A Hydrogen-Bonded [(Mercuracarborand–Water)$_2$–Benzene] π-Sandwich Complex**

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Benzene–water, π-hydrogen bond complexes have been extensively studied by a variety of theoretical and experimental methods.[1–5] The structural basis of such complexes is a π-hydrogen bond involving hydrogen atom(s) of water and the π-electron cloud associated with the benzene ring. These benzene–water complexes serve as prototypes for the generic $O{-}H\cdots\pi$ interaction.[3–6] The number of hydrogen atoms of water directed toward the benzene π-electron cloud is yet to be clearly determined.[5–7] Most of these experiments involved gas-phase results and the main structural information was obtained by comparison with data from ab initio calculations. The structure derived from these gas-phase studies is a benzene/(water)$_2$ complex with dimeric H_2O bound to only one side of the aromatic ring.

Mercuracarborands, cyclic multidentate Lewis acids composed of alternating units of carborane cages and mercury atoms (Figure 1), readily form complexes with electron-donor molecules such as tetrahydrofuran,[8] acetonitrile,[9] nitrate ion,[10] halide anions (Cl^-, Br^-, I^-),[11, 12] and the polyhedral *closo*-$B_{10}H_{10}^{2-}$ ion among others.[12, 13] Also, mercuracarborands have been demonstrated to complex and activate an uncharged nucleophilic species for catalysis.[14]

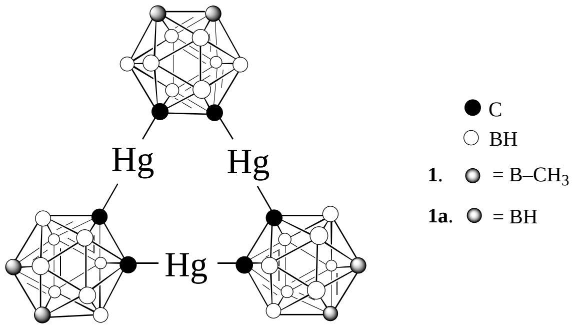

Figure 1. Representation of *B*-hexamethyl-[9]mercuracarborand-3 (**1**) and [9]mercuracarborand-3 (**1a**).

Here we report the structural characterization of trimeric 9-mercuracarborand-3, $(C_2B_{10}H_{10}Hg)_3$, (**1a**) in which the mercuracarborand is η^3-coordinated by the oxygen atom of a water molecule, and the first solid-state structure of a benzene–water complex, [$(\mathbf{1}\cdot\text{water})_2\cdot\text{benzene}$]. The latter is composed of two electroneutral trimeric *B*-hexamethyl-9-mercuracarborand-3, $(9,12\text{-}(CH_3)_2\text{-}C_2B_{10}H_8Hg)_3$, (**1**) receptors, each of which hosts a single water molecule. The benzene molecule is situated between two such water molecules in a sandwich fashion.

A single crystal of the simple benzene-free complex, [$\mathbf{1a}\cdot(OH_2)\cdot((CH_3)_2CO)_3$], (**2**) grown from acetone/water (50:1) was selected for an X-ray diffraction study.[15,19b] Compound **2** is an air- and moisture-stable solid which crystallized in the rhombohedral space group $R\bar{3}$. The cyclic tridentate host **1a** is coordinated to water and to three acetone molecules (Figure 2).

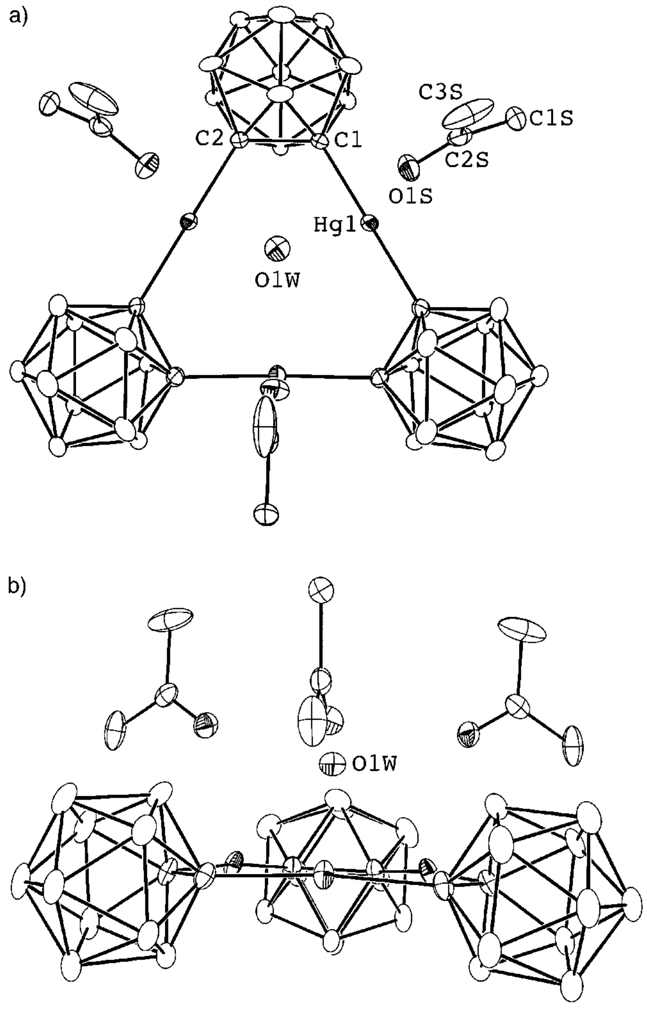

Figure 2. Structure of **2** (ORTEP plot; hydrogen atoms omitted for clarity). a) Top view. b) Side view. Selected distances [Å]: Hg1-O1W 2.915(5), Hg1-O1S 2.762(4), $Hg\cdots Hg$ 3.7329(6), $O1W\cdots O1S$ 3.014(4), $Hg_3(\text{centroid})\cdots O1W$ 1.963(7).

The three mercury atoms present in complex **2** are arranged in an equilateral triangle ($Hg\cdots Hg$ 3.7329(6) Å; Hg-Hg-Hg 60°); the Hg_3C_6 ring is nearly planar and the Hg-C-C-Hg torsion angle is 1.0(6)°. The water molecule lies on the threefold axis and is located 1.824 Å above the Hg_3 plane. The oxygen atom of water is η^3-coordinated to the three mercury atoms ($Hg1\cdots O1W$ 2.915(5) Å). This distance is within the sum of the van der Waals separation of 3.13 Å (Hg = 1.73[16] and O = 1.40[17] Å). The hydrogen atoms of water were

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crystallographically disordered and not located. The carbonyl oxygen atom of each acetone molecule is coordinated to its corresponding mercury center (Hg1 ··· O1S 2.762(4) Å) forming a 1:1 acetone to mercury center complex. The observed Hg ··· O=C distance is consistent with previously reported Hg ··· O=C intermolecular distances.[18] Interestingly, water and acetone molecules are located on the same cavity face of **1a**. A short O1W ··· O1S distance of 3.014(4) Å may indicate the presence of a hydrogen bond between the water and acetone molecules. The oxygen atom of water is η^3-coordinated to the mercury centers and is in close proximity to the carbonyl oxygen atom of acetone ligands. The water molecule may serve as a template for the acetone molecules.

Compound **1** dissolves in a hot dichloromethane/benzene/water (20:10:1) solution. A single crystal of $[(\mathbf{1}\cdot OH_2)_2\cdot C_6H_6]$ (**3**) was grown by slow evaporation of solvent and was selected for an X-ray diffraction study.[19] Species **3** is an air- and moisture-stable crystalline solid which crystallized in the rhombohedral space group $R\bar{3}$. Each water molecule is η^3-coordinated at the center of a host, **1**, forming a $[\mathbf{1}\cdot OH_2]$ complex, similar to the $[\mathbf{1a}\cdot OH_2]$ component of complex **2**. The benzene ring of **3** is sandwiched between two $[\mathbf{1}\cdot OH_2]$ complexes (Figure 3) with the acidic water protons of the complexed water molecules forming hydrogen bonds with available π electrons of the benzene ring.

The three mercury atoms present in each of the two hosts in complex **3** are arranged in an equilateral triangle (Hg ··· Hg 3.7346(7) Å; Hg-Hg-Hg 60°) and the Hg-C-C-Hg torsion angle (2.8(8)°) shows these four atoms are not coplanar. Each water molecule lies on a threefold axis and is located 2.08(1) Å from its respective Hg_3 plane in **3**. The oxygen atom of water is equidistant to three mercury atoms (Hg ··· O 2.994(8) Å), which is less than the sum of the van der Waals radii (3.13 Å). The hydrogen atoms of water are crystallographically disordered and not located. However, in the solid state, both hydrogen atoms of water must be oriented toward and bonding with the π system of benzene. The benzene centroid ··· oxygen distance is 2.99(1) Å, which is closer than the reported spectroscopic (3.32 – 3.35 Å)[2] and theoretically calculated distances (3.20 – 3.32 Å)[2, 5] of a benzene – water complex (single O–H ··· π interaction). Thus, host **1** increases the acidity of the hydrogen atoms of η^3-coordinated water in the $[(\mathbf{1}\cdot OH_2)_2\cdot C_6H_6]$ complex which, in turn, increases the O–H ··· π hydrogen bond affinity. This increased bond affinity may explain the apparent ability of benzene to simultaneously coordinate four hydrogen atoms.

The two trimeric hosts of **3** are inverted with respect to each other and separated by 10.126(3) Å. For comparison, the two trimeric hosts of the $[\mathbf{1}_2\cdot I]^-$ sandwich complex are separated by 4.902 Å.[11] The distance between the C–C centroid of benzene and the mercury centers (5.19 Å) is much longer than those (3.36 Å) reported by Tsunoda and Gabbaï[20] and presumably, the mercury centers of **3** are not directly coordinated to the benzene ring.

The correct formulation of the hydrogen bonding present in **3** is not possible without knowledge of the disposition of the water protons. However, in the solid state, we assume both hydrogen atoms of water must be oriented toward and bonding with the π system of benzene.

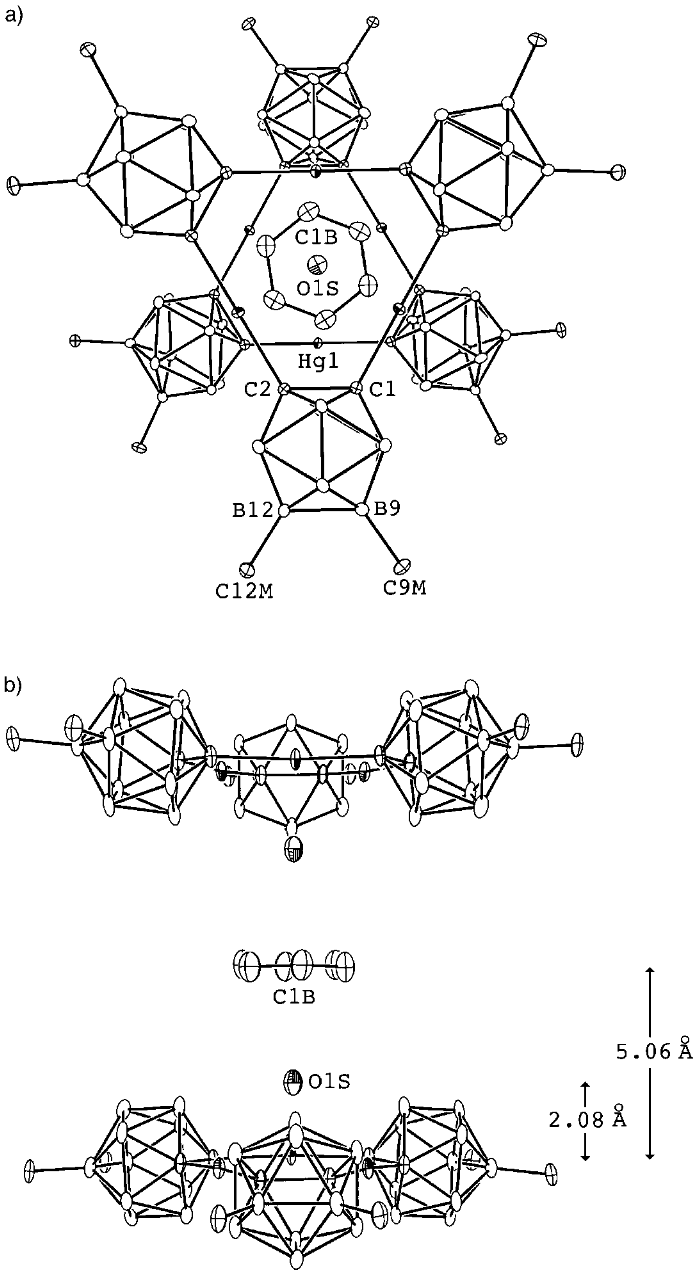

Figure 3. Structure of **3** (ORTEP plot; hydrogen atoms omitted for clarity). a) Top view. b) Side view. Selected distances [Å]: Hg1-O1S 2.994(8), Hg_3(centroid) ··· O1S 2.08(1), Hg ··· Hg 3.7346(7), O1S ··· C1B 3.28(2), O1S ··· C1B′ 3.32(2), O1S ··· benzene centroid(π) 2.99(1).

Experimental Section

$[\mathbf{1a}\cdot(OH_2)\cdot((CH_3)_2O)_3]$ (**2**): Compound **1a**[9] (20 mg, 19 µmol) was dissolved in an acetone/water (1 mL/0.02 mL) mixture. Slow evaporation of the solvent yielded clear crystals.

$[(\mathbf{1}\cdot OH_2)_2\cdot C_6H_6]$ (**3**): Compound **1**[21] (10 mg, 9 µmol) was dissolved in a hot methylene chloride/benzene/water (1 mL/0.5 mL/0.02 mL) mixture. Slow evaporation of the solvent yielded clear crystals.

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[15] Crystallographic data collection for $[\mathbf{1a}\cdot(H_2O)\cdot((CH_3)_2O)_3]$ (**2**): $C_{15}H_{48}B_{30}Hg_3O_4$, $M_r = 1218.6$, crystal dimensions $= 0.2 \times 0.25 \times 0.5\,\text{mm}^3$, rhombohedral, space group $R\bar{3}$, $a = 21.565(3)$, $c = 15.455(3)$ Å, $V = 6225(2)$ Å^3, $Z = 6$, $\rho_{calcd} = 1.951\,\text{mg}\,\text{cm}^{-3}$, $T = 100(2)$ K, absorption coefficient $\mu = 11.098\,\text{mm}^{-1}$. Data were collected on a Bruker SMART CCD diffractometer, using Mo$_{K\alpha}$ radiation ($\lambda = 0.71073$ Å). Unit cell parameters were determined from a least-squares fit of 976 accurately centered reflections ($6.345° < 2\theta < 55.785°$). A total of 3361 unique reflections were measured, of which 2990 reflections were considered observed with $I > 2\sigma(I)$. All reflections were used for structure analysis. The intensity data were corrected for Lorentz and polarization effects, absorption, and secondary extinction. Atoms were located by use of statistical methods. All non-hydrogen atoms were refined with anisotropic parameters. With the exception of the hydrogen atoms of water (not located), all hydrogen atoms were included in structure factor calculations but parameters were not refined. The hydrogen atoms were assigned isotropic displacement values based approximately on the value for the attached atom. The final discrepancy index was $R = 0.032$, $R_w = 0.074$ ($w = 1/\sigma^2(|F_o|)$ for 2990 independent reflections with $I > 2\sigma(I)$. The largest peak maximum and minimum on a final difference electron density map were 2.19 and -3.43 e Å^{-3}, both near Hg. Data were processed by using programs supplied with the Bruker SMART CCD diffractometer.[19b]

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[19] a) Crystallographic data collection for $[(\mathbf{1}\cdot H_2O)_2\cdot C_6H_6]$ (**3**): $C_{15}H_{45}B_{30}Hg_3O$, $M_r = 1167.58$, crystal dimensions $= 0.15 \times 0.15 \times 0.05\,\text{mm}^3$, rhombohedral (obverse), space group $R\bar{3}$, $a = 20.763(3)$, $c = 15.944(4)$ Å, $V = 5953(2)$ Å^3, $Z = 6$, $\rho_{calcd} = 1.954\,\text{mg}\,\text{cm}^{-3}$, $T = 100(2)$ K, absorption coefficient $\mu = 11.594\,\text{mm}^{-1}$. Data were collected on a Bruker SMART CCD diffractometer, using Mo$_{K\alpha}$ radiation ($\lambda = 0.71073$ Å). Unit cell parameters were determined from a least-squares fit of 959 accurately centered reflections ($6.794° < 2\theta < 56.532°$). A total of 3202 unique reflections were measured, of which 2505 reflections were considered observed with $I > 2\sigma(I)$. All reflections were used for structure analysis. The intensity data were corrected for Lorentz and polarization effects, absorption, and secondary extinction. Atoms were located by use of statistical methods. All non-hydrogen atoms were refined with anisotropic parameters. With the exception of the hydrogen atoms of water (not located), all hydrogen atoms were included in structure factor calculations but parameters were not refined. The hydrogen atoms were assigned isotropic displacement values based approximately on the value for the attached atom. The final discrepancy index was $R = 0.041$, $R_w = 0.105$ ($w = 1/\sigma^2(|F_o|)$ for 2505 independent reflections with $I > 2\sigma(I)$. The largest peak maximum and minimum on a final difference electron density map were 3.37 and -3.41 e Å^{-3}, both near Hg. Data were processed using programs supplied with the Bruker SMART ccd diffractometer. b) Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-160758 (**2**) and CCDC-160759 (**3**). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: (+44)1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

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An Efficient Synthesis of (±)-Narwedine and (±)-Galanthamine by an Improved Phenolic Oxidative Coupling

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(−)-Galanthamine (**1**; Scheme 1),[1] an alkaloid isolated from the *Amaryllidaceae* family, has been approved in Austria and the United Kingdom for the treatment of Alzheimer's disease as a selective acetylcholinesterase inhibitor.[2, 3] Because of the limited supplies and the high cost of its isolation from natural sources[4], several syntheses of galanthamine have been reported which use a phenolic oxidative coupling.[5] Recent syntheses make use of an asymmetric Heck reaction.[6a] (−)-Galanthamine (**1**) is considered to be synthesized biologically by the phenolic oxidative coupling[7] of norbelladine derived from L-tyrosine. Since the first synthesis of galanthamine by Barton and Kirby[5a] in 1960 by the biomimetic phenolic oxidative coupling of the biogenetic precursor norbelladine by using potassium ferricyanide, several methods have been designed to improve the low yield of this coupling reaction: for example, blocking one of the *ortho* positions on the norbelladine derivative with a bromo[5b,e–g,i,j, 8b] or a trimethylsilyl[5h] group, which could be easily be substituted by a hydrogen atom, changing the oxidant,[5c,d,h] and using symmetrical substrates.[5c,d] Despite these efforts, the yield of the pivotal step in these syntheses still remains only moderate (~50%). Therefore, an efficient synthesis of **1** is highly desirable and useful.

Since (−)-galanthamine (**1**) has been efficiently obtained from (±)-narwedine (**2**)[8] by crystallization-induced chiral

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