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Synthesis and inclusion properties of a novel macrocyclic hexaketone monohydrate with a hemiacetal structure

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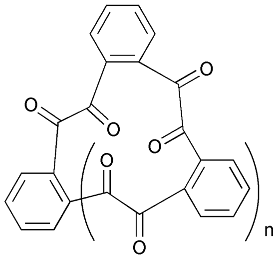
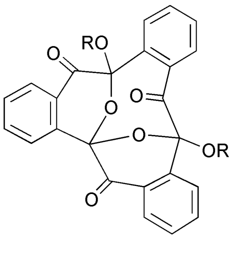
A macrocyclic hexaketone monohydrate was synthesized by the oxidation of either tribenzohexadehydro[12]annulene or tribenzotetradehydro[12]annulene-1,2-dione with ruthenium catalysts; the hexaketone monohydrate incorporates small molecules with a hydroxy, carbonyl or ether group in the crystalline lattice to form inclusion complexes.

Although macrocyclic conjugated π-systems such as annulenes, cyclic polyaromatics, and large membered cyclophanes have been investigated extensively in the last three decades,[1] until now only a limited number of corresponding polyketones have been reported.[2] Macrocyclic polyketones **1** ($n = 1, 2, 3$, *etc.*) have a unique structure with regularly arranged carbonyl groups. In order to synthesize **1** ($n = 1$), ruthenium-catalyzed oxidation of the corresponding annulene and annulenedione was investigated, which gave the monohydrate **2** having a nonsymmetrical structure with two dihydrobenzopyranone units. Herein, we report the synthesis and properties of cyclic hexaone monohydrate **2**.



1: n = 1

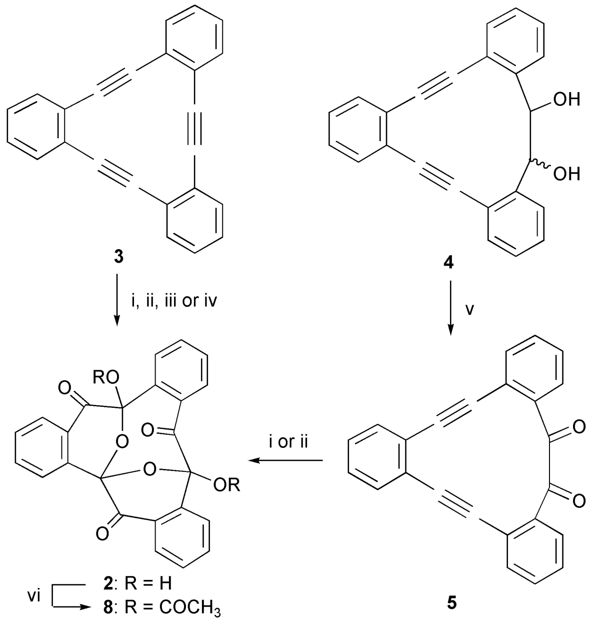


2

We tried ruthenium-catalyzed oxidation of the acetylene units of **3**[3,4] and **5**, to produce cyclic polyketone **1** (Scheme 1).[5] When tribenzohexadehydro[12]annulene **3** was oxidized with $RuO_2\cdot2H_2O$ in the presence of $NaIO_4$ in CCl_4–CH_3CN–H_2O at room temp., hexaone hydrate **2** was formed in 13% yield, together with dione **5** (Table 1; entry 1). Since **1** has a small inner cavity, H_2O may attack the carbonyl group to easily form a cyclic structure. By using $RuCl_3\cdot3H_2O$–PhI=O for the oxidation, **2** was obtained in 31% yield as a major product, together with a small amount of **5** (entry 2). When the reaction of **3** was carried out using $RuCl_2(PPh_3)_3$–PhI=O or $RuCl_2(CH_3CN)_2(PPh_3)_2$–PhI=O in dry CH_2Cl_2, the oxidation proceeded slowly and most of the starting **3** was recovered (entries 3 and 4). In a similar manner, when dione **5** prepared from **4**[6] was treated with $RuO_2\cdot2H_2O$ (10 mol%) in the presence of $NaIO_4$ in CCl_4–CH_3CN–H_2O, **2** was obtained in 39% yield, together with phthalic anhydride (3%). Oxidation of **5** with $RuCl_3$–PhI=O in acetone-H_2O at room temp. produced the best yield of **2** (46%).

Hexaone hydrate **2** has very low solubility in common organic solvents such as CH_2Cl_2, benzene and alcohols, but is soluble to some extent in acetone, ethyl acetate and THF. Although dehydration of **2** was attempted under vacuum or by using dehydrating reagents (dry $MgSO_4$, dry K_2CO_3, anhydrous $CuSO_4$, *etc.*), **2** was recovered unchanged. Treatment of **2** with H_2SO_4 in methanol at room temp. afforded only starting **2** without decomposition. Thus, the hemiacetal structure in **2** is stable to acids and bases. In addition, the hydroxyl groups in **2** were acetylated to give **8** in 68% yield by reaction with acetic anhydride in the presence of *p*-TsOH at 110 °C for 16 h.

Since **2** was not fully characterized by spectroscopic analyses, the structure was determined unambiguously by X-ray analysis. Hexaone hydrate **2** was recrystalized from AcOEt–MeOH to form single crystals. Interestingly, these crystals incorporate MeOH tightly to afford a 1 : 1 complex **2a**† (Fig. 1).‡ In the crystal of **2a**, the bond lengths and angles of **2** containing two dihydrobenzopyranone rings have the normal values, reflecting a stable, strain-free structure. Although there is no intramolecular hydrogen bond in **2a**, three types of intermolecular hydrogen bonds are formed in the crystal. Thus, two methanol molecules are incorporated in the cavity composed of the four molecules of **2**. The strongest hydrogen bond is the one between the hydroxyl hydrogen in **2** and the oxygen



Scheme 1 *Reagents and conditions*: i, $RuO_2\cdot2H_2O$, $NaIO_4$, CCl_4–CH_3CN–H_2O (1 : 1 : 2); ii, $RuCl_3\cdot3H_2O$, PhIO, acetone–H_2O (9 : 1); iii, $RuCl_2(PPh_3)_2$, PhIO, CH_2Cl_2; iv, $RuCl_2(CH_3CN)_2(PPh_3)_2$, PhIO, CH_2Cl_2; v, $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2 (78%); vi, *p*-TsOH, Ac_2O (68%).

Table 1 Reactions of [12]annulene **3** with ruthenium catalysts[a]

Entry	Ru species	Co-oxidant	Yields (%)[b] **2**	**5**	**3**
1[c]	$RuO_2\cdot2H_2O$	$NaIO_4$	13	27	16
2[d]	$RuCl_3\cdot3H_2O$	PhIO	31	6	8
3[e]	$RuCl_2(PPh_3)_2$	PhIO	trace	21	25
4[e]	$RuCl_2(CH_3CN)_2(PPh_3)_2$	PhIO	trace	26	40

[a] A mixture of **3** (0.20 mmol), ruthenium salt or complex (0.020 mmol) and co-oxidant (1.80 mmol) was stirred for 20 min at room temp. [b] Isolated yield. [c] In CCl_4, CH_3CN and H_2O. [d] In acetone and H_2O. [e] In CH_2Cl_2.

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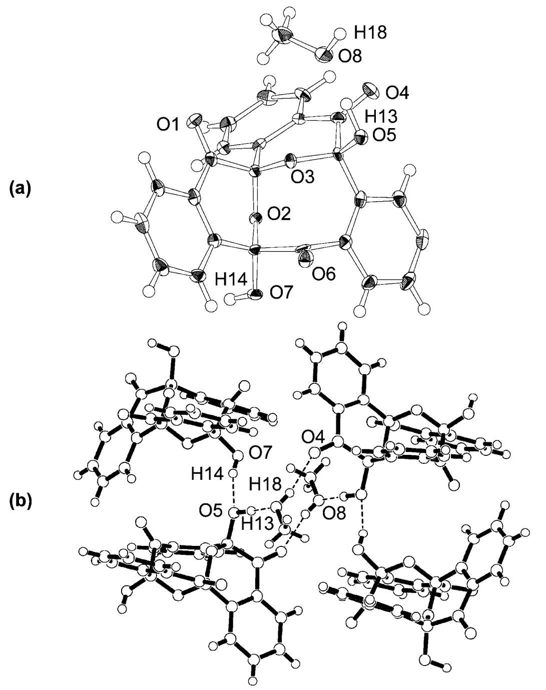

Fig. 1 a) ORTEP (50% probability ellipsoids) diagram of **2a**. b) Intermolecular hydrogen bond networks in **2a**. Interatomic distances (Å) are as follows: H(13)···O(8), 1.60(7) [O(5)···O(8), 2.659(4)], H(14)···O(5), 1.94(5) [O(5)···O(7), 2.756(4)], H(18)···O(4), 1.99(5) [O(8)···O(4), 2.790(4)], H(18)···O(8), 3.31(4) [O(8)···O(8), 3.594(4)].

in methanol [H(13)···O(8)]. The O(5)···O(8) distance is 2.659(4) Å. The other two hydrogen bonds are between the carbonyl oxygen in **2** and the methanol hydroxyl group [O(4)···H(18)], and between the two hydroxy groups in **2** [O(5)···H(14)]. The distances between O(4)···O(8) and O(5)···O(7) are 2.790(4) and 2.756(4) Å, respectively.

In the crystals hexaone hydrate **2** exhibits interesting inclusion properties for alcohols, esters and ethers.[7] By analogy with methanol, recrystallization from ethyl acetate containing ethanol, 2-propanol or 1-propanol forms tightly incorporated 1 : 1 complexes **2b**, **2c** and **2d**, respectively, whereas recrystallization from methyl formate or ethyl acetate affords 3 : 2 complexes **2e** and **2f**, respectively (Table 2). In addition, THF and ether are incorporated loosely to form 1 : 2 complexes **2g** and **2h**. The crystalline ether complex **2h** is unstable and dissociates gradually at ambient temperature to give **2** as a powder. In contrast, acetone and hydrophobic molecules such as hexane, benzene and CH_2Cl_2 afford no inclusion complex. In the case of 1-butanol and water, where **2** is only very slightly soluble, no crystalline complexes are formed by recrystallization of **2** from 1-butanol–acetone and aq. acetone. However, 1-butanol and water are incorporated directly by contact with **2** through the solid–liquid interface.

Table 2 Formation of inclusion complexes **2a–2g** and their dissociation temperatures

Complex	Included molecule	Ratio[a] (**2** : guest)	Dissociation temp.[b]/°C
2a	MeOH	1 : 1	171.6
2b	EtOH	1 : 1	168.3
2c	2-PrOH	1 : 1	162.2
2d	1-PrOH	1 : 1	159.5
2e	HCO_2Me	3 : 2	139.0
2f	CH_3CO_2Et	3 : 2	135.1
2g	THF	1 : 2	110.6

[a] Ratios of **2** and guest molecule were determined by ^1H NMR and elemental analyses. [b] Dissociation temperatures were determined by DSC and TG measurements.

As shown in Table 2, the tightness of inclusion in the crystal is in the order of **2a** > **2b** > **2c** > **2d** > **2e** > **2f** > **2g** > **2h**. Complex formation was also observed on exposure of **2** to the vapor of alcohols, and **2a**, **2b** and **2c** were obtained when **2** was exposed to vaporized methanol, ethanol or 2-propanol, respectively. Interestingly, **2a** produced **2b** when exposed overnight to ethanol vapor at room temp. The reverse change from **2b** to **2a** proceeded more smoothly upon contact with the vaporized methanol.

Since methanol and ethanol are incorporated in the crystalline lattice of **2** more strongly than 1-propanol, 1-butanol and water, separation of a small amount of methanol and ethanol contaminant in 1-propanol, 1-butanol and water was investigated using **2** as a capturing agent. When 1-propanol, 1-butanol and water containing 0.05 mol% methanol were passed through a column containing 100 mol equiv. of **2** dispersed in celite, methanol was removed from 1-propanol, 1-butanol and water. As a result, 27, 62 and 28% of methanol was removed from the solutions of 1-propanol, 1-butanol and water, respectively. Methanol captured in the crystal lattice of **2** can be dissociated upon heating, so **2** can be used repeatedly. A similar separation of ethanol from 1-propanol, 1-butanol and water was observed using a column containing **2** dispersed in celite.

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Notes and references

† **2a**: colorless plates (from AcOEt–MeOH), mp *ca.* 206 °C (dec); ^1H NMR (500 MHz, acetone-d_6) δ 3.19 (q, J = 5.3 Hz, 1H, MeOH), 3.30 (d, J = 5.3 Hz, 3H, MeOH), 6.99 (s, 1H), 7.21 (s, 1H), 7.25 (d, J = 8.3 Hz, 1H), 7.29 (d, J = 8.3 Hz, 1H), 7.42–7.45 (m, 2H), 7.50 (t, J = 8.0 Hz, 1H), 7.68–7.79 (m, 3H), 7.91–7.94 (m, 2H), 8.07 (d, J = 8.0 Hz, 1H), 8.14 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, acetone-d_6) δ 47.99 (MeOH), 98.09, 98.83, 99.94, 126.30, 127.41, 127.46, 128.81, 129.27, 129.55, 129.89, 130.15, 130.30, 130.42, 130.71, 131.36, 135.01, 135.55, 136.88, 137.16, 138.28, 142.17, 186.97, 191.07, 201.91; EI-MS: *m/z* 396 ($M^+ - 18$); FAB-MS: *m/z* 415 ($M^+ + 1$), 397 ($M^+ - 17$); IR (KBr) 3500, 3347, 3116, 2847, 1725, 1698, 1693, 1598, 1454 cm^{-1}; Anal. Calcd for $C_{24}H_{14}O_7$–CH_3OH: C, 67.26; H, 4.06; Found: C, 67.11; H, 4.10%.

‡ Crystal data for **2a**: $C_{25}H_{18}O_8$, M_w 446.41, monoclinic, space group $C2/c$ (No. 15), a = 20.486(7), b = 19.08(1), c = 13.742(5) Å, β = 131.58(1)°, V = 4018(3) Å^3, Z = 8, D_c = 1.476 g cm^{-3}, $F(000)$ = 1856, μ(MoKα) = 1.10 cm^{-1}, R = 0.044, Rw = 0.054, GOF = 1.14. All measurements were performed on a Rigaku AFC7R diffractometer with graphite monochromated Mo-Kα (λ = 0.71069 Å) radiation at 23 °C. Among a total of 4887 reflections measured, 4616 were unique and the observed (I > 3.00σ(I)) 1850 reflections were used for the refinement. The crystal structure was solved by the direct method and refined by the full matrix least-squares method. CCDC 215698. See http://www.rsc.org/suppdata/cc/b3/b308167b/ for crystallographic data in CIF or other electronic format.

1 For recent reviews: R. D. Kennedy, D. Lloyd and H. McNab, *J. Chem. Soc., Perkin Trans. 1*, 2002, 1601; U. H. F. Bunz, Y. Rubin and Y. Tobe, *Chem. Soc. Rev.*, 1999, **28**, 107.
2 For examples of macrocyclic polyketones: W. Y. Lee, *Synlett*, 1994, 765; S. W. McElvany, M. M. Ross, N. S. Goroff and F. Diederich, *Science*, 1993, **259**, 1594; Y. Rubin, T. C. Parker, S. J. Pastor, S. Jalisstgi, C. Boulle and C. L. Wilkins, *Angew. Chem., Int. Ed.*, 1998, **37**, 1226.
3 For a review: W. J. Youngs, C. A. Tessier and J. D. Bradshaw, *Chem. Rev.*, 1999, **99**, 3153.
4 M. Iyoda, A. Vorasingha, Y. Kuwatani and M. Yoshida, *Tetrahedron Lett.*, 1998, **39**, 4701.
5 P. Müller and J. Godoy, *Helv. Chim. Acta*, 1981, **64**, 2531; P. H. J. Carlsen, T. Katsuki, V. S. Martin and K. B. Sharpless, *J. Org. Chem.*, 1981, **46**, 3936; R. Zibuck and D. Seebach, *Helv. Chim. Acta*, 1988, **71**, 237.
6 M. Iyoda, K. Fuchigami, A. Kusaka, T. Yoshida, M. Yoshida, H. Matsuyama and Y. Kuwatani, *Chem. Lett.*, 2000, 860.
7 For a review: F. Toda, *Diol, Bisphenol and Diamide Host Compounds*, in *Comprehensive Supramolecular Chemistry*, ed. D. D. MacNicol, F. Toda and R. Bishop, Pergamon, Oxford, 1996, **vol. 6**, p. 465.