

Host-Guests Binding by a Simple Detergent Derivative: 'Tentacle Molecules'

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Benzene 1,3,5-tris(11-pyridiniumundecanyl)tricarboxylate trichloride forms complexes with small aromatic compounds in solution in methanol or acetonitrile and inhibits the chlorination of phenol by protective binding.

In recent years, a wide variety of novel compounds has been found to act as hosts for molecular inclusion compounds, consisting chiefly of macrocyclic molecules.¹ Relatively little attention has, however, been paid to synthetic reactions.² As a result of our studies on the effects of detergent-like compounds upon aromatic substitution reactions,³ and the behaviour of *N*-alkyl-2-hydroxybenzylamines,⁴ we felt that it would be possible to construct a simple detergent analogue that would act as a host for small aromatic molecules. Such a compound would be a valuable structural base for the design of selective functionalisation systems devoid of the complex association/dissociation equilibria found in micelles. Menger⁵ has reasoned along similar lines and has synthesised a six-armed covalently linked detergent molecule called 'hexapus'. This compound is most effective in solubilising a range of organic solutes in water. Our micellar studies, however, suggested that three covalently linked detergent chains might prove sufficient and accordingly we based our synthesis upon the readily available benzene-1,3,5-tricarboxylic acid (1). Treatment of (1) with an excess of thionyl chloride afforded the acid chloride (2) which was esterified with 3 mol. equiv. of 11-bromoundecanol in the presence of pyridine. The triester (3) was obtained as a viscous oil, but analytically pure, and was converted into the first 'tentacle' molecule (4) by heating with an excess of pyridine. The triundecylpyridinium tribromide was converted into the trichloride with aqueous hydrochloric acid and was isolated as a waxy solid, analytically pure after prolonged drying. The tentacle molecule (4) was soluble in water, methanol, and acetonitrile and slightly soluble in chlorinated organic solvents.

To investigate the ability of (4) to bind small aromatic substances, we first used high-field ¹H n.m.r. spectroscopy which had demonstrated binding in micellar systems by virtue of differential chemical shift changes between *ortho*-, *meta*-, and *para*- protons of the solubilisate.^{3,4} In methanol, no differential shifts were observed when phenol and (4) were the solutes (each 3.3×10^{-3} M). However an equimolar (3.3×10^{-3} M) solution of phenol and (4) in acetonitrile showed substantial changes when compared with phenol alone at the same concentration (Figure 1). The *para*- and *meta*- resonances were shifted upfield whereas the *ortho*-resonance moved downfield. Such a significant alteration of the spectrum of phenol in detergent solution was only observed at a detergent concentration of fifty to one hundred times the tentacle concentration.^{3,4} If these differential shifts are caused by binding of phenol, then increasing the phenol concentration should reduce the differential shift. The results shown in Figure 2 show that this is indeed the case. Further, by extrapolation of the linear plots to determine the maximum differential shifts to be expected when phenol is fully bound at low phenol concentration, it can be estimated that at equimolar concentrations (3.3×10^{-3} M), 85–90% of the phenol is bound by the tentacle molecule (4). Scatchard analysis⁶ of the n.m.r. data suggests that at high phenol concentration, several phenol molecules interact with the tentacle molecule.

The ability of (4) to bind organic molecules was independently demonstrated using sodium 4-nitrophenolate as solubilisate. Addition of a solution of (4) in methanol or

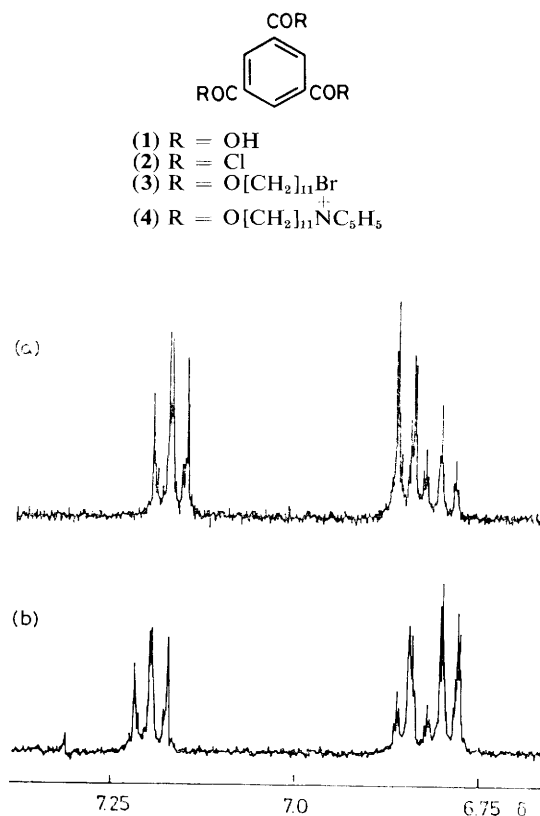


Figure 1. High-field 360 MHz n.m.r. spectra of (a) an equimolar solution of phenol and tentacle molecule (4), (b) phenol alone in acetonitrile (see the text).

acetonitrile to a yellow solution of sodium 4-nitrophenolate in the same solvent caused a shift of the absorption of the anion from the visible (400–410 nm) to the u.v. (310–315 nm) region. The reaction showed good isosbestic behaviour and the colour could be regenerated by adding water. Application of Scatchard analysis⁶ to the spectroscopic data suggests that the stoichiometry of the complex is 1:1 with a dissociation constant of *ca.* 6×10^{-7} M and 2×10^{-7} M for acetonitrile and methanol, respectively.†

Our interest in tentacle molecules is in the development of selective functionalisation systems and accordingly we assessed the ability of tentacle molecule (4) to modulate the chlorination of phenol by *t*-butyl hypochlorite. Solutions of (4) and phenol at several molar ratios were treated with *t*-butyl hypochlorite (0.5 mol. equiv. based upon phenol) and the chlorophenol products analysed by g.l.c. (using 5% FFAP on Chromosorb G at 210 °C, the column being precalibrated with a standard solution). The results are shown in Table 1. In

† Results determined by Dr. D. I. Robinson.

methanol solution, within experimental error, no change in the chlorination pattern was observed. Notably, this result agrees with the lack of binding shown by the n.m.r. spectra. However

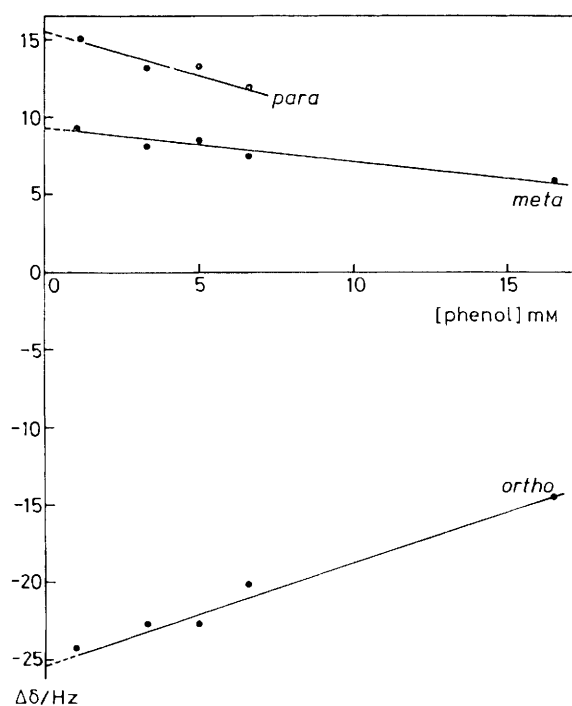


Figure 2. Variation of differential shifts in *ortho*-, *meta*-, and *para*-resonances with phenol concentration.

Table 1. Chlorination of phenol by Bu^tOCl in the presence of (4).

| [phenol]/[tentacle] | Total % yield ^c | % chlorophenols ^d | | |
|---------------------|----------------------------|------------------------------|----|--------|
| | | 2- | 4- | 2,4,6- |
| 0 ^a | 100 | 28 | 72 | — |
| 1 ^a | 82 | 28 | 72 | — |
| 1.5 ^a | 60 | 27 | 73 | — |
| 2 ^a | 56 | 28 | 72 | — |
| 4 ^a | 72 | 32 | 68 | — |
| 0 ^b | 100 | 15 | 85 | — |
| 1 ^b | 86 | — | — | 100 |
| 1.5 ^b | 84 | 8 | 37 | 55 |
| 2 ^b | 100 | 10 | 46 | 43 |
| 4 ^b | 100 | 14 | 62 | 23 |

^a In MeOH. ^b In MeCN. ^c Based upon chlorine consumed.

^d Normalised proportions of chlorinated products.

in acetonitrile, at equimolar concentrations, the only product was 2,4,6-trichlorophenol and 86% unchanged phenol was recovered. The proportion of recovered phenol corresponds remarkably closely to the proportion estimated to be bound by the tentacle (4) from the n.m.r. spectroscopic studies mentioned above. Evidently the tentacles protect the bound phenol from chlorination and the free phenol is trichlorinated. Again consistent with the n.m.r. results was the observation that as the fraction of phenol bound was decreased by increasing phenol concentration, so the proportion of trichlorination decreased. The high proportion of trichlorophenol produced even at high phenol/tentacle ratios is unexpected in view of the absence of trichlorophenol in the control experiment. However this behaviour is understandable if the tentacle molecule accommodates more than one molecule of phenol and can also protect monochlorophenols from further chlorination. The n.m.r. data described above are consistent with the former condition and further n.m.r. experiments showed strong similar interactions of both monochlorophenols with the tentacle system, consistent with the latter condition.

From our results and those of Menger,^{4,5} it seems very probable that remarkably simple functional enzyme analogues will become available in the near future.

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