Synthesis and Crystal Structure of a Novel Hexahomotrioxacalix[3]cryptand

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A novel hexahomotrioxacalix[3]cryptand was synthesized and its crystal structure has been determined. The crystals obtained by recrystallization from ethanol, are single clinic, space group is C2/c, $a = 19.6831(16)\text{\AA}$, $b = 16.8180(16)\text{\AA}$, $c = 29.267(3)\text{\AA}$, $\alpha = 90.00^\circ$, $\beta = 105.222(4)^\circ$, $\gamma = 90.00^\circ$. ¹H NMR spectroscopy and X-ray single-crystal structure results suggested that this compound was fixed in a cone conformation.

Key Words: Oxacalix[3]arene derivative, Synthesis, Crystal structure, Cone conformation.

INTRODUCTION

In past decade, calixarenes have been attracted considerable attention due to their molecular recognition properties¹. To enhance molecular/ionic binding ability and altered selectivity more efficient compared with the parent calixarenes, calixarenes generally be modified into different conformation isomers by introduction of large bulky substituents on their phenolic oxygens, blocking interconversion by oxygen-through-the-annulus rotation². For example, one of the method is to build a bridge on the lower or up rim. As a result, many tripodal calixarene cryptands such as tripodal calix[4]cryptand³, tripodal calix[6]cryptand⁴ were prepared.

Hexahomotrioxacalix[3]arene has more flexible conformation than calix[4]arene, because of the ether linkage. The presence of oxygen atom in oxacalixarenes is envisioned to adding the binding site and other specific features, such as building sophisticated ligand system. Indeed, such sophisticated ligands could be easily obtained by functionalization at the upper rim and/or lower rim, as usually done for classical calixarenes. Some examples have been given leading to an improvement of their ability to complex.

Recently, we synthesized a novel rhodamine amide-arm homotrioxacalix[3]arene, which shown excellent complexation ability for antimony and transition metal cations⁵. In order to further understanding of the relationship between the structure and molecular/ionic recognition ability of oxacalix[3]-arene derivatives, and continue our previous work, herein, we report the synthesis and crystal structure of a hexahomotri-oxacalix[3]-cryptand.

EXPERIMENTAL

The melting points were measured by an X-5 apparatus and are uncorrected. ¹H NMR spectra were measured with JEOL-ECX 500 MHz NMR spectrometers at room temperature using TMS as an internal standard. Crystal X-ray diffraction was conducted on a Bruker Smart ApexII CCD diffractometer. IR spectra were obtained using a Bruker Vertex 70 FT-IR spectrometer.

Synthetic procedures:

Preparation of compound 2a and 2b: The *p*-tert-butyl-homooxacalix[3]arene can be easily prepared by the condensation of *p*-tert-butylphenol and formaldehyde. Tricalix[3]arene (**1**) (2g, 3.44 mmol) and dry THF (100 mL) were added in round bottom flask, then added NaH (840 mg, 60 %, 21 mmol). The mixed solution was refluxed for 1 h, then added ethyl chloroacetate (2.65 g, 21 mmol), the solution was refluxed for 2 days and cooled to room temperature. Removed the THF under reduced pressure, the residue was dissolved in ethyl acetate (120 mL), washed with 10 % HCl (50 mL), water (50 mL $\times$ 2), brine (50 mL) and dried with anhydrous sodium sulphate. The filtrate was evaporated to get light yellow solid. Chromatographed over silica gel using CH₂Cl₂/acetone (14:1) as eluent to give a colourless solid, recrystallized from methanol to give pure white crystal, cone compound (**2a**) 1.8 g, yield 28 %. m.p. 70-72 °C; ¹H NMR (500 MHz, CDCl₃): δ (ppm) 1.09 (s, 27H, *t*-Bu), 1.34 (t, 9H, $J = 16$ Hz, CH₂CH₃), 4.27 (q, 6H, $J = 6.8$ Hz, OCH₂CH₃), 4.50 (s, 6H, OCH₂CO), 4.53 (d, 6H, $J = 16$, OCH₂), 4.91 (d, 6H, $J = 16$ Hz, OCH₂), 6.95 (s, 6H, ArH); IR (KBr, ν_{max} , cm⁻¹): 1750, 1190.

The partial cone compound (**2b**) 0.28 g, yield 58 %, m.p. 146–148 °C; ^1H NMR (500 MHz, CDCl_3): δ (ppm) 1.09 (t, 3H, CH_2CH_3), 1.22 (t, 6H, CH_2CH_3), 1.25 (s, 18H, *t*-Bu), 1.33 (s, 9H, *t*-Bu), 3.22 (s, 2H, OCH_2CO), 4.22 (d, 2H, OCH_2CO), 4.51 (d, 2H, OCH_2CO), 3.79 (q, 2H, OCH_2CH_3), 4.10 (q, 4H, OCH_2CH_3), 4.17 (d, 2H, OCH_2Ar), 4.23 (d, 2H, OCH_2Ar), 4.34 (d, 2H, OCH_2Ar), 4.63 (d, 2H, OCH_2Ar), 4.95 (d, 2H, OCH_2Ar), 5.05 (d, 2H, OCH_2Ar), 7.19 (d, 2H, ArH), 7.23 (d, 2H, ArH), 7.28 (d, 2H, ArH); IR (KBr, ν_{max} , cm^{-1}): 1750, 1190.

Preparation of compound 3: Compound **2a** (0.54 g, 0.64 mmol) added in 20 mL mixed solution of methanol/toluene (1:1, v/v), then added *tris*-(2-amino-ethylamine) (0.1 g, 0.64 mmol). The solution was refluxed for 2 days under the nitrogen atmosphere and then cooled to room temperature. Removed the solution under reduced pressure, the residue was recrystallized with ethanol, get pure white crystals (**3**) (0.21g, 38%). m.p. > 300 °C. ^1H NMR (500 MHz, CDCl_3): δ (ppm) 1.14 (s, 27H, *t*-Bu), 2.72 (t, 6H, NCH_2), 3.40 (t, 6H, NHCH_2), 4.23 (s, 6H, OCH_2CO), 4.36 (d, 6H, ArCH_2O), 4.60 (d, 6H, ArCH_2O), 6.95 (s, 6H, ArH), 8.02 (s, 3H, NH). IR (KBr, ν_{max} , cm^{-1}): 3412, 3376, 2960, 2864, 1678, 1450, 882.

Preparation of compound 4: Compound **3** was acidified with hydrochloric acid (pH = 3) and recrystallized from ethanol to give compound **4**, m.p. 215–217 °C. ^1H NMR (500 MHz, CDCl_3): δ (ppm) 1.140 (s, 27H), 2.724 (t, 6H), 3.385 (t, 6H), 4.214 (s, 6H), 4.405 (d, 6H, $J = 12$), 4.886 (d, 6H, $J = 12$), 6.951 (s, 6H). IR (KBr, ν_{max} , cm^{-1}): 3432, 3283, 3070, 2959, 2907, 2868, 1678, 1564, 1454, 1258, 1062.

Crystallography: Crystals of compound **4** suitable for X-ray investigation was obtained from ethanol by slow evaporation solvents. Determination of the unit cell and data collection (Table-1) was performed on a Bruker Apex-II CCD diffractometer using graphite monochromated MoK_α radiation ($\lambda = 0.71073\text{\AA}$) at 293 (2)K with crystal size $0.20 \times 0.15 \times 0.25\text{ mm}^3$. A total of 55377 ($R_{\text{int}} = 0.0485$) independent reflections were collected by ω -2 θ scan technique in the range $1.44 \leq \theta \leq 27.52^\circ$ from which 6565 [$I > 2\sigma(I)$] reflection were corrected for Lorentz and polarization factors. The structure was solved by direct method using SHELXS-97 and refined using a full-matrix least-squares procedure on F^2 in SHELXS-97. All non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms were added theoretically and refined with riding model position parameters and fixed with isotropic thermal parameters. (CCDC: 759964).

RESULTS AND DISCUSSION

The synthetic route of compound **4** is presented in **Scheme-I**. The key process of synthesis of compound **4** is making sure that get a fixed cone conformation, because the specific conformation is not only depends on temperature and solvent, but is also controls by the introduced functional moiety. Compound **4** was synthesized using compound **2a** and the *tris*-(2-amino-ethylamine) as the starting materials with a high yield.

The molecular structure of compound **4** is illustrated in Fig. 1. Its crystallization in the monoclinic system (space group C 2/c 1), $a = 19.6831(16)\text{\AA}$, $b = 16.8180(16)\text{\AA}$, $c = 29.267(3)\text{\AA}$, $\alpha = 90^\circ$, $\beta = 105.222(4)^\circ$, $\gamma = 90^\circ$. It is clearly suggested

TABLE-1
DATA COLLECTION AND PROCESSING
PARAMETERS FOR COMPOUND 4

Formula	$\text{C}_{48}\text{H}_{66}\text{N}_4\text{O}_9$	Volume ($\text{\AA}^3$)	9348.2(14) $\text{\AA}^3$
Formula weight	843.5	Z	8
Crystal system	Monoclinic	D(calc), Mg cm^{-3}	1.198
Space group	C 2/c 1	μ (mm^{-1})	0.86
Temperature	293 K	2 θ max ($^\circ$)	50
No. of params	550	N ind	10626
R	0.0541	GOF	1.033
Rw	0.1335	F(000)	3632

that compound **4** adopts a cone conformation, three calix benzene rings tilt towards the cavity and maintain a normal cone conformation; the dihedral angles of the three calixarene benzene Ring 1 (C5–C6–C7–C8–C9–C10) and Ring 2 (C21–C22–C23–C24–C25–C26), Ring 2 and Ring 3 (C37–C38–C39–C40–C41–C42), Ring 3 and Ring 1 have the values $80.56(6)^\circ$, $33.56(5)^\circ$ and $55.48(7)^\circ$, respectively. The carbonyl oxygens (O1, O4, O7) are orientated outside, against the concave cavity. The torsion angles N1–C1–C2–N2, N1–C17–C18–N3, N1–C33–C34–N4 are $-67.6(3)^\circ$, $-70.8(2)^\circ$, and $-59.6(3)^\circ$. The ether linkage C15–O9–C16, C31–O3–C32 are $111.84(14)^\circ$, $115.76(15)^\circ$. Orientated downward, and the C47–O6–C48 is orientated upward. Three aliphatic chains (N1–C1–C2–N2–C3–C4–O8, N1–C17–C18–N3–C19–C20–O2, N1–C33–C34–N4–C35–C36–O5) are oriented randomly between the top nitrogen atom and calix benzene, they do not adhere to the C_{3v} -symmetrical conformation. For example, the distances between the carbonyl carbon atoms (C3–C19–C35–C3) are $5.278\text{\AA}$, $5.248\text{\AA}$, and $6.894\text{\AA}$, respectively.

Scheme-I: Synthetic scheme for the preparation of capped hexahomotri-oxacalix[3]arene derivative

Conclusion

In summary, the structure of compound **4** has been first determined by X-ray analysis, which showed a fixed cone conformation and capped by *tris*-(2-amino-ethylamine) at the lower rim. This compound has such advantages as easily synthesis, highly yield and controllable conformation. The special novel configuration give this molecule better performance, the properties of the compound need further experimental and theoretical study.

Fig. 1. X-ray structure of capped compound **4**, hydrogen atoms are omitted for clarity. (a) The side view of X-ray structure of compound **4**. (b) The top view of X-ray structure of compound **4**

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