The Molecular Complexes of Calix[4]resorcinolarene with Diglycidylmethyl Phosphonate

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Abstract. The formation of strong molecular complexes of calix[4]recorcinolarene with the polyfunctional phosphoorganic compound diglycidylmethyl phosphonate was observed in organic media. Complexes of different compositions were obtained with the ratio of the initial reagents of 1:1 and 1:4. Three complexes were isolated and characterized by elemental analysis; their ^{1}H and ^{13}C NMR spectroscopic parameters are also discussed.

Key words: calix[4]resorcinolarene, diglycidylmethyl phosphonate, complexation, NMR.

1. Introduction

The different noncovalent interactions play leading roles as driving forces in molecular assembling processes; one such interaction being that of protons with heteroatoms. They are weak and noneffective if separated, but if they are organized into multipoint interactions they lead to the formation of strong supramolecular complexes. The role of such interactions in molecular recognition is well known, they are widely realized as biological [1] and synthetic molecular receptors [2].

In the host-guest complexes with metal ions, e.g., complexes of crown-ethers with different metal cations [3] the binding is provided by the polydentate interactions of cations with electron donors – oxygen, nitrogen or sulfur atoms [4–8]. Organic guest-molecules generally form weaker complexes than inorganic ions. Cyclodextrin and calixarene host-molecules, in addition to the upper rim hydrogen binding, can give a lipophilic cavity to the host-guest interactions.

Aoyama and co-workers demonstrated that water-soluble calix[4]resorcinolarene binds a variety of guest molecules – polyols, aminoacids and different aromatic derivatives in water due to the incorporation of the apolar part of the guest into

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the calixarene cavity. The bound guests exhibited significant ^{1}H NMR up-field shifts due to the ring-current effects of the host; the complexation-induced shifts at saturation binding usually fall in the range of 1–3 ppm. The chiral host-guest interaction makes it possible to distinguish the enantiomer protons of aromatic guests [9]. On the other hand it was shown [7, 8, 10, 11] that in the case of neutral molecules binding in an organic apolar solvent the upper rim of the cavity plays an important role, while the cavity is not so important, because of its competition with the apolar media. Binding constants increase due to the increase in the number of hydroxy groups of the polyols, which provide multipoint binding in these complexes. The values of the binding constants of the reported complexes are small, therefore, they were not isolated. In several cases there were no changes in the ^{1}H NMR spectra of complexes in comparison with the spectra of the initial reagents. The binding of these guests was confirmed by changes of CD spectra [8].

The ability of calixarenes to form molecular compounds with small molecules of organic solvents in the solid state is well-known. It largely depends on the experimental conditions [12]. The complexes with guest molecules inside and outside the macrocycle cavity were reported in [13, 14].

In this paper we report unexpected results of the formation of strong complexes between calix[4]resorcinolarene and a phosphorus compound in organic media. The complexes were obtained during the attempt to alkylate calix[4]resorcinolarene by methyldiglycidyl phosphonate (**I**) in CH_2Cl_2. **I** was produced as described in [15].
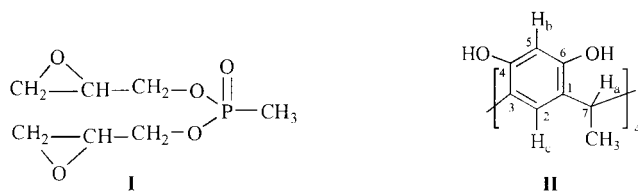
2. Experimental

The ^{1}H, ^{13}C, ^{31}P and 2D NOESY NMR spectra of the compounds were recorded using a multifunctional pulsed FT NMR spectrometer "UNITY-300" (Varian Associates Inc. (USA)) operating at 300 MHz. The ^{1}H and ^{13}C NMR spectral shifts were measured in ppm relative to $SiMe_4$. The ^{31}P NMR spectral shifts were measured in ppm relative to H_3PO_4.

The reactions of calix[4]resorcinolarene **II** with **I** were carried out in a boiling mixture of the heterogeneous system for 10 hours, the process was monitored by TLC. The eluent composition benzene-dioxane-acetonitrile in the ratio 1 : 1 : 8 was used.

Compound III: To a suspension of calix[4]resorcinolarene **II** (3 g, 5.5 mmol) in 50 mL of CH_2Cl_2 two drops of $TiCl_4$ and 1.14 g (5.5 mmol) of **I** were added. The reaction mixture was stirred for 10 h at room temperature and then refluxed
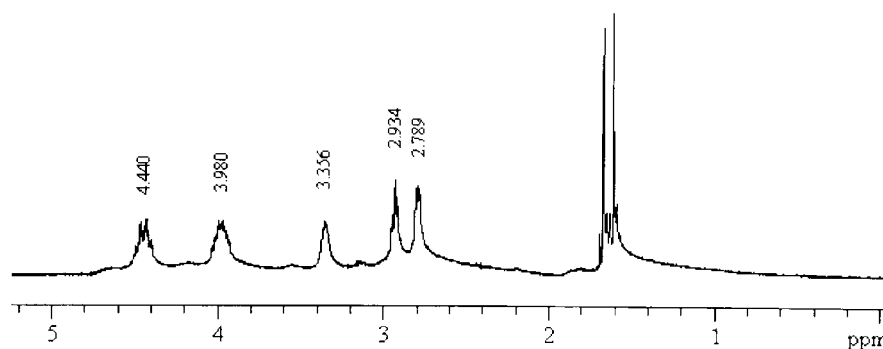
Figure 1. ^{1}H NMR spectrum of diglycidylmethyl phosphonate (**I**) in $(CD_3)_2CO$.

for 10 h. The solid was filtered, washed and dried. The product was dissolved in acetone, filtered and dried. **III** is a solid powder with m.p. 244–247 °C, δ_P 32.148 ppm. Yield 3.47 g (83.7%). Found,%: C 62.69, H 6.45, P 3.86. $C_{39}H_{45}O_{13}P$. Calculated,%: C 62.23, H 5.98, P 4.12.

Compound IV: To a suspension of calix[4]resorcinolarene **II** (3 g, 5.5 mmol) in 50 mL of CH_2Cl_2 two drops of $TiCl_4$ and 4.59 g (22 mmol) of **I** were added. The reaction mixture was stirred for 10 h at room temperature and then refluxed for 10 h. The solid was filtered, washed and dried. The product was dissolved in acetone, filtered and dried. **IV** is a solid powder with m.p. 197–200 °C, δ_P 31.47, 32.74 ppm. Yield 3.3 g (62.3%). Found,%: C 57.8, H 5.64, P 5.96. $C_{46}H_{58}O_{18}P_2$. Calculated,%: C 57.5, H 6.04, P 6.46.

Compound V: After the solvent was removed from the initial solution of **IV** under vacuum a brown oil was isolated. It was dissolved in 25 mL of CH_2Cl_2 and washed with 30 mL of water at room temperature. The solvent was removed and the solid was dried for 10 h at 70 °C under vacuum. **V** is semi-crystalline with δ_P 31.37 ppm. Yield 1.80 g (23.8%). Found,%: C 51.73, H 6.39 , P 9.05. $C_{60}H_{84}O_{28}P_4$. Calculated,%: C 52.3, H 6.1, P 9.01.

3. Results

The reaction of calix[4]resorcinolarene **II** with **I** was carried out with the ratio of reagents of 1 : 1 and 1 : 4 in CH_2Cl_2 under reflux conditions or for a long time standing with stirring. It is proposed that the epoxy ring of **I** is destroyed under the Lewis acid ($TiCl_4$) catalysis giving a three dimensional partially fixed structure. The disappearance of the phosphonate spot on TLC was a criterion of the end of the reaction. In both cases the solid powder products were isolated. In contrast to the initial reagents solid complexes **III** and **IV** have well defined melting points (Table I).

^{1}H NMR spectra of products **III**, **IV** and **V** did not show the epoxy ring destruction or the formation of other new bonds. Identical product **III** was isolated
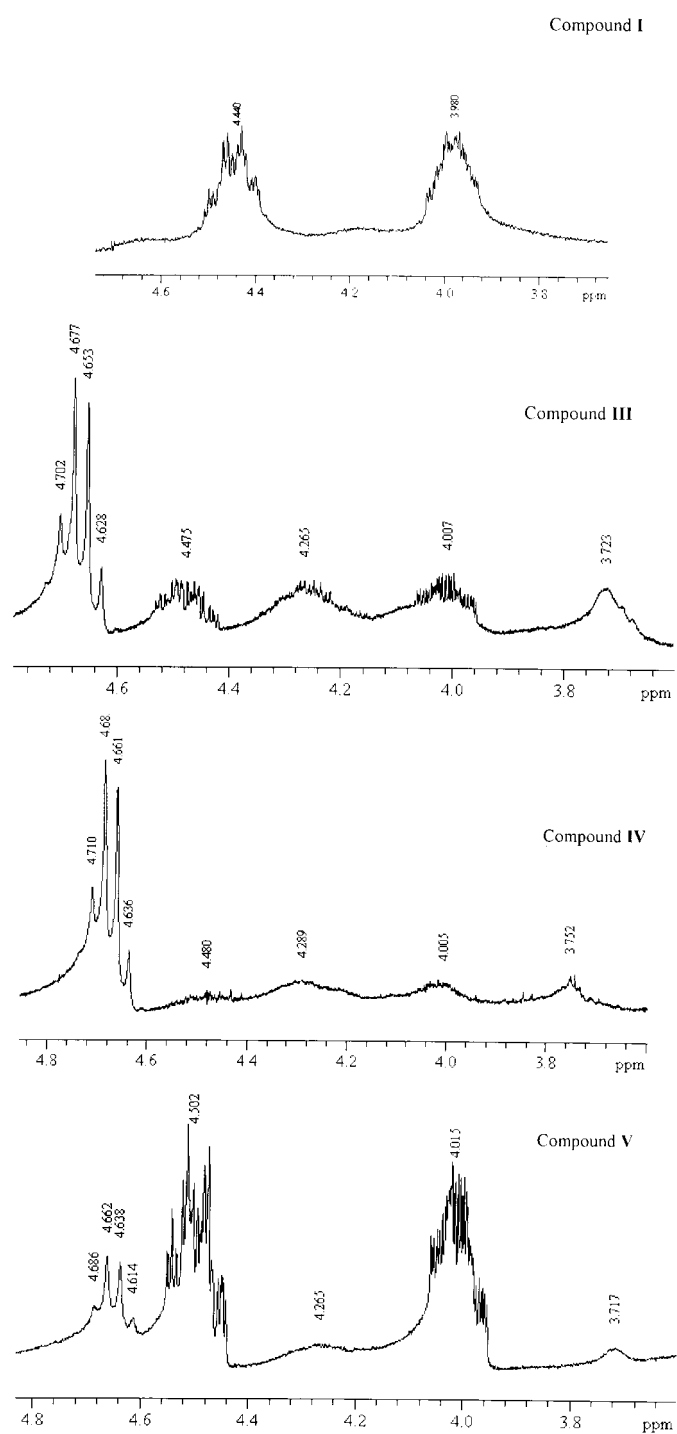
Figure 2. Partial ^{1}H NMR spectra of H_a, CH_2—O—P in compounds **I**, **III–V** in $(CD_3)_2CO$.

Table I. Melting points, formula, ^{31}P, and ^{1}H NMR data for compounds **I–V**

Compound		**I**	**II**	**III**	**IV**	**V**
Composition		Initial reagents		1 : 1	1 : 2 from 1 : 4	1 : 4 from 1 : 4
Melting point, °C		Liquid	Decomposes at 360	244–247	197–200	Oil
Formula		$C_7H_{13}O_5P$	$C_{32}H_{32}O_8$	$C_{39}H_{45}O_{13}P$	$C_{46}H_{58}O_{18}P_2$	$C_{60}H_{84}O_{28}P_4$
$\delta\,^{31}$P NMR, ppm		31.416	–	31.148	32.74, 31.47	31.37
δ^1H	CH$_3$—P	d, 1.66 (17.67)	–	d, 1.67; 0.01 (17.7)	d, 1.71; 0.05 (17.7)	d, 1.70; 0.04 (17)
NMR,	CH$_2$ (epoxy)	d/m, 2.715 (33)	–	d/m, 2.85; 0.135 (39)	d/m, 2.86; 0.145 (36)	d/m 2.85; 0.045 (42)
ppm;						
$\Delta\delta$, ppm	CH (epoxy)	m, 3.36	–	m, 3.354; 0.006	m, 3.38; 0.02	m, 3.35; −0.01
(J, Hz)	CH$_2$—O—P	d/m, 4.045 (129)	–	d/d/m, 3.99 (161.4), 4.187 (171.9)	d/m, 4.05; 0.015 (126)	d/m, 4.35; 0.315 (141)
	H$_a$	–	q, 4.47 (7.5)	q, 4.63; 0.13 (7.2)	q, 4.6; 0.13 (6)	q, 4.61; 0.14 (7.14)
	H$_b$	–	7.65	7.8; 0.15	7.9; 0.25	7.76; 0.11
	H$_c$	–	6.21	6.4; 0.19	6.38; 0.17	6.4; 19
	OH	–	8.56	8.7; 0.14	8.52; −0.04	8.94; 0.38
	CH$_3$	–	d, 1.765 (7.5)	d, 1.92; 0.155 (7.2)	d, 1.91; 0.145 (7.2)	d, 1.85; 0.085 (7.2)

after noncatalytic interactions of **II** and **I** with the ratio of reagents of 1 : 1 under the same conditions.

All compounds were characterized by elemental analysis, ^{1}H, ^{31}P and ^{13}C NMR spectroscopy (Table I). There is a good correlation between the elemental analysis and NMR spectroscopic data for the composition of compounds **III**, **IV** and **V**. 2D NOESY experiments for compound **III** did not show any interactions of the calix-arene and phosphorus-containing component protons. To destroy the complex of **II** with phosphonate **III** was treated with triethylamine in acetonitrile. In consequence the complex (**III** · 2 Et$_3$N) was isolated. Thus, the formation of strong molecular complexes of calix[4]recorcinolarene with the polyfunctional organic compound **I** in the organic media was suggested.

4. Discussion

The reaction of **II** and **I** was carried out with the ratio of reagents of 1 : 1 both in the presence and absence of Lewis acid. The same product **III** was obtained in the both cases. The disappearance of the phosphonate spot of **I** on TLC was a criterion of the end of the reaction. This happened in all cases indicating there was no free diglicidyl methyl phosphonate in the reaction mixture. Products **III–V** had well-defined melting points in contrast to the initial reagent **II**, which decomposes at 360 °C. Elemental analysis data are in a good agreement with the proposed composition of compounds **III–V**. The ^{31}P NMR signal of the phosphonate group displayed a negligible down-field shift for product **V** ($\Delta\delta \sim 0.09$ ppm) and a small up-field shifts for products **III** and **IV** (-0.268 ppm and -1.28 ppm respectively). That might be assigned to the change of the phosphonate group environment from that in the initial compound **I**. ^{1}H NMR spectra of **III**-**V** demonstrated down-field shifts of all the proton signals. The small values of down-field shifts of the aromatic ring protons were ascribed to the conformational changes of the calix[4]resorcinolarene skeleton which accompanied the formation of the products **III–V**. ^{13}C NMR spectra of **III–V** exhibited several changes of carbons signals, but these changes are different for each product, thus compounds **III–V** seem to have different structures.

The ^{1}H and ^{13}C NMR spectra of compound **III** (composition 1 : 1) demonstrated considerable changes (Tables I and II). A remarkable perturbation of protons and carbons of the CH_2—O—P groups in **III** were discovered. In the ^{1}H NMR spectrum of **I** these groups appeared as a doublet of multiplets, while in the case of **III** they appeared as a pair of doublets with multiple character. In the ^{13}C NMR spectrum CH_2—O—P carbons appeared as a pair of doublets at 64.02 ppm and 70.75 ppm. This fact indicates the loss of two CH_2—O—P groups equivalency which can be a consequence of the different environment of the two glycidol chains in complex **III**. The formation of the stable complex (**III** $\cdot$ 2 Et_3N) by treatment of **III** with triethylamine confirms the stability of **III**.

The reaction of **II** and **I** with the ratio of initial reagents of 1 : 4 led to the formation of two different products **IV** and **V** with 1 : 2 and 1 : 4 composition. They were produced in the ratio 3 : 1, while with the ratio of initial reagents of 1 : 1 only one product **III** was obtained. For both **IV** and **V** the CH_2-O-P groups of the phosphonate component retained their equivalency in the complexes.

Tables I and II present the greatest changes displayed in the ^{13}C NMR spectra of compounds **IV** and **V**. They are different from those in the 1 : 1 complex (**III**) indicating they have a different arrangement of the **II** and **I** moieties than in compound **III**. The most significant complexation-induced shifts for both **IV** and **V** were seen for the carbon atoms of CH_3—P and CH_2—O—P (for **I**) and for C-2 atoms of the calixarene moiety ($\Delta\delta \sim 1.80$, 1.77 ppm, respectively). Additionally for compound **V** a down-field shift for the C-7 atom ($\Delta\delta \sim 0.59$ ppm) was observed, while for product **IV** such a shift was not found.

Table II. ^{13}C NMR data for compounds **I–V**

Compound		**I**	**II**	**III**	**IV**	**V**
$\delta\,^{13}$C	CH$_3$—P	d, 11.44 (143)	–	d, 11.57; 0.13 (144.3)	d, 11.06; −0.38 (144)	d, 11.13; −0.31 (142.7)
NMR,	CH$_2$ (epoxy)	44.77	–	45.08; 0.91	44.79; 0.02	44.75; −0.02
$\Delta\delta$, ppm	CH (epoxy)	51.10	–	51.45; 0.35	51.11; 0.01	51.13; 0.03
(J, Hz)	CH$_2$—O—P	67.18	–	d, 64.02, d, 70.75	67.69; 0.51	67.55; 0.37
	C-1, 3	–	126.50	124.58; −0.92	126.48; 0.02	126.36; 0.14
	C-2	–	102.20	103.55; 1.35	104.00; 1.80	103.97; 1.77
	C-5	–	125.50	126.74; 1.24	125.45; 0.05	125.46; 0.04
	C-4, 6	–	152.70	153.36; 0.66	152.56; −0.01	152.67; −0.03
	C-7	–	29.10	30.97; 1.87	29.06; −0.04	29.69; 0.059
	CH$_3$	–	20.70	22.94; 2.24	20.62; −0.08	20.56; −0.14

It is noteworthy in the ^{1}H NMR spectra of **IV** and **V** that nonequivalency of the CH$_2$—O—P groups protons did not appear. The same changes as those for **III** were observed for the ^{1}H NMR signals of H$_a$, H$_b$, H$_c$ and CH$_3$ (but only for **IV**). The protons of the calixarene OH groups displayed different complexation-induced shifts for all products **III–V**. The phosphorus-containing component for all products showed inconsiderable changes of the CH$_3$-P and CH (epoxy) protons. The CH$_2$ (epoxy) and CH$_2$—O—P protons in all cases allow us to propose participation of these groups in the formation of complexes **III–V**.

The results obtained motivated us to simulate electron density and charge distribution in the diglycidyl ether of methylphosphonic acid to propose the most important potential electron donor and electron acceptor centers.

Table III presents the results of semi-empirical calculations using the MOPAC 7.0 program. As the simulation results show, carbon atoms C(1) and C(2) of the CH$_2$ groups in compound **I** have less electron density than the epoxy carbon atoms C(3), C(21), C(4) and C(22). The ether oxygens (O(11), O(12)) have a higher electron density than the epoxy oxygen atoms O(5) and O(23). That provides the possibility of electron donor interactions with the CH$_3$—P=O, CH$_2$—O—P groups participation because of the more positively charged carbon atoms and proton donor interaction with ether oxygens participation as they possess more negative charge than the epoxy oxygen atoms.

Therefore, well-defined melting points, shifts values of ^{1}H and ^{13}C NMR spectral signals and the clearly determined stoichiometry of the isolated complexes allow us to suggest the presence of a solvation interaction mode between **II** and **I**.

Table III. Electron density and charge distribution in the diglycidylmethylphosphonate molecule, results of PM3 MOPAC calculations

No. of atom	Element	Charge	Electron density
1	C	0.1358	3.8642
2	C	0.1468	3.8532
3	C	−0.0340	4.0340
4	C	−0.0071	4.0071
5	O	−0.2635	6.2635
6	H	0.1072	0.8928
7	H	0.0658	0.9342
8	H	0.0700	0.9300
9	P	2.0741	2.9259
10	C	−0.5108	4.5108
11	O	−0.6419	6.6419
12	O	−0.6412	6.6412
13	O	−0.8538	6.8538
14	H	0.0844	0.9156
15	H	0.0834	0.9166
16	H	0.0875	0.9125
17	H	0.0455	0.9545
18	H	0.0410	0.9590
19	H	0.0387	0.9613
20	H	0.0306	0.9694
21	C	−0.0258	4.0258
22	C	−0.0135	4.0135
23	O	−0.2650	6.2650
24	H	0.1033	0.8967
25	H	0.0656	0.9344
26	H	0.0770	0.9230
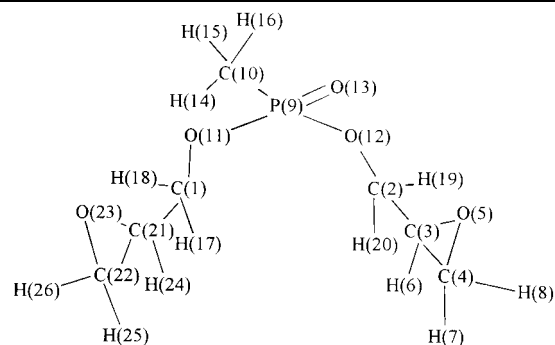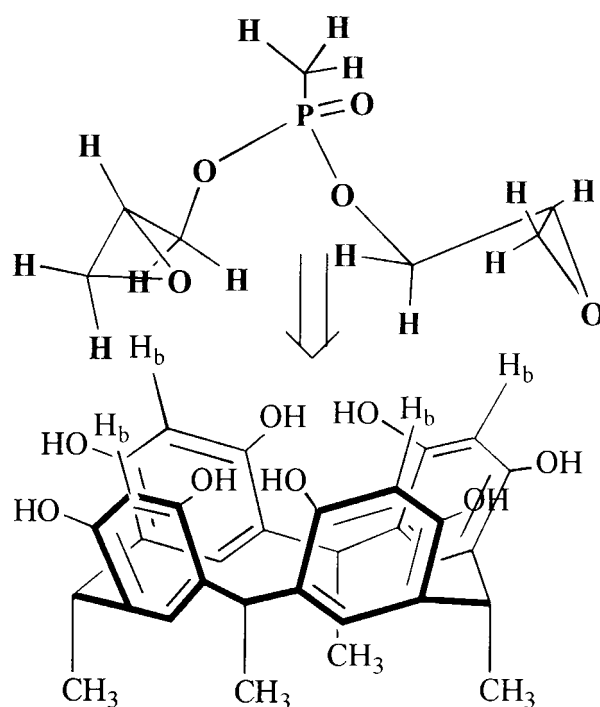
Scheme 1. Formation of the 1 : 1 complex between calix[4]resorcinolarene and diglycidyl methylphosphonate (**III**).

In this molecular complex **I** plays the role of solvent and calix[4]resorcinolarene the role of solvated substance. Unfortunately the data available are not enough to propose an unambiguous structure for this complex. However, it is obvious that **II** forms strong complexes with the polar polyfunctional compound **I** in organic media due to the multipoint weak interactions.

Acknowledgments

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