

News Item

New Synthetic Receptors

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The revolution in the development of synthetic receptor molecules recognized by the award of the 1987 Nobel prize in chemistry to Charles Pedersen, Donald Cram and Jean-Marie Lehn continues. Three reports in *Angewandte Chemie (Int. Ed. Engl.)* give details of new receptors (hosts) incorporating boron atoms in their structures. All are cyclic compounds containing a central binding cavity and in each case their synthesis represents an important and novel addition to the expanding field of synthetic host-guest chemistry with implications for the future development of more efficient molecular catalysts. A common feature of each study is the use of molecular architecture to achieve spatial and/or electronic complementarity between the host and guest species. New receptors, adept at the selective capture of anions, are the result.

The first report by Hawthorne and colleagues (X. Yang, C. B. Knobler and M. F. Hawthorne, *Angew. Chem.* **30**, 1507–1508 (1991)), describes the synthesis of 12-mercurocarborand-4 (Figure 1), the initial representative of a new class of rigid macrocycles that are capable of binding an anion such as chloride in the central cavity. The chloride-ion complex can be considered to be a charge-reversed analogue of the alkali-metal complexes of the well-studied cyclic polyether 12-crown-4. The very stable chloride complex of 12-mercurocarborand-4 is obtained in high yield simply by reacting the dilithiated borane cage 1,2-C₂B₁₀H₁₂ with mercuric chloride. The authors propose that the chloride ion serves as a template in cyclizing the mercury ions and their carborane ligands; an X-ray diffraction study shows that the cyclic tetrameric product contains the chloride in the central cavity with each mercury distorted towards it. This arrangement results in unprecedented square-planar coordination of the central chloride ion by the four mercury sites. It appears that the electron-withdrawing properties of the carborane cages greatly enhance the attraction of the mercury centres for the central chloride anion.

A key observation is that reaction of the chloride complex with silver ions results in removal of the chloride from the central cavity without causing the host molecule to decompose. The shape and electronic nature of the cavity appear suitable for the binding of a range of other inorganic and organic anions; and it seems likely that the system might act as a homogeneous catalyst for promoting particular reactions, a possibility now being explored.

Reetz and coworkers describe in a pair of reports (M. T. Reetz, C. M. Niemeyer and K. Harms **30**, 1472–1474, 1474–1476 (1991)) the synthesis of the first examples of a new class of selective boron-containing hosts which are capable of performing

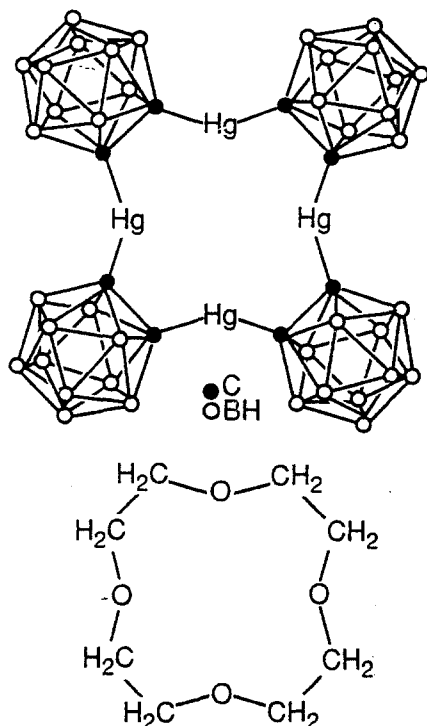


Fig. 1. 1,2-Mercurocarborand-4 (top) binds chloride anions in its interior just as its charge-reversed analogue 12-crown-4 (below) binds alkali metal atoms.

the dual role of binding both a cation and an anion *simultaneously* using different sites within the host. This has been achieved by incorporating both a cyclic crown ether backbone and a boron-containing (electron starved) site in the host (Figure 2). Such a molecule may bind a cation using the polyether crown ring and either leave the corresponding counter anion unbound or bind it simultaneously at the boron site. The latter effect can be employed to achieve 'salt selectivity'. For

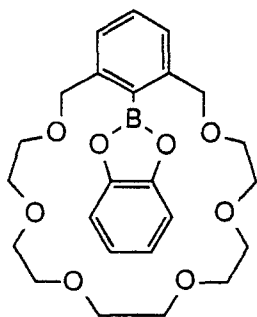


Fig. 2. This difunctional receptor is capable of simultaneous binding of a cation to its polyether (crown) ring and an anion to its boron site.

example, this host shows remarkable selectivity in preferentially binding KF from a mixture of KF, KCl, KBr and KI. In this case the discrimination is associated with the simultaneous binding of cation and anion to the host, a situation shown to persist in the solid state by means of X-ray diffraction. In solution, the binding of the potassium and the fluoride to the host is synergistic: in part, the arrangement adopted in the KF adduct is undoubtedly influenced by the strong affinity of the fluoride ion for the boron centre, although a number of other factors are also important.

Reetz and coworkers also show that their host binds alcohols and amines simultaneously (as well as selectively). The overall reaction (see Figure 3) involves the spontaneous deprotonation of the alcohol and corresponding protonation of the amine to produce alkoxy and alkyl ammonium ions; the former binds to the boron receptor site and the latter hydrogen bonds to the oxygens of the crown polyether ring. Thus, in mimicry of many biological systems, the synthetic host is capable of recognizing and binding more than one organic guest molecule. The initial experiment involved the interaction of the difunctional host with a 1:1 mixture of methanol and benzylamine in dichloromethane. An X-ray structure of the product shows that there is communication between the guests: the ammonium ion is contained in the cavity of the crown ring and is hydrogen bonded to the oxygens of the crown as well as to that of the methoxy group (which is bound at the boron acceptor site). Competition experiments involving benzylamine and two alcohols

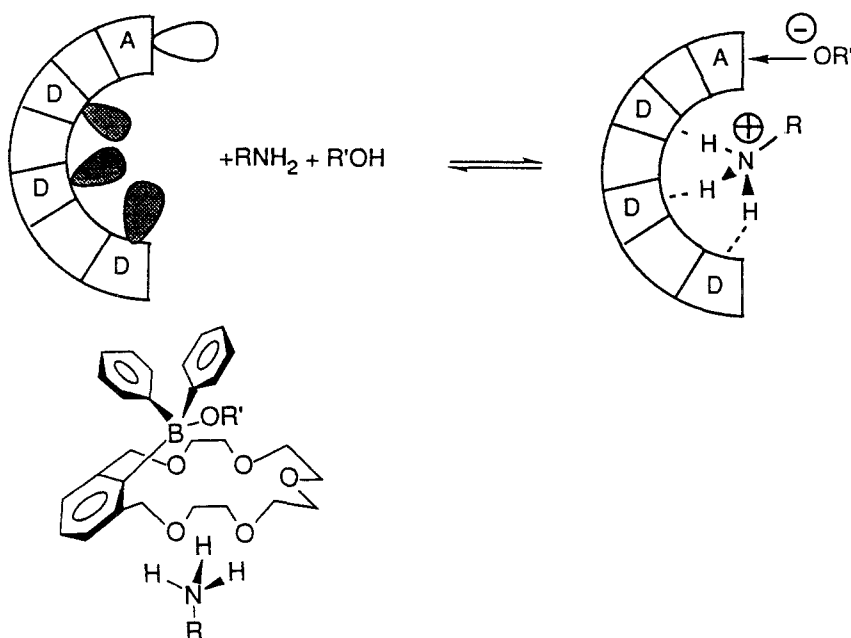


Fig. 3. The binding of amines and alcohols to Reetz and coworkers' difunctional hosts. Above, the lone pair (filled lobes) on each donor ether oxygen (D) is capable of binding to a hydrogen on the protonated amine, while the empty orbital (blank lobe) on the boron acceptor site (A) can bind to the deprotonated alcohol. Left, with a smaller crown, amines are unable to penetrate so deeply into the ring and the host is less selective.

indicate that selective alcohol binding occurs. For example, methanol binding is favoured over ethanol binding by a ratio of approximately 3:1. Such potentially useful molecular recognition appears to be largely controlled by steric factors.

Because the X-ray structure shows incorporation of benzylamine in the crown's cavity, the authors expected that the host might recognize amines selectively based on their size. Again, competition experiments with benzylamine and α -methylbenzylamine together with different alcohols show that, in each case, only a benzylamine/alcohol combination was selected.

Similar competition experiments involving a smaller version of the host (incorporating five oxygen atoms in the crown ring, instead of six) resulted in lower amine selectivity. Reetz and coworkers ascribe this to the inability of the respective ammonium groups to penetrate as deeply into this smaller crown (Figure 3). This latter observation is in accordance with the X-ray structure of the ethanol/benzylamine adduct. But this smaller host yields increased selectivity for methanol; for example, in association with benzylamine, methanol is bound exclusively over ethanol.

The present innovations in receptor design have wider implications. These include the development of new anion sensing devices, new chromatography materials and new boron-containing reagents for use in neutron-capture therapy for the treatment of cancer.