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Supplementary Material Available: Experimental procedures for production of ^{13}C-labeled peptone, fermentation and isolation of leucocin A, and acquisition of NMR data, as well as tables of ^{1}H and ^{13}C NMR assignments (11 pages). Ordering information is given on any current masthead page.

Intermolecular versus Intramolecular Hydrogen-Bonding Competition in the Complexation of Cyclitols by a Twisted Polyaza Cleft

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The complexation of monomers of biomacromolecules via hydrogen bonding and π-stacking is receiving increased attention.[1] Foremost are synthetic receptors for nucleotide bases.[2] In contrast, only a small number of hosts for monosaccharides have been developed,[3] even though practical applications for carbohydrate hosts are possible.[4] The parallel alignment or divergence of hydrogen bond donors and acceptors within nucleotide bases does not allow substantial intramolecular hydrogen bonding. Conversely, we find that the ability to form intramolecular hydrogen bonds within carbohydrate analogues (cyclitols) dominates the selectivity and strength of binding to polyaza cleft **1**.

Key steps in the synthetic pathway to **1**[5] (Scheme I) are as follows: (a) formylation of the aldol product[6] **3** with *N*,*N*-dimethylformamide dimethyl acetal,[7] (b) protection of ethyl 3,3-diaminopropenoate[8] with 3,4-dimethoxybenzyl (**4**), (c) enamine formation from **5** using trimethylsilylpyrrolidine,[9] (d) vacuum flash pyrolysis addition of ethyl glyoxylate[10] to **6**, and (e) after central pyridine formation,[11] deprotection of the amines with CF_3CO_2H.[12]

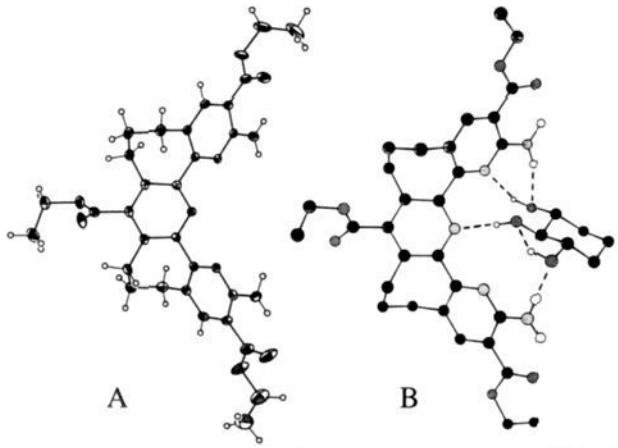


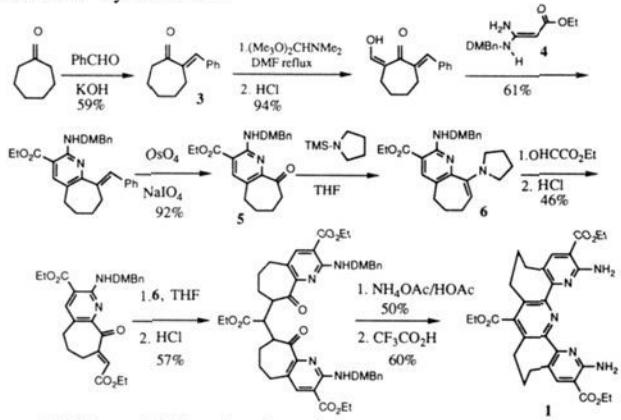
Figure 1. (A) Crystal structure of **1**. (B) Molecular dynamics derived structure for the complexation of 1,3/2-cyclohexanetriol by **1**.

Table I. Binding Constants (M^{-1})[a]

	host	
guest	**1**	**2**
cis 1,2-diol	12[a]	--
trans 1,2-diol	18[a]	2[c]
1,3/2-triol	110[b]	35[b]
1,2/3-triol	47[b]	12[a]
1,2,3-triol	39[b]	14[a]

[a] Error estimated from the percent saturation achieved is (a) 15%, (b) 10%, and (c) 100%.

Scheme I. Synthesis of **1**[a]



[a] DMBn = 3,4-dimethoxybenzyl.

Host **1** is twisted in the solid state[13] with a dihedral angle between the peripheral pyridines of 79.8° (Figure 1A). This twist opens up the cavity and allows the complexation of nonplanar substrates such as cyclitols. Figure 1B displays the dominant

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(5) Compound **1**: ^{1}H NMR ($CDCl_3$, 300 MHz), δ 7.99 (s, 2 H), 6.60 (br, 4 H), 4.46 (q, 2 H), 4.34 (q, 4 H), 2.48 (t, 8 H), 2.18 (t, 4 H), 1.41 (m, 9 H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 75 MHz) δ 167.4, 166.3, 158.0, 154.0, 148.8, 142.0, 141.3, 132.0, 123.6, 107.0, 62.0, 61.1, 31.9, 28.4, 27.4, 14.3; high-resolution MS (100 eV, CI) *m/e* calcd for $C_{30}H_{33}N_5O_6$ 559.243 084, measured 559.243 432.

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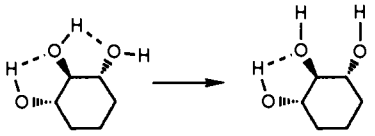
low-energy structure of **1** and 1,3/2-cyclohexanetriol generated by a molecular dynamics[14] run from 0 to 300 K with 5-fs step sizes, a path length of 105 ps, and the Amber force field,[15] followed by minimizing random structures generated after multiple 4-ps intervals. The four hydrogen bonds indicated between **1** and the guest are those with interheteroatom distances of 2.9 Å or less and hydrogen bonds angles greater than 160°.[16] The molecular dynamics suggests that 1,3/2-cyclohexanetriol undergoes a reorganization to break one intramolecular hydrogen bond upon complexation as shown.



Binding constants (Table I) in chloroform were determined by ^{1}H NMR titrations of host into constant concentrations of cyclitols. Upfield chemical shifts of the guest C*H*OH resonances versus host concentration were fit to the typical binding algorithm,[17] and downfield shifts of the CHO*H* resonances were observed.[18] Host **1** binds stronger than **2**,[19] indicating cooperativity between the C_2 symmetric halves of **1**. Within a series of guests (diols or triols), trans arrangements of hydroxyls yield larger binding constants. Furthermore, the binding constants are lower than predicted by comparison to complexes that possess four hydrogen bonds between relatively nonacidic donors and nonbasic acceptors.[20]

The selectivity is postulated to arise from competition between intramolecular hydrogen bonds in the guests and intermolecular hydrogen bonds with the host. Cis 1,2-hydroxyls form stronger intramolecular hydrogen bonds than trans 1,2-hydroxyls.[21] Infrared spectroscopy of the cyclitols in chloroform confirmed the intramolecular hydrogen bonds and indicated no guest oligomerization. In addition, the IR spectra of the diols confirmed the relative strength of cis versus trans intramolecular hydrogen bonds. Thus, trans hydroxyl stereochemistry leads to stronger complexation since the weaker intramolecular hydrogen bonds are broken. The intramolecular hydrogen bonds also depress the binding since the energy required to partially break them must be paid upon complexation. This competition will likely play a similar role in the complexation of saccharides with synthetic hosts in aprotic low dielectric solvents. Future saccharide receptors for such solvents will need to effectively compete with the intramolecular hydrogen bonds to achieve large association constants. The competition is another factor in addition to secondary interactions,[22] electronic arguments,[23] and strength of acid-base considerations,[24] which should be considered in the interpretation of binding constants.

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Registry No. 1, 138722-49-3; **1** dimeric precursor, 138753-37-4; **3**, 42063-01-4; **3** hydroxymethylene derivative, 138722-50-6; **4**, 138722-51-7; **5**, 138722-53-9; **5** phenylmethylene precursor, 138722-52-8; **5** 8-(ethoxycarbonylmethylene) derivative, 138722-55-1; **6**, 138722-54-0; 1-(trimethylsilyl)pyrrolidine, 15097-49-1; cycloheptanone, 502-42-1; *cis*-1,2-cyclohexanediol, 1792-81-0; *trans*-1,2-cyclohexanediol, 1460-57-7; (1α,2β,3α)-1,2,3-cyclohexanetriol, 2630-65-1; (1α,2α,3β)-1,2,3-cyclohexanetriol, 10515-21-6; (1α,2α,3α)-1,2,3-cyclohexanetriol, 2630-64-0.

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Formation of Gaseous π and Ion-Neutral Complexes As Probed by Interannular *tert*-Butyl Cation Transfer in Protonated *tert*-Butyl-Substituted Diphenylalkanes†

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The role of π and σ complexes as reactive intermediates in electrophilic aromatic substitution reactions has become common textbook knowledge.[2-4] However, detailed information on the structure, reactivity, and energetics is only available for σ complexes, both in solution[5] and in the gas phase.[6] In contrast, the occurrence and properties of π complexes, at least in the gas phase,[4] are much less clear.

The existence of gaseous π complexes along with the corresponding σ complexes has been shown in some cases by utilizing sophisticated mass spectrometric techniques.[7-9] Moreover, the unimolecular formation of noncovalent, i.e., purely *electrostatically bound*, ion-neutral complexes during the fragmentation of gaseous organic ions has been studied in greater detail.[10-17] For protonated

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