Table I. Spectral Data for Copper(I) Complexes and Ligands[a]

complex	λ_{max}[b] (ϵ)[c]	ligand	λ_{max}[b] (ϵ)[c]
two-coordinate[d]			
$Cu(DMP)_2^+$	209 (20.8), 234 (24.8)	DMP	214 (6.4)
$Cu(TMP)_2^+$	215 (23.5), 239 (23.1)	TMP	220 (7.8)
$Cu(4\text{-MeIm})_2^+$	207 (28.2)	4-MeIm	201 (9.7)
three-coordinate			
$Cu(pza)^+$[e]	220 (17.2), 231 (sh), 254 (16.5), 299 (1.6)	pza	220 (13.2)
$[Cu(timm)]_2^{2+}$[f]	232 (28.9), 287 (3.75)	timm	225 (23.7)
four-coordinate[g]			
$Cu(trpyn)^+$	215 (17.2), 261 (16.5)	trpyn	216 (19.8)
$Cu(Me_6trpyn)^+$	218 (21.4), 265 (19.1)	Me_6trpyn	220 (25.1)

[a] In methanol. [b] nm. [c] mM^{-1} cm^{-1}, sh = shoulder. [d] Reference 7. [e] Reference 8. [f] Reference 5. [g] Reference 9.

π-π^* excited states can be seen in the altered enhancement patterns, reflecting different Franck-Condon factors. Thus the 218-nm-excited spectrum is dominated by the 1467-cm^{-1} band, while the 266-nm-excited spectrum has a more even intensity distribution. The relative intensities of the 1235- and 1395-cm^{-1} bands are much higher with 266- than 218-nm excitation. Similar spectra are obtained for the Ag(I) complex with 218- but *not with 266-nm* excitation.

Thus, selecting laser lines which correspond to the MLCT absorption bands of the Cu(I) complex provides specific enhancement of the coordinated ligand modes. This effect should prove useful in probing the structure of the coordination group in reduced copper proteins. Moreover, their UVRR spectra and excitation profiles should aid in delineating the MLCT absorption bands, which are likely to be hidden among the aromatic side-chain absorptions.

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Molecular Recognition: Ionic and Aromatic Stacking Interactions Bind Complementary Functional Groups in a Molecular Cleft

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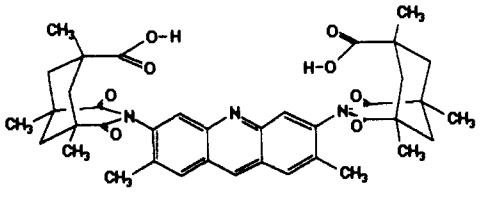
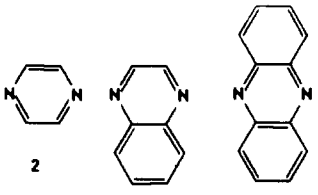
We recently introduced the model receptor **1** and showed its affinity for molecules of complementary size and shape.[1] The



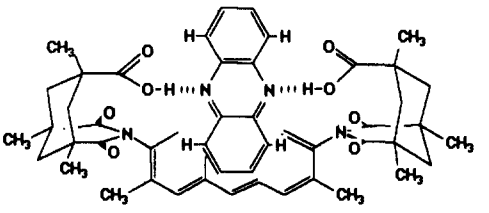
1



2 **3** **4**

structure features a rapidly assembled *molecular cleft* defined by the convergence of two carboxyl groups and the acridine nitrogen. The cleft provides a highly polar microenvironment in an otherwise lipophilic skeleton, a feature that proves useful in the transport of amino acids across liquid membranes.[2] In this paper we explore the selectivity that the system shows toward molecules of complementary functionality.

Table I Association Constants[a] for Complexes of **1** ($CDCl_3$, 25 °C)



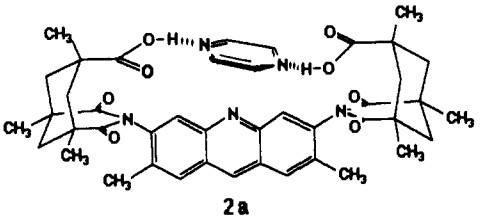
4a

5

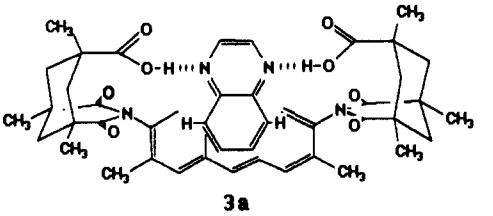
base	K_a, M^{-1} L	pK_a[b](BH^+)
pyrazine (**2**)	1.4×10^3	0.65
quinoxaline (**3**)	23×10^3	0.56
phenazine (**4**)	2.2×10^3	1.2
pyrimidine (**5**)	0.7×10^3	1.3
quinazoline (**6**)	1.6×10^3	1.9[c]
imidazoline (**7**)	$K_1 = 1.0 \times 10^6$, K_2[d] $= 5.5 \times 10^4$	6.9
benzmidazole (**8**)	$K_1 = 1.5 \times 10^4$, K_2[d] $= 7.5 \times 10^3$	5.5
purine[e] (**9**)	$\sim 8 \times 10^3$	2.4
pyridine	$K_1 = 1.2 \times 10^2$, K_2[d] = <1	5.2

[a] Obtained from Eadie-Hofstee plots[4] involving chemical shift changes as a function of receptor/substrate ratios. Saturation of the receptor (>95% sites occupied) was attained with all bases except pyridine. [b] Albert, A. In *Physical Methods in Heterocyclic Chemistry*; Katritsky, A., Ed.; Academic Press: New York, 1963; Vol. I, chapter 1. [c] For the unhydrated form: *The Chemistry of Heterocyclic Compounds*; Brown, D. J., Ed.; Interscience: New York, 1967; Vol. 24. Part 2 (Quinalzolines), Ch. II. [d] M^{-2} L^2. [e] Low solubility of this base required sufficiently high dilution that NMR shifts were difficult to assess.

The binding of **1** to heterocyclic diamines was studied by using the NMR techniques described previously,[1] and association constants are reported in Table I. For example, the binding of aromatic amines such as pyrazine **2** causes upfield shifts for the signals for the interior protons of the cleft (H_4, H_5) whereas mere deprotonation by conventional bases such as triethylamine causes downfield shifts in these signals. The most likely structure for the pyrazine complex involves a perpendicular arrangement of the two aromatic systems shown in **2a**. The selectivity for the



2a



3a

diamine pyrazine vs. pyridine can be seen in Table I: **1** recognizes and preferentially complexes pyrazine *in the presence of* the stronger base, pyridine.

Similiar studies involving the benzo derivatives of pyrazine reveal how stacking interactions and steric effects alter association constants. Thus, quinoxaline **3** shows a 15-fold enhancement in binding over **2**, and the stacking interaction between aromatic

(1) Rebek, J., Jr.; Askew, B.; Islam, N.; Killoran, M.; Nemeth, D.; Wolak, R. *J. Am. Chem. Soc.* **1985**, *107*, 6736-6738.

(2) Rebek, J., Jr.; Nemeth, D. *J. Am. Chem. Soc.* **1985**, *107*, 6738.

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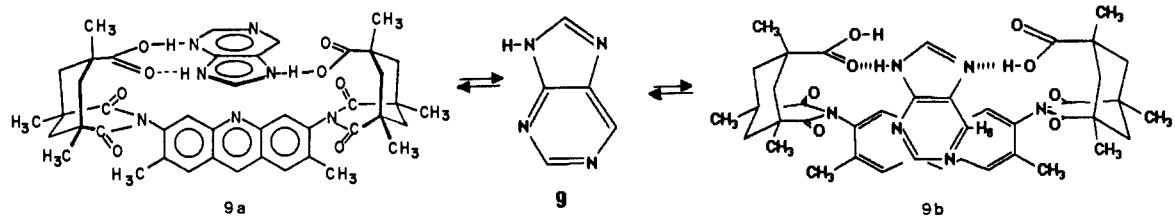
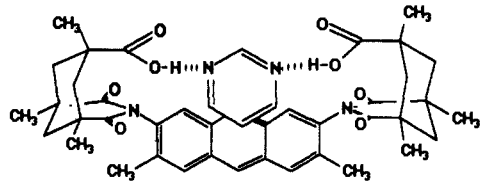
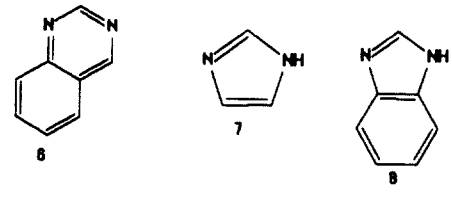


(2)

subunits in the receptor and substrate is revealed by *upfield*[3] shifts in **3**. Accordingly, the parallel arrangement of aromatics, shown in **3a**, is indicated. The diacid functions as a *molecular chelate* that positions the substrate for optimal stacking interactions. With phenazine **4**, this geometry creates steric effects involving the carbonyl oxygen of the carboxyl and the peri hydrogens of the remote (unstacked) ring and results in reduced binding. The chemical shifts observed[3] for these protons in the complex **4a** are those expected for a system showing rapid exchange between two stacking sites.

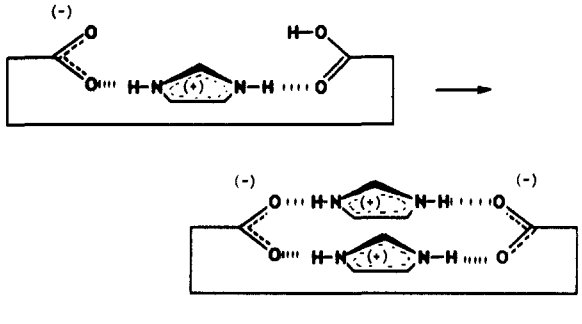
Chelation of pyrimidine **5** is slightly less favorable than that of **2** even though **5** is a stronger base and stacking interactions





can be seen in its complex with the receptor.[3] The reduced affinity of pyrimidine must be attributed to its shape: The N–N distance of about 2.5 Å is 0.3 Å shorter than in pyrazine and the orientation of the lone pairs is inferior for complexation, at least if idealized, linear hydrogen bonds are assumed. Again, the benzo derivative quinazoline **6** shows improved binding.

Yet another type of binding interaction available to **1** is revealed in its complexation with imidazole **7**, a heterocycle that can act as both hydrogen bond donor and acceptor. Here, curvature[5] of the plots indicated the binding of two molecules of **7**, with $K_2 \approx K_1$. The complexation of this relatively strong base probably involves some ionization (eq 1), a process which should improve



(1)

the hydrogen-bonding capabilities of the 1:1 complex: the carboxylate becomes a better lone pair donor while the acid becomes a better proton donor.[6] Even so, the common test for cooperativity, the Hill plot,[7] showed a slope of 0.4 indicating that the binding of a second imidazole was a factor of 20 times less favorable than binding the first. This result is most likely due to electrostatic repulsion between the two bound imidazolium ions. With the benzo derivative **8** 2 equiv of the amine were bound but somewhat less effectively and again without cooperativity. Even so, it should be possible to engineer cooperativity into this system by selecting substrates that minimize repulsions in the 2:1 complex.[8]

Finally an intramolecular competition between the two heterocyclic nuclei imidazole and pyrimidine was staged by examining the mode of binding to purine **9**. Here, as with **2**, upfield shifts are observed for the protons lining the cleft of the receptor and modest shifts are observed in the pyrimidine nucleus. These changes are best accommodated by contributions from both the perpendicular arrangement **9a** and the stacking of **9b** (eq 2) rather than direct chelation of the pyrimidine nucleus.

In summary, the arrangement of carboxyl groups and the aromatic surface of the model receptor present a number of binding possibilities to diamines. We are currently exploring the catalytic advantages offered by the convergent functionality of **1**.

Acknowledgment. We are grateful to the National Institutes of Health for financial support of this research.

(3) Upfield shifts (ppm) observed in the diamine portions of the various complexes: **2a** (none); **3a** ($H_{5,8}$ 0.1; $H_{6,7}$ 0.25); **4a** ($H_{2,3,7,8}$ 0.1); **5a** (H_5 0.15); **6a** (H_5 0.2, H_7 0.15, H_8 0.1); **7a** ($H_{4,5}$ 0.45); **8a** ($H_{4,7}$ 0.51, $H_{5,6}$ 0.53); **9a** (H_2 0.13, H_6 0.18).

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(7) For an excellent discussion, see: Levitzki, A. *Mol. Biol., Biochem., Biophys.* **1978**, *28*, 15–29.

(8) For a related case in crown ether chemistry, see: Rebek, J., Jr.; Costello, T.; Marshall, L.; Wattley, R.; Gadwood, R. C.; Onan, K. *J. Am. Chem. Soc.* **1985**, *107*, 7481–7487.

Facile Enzymatic Preparation of Monoacylated Sugars in Pyridine

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Regioselective modification, e.g., acylation of sugars, is a fundamental and difficult task in organic chemistry.[1] Even preferential acylation of primary over secondary hydroxyl groups can only rarely be efficiently carried out with free sugars;[1,2] this

†On leave from Universite Paris-Sud, Orsay, France.

(1) Sugihara, J. M. *Adv. Carbohydr. Chem.* **1953**, *8*, 1–44. Haines, A. H. *Adv. Carbohydr. Chem. Biochem.* **1976**, *33*, 11–109.

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