Pergamon

Tetrahedron Letters 42 (2001) 8861–8864

TETRAHEDRON
LETTERS

Synthesis and crystal structure of a novel triangular macrocyclic molecule, tris(H_2saloph),[†] and its water complex

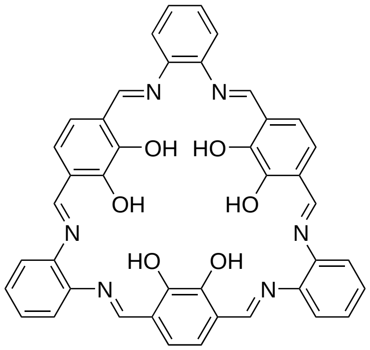
Shigehisa Akine, Takanori Taniguchi and Tatsuya Nabeshima*

Department of Chemistry, University of Tsukuba, Tsukuba, Ibaraki 305-8571, Japan

Received 6 August 2001; revised 9 October 2001; accepted 12 October 2001

Abstract—Condensation of 2,3-dihydroxybenzene-1,4-dicarbaldehyde and 1,2-phenylenediamine afforded a novel 30-membered macrocyclic hexaimine bearing six hydroxyl groups, in which a water molecule is trapped in the crystalline state. © 2001 Elsevier Science Ltd. All rights reserved.

Macrocyclic molecules containing a Schiff base and hydroxyl moieties have attracted considerable attention due to formation of a variety of multi-metal complexes,[1] which exhibit catalytic activity for epoxidation of olefins,[2] asymmetric ring-opening of epoxides,[3] NLO behavior,[4] etc. Application of the macrocycles to model systems for active sites of metalloproteins and magnetic materials may be expected. Furthermore, metallohosts bearing a salen[‡] analogue provide a unique and cooperative binding site for both neutral guests and cations.[5] Hydrogen bonding through the hydroxyl groups of salicylaldimine is also expected to be useful for molecular recognition, because a well-arranged, multi-hydrogen bonding network can be available. There is, however, no example of host–guest systems by using intermolecular hydrogen bonding of an oligo(H_2salen) macrocyclic compound as a host, although interesting synthetic applications of intramolecular hydrogen bonds to cyclization of H_2salen analogues and the absolutely template-dependent synthesis of bis- and tris(H_2salen) ligands and their complexes were reported.[6,7] Cyclic oligo(H_2salen) derivatives possessing a triangular arrangement of three salicylaldimine[8] are very attractive and important target molecules, because this arrangement is fit for the shape of guests with C_3 symmetry such as ammonium salts and spherical guests such as alkali and alkaline earth metal ions.[7,9] Here we report synthesis of a triangular 30-membered macrocyclic oligo(H_2salen) analogue **1**, tris(H_2saloph), without a template and the crystal structure of a complex of **1** and a water molecule via multi-hydrogen bonds.



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Synthesis of the cyclic hexaimine **1** is shown in Scheme 1. Dilithiation[10] of 1,2-dimethoxybenzene (**2**) followed by the reaction with *N*,*N*-dimethylformamide gave 2,3-dimethoxybenzene-1,4-dicarbaldehyde (**3**). Treatment of **3** with boron tribromide afforded **4** in 92% yield. The macrocyclic compound **1** was obtained in a remarkably high yield (91%) by condensation of **4** and **5** (4×10^{-2} M) in acetonitrile (rt, 2 weeks). Under lower concentrations ($2.5–4.0\times10^{-3}$ M, rt, 1 month), the yield decreased considerably (19%). Pure compound **1** gradually precipitated during the reaction. The IR spectrum of **1** suggested an imine functionality. The C=N stretching band appeared at 1620 cm^{-1}, while the C=O absorption around 1660 cm^{-1} of the dialdehyde **4** disappeared.

The structure of **1** was supported by NMR in DMF-d_7 and analytical data,[§] and finally determined to be a 3:3

Keywords: imines; macrocycles; X-ray crystal structures.

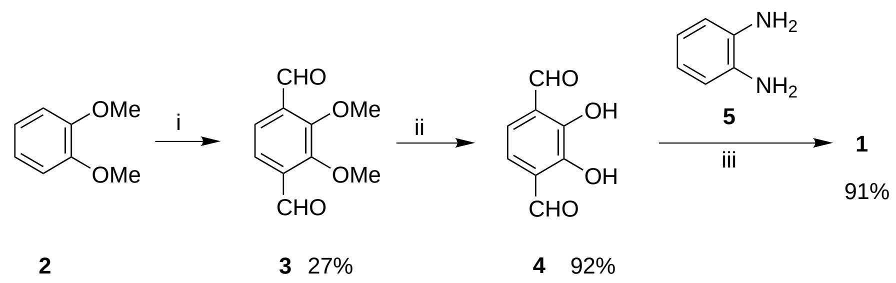
* Corresponding author. Tel.: +81-298-53-4507; fax: +81-298-53-6503; e-mail: nabesima@chem.tsukuba.ac.jp

[†] H_2saloph = *N*,*N*′-disalicylidene-*o*-phenylenediamine.

[‡] H_2salen = *N*,*N*′-disalicylideneethylenediamine.

[§] ^{1}H NMR (400 MHz, DMF-d_7) δ 7.29 (s, 6H), 7.50–7.52 (m, 6H), 7.62–7.64 (m, 6H), 9.07 (s, 6H), 13.54 (s, 6H); ^{13}C NMR (100 MHz, DMF-d_7) δ 119.74, 121.24, 121.69, 128.63, 142.51, 151.49, 164.61. Anal. calcd for $C_{42}H_{30}N_6O_6\cdot 2H_2O$: C, 67.19; H, 4.56; N, 11.19. Found: C, 67.51; H, 4.73; N, 11.15.

PII: S0040-4039(01)01943-8



Scheme 1. *Reagents and conditions*: (i) (1) *n*-BuLi, TMEDA, ether, (2) DMF then H_2O; (ii) BBr_3, dichloromethane, then H_2O; (iii) acetonitrile.

macrocycle by X-ray crystallographic analysis (Fig. 1).[¶] This is the first example of X-ray crystallographic identification of a tris(H_2saloph) derivative. Compound **1** has a triangular shape with three apexes of the phenylenediamine moieties and was located on the crystallographic two-fold axis. Each hydroxyl group points to a nitrogen atom of the imine moieties with O–N distance of ca. 2.6 Å, indicating existence of a strong intramolecular hydrogen-bond network. However, no intermolecular hydrogen bond was observed. While the three benzene rings of the phenylenediamine moieties lie on the average plane of the molecule (defined as the least-square plane of whole non-hydrogen atoms of **1**), the dihedral angles between the catechol rings and the average plane are about 30°. Thus, four of the six hydroxyl groups (O(1)*, O(2)*, O(3), and O(4)) stick out to one side of the molecular plane and the other two (O(1) and O(2)) to the opposite side.

Interestingly, a hydrate, **1**·H_2O·MeCN, was also obtained from the reaction mixture. X-Ray crystallography[¶] revealed that a water molecule is captured in the cavity of the cyclic compound **1** (Fig. 2).[11] The two hydrogen atoms of the water molecule make effective

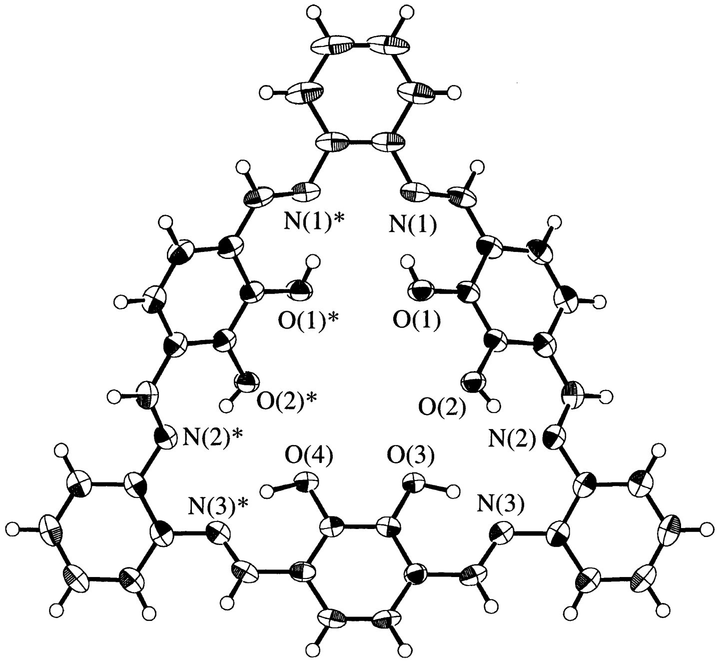


Figure 1. Crystal structure of **1**·3MeCN (ORTEP, 50% probability). Disordered atoms and solvent molecules are omitted. Selected interatomic distances (Å): N(1)–O(1) 2.597(3), N(2)–O(2) 2.593(3), N(3)–O(3) 2.568(4), N(3)*–O(4) 2.603(4), O(1)–O(1)* 3.376(4), O(1)–O(2) 2.647(3), O(2)–O(3) 3.165(4), O(3)–O(4) 2.677(5), O(4)–O(2)* 2.930(4).

[¶] Crystallographic analysis of **1**·3MeCN: deep red prism (0.40×0.40×0.30 mm^3), $C_{48}H_{39}N_9O_6$ ($M=837.88$), trigonal, $a=18.2013(6)$, $c=10.7814(4)$ Å, $V=3093.2(2)$ $Å^3$, space group, $P3_121$ (No. 152) or $P3_221$ (No. 154), $Z=3$, $\rho_{calcd}=1.349$ g/cm^3, $T=120$ K, μ(MoKα)$=0.092$ mm^{-1}, collected reflections, 22827, unique, 4725 ($R_{int}=0.0682$), $R_1=0.0527$ ($I>2\sigma(I)$), $wR_2=0.1342$ (all data).[13] The chirality of the crystal was not reliably determined by the refinement, which left ambiguity in the determination of the space group. In the crystal of **1**·3MeCN, the cavity of **1** surrounded by the six oxygen atoms was partially filled by the methyl groups of two acetonitrile molecules.

Crystallographic analysis of **1**·H_2O·MeCN: deep red needle (0.40×0.10×0.05 mm^3), $C_{44}H_{35}N_7O_7$ ($M=773.79$), monoclinic, $a=9.646(3)$, $b=18.910(2)$, $c=21.032(9)$ Å, $\beta=95.519(3)$°, $V=3819(2)$ $Å^3$, space group, $P2_1/c$ (No. 14), $Z=4$, $\rho_{calcd}=1.346$ g/cm^3, $T=120$ K, μ(MoKα)$=0.093$ mm^{-1}, collected reflections, 22311, unique, 6671 ($R_{int}=0.1898$), $R_1=0.0935$ ($I>2\sigma(I)$), $wR_2=0.2472$ (all data).[13]

Crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 166254 (**1**·3MeCN) and 166255 (**1**·H_2O·MeCN).

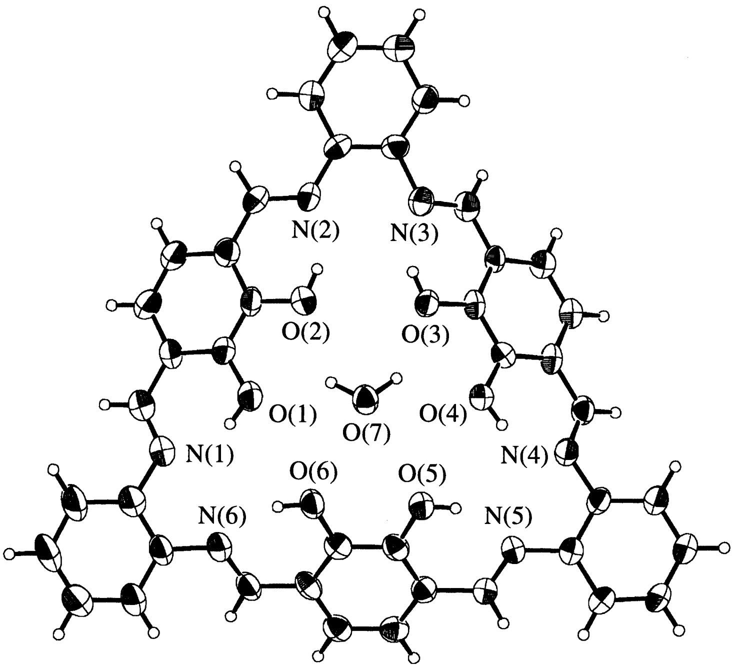
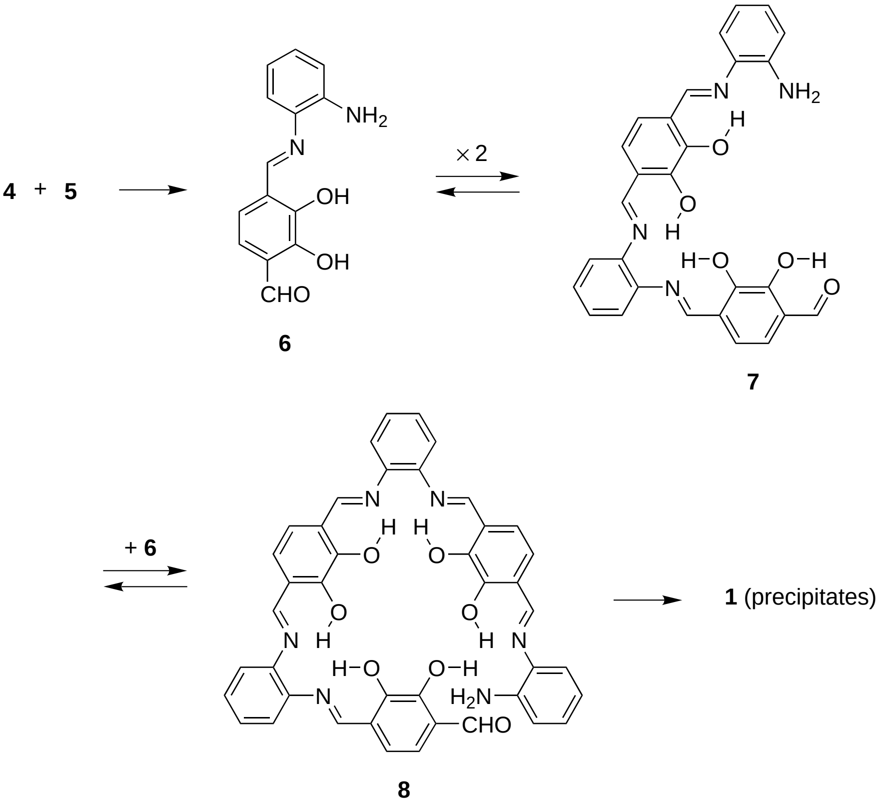


Figure 2. Crystal structure of **1**·H_2O·MeCN (ORTEP, 30% probability). Disordered atoms and acetonitrile molecules are omitted. Selected interatomic distances (Å): N(1)–O(1) 2.645(8), N(2)–O(2) 2.628(7), N(3)–O(3) 2.573(6), N(4)–O(4) 2.590(6), N(5)–O(5) 2.657(7), N(6)–O(6) 2.655(7), O(1)–O(2) 2.671(6), O(2)–O(3) 3.006(6), O(3)–O(4) 2.640(6), O(4)–O(5) 3.053(6), O(5)–O(6) 2.646(6), O(6)–O(1) 3.032(6), O(1)–O(7) 2.940(6), O(2)–O(7) 2.939(6), O(3)–O(7) 2.975(6), O(4)–O(7) 3.023(6), O(5)–O(7) 2.997(6), O(6)–O(7) 2.947(6).



Scheme 2. Plausible mechanism for the formation of **1**.

hydrogen bonding to four oxygen atoms of **1** because of complementary geometrical fit. Compound **1** adopted a shallow bowl conformation with all the six hydroxyl groups sticking out to the same side. Rather long O(water)–O(catechol) distances (2.94–3.02 Å) suggest delocalization of protons in ways like O···H···N and O···H···O.

Selective formation of cyclic compound **1** is probably explained by stabilization of the favorable conformation of the transition state and/or intermediates in the cyclization due to intramolecular hydrogen bonds. The initial cyclization process was monitored by ^{1}H NMR spectroscopy in CD_3CN. Only two compounds (major and minor, 4:1) were formed (Scheme 2). The major component was easily assigned to be 1:1 adduct **6**,[||] and the minor component was considered to be a linear 2:2 adduct **7**. It is noteworthy that hydroxyl protons of the salicylaldimine moieties were observed at 13.5 and 13.2 ppm during the course of the reaction, indicating existence of strong hydrogen bonds. The conformation of the precursor **8** is restricted by multiple hydrogen bonds in such a way that the amino group can easily attack the formyl group. The driving force for formation of the cyclic trimer is considered to be the extremely low solubility of the product in acetonitrile,[**] as well as the multiple hydrogen bonds as mentioned above.

It is well known that the oxygen atoms of metal complexes of salen-type ligands have anionic character, which sometimes enhances coordination strength to other metal ions.[12] We are currently investigating the synthesis of transition metal complexes of **1** and preparing more soluble tris(H_2saloph) as a sophisticated host molecule by introducing hydrophobic groups such as an alkyl chain into the benzene rings of **1**.

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[||] ^{1}H NMR signals assigned to intermediate **6** are as follows (400 MHz, CD_3CN): $\delta=4.4$ (brs, 2H), 6.74 (td, $J=7.6$, 1.2 Hz, 1H), 6.82 (dd, $J=7.6$, 1.2 Hz, 1H), 7.10 (td, $J=7.6$, 1.2 Hz, 1H), 7.17 (dd, $J=7.6$, 1.2 Hz, 1H), 7.20 (d, $J=8.4$ Hz, 1H), 7.27 (d, $J=8.4$ Hz, 1H), 8.78 (s, 1H), 10.02 (s, 1H), 10.5 (brs, 1H), 13.5 (brs, 1H).

[**] The product was also insoluble in chloroform, methanol, and water.