guanines with relative rates of 0.03 and 0.06 that of the major site of reaction. Apparently, there exists sufficient flexibility in the linker arm and/or the junction of the local triple-helical complex to access all three guanine bases for modification to some extent.[19]

A plot of ln $[DNA]_{intact}/[DNA]_{total}$ vs time (pseudo-first-order conditions) indicates that the reaction between bromoacetyl-oligonucleotide **3** and the double-helical DNA is first order in target DNA concentration with a pseudo-first-order rate constant of 3.1×10^{-5} s^{-1} at 37 °C. This corresponds to a half-life for alkylation within the triplex of 6.2 h (37 °C).[20] Separate experiments with *N*-iodoacetyl- and chloroacetyloligonucleotides indicate that these moieties react with relative rates of $k_{iodo}/k_{bromo} = 0.2$ and $k_{chloro}/k_{bromo} = 0.06$. The slower rates of reaction for both the chloroacetyl and iodoacetyl derivatives parallel the relative rates at N-3 of adenine seen with the reactions of *N*-bromo-, chloro-, and iodoacetyldistamycin bound in the minor groove of double-helical DNA.[6c]

In conclusion, this work demonstrates that a nondiffusible electrophile judiciously attached to the 5'-end of an oligonucleotide is capable of modification of intact double-helical DNA at a single base position in high yield.[19] Because the oligonucleotide-directed triple-helix motif is sufficiently generalizable and specific for the recognition of single sites in genomic DNA,[22] modification of a single base within megabase-sized chromosomes using strictly chemical methods should be possible.

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(19) Undoubtedly there will be sequence composition effects, which will make the absolute and relative rates of reaction vary. By replacement of the targeted sequence 5'-GGG-3' with 5'-(A,T,C)G(A,T,C)-3' proximal to the triplex binding site, reaction at a single base position (G) would be expected.

(20) For a report on modification of duplex DNA by 5'-*p*-[*N*-(2-chloroethyl)-*N*-(methylamino)]benzamide of oligodeoxyribonucleotide, $ClRCH_2NH(dC)_n$ (n = 9, 15) at pH 4.5 see: (a) Fedorova, O. S.; Knorre, D. G.; Podust, L. M.; Zarytova, V. F. *FEBS Lett.* **1988**, *228*, 273. (b) Vlassov, V. V.; Gaidamakov, S. A.; Zarytova, V. F.; Knorre, D. G.; Levina, A. S.; Nekona, A. A.; Podust, L. M.; Fedorova, O. A. *Gene* **1988**, *72*, 313.

(21) Iverson, B. L.; Dervan, P. B. *Nucleic Acids Res.* **1987**, *15*, 7823.

(22) (a) Strobel, S. A.; Moser, H. E.; Dervan, P. B. *J. Am. Chem. Soc.* **1988**, *110*, 7927. (b) Strobel, S. A.; Dervan, P. B. *Science* **1990**, *249*, 73.

Vibrationally Induced Ring Currents? The Vibrational Circular Dichroism of Methyl Lactate

R. Bursi, F. J. Devlin, and P. J. Stephens*

Department of Chemistry
University of Southern California
Los Angeles, California 90089-0482

Received April 9, 1990

It has recently been proposed that ring currents contribute significantly to the magnetic dipole transition moments and rotational strengths of the vibrational transitions of chiral molecules containing rings.[1] This hypothesis has been the basis for the interpretation of the vibrational circular dichroism (VCD) spectra of a variety of molecules.[2] It has been invoked most extensively in studies of molecules capable of ring formation via intramolecular hydrogen bonding (H bonding).

We have recently developed[3] and implemented ab initio[4] an a priori theory of vibrational rotational strengths. Comparisons of predicted and experimental VCD spectra have exhibited substantial agreement.[5] This theory provides a general basis for the

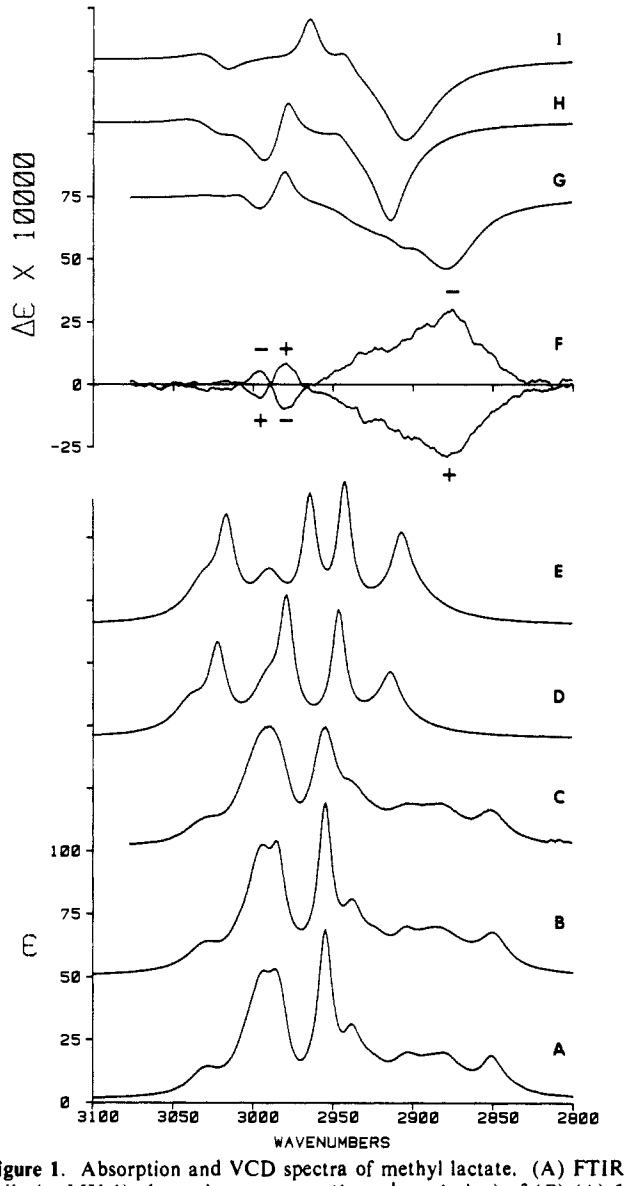

Figure 1. Absorption and VCD spectra of methyl lactate. (A) FTIR (Nicolet MX-1) absorption spectrum (1-cm^{-1} resolution) of (*R*)-(+)-**1** (Aldrich) (0.015 M in CCl_4). (B) Lorentzian fit to A. (C) Absorption spectrum of (*R*)-(+)-**1** under VCD measurement conditions (see F). (D) Absorption spectrum predicted for **1a** (γ values from Table I). (E) Absorption spectrum predicted for **1b** (γ values as in D). (F) VCD spectra of (*R*)-(+)- and (*S*)-(−)-**1** (Aldrich; $[\alpha]^{21}_D$(neat) = +8.1° and −8.4°, respectively). VCD measured by using instrumentation previously described.[10] Resolution 9.6 (at 2800) to 11.7 (at 3100) cm^{-1}. (G) Lorentzian fit to F for (*R*)-(+)-**1**. (H) VCD spectrum predicted for (*R*)-**1a** (γ values from G). (I) VCD spectrum predicted for (*R*)-**1b** (γ values as in H).

(1) (a) Nafie, L. A.; Oboodi, M. R.; Freedman, T. B. *J. Am. Chem. Soc.* **1983**, *105*, 7449. (b) Oboodi, M. R.; Lal, B. B.; Young, D. A.; Freedman, T. B.; Nafie, L. A. *J. Am. Chem. Soc.* **1985**, *107*, 1547. (c) Freedman, T. B.; Balukjian, G. A.; Nafie, L. A. *J. Am. Chem. Soc.* **1985**, *107*, 6213. (d) Nafie, L. A.; Freedman, T. B. *J. Phys. Chem.* **1986**, *90*, 763.

(2) Freedman, T. B.; Nafie, L. A. In *Topics in Stereochemistry*; Eliel, E. L., Wilen, S. H. Eds.; Wiley: New York, 1987; Vol. 17, pp 113-206 and references therein.

(3) Stephens, P. J. *J. Phys. Chem.* **1985**, *89*, 748; **1987**, *91*, 1712.

(4) (a) Lowe, M. A.; Segal, G. A.; Stephens, P. J. *J. Am. Chem. Soc.* **1986**, *108*, 248. (b) Amos, R. D.; Handy, N. C.; Jalkanen, K. J.; Stephens, P. J. *Chem. Phys. Lett.* **1987**, *133*, 21. (c) Amos, R. D.; Jalkanen, K. J.; Stephens, P. J. *J. Phys. Chem.* **1988**, *92*, 5571.

(5) (a) Lowe, M. A.; Stephens, P. J.; Segal, G. A. *Chem. Phys. Lett.* **1986**, *123*, 108. (b) Jalkanen, K. J.; Stephens, P. J.; Amos, R. D.; Handy, N. C. *J. Am. Chem. Soc.* **1987**, *109*, 7193. (c) Jalkanen, K. J.; Stephens, P. J.; Amos, R. D.; Handy, N. C. *J. Am. Chem. Soc.* **1988**, *110*, 2012. (d) Kawiecki, R. W.; Devlin, F.; Stephens, P. J.; Amos, R. D.; Handy, N. C. *Chem. Phys. Lett.* **1988**, *145*, 411. (e) Kawiecki, R. W. Ph.D. Thesis, University of Southern California, 1988. (f) Stephens, P. J. *Croat. Chem. Acta* **1989**, *62*, 429. (g) Jalkanen, K. J. Ph.D. Thesis, University of Southern California, 1989. (h) Kawiecki, R. W.; Devlin, F.; Stephens, P. J.; Amos, R. D. *J. Phys. Chem.*, in press. (i) Devlin, F.; Jalkanen, K. J.; Stephens, P. J.; Polonski, T. To be submitted. (j) Jalkanen, K. J.; Stephens, P. J.; El-Azhary, A.; Keiderling, T. A., to be submitted. (k) Bursi, R.; Devlin, F. J.; Forni, A.; Stephens, P. J., to be submitted.

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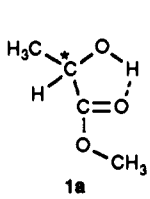
Table I. Frequencies and Dipole and Rotational Strengths of Methyl Lactate[a]

1a											1b		
unscaled calcn[b]			scaled calcn[b,c]			C–H	expt[d]				scaled calcn[b,f]		
$\bar{\nu}$	D	R	$\bar{\nu}$	D	R	stretching mode	$\bar{\nu}$	D	R	γ^e	$\bar{\nu}$	D	R
3357*	27.9	1.1	3039	30.8	1.1	O–CH_3 as	3031*	11.1	0.5	13.0	3031	36.7	1.4
3339	32.6	−0.7	3022	36.0	−0.7	O–CH_3 as	3009	2.0	0.9	6.2	3016	40.3	−1.2
3305*	30.7	−5.1	2992	34.0	−5.1	*C–CH_3 as	2995*	43.3	−2.2	10.5	2990	32.8	0.3
3291*	43.6	3.0	2979	48.2	3.0	*C–CH_3 as	2984*	14.7	2.4	5.3	2964	46.1	3.0
3255*	40.2	0.7	2946	44.4	0.7	O–CH_3 ss	2955*	29.8	0.0	5.1	2943	49.4	1.3
							2938	13.7	−0.7	7.6			
							2924	7.9	−2.5	10.4			
3221*	41.5	−12.3	2916	45.9	−12.3	*C–H	2885*	38.1	−15.8	22.7	2903	58.6	−16.2
3219	17.8	−4.0	2914	19.7	−4.0	*C–CH_3 ss	2905	4.1	−1.4	6.9	2907	30.8	−1.1
							2849	13.0	0.2	10.5			

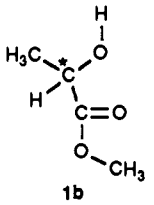
[a] $\bar{\nu}$ and γ in cm^{-1}, D in 10^{-40} esu^2 cm^2, R in 10^{-44} esu^2 cm^2. Rotational strengths are for the R enantiomer. [b] Calculations were carried out as described previously.[4,5] Ab initio calculations were carried out by using a CRAY-XMP version of CADPAC (version 4.0). [c] Scaling used asterisked calculated and experimental frequencies; the scale factor is 0.819; the RMS deviation of calculated and experimental frequencies is 15 cm^{-1}. [d] See Figure 1 for experimental details. [e] Lorentzian bandwidth parameter;[5d] values are from fit to 1-cm^{-1}-resolution absorption spectrum (Figure 1B). [f] Scale factor 0.819.

interpretation of VCD spectra. Here it is used to examine the "ring-current mechanism" of VCD, specifically for the methine stretching mode of methyl lactate (**1**), a molecule exhibiting internal H bonding when dilute in nonpolar solvents. We compare the VCD predicted for internally H bonded **1** and for the analogous conformation of **1** in which the internal H bond is broken. The reliability of the calculations for the former conformer is assessed by comparison to experiment.

The C–H stretching absorption and VCD spectra of **1** in CCl_4 are presented in Figure 1. Infrared spectroscopy of **1**, dilute in CCl_4, indicates preponderant internal H bonding to carbonyl O (**1a**):[6]



1a



1b

Ab initio SCF 6-31G*[7] geometry optimizations of several conformers of **1**[8] find **1a** to be lowest in energy and (i) the methoxy C to be cis to carbonyl O and (ii) the *C(OH)COOC moiety to be planar. Comparison of predicted absorption and VCD spectra of the various conformers of **1** to experimental spectra confirms that **1a** is indeed the preponderant conformer.[8] For **1a** the C–H stretching frequencies, dipole strengths, and rotational strengths predicted from the 6-31G* SCF force field, atomic polar tensors, and atomic axial tensors (the last in the distributed origin gauge[3,4]) are given in Table I. The calculations permit assignment of the experimental spectra. The strong absorption and bisignate VCD at ~2990 cm^{-1} are assigned to the two *C–CH_3 asymmetric CH_3 stretches. The weaker absorption at 3031 cm^{-1} having barely detectable VCD is assigned to the higher of the OCH_3 asymmetric CH_3 stretches; the lower is placed under the *C–CH_3 absorption. The absorption and strong VCD at 2885 cm^{-1} are assigned to the *C–H stretch. The absorptions at 2955 and 2905 cm^{-1} are attributed to the OCH_3 and *C–CH_3 symmetric stretches, respectively. Other features are assigned as overtone/combination bands. Lorentzian fits[5d] to the experimental spectra shown in Figure 1 yield the frequencies, dipole and rotational strengths in Table I. Uniform scaling of the SCF force field using experimental C-H stretching frequencies gives the frequencies and dipole and rotational strengths in Table I. The frequencies are now in the experimental range; the pattern of dipole and rotational strengths is unaffected. Predicted C–H stretching frequencies could be brought into closer agreement with experiment by further scaling[9] of the force field.[8] However, this would be of arguable significance in view of the probable importance of anharmonicity to these experimental frequencies. Spectra obtained by using predicted frequencies, dipole and rotational strengths, and experimental bandwidths are shown in Figure 1. Overall, except for the consequences of anharmonicity, calculation and experiment agree well. In particular, the principal features of the VCD spectrum are reproduced.

Table II. *C–H Stretching Rotational Strengths of Methyl Lactate and Methyl Lactate-d_6[a]

	R_{xx}	R_{yy}	R_{zz}	R
1a	1.3	−18.5	4.9	−12.3
1a-d_6	1.9	−26.6	7.8	−16.9
1b	6.7	−24.2	1.4	−16.2
1b-d_6	10.0	−30.2	11.7	−8.6

[a] Rotational strengths in 10^{-44} esu^2 cm^2 are for R enantiomers and are independent of (uniform) scaling. $R_{\alpha\alpha}$ gives the contribution to R of the α-components of the electric and magnetic dipole transition moments. The C(OH)COOC moiety is (to a very good approximation) in the xz plane. The origin is the center of mass of **1a** or **1b**.

The *C–H stretch has the largest rotational strength of the seven C–H stretching modes of **1**. The predicted (-1.07×10^{-4}) and observed (-1.66×10^{-4}) anisotropy ratios ($4R/D = \Delta\epsilon/\epsilon$) are in excellent agreement. The "ring-current hypothesis" would attribute this rotational strength predominantly to ring current induced in the internally H bonded ring by the *C–H stretching motion.[1,2] The predominance of the contribution to the rotational strength of the electric and magnetic dipole transition moment components perpendicular to the ring, R_{yy} (Table II), is consistent with this hypothesis. Prediction of the VCD spectrum of the conformer of **1** most similar to **1a** but not possessing an internally H bonded ring, **1b**, provides a further test. The geometry of **1b** is virtually superposable on that of **1a** except for the rotation of the hydroxyl H by ~180°.[8] **1b** is predicted to be 5.0 kcal/mol more energetic than **1a**, consistent with the loss of a H bond. The geometry of **1b** shows that the *C(OH)COOC moiety of **1a** is not planar *because of* the H bond. Predicted frequencies, dipole and rotational strengths, and absorption and VCD spectra of **1b** are given in Table I and Figure 1. The predicted spectra of **1a** and **1b** are similar. The rotational strength and VCD of the *C–H stretch are predicted to be even larger in **1b** than in **1a**. As shown in Table II, R_{yy} is also larger in **1b** than in **1a**. Thus, the large VCD of the *C–H stretch of **1a**, and, in particular, the large contribution of R_{yy}, does not owe its existence to the presence of the internally H bonded ring.

(6) Mori, N.; Omura, S.; Kobayashi, N.; Tsuzuki, Y. *Bull. Chem. Soc. Jpn.* **1965**, *38*, 2149.
(7) Hehre, W. J.; Radom, L.; Pople, J. A.; Schleyer, P. v. R. *Ab Initio Molecular Orbital Theory*; Wiley: New York, 1986.
(8) Bursi, R.; Devlin, F.; Stephens, P. J., to be submitted.
(9) Fogarasi, G.; Pulay, P. *Annu. Rev. Phys. Chem.* **1984**, *35*, 191; *Vib. Spectra Struct.* **1985**, *14*, 125.
(10) (a) Nafie, L. A.; Keiderling, T. A.; Stephens, P. J. *J. Am. Chem. Soc.* **1976**, *98*, 2715. (b) Stephens, P. J.; Clark, R. In *Optical Activity and Chiral Discrimination*; Mason, S. F.; Ed.; D. Reidel Pub.: Dordrecht, 1979; p 263. (c) Devlin, F.; Stephens, P. J. *Appl. Spectrosc.* **1987**, *41*, 1142.

The coupling of the *C-H stretch and other C-H stretching coordinates in **1a** and **1b** is removed by deuteration of their methyl groups. Calculations for **1a**-d_6 and **1b**-d_6 (Table II) also predict large *C-H stretching VCD in both conformers. In particular, R_{yy} is again large in both conformers and larger in **1b**-d_6 than in **1a**-d_6. We therefore predict that study of the (simpler) C-H stretching absorption and VCD spectra of **1**-d_6 will yield identical conclusions.

VCD of magnitude comparable to that of the *C-H stretch of methyl lactate has been observed in the *C-H stretches of similar molecules and attributed to intramolecular ring currents around internally H bonded rings.[1,2] Our results are in direct conflict with these analyses and lead to the conclusion that large methine stretch VCD cannot be uniquely correlated with the presence of a ring. More generally, our results do not support the invocation of the "ring-current mechanism" in the elucidation of the unknown stereochemistry of chiral molecules from their VCD spectra.

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Probing Microstructures in Double-Helical DNA with Chiral Metal Complexes: Recognition of Changes in Base-Pair Propeller Twisting in Solution

Anna Marie Pyle,† Takashi Morii, and Jacqueline K. Barton*

Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, California 91125

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That DNA base pairs are propeller twisted in a sequence-dependent manner has been evident only in viewing crystal structures of oligonucleotides.[1-7] Here we report that shape-selective DNA-binding molecules can recognize and distinguish propeller twisted DNA sites in solution on the basis of shape and symmetry. Enantioselective discrimination is apparent in photocleavage by $Rh(phen)_2phi^{3+}$ (phen = 1,10-phenanthroline; phi = 9,10-phenanthrenequinone diimine) at 5′-pyr-pyr-pur-3′ steps which are characterized by a high degree of differential propeller twist[8] but not at homopyrimidine-homopurine segments. Neither isomer targets 5′-pur-pyr-3′ steps.

Previously we reported that $Rh(phen)_2phi^{3+}$, which binds DNA avidly by intercalation and upon photolysis promotes DNA strand scission, targets DNA sites where the major groove is open and accessible.[9,10] *rac*-$Rh(phen)_2phi^{3+}$ primarily targets two families of sequences, 5′-pyr-pyr-pur-3′ segments,[2,5,6,11-13] and homopyrimidine sites.[5,14,15] Resolution of $Rh(phen)_2phi^{3+}$ into its Δ and Λ enantiomers yields mirror-image probes with different specificities for these two target sequences. As can be seen in parts A and B of Figure 1, the Δ isomer cleaves strongly at the 5′-CCAG-3′ sequences and throughout the homopyrimidine region while both Δ and Λ isomers cleave to equivalent extents in the homopyrimidine segments of the fragment. The chiral discrimination evident at 5′-pyr-pyr-pur-3′ steps must therefore result from sensing an asymmetry in these steps which is absent at homopyrimidine-homopurine sites.

Cleavage by the enantiomers was next examined on the well-characterized dodecamer[3,13] $d(CGCGAATTCGCG)_2$ (Figure 1C,D). Here, Δ-$Rh(phen)_2phi^{3+}$ cleaves predominantly at the C9 site whereas the Λ isomer cleaves only weakly at C9. The high level of enantioselectivity is understandable since this C9-G10 step has the highest associated differential propeller twist (-11.8°) within the dodecamer. This high differential propeller twist creates a large chiral pocket in the major groove. The cleavage seen at T8 can be accounted for in terms of base tilting (1.1° at T8 and 1.6° at A17) which opens the major groove,[14] and here, where the differential propeller twist is -1.0°, there is no associated enantioselectivity. Helical twist provides the only alternate structural parameter which is intrinsically chiral,[16] but helical twisting cannot account for the chiral discrimination observed here. On the basis of the chirality of helical twisting, we would expect[17,18] low enantioselectivity at the C9-G10 step, which is undertwisted (32.3°), and high enantioselectivity at the G10-C11 step, which is overtwisted (44.7°), contrary to what we observe. Instead, therefore, *the chiral discrimination in site recognition must depend upon the asymmetry associated with propeller twisting.*

It is curious that intercalation which itself produces a structural perturbation at the binding site is still able to sense propeller twisting. Likely the propeller twisting is stabilized by the stacking of purine bases. Perhaps intercalative stacking reinforces this.[19]

The chiral discrimination apparent in the recognition of sites with large differential propeller twist and the absence of such discrimination at homopyrimidine segments which lack differential propeller twisting reflect the different symmetries associated with these steps. The 5′-pyr-pur-3′ step, in contrast to the 5′-pyr-pyr-3′ step, contains a C_2 axis, the basis for chiral discrimination, perpendicular to the helix along the pseudodyad axis. As shown in Figure 2, the propeller twist of purines at the 5′-pyr-pur-3′ site is disposed in an orientation that permits facile intercalation by Δ-$Rh(phen)_2phi^{3+}$, but the alignment of the ancillary phenanthroline ligands in the Λ isomer, with a contrary orientation

* To whom correspondence should be addressed.
† Present address: Department of Chemistry and Biochemistry, University of Colorado, Boulder, CO 80309.

(1) Saenger, W. *Principles of Nucleic Acid Structure*; Springer-Verlag: New York, 1984.
(2) Wing, R.; Drew, H.; Takano, T.; Broka, C.; Tanaka, S.; Itakura, K.; Dickerson, R. E. *Nature* **1980**, *287*, 755-758. Wang, A. H.-J.; Fujii, S.; van Boom, J. H.; Rich, A. *Proc. Natl. Acad. Sci. U.S.A.* **1982**, *79*, 3968-3972. Shakked, Z.; Rabinovich, D.; Cruse, W. B. T.; Egert, E.; Kennard, O.; Sala, G.; Salisbury, S. A.; Viswamitra, M. A. *Proc. R. Soc. London, B* **1981**, *231*, 479-487.
(3) Dickerson, R. E. *J. Mol. Biol.* **1983**, *166*, 419-441.
(4) Calladine, C. R. *J. Mol. Biol.* **1982**, *161*, 343-352.
(5) Coll, M.; Frederic, A.; Wang, A. H. J.; Rich, A. *Proc. Natl. Acad. Sci. U.S.A.* **1987**, *84*, 8385-8389. Nelson, H. C.; Finch, J. T.; Luisi, B. F.; Klug, A. *Nature* **1987**, *330*, 221-226.
(6) Timsit, Y.; Westhof, E.; Fuchs, R. P. P.; Moras, D. *Nature* **1989**, *341*, 459-462.
(7) Nadeau, J. G.; Crothers, D. M. *Proc. Natl. Acad. Sci. U.S.A.* **1989**, *86*, 2622-2626. Banks, K. M.; Hare, D. R.; Reid, B. R. *Biochemistry* **1989**, *28*, 6996-7010.
(8) We define differential propeller twist as the angle between the two purine bases projected onto the plane defined by the helical and dyad axes.
(9) Pyle, A. M.; Long, E. C.; Barton, J. K. *J. Am. Chem. Soc.* **1989**, *111*, 4520-4522. Uchida, K.; Pyle, A. M.; Morii, T.; Barton, J. K. *Nucleic Acids Res.* **1989**, *17*, 10259-10265.
(10) Both spectroscopic analyses on phi complexes of ruthenium and product analyses after cleavage by phi complexes of rhodium(III) are consistent with a single intercalative interaction in the major groove of the helix. See: Pyle, A. M.; Rehmann, J. P.; Meshoyrer, R.; Kumar, C. V.; Turro, N. J.; Barton, J. K. *J. Am. Chem. Soc.* **1989**, *111*, 3051. Pyle, A. M. Ph.D. Dissertation, Columbia University, 1989. Long, E. C.; Absalon, M. J.; Stubbe, J. A.; Barton, J. K., submitted for publication.
(11) Hunter, W. N.; D'Estaintoto, B. L.; Kennard, O. *Biochemistry* **1989**, *28*, 2444-2451.
(12) Heinemann, U.; Lauble, H.; Frank, R.; Blöcker, H. *Nucleic Acids Res.* **1987**, *15*, 9531-9550.
(13) Dickerson, R.; Drew, H. R. *J. Mol. Biol.* **1981**, *149*, 761-786.
(14) Drew, H. R.; Travers, A. A. *Cell* **1984**, *37*, 491-502.
(15) Ulanovsky, L. E.; Trifonov, E. N. *Nature* **1987**, *326*, 720-722. Marini, J. C.; Levene, S. D.; Crothers, D. M.; Englund, P. T. *Proc. Natl. Acad. Sci. U.S.A.* **1982**, *79*, 7664-7668. Burkhoff, A. M.; Tullius, T. D. *Cell* **1987**, *48*, 935-943. Burkhoff, A. M.; Tullius, T. D. *Nature* **1988**, *331*, 455-457.
(16) Besides this, both the variations in sugar puckering and the rise per base pair also contribute to the opening of the site. These are all, however, not independent parameters. To account for sequence-dependent chiral discrimination, only propeller twisting and helical twisting, the parameters that are asymmetric and potentially sequence dependent, need be considered.
(17) Barton, J. K. *Science* **1986**, *233*, 727-733.
(18) Overall cleavage favors the Δ isomer consistent with the right-handed DNA helicity.
(19) Wilson, W. D.; Strekowski, L.; Tanious, F. A.; Watson, R. A.; Mokerosz, J. L.; Strekowska, A.; Webster, G. D.; Neidle, S. *J. Am. Chem. Soc.* **1988**, *110*, 8292-8299.
(20) Maxam, A.; Gilbert, W. *Methods Enzymol.* **1980**, *65*, 499-560.
(21) Dollimore, L. S.; Gillard, R. D. *J. Chem. Soc.* **1973**, 933.
(22) Bosnich, B. *Acc. Chem. Res.* **1969**, 2, 266.

0002-7863/90/1512-9432$02.50/0