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Preparation of 4,13,19,28-Tetrahydroxy-9,9,24,24-tetramethyl[2.1.2.1]metacyclophane, a Novel *exo*-Hydroxycalixarene Analogue†

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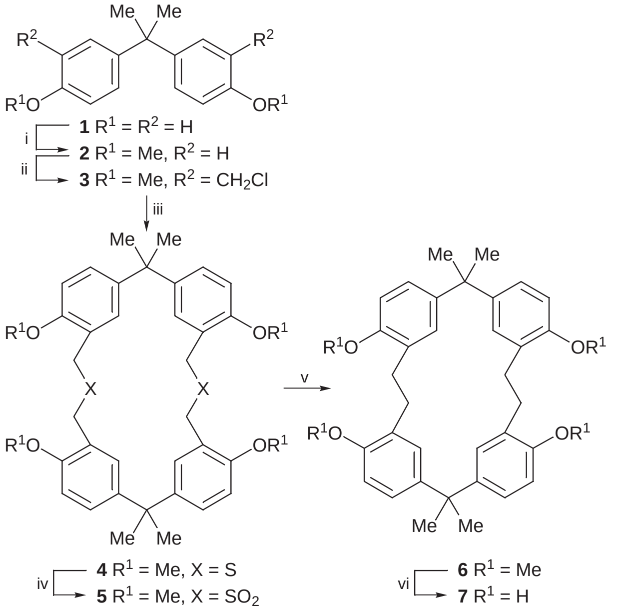
A novel 4,13,19,28-tetrahydroxy-9,9,24,24-tetramethyl[2.1.2.1]metacyclophane is prepared from bisphenol A in six steps and found to have a saddle structure in solid state.

We have reported that a series of [2.*n*.2.*n*]metacyclophanes ($n = 1, 2$) are useful building blocks for supramolecular assemblies by fuctionalization of hydroxy groups introduced at internal positions.[1–3] Recently, *exo*-calixarene derivatives containing hydroxy groups at the outer positions have been central for novel supramolecular assemblies.[4–7] Here, we report the preparation of *exo*-tetrahydroxy[2.1.2.1]metacyclophane and the crystal structure of its tetramethylated derivative.



Scheme 1 *Reagants and conditions*: i, MeI, K_2CO_3 (72%); ii, $(HCHO)_x$, HCl, AcOH, H_3PO_4 (56%); iii, Na_2S (62%), iv, *m*-CPBA (82%); v, 450 °C (1 Torr) 44%; vi, BBr_3 (66%)

exo-Tetrahydroxy[2.1.2.1]metacyclophane **7** was prepared from bisphenol A **1** in six steps (Scheme 1). The bis-(chloromethyl) derivative **3** was prepared according to the method reported previously.[8] Cyclization of **3** with sodium sulfide under high-dilution conditions afforded the corresponding dithiacyclophane **4** in 62% yield. Oxidation of **4** with *m*-CPBA, followed by flash vacuum pyrolysis (450 °C, 1 Torr) gave 4,13,19,28-tetramethoxy-9,9,24,24-tetramethyl[2.1.2.1]metacyclophane **6** in 14% yield. Demethylation leading to the desired 4,13,19,28-tetrahydroxy-9,9,24,24-tetramethyl[2.1.2.1]metacyclophane **7** in 66% yield was carried out by reaction with BBr_3. According to ^{1}H NMR spectroscopy, compound **7** is conformationally flexible in solution. The ^{1}H NMR spectrum of **7** shows two singlets assigned to four methyl groups (δ 1.49, 12H) and eight protons (δ 2.87, 8H) of bridging CH_2 at 273 K. No significant change in the ^{1}H NMR spectrum was observed in the temperature range 173—273 K.

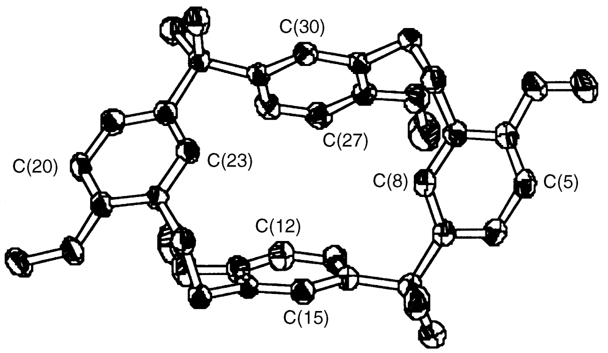


Fig. 1 Top view of the molecular structure of **6** showing the atom numbering scheme (hydrogen atoms are omitted for clarity). Selected atom distances in Å: C(5)–C(20), 10.655, C(8)–C(23), 5.668, C(12)–C(27), 3.710, C(15)–C(30) 5.833.

The molecular structure of **6** (satisfactory crystals of **7** could not be obtained) was determined by single crystal X-ray crystallographic analysis (Fig. 1). Two phenyl rings which face each other incline into the cavity whereas the other two phenyl rings point outwards and the conformation of **6** can be described as saddle like in the solid state. Bond distances and angles are unexceptional.

Functionalization of the hydroxy groups leading to supramolecular assemblies is in progress.

Experimental

All melting points are uncorrected. ^{1}H NMR spectra were recorded on a Nippon Denshi JEOL GSX-270 spectrometer in $CDCl_3$ with Me_4Si as internal reference. IR spectra were measured for KBr pellets on a Perkin Elmer Paragon1000 spectrometer. Mass spectra were obtained on a Hitachi M-80B spectrometer utilizing a 75 eV direct inlet system. X-Ray crystallographic analysis was performed on an Enraf-Nonius CAD4 diffractometer. Column chromatography was carried on silica gel (Wako gel, C300).

Cyclization of **3** *with* Na_2S.—A solution of 4.0 g (11.3 mmol) of dichloride **3** in 300 mL of benzene was added dropwise over a period 12 h to a solution of 5.43 g (22.6 mmol) of sodium sulfide nonahydrate

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in 1 l of EtOH with stirring at room temperature under an N_2 atmosphere. After addition was complete, the reaction mixture was evaporated to leave a residue from which organic materials were extracted with chloroform. The chloroform solution was washed with water and brine, dried with Na_2SO_4, and evaporated to leave a residue which was chromatographed on SiO_2 with hexane–AcOEt (9:1 v/v) as eluent to give a colorless solid, which was recrystalized from hexane–chloroform to yield 2.20 g (62%) of 2,18-dithia-5,14,21,30-tetramethoxy-10,10,26,26-tetramethyl[3.1.3.1]metacyclophane **4** as colorless prisms; mp 237–238 °C; ν_{max}/cm^{-1} 811, 1031, 1249, 1503, 1606, 2917, 2963, 2996; δ_H 1.55 (12H, s), 3.25 (8H, s), 3.81 (12H, s), 6.56 (4H, d, $J = 2.4$ Hz), 6.80 (4H, d, $J = 8.6$ Hz), 7.28 (4H, dd, $J = 2.4$, 8.6 Hz); m/z 628 (M^+) (Found: C, 72.33; H, 7.12. $C_{38}H_{44}O_4S_2$ requires C, 72.59; H, 7.05%).

Oxidation and Flash Vacuum Pyrolysis.—To 3.66 g (5.82 mmol) of **4** in 90 mL of dry chloroform was added 5.52 g (25.6 mmol) of *m*-CPBA and the solution stirred for 1 h under an N_2 atmosphere. The reaction mixture was poured into 100 mL of aqueous NaOH, 10%. The organic phase separated, dried with Na_2SO_4 and evaporated to give the disulfone **5** (3.30 g, 82%) as a white powder; mp > 300 °C; ν_{max}/cm^{-1} 822, 1026, 1119, 1253, 1304, 1503, 1612, 2935, 2968, 3009; δ_H 1.60 (12H, s), 3.85 (12H, s), 4.12 (8H, s), 6.85 (4H, d, $J = 8.6$ Hz), 6.95 (4H, d, $J = 2.4$ Hz), 7.33 (4H, dd, $J = 2.4$, 8.6 Hz).

Without further purification, sulfone **5** (3.5 g, 5.05 mmol) was pyrolyzed at 450 °C (1 Torr) according to the literature.[9] The sublimed product was collected and chromatographed on SiO_2 with hexane–$CHCl_3$ (1/1, v/v) as eluent to give 4,13,19,28-tetrahydroxy-9,9,24,24-tetramethyl[2.1.2.1]metacyclophane **6** (1.26 g, 44%) as colorless prisms (hexane); mp 213–214 °C; ν_{max}/cm^{-1} 803, 1035, 1243, 1257, 1502, 1605, 2926, 2956; δ_H 1.47 (12H, s), 2.84 (8H, s), 3.60 (12H, s), 6.56 (4H, d, $J = 2.3$ Hz), 6.61 (4H, d, $J = 8.6$ Hz), 6.88 (4H, dd, $J = 2.3$, 8.6 Hz); m/z 564 (M^+) (Found: C, 80.77; H, 7.79. $C_{38}H_{44}O_4$ requires C, 80.81; H, 7.85%).

Demethylation of **6**.—To a solution of 400 mg (0.71 mmol) of **6** in 50 mL of dry CH_2Cl_2 was added dropwise 4.25 mL (4.25 mmol) of BBr_3 with stirring at 0 °C under an N_2 atmosphere. After addition was complete, the reaction mixture was poured into a large volume of ice/water. The organic layer was washed with water and brine, dried with Na_2SO_4, and evaporated to leave a residue. The resulting residue was chromatographed on SiO_2 with $CHCl_3$ as eluent to give the 4,13,19,28-tetrahydroxy-9,9,24,24-tetramethyl[2.1.2.1]metacyclophane **7** (238 mg, 66%) as colorless prisms from hexane; mp 238–240 °C; ν_{max}/cm^{-1} 820, 1100, 1157, 1255, 1416, 1503, 1611, 2930, 2960, 3017, 3420; δ_H 1.49 (12H, s), 2.87 (8H, s), 4.23 (4H, s, D_2O exchangeable), 6.55 (4H, d, $J = 2.3$ Hz), 6.61 (4H, d, $J = 8.6$ Hz), 6.87 (4H, dd, $J = 2.3$, 8.6 Hz); m/z 508 (M^+) (Found: C, 80.15; H, 7.25. $C_{34}H_{36}O_4$ requires C, 80.28; H, 7.13%).

X-Ray Crystal Structure Determination of **6**. *Crystal Data*.—$C_{38}H_{44}O_4$, $M = 564.77$, triclinic, space group P-1 (no. 2), $a = 11.066(2)$, $b = 14.832(1)$, $c = 9.690(1)$ Å, $\alpha = 91.71(1)$, $\beta = 93.15(1)$, $\gamma = 90.38(1)$, $V = 1587.1(4)$ Å^3, (by least-squares refinement on diffractometer angles for 23 automatically centered reflections, $\lambda = 1.541\,84$ Å), $Z = 2$, $D_c = 1.1817$ g cm^{-3}, colorless prism, crystal size $0.10 \times 0.15 \times 0.17$ mm. μ(Cu-Kα) = 0.587 mm^{-1}.

Data Collection and Processing.—CAD4 FR590 diffractometer, $\omega - 2\theta$ mode with ω scan width $= 0.8 + 0.360 \tan\theta$, scan speed 2–20 ° min^{-1}, graphite-monochromated Cu-Kα radiation; 5714 reflections were measured ($2.98 \le \theta \le 64.94$, $+h$, $\pm k$, $\pm l$). 5401 unique [merging $R = 0.0235$ after absorption correction (max, min. transmission factor = 0.9663, 0.9990)], linear and approximately isotopic crystal decay, *ca.* −0.0% corrected during procedure.

Structure Analysis and Refinement.—The structure was solved by direct methods (SIR92).[10] Full-matrix least-squares refinement on F^2 with all non-hydrogen atoms anisotropic and hydrogens in calculated positions with $U_{iso} = 1.3$ times of U (bonded atoms). The weighting scheme $w = 1/[\sigma^2(F_0^2) + (0.1687P)^2 + 26.0206P]$ where $P = (F_0^2 + 2F_c^2)/3$. Final R and R_w values are 0.0477, 0.1269 (refined on F^2). All calculations were performed on a MicroVAX3100 and IBM RISC System/6000 3100 using MolEN[11] and SHELXL-93.[12]

Full crystallographic details, excluding structure factors, have been deposited at the Cambridge Crystallographic Data Centre (CCDC). See Instructions for Authors, *J. Chem. Research (S)*, 1998 Issue 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 423/23.

See http://www.rsc.org/suppdata/jc/1999/426 for crystallographic files in .cif format.

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References

1 M. Tashiro, A. Tsuge, T. Sawada, T. Makishima, S. Horie, T. Arimura, S. Mataka and T. Yamato, *J. Org. Chem.*, 1990, **55**, 2404.
2 A. Tsuge, T. Sawada, S. Mataka, N. Nishiyama, H. Sakashita and M. Tashiro, *J. Chem. Soc., Perkin Trans. 1*, 1992, 1489.
3 T. Sawada, A. Tsuge, T. Thieman, S. Mataka and M. Tashiro, *J. Inclusion Phenom. Mol. Recognit. Chem.*, 1994, **19**, 301.
4 D. W. Chaser, *J. Org. Chem.*, 1985, **50**, 545.
5 G. Sartori, R. Maggi, F. Bigi, A. Arduini, A. Pastorio and C. Porta, *J. Chem. Soc., Perkin Trans. 1*, 1994, 1657.
6 V. Böhmer, R. Dorrenbacher, M. Frings, M. Heydenreich, D. de Paoli, W. Vogt, G. Fergunson and I. Thondorf, *J. Org. Chem.*, 1996, **61**, 549.
7 T. N. Sorrell and H. Yuan, *J. Org. Chem.*, 1997, **62**, 1899.
8 US *Pat*. 2884462, 1956 (*Chem. Abstr*., 1956, **74**, 87599).
9 M. Tashiro and T. Yamato, *J. Org. Chem.*, 1985, **50**, 2939.
10 SIR92: M. C. Altmare, M. Burla, G. Camalli, C. Cacarano, A. Giacovazzo, G. Guagliardi and J. Polidori, *J. Appl. Crystallogr.*, 1994, **27**, 435.
11 MolEN: An Interactive Structure Solution Procedure, Enraf-Nonius, Delft, The Netherlands, 1990.
12 SHEXL-93: G. M. Sheldrick, University of Göttingen, Germany, 1993.