for **7b**. Thus **5a** should rearrange faster than **5b**, which is in accord with the experiment.

Since both steric and electronic effects lead to the same result, the obtained kinetics permit no conclusion, whether a [5,5]-sigmatropic shift is contributing to the isomerization of **5a**.

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Supplementary Material Available: Experimental procedure and reaction scheme for fomation of **5a,b** and **6a,b** and tables of experimental raw data for and composition of reaction mixture during isomerization of **5a,6** (4 pages). Ordering information is given on any current masthead page.

Sequence-Specific Recognition of B DNA by Bis(EDTA–distamycin)fumaramide

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One approach for the design of sequence-specific DNA binding molecules that read large sequences of double-helical DNA is to couple DNA binding units of similar or diverse base pair specificities.[1-6] The base-specific recognition elements of each unit and the linkers connecting them must be compatible with the same groove (e.g., major or minor in B DNA) and conformational state of the DNA (e.g., B, A, Z). We have shown that oligo-*N*-methylpyrrolecarboxamides containing 4–7 amide NHs bind sites of A·T rich DNA consisting of 5–8 contiguous base pair in size.[3-6] The general rule of n amide NHs affording binding site sizes of $n + 1$ base pairs is consistent with the oligopeptide binding in the minor groove of right-handed B DNA with the amide NH groups

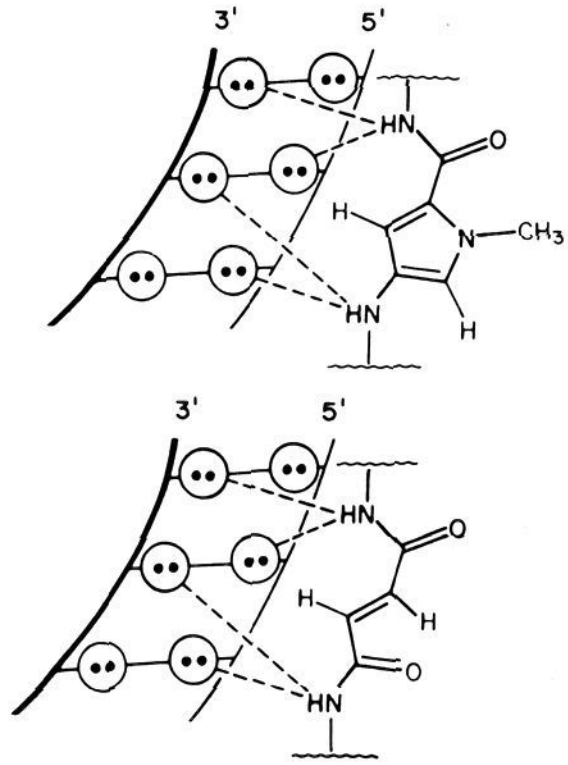

Figure 1. Circles with two dots represent lone pairs of electrons on N3 of adenine (A) and O2 of thymine (T) at the edges of the base pairs on the floor of the minor groove of the right-handed B DNA helix. Dotted lines are bridged hydrogen bonds to the amide NHs.[7] (Top) Model of *N*-methylpyrrolecarboxamide binding in the minor groove of A·T rich DNA.[7] (Bottom) Model of fumaramide binding in the minor groove of A·T rich DNA.

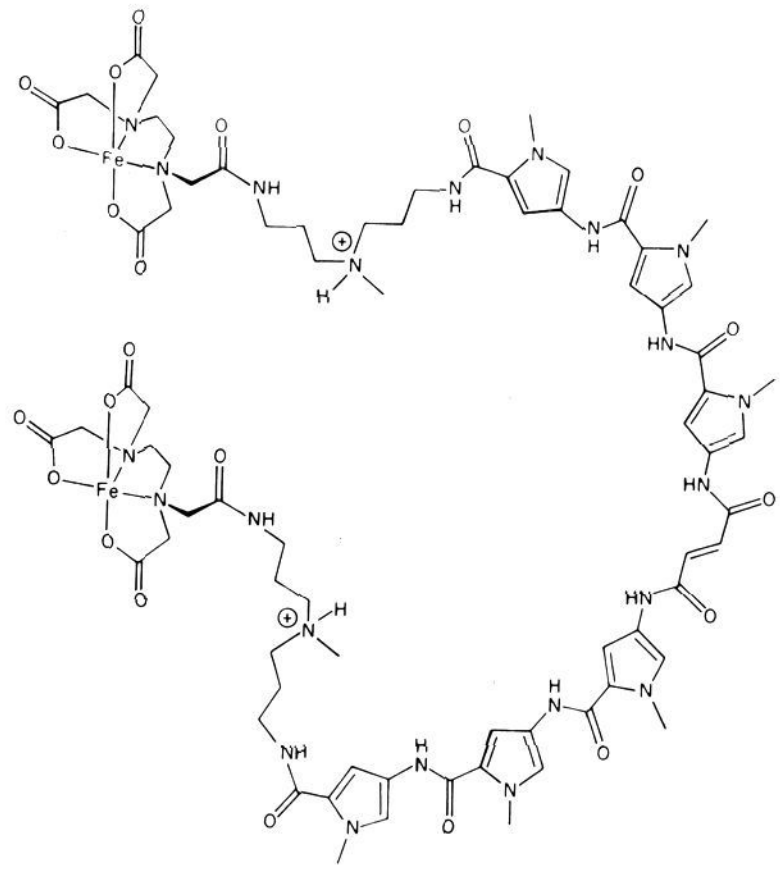

Figure 2. Bis(Fe^{II}·EDTA–distamycin)fumaramide (BEDF·Fe^{II}).

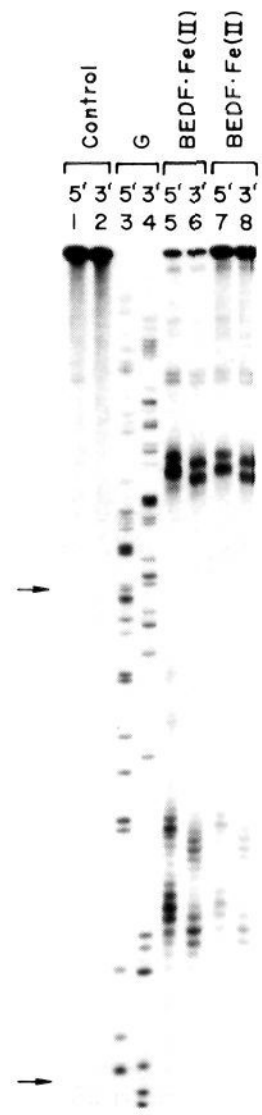

Figure 3. Autoradiogram of 5′ (odd-numbered lanes) and 3′ (even-numbered lanes) ^{32}P end-labeled 517 bp DNA restriction fragment (*Eco RI/Rsa I*) from plasmid pBR322 on a high-resolution denaturing gel.[9] Lanes 1 and 2, intact DNA; lanes 3 and 4, Maxam-Gilbert chemical sequencing G reaction;[10] lanes 5 and 6, BEDF·Fe^{II} at 1.5 μM concentrations; lanes 7 and 8, BEDF·Fe^{II} at 0.5 μM concentrations. Bottom to arrow at the middle of the autoradiogram is the sequence left to right in Figure 4.

(1) Schultz, P. G.; Taylor, J. S.; Dervan, P. B. *J. Am. Chem. Soc.* **1982**, *104*, 6861–6863.
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(3) Schultz, P. G.; Dervan, P. B. *Proc. Natl. Acad. Sci. U.S.A.* **1983**, *80*, 6834–6837.

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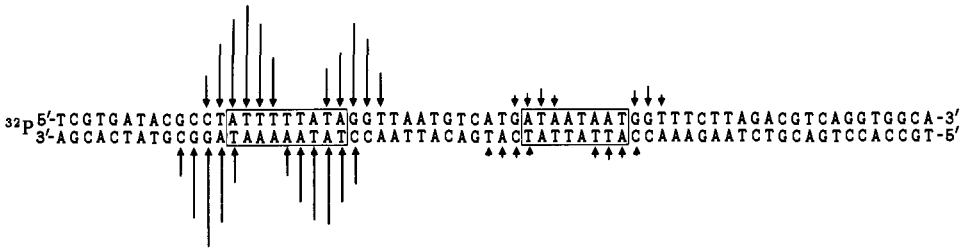

Figure 4. Histograms of BEDF·Fe^{II} cleavage patterns on 517 bp DNA restriction fragment (base pairs 4337–4296 on plasmid pBR322) from high-resolution denaturing gel (Figure 3). Arrows represent amount of cleavage resulting in removal of indicated base. Boxes define binding site location and size based on model described in ref 4.

forming bridges between adjacent N3 or O2 atoms of adenine (A) and thymine (T) on opposite strands of the DNA helix.[4-7] We anticipate there is a point where an oligo-*N*-methylpyrrolecarboxamide will no longer fit the natural twist of the B helix.[6] The recognition of DNA sequences larger than the upper limit permissible with oligo-*N*-methylpyrrolecarboxamides will require linkers compatible with both these DNA binding units and the minor groove of A·T rich sequences of B DNA. The question arises whether the *N*-methylpyrrolecarboxamide ring, a two base pair DNA recognition element, can be replaced by structurally similar moiety. For example, the diamide of fumaric acid might mimic *N*-methylpyrrolecarboxamide with regard to shape and distance between the amide NHs (Figure 1).

We report a new sequence-specific DNA binding molecule, bis(EDTA–distamycin)fumaramide (BEDF)[8] (Figure 2). This crescent-shaped octaamide contains two *N*-methylpyrrole tripeptide units[1-6] coupled at the amino termini via fumaric acid (Figure 2). Attachment of EDTA to the carboxy terminus of each tripeptide allows use of the affinity cleaving method[4-6] to visualize the sequence and size of the DNA recognition site by analysis of DNA cleavage patterns on ^{32}P-end-labeled DNA restriction fragments by high-resolution denaturing gel electrophoreses.[1-6]

A 517 base pair *Rsa I/Eco RI* restriction fragment (3848–4362 bp) from plasmid pBR322 DNA was labeled separately with ^{32}P on the 5′- and 3′-ends.[2,3] The DNA restriction fragments were allowed to react with BEDF·Fe^{II} (1.5 μM concentration) at dimer/DNA base pair ratios of 0.015 in the presence of dithiothreitol (5 mM) for 2 h (37 °C, pH 7.9).[9] The DNA cleavage sites were visualized by high-resolution gel electrophoreses (Figure 3). From densitometric analysis of the autoradiogram, the DNA cleavage patterns reveals major cleavage sites flanking two sequences 5′-ATTTTTATA-3′ and 5′-ATAATAAT-3′ (Figure 4).

According to the "$n + 1$ rule", a functional octamide in the minor groove should bind nine base pairs. The observation of eight and nine base pair binding in the absence of five base pair binding suggests that BEDF is binding DNA exclusively in the dimeric mode. This is in contrast to results with a dimer of the same tripeptide coupled with heptanedioic acid, a flexible C-7 hydrocarbon linker.[2] In this case, monomeric binding at one site, 5′-atAATAAt-3′, was competitive with dimeric binding at the 5′-TTTTTATA-3′ site on the same restriction fragment.[2] The fact that we observe eight as well as nine base pair binding site sizes for BEDF may be due to our inability to assign exactly the binding site boundaries based on the asymmetric cleavage pattern model.[4-6] Alternatively, the appearance of an eight base pair binding site may indicate that there are other binding options for the fumaramide linker.

In summary, the dimer of tris-*N*-methylpyrrolecarboxamide connected by a flexible C-7 linker, which had the property of monomeric binding competitive with dimeric binding,[2] was redesigned with a shorter rigid C-4 linker of favorable curvature affording a new molecule, BEDF, that has the property of exclusive dimeric binding which results in the recognition of eight–nine contiguous base pairs of A·T rich double helical DNA.

Acknowledgment. We are grateful to the National Institutes of Health for grant support (GM-27681).

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(7) A molecular basis for DNA recognition by *N*-methylpyrrolecarboxamide is provided by a recent X-ray crystal structure of netropsin and B DNA dodecamer of sequence 5′-CGCGAATTCGCG-3′. Kopka, M. L.; Yoon, C.; Goodsell, D.; Pjura, P.; Dickerson, R. E. *Proc. Natl. Acad. Sci. U.S.A.* **1985**, *82*, 1376–1380.
(8) The NMR, IR, UV, and mass spectral data are consistent with the assigned structure. The synthetic details, similar to methods described in ref 2 and 4, will be published elsewhere.
(9) The cleavage reactions were run with >600 cpm of ^{32}P end-labeled restriction fragments and made up to a total DNA concentration of 100 μM (bp) with sonicated calf thymus DNA. The samples were equilibrated with the DNA at 37 °C for 2 h and reaction was initiated by the addition of a dithiothreitol solution. The reactions were run at 37 °C for 2 h and terminated by freezing followed by lyophilization and suspension in 4 μL of a pH 8.3 100 mM Tris-borate, 50% formamide solution. These solutions were heat denatured and loaded on a 0.4 mm thick, 40 cm long, 8% polyacrylamide, 1:20 cross-linked, 50% urea gel and electrophoresed at 1500 V. Autoradiography of the gels was carried out at −50 °C on Kodak, X-Omat AR film, and the autoradiograms were scanned at 485 nm. The relative peak area for each site was equated to the relative cleavage efficiency.

Formation of Acrylic Acid Derivatives from the Reaction of CO_2 with Ethylene Complexes of Molybdenum and Tungsten†

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There is at present a great deal of interest in the organometallic chemistry of carbon dioxide, largely aimed at finding new catalytic processes for the conversion of abundant CO_2 into organic chemicals of commercial interest.[2] In the course of our studies on CO_2 chemistry,[3] we have found that the complexes *trans*-M-

† Dedicated to Professors Gonzalez Garcia and Gutiérrez Rios on the occasion of their retirement.
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