Pure & Appl. Chem., Vol. 68, No. 8, pp. 1561–1567, 1996.
Printed in Great Britain.
© 1996 IUPAC

Molecular recognition of dihydroxy-aromatics with *bis-o*-xylyleneglycoluril hosts

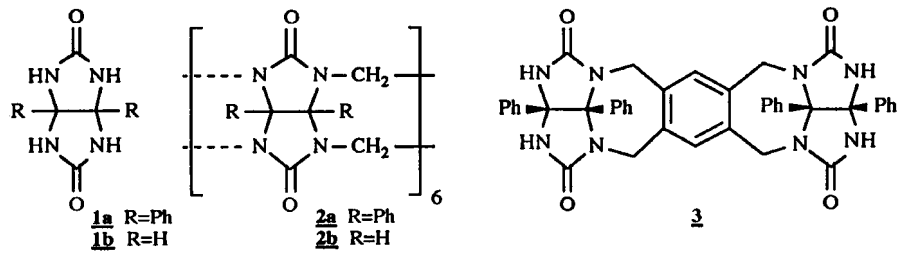
Brian A. Murray[a,b] and Giuseppe S. Whelan[a].

a) Department of Chemistry, University College Dublin, Dublin 4, Ireland; b) Department of Applied Sciences, Regional Technical College Tallaght, Dublin 24, Ireland.

ABSTRACT: a variety of 'molecular clip' host molecules based on glycoluril have been synthesised and their binding to resorcinol and catechol guests in chloroform investigated by NMR, IR and phase transfer. The glycoluril unit provides two convergent hydrogen-bond acceptors, and two xylylene 'walls' complete a cleft which further binds the guest by aryl stacking; 1:1 binding constants of up to 2500 M^{-1} are obtained. Modelling suggests that the systems have moderate conformational flexibility, allowing for an induced fit to the guest. Placing π-electron-donating substituents on the walls enhances binding, despite the presence of such substituents on the target guests: this has been explained in terms of the interactions of π-poor and π-rich atoms at the points of contact of the host and guest.
The host molecules catalyse the transport of resorcinol from water into chloroform.

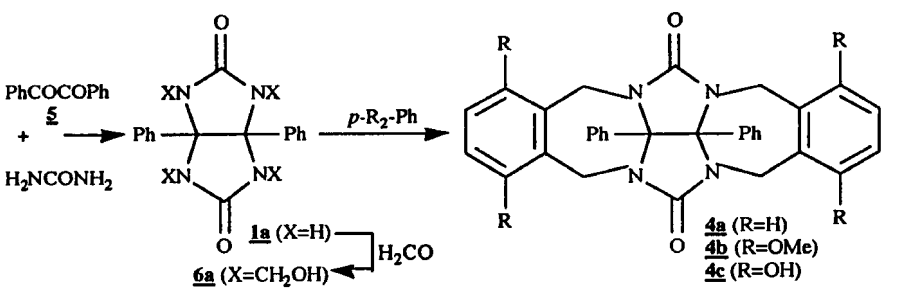
INTRODUCTION

Cram has pointed out that most guests are relatively small convex molecules with diverging binding sites (1). So hosts which are to bind such targets should be complementary in structure: they should be sufficiently large so as to contain intramolecular cavities delineated by molecular segments which bear the interaction sites i.e. converging binding sites. A number of host systems exhibiting such features incorporate the V-shaped glycoluril unit **1**, with two carbonyl oxygens as hydrogen-bond acceptors, and four ureido hydrogens providing hydrogen-bond donors, or alternatively providing functionality for further structural elaboration. Examples include Mock's Cucurbituril **2b**, (prepared from urea, glyoxal and formaldehyde, it binds diammonium ions internally) (2), Rebek's *bis*(glycoluril)durene **3** (a self-complementary molecule which forms a 'tennis ball' dimer) (3), and Nolte's *bis(-o*-xylylene)diphenylglycoluril 'molecular clip' **4a** (see Scheme 1), which binds resorcinol and catechol between its xylylene 'walls' (4).



In unsuccessful attempts to prepare **2a** (substituting benzil **5** for glyoxal), we often produced derivatives of diphenylglycoluril **1a**, which were precursors to the molecular clip (see Scheme 1). Scheme 2 shows a stylised representation of a clip binding a resorcinol guest *via* hydrogen-bonding to the carbonyls and aryl stacking between the upward-facing xylylenes. The phenyl substituents maintain a conformational 'lock', preventing the xylylenes equilibrating into downward-facing conformations (4b).

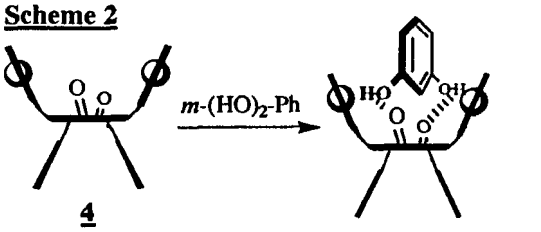
Scheme 1



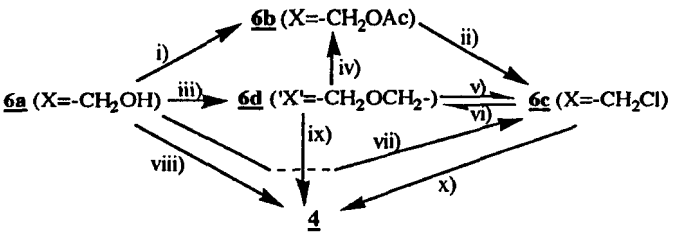
A particularly attractive feature of Nolte's clip is the synthesis: the last step is an electrophilic aromatic substitution, opening up the possibility of a wide variety of clips with e.g. oxidisable (5) and/or basic (6) 'walls', which should both modify binding and also be themselves switchable between two states by a change in environment (e.g. voltage or pH change, etc.).

The capacity for binding dihydroxybenzenes (4d) suggests that such hosts may be useful in molecular recognition of, for example, dihydroxyphenethylamines such dopamine, DOPA, and (nor)adrenaline.

Scheme 2



Scheme 3



i), iv) Ac_2O/*p*-TsOH
ii) $SOCl_2/CH_2Cl_2$/RT/15h
iii) H^+(aq.)/Δ
v), vii) $SOCl_2$/RT/15h
vi) Air (standing)
viii) H_2SO_4/RT
ix) H_2SO_4 or TFA *[or x)]*
x) $SnCl_4/AlCl_3/Cl(CH_2)_2Cl$

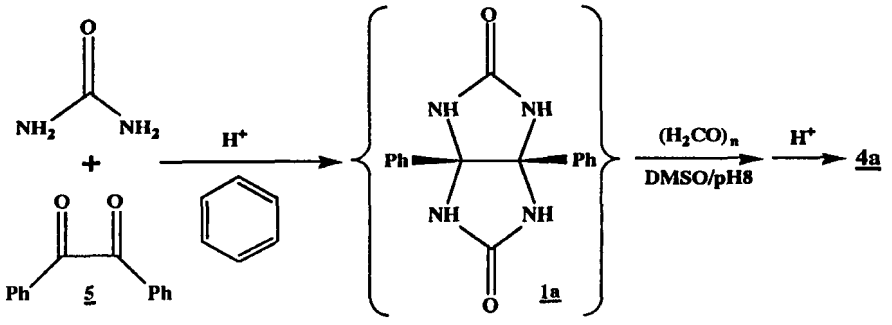
EXPERIMENTAL

Molecular modelling: using the COSMIC force field (7), the total energy of each clip structure was minimised and significant geometric parameters measured. Examples include the intercarbonyl (O<->O) distance, which indicates the molecule's 'bite' as a two-hydrogen-bond acceptor, and the distance and angle between the xylylene 'walls', as an indication of its potential to bind an aromatic guest by aryl stacking.

Synthesis: another attraction of the clips is their very simple and inexpensive synthons (4b): condensation of benzil **5** and urea (benzene/trifluoroacetic acid/azeotropic reflux) gives diphenylglycoluril **1a** (Scheme 1); addition of 4 equivalents of paraformaldehyde (DMSO/pH8) yields the tetraol **6a**; addition of an appropriate aromatic with an acid catalyst then gives clip **4**. A number of more activated diphenylglycoluril derivatives were introduced by Nolte (4d), including the tetra(acetoxymethyl) **6b**, the tetra(chloromethyl) **6c**, and the *bis*ether **6d** (see Scheme 3). We have further optimised these routes, and added a new one [*vii)* in Scheme].

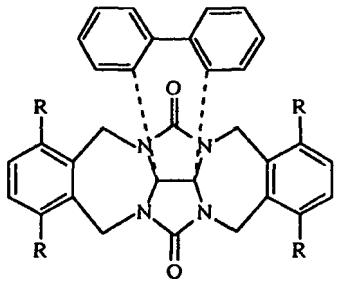
As befits a convergent host molecule, we have also demonstrated how highly convergent the synthesis is by converting it to a one-pot reaction (see Scheme 4) with four steps controlled by sequential pH changes; note that the solvent in the first step becomes a reactant in the last. As well as eliminating a number of tedious isolations, this method proceeds with higher overall yield.

Scheme 4

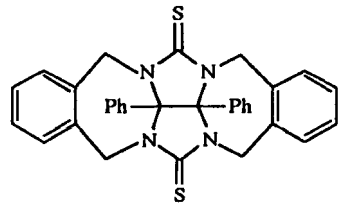


An alternative synthesis is base-catalysed reaction of diphenylglycoluril **1a** with *o-bis*(bromomethyl)xylene to give the clip **4a**; this has also been carried out in one pot, starting with urea, with comparable efficiency.

Other clips based on diphenylglycoluril **1a** which have been prepared include: (i) the tetramethoxy **4b** and the tetraol **4c** (see Scheme 2), (ii) a tetramethyl clip **4d** (R=Me), and (iii) two potentially pH- and redox-switchable *p*-phenylenediamine hosts **4e** ($R=NH_2$) and **4f** ($R=NMe_2$); the latter two are unfortunately too unstable in air to be studied conveniently.



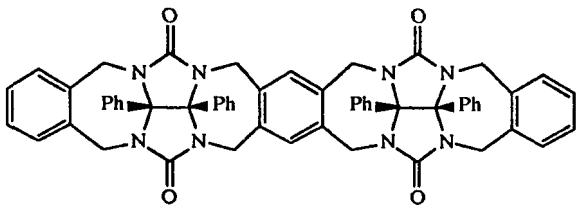
7a (R=H)
7b (R=OMe)



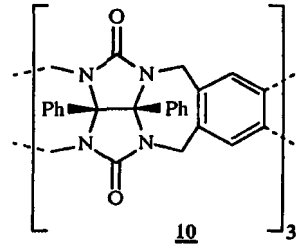
8

Other modifications of the host architecture include: (i) two phenanthro-clips **7a** and **7b**, - in which the two phenyl substituents are *ortho*-linked to form a biphenyl unit - prepared by replacing benzil **5** with 9,10-phenanthraquinone, and (ii) a dithio-clip **8**, prepared using thiourea.

Host **9** is a "2.5-mer", formed by reacting Rebek's monomer **3** with two moles of *o-bis*(bromomethyl)-xylene: it has two clefts which share a central durene unit, so although it has two degenerate binding sites, it should only accommodate one guest.



9



10

Cyclotrimer **10** was made by a similar route: its NMR spectrum indicates it is highly symmetrical. Potentially a triply-degenerate host, it has structural similarities to (dodecaphenyl)cucurbituril **2a**.

Full details of the above syntheses will be reported elsewhere.

Binding constants by NMR titration: all titrations were carried out in $CDCl_3$ at 25°. Where possible, the concentration of the component of which the ^{1}H-NMR signal was monitored (host or guest) was kept constant by making up the other component in the stock solution of the one being measured. This ensured that the concentration of the monitored component was not diluted by additions of the other component; it also simplified calculation of the binding constant. A spectrum of the monitored component was taken, then further spectra as aliquots of the other component were added by microlitre syringe, concentrations covering the range from deficiency through to large excess.

In all cases, fast exchange was observed i.e. on the NMR timescale, individual peaks due to host and complex were not seen (contrast IR spectra below): rather, an 'average' peak was seen, with its chemical shift moving as the titration proceeded. Significant shifts were typically seen in the methylenes (CH_aH_b) attaching the aromatic walls to the glycoluril framework, as the shifts of these hydrogens are conformationally very sensitive to wall movement induced on binding. The largest binding-induced shift, as expected, was in the guest phenolic hydrogens undergoing hydrogen bonding, but exchange-broadening hampered monitoring of this change in many cases.

The reverse titration, where the other component becomes the monitored species, was always taken and both sets of data compared. Each host and guest were also checked for dimerisation, by carrying out a dilution study, where the peaks of the host or guest were examined for movement over a number of concentrations.

Guest Phase-Transfer: a 1.2 cm diameter U-tube was used to measure the rate of transfer of guest (resorcinol) from an aqueous 'source' phase, through chloroform, into an aqueous 'sink'. The bend was filled with 0.01 mol dm^{-3} host in chloroform, then 0.5 mol dm^{-3} resorcinol in water was placed on one side, and pure water on the other. A magnetic stirring bar in the chloroform helped achieve a reasonable rate of transfer, which was monitored by taking microsamples of the sink phase at intervals and analysing them by UV. The resulting absorbances were plotted against time and compared to that of a blank run (containing no host). An exponential approach to equilibrium was expected and was confirmed in one case, but typically transfers were only run for ~10% of this (to avoid lengthy run times), giving a pseudo-linear absorbance increase with time. Acceleration due to the host was then approximated by the ratio of slopes in the presence and absence of host.

Infra-Red spectroscopy: all spectra were taken in chloroform using a Mattson Galaxy FT-IR 3000. Typically spectra of pure host, pure guest, and a 1:1 mixture were taken; comparison was facilitated by having the stoichiometric concentrations of each species in the latter the same as in the pure solutions. The most obvious manifestation of binding was a decrease in the intensity of the host carbonyl stretching band, together with a new peak at lower wavenumber due to the same feature in the complex. The corresponding shift in the OH stretch of the guest could also be observed in many cases.

A spectrum of the 'pure complex' could also be obtained by subtracting the pure host and pure guest spectra from that of the mixture, using an appropriate scaling factor determined from the decrease in absorbance of an isolated peak associated with each uncomplexed species.

RESULTS

Molecular modelling: Table 1 shows some of the molecular parameters for some of the clips studied. Typically the carbonyl oxygens are 5.8 Å apart, and the xylylene walls are disposed at 15-30° to each other, with ~6 Å between their centres; an obvious exception to the latter is the phenanthro-clip **7a** (shown in Fig. 1 below). Several of the clips appear to have low barriers to variation of the interwall angle/distance (4e). The dithio-clip **8** has its sulphurs spaced more widely (7.0 Å), due both to the C=S bond being longer, and the thiocarbonyls being slightly more divergent from the cavity.

Binding constants by NMR titration: denoting host, guest and 1:1 complex as H, G & HG, the equilibrium constant, K, can be obtained by analysing a peak movement in either host or guest. If the initial concentrations of reactants are H_i & G_i, solving for the concentration of complex yields eqn. (1):

$$[HG] = b - (b^2 - 4H_iG_i)^{0.5}/2 \qquad (where\ b = H_i + G_i + 1/K) \tag{1}$$

Taking the case of a host peak of shift, δ_H, moving to shift, δ_{HG}, when complexed, the observed shift is:

$$\delta_{obs} = \{[H]\delta_H + [HG]\delta_{HG}\}/H_i \tag{2}$$

leading to:
$$[HG] = H_i(\delta_{obs}-\delta_H)/(\delta_{HG}-\delta_H) \tag{3}$$

Comparison of eqns. (1) and (3) yields the NMR-fitting eqn. (4):

$$2H_i(\delta_{obs}-\delta_H)/(\delta_{HG}-\delta_H) = (H_i + G_i + 1/K) - \{(H_i + G_i + 1/K)^2 - 4H_iG_i\}^{0.5} \tag{4}$$

This equation has 3 variables (H_i, G_i & δ_{obs}) and 3 parameters (δ_H, δ_{HG} & K), one of which (δ_H) can be determined from the pure host spectrum.

Data sets were fitted to eqn. (4) using an iterative least-squares curve-fitting routine implemented on the SYSTAT statistical package (8), and the results are shown in Table 1.

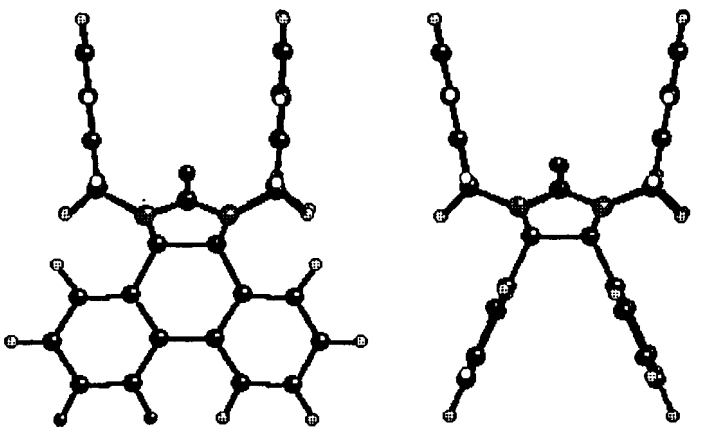


Fig. 1.
Calculated structures of *bis(-o-*xylylene)-(9,10-phenanthro)glycoluril **7a** (left) and *bis(-o-*xylylene)- diphenylglycoluril **4a**, viewed with the xylylenes upwards and one carbonyl oxygen obscured by the other.

Guest Phase-Transfer: the potentially complicated equilibria involved in phase-transfer simplify considerably in the present case. The dihydroxy guest in this study, resorcinol, is more soluble in water than chloroform i.e. its distribution constant, K_d (=$[G]_{org}/[G]_{aq}$), is <<1. The corresponding constant for the host is >>1, and the complex is similar. Therefore the complex formation constant will be negligible in water, while that in chloroform (K) is already known from the NMR binding studies above. An extraction constant, K_e, can be defined for the overall process:

$$G_{aq} + H_{org} = HG_{org}; \qquad K_e = [HG]_{org}/\{[G]_{aq}[H]_{org}\} \tag{5}$$

and clearly:
$$K_e = K_dK \tag{6}$$

Hence extraction into the chloroform phase will be more favourable for strongly-binding clips, and we expect transport accelerations to have a similar proportionality. The accelerations observed are shown in Table 1, and while the relationship is not necessarily linear, their rank order clearly follows that of the binding constants.

TABLE 1. Calculated geometry, binding constants with resorcinol by NMR & IR, and accelerations of resorcinol transport through chloroform for a variety of molecular clip host molecules.

Host:	*Calculated host parameter:* O<>O[a]	Wall separation[b]	*Binding constant, K/M-1* NMR	IR[c]	*Phase-Transfer:* Acceleration
4a	5.77 Å	5.83 Å; 20°	195[d,e] (±20)	135	5
4b			2500[d,f] (±400)	1900	15
4c	5.81 Å	6.19 Å; 30°	400[d] (±25)	230	5-6
7a	5.80 Å	5.11 Å; 6°	90 (±15)	35	4
7b	5.81 Å;	6.02 Å; 28°	150 (±70)	75	5
8	6.97 Å	5.64 Å; 16°	30 (±10)	10	3
9			250 (±30)		

a) Distance between carbonyl oxygens *(sulphurs in the case of 8)*. b) Between xylylene ring centres; angle between ring planes. c) Error ~±30%; probably larger for smaller values. d) For **4a**, **4b** & **4c**, the corresponding values with catechol guest are 70, 50 & 55, respectively, each ~±10; for **4a** & **4b**, literature (4d) gives 80±6 & 60±10. e, f) Literature (4d) gives 200 & 2600.

Infra-Red spectroscopy: typically, the carbonyl stretching frequency of the host was lowered by 15-25 cm^{-1} on complexation: this is in close agreement with hydrogen-bonded complexes of other urea derivatives with phenols (9). Nolte also reports $\Delta\nu(C{=}O) = -20\ cm^{-1}$ and $\Delta\nu(OH) = -233\ cm^{-1}$ for **4b** & resorcinol (4d).

The decrease in the absorbance of the host carbonyl band was used - together with H_i & G_i - to calculate [H], [G] & [HG], and hence K. A simple error analysis suggests that - with $H_i = G_i$ - this is most accurately calculated when all three equilibrium concentrations are comparable i.e. for ~50% complexation. The convenience of the IR experiment allowed initial concentrations to be adjusted (subject to limits of solubility) to achieve this in most cases.

Binding constants determined in this way are listed in Table 1, and the error is estimated at ~30% for a single determination. Comparison with the values determined by NMR shows that the results are comparable (allowing for the error on each), and both give the same ranking of K values.

DISCUSSION

Synthesis: a wider variety of glycoluril-based molecular clips than heretofore reported (4) has been prepared, in part through the improvement of existing routes as well as the development of new ones, so that a choice of several functionalised glycolurils (e.g. **6a**/**b**/**c**/**d**) are now available in high yield as reactants for the final clip-forming step.

The development of the one-pot reaction allows the elegant preparation of e.g. **4a** from a total of 9 reactants (a molecule of benzil **5**, two ureas, four formaldehydes & two benzenes) in high yield, even though this involves 4 bimolecular condensations, 6 cyclocondensations and 4 addition reactions.

The clip architecture has also been varied on its convex side, *via* the replacement of diphenylglycoluril **1a** with its 9,10-phenanthro-analogue, and sulphurs can be used as hydrogen-bond acceptors, as in **8**. The syntheses developed are easily adapted to the more complex folded and cyclised degenerate hosts, **9** and **10**.

Monitoring and Applying Binding: the commonly-used NMR titration has been complimented by direct IR measurement of the binding constant: the IR technique gives comparable results, complimentary structural information, and is a quick and useful technique for screening new host-guest combinations. Similarly, host-catalysed transport is easily measured (albeit time-consuming), yielding accelerations consistent with the trends seen in binding by NMR and IR.

Binding Constants: the carbonyl host molecules in this study complex resorcinol in chloroform with the net formation of two hydrogen bonds and two simple (benzenoid) aryl stacking interactions, with binding constants in the range 100-2500 M^{-1}. This is not untypical of hosts using such binding motifs in this solvent. In Zimmerman's (clip-like) tweezers (10), two acridines (three aryl rings each) sandwich a variety of fluorenones (two aryl rings) with complexation constants of 700-3400 M^{-1}; when the highly-polarised adenine is the guest and two hydrogen bonds are added, K goes up to 25000 M^{-1} (11). Rebek's molecular clefts based on Kemp's triacid form two hydrogen bonds with a similar guest with average complexation constants 50-75 M^{-1}; on appropriate placement of an aryl surface in the host, the binding constant approximately doubles for each benzene ring added (12).

Selectivity for Resorcinol: the data in Table 1 gives rise to several interesting comparisons:
(i) resorcinol binds more strongly than catechol; (ii) resorcinol binds more strongly when hydroxy or methoxy functions are added to the host's xylylene walls - this is observed in both the diphenyl **4** and phenanthro **7** compounds; and (iii) such selectivity for the host is not seen for catechol.
A major cause of the preference for resorcinol is the relative geometry of the OH groups in the guests. In catechol, the oxygens are only ~2.8 Å apart, allowing formation of an intramolecular hydrogen bond. This bond must therefore be broken before the two simultaneous hydrogen bonds with the host carbonyls can be formed, giving a net stabilisation of only one intermolecular hydrogen bond. Assuming the intermolecular hydrogen bonds are linear (13), molecular modelling suggests an unfavourable geometry for acceptors 5.8 Å apart (see Table 1). In contrast, resorcinol has two free hydroxyls, optimally spaced for bonding.

The increase in binding to a dihydroxy guest when the host is also hydroxylated/methoxylated is surprising. At first sight, the Hunter/Sanders model of π-π interactions (14) would suggest that π-π repulsions would be increased if host and guest rings become π-rich due to donating substituents. However, they emphasise that it is the properties of the atoms at the points of intermolecular contact rather than the overall redox properties of the molecules which determine how the π-systems interact. While the aromatic ring of the guest molecule can be considered to be π-rich overall, the position of the substituents determines the property for individual atoms (see Fig. 2). The walls of the hydroxy- and methoxy-hosts should have a similar distribution to hydroquinone.

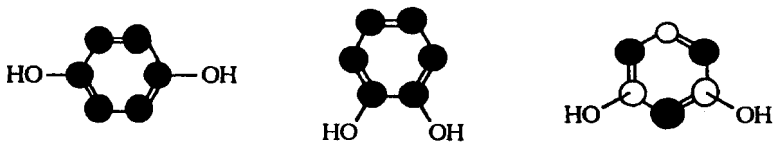


Fig 2. Schematic of π-rich (shaded circle) and π-poor (empty circle) atoms in the aromatic rings of *p*-, *m*-, and *o*-dihydroxybenzene (*i.e.* hydroquinone, resorcinol and catechol).

The Hunter/Sanders model predicts that with two π-rich systems (without highly-charged atoms), offset stacking is generally attractive and face-to-face stacking is repulsive. NMR titration shows that resorcinol's OH groups point into the cavity in a downwards direction (4d): H-2 experiences a large complexation-induced shift, but H-4/5/6 do not, suggesting that they are outside the cavity and hence are not affected by the aromatic deshielding region (see Fig. 3); i.e. a substantial offset exists.

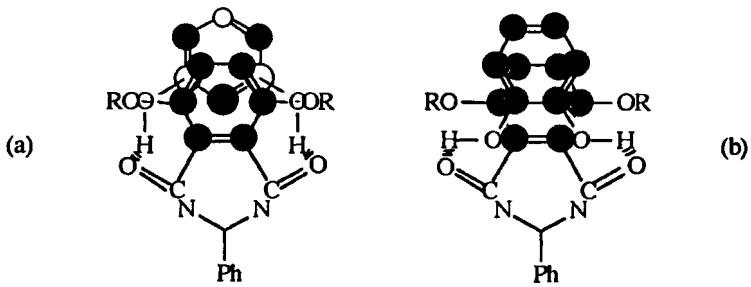


Fig 3. Schematic of complexes involving host **4b/c**: (a) resorcinol {π-rich and π-poor} binding a π-rich host; and (b) catechol {π-rich} binding the same (only one xylylene ring in each host shown, for clarity).

Both guests must adopt a translationally offset geometry as they cannot fit completely into the host; however the very structure of resorcinol means it is also offset by a 30° rotation and therefore adopts a twisted offset geometry, which can maximise attractions and minimise repulsions. The π-poor regions in resorcinol also account for the increased binding constants observed when the host becomes more π-rich. Thus the higher binding constant of resorcinol (relative to catechol) with the xylylene host **4a** may involve a larger stacking component (as well as better hydrogen-bonding), and the ability of resorcinol to take advantage of π-enrichment of the host walls in **4b/c** is also rationalised. Of course it is unlikely that these are the only factors operating: the factor of six difference in binding constant between **4b** and **4c** appears inconsistent with their electronic similarity, and the partial conformational freedom for the clip walls mentioned in the Results suggests that the free hosts and/or the complexes may significantly differ for the hydroxy- and methoxy-cases (4c, 4e).

Diphenyl vs. Phenanthro derivatives: modelling and crystal structures (4b) clearly show that the conformation-locking phenyls in clips **4** are at 90° to the glycoluril C-C bond (see Scheme 2). Joining them together as in the phenanthro-derivatives **7** makes them co-planar, and modelling (see Fig. 1) suggests this may cause crowding of the xylylene walls: **7a**, for example, has the walls compressed to being nearly parallel. This might have excluded the guest, but the results show only a halving of the binding constant: 90 vs. 195 M^{-1}. This is consistent with the shallow minima found in the molecular modelling: the guest can insert with an induced fit (4e), and in this case widening the cavity is not particularly unfavourable. This is quite promising for the development of a new generation of clips with e.g. a phenanthroline function for proton or metal ion binding on the back of the clip (15).

Clip vs. 'Double Clip': the degenerate host **9**, if it bound resorcinol in a similar way to the simple clip **4a**, would be expected to have a binding constant twice as high. At 250 M^{-1}, it is only a factor of ~1.5 short of 2 x 195 M^{-1}, suggesting that it is indeed similar, but the guest's entry to the cavity may be slightly hindered.

*The Dithio-Host, **8**:* a low complexation constant was expected as sulphur is not a very good hydrogen-bond acceptor, although weak bonds to thioketones have been observed (16). The S-S separation (7 Å) also appears unfavourable. Therefore the fact that there was only a decrease of a factor of ~7.5 (±3) [equivalent to ~5(±1) kJ/mol in free energy] is perhaps surprising. Binding is taking place but the exact contributions from the two modes (hydrogen bonding and aryl stacking) is unknown. It could be suggested that much of the binding is being carried by the aryl stacking but that two hydrogen bonds to sulphur - albeit weak - are considerably more favourable than allowing the two free OH's of resorcinol to be exposed to chloroform.

ACKNOWLEDGEMENTS

BAM wishes to thank Syntex, Forbairt (the Irish Science & Technology Agency) (Grant SC/91/227) and the Ireland-US Council for Educational Exchange for financial support, and the Organising Committee of the 24th IUPAC Conference on Solution Chemistry for the invitation to present this paper.

REFERENCES

1. D J Cram; *Angew Chem Int Ed Engl* **15**, 1039 (1986).
2. a) W Freeman, W Mock and N-YShih; *J Am Chem Soc* **103**, 7367 (1981); b) W Mock, T Irra, J Wepsiec and T Manimaran; *J Org Chem* **48**, 3619 (1983); c) W Mock and N-YShih; *ibid.* **48**, 3618 (1983); d) W Mock and N-YShih; *J Am Chem Soc* **110**, 4706 (1988); e) Cucurbituril **2b** was first prepared by Behrend, Meyer and Rusche; *Justus Liebigs Ann Chem* **339**, 1 (1905).
3. J Rebek Jr., J Mendoza and R Wyler; *Angew Chem Int Ed Engl* **32**, 1699 (1993).
4. a) F G M Niele, J W Zwikker and R J M Nolte; *Tetrahedron Letters* **27**, 243 (1986); b) J W H Smeets, R P Sijbesma, F G M Niele, A L Spek, W J J Smeets and R J M Nolte; *J Am Chem Soc* **109**, 928 (1987); c) R P Sijbesma, W P Bosman and R J M Nolte; *J Chem Soc, Chem Commun* 885 (1991); d) R P Sijbesma, A P M Kentgens and R J M Nolte; *J Org Chem* **56**, 3199 (1991); e) R P Sijbesma, S S Wijmenga and R J M Nolte; *J Am Chem Soc* **114**, 9807 (1992); f) R P Sijbesma, PhD thesis, University of Nijmegen, The Netherlands (1992).
5. For a review of redox-responsive hosts, see: P D Beer; *Chem Soc Rev* **18**, 409 (1989).
6. For examples of pH-responsive crown ethers, see: (a) H Stetter and W Frank; *Angew Chem Int Ed Engl* **15**, 686 (1976); (b) A Hriciga and J-M Lehn; *Proc Natl Acad Sci USA* **80**, 6426 (1983).
7. a) Vinter et al; *J Comput-Aided Mol Design* **1**, 31 (1987); b) Morley et al; *ibid.* **5**, 475 (1991).
8. SYSTAT 5.2; © (1992) Systat Inc., 1800 Sherman Avenue, Evanston, Illinois 60201-3793, USA.
9. J Muller, G Vercruysse and T Zeeger-Huyskens; *J Chem Phys* **69**, 1439 (1972).
10. M Baloga, M Mrksich and S Zimmermann; *J Am Chem Soc* **111**, 8528 (1989).
11. S Zimmermann and W Wu; *J Am Chem Soc* **111**, 8054 (1989).
12. B Askew, P Ballester, C Buhr, S Jones, D Nemeth, J Rebek, Jr. and K Williams; *J Am Chem Soc* **109**, 5033 (1987).
13. a) P-G Jönsson and I Olovsson; "The Hydrogen Bond" Vol **2**, 393; Oxford (1976); b) M Joesten, L Schard; "The Hydrogen Bond"; Dekker, New York (1974).
14. C Hunter and J Sanders; *J Am Chem Soc* **112**, 5525 (1990).
15. For an example of 1,10-phenanthroline as an indicator, see: S C Watson and J F Eastham; *J Organomet Chem* **9**, 165 (1967).
16. Drago and Vogel; *J Am Chem Soc* **92**, 5347 (1970).