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A highly selective host–guest system formed and stabilized due to concerted halogen···oxygen and C-H···O non-bonded interactions:† X-ray structures of racemic 1,2,3,4,5-penta-*O*-benzoyl-6-*O*-tosyl *myo*-inositol–dihalomethane (CH_2X_2, X = Cl and Br) inclusion complexes

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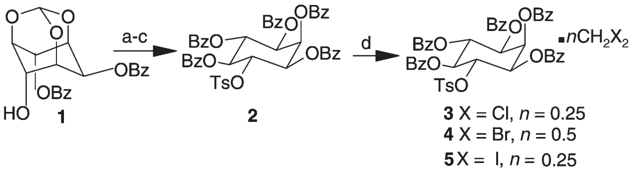
***myo*-Inositol derivative as a host assembles around crystallographic 2-fold axis selectively accommodating dihalomethanes as guests having a C_2 symmetry; formation of highly stable host–guest complexes is attributed to halogen···oxygen and C–H···O interactions.**

An intermolecular recognition process is a result of a number of non-covalent interactions that exist between the molecules.[1] Recently much effort has been concentrated upon recognizing and analyzing the nature of such interactions due to the demands of designing the functional molecular assemblies[2] which span wide areas—from molecular selectivity in separation techniques to drug–receptor interactions in drug design and to material science. In this paper we report a serendipitous discovery of highly selective encapsulation of dihalomethanes by the *myo*-inositol derivative **2**‡ (Scheme 1) due to halogen···oxygen interactions.

The compound **2**, which resisted crystallization in most of the common solvents like chloroform, ethyl acetate, carbon tetrachloride *etc*. readily formed good quality crystals when crystallized from dichloromethane. We further noted that this 'spontaneous' crystallization of **2** occurred only from dihalomethanes, (CH_2X_2, X = Cl, Br and I). So much was the dependence on CH_2X_2 in crystal formation that even their presence at 2.5% (v/v) along with other solvents induced crystallization of **2**. The presence of dihalomethanes in these crystals was revealed by elemental analysis§ and ^1H NMR spectroscopy. The DSC¶ of **3** and **4** indicated that dihalomethanes were retained in crystals close to their melting points (183–192 °C for **3** and 186–188 °C for **4**), suggesting a strong association of the guest molecules with the host.‖ The X-ray structures** of two inclusion complexes of **2** with dihalomethanes revealed that halogen···oxygen interactions, or what is termed as 'halogen bonding',[3] played a vital role in forming a stable host–guest assembly, a bonding recognized as a strong driving force in formation of co-crystals and controlling the construction of supramolecular architectures. It is thought that the remarkable specificity for dihalomethanes in the formation of crystals with **2** will have applications in the separation of halocarbon compounds, through the design of suitable organic hosts such as compound **2**.

View of the molecular packing of **3** down the *c*-axis (Fig. 1) clearly reveal the thorough open channels of dimensions ~6.5 × 4.5 Å formed by the host assembly containing the guest molecules. Amongst all possible host–guest interactions, notable ones are halogen···oxygen short contacts (Fig. 2) in **3** (Cl···O = 2.968 (9) Å) as well as in **4** (Br···O = 3.336 (7) Å) which are shorter than the sum of their van der Waal's radii (3.20 and 3.35 Å respectively). The short halogen···oxygen distances were analyzed earlier[4] to understand the exact nature and favored geometry of their interactions.[5] Although C–X···O linear geometry is suggested for stronger interactions, the present structure shows some deviation from linearity (139.5° (4) and 142.1° (2) for **3** and **4** respectively).[6] Even then it is striking that this 'halogen bonding' has induced the assembly of the host. However, solvent retention is a multi-point recognition phenomenon[7] as evidenced by other weak interactions between the CH_2X_2 guest molecules and the host, which certainly aid in the host–guest stabilization. For instance, there are C–H···O contacts[8] between the CH_2 hydrogens of the guest with the carbonyl oxygens O2 and O4 of the host in both **3** and **4**. The halogen atoms are also involved in weak C–H···X interactions with the phenyl C–H groups of the neighbouring assembly.

It is noteworthy that solvents CH_2Cl_2, CH_2Br_2 and CH_2I_2 readily form crystals with **2,** whereas halogenated solvents



Scheme 1 (a) Pyridine–tosyl chloride, reflux 24 h; (b) pTsA·H_2O–methanol 60 °C, 24 h; (c) pyridine–benzoyl chloride, 0 °C to rt, 24 h, 89% (for 3 steps); (d) crystallization from CH_2X_2 or $CHCl_3$–CH_2X_2 mixture.

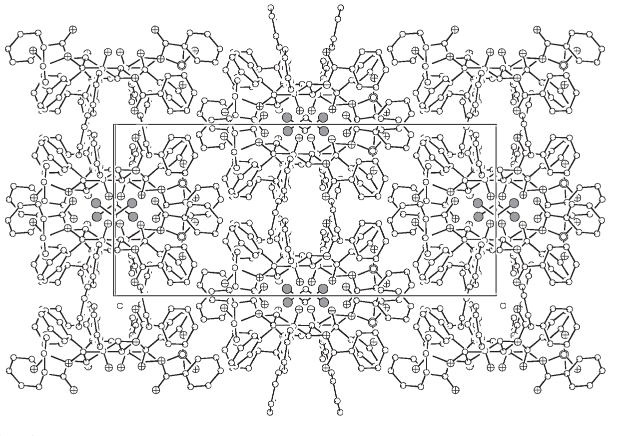


Fig. 1 Molecular packing of **3** viewed down the *c*-axis showing the open framework containing CH_2Cl_2 guest molecules. H-atoms are omitted for clarity. Atom code: ● chlorine, ⊕ oxygen, ○ carbon and ◎ sulfur.

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† Electronic supplementary information (ESI) available: a table of intermolecular interactions. See http://www.rsc.org/suppdata/cc/b1/b101394g/

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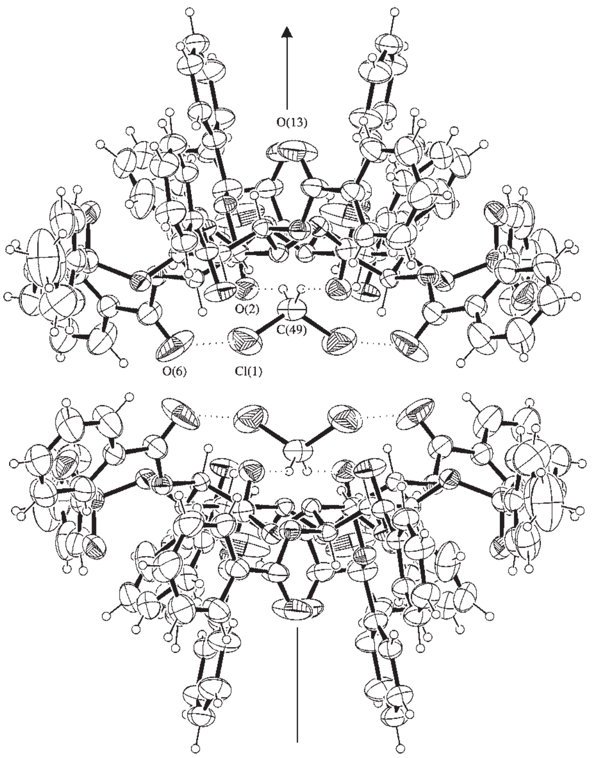

Fig. 2 Formation of an elliptical open channel with the guests in **3**; twofold related host–guest association showing Cl···O and significant C–H···O interactions. Ellipsoids are drawn at the 30% probability level for non-H atoms.

which lack C_2 symmetry (chloroform, methyl iodide) do not yield crystals. Clathrating hosts with open channel formation around the two fold symmetry axis have been reported,[9] but the inclusion of the guest was found to be non-specific, accommodating a wide range of guest molecules; whereas the host **2** is highly specific to dihalomethanes which occupy a crystallographic two-fold axis. But there seems to be a restriction on the steric size of the guest—only the guests having a C_2 symmetry of molecular diameter of ~6.0 Å such as CH_2X_2 are accommodated (to produce crystals), while the higher homologues like 1,2-dichloroethane or 1,2-dibromoethane are not. We believe that the guest induces the assembling process by bringing the second molecule of the host (related by a crystallographic two-fold axis) around it (Fig. 2) making strong halogen···oxygen contacts. The other half of the cavity is completed by the two host molecules related by a center of symmetry (Fig. 2). These two halves are cemented to each other by significant C–H···O interactions to complete the elliptical open framework. All the hydrophobic phenyl groups point outward while the hydrophilic carbonyl oxygens point toward the center of the cavity.

In summary, a novel host–guest assembly held together, notably by halogen···oxygen non-bonded contacts, has been prepared and characterized. Study of such systems, which lack polar groups (OH, COOH, NH_2 *etc.*) is essential to further extend our knowledge of weak interactions among molecules, which play a vital role in crystal growth, enzyme–substrate recognition and ligand–receptor binding.[10] The present adducts re-emphasize the role of 'halogen bonding' in self-assembly and molecular recognition. The work presented shows there is potential for the exploitation of these interactions in the separation of traces of dihalomethanes from other organic compounds or solvents.

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Notes and references

‡ All the compounds in Scheme 1 are racemic. The dibenzoate **1** was prepared as reported earlier.[11] All the compounds gave satisfactory spectroscopic data (IR, ^1H and ^{13}C NMR) and elemental analysis.

§ Analytical data for **3**: calc. for $C_{48}H_{38}O_{13}S \cdot 0.25CH_2Cl_2$: C, 66.13%; H 4.43%; found: C, 66.16%; H, 4.43%. **4**: calc. for $C_{48}H_{38}O_{13}S \cdot 0.50CH_2Br_2$: C, 61.84%; H, 4.17%; found: C, 62.38%; H, 4.16%. **5**: Calc. for $C_{48}H_{38}O_{13}S \cdot 0.25CH_2I_2$: C, 62.87%, H, 4.32%. found: C, 62.73%, H, 4.45%.

¶ The DSC was performed on a Perkin-Elmer DSC 7 instrument in open aluminium crucibles, sample wt. 5 mg (approx), heating rate of 10 K min^{-1}, and nitrogen as purge gas for all the measurements.

‖ Melting point of **2** without dihalomethane was 240–241 °C.

** Crystals of **3** and **4** are isomorphous. *Crystal data* for **3**: $C_{48}H_{38}O_{13}S \cdot 0.25\ CH_2Cl_2$, $M = 876.08$, crystal dimensions 0.20 × 0.19 × 0.11 mm, monoclinic, space group $C2/c$, $a = 26.771(4)$, $b = 11.608(3)$, $c = 30.783(6)$ Å, $\beta = 105.176(6)°$, $V = 9232(3)$ Å^3, $Z = 8$, $D_c = 1.261$ g cm^{-3}, $\mu = 0.162$ mm^{-1}, 22 898 reflection measured, 6618 unique [$I > 2\sigma(I)$], R value 0.056 ($R_w = 0.1280$). *Crystal data* for **4**: $C_{48}H_{38}O_{13}S \cdot 0.50CH_2Br_2$, $M = 941.77$ crystal dimensions 0.24 × 0.22 × 0.16 mm, monoclinic, space group $C2/c$, $a = 26.927(17)$, $b = 11.716(8)$, $c = 30.874(2)$ Å, $\beta = 105.998(10)°$, $V = 9362.7(11)$ Å^3, $Z = 8$, $D_c = 1.336$ g cm^{-3}, μ(Mo-Kα) = 0.986 mm^{-1}, 26 695 reflections measured, 6718 unique [$I > 2\sigma(I)$], R value 0.0664 ($R_w = 0.2172$). Data of both the compound were collected on a Bruker SMART 1000 diffractometer (CCD) (Mo-Kα, $\lambda = 0.71073$ Å) at $T = 293(2)$ K. All the data were corrected for Lorentzian, polarisation and absorption effects. SHELX-97[12] was used for structure solution and full-matrix least squares refinement on F^2. Hydrogen atoms were included in the refinement as per the riding model. CCDC 147891 and 147892. See http://www.rsc.org/suppdata/cc/b1/b101394g/ for crystallographic data in .cif and other electronic formats.

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