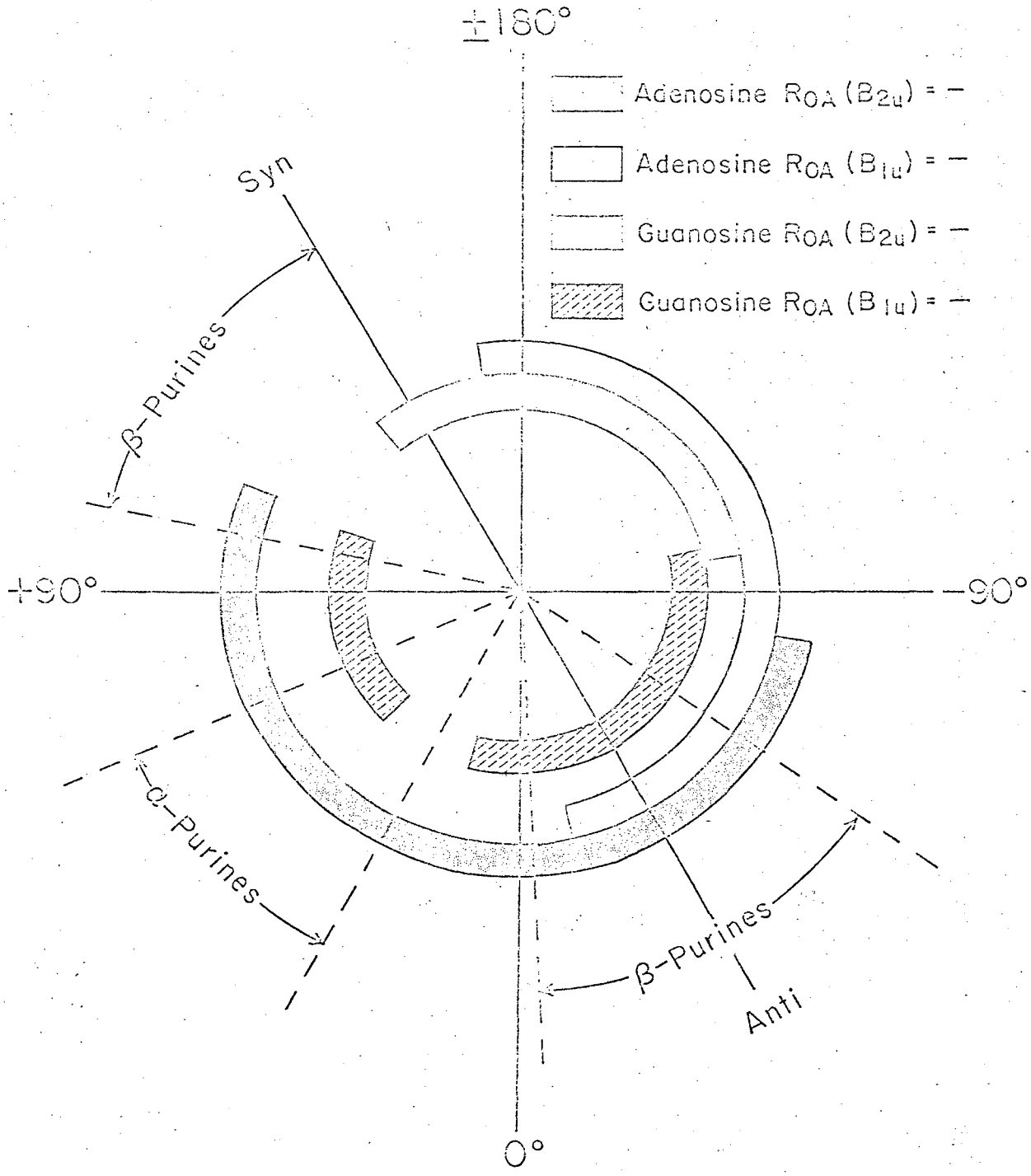
Figure 3



XBL 7012-4956

Figure 4a

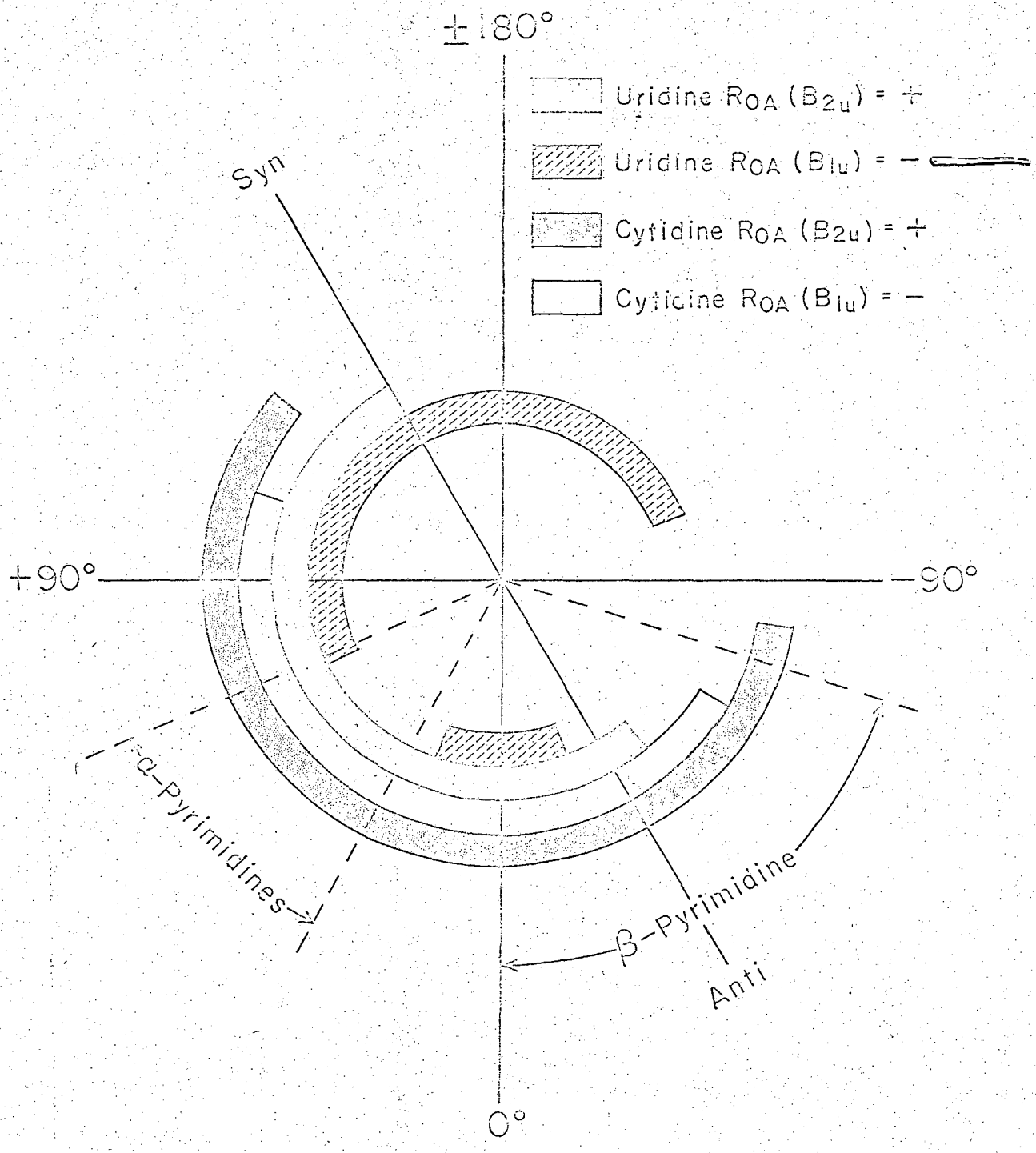

±180°
Uridine ROA (B2u) = +
Uridine ROA (B1u) = −
Cytidine ROA (B2u) = +
Cytidine ROA (B1u) = −
Syn
+90°
−90°
α-Pyrimidines
β-Pyrimidine
Anti
0°
XBL7012-4957

Figure 4b

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LAWRENCE RADIATION LABORATORY
UNIVERSITY OF CALIFORNIA
BERKELEY, CALIFORNIA 94720