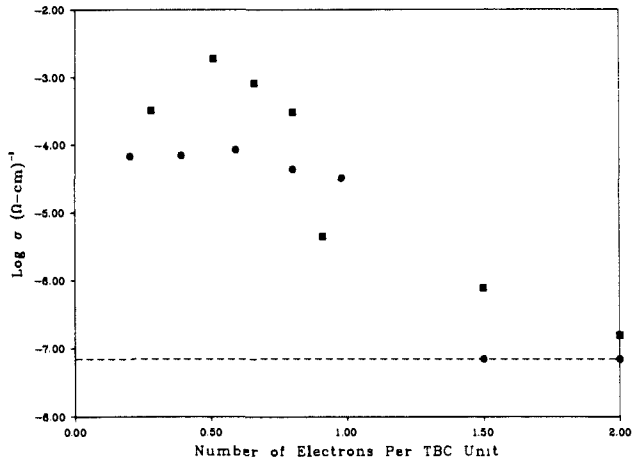

Figure 1. Conductivity versus number of electrons based upon initial stoichiometry for the doping study of Ni(TBC) with $[K(C222)]_2[Ni(TBC)]$ (squares) and TBC with $[K(C222)]_2(TBC)$ (circles). The dashed line represents the lower limit for conductivity measurements with the device used.

creasing proportion of $Ni(TBC)^{2-}$, while the band for $Ni(TBC)^{1-}$ increases. The number of electrons per Ni(TBC) as determined by initial stoichiometry is consistent with the relative amounts of Ni(TBC) and $Ni(TBC)^{1-}$ as determined by IR.

Efforts are currently underway to determine the mechanism of conductivity in Ni(TBC). In particular, two mechanisms of conductivity are under consideration, conductivity via the interacting π-orbitals as in $Ni(Pc)I_x$[3a] or conductivity via the metal spine as in $Co(Pc)I_x$.[3b] Electrochemical, EPR and infrared results, and theoretical calculations[6] indicate the LUMO of Ni(TBC) is primarily ligand centered and antibonding with respect to the alkyne bonds. Ni(0) is a d^{10} species requiring the 4s or 4p orbitals to interact in order to form a conduction band for metal-centered conductivity in this n-doped system. To determine if the nickel was essential to the conductivity in this system a similar study on the free ligand TBC was undertaken.[11] The IR spectrum of reduced TBC shows two bands at 2089 and 2036 cm^{-1} which have been assigned to the monoanion and dianion, respectively. The results of n-doping of TBC show a weak maximum at 0.6 e^-/TBC with a conductivity of 8×10^{-5} $(\Omega\text{-cm})^{-1}$, 25 times lower than the maximum observed for Ni(TBC). This indicates that while the presence of the nickel atom is not essential for conductivity it does strongly influence the conductivity.

The conductivities of reductively doped Ni(TBC) are comparable to p-doped metallophthalocyanine complexes with the four-probe powder conductivity for $Ni(Pc)(I)_x$ at room temperature being 7.7 $(\Omega\text{-cm})^{-1}$.[3a] The conductivities for many other p-doped phthalocyanine complexes lie in this region.[3] The reductive doping of phthalocyanine complexes has been explored recently with room temperature conductivities of $\{K[SiO(Pc)]\}_n$,[3e] $K_2[Co(Pc)]$,[3f] and $K_2[Fe(Pc)]$[3f] of 2×10^{-5}, 5×10^{-3}, and 2×10^{-4} $(\Omega\text{-cm})^{-1}$, respectively. These were measured by the four-probe technique.[8] As with the above materials the conductivity of doped Ni(TBC) is expected to be highly anisotropic.

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Registry No. Ni(TBC), 98779-78-3; Li, 7439-93-2; Na, 7440-23-5; K, 7440-09-7; I_2, 7553-56-2.

(10) Perlstein, J. H. *Solid State Chemistry and Physics An Introduction*; Weller, P. F., Ed.; Marcel Dekker, Inc.: New York, 1973; Vol. 1, pp 275-278.
(11) A procedure similar to that in ref 9 was followed for the doping of TBC with $[K(C222)]_2(TBC)$.
(12) Shriver, D. F.; Drezdzon, M. A. *The Manipulation of Air Sensitive Compounds*, 2nd ed.; John Wiley & Sons: New York, 1986.

Molecular Recognition: Hydrogen Bonding and Aromatic Stacking Converge To Bind Cytosine Derivatives

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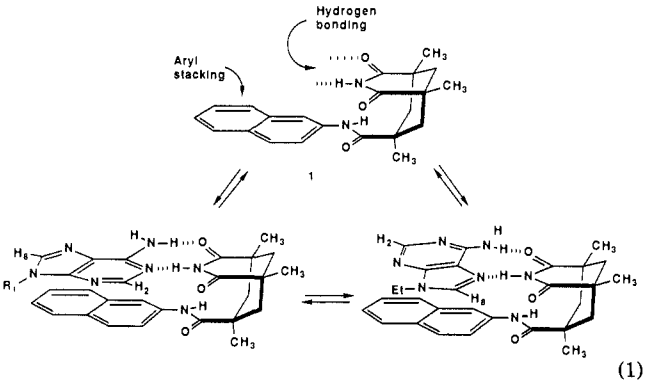
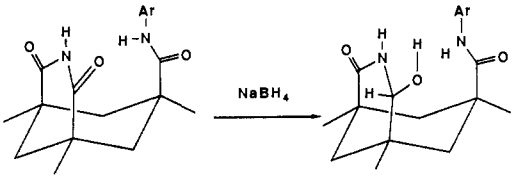
In recent communications from this laboratory we have described model receptors for nucleic acid components.[1] Such structures (eq 1) feature hydrogen bonding and aryl stacking



(1)

surfaces which converge from perpendicular directions to provide a microenvironment complementary to adenine derivatives. Watson-Crick, Hoogsteen, and bifurcated hydrogen bonds are present, and remote structural features influence the subtleties of base-pairing in the recognition event. We now describe modification of these systems that results in their selective binding of cytosine derivatives.

The new molecules are prepared by mere $NaBH_4$ reduction[2] of the imide amides. Specifically, the naphthyl **1**, phenyl **2**, and anthryl **3** derivatives were reduced to give the corresponding hydroxylactam structures **3a-c**. This reaction effectively changes the hydrogen bonding pattern of the imide to a structure complementary to acylated amidines (eq 2). The structures follow



(2)

1 Ar=2-naphthyl
2 Ar=phenyl
3 Ar=2-anthryl

3a Ar=2-naphthyl
3b Ar=phenyl
3c Ar=2-anthryl

from spectroscopic features[3] which indicate an intramolecular hydrogen bond between the hydroxyl and the neighboring amide carbonyl. This is revealed by a large coupling constant of the hydroxyl and the α-methine proton (13 Hz) and NOE experiments which indicate that this intramolecular hydrogen bond limits considerably the internal rotations of the structure. The NOE results for **3a** are summarized on the structure. (The proton at

(1) Rebek, J., Jr.; Askew, B.; Ballester, P.; Buhr, C.; Jones, S.; Nemeth, D.; Williams, K. *J. Am. Chem. Soc.* **1987**, *109*, 5033-5035. Rebek, J., Jr.; Askew, B.; Ballester, P.; Buhr, C.; Costero, A.; Jones, S.; Williams, K. *J. Am. Chem. Soc.* **1987**, *109*, 6866-6867. Rebek, J., Jr.; Williams, K.; Parris, K.; Ballester, P.; Jeong, K. S. *Angew. Chem., Int. Ed. Engl.* **1987**, *26(12)*, 1244-1245. For a macrocyclic system with similar recognition capabilities see: Hamilton, A.; Van Engen, D. *J. Am. Chem. Soc.* **1987**, *109*, 5035-5036.
(2) Hubert, J. C.; Wijnberg, J. B. P. A.; Speckamp, W. N. *Tetrahedron* **1975**, *31*, 1437-1441.
(3) All new compounds were characterized by a full complement of high-resolution spectra. For **3a** (mp 186-189 °C): ^1H NMR (300 MHz, $CDCl_3$) δ 5.16 (d, J = 13 Hz, 1 H, OH) δ 4.57 (d, J = 13 Hz, 1 H, CH). Similar signals were observed for **3b** (mp 201-204 °C) and for **3c** (mp 223-225 °C).

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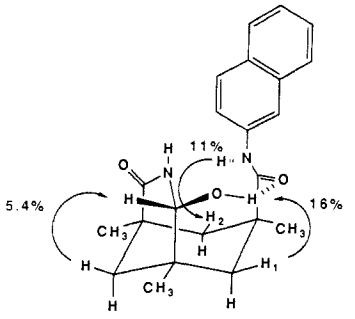
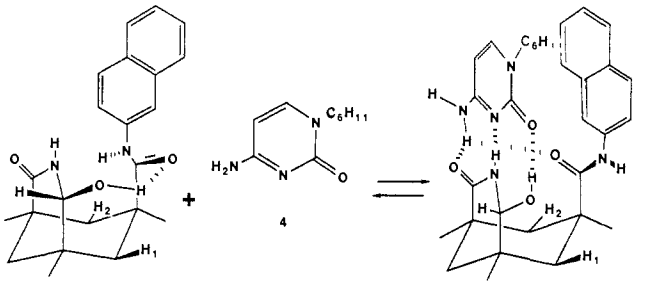
the tail of the arrow was irradiated and the percent enhancement was observed on the proton at the head of the arrow.)



3a

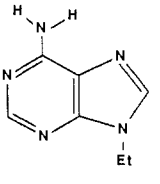
Titration of either **3a**, **3b**, or **3c** with cyclohexyl cytosine[4] **4** in $CDCl_3$ gave changes consistent with simultaneous hydrogen bonding and stacking interactions as suggested in eq 3. Downfield



4 5

(3)

shifts of the lactam NH (δ 5.5 → δ 11.4) or the corresponding upfield shifts in the aromatic signals could be used to generate saturation curves. Association constants were obtained from Eadie plots.[5] The titration could even be followed by observing the change in coupling constant between the OH and methine proton which decreases from 13 to 3 Hz during the course of the complexation. For the naphthalene derivative **3a**, K_a was observed to be 260 M^{-1}. For the phenyl derivative **3b** the corresponding value was 100 M^{-1}, while the anthracyl **3c** gave 290 M^{-1}. The naphthalene surface appears to offer all the aryl stacking interactions there are to be had in this system. Studies at various temperatures with **3a** gave $\Delta H = -8.65$ kcal/mol and $\Delta S = -18$ eu, figures which are in reasonable agreement with models for cytosine–guanine base pairing in organic solvents.[6] Parallel titration of **3a** with 9-ethyladenine **6** gave a value of $K_a \leq 25$ M^{-1}.

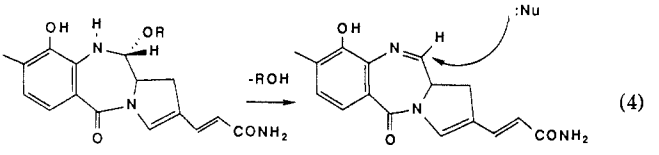


6

The selectivity of the new systems for cytosine over adenine is therefore at least 10-fold. For the binding shown in eq 1, K_a = 220 M^{-1} was observed,[1] but the (mismatched) interaction[7] of cytosine **4** with **1** shows $K_a < 10$ M^{-1}. The reversal of selectivities generated by altering a single hydrogen bonding site is quite satisfactory.

The structural details of the complex **5** were explored with NOE methods. Irradiation of the aryl N–H at 63% complex (37% free **3a**) gave enhancements of 8.5% at H_1 and 6.2% at H_2 (58:42). At 70% complex the corresponding values were 10% and 5.1% (66:34). Thus, complexation forces the rotation of the aryl carboxamide by ~180°, presumably because a bifurcated hydrogen bond can be formed with the amino group of cytosine. The net increase is two hydrogen bonds, since the intramolecular hydrogen bond of **3a** becomes broken on complexation. As a result the association constants are in the hundreds rather than the thousands that might be expected for three new hydrogen bonds.[8]

Finally, structures **3** incorporate the functional aspects of anthramycins **7**, agents that alkylate double-stranded DNA by way of their dehydration products (eq 4).[9] It should be possible to "tune" the new molecules for similar activity, and we are working toward this goal with suitable modifications.



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(4)

Acknowledgment. This work was supported by the National Science Foundation.

(4) Okano, T.; Goya, S.; Takahashi, T. *Yakugaku Zasshi* **1968**, *88*, 1112–1117 (*Chem. Abst.* **1969**, *70*, 37756x). See, also: Fox, J. J.; Van Praag, D.; Wempen, I.; Doerr, I. L.; Cheong, L.; Knoll, J. E.; Eidinoff, M. L.; Bendich, A.; Brown, G. B. *J. Am. Chem. Soc.* **1959**, *81*, 178–187.

(5) Eadie, G. S. *J. Biol. Chem.* **1942**, *146*, 85–93. Hofstee, B. H. J. *Nature (London)* **1959**, *184*, 1296–1298.

(6) Pohorille, A.; Burt, S. K.; MacElroy, R. D. *J. Am. Chem. Soc.* **1984**, *106*, 402–409.

(7) For a similar mismatch see: Williams, L. D.; Shaw, B. R. *Proc. Natl. Acad. Sci. U.S.A.* **1987**, *84*, 1779–1783.

(8) Kyogoku, Y.; Lord, R. C.; Rich, A. *Science (Washington, D.C.)* **1966**, *154*, 518–520. Pitha, J.; Jones, R. N.; Pithova, P. *Can. J. Chem.* **1966**, *44*, 1045–1050.

(9) Barkley, M.; Cheatham, S.; Thurston, D. E.; Hurley, L. H. *Biochemistry* **1986**, *103*, 7629.

Experimental Tests of Models To Predict Nucleophilic Addition Stereochemistries

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Many models have been proposed to explain the stereochemistries of nucleophilic additions, especially lithium aluminum hydride reductions, of both acyclic and cyclic carbonyl compounds.[4] While there are conceptual differences in these models, they rationalize the same body of experimental data, and consequently they have not been distinguishable by direct experimental tests. However, we have identified several new compounds for which different models predict different stereoselectivities in LAH reductions. We describe here these predictions and the experimental tests subsequently performed in our laboratories.

Various literature models for cyclohexanone reduction are summarized here with reference to cyclohexanones **1a–c**. LAH reduction of each of these compounds proceeds preferentially from the axial direction to give axial/equatorial attack ratios of 92:8, 83:17, and 53:47, respectively.[4] As generalized by Barton, axial attack of nucleophiles is favored when steric hindrance is negligible.[5] Dauben proposed that "product development control"

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(4) Boone, J. R.; Ashby, E. C. *Topics in Stereochemistry*; Eliel, E. L., Allinger, N. L., Eds.; Vol. 11, p 53.

(5) Barton, D. H. R. *J. Chem. Soc.* **1953**, 1027, footnote 23.