

Synthesis, Structural and Antioxidant Properties of C-p-methoxyphenylcalix[4]resorcinarene

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Abstract— The structure of Calix[4]resorcinarene is less reported compare to other calixarene derivatives because of its conformational flexibility and stability when exposed to air. The presence of solvent molecules is important for its stability in the solid state. On the other hand, the presence of several phenol groups make it a good candidate for antioxidant study. Some of them have also shown good antibacterial activity. p-methoxyphenyl calix[4]resorcinarene was synthesized and characterized by infrared and (¹H, ¹³C) NMR spectroscopic techniques. After several attempts suitable crystals were obtained and with the help of a special oil an X-ray investigation was carried out at low temperature. The calix crystallized in triclinic system with space group $P\bar{1}$, $a=10.6958(5)$, $b=13.5781(7)$, $c=16.3334(8)\text{\AA}$, $\alpha=68.284(4)$, $\beta=74.275(5)$, $\gamma=82.589(5)^\circ$, $Z=2$ and $V=2121.15(8)\text{\AA}^3$. The compound exhibits chair conformation with two resorcinol groups in anti-parallel position. The conformation is supported by eight DMSO and two DMF solvated molecules. It has a moderate antioxidant property.

Keywords— Calix[4]resorcinarene, p-methoxyphenyl and X-ray single crystal.

I. INTRODUCTION

Calix[n]arenes represent macrocyclic compounds are widely used in supramolecular chemistry for the construction of various receptors for the complexation of charged or neutral molecules [1]. Their unique three-dimensional structures with almost unlimited derivatization abilities and a tuneable shape of the molecules make calixarenes ideal candidates for building blocks and/or molecular scaffolds in the design of new and more sophisticated molecules[2,3]. Calix[4]resorcinarene possesses two hydroxy groups benzene rings at extra annular position that form the macrocycle nature have been synthesized generally by the acid-catalyzed cyclocondensation of resorcinol with various aliphatic or aromatic aldehydes [4]. The rapid development on these compounds was driven by their application as macrocyclic receptor, dendrimers in biological systems [5], nano-capsule [6], nano-particles [7] and optical chemosensors [8]. although the present calix has been reported the Cambridge Data base search gave no report on the molecular structure of the calix. It is known that most calix[4]resorcinarene derivatives are not stable in the air and transformed into powder in a very short time.

Special effort is needed in order to collect the reflections within the experimental time. After several attempts a reasonable good data was obtained and the crystal structure of p methoxyphenyl calix[4]resorcinarene is reported to support the normal chemical characterisation data.

II. METHODS

A. Chemicals and instrumentation

Most of organic compounds utilized in this research were commercial products of high purity purchased from Acros and Sigma and used as such without any further purification.

The microelemental analysis, CHNS-O was carried out by using Carlo Erba 1108. The infrared spectra (IR) of the products were recorded by using the Perkin Elmer Spectrum GX spectrophotometer in the range $400-4000\text{cm}^{-1}$. Nuclear Magnetic Resonance (NMR) for ¹H and ¹³C experiment were performed with Joel ECP 600 MHz in d_6 -DMSO as solvent. X-Ray data were collected at the low temperature with Oxford instrument at Universiti Pitra malaysia spectrometer using Mo K α radiation ($\lambda=0.71073\text{\AA}$).

B. Preparation of C-p-methoxyphenylcalix[4]resorcinarene

7 ml of concentrated hydrochloric acid was added into a round-bottom flask containing a solution of 4-Anisaldehyde (0.01mol, 1.36gm) in absolute ethanol (60ml). The solution mixture was stirred for 30 minutes and a solution of resorcinol (0.01mol, 1.101gm) in absolute ethanol (20 ml) was added to the mixture. The mixture was refluxed for 10 hours at 80°C. The purple precipitate was collected by filtration, washed with distilled water and acetone several times. The colorless crystals were obtained by recrystallization of the precipitate in DMSO suitable for X-ray analysis in good yield (74.23%, 1.23gm).

FTIR (KBr, cm^{-1}): 3399.92 (OH), 2998.01 (CH aromatic), 2835.99 (OCH_3), 1608.71 and 1510.51 (C=C Aromatic); δ_{H} (600 MHz; DMSO) 3.69 (3H, s, OCH_3), 5.57 (CH methine bridge), 6.12 (2H, s, CH_{Ar}), 6.53 (2H, d, $J = 8$, CH_{Ar}), 6.60 (2H, d, $J = 8$, CH_{Ar}), 8.51 (2H, s, OH); δ_{C} (600 MHz; DMSO) 55.1 (OCH_3), 102.3 (CH-methine bridge), 112.9 (2 x CH_{Ar}), 121.2 (2 x CH_{Ar}), 129.8 (2 x CH_{Ar}), 138.2 (2 x C_{Ar}), 152.9 (2 x C_{Ar}), 156.9 (2 x C_{Ar}); Anal Calculated for the compound ($\text{C}_{56}\text{H}_{48}\text{O}_{12}$): C=73.67 and H= 5.30, Found: C, 73.08 and H,4.89.

C. Antioxidant studies

A stock solution of DPPH was prepared by dissolving 0.4gm of DPPH in 1L methanol and the solution was kept in the dark at 4°C. A stock solution of the C-p-methoxyphenylcalix[4]resorcinarene was prepared at 10 mg/5ml in DMSO. 100 μ l from the stock solution of the compound was added to the 1ml of DPPH (Abs:1.012nm). The mixture was shaken well and kept in dark at room temperature for 2 hour. The absorbance of the mixture was measured at 517 nm by using spectrophotometer (Abs: 0.33nm). The present inhibition of radical scavenging ability was calculated as:

$$\% \text{ inhibition} = [(A_{\text{DPPH}} - A_{\text{Sample}}) / A_{\text{DPPH}}] * 100 = [(1.012 - 0.33) / 1.012] * 100 = 67.39\%$$

III. RESULTS AND DISCUSSION

The FTIR spectrum of calix showed characteristics absorption at 3399.92 cm^{-1} corresponds to O-H stretching vibration. A much weaker band at 2998.01 cm^{-1} is for the C-H stretching frequencies. The peak at 2835.99 cm^{-1} is typical of a methoxy group on an aromatic ring and the C=C aromatic ring appeared at 1510.51 cm^{-1} .

The ^1H NMR assignment for the calix was straightforward. The OH group of resorcinol ring was assigned at 8.51 ppm. The appearance of singlet multiplicity signal indicated that this hydroxyl has a same chemical environment. A two doublet peaks at 6.54 and 6.60 ppm ($J = 8$) are well defined peak assignable for equal amount of the aromatic linker protons. Two C-H aromatic resorcinol displayed a singlet at 6.11 ppm, a singlet at 5.57 ppm for

methine bridge and another singlet at 3.69 was assigned for methoxy proton. (Fig. 1)

X-Ray Crystallography study

X-ray investigation showed that the compound crystallized in triclinic system with space group of $\text{P}\bar{1}$. The unit cell dimension are $a = 10.6958(5)$, $b = 13.5781(7)$, $c = 16.3334(8)$ Å, $\alpha = 68.284(5)$, $\beta = 74.375(4)$, $\gamma = 82.579(4)^\circ$, $Z = 2$ and $V = 2121.15(8)$ Å³. The crystal system and refinement parameters are given in Table 1.

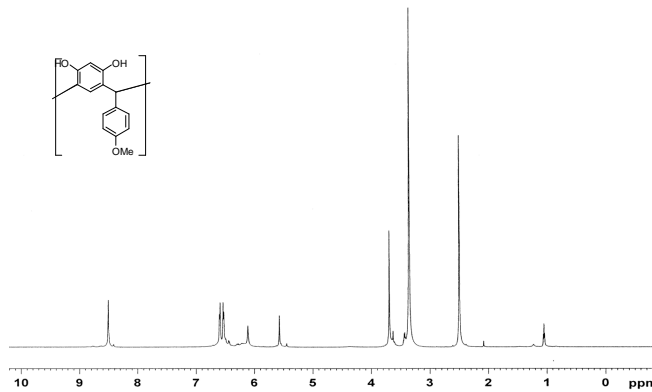


Fig. 1. ^1H NMR spectrum of C-p-methoxyphenyl calix[4]resorcinarene in d_6 -DMSO,

TABLE I
CRYSTAL DATA AND STRUCTURE REFINEMENT FOR C-p-METHOXYPHENYLCALIX[4]RESORCINARENE

Empirical formula	$\text{C}_{78}\text{H}_{110}\text{N}_2\text{O}_{22}\text{S}_8$
Formula weight	1684.24
Temperature	293(2) K
Wavelength	1.54178 Å
Crystal system	Triclinic
Space group	$\text{P}\bar{1}$
Unit cell dimensions	$a = 10.6958(5)$ Å $b = 13.5781(7)$ Å $16.3334(8)$ Å, $\alpha = 68.285(5)^\circ$, $\beta = 74.375(4)$ and $\gamma = 82.579(4)^\circ$
Volume	2121
F(000)	836
Crystal size	0.3 x 0.36 x 0.42 mm ³
Theta range for data collection	3.00 to 71.58°.
Index ranges	-
	$13 \leq h \leq 13$, $-16 \leq k \leq 16$, $-19 \leq l \leq 19$
Reflections collected	28842
Independent reflections	8144 [R(int) = 0.0240]
Completeness to theta	= 71.58° 98.4 %
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	8144 / 0 / 503
Goodness-of-fit on F^2	3.850
Final R indices [$I > 2\sigma(I)$]	$R_1 = 0.1356$, $wR_2 = 0.4627$
R indices (all data)	$R_1 = 0.1403$, $wR_2 = 0.4767$
Extinction coefficient	0.0000(7)
Largest diff. peak and hole	3.974 and -2.802 e.Å ⁻³

The asymmetric unit consists of one C-p-methoxyphenylcalix[4]resorcinarene at special position with centre of inversion, eight DMSO and two DMF molecules of crystallization (Fig.2). The N1 and O11 atoms are

disordered and were not treated. The calix[4] moiety adopts a chair conformation. The two pairs of opposite resorcinol rings are coplanar and a pair of it is antiparallel.

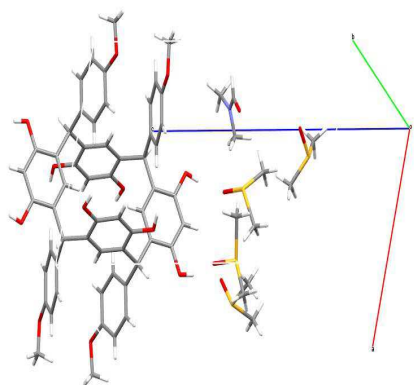


Figure 2. The asymmetric unit of *C-p*-methoxyphenyl calix[4]resorcinarene

The calix molecule adopts a chair conformation with two opposite resorcinol groups are almost coplanar to each other but a pair of them is in the anti-parallel position

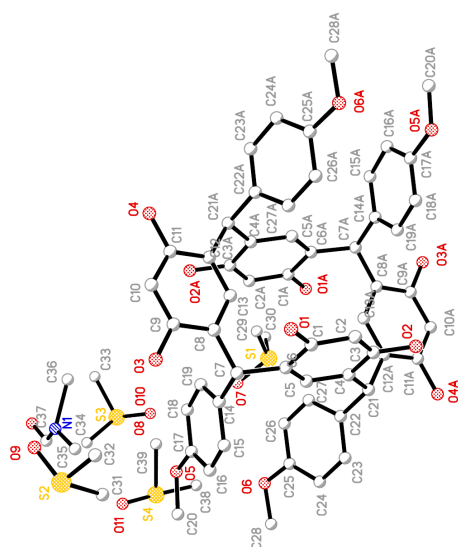


Figure 3. The molecular structure of *C-p*-methoxyphenyl calix[4]resorcinarene drawn at 50% probability ellipsoid. The hydrogen atoms were omitted for clarity.

The opposite resorcinol rings are perfectly planar as indicated by the clean NMR spectrum. The dihedral angle between the alternate (C1-C6) and (C8-C13) resorcinol rings is $77.7(2)^\circ$ whereas with the linkage benzene ring (C14-C19) is $85.1(2)^\circ$. The two methoxyphenyl linkage groups that attached to the coplanar resorcinol rings are at the opposite directions but the two groups attached to the anti-parallel resorcinol rings are in the same directions. Similar conformation with approximately C_{2h} symmetry due to the presence of crystallographic inversion center was also observed for tetraarylboronic acid resorcinarene[9]. The bond lengths and angles are in normal ranges and comparable with other resorcinarene[10]. The structure is

stabilized by extensive O-H...O, O-H...S, and C-H...O intermolecular hydrogen bonds.

Antioxidant property

Antiradical properties of *C-p*-methoxyphenyl calix[4]resorcinarene was monitored by the decrease in absorbance of 1,1-diphenyl-2-picrylhydrazyl radical (DPPH). Calix[4]resorcinarene which can donate hydrogen atoms to the non-radical form of DPPH is highly efficient antioxidant agents [11]. The free radical scavenging activity of *C-p*-methoxyphenyl calix[4]resorcinarene of 67.30% is a moderate antioxidant and comparable to 5,11,17,23,-tetra-*tert*-butyl-25,27-bis(5-(henyl)-1,3,4-oxadiazole-2-thiacarbonylmethoxy)-26,28-dihydroxycalix[4]arene[12].

IV. CONCLUSION

The *C-p*-methoxyphenyl calix[4]resorcinarene has been synthesized and fully characterised by FTIR and NMR techniques. The X-ray crystallographic data were obtained to support the structural study despite the instability of the crystal upon exposure to the air. It showed a moderate antioxidant.

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