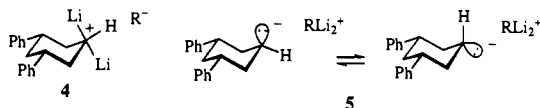


a preponderance of equatorial lithium reagent **2e** and equilibrated to the same 8/92 mixture of **2a** and **2e** (see Figure 1). These results represent the first example of a non-cyclopropyl hydrocarbon alkylolithium reagent with useful configurational stability on the laboratory time scale in THF or any ether solvent.

The rate of equilibration was accelerated by lithium iodide and was strongly dependent on the total organolithium concentration.<sup>12b</sup> Reasonable pseudo-first-order kinetics were obtained when the concentration of *sec*-butyllithium was optimum (36 mM,  $t_{1/2}$  = 9 min), as shown in Figure 1. At 96 mM,  $t_{1/2}$  was 3 min, at 24 mM, approximately 18 min, but considerable scatter was observed at both the higher and lower concentrations, the former because the rate was too fast, and the latter because the concentration of RLi was too low for accurate work.

A reasonable interpretation of this concentration dependence is that the inversion process involves an aggregation state higher than that present in THF. If **2**, like *sec*-butyllithium,<sup>15</sup> is largely monomeric in THF, then the inversion may involve a dimer (this fits our rate data best) or a higher aggregate. The concentration dependence of primary Grignard reagent inversion has been rationalized by invoking aggregate formation.<sup>16</sup> An aggregate may provide mechanistic opportunities for moving a cation from one face of a carbanion to the other not available to a monomer, for example, by formation of a rapidly inverting free carbanion **5** or a triple ion intermediate such as **4** with a symmetrically dilithiated planar carbanion,<sup>17</sup> or by related pathways as explored theoretically for methylolithium dimer.<sup>18</sup>



We have tested the aggregation hypothesis. A complexing agent that effectively prevents dimerization might enhance the configurational stability of **2a** by preventing aggregate-based lithium exchange. The tridentate ligand *N,N,N',N'',N'''*-pentamethyldiethylenetriamine (PMDTA) is uniquely suited for the purpose: it is a strong complexing agent<sup>16,19</sup> and is capable of occupying the three free coordination sites of a monomeric organolithium reagent, thus inhibiting dimerization.<sup>15,20</sup>

The cleavage of the tellurides **1a** and **1e** was repeated in the presence of PMDTA (1/3/15 ratio of telluride, *sec*-butyllithium, and PMDTA), with the results shown in Figure 1. The isomerization rate was reduced by a factor of 20, with a half-life for

equilibration longer than 2 h. The equilibration constant was not significantly affected by the presence of PMDTA (a ratio of 7/93 **3a**/**3e** was obtained at -45 °C). Furthermore, the rate of isomerization was unaffected by an 8-fold increase in the concentration of PMDTA over lithium, provided that at least a 5-fold excess of PMDTA over lithium was maintained.<sup>21</sup> Under optimum conditions at -78 °C with short reaction times, **1a** gave 94% axial sulfide **3a**, and **1e** gave 98% equatorial sulfide **3e**. In contrast, the rate of epimerization increased when run in ether/THF mixtures compared to pure THF (most lithium reagents form higher aggregates in ether than in THF). The bidentate complexing agent tetramethylethylenediamine (TMEDA, 5 equiv per RLi) produced no significant change in the rate of isomerization of **2a**.<sup>22</sup>

We believe that this is the first example in which configurational isomerization of a lithium reagent was slowed by increase in the strength of lithium coordination.<sup>23</sup> However, the configurational isomerization of neohexylmagnesium chloride<sup>16a</sup> and 3-cyclohexenylmagnesium bromide is slower in diglyme and THF than in ether.<sup>16a</sup> We speculate that there may be two "islands" of relatively high configurational stability for alkylolithium reagents as solvent polarity is changed. One is in hydrocarbon solvents in which the charge separation needed for C-Li bond reorganization is energetically costly, and a second is in more polar solvents containing predominantly monomeric species where aggregate-assisted isomerization is inhibited, as proposed in the current study. One might anticipate that further increases in solvent polarity could again facilitate isomerization by stabilizing separated ion pairs, the mechanism usually invoked for polar-solvent-accelerated isomerizations.<sup>2b,c,6a,c,12</sup>

**Acknowledgment.** We thank the National Science Foundation for support of this work.

(21) Use of much less than 5 equiv of PMDTA per lithium results in only partial reduction of the isomerization rate; above 5 equiv, no significant additional decrease in rate was observed.

(22) Collum, D. B. *Acc. Chem. Res.* **1992**, *25*, 448. Bernstein, M. P.; Romesberg, F. E.; Fuller, D. J.; Harrison, A. T.; Collum, D. B.; Liu, Q.-Y.; Willard, P. G. *J. Am. Chem. Soc.* **1992**, *114*, 5100.

(23) The opposite is usually observed: 1-substituted cyclopropyllithium,<sup>12</sup> 1-styryllithium,<sup>2b,c</sup> ( $\alpha$ -aminoalkyl)lithium.<sup>6a,c</sup>

## Reduction and Electrochemistry of $\text{C}_{60}$ in Liquid Ammonia

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We report here the reduction of  $\text{C}_{60}$  slurries by solvated electrons ( $e_s^-$ ) generated electrochemically in liquid ammonia and the cyclic voltammetry (CV) of the  $\text{C}_{60}^-$  solution produced. Waves corresponding to both soluble and insoluble forms of  $\text{C}_{60}^-$  were observed, with  $n$  spanning the range 0-6 (depending on the supporting electrolyte used).  $\text{C}_{60}$  in solvents in which  $\text{C}_{60}$  and its reduced products are soluble, e.g.,  $\text{CH}_2\text{Cl}_2$ , benzene, and toluene, showed up to five CV waves,<sup>1-4</sup> and by use of mixed solvents at low temperature, the presence of six CV redox waves for  $1e^-$

(1) Allemand, P.-M.; Koch, A.; Wudl, F.; Rubin, Y.; Diederich, F.; Alvarez, M. M.; Anz, S. J.; Whetten, R. L. *J. Am. Chem. Soc.* **1991**, *113*, 1050.

(2) Cox, D. M.; Behal, S.; Disko, M.; Gorun, S. M.; Greaney, M.; Hsu, C. S.; Kollin, E. B.; Millar, J.; Robbins, J.; Robbins, W.; Sherwood, R. D.; Tindall, P. *J. Am. Chem. Soc.* **1991**, *113*, 2940.

(3) Dubois, D.; Kadish, K. M.; Flanagan, S.; Haufler, R. E.; Chibante, L. P. F.; Wilson, L. J. *J. Am. Chem. Soc.* **1991**, *113*, 4364.

(4) Dubois, D.; Kadish, K. M.; Flanagan, S.; Wilson, L. J. *J. Am. Chem. Soc.* **1991**, *113*, 7773.

(15) Bauer, W.; Winchester, W. R.; Schleyer, P. v. R. *Organometallics* **1987**, *6*, 2371.

(16) DNMR studies of alkyl Grignard reagents:<sup>7a</sup> (a) Whitesides, G. M.; Roberts, J. D. *J. Am. Chem. Soc.* **1965**, *87*, 4878. (b) Pechhold, E.; Adams, D. G.; Fraenkel, G. *J. Org. Chem.* **1971**, *36*, 1368. (c) Maercker, A.; Geuss, R. *Angew. Chem., Int. Ed. Engl.* **1971**, *10*, 270.

(17) Eaborn, C.; Hitchcock, P. B.; Smith, J. D.; Sullivan, A. C. *J. Chem. Soc., Chem. Commun.* **1983**, 827. Jackman, L. M.; Scarmoutzos, L. M.; Porter, W. *J. Am. Chem. Soc.* **1987**, *109*, 6524. Collum, D. B.; Romesberg, F. E. *J. Am. Chem. Soc.* **1992**, *114*, 2112. Collum, D. B.; Romesberg, F. E.; Gilchrist, J. H.; Harrison, A. T.; Fuller, D. J. *J. Am. Chem. Soc.* **1991**, *113*, 5751.

(18) Clark, T.; Schleyer, P. v. R. *J. Chem. Soc., Chem. Commun.* **1978**, 137.

(19) Lappert, M. F.; Engelhart, L. M.; Raston, C. L.; White, A. H. *J. Chem. Soc., Chem. Commun.* **1982**, 1323. Klumpp, G. W.; Luitjes, H.; Schakel, M.; de Kantner, F. J. J.; Schmitz, R. F.; Hommes, N. J. R. v. E. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 633.

(20) (a) Fraenkel, G.; Chow, A.; Winchester, W. R. *J. Am. Chem. Soc.* **1990**, *112*, 6190. (b) Johns, D.; Edlund, U. *J. Organomet. Chem.* **1990**, C35. (c) Schumann, U.; Kopf, J.; Weiss, E. *Angew. Chem.* **1985**, *97*, 222.

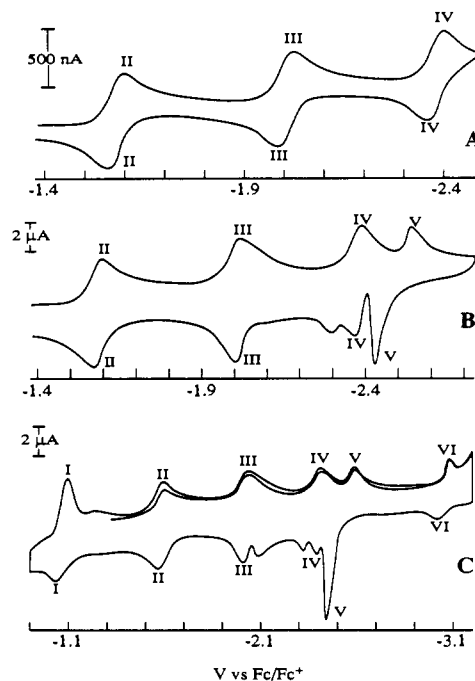
**Table I.** Peak Potentials in Liquid Ammonia and Comparison to Solution Data<sup>a</sup>

wave	species	ammonia/KI <sup>b</sup>		ammonia/LiI		MeCN <sup>c</sup>	toluene/MeCN <sup>d</sup>
		$E_{pa}$ (V)	$E_{pc}$ (V)	$E_{pa}$ (V)	$E_{pc}$ (V)	$E_{pc}$ (V)	$E_{1/2}$ (V)
I	(0,-1)	-1.04	-1.10 (f + s)	-1.06	-1.21 (f + s)	-1.17	-0.98
II	(-1,-2)	-1.56	-1.60 (s)	-1.52	-1.60 (s)	-1.39	-1.37
III	(-2,-3)	-2.00	-2.03 (s)	-1.85	-1.98 (f + s)	-1.88	-1.87
IV	(-3,-4)	-2.37	-2.40 (s)	-2.29	-2.39 (f + s)	-2.24	-2.35
V	(-4,-5)	-2.43	-2.58 (f + s)	-2.68	-2.78 (f + s)		-2.85
VI	(-5,-6)	-3.03	-3.08 (f + s)				-3.26

<sup>a</sup> All potentials are referenced to the Fc/Fc<sup>+</sup> couple. In ammonia, the potentials were referenced to the potential for solvated electron generation (at 2 mA/cm<sup>2</sup>) and then referenced to the Fc/Fc<sup>+</sup> couple.<sup>15,16</sup> Surface wave, f; solution wave, s. <sup>b</sup> See Figure 1. <sup>c</sup> Reference 7. <sup>d</sup> Reference 5a.

reduction steps up to C<sub>60</sub><sup>6-</sup> was demonstrated,<sup>5</sup> showing complete filling of the three degenerate molecular orbitals of C<sub>60</sub>.<sup>6</sup> We previously showed<sup>7,8</sup> that C<sub>60</sub> was insoluble in MeCN and that redox processes of films of C<sub>60</sub>, involving doping of the films with electrolyte cation, M<sup>+</sup> [M<sup>+</sup> = tetra-*n*-butylammonium (TBA<sup>+</sup>), Li<sup>+</sup>, K<sup>+</sup>], could be observed. Studies of film mass changes with the quartz crystal microbalance (QCM)<sup>9,10</sup> have indicated higher solubility of the reduced forms in MeCN, with the C<sub>60</sub><sup>3-</sup> form soluble in TBA<sup>+</sup> solutions. Indeed, slurries of C<sub>60</sub> could be reduced electrochemically in MeCN to the -3 form, which could then be oxidized to insoluble films on the electrode.<sup>10</sup> We now describe experiments in liquid NH<sub>3</sub> at -70 °C, where C<sub>60</sub> slurries are dissolved by reaction with e<sub>s</sub><sup>-</sup>.

C<sub>60</sub> is insoluble and chemically inert in liquid NH<sub>3</sub>.<sup>11</sup> A mass spectrum of a C<sub>60</sub> sample which had been exposed to liquid NH<sub>3</sub> at -60 °C for 5 h followed by removal of the NH<sub>3</sub> at room temperature showed only one peak (*m/z* = 720), and the visible spectrum of the same sample in a toluene solution was identical to that of untreated C<sub>60</sub>. However, the C<sub>60</sub><sup>-</sup> form is soluble in a NH<sub>3</sub>/KI solution. After 1 equiv of e<sub>s</sub><sup>-</sup> was generated to reduce the C<sub>60</sub> slurry, a red-brown solution appeared with no C<sub>60</sub> particles remaining in the cell. In a typical experiment, 14 mg of C<sub>60</sub> in 10 mL of NH<sub>3</sub> was reduced by 1 equiv of e<sub>s</sub><sup>-</sup>, generated at a constant current at a Pt mesh electrode, to form a 1.9 mM C<sub>60</sub><sup>-</sup> solution, which was then studied by CV.<sup>14</sup> CV scans in this solution toward negative potentials performed at a 1-mm-diameter Pt disk electrode, starting at the rest potential, E<sub>r</sub> [ca. -1.37 V vs Fc/Fc<sup>+</sup> (Fc = ferrocene)], at a scan rate, *v*, of 20 mV/s, produced a series of reduction waves. If the scan was reversed after wave IV (reduction to C<sub>60</sub><sup>4-</sup>), the CV scan toward positive potentials showed three stepwise oxidations to soluble -3, -2, and -1 forms of C<sub>60</sub> (Figure 1A). The peak potential splittings ( $\Delta E_p$ ) for waves II, III, and IV were 40 mV (RT/F at -70 °C), and *i*<sub>p</sub> for each peak was proportional to *v*<sup>1/2</sup>. Thus C<sub>60</sub><sup>-</sup>, C<sub>60</sub><sup>2-</sup>, C<sub>60</sub><sup>3-</sup>, and C<sub>60</sub><sup>4-</sup> are all soluble and the corresponding CV waves are reversible. If the CV scan is continued beyond wave V, a film of the K salt of C<sub>60</sub><sup>5-</sup> forms and the corresponding oxidation on reversal resembles a stripping peak to form dissolved C<sub>60</sub><sup>4-</sup> (Figure



**Figure 1.** Cyclic voltammograms of a 1.9 mM C<sub>60</sub><sup>-</sup> solution prepared after generating 1 equiv of e<sub>s</sub><sup>-</sup> in liquid ammonia/KI (0.1 M) at -70 °C, when (A) the potential was scanned at *v* = 20 mV/s and reversed beyond wave IV; (B) the potential was scanned at 500 mV/s and reversed beyond wave V; and (C) the whole potential range of the solution was scanned at *v* = 500 mV/s. The working electrode was a 1-mm-diameter Pt disk electrode, and the concentration of KI was 0.1 M.

1B). However, two additional small peaks appear, together with the oxidation waves of dissolved C<sub>60</sub><sup>4-</sup> and C<sub>60</sub><sup>3-</sup>. In this case, these waves have the characteristics of surface CV waves and probably represent the oxidation of some undissolved C<sub>60</sub><sup>4-</sup> and C<sub>60</sub><sup>3-</sup> forms. When the scan continues to more negative potentials, a wave corresponding to reduction of the insoluble C<sub>60</sub><sup>5-</sup> salt to an insoluble -6 form (based on the *i*<sub>p</sub>-*v* behavior) occurs (Figure 1C). A scan from the C<sub>60</sub><sup>-</sup> E<sub>r</sub> toward positive potentials produces an anodic wave corresponding to the oxidation of C<sub>60</sub><sup>-</sup> to C<sub>60</sub> (wave I), and on reversal, the reduction of C<sub>60</sub> (present in the form of both film and dissolved species) occurs at -1.10 V.

Coulometric titration with e<sub>s</sub><sup>-</sup> was carried out to confirm the formation of the C<sub>60</sub><sup>6-</sup> species. In such an experiment, a known excess of e<sub>s</sub><sup>-</sup> was generated at constant current and the initially red-brown solution became a suspension of black particles (the K salt of C<sub>60</sub><sup>6-</sup>). A back-titration was then conducted by holding the potential constant at -3.14 V, just beyond wave VI, where e<sub>s</sub><sup>-</sup> is oxidized. The end point was determined by measuring the rest potential of the microelectrode until it reached a potential of -3.14 V. The net amount of e<sub>s</sub><sup>-</sup> consumed corresponded to 5.81 mol of e<sub>s</sub><sup>-</sup>/mol of C<sub>60</sub><sup>6-</sup>. A similar experiment was conducted in NH<sub>3</sub>/(TBA)CF<sub>3</sub>SO<sub>3</sub> solution, where the TBA<sup>+</sup> salts of all forms (C<sub>60</sub><sup>n-</sup>, *n* = 1-6) are insoluble. Generation of excess e<sub>s</sub><sup>-</sup> followed by back-titration yielded 6.19 e<sub>s</sub><sup>-</sup> per C<sub>60</sub>.

If the supporting electrolyte was a Li salt, the CV of the C<sub>60</sub><sup>-</sup> solution was very different. A cathodic CV scan from the E<sub>r</sub> at ca. -1.51 V showed only four reductions, suggesting that only C<sub>60</sub><sup>5-</sup>

(5) (a) Xie, Q.; Perez-Cordero, E.; Echegoyen, L. *J. Am. Chem. Soc.* **1992**, *114*, 3978. (b) Ohsawa, Y.; Saji, T. *J. Chem. Soc., Chem. Commun.* **1992**, 781.

(6) Haddon, R. C.; Brus, L. E.; Raghavachari, K. *Chem. Phys. Lett.* **1986**, *125*, 459.

(7) Jehoulet, C.; Bard, A. J.; Wudl, F. *J. Am. Chem. Soc.* **1991**, *113*, 5456.

(8) Jehoulet, C.; Obeng, Y. S.; Kim, Y.-T.; Zhou, F.; Bard, A. J. *J. Am. Chem. Soc.* **1992**, *114*, 4237.

(9) Zhou, F.; Yau, S.-L.; Jehoulet, C.; Laude, D. A., Jr.; Guan, Z.; Bard, A. J. *J. Phys. Chem.* **1992**, *96*, 4160.

(10) Koh, W.; Dubois, D.; Kutner, W.; Jones, M. T.; Kadish, K. M. *J. Phys. Chem.* **1992**, *96*, 4163.

(11) Experimental procedures followed previous reports.<sup>12,13</sup> The solutions, before addition of C<sub>60</sub>, were treated with electrogenerated e<sub>s</sub><sup>-</sup> (followed by oxidation of e<sub>s</sub><sup>-</sup>) to scavenge any reducible impurities.

(12) Demortier, A.; Bard, A. J. *J. Am. Chem. Soc.* **1973**, *95*, 3495.

(13) Teherani, T.; Itaya, K.; Bard, A. J. *Nouv. J. Chim.* **1987**, *2*, 481.

(14) The electrochemical experiments were performed with a PAR 173 potentiostat and a PAR 175 universal programmer (Princeton Applied Research Corp., Princeton, NJ). Potentials were measured versus either Ag/AgNO<sub>3</sub> (in coulometric titrations) or a Ag quasireference electrode and referenced to the solvated electron potential.

(15) Itaya, K.; Malpas, R. E.; Bard, A. J. *Chem. Phys. Lett.* **1979**, *63*, 411.

(16) Bauer, D.; Breant, M. In *Electroanalytical Chemistry*; Bard, A. J., Ed.; Marcel Dekker: New York, 1975; Vol. 8.

was produced before generation of  $e_s^-$ . On the basis of the CV behavior for each reduction, the only soluble species were the -1 and -2 ions; all other anions were either insoluble or partially soluble. Note that in the LiI CV, all of the reduction waves were about equally spaced in potential, while wave V in Figure 1B is shifted to a less negative potential, probably because of the precipitation of  $K_5C_{60}$  from soluble  $C_{60}^{4-}$ . The potentials of the different waves in both  $NH_3/LiI$  and  $NH_3/KI$  solutions and a comparison to those in other solvents are given in Table I.<sup>14</sup>

These results support the strong dependence of the redox chemistry of  $C_{60}$  on both solvent and cation of the supporting electrolyte and demonstrate that electrochemical reduction to the -6 state can be accomplished in liquid  $NH_3$  in the presence of  $K^+$ . Electrolysis of  $C_{60}$  slurries by  $e_s^-$  generated electrochemically is quantitative and provides a useful new approach in the preparation of  $C_{60}$  compounds and films.

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### Ligand-Promoted Dimerization of Oligonucleotides Binding Cooperatively to DNA

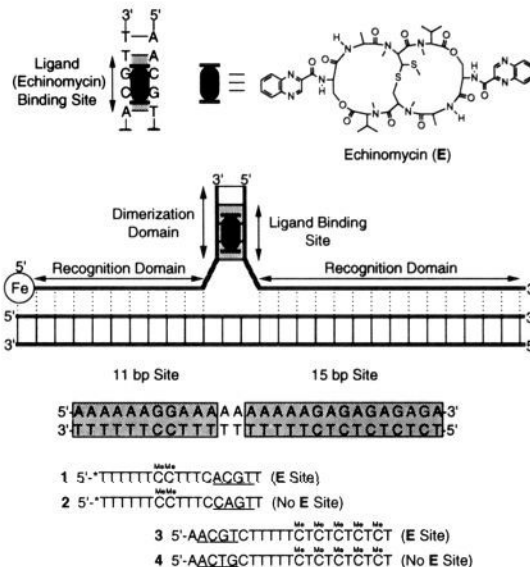
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In biological systems, specific protein-DNA interactions are often modulated by ligands as in the regulation of gene expression.<sup>1</sup> Many transcription factors are active as dimers, but inactive as monomers. In at least one case, dimerization is regulated by an additional protein cofactor.<sup>2</sup> We recently described the design of a triple helical complex comprising two oligonucleotides which bind adjacent sites on DNA cooperatively through dimerization.<sup>3</sup> If dimerization could be controlled by additional ligands, such an artificial nucleic acid system would be analogous to the naturally occurring inducible protein systems. We now report that the stability of the dimerization domain can be enhanced by a small molecule, echinomycin (E). The strengths of ligand-promoted control of oligonucleotides binding cooperatively to DNA are quantitated by affinity cleavage.

Our design begins with a Y-shaped structure consisting of two oligonucleotides (Figure 1).<sup>3</sup> Each of these oligonucleotides contains a recognition domain (11 or 15 bases) and a dimerization domain (5 bases) separated by a one-base linker.<sup>3</sup> Site-specific DNA recognition is achieved through specific Hoogsteen hydrogen bonding and local triple helix formation (T·AT and C+GC triplets)<sup>4</sup> while dimerization occurs through Watson-Crick hydrogen bonding. The stability of the Watson-Crick dimerization domain can be controlled both by length and/or by the addition of sequence-specific DNA-binding peptides or proteins. In order to minimize dimerization in the absence of ligand, a 5-bp mini-helix was used (Figure 1). To obtain ligand-mediated control of dimerization, a specific 4-bp recognition sequence for the DNA-binding drug echinomycin (E) was incorporated into the dimerization domain. Echinomycin (E), a bis-intercalating minor



**Figure 1.** Schematic representation of a Y-shaped nucleic acid complex composed of two triple helix forming oligonucleotides which dimerize through formation of a small segment of Watson-Crick double helical DNA. Contained within the mini-helix is a high-affinity site for the DNA-binding molecule, echinomycin (E).

groove-binding molecule, is known to bind sequence specifically to the 4-bp site 5'-ACGT-3' and stabilize duplex DNA formation at micromolar concentrations (Figure 1).<sup>5-8</sup> Echinomycin (E) binding should therefore augment the stability of the 5-bp dimerization domain and increase the affinity of the resulting dimeric oligonucleotide complex for its specific DNA target site.

Four oligonucleotides, 1-4, were synthesized to test this design (Figure 1). Oligonucleotides 1 and 3 contain the echinomycin recognition sequence 5'-ACGT-3' in the dimerization domain while 2 and 4 do not. The modified base thymine-EDTA (T\*) was incorporated at the 5'-termini of oligonucleotides 1 and 2, each targeted to the 11-bp site, to allow analysis of site-specific binding by the affinity cleavage method.<sup>4a,9</sup> The binding affinities of oligonucleotide pairs 1,3 and 2,4 in the presence and absence of echinomycin (E) were measured.

Affinity cleavage experiments were performed on a <sup>32</sup>P-end-labeled restriction fragment (852 bp) containing the adjacent 11- and 15-bp target sites (Figure 2).<sup>3</sup> Reaction of oligonucleotide-EDTA-Fe 1 (100 nM) with the target DNA (pH 7.0, 37 °C) alone or in the presence of echinomycin (E) results in little cleavage (Figure 2, lanes 2 and 3). A reaction of 1 in the presence of 3 (1.0 μM)<sup>10</sup> affords a modest increase in cleavage, revealing that some cooperativity occurs even with a 5-bp dimerization domain (lane 4). Upon addition of echinomycin (E) (50 μM) to the reaction containing oligonucleotides 1 and 3, a dramatic increase in cleavage occurs (lane 5). This demonstrates that the small ligand E significantly enhances the affinity of oligonucleotides 1 and 3 for its site. Only minimal cleavage is obtained in the reaction containing 2, 4, and E (lane 10), demonstrating that this result depends on a sequence-specific ligand-binding site within the dimerization domain. For comparison, significant cleavage is obtained in a reaction containing 2 and 4 when the concentration of 2 is raised by a factor of 10 from 100 nM to 1.0 μM (lane 11). This demonstrates that oligonucleotide 2 binds

(1) Lewin, B. *Genes IV*; Oxford University Press: New York, 1990.  
(2) Mendel, D. B.; Khavari, P. A.; Conley, P. B.; Graves, M. K.; Hansen, L. P.; Admon, A.; Crabtree, G. R. *Science* 1991, 254, 1762.  
(3) Distefano, M. D.; Shin, J. A.; Dervan, P. B. *J. Am. Chem. Soc.* 1991, 113, 5901.  
(4) (a) Moser, H. E.; Dervan, P. B. *Science* 1987, 238, 645. (b) Praseth, D.; Perroault, L.; Doan, T. L.; Chassignol, M.; Thuong, N.; Helene, C. *Proc. Natl. Acad. Sci. U.S.A.* 1988, 85, 1349. (c) Rajagopal, P.; Feigon, J. *Biochemistry* 1989, 28, 7859. (d) de los Santos, C.; Rosen, M.; Patel, D. *Biochemistry* 1989, 28, 7282.

(5) (a) Waring, M. J.; Wakelin, L. P. G. *Nature* 1974, 252, 653. (b) Wakelin, L. P. G.; Waring, M. J. *Biochem. J.* 1976, 157, 721.  
(6) Van Dyke, M. M.; Dervan, P. B. *Science* 1984, 225, 1122.  
(7) Ughetto, G.; Wang, A. H.-J.; Quigley, G. J.; van der Marel, G. A.; van Boom, J. H.; Rich, A. *Nucleic Acids Res.* 1985, 13, 2305.  
(8) Gao, X.; Patel, D. J. *Biochemistry* 1988, 27, 1744.  
(9) Dreyer, G. B.; Dervan, P. B. *Proc. Natl. Acad. Sci. U.S.A.* 1985, 82, 968.  
(10) At 1.0 μM concentration, oligonucleotides 3 and 4 should nearly saturate their cognate binding sites (>90% occupancy).<sup>11</sup> Similarly, echinomycin at 50 μM concentration should be saturating.<sup>8</sup>