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ONE STEP SYNTHESIS OF A BULKY COMPOUND AND ITS ABILITY TO FORM INCLUSION CRYSTALS WITH SMALLER ORGANIC MOLECULES

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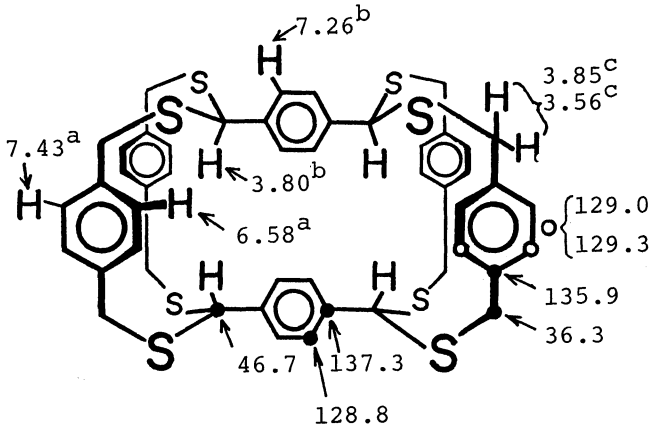
The reaction of terephthalaldehyde with 1,4-bis(mercaptomethyl)benzene leads to a novel macrocyclic thioacetal (1) which specifically and strongly forms inclusion crystals with organic solvents. The X-ray crystallographic examination of 1-benzene (2:3) complex revealed that the crystal is a crystalline solvate containing the benzene molecules as part of its lattice.

The design and synthesis of host molecules possesing cavity for the specific complexation of guest species is recognized currently as an important objective in the area of biomimetic chemistry.[1] Since the discovery of inclusion phenomenon by a macrocyclic cyclophane,[2] new and more complex structures such as cavitands[1b,3] and other synthetic molecular receptors[1] have become available. Constructing such three-dimensional compounds, however, generally requires rather complicated strategies. We report here the one-step high-yield synthesis of the novel "bulky cyclophane" (formula 1, $C_{48}H_{44}S_8$) which is useful to specifically trap a variety of organic molecules in the solid state.

Cyclophane 1 was synthesized by high-dilution reaction of terephthalaldehyde with 1,4-bis(mercaptomethyl)-benzene in the molar ratio 1:2 in boiling benzene containing a catalytic amount of p-toluenesulfonic acid. The usual work-up procedure afforded a white solid consisting mainly of 1, which was chromatographed on silica: colorless needles from benzene, yield 66%. After drying in vacuum at 80 °C for 24 h, the crystal was composed of 1 and benzene in a 2:3 ratio and decomposed above 292 °C. The elemental



(1)

Fig. 1. ^1H (400 MHz) and ^{13}C (25 MHz) Chemical shifts (δ) in $CDCl_3$ of 1; (a) broad singlet, (b) singlet, (c) AB type quartet (J_{AB} = 13.7 Hz).

analysis, mass spectrum (m/z 877, M^+) as well as ^1H and ^{13}C NMR data (Fig. 1) were in agreement with the assigned structure 1.

When crystallized from several organic solvents, 1 specifically formed inclusion compounds which were stable in air and lost the guest solvent only upon prolonged heating under vacuum to regenerate 1. Results are summarized in Table 1. The guest ranged in size from benzene (MW 78) to 1,1,2,2-tetrachloroethane (MW 168). It is of interest that the cyclophane 1 (i) discriminates between p-xylene and mesitylene, and between cyclohexane and dioxane, (ii) expels a smaller molecule, acetone (MW 58), and (iii) forms solvates with halogen compounds. Thus, 1 can act as a host compound which discriminates differences in shape and size and recognizes existance of heteroatoms in organic molecules. The non-stoichiometric ratios for the inclusion compounds imply that the complexes do not have intramolecular host-guest character.[1a)]

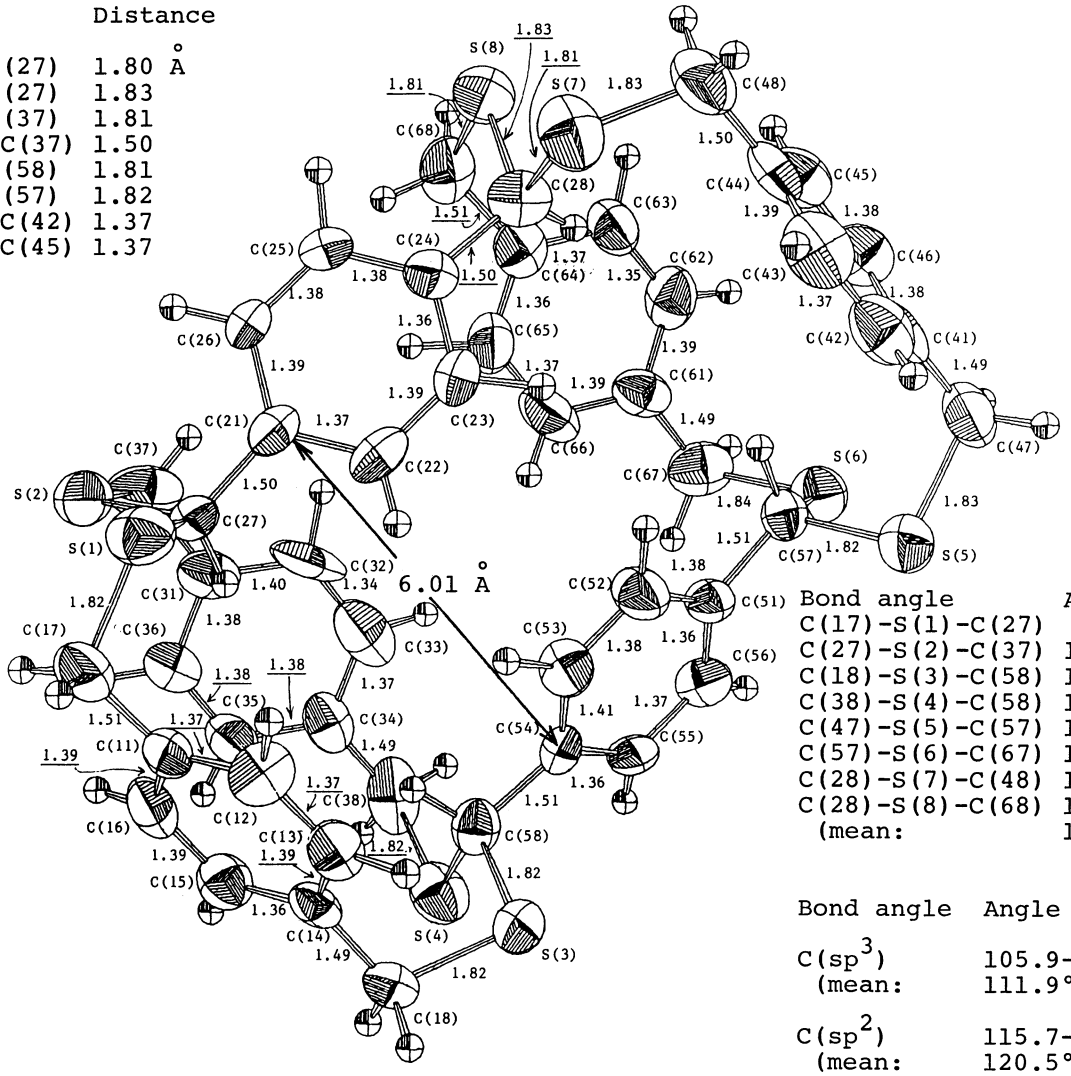
Table 1. ^1H NMR results for the ability of 1 to include solvents on crystallization[a,b,c)]

Recrystallization solvent	Heating under vacuum (<1 mmHg)			
	Rt, 3 h	80 °C, 24 h	80 °C, 24 h + 120 °C, 19 h	80 °C, 24 h + 120 °C, 33 h
Benzene	I (3.3)	I (1.5)[d]	I (0.2)	N
p-Xylene	I (2.3)	I (0.9)	N	
Mesitylene	N			
Acetone	N[d]			
Cyclohexane	N			
Dioxane	I (2.5)	I (1.2)	I (0.3)	
1,2-Dichloroethane	I (1.1)	I (0.4)	I (0.1)	
1,1,2,2-Tetrachloroethane	I (2.2)		N	

a) Value in parentheses denotes the molar ratio of solvent molecule to 1 determined from the ^1H NMR spectra in $CDCl_3$. b) I: included. c) N: not included.
d) Elemental analyses; from benzene, Found: C, 68.74; H, 5.33%. Calcd for $C_{48}H_{44}S_8 \cdot 1.5C_6H_6$: C, 68.84; H, 5.37%; from acetone, Found: C, 65.57; H, 5.15%. Calcd for $C_{48}H_{44}S_8$: C, 65.71; H, 5.06%.

The X-ray crystallographic examination of the above mentioned 1-benzene (2:3) solvate revealed that cyclophane 1 adopts a strain-free structure with normal bond distances and angles (Fig. 2). The cavity of 1 seems too shallow (e.g. distance between C(21) and C(54) is 6.01 Å) to intramolecularly include benzene molecules. The crystal is not a molecular complex but a crystalline solvate containing the benzene molecules as part of its lattice (Fig. 3). There are two crystallographically different kinds of guest benzene molecules; one (hereafter Bz(G)) is arranged at the general position (four molecules in a unit cell, Fig. 3a), and the other (hereafter Bz(C)) is situated at the centre of symmetry (two molecules in a unit cell, Fig. 3b). The temperature parameters of carbon atoms of Bz(G) (B_{eq} =

Bond	Distance
	Å
S(1)-C(27)	1.80
S(2)-C(27)	1.83
S(2)-C(37)	1.81
C(31)-C(37)	1.50
S(4)-C(58)	1.81
S(6)-C(57)	1.82
C(41)-C(42)	1.37
C(44)-C(45)	1.37



Bond angle	Angle
C(17)-S(1)-C(27)	99.5°
C(27)-S(2)-C(37)	102.6
C(18)-S(3)-C(58)	100.3
C(38)-S(4)-C(58)	102.9
C(47)-S(5)-C(57)	100.9
C(57)-S(6)-C(67)	102.0
C(28)-S(7)-C(48)	100.1
C(28)-S(8)-C(68)	101.1
(mean:	101.2°)

Bond angle	Angle
$C(sp^3)$	105.9-116.9°
(mean:	111.9°)
$C(sp^2)$	115.7-124.9
(mean:	120.5°)

Fig. 2. ORTEP drawing[8] of bulky cyclophane 1 (e.s.d.'s; S-S: 0.004 Å, S-C and C-C: 0.01 Å, C-S-C: 0.4-0.5°, C-C-C: 0.8-0.9°, S-C-C: 0.6-0.7°, and S-C-S: 0.5°).

(a) (b)

Fig. 3. Illustrations of the included benzene molecules with their surroundings: (a) Bz(G) projected onto (010), and (b) Bz(C) onto $(1\bar{1}0)$, respectively.

7.8-9.6 Å^2), are larger than those of Bz(C) (B_{eq} = 4.7-5.1 Å^2), which are almost equal to those of 1.

Synthesis of further representatives of this type which have cavities different in shape and size from 1 is in progress.

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4) Crystal data: $C_{48}H_{44}S_8 \cdot 1.5C_6H_6$, F. W. = 994.53, monoclinic, space group $P2_1/c$, a = 17.858(3), b = 17.783(4), c = 16.243(3) Å, β = 98.18(2)°, U = 5105(2) Å^3 (22°C), Z = 4, D_c = 1.29, D_m = 1.28 g cm^{-3}(by flotation), μ(Mo-Kα) = 3.73 cm^{-1}. The intensity data were collected on a Rigaku AFC-4 four-circle diffractometer using graphite-monochromated Mo-Kα radiation and the θ-2θ scanning technique, corrected for Lorentz and polarization effects, but not for absorption (crystal size: 0.42 X 0.30 X 0.25 mm). Of the unique 12196 reflections (2θ ≦ 55°) measured, observed 3594 ($|F| \geq 3\sigma(|F|)$) were used for calculations. The structure was solved by direct method using MULTAN 78[5] and refined by block-diagonal least-squares method.[6] All the hydrogen atoms were found from difference-Fourier maps. The final conventional R was 0.083 with anisotropic temperature parameters for non-hydrogen atoms, constant isotropic temperature parameter, B = 4.0 Å^2, for hydrogen atoms, and anomalous dispersion correction for sulfur atoms.[7] Highest peak in the final difference-Fourier map was 0.5 e Å^{-3}.

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