Journal of Inclusion Phenomena **5** (1987), 161–164.

MULTIPLE RECOGNITION IN POLYTOPIC ANION HOSTS

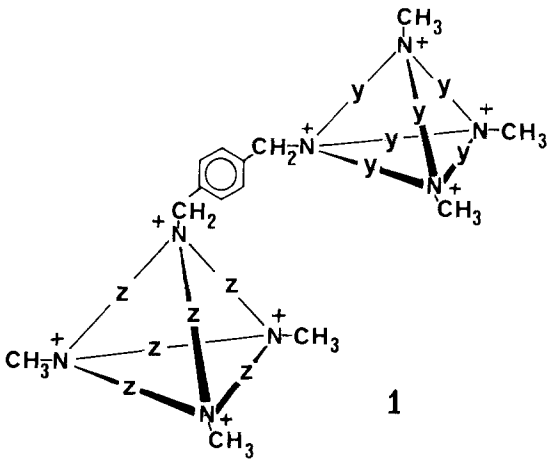
Franz P. Schmidtchen
Lehrstuhl für Organische Chemie und Biochemie der TU München
D-8046 Garching, Lichtenbergstr. 4, FRG

Selectivity in guest binding by biogenic or abiotic receptors depends on the type, number, spatial orientations and overall flexibility of the ensemble of recognition sites interacting with the substrates. The putatively optimal approach to construct a selective host compound is to arrange anchor groups on a rigid concave molecular framework capable of inclusion of the guest species. This route, however, may soon reach the limits of synthesizability if polyfunctional biologically relevant guests (nucleotides, hormones, coenzymes) are to be selectively bound.

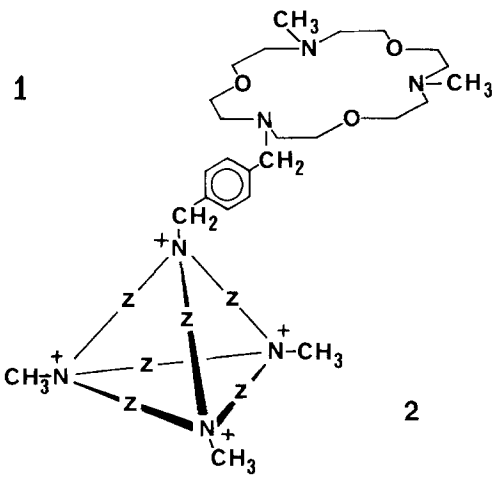
An alternative is to connect modular receptor sites in a linear (branched or unbranched) open chain fashion to constitute a receptor which must be folded by the guest template for binding. Though the selectivity features may be inferior to a rigid host compound possessing the same types and numbers of anchor groups, substrate specificity in the former approach may easily be altered or enforced by simple attachment of supplementary recogniton sites.

In order to probe this concept the substrate specificities of two artificial ditopic receptors 1 and 2 [1] have been studied, each of which is composed of two different and independent anchor groups interlinked by a freely rotatable p-xylene spacer unit. The monotopic receptor 3, a common building block of either ditopic receptor 1 or 2 is known [2] to bind hydrophobic preferentially anionic guest species whereas the other subsites of 1 and 2 have been shown to complex hydrophic anions [2a] and prim. ammonium cations [3a], respectively.

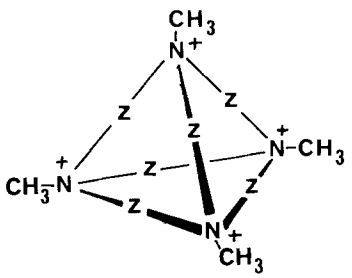
The selectivity advantage of the ditopic design of 1 in relation to its monotopic parent compound 3 was investigated using the dimensional probes 4 – 8 each containing two anionic functions at a fixed distance. Analysis of the UV-absoption band shifts experienced by these solvatochromic probes on inclusion into the molecular cavity of the larger tetrahedral receptor site 3 yielded the 1 : 1 association constants in water.



1



2



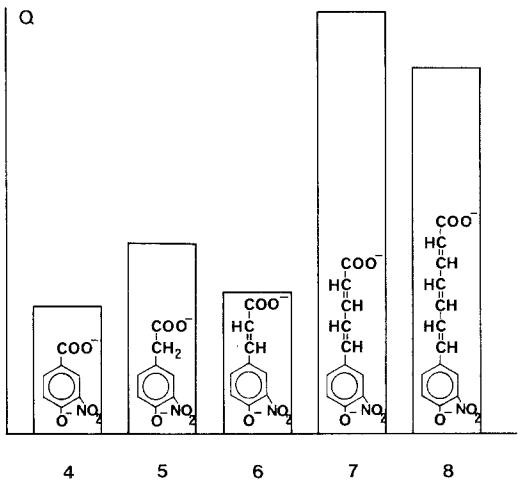
3

y = $-(CH_2)_6-$

z = $-(CH_2)_8-$

The complexes with 1 are generally more stable than those with 3 owing to increased electrostatic attractions. In addition to this unspecific binding enhancement the specific interaction of suitably large substrates with both receptor subsites becomes apparent from inspection of the selectivity factor Q. Whereas the smaller substrates 4, 5, 6 are confined to the interaction with the big subsite in 1 due to insufficient spacing of the anionic moieties. The more extended probes 7 and 8 can span the gap between the receptor subsites in 1. This additional interaction mode translates as a threefold increase in Q, although rotation of the subunit with respect to each other could paralyze simultaneous recognition of both anionic moieties of the probe.

$$Q = \frac{K_{ass}\ (\text{guest} \subset 1)}{K_{ass}\ (\text{guest} \subset 3)}$$



Association constants K_{ass} $[M^{-1}]$ and selectivity factors Q of the dimensional probes 4 - 8 with the monotopic (3) and ditopic (1) receptor in water, pH 8.8, 27°C.

substrate		4	5	6	7	8
K_{ass}	1	714	322	2041	5265	10 000
	3	208	62	556	476	1042
	Q	3.4	5.1	3.7	11.1	9.6

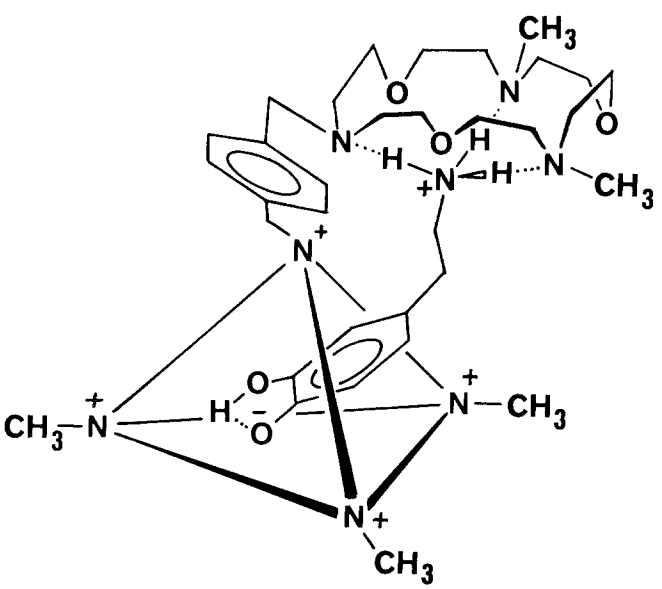


Fig. 1:

The combination of a receptor unit for hydrophobic (anionic) species (3) with a prim. ammonium anchor group (the azacrown ether [3]) is expected to yield a ditopic receptor for biogenic amines. A possible complex structure is depicted in Fig. 1.

Preliminary measurements of the association constants by a competition method with K^+ ion using K^+ selective electrodes reveal that the ditopic receptor 2 preferentially binds hydrophobic amines.

Association constants K_{ass} $[M^{-1}]$ of amine guest compounds in 80 wt% aqueous methanol; pH_{obs} = 10.00; μ = 1.0, 25°C.

substrate	K_{ass}
K^+	246
5-aminopentanol	83
tyramine	184
dopamine	134
tyrptamine	183

Conclusion:

Even the first and simplest member of the family of linear modular receptors, the ditopic host 1, exhibits a measurable selectivity advantage solely attributable to the ditopic design. It amounts to a factor of 3 with respect to binding homologous substrates.

References:

1) F.P. Schmidtchen, Tetrahedron Lett. 27, 1987 (1986); see also: F.P. Schmidtchen, ibid. 25, 4361 (1984)

2) F.P. Schmidtchen, Chem.Ber. 114, 597 (1981); F.P. Schmidtchen J.Chem.Soc.Perkin Trans. II, 1986, 135.

3) J.-M. Lehn, P. Vierling, Tetrahedron Lett. 21, 1323 (1980)