The use of ^{171}Yb NMR spectroscopy as a valuable structural and mechanistic probe is expected to catalyze a rapid expansion in Yb(II) chemistry.

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Nucleotide Base Recognition: A Macrocyclic Receptor for Adenine Employing Hydrogen Bonding and Aromatic Stacking Interactions

Shyamaprosad Goswami† and Andrew D. Hamilton*

Department of Chemistry, University of Pittsburgh Pittsburgh, Pennsylvania 15260

Donna Van Engen

Department of Chemistry, Princeton University Princeton, New Jersey 08544

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Effective molecular recognition requires a precise complementarity between several binding regions on the receptor and the different chemical features of the substrate. We have recently introduced[1] such a *multi-site* approach for the recognition of nucleotide bases in which hydrogen bonding and aromatic stacking groups within a macrocyclic receptor bind simultaneously to the substrate. Varying the hydrogen bonding region has led to selective receptors for thymine[2a] and guanine,[2b] while changing the electronic characteristics of the stacking group results[2c] in different geometries for the aromatic–aromatic interaction.[3] In this paper we report the further development of this approach with the synthesis, structure, and binding properties of a family of receptors for adenine derivatives.[4]

The periphery of adenine offers four readily accessible hydrogen bonding sites, the pyrimidine-N,NH of Watson–Crick and the imidazole-N,NH of Hoogsteen base-pairing.[5] Molecular modelling studies suggested that all four of these could be complexed by a 1,2-bis(2-amino-6-pyridyl)ethane derivative in an anti conformation and with inwardly pointing pyridine and amide groups (Chart I).[5] This particular orientation of hydrogen bonding groups should be favored by incorporating the dipyridylethane into a macrocycle which also contains a suitable π-stacking component.

The synthesis of the adenine receptors is shown in Chart II. Protection of 2-amino-6-picoline as its phthalimide derivative **1** followed by NBS bromination gave bromomethylpyridine **2** in 60% yield. Reductive dimerization[6] of **2** using chlorotris(triphenylphosphine)cobalt(I)[7] afforded a 50% yield of **3**[8] which was then

Chart I

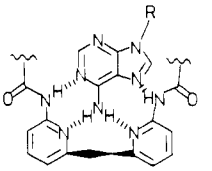
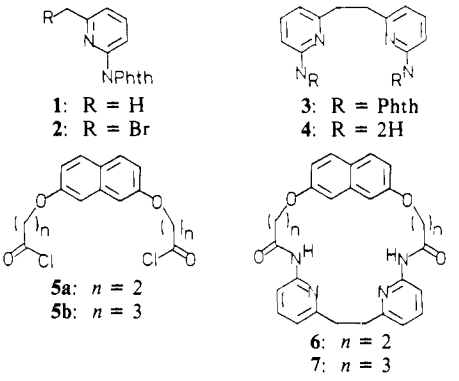


Chart II



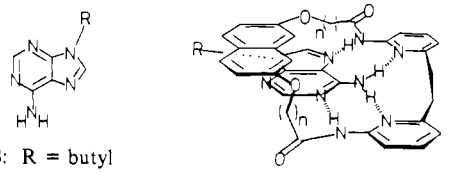
1: R = H
2: R = Br

3: R = Phth
4: R = 2H

5a: n = 2
5b: n = 3

6: n = 2
7: n = 3

Chart III



8: R = butyl

deprotected via hydrazinolysis (70% yield) to diamine **4**.[8] High dilution coupling of **4** (CH_2Cl_2, Et_3N) with the appropriate naphthalene diacid chloride **5a**,**b**[2a,9] gave macrocyclic receptors **6** and **7**[8,10] in 17 and 19% yield, respectively.

The proposed binding orientation of the receptors (Chart I) is supported by the X-ray crystal structure of macrocycle **6** (Figure 1a). Two intramolecular hydrogen bonds between the amide-NHs and ether-Os (H···O, 1.95 Å, 2.00 Å) stabilize a conformation for the macrocycle in which the two amidopyridines are anti to each other and approximately in the same plane. This places the pyr-Ns at 5.04 Å and the amide-NHs at 7.33 Å apart from each other with good binding complementarity to the amino group and purine-Ns of adenine. In contrast, the crystal structure of receptor **7** (Figure 1b) shows a more open conformation with the dipyridylethane unit in a gauche arrangement. A 60° rotation around the central C–C bond is required to form the binding orientation.

The adenine-binding properties of the receptors were followed by ^{1}H NMR and showed a strong dependence on ring size. Titration of **7** in $CDCl_3$ with 9-butyladenine **8**[11] caused large downfield shifts in the receptor-NH (2.0 ppm) and adenine-NH_2 (2.4 ppm) resonances consistent with the formation of a tetrahydrogen bonded complex, as in Chart I. In addition, upfield shifts in the naphthalene-1,8- (0.4 ppm), 4,5- (0.16 ppm), and 3,6- (0.17

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(8) All new compounds gave satisfactory spectroscopic and analytical and/or high resolution mass spectral data.

(9) Prepared by alkylating 2,7-dihydroxynaphthalene with the appropriate bromoester (acetone, K_2CO_3) followed by hydrolysis and acid chloride formation (oxalyl chloride).

(10) **7**: ^{1}H NMR ($CDCl_3$) 8.30 (2 H, br s, NH), 7.95 (2 H, d, J = 7.6 Hz, pyr-2H), 7.59 (2 H, d, J = 8.8 Hz, naphth-4,5H), 7.54 (2 H, t, J = 7.6 Hz, pyr-4H), 7.28 (2 H, d, J = 2.0 Hz, naphth-1,8H), 6.95 (2 H, dd, J = 2.0, 8.8 Hz), 6.82 (2 H, d, J = 7.6 Hz, pyr-5H), 4.21 (4 H, t, J = 5.8 Hz, CH_2O), 2.91 (4 H, s, pyrCH_2), 2.61 (4 H, t, J = 5.9 Hz, CH_2CO), 2.27 (4 H, m, $CH_2CH_2CH_2$).

(11) Synthesized by a modification of Carraway et al. (Carraway, K. L.; Huang, P. C.; Scott, T. G. In *Synthetic Procedures in Nucleic Acid Chemistry*; Zorbach, W. W., Tipson, R. S., Eds.; Interscience: New York, 1986; p 3).

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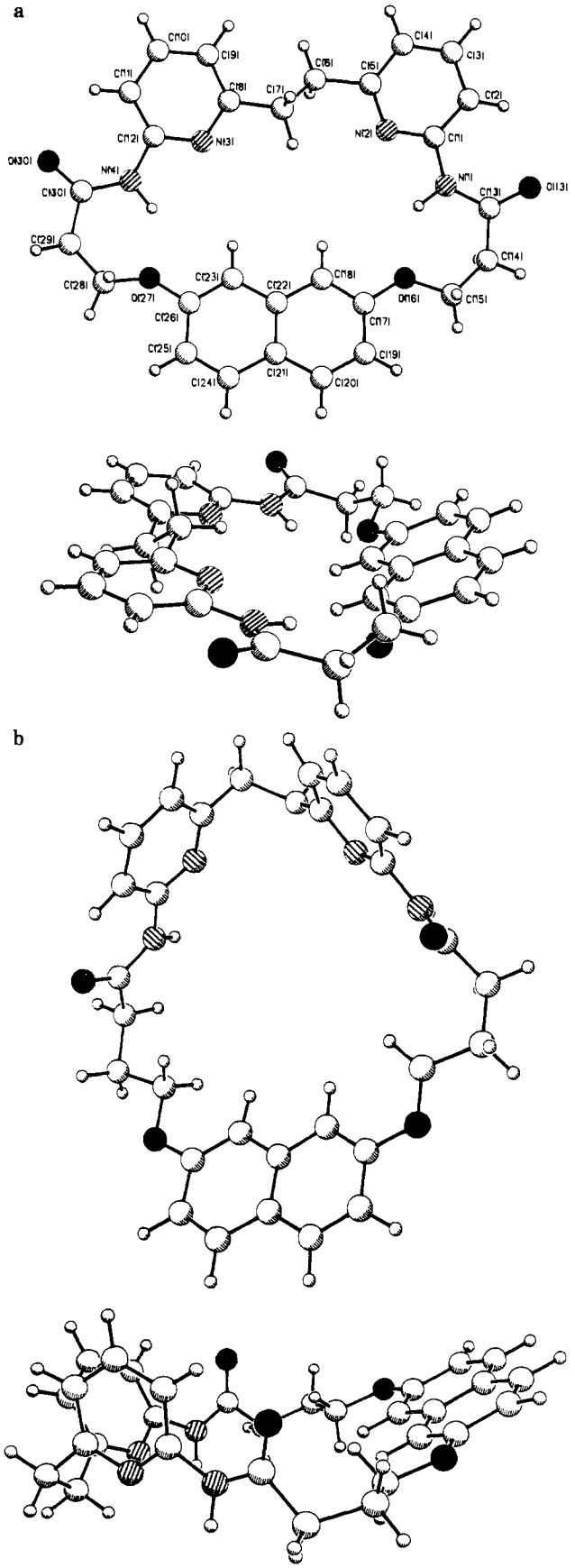

Figure 1. (a) X-ray structure of **6** and (b) X-ray structure of **7**.

ppm) and adenine-2- (0.08 ppm) and 8- (0.05 ppm) proton resonances are seen, reflecting the close approach of the two rings in an aromatic stacking interaction (Chart III).[2a,b] All of the shifts showed clear saturation behavior, and from these curves an association constant (K_s) of 3200 M^{-1} for **7**:**8** was determined.[12] This value is substantially larger[4] than related triple hydrogen bonding receptors for thymine,[2a] guanine,[2b] and cytosine[3b] thus confirming that simultaneous Watson-Crick and Hoogsteen interactions are present in complex **7**:**8**. The complementarity and selectivity of this arrangement for adenine is further supported by the weak association between **8** and 1-butylthymine ($K_s < 23$ M^{-1}) or tripentanoylguanosine ($K_s < 10$ M^{-1}). Despite the high level of preorganization apparent in Figure 1a, receptor **6** shows much weaker binding to **8** ($K_s = 73$ M^{-1}). This is possibly due to the two intramolecular hydrogen bonds, shown in solution by their downfield shifted NH resonances (δ 9.5 ppm in **6** compared to 8.30 ppm in **7**), which block the cavity and must be broken for adenine binding to occur. Thus, the structure of **6** with two *intramolecular* H-bonds between the pyr-NH and the rigid 2,7-dioxynaphthalene provides a model for the conformational change that accompanies the *intermolecular* H-bonding interaction between **7** and 9-alkyladenine **8**.

In summary, we have shown that semirigid receptors with oriented hydrogen bonding sites can form strong and selective complexes with complementary substrates. X-ray structural characterization provides important insights into the conformational changes involved in complexation.

Acknowledgment. We thank the National Institutes of Health for partial support of this work and Nalin Pant for helpful discussions.

Supplementary Material Available: Crystallographic details for **6** and **7** including tables of atomic coordinates, thermal parameters, bond angles, and bond lengths (18 pages). Ordering information is given on any current masthead page.

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Catalytic Asymmetric Hydroboration of Styrenes

Tamio Hayashi,* Yonetatsu Matsumoto, and Yoshihiko Ito*

Department of Synthetic Chemistry, Faculty of Engineering, Kyoto University, Kyoto 606, Japan

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We report here novel catalytic asymmetric synthesis of optically active 1-arylalkanols (up to 96% ee) through asymmetric hydroboration of styrenes catalyzed by a chiral cationic rhodium complex, which complements the uncatalyzed asymmetric hydroboration with chiral alkylboranes derived from α-pinene that has been successfully used for internal alkenes.[1,2]

Since Mannig and Noth reported in 1985 that rhodium complexes catalyze the hydroboration with catecholborane,[3] a few reports have appeared on application of the catalyzed hydroboration for organic synthesis, i.e., control of regio- and stereochemistry in the hydroboration of allylic alcohol derivatives[4] and catalytic asymmetric hydroboration of 1,2- and 1,1-disubstituted alkenes.[5] We found that the use of a certain cationic phos-

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