CHAPTER 7

Interaction between Water-Soluble Tetrasulfonatatomethyl Calix[4]resorcinarene and Cationic Surfactants in Aqueous Solution
Resume

Water-soluble tetrasulfonatomethylcalix[4]resorcinarene was synthesized by microwave irradiation method. It was characterized by elemental analysis, FT-IR, \textsuperscript{1}HNMR and ESI-MS. The water-soluble compound has been studied for its interaction with cationic surfactants differing in nonpolar tail, polar head group and counter ions, by turbidimetry, tensiometry and by dynamic light scattering. The addition of cationic surfactants to the compound solution induces turbidity at concentrations much lower than the critical micelle concentration (cmc) and is followed by precipitation. The clear water-soluble compound solutions turn progressively turbid on gradual addition of cationic surfactant and these stable bluish solutions when examined by dynamic light scattering showed nearly monodispersed nano size particles of diameters ranging from 50-300nm. Normal micelles of surfactant are seen separately at higher surfactant concentrations. Surface tension measurements show that the compound is weakly surface active but in the presence of cationic surfactant, it shows high surface activity and the cmc of the surfactant is greatly reduced in the presence of water-soluble tetrasulfonatomethyl calix[4]resorcinarenes.
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1. Introduction

One of the objectives of supramolecular chemistry is to mimic nature in its development of specific receptor molecules\(^1\). The host-guest interaction of calixarenes in water is a recent significance in supramolecular chemistry\(^2\). Calixarene are macrocyclic compounds in which phenolic units are connected by methylene bridges to form a hydrophobic cavity\(^3, 4\). These cavity-shaped cyclic molecules can form inclusion complexes with a variety of molecules. calix[4]arenes, calix[6]arenes, and calix[8]arenes have been extensively studied. The cavity sizes of calix[4]arene, calix[6]arene, and calix[8]arenes are 3.0, 7.6, and 11.7 Å, respectively. Their low toxicity and the lack of immune response enable new applications of these macrocycles in biomedical and pharmaceutical sciences.

In the case of spontaneous self-assembled calix[8]arenes derivatives, static and dynamic light scattering and electrophoretic mobility is used to study their structure and conformation\(^5\).

The chemistry of calix[n]arenes and of calix[4]resorcinarene\(^6-9\) in particular, is one of the most promising and fast developing branches of organic chemistry. The simplicity of their synthesis and their ability to form complexes of the "guest-host" type with various organic compounds and metal ions have lead them to receive considerable attention as host molecules. Calix[4]resorcinarenes are interesting for their receptor properties and as building blocks for large supramolecular assemblies of a fascinating architecture. The bridging of hydroxyl groups of calix[4]resorcinarenes leads to cavatands which are bowl-shaped species serving as synthetic receptors that are able to assembly into capsules. The chemistry of these bowl-shaped macrocyclic compounds that can function as complex organic and inorganic guests have received significant attention in the field of supramolecular chemistry.

The preparation of calix[4]resorcinarene using gentle procedures that effectively embrace the principles of green chemistry has witnessed much progress. These green routes provide a fast, simple, high-yielding, and non-polluting synthetic methodology of resorcinarene and these efficient processes

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should be potentially applicable to the preparation of other calix[4]resorcinarene systems too. Herein, we report the synthesis of water-soluble tetrasulfonatomethylcalix[4]resorcinarene (1) under microwave irradiation.

The anionic water-soluble compound (1) was examined for interaction with cationic surfactants. There have been several reports in literature on the interaction of water-soluble polyelectrolytes with oppositely charged surfactant both as polymer-surfactant interaction \[^{10}\] and polyelectrolyte – micelle complex\[^{11}\]. However, no study on the interaction of anionic tetrasulfonatomethylcalix[4]resorcinarene (1) with a surfactant has been reported so far.

Surface active agents (or surfactants, amphiphiles, tensides) constitute an interesting class of substances with unique structural features that render them highly useful in industry and geology. The word surfactant points to the surface active nature of these classes of compounds and their tendency to get adsorbed at interfaces. A surfactant molecule has a hydrophilic (water-loving) head and a long hydrophobic (water-hating or oil-loving) tail. For this reason, we often describe surfactants as amphilic molecules—they love everything. This amphipathic nature of the surfactant is responsible for the uniqueness and versatility of these compounds.

Surfactants are said to have a “head” and a “tail”. The head is hydrophilic which means that it is water-loving, and it is generally depicted as a circle. The tail is generally a long hydrocarbon chain and is hydrophobic, which means it is water-hating (therefore oil-loving). The tail may be depicted either as a straight line or a wavy tail.
Soaps and detergents are commonly used terms for surfactants. In fact soaps are the oldest surfactants. However, besides cleaning dirty cloths and surfaces, a surfactant is also an emulsifier, a suspending agent, a foaming agent, a solubilizing agent, a viscosity modifier, etc.

Surfactants play an important role in many human endeavors ranging from mundane (laundrying) to very sophisticated (microelectronics). The science of surfactant behavior in solution is a rapidly developing field with wide applications in different industries, medical sciences, life sciences, analytical chemistry and pollution control and even in the fields of physics and engineering.

**Classification of surfactants**

Surfactants are classified into several groups on the nature of their hydrophilic head group charge as

- Anionics (having a negative charge),
- Cationics (with a positive charge),
- Nonionics (with no charge) and
- Amphoterics or zwitterionics (whose charge depends upon the pH of the solution).

**Anionic surfactants:**

The defining feature of the anionic surfactant is, of course, that it is an anion (i.e., a negatively charged ion). All soaps (the fatty acid salts) are anionic surfactants

\[
\begin{align*}
\text{A} & \text{O} - \text{C}_n \text{H}_{2n+1} - \text{O} - \text{H} \\
\text{H} & \text{O} - \text{C}_m \text{H}_{2m+1} - \text{O} - \text{H} \\
\end{align*}
\]

Anionic surfactants are used all over the places. They make up around 49% of all surfactants made. They are used in shampoos, dishwashing detergents and in
washing powders. In many industrial and commercial applications, anionic surfactants are no longer used on their own. Typically, they are used in conjunction with nonionic surfactants to provide even greater stability.

**Cationic surfactants:**

Like anionic surfactants, it is fairly easy to recognize the cationic surfactants; it has a positive charge. Fatty amine salts (or ammonium salts) were developed as the first cationic surfactants.

![Ammonium carboxylate](image1)

![Ammonium sulfate](image2)

![Amine oxide](image3)

Cationic surfactants are typically used in things like hair-conditioner and fabric softeners. The fatty amine salts have proved quite useful in blends with nonionic surfactants, giving good stability over a range of pH levels.

**Nonionic surfactants:**

These types of surfactants are different from both cationic and anionic surfactants in that the molecules are actually uncharged. The hydrophilic group is made up of some other very water-soluble moiety, (e.g., a short, water-soluble polymer chain) rather than a charged species. Traditionally, nonionic surfactants have used poly (ethylene oxide) chains as the hydrophilic group. Poly (ethylene oxide) is a water-soluble polymer; the polymers used in nonionic surfactants are typically 10 to 100 units long.

Two common classes of surfactants which use poly (ethylene oxide) chains as their hydrophilic groups are alcohol ethoxylates and alkyl phenol ethoxylates.
The predominant uses of these surfactants are in food and drinks, pharmaceuticals and skin-care products.

**Zwitterionic Surfactants:**

Zwitterionic surfactants are a zwitterion that has surface-active properties. (A zwitterion is also known as an internal salt, having an anion and a cation in the same molecule, chemically joined together) Zwitterionic surfactants are also called amphoteric surfactants as they often comprise a base coupled with an acid.

Zwitterionic surfactants are considered to be specialty surfactants as their uses are fairly limited. The one area where these surfactants have become very popular is in skin-care products. This is because, they have a good skin feel.

In this chapter, synthesis of water-soluble tetrasulfonatomethyl calix[4]resorcinarene using microwave-irradiation technique and was used for studying interaction with cationic surfactant by turbidity, surface tension and dynamic light scattering (DLS) measurements.
2. Experimental

2.1. Materials

All chemicals used in the synthesis of tetrasulfonatomethylcalix[4]resorcinarene (1) were obtained from Sigma-Aldrich or fluka and were used without further purification. The cationic surfactants used were tetradecyltrimethylammonium bromides (C\textsubscript{14}TABr), hexadecyltrimethylammonium bromides (C\textsubscript{16}TABr), dodecylpyridinium bromide (C\textsubscript{12}PyBr), dodecylpyridinium chloride (C\textsubscript{12}PyCl), dodecylpyridinium iodide (C\textsubscript{12}Pyl), hexadecylpyridinium bromide (C\textsubscript{16}PyBr), and alkyltriphenylphosphonium bromide (C\textsubscript{12}TPPBr, C\textsubscript{14}TPPBr, C\textsubscript{16}TPPBr). These were purchased from Aldrich/Fluka (purity 99%) and were used as supplied. Their CMCs determined from surface tension are reported in (Table 1) which agrees with those reported in literature\textsuperscript{[12]}

Table 1. Critical micelle concentration (cmc in mmol/L) of cationic surfactants in water at 30 °C.

<table>
<thead>
<tr>
<th>Cationic surfactants</th>
<th>CMC (mM)</th>
<th>Literature</th>
</tr>
</thead>
<tbody>
<tr>
<td>γ</td>
<td></td>
<td>Y</td>
</tr>
<tr>
<td>C\textsubscript{14}TABr</td>
<td>3.98</td>
<td>3.83\textsuperscript{[13]}</td>
</tr>
<tr>
<td>C\textsubscript{16}TABr</td>
<td>1.00</td>
<td>1.00\textsuperscript{[13]}</td>
</tr>
<tr>
<td>C\textsubscript{12}PyBr</td>
<td>11.85</td>
<td>10.00\textsuperscript{[14]}</td>
</tr>
<tr>
<td>C\textsubscript{12}PyCl</td>
<td>17.50</td>
<td>17.00\textsuperscript{[15]}</td>
</tr>
<tr>
<td>C\textsubscript{12}Pyl</td>
<td>5.30</td>
<td>6.6\textsuperscript{[16]}</td>
</tr>
<tr>
<td>C\textsubscript{12}TPPBr</td>
<td>1.88</td>
<td>1.88\textsuperscript{[17]}</td>
</tr>
<tr>
<td>C\textsubscript{14}TPPBr</td>
<td>0.60</td>
<td>0.60\textsuperscript{[17]}</td>
</tr>
<tr>
<td>C\textsubscript{16}TPPBr</td>
<td>0.20</td>
<td>0.20\textsuperscript{[17]}</td>
</tr>
</tbody>
</table>
2.2. Instrumentation

Melting points were taken in a single capillary tube using a Veego based (Model: VMP-DS) melting point apparatus and were uncorrected. Elemental analysis was done on Heraeus CarloEbra 1108 elemental analyzer. IR spectra were recorded on Bruker as KBr pellets and expressed in cm\(^{-1}\). \(^1\)HNMR spectra were recorded on DRX 300 operating at 300MHz for proton in D\(_2\)O with tetramethylsilane as internal standard. Mass spectra were also obtained by the electrospray technique (positive mode) on a MICROMASS QUATTRO II triple quadrupole mass spectrometer. The samples (dissolved in suitable solvents) were introduced into the ESI source through a syringe pump at the rate of 5 \(\mu\)L/minute. The ESI capillary was set at 3.5 KV and the cone voltage was 60 V. Electronic spectra were recorded on Jasco V-570 UV-Visible spectrophotometry with matching 10 mm quartz cells. The antibacterial studies were carried out using Muller Hinton Agar media (Hi media).


The synthesis of tetrasulfonatomethylcalix[4]resorcinarene involves the following steps:

1. Preparation of calix[4]resorcinarenes; and


Calix[4]resorcinarene was synthesized as described by a previously reported method\(^{18}\).


Conventional method

Water-soluble tetrasulfonatomethyl calix[4]resorcinarene was synthesized as described by a previously reported method\(^{19}\).

Microwave method

A mixture of calix[4]resorcinarene 5.44g (0.01 mol), a solution of 37% formaldehyde 4.1g (0.05 mol) and sodium sulfite 6.3g (0.05 mol) in H\(_2\)O (15 ml) were placed in Kenstar domestic microwave oven at 48% output for 5 minutes.
Dilute hydrochloric acid was added until the pH became 7, then acetone (30ml) was added to precipitate out the product (1). The solid was filtered off, washed with acetone and dried. The microwave-assisted synthetic route is simple, efficient, time saving and enhances the yield (Table 2) of the reaction. The isolation of the product is simple. The microwave-assisted synthetic route of water-soluble tetrasulfonatomethyl calix[4]resorcinarene is shown in (Scheme 1).

Data

Compound (1) is a light yellow powder, with mp>360°C.

Yield (90%), FT-IR for (1): 3250 cm\(^{-1}\)(-OH), 2966 cm\(^{-1}\)(ArCH), 2931cm\(^{-1}\)(-CH), 836 cm\(^{-1}\)(C\(_6\)H\(_5\));

\(^1\)H NMR for (1): 1.69 (-CH\(_3\)), 4.65 (-CH), 4.21 (-CH\(_2\)), 6.79 (ArH);

ESI/MS of (1) M.wt. = 1009 gm; and

Elemental analysis for (1): C= Calcd: 42.81%, Found: 42.75 %, H = Calcd: 3.57 %, Found: 3.45 %, S= Calcd: 12.71%, Found: 12.60%.

<table>
<thead>
<tr>
<th>No.</th>
<th>Conventional method</th>
<th>Microwave assisted method</th>
<th>Conventional method</th>
<th>Microwave assisted method</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Reaction time (minutes)</td>
<td>Reaction time (minutes)</td>
<td>Yield(%)</td>
<td>Yield(%)</td>
</tr>
<tr>
<td>1</td>
<td>240</td>
<td>5</td>
<td>52%</td>
<td>90%</td>
</tr>
</tbody>
</table>

Table 2. Comparison of reaction time and Yield of water soluble calix[4]resorcinarene under classical and microwave method
2.4 Antimicrobial activities

The antimicrobial activity of Compound (1) was carried out as described in Chapter 6.

3. Results and discussion

The compound was characterized by elemental analysis, FTIR, $^1$HNMR, and Mass. The FTIR Spectra of compound (1) showed at 3250 cm$^{-1}$ corresponding to -OH. A weak band or shoulder located at 2966 cm$^{-1}$ is assigned to aromatic C-H. Also a peak at 2931 cm$^{-1}$ for aliphatic C-H.

The $^1$H-NMR (H$_2$O-d$_2$) spectrum showed a doublet at 1.69 ppm for (-CH$_3$), a quartet at 4.65 ppm (-CH), a peak at 6.79 ppm for aromatic protons (ArH) and a singlet at 4.21 ppm for (-CH$_2$).

Antibacterial activity:

The antibacterial activity of the compounds against *E.coli* and *S.aureus* were carried out using Muller Hinton Agar media (Hi media). The activity was carried out using paper disc method. Base plates were prepared by pouring 10 ml of autoclaved Muller-Hinton agar into sterilized Petri dishes and allowing them to settle. Molten autoclaved Muller Hinton that had been kept at 48°C was
incubated with a broth culture of the *E. coli* or *S. aureus* and then poured over the base plate. The discs were air dried and placed on the top of agar layer. The solutions of all compounds were prepared at two different concentrations and chloramphenicol was used as a reference. The plates were then incubated for 18 hours at room temperature. Activity of (1) against *E. coli* was 8 mm and against *S. aureus* was 10 mm. Its antibacterial activity was found maximum against *S. aureus*.

(Figures 1, 2, and 3) show the turbidity results for 0.1% solution of compound (1) in water in the presence of varying concentration of different cationic surfactants. The solution of (1) was optically clean with 100% transmittance at $\lambda_{\text{max}} = 600$ nm. The addition of cationic surfactant brings down the transmittance but the solutions were stable and showed no time dependant changes in transmittance. The concentrations of surfactants used were less than their CMC values as the solution undergoes precipitation at higher concentration. The surfactant concentration was increased till solution showed 60% T and above this concentration solutions become unstable.

![Figure 1](image_url)

**Figure 1.** Transmittance values for 0.1% calix [4] resorcinarene in the presence of cationic surfactants (■) C$_{12}$TPPBr (●) C$_{14}$TPPBr (▲) C$_{16}$TPPBr
Figure 2. Transmittance values for 0.1% calix [4] resorcinarene in the presence of cationic surfactants (●) C_{12}PyBr (■) C_{12}PyI (▲) C_{12}PyCl

Figure 3. Transmittance values for 0.1% calix [4] resorcinarene in the presence of cationic surfactants (■) C_{16}TABr (●) C_{16}TPPBr (▲) C_{16}PyBr

The minimum concentration of surfactant required to bring down % T below 100 was taken for comparison. This value is reported for surfactant with varying nonpolar concentration, nonpolar carbon chain length, polar head group and
counter ion in (Tables 3, 4, 5). A perusal of the data in these tables clearly reflects the effect:

- Surfactants with larger nonpolar tail decrease %T at larger concentration than surfactants with shorter nonpolar tail.
- Strongly bound counter ions in surfactant were needed in small amounts. The effect was I⁻ > Br⁻ > Cl⁻.
- Smaller polar head group of surfactant was more effective in decreasing % T.

**Table 3.** Concentration of cationic surfactants in mM needed to decrease % T of 0.1% copolymer solution from 100 (effect of nonpolar tail)

<table>
<thead>
<tr>
<th>Cationic Surfactants, mM</th>
<th>0.1% Calix [4] resorcinarene</th>
</tr>
</thead>
<tbody>
<tr>
<td>C_{12}TPPBr</td>
<td>0.017</td>
</tr>
<tr>
<td>C_{14}TPPBr</td>
<td>0.020</td>
</tr>
<tr>
<td>C_{16}TPPBr</td>
<td>0.027</td>
</tr>
</tbody>
</table>

**Table 4.** Concentration of cationic surfactants in mM needed to decrease % T of 0.1% copolymer solution from 100 (effect of counter ion)

<table>
<thead>
<tr>
<th>Cationic Surfactants, mM</th>
<th>0.1% Calix [4] resorcinarene</th>
</tr>
</thead>
<tbody>
<tr>
<td>C_{12}PyCl</td>
<td>0.046</td>
</tr>
<tr>
<td>C_{12}PyBr</td>
<td>0.025</td>
</tr>
<tr>
<td>C_{12}Pyl</td>
<td>0.031</td>
</tr>
</tbody>
</table>
Table 5. Concentration of cationic surfactants in mM needed to decrease % T of 0.1% copolymer solution from 100. (effect of polar head group)

Effect of Polar Head Group

<table>
<thead>
<tr>
<th>Cationic Surfactants, mM</th>
<th>0.1% Calix [4] resorcinarene</th>
</tr>
</thead>
<tbody>
<tr>
<td>C\textsubscript{16}TABr</td>
<td>0.026</td>
</tr>
<tr>
<td>C\textsubscript{16}PyBr</td>
<td>0.018</td>
</tr>
<tr>
<td>C\textsubscript{16}TPPBr</td>
<td>0.027</td>
</tr>
</tbody>
</table>

The surface tension results for cationic surfactants in water were measured over a large range of concentrations from 0.01mM to 10mM in the presence of different concentrations of (1). All the solutions so measured were clear and stable.

(Figure 4) shows representative plot of surface tension vs. surfactant concentration. The nature of curve is typical of surfactants.
Figure 4. Surface tension behavior of different concentrations of tetra sulfonatomethylcalix[4]resorcinarene (1) in presence of C$_{14}$TABr at 30°C

(■)0.01% (●) 0.05% (▲)0.075% (▼)0.1%

Though the pure compound (1) in water in the concentration range (0.01 to 0.1%) did not change the surface tension of water, it showed synergistic effect in the presence of surfactants. The critical aggregation concentration of C$_{14}$TABr in the presence of compound (1) is reported in the (Table 6) which is much less than CMC of the surfactant itself. These studies thus clearly reveal the interaction of (1) with cationic surfactants and an electrostatic interaction that finally leads to turbidity seems to be operating pronominally.
Table 6. Critical aggregation concentration of TTAB in the presence of compound (1) at 30°C.

<table>
<thead>
<tr>
<th>No</th>
<th>[tetrasulfonatomethylcalix[4]resorcinarene], %</th>
<th>Critical aggregation concentration of TTAB, mM</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.01</td>
<td>3.2284</td>
</tr>
<tr>
<td>2</td>
<td>0.05</td>
<td>0.95842</td>
</tr>
<tr>
<td>3</td>
<td>0.075</td>
<td>0.07958</td>
</tr>
<tr>
<td>4</td>
<td>0.1</td>
<td>0.05655</td>
</tr>
</tbody>
</table>

Several dynamic light scattering measurements were done to examine the morphological features of the particles obtained as a result of this interaction. (Figure 5) shows the DLS results as representative plots.

Figure 5. Hydrodynamic diameter values of 0.1% of tetrasulfonatomethylcalix [4] -resorcinarene (1) in presence of C_{14}TABr at 30°C.
Size Distribution

![Size Distribution Graphs]

- Diameter (nm) range from 5 to 5000 nm.
- % in Class indicates the percentage of particles within each diameter range.

Size distribution graphs show the percentage of particles per diameter class.
Following are the observations obtained from the dynamic light scattering measurements.

The interaction is very strong and is governed by the cationic surfactant concentration. The size increases initially with increasing concentration of cationic surfactant. Maximum size increases as the surfactant chain length increases. Initially, the size of the clusters increases with an increase in surfactant concentration but at higher concentrations, the size of the clusters was found to reduce because of disintegration which is due to stronger hydrophobic interaction between surfactant molecules. Polydispersity decreases with an increase in surfactant concentration.
Conclusion

The anionic water-soluble compound tetrasulfonatomethylcalix[4]resorcinarene (1) was examined for interaction with cationic surfactants. From turbidity measurements, we have reported that the addition of cationic surfactant brings down the transmittance but the solutions were stable and showed no time-dependant changes in transmittance. Surface tension measurement reveals that the critical aggregation concentration of C_{14}TABr decreases with increasing concentrations of compound (1). From the dynamic light scattering measurements, it was observed that the interaction is very strong and is governed by the cationic surfactant concentration.
References

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19. (a) Kazakova, E. Kh.; Makarova, N. A.; Ziganshina, A. U.; Muslinkina, L.
(b) Morozova, Yu. E.; Shalaeva, Ya. V.; Makarova, N. A.; Syakaev, V. V.;