Co.) and 200 mg of diamine 3 [prepared from trisnorsqualene aldehyde (4)[9] and ethylenediamine][10] in 2 mL of ethanol at 23 °C for 12 h, filtration, and washing with 250 mL of ethanol followed by 250 mL of distilled, deionized water. The resulting affinity matrix 5, which was chosen because it retains both the H bond accepting capabilities and the C(4) → C(30) hydrophobic structure of the normal substrate 1, is the first such reagent to function effectively in the purification of the sterol cyclase.

The purified sterol cyclase can be stored for at least 2 weeks at 0 °C without significant loss of activity. We believe that the way is now clear for the cloning of the gene for the yeast sterol cyclase and for the eventual determination of its structure.[11]

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(10) To 1.00 g of trisnorsqualenal[9] (4) (2.60 mmol) in 260 mL of anhydrous methanol at 0 °C was added 1.56 g of ethylenediamine (26.0 mmol, 10 equiv). Concentrated hydrochloric acid (0.43 mL, 5.2 mmol) was added, followed by 327 mg of sodium cyanoborohydride (5.2 mmol) in one portion. After 2 h at 0 °C, the methanol was removed in vacuo, and the residue was taken up in 200 mL of hexane and 300 mL of 1 M sodium bisulfate. The hexane layer was removed, and the aqueous layer was washed with another 200-mL portion of hexane. The aqueous layer was brought to pH 13 with solid sodium hydroxide and extracted with 3 × 200 mL of ether. The combined ether fractions were washed once with brine and then dried with anhydrous sodium sulfate. Concentration afforded 840 mg (76%) of monoalkylated diamine 3: 400-MHz ^{1}H NMR ($CDCl_3$) δ 1.60 (s, 12 H), 1.68 (s, 3 H), 1.72 (s, 3 H), 2.04 (m, 18 H), 2.07 (t, 2 H, J = 7.1), 2.59 (t, 2 H, J = 7.4), 2.67 (t, 2 H, J = 5.8), 2.81 (t, 2 H, J = 6.1), 5.14 (m, 5 H).

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Mirror-Image DNA

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D-Deoxyribose is the only asymmetric unit of DNA. Chiral molecules have two possible enantiomers, possibly possessing the same chemical and physical properties, although the energy difference between the enantiomers, particularly at a nuclear physics level, is quite small.[1] The features of single-stranded L-oligonucleotides have been reported.[2] However, whether the duplex structure of a DNA composed of L-deoxyribose is also an exact mirror image of the natural one has yet to be determined. Thus, a conformational study was conducted on the self-complementary hexanucleotide d(CGCGCG) composed of L-deoxyribose.

L-Deoxycytidine was synthesized via the L-deoxyuridine derivative by glycosylation[3] of silylated uracil with 1-chloro-2-deoxy-3,5-di-*O*-toluoyl-L-*erythro*-pentofuranose (prepared from L-arabinose[4]) and subsequent conversion to L-deoxycytidine.[5] L-Deoxyguanosine[6] was synthesized by direct glycosylation as described by Robins et al.[6,7] L-Deoxynucleosides were protected in the usual way, and D- and L-d(CGCGCG) were synthesized by the β-cyanoethylphosphoramidite method.[8]

On reversed-phase HPLC, the retention time of L-d(CGCGCG) was consistent with that of the corresponding natural D-hexamer synthesized as a control. The purity of both hexamers was more than 95%. The enzymatic digestion of D-d(CGCGCG) with

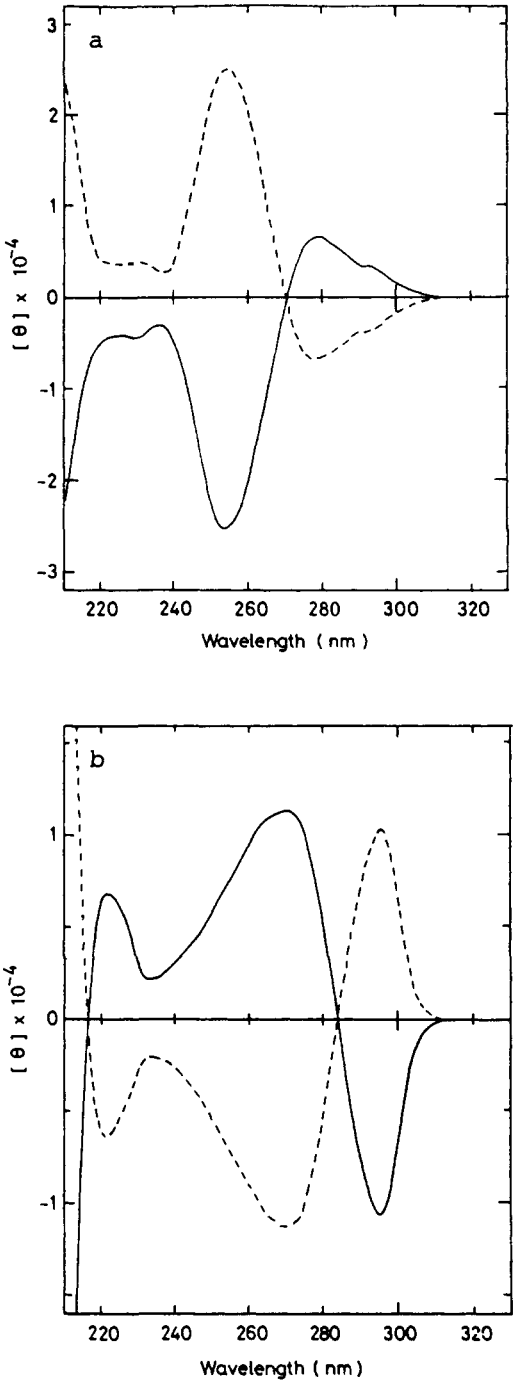

Figure 1. Circular dichroism spectra of D-d(CGCGCG) (solid line) and L-d(CGCGCG) (dashed line) at 0 °C. Samples (10 A_{260}/mL) were dissolved in 10 mM sodium phosphate buffer (pH 7) containing (a) 0.1 M NaCl and (b) 4 M NaCl. Strand concentration was estimated by absorbance values at 80 °C and a molar extinction coefficient of 51 400 L/(mol·cm) at 260 nm calculated for D- and L-d(CGCGCG).[12]

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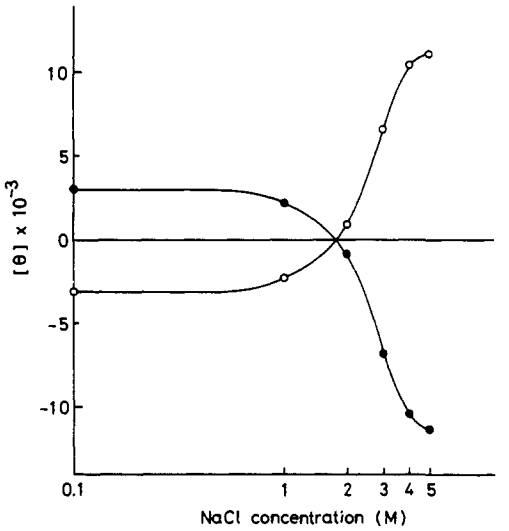

Figure 2. Salt concentration dependence of the B to Z transition for D-d(CGCGCG) (closed circles) and L-d(CGCGCG) (open circles) at 0 °C. [θ] values at 295 nm were plotted for each salt concentration. Experimental conditions were the same as those described in the caption below Figure 1 except for NaCl concentration.

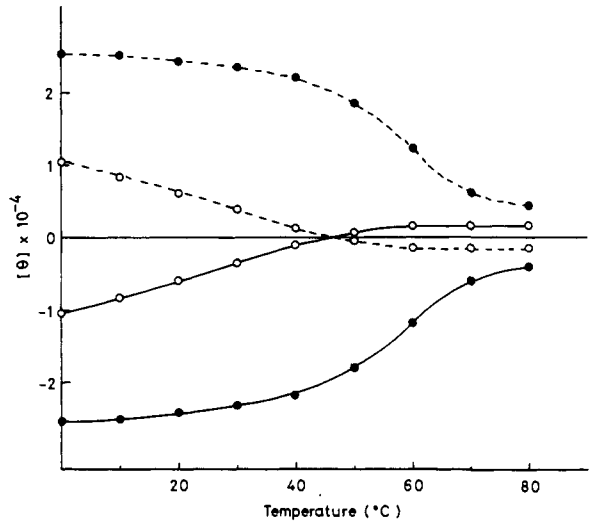

Figure 3. Temperature dependence of CD strength of D-d(CGCGCG) (solid line) and L-d(CGCGCG) (dashed line) under low salt conditions (0.1 M NaCl, closed circles) at 254 nm and under high salt conditions (4 M NaCl, open circles) at 295 nm.

nuclease P1 afforded the expected nucleotides and 5'-end deoxycytidine, but the L-isomer was resistant to digestion by this enzyme under the same conditions, as expected. This result indicates that the optical isomer of natural DNA cannot be recognized by natural enzymes consisting of L-amino acids.

The conformational properties of DNA oligomers or polymers containing the alternating C–G sequence have been well documented by circular dichroism (CD) spectra.[9] In 0.1 M NaCl solution, the CD spectrum of the D-hexamer showed a profile of the standard B form[10] (Figure 1a, solid line). The same magnitude but opposite sign was observed for the CD spectrum of L-d(CGCGCG) (Figure 1a, dashed line). The L-oligonucleotide thus adopts a mirror-image B form with left-handed double-helical conformation. The inversion of the CD band at 295 nm of the alternating C–G sequences under high salt conditions is known to be due to the conformational transition from the right-handed B form to the left-handed Z form.[11] The CD spectrum of D-d(CGCGCG) showed the characteristic negative band of the Z form at 295 nm in 4 M NaCl solution (Figure 1b, solid line), and that of the L-isomer showed an inversion profile (Figure 1b, dashed line). Both spectra were the same in magnitude at each wavelength. The L-hexamer thus adopts a mirror-image Z form with right-handed double-helical conformation.

The dynamic properties of both hexanucleotides were also compared. Both were noted to have the same salt concentration dependence on the B to Z conformational transition, whose midpoint was at 2.6 M NaCl (Figure 2). The same dependency on temperature, with opposite signs, was also noted for both isomers within experimental error under both low and high salt conditions (Figure 3). D- and L-DNA thus have the same type and strength of hydrogen bonding and base–base stacking interactions.

The present data clearly show both D- and L-DNA to possess the same conformation and dynamic properties except for chirality. The higher order structures of L-DNA are also the exact mirror images of that of natural DNA.

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Nearest-Neighbor Recognition in Phospholipid Bilayers. Probing Lateral Organization at the Molecular Level[1]

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Developing a detailed understanding of supramolecular structure–function relationships within biological membranes represents one of the most important challenges presently facing chemists and biologists.[3] Although the lipid bilayer provides the basic structural element for all biological membranes, its precise lateral organization remains poorly defined. In particular, the question of whether or not lipids organize themselves into nonrandom clusters (i.e., domains) remains enigmatic.[4] The fact that natural phospholipids are rich in structural diversity could mean that a hierarchy of domains exists and that certain of these domains have functional importance, e.g., membrane fusion, transport, recognition, and catalysis.[5-7]

In this report we describe an experimental method that probes the thermodynamic preference for one phospholipid unit to become a *covalently attached nearest neighbor* of another in the bilayer state. We define such a preference as "nearest-neighbor recognition" (NNR). If the packing forces that govern NNR are the same as those that govern domain formation, then a systematic analysis of NNR should provide molecular-level insight into how the structure and composition of phospholipids influence their tendency to segregate within the lamellar phase. Our approach

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