The Ar–Cl···HO hydrogen bond of 6-chloro-9-hydroxy-[3.3]metacyclophane

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The chlorophenol moiety of the titled cyclophane showed intermolecular hydrogen bonds, O–H···OH and C–Cl···HO, in the crystals.

Keywords: C–Cl···HO hydrogen bond, C–F···HO hydrogen bond, cyclophane

The halogen atoms covalently bonded to a carbon atom (C–X, X = F, Cl, Br, I) are very poor proton acceptors. Different from H–X or M–Cl, halocarbons (C–X) are inert to proton donors and thus, C–X···HO appears very rarely in crystal structures.[1] A statistical study of this hydrogen bond was done by Orpen *et al.* who concluded that M–Cl are good hydrogen bond acceptors, while C–Cl is a very poor proton acceptor.[2]

Recently, we observed the C–F···HO hydrogen bond in 6-fluoro-9-hydroxy-[3.3]metacyclophane.[3] During the course of this study, we found the above mentioned Ar–Cl···HO hydrogen bond in the crystals of 6-chloro-9-hydroxy-[3.3]metacyclophane **1**.

The synthesis of the cyclophane was achieved by a coupling reaction between 4-chloro-2,6-bis(bromomethyl)-1-benzyloxybenzene and 1,3-bis[2-isocyano-2-(toluenesulfenyl)ethyl]benzene under phase-transfer conditions (Bu_4NI in CH_2Cl_2/aq. NaOH).[4] The obtained cyclophane-dione **4** was converted to 6-chloro-9-benzyloxy-[3.3]metacyclophane **3** (52.9 %) and 6-chloro-9-hydroxy-[3.3]metacyclophane **1** (16.8 %) by the Wolff–Kishner reduction.

Figure 1 shows the molecular packing of the cyclophane in which each *p*-chlorophenol moiety is bound by HO···HO and Cl···HO hydrogen bonds.[5] Figure 2 shows the partial hydrogen bond pattern which is picked up from the crystal structure. The HO···H distance (197.3 pm) is shorter than the sum of the van der Waals radii (272 pm) of H and O atoms, and the Cl···HO distance of 258.4 pm is shorter than that of Cl and H (295 pm).[6] The angle Ar-Cl···H–O (92.5°) is much more acute compared to the two O–H···HO angles (146.8° and 132.2°, respectively). These values reflect the weakness of the Cl···H–O hydrogen bond.

In the IR spectra (KBr) of **1**, a sharp ν_{OH} band at 3564 cm^{-1} and broad band at 3457 cm^{-1} appeared (Figure 3). As previously reported, the spectra in KBr is identical to those in the transmittance IR spectra of the cyclophane crystals.[3] Therefore, the IR spectra were measured in KBr for all cases in this study. 9-Hydroxy-[3.3]metacyclophane **2** was chosen as the reference material which was previously reported.[3] In the case of **2**, a sharp, but weak ν_{OH} band appeared at 3541 cm^{-1} accompanied by a broad and strong band at 3471 cm^{-1}. The broad bands and the sharp bands are assigned to $\nu_{OH\cdots OH}$, and $\nu_{Cl\cdots HO}$ or ν_{OH} free from hydrogen bond, respectively. In general, free OH bands of simple phenols appear in the gas phase IR spectra or the spectra of a highly-diluted solution in nonpolar solvents, but these are not observed in KBr or other crystallines. Therefore, the bands are characteristic of cyclophanes **1** and **2**. The intermolecular HO···HO hydrogen bond of **1** should be stronger than that of **2** due to the presence of the electron-withdrawing chloro atom. Therefore, the red shift of the broad band of **1** is quite reasonable. On the other hand, the reason why the sharp band of **1** (3564 cm^{-1}) blue-shifted (23 cm^{-1}) as compared to that of **2** (3541 cm^{-1}) is

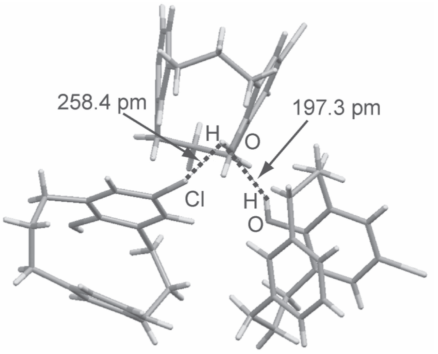

Fig. 1 Crystal structure of cyclophane **1**. Hydrogen bonds are represented by dotted lines.

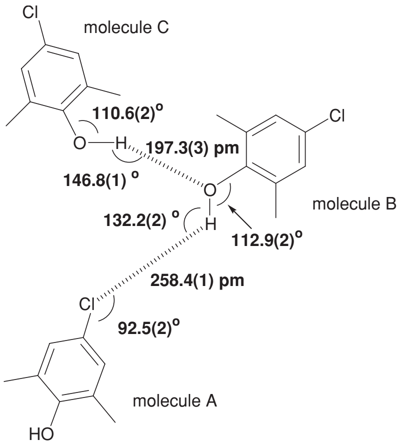

Fig. 2 Hydrogen bond patterns among three cyclophane molecules. Partial molecular structures of the cyclophanes are drawn for clarity.

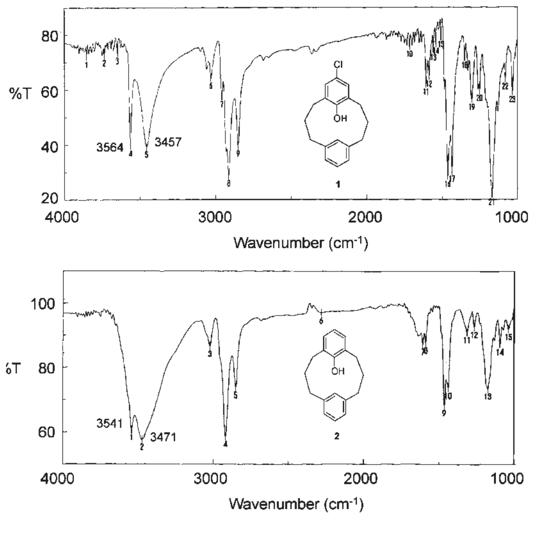

Fig. 3 IR spectra of cyclophane **1** and **2** in KBr.

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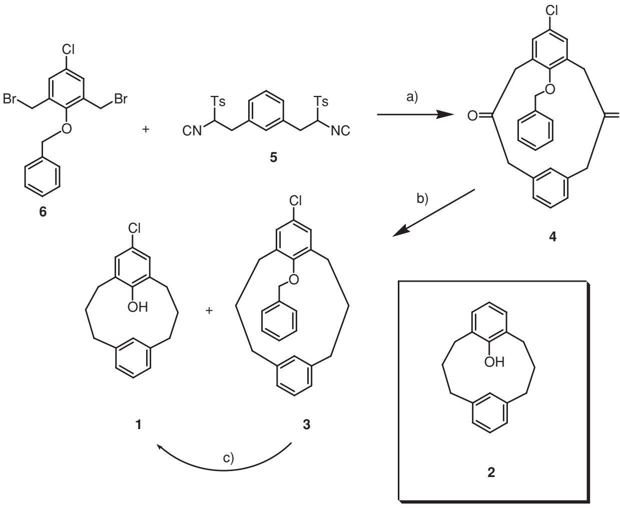

Scheme 1 Synthesis of cyclophanes. (a) CH_2Cl_2/aq. KOH, Bu_4NI; (b) NH_2NH_2-H_2O, diethyleneglycol, 120°C –180°C.

unclear. If the Ar–Cl···HO hydrogen bond has an anti-hydrogen bond character, the blue shift of the band is reasonable. [7]

As a result, the very rare Ar–Cl···HO hydrogen bond is found in the crystalline structure of 6-chloro-9-hydroxy-[3.3]meta-cyclophane **1**. The Ar-Cl···HO hydrogen bond is very weak compared to the OH···OH hydrogen bond, thus, it is possible to observe it only in crystalline structure.

Experimental

Melting points: Yanaco MP-500D apparatus in Ar sealed tubes, and are uncorrected. NMR: Bruker DPX-400 (400.1 MHz for ^{1}H with TMS as internal references). IR: JASCO IR-700. FAB MS: JEOL JMS-SX/SX102A.

6-Chloro-9-benzyloxy-[3.3]metacyclophane-2,11-dione **(4)**: A mixture of CH_2Cl_2 (1.3 l), 40 % aq. NaOH (50 ml), and *n*-Bu_4NI (1.69 g, 4.58 mmol) was heated under reflux with vigorous stirring. To this mixture, a solution of 4-chloro-2,6-bis(bromomethyl)-1-benzyloxybenzene **6**[3] (4.05 g, 10.0 mmol) and 2,6-bis[2-isocyano-2-(toluenesulfenyl)ethyl]benzene **5** (5.62 g, 11.0 mmo1) in 250 ml of CH_2Cl_2 was added dropwise over a period of 6 h. Additional heating and stirring was continued for 5 h. After cooling, the organic phase was separated and washed with brine. After the solution was concentrated to *ca*. 300 ml, 30 ml of conc. HCl was added and stirred for 40 min at room temperature. The organic phase was separated and washed with water and dried over $MgSO_4$. The solvent was removed under reduced pressure and to the resultant colourless oil was added a small amount of diethyl ether. The precipitated colourless powder was collected and washed with a small amount of diethyl ether (2.12 g, 50.1 %). m.p. 87.9–88.5°C; ^{1}H NMR (CDC1$_3$): δ = 7.34–7.27 (m, 3H, ArH), 7.21 (s, 2H, ArH), 7.07–7.01 (m, 5H, ArH), 4.43 (s, 2H, CH_2), 3.64, 3.16 (dd, ^2J (H, H) = 15 Hz, 4H, CH_2), 3.51, 3.48 (dd, ^2J (H, H) = 14 Hz, 4H, CH_2); HRMS (FAB): calcd (%) for $C_{25}H_{21}O_3Cl$: *m/z* = 404.1179 (^{35}Cl); found: 404.1200.

6-Chloro-9-benzyloxy-[3.3]metacyclophane **(3)** and 6-chloro-9-hydroxy-[3.3]metacyclophane **(1):** A mixture of **4** (252 mg, 0.622 mmol), hydrazine hydrate (4.0 ml, 82.5 mmol), and diethylene glycol (6.0 ml) was heated at 100°C for 1 h. Potassium hydroxide (380 mg, 5.76 mmol) was added in the solution and the temperature was raised to 120°C. After 2 h, the temperature was raised to 180°C and heating was continued for more 2 h. The solution was then cooled and poured into 20 ml of water. The mixture was extracted with ether (5 ml × 4), and the combined ether solution was washed twice with water. The solution was dried over $MgSO_4$ and evaporated. The resultant oily material was purified by preparative TLC (Merck 60F$_{254}$) with CH_2Cl_2/*n*-hexane = 1/2, v/v) as the eluent. Compound **3** (Rf = 0.5) and **1** (Rf = 0.1) were obtained as colourless crystals.

*Compound **3** (124 mg, 52.9 %)*: m.p. 76.4–76.8°C; ^{1}H NMR (CDC1$_3$): δ = 7.55–7.35 (m, 5H, ArH), 7.26 (s, 1H, ArH), 6.91 (t, ^3J(H, H) = 7.6 Hz, 1H, ArH), 6.62 (d, ^3J(H, H) = 7.6 Hz, 2H, ArH), 6.53 (s, 2H, ArH), 4.73 (s, 2H, CH_2), 3.04–2.27 (m, 10H, CH_2), 1.80–1.67 (m, 2H, CH_2); HRMS (FAB): calcd (%) for $C_{25}H_{25}OCl$: *m/z* = 376.1594 (^{35}Cl); found: 376.1590.

Compound 1 (30 mg, 16.8 %): m.p. 108.7–109.5°C; ^{1}H NMR (CDC1$_3$): δ = 7.09 (s, 1H, ArH), 6.96 (t, ^3J (H, H) = 7.3 Hz, 1H, ArH), 6.67 (dd, ^3J (H, H) = 7.3 Hz, 2H, ArH), 6.48 (s, 2H, ArH), 4.62 (s, 1H, OH), 2.92–2.28 (m, 10 H, CH_2), 1.89–1.74 (m, 2H, CH_2); HRMS (FAB): calcd (%) for $C_{18}H_{19}OCl$: *m/z* = 286.1124 (^{35}Cl); found: 286.1122.

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5 Crystal data for **1**: $C_{18}H_{19}OCl$, Mr = 286.80 g mo1^{-1}, colorless block (grown from *n*-hexane), size 0.90 × 0.55 × 0.18 mm, monoclinic, space group P2$_1$/a (#14), a = 13.839(1), b = 9.0890(6), c = 23.122(2) Å, β = 93.165(3)°, V = 2903.8(4) Å^3, Z = 8, ρ_{calcd} = 1.312 g cm^{-3}, μ(Mo-Kα) = 2.56 cm^{-1}, F(000) = 1216.00, T = – 150.0 ± 1°C using the ω-2θ scan technique to a maximum 2θ value of 0.0°. A total of 25690 reflections were collected. The final cycle of the full-matrix least-squares refinement was based on 4173 observed reflections (I > 2.00σ (I)) and 373 variable parameters and converged with unweighted and weighted agreement factors of R = 0.079, Rw = 0.254, and GOF = 0.95. The maximum and minimum peaks on the final difference Fourier map corresponded to 0.50 and – 1.09 e$^-$/Å^3, respectively. Crystallographic data (excluding structure factor) for structure of **1** reported in this paper has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-230865. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: (+44)1223-33603; e-mail: deposit@ccdc.cam.ac.uk).

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