Chapter - 2

Resume

This chapter deals with the synthesis of parent calix[4]resorcinarene and its tetrahydrazide derivative. The compounds were checked for their purity by melting point, TLC and characterized by various physico-chemical techniques such as, FT-IR, $^1$H NMR, ESI-MS, $^{13}$C NMR and DEPT. Further the hydrazide derivative of parent calix[4]resorcinarene was explored as reducing and capping agent in the synthesis of water dispersible stable metal [AuNps, AgNps and (AuAgNps)] nanoparticles, which have been proposed in their respective chapter of application.
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1. Introduction

In the field of supramolecular chemistry, calixarene and calix[4]resorcinarene are well known host molecules [1]. Various analytical techniques have been utilized to investigate interactions and sensing processes of different analytes with calixarenes and related compounds [2-4]. Fluorescent sensors have become increasingly important as tools for the quantitative real-time monitoring of metal ion concentration in biological samples [5-7]. The development of receptors, with the goal of achieving a higher level of control over recognition, has intrigued researchers in supramolecular chemistry due to their importance in a wide range of chemical, environmental and biological processes [8-14].

Calix[4]resorcinarenes the most stable conformer having a bowl shaped molecular cavity have attracted great interest in recent years due to their versatile complexing properties, conformational flexibility, a great variety of ways for their further functionalization, easy synthetic and commercial availability and so in recent years aromatic macrocyclic chemistry has attracted the attention of many chemists [15, 16].

Calix[4]resorcinarenes embraces wide range of applications since their synthesis. The utility has been recognized as starting materials for the synthesis of macrocyclic compounds (e.g. cavitands and carcerands) [17], for the separation of pyrimidine bases [18], GC separations [19], HPLC stationary phases [20], imaging material for organic electronics [21], molecular receptors [22-24], multifunctional antiradical and antioxidant agents [25], NMR chiral shift agents [26] and photo resist material [27]. A few reviews on different aspects of these molecules have been published [28-30].
Calix[4]resorcinarenes [28, 31] are resorcinol-derived calixarenes, which are synthesized by acid-catalysed condensation of resorcinol and with different type of aldehyde. C-alkyl- and C-arylcalix[4]resorcinarenes can also be prepared from 2-alkyl- and 2-hydroxyresorcinol [32].

Calix[4]resorcinarenes are three-dimensional cyclic aromatic tetramers with relatively shallow conical cavity that can be extended by suitable substitution and further functionalization. Calix[4]resorcinarene has an important advantage over calix[n]arenes as they are readily obtainable with various substituent’s at the sites of the bridging methylene groups and various functionlization on the hydroxy group as well as on upper rim.

Herewith, the –COOH group was exploited and the hydrazide derivative was synthesized. Hydrazides moieties are well known excellent reagents for reducing and stabilizing metal salt precursors for synthesizing nanoparticles. Resorcinarene and other calixarene derivatives have been widely used to enhance the dispersion of colloidal metal particles in various organic solvents, as well as their self-assembly into well-defined nanostructures with novel collective properties [33]. Calix[4]resorcinarenes derivatives as a reducing agent has been used previously but, the stabilizing property is newly known [34, 35].

Herein, the hydrazide derivative of calix[4]resorcinarene has been synthesized in two step process and further exploited to synthesize metal and alloy nanoparticles. The steps include synthesis and characterization of


The parent calix[4]resorcinarene has been further functionalized to its hydrazide derivative in simple one step reaction. Calix[4]resorcinarene hydrazide derivatives have been used (Chapter 3, 4 and 5) for the formation of gold, silver and bimetallic nanoparticles.

2. Experimental section

2.1. Chemicals and reagents

All the reagents and metal salts of AR grade were purchased from Sigma-Aldrich and used without further purification. Solvents used for spectroscopic studies were purified and dried before use. All aqueous solutions were prepared from quartz distilled deionized water which was further purified by a Millipore Milli-Q water purification system (Millipack 20, Pack name: Simpak 1, Synergy).

2.2. Instruments

The melting points (uncorrected) were obtained from a VEEGO (Model; VMP-DS) melting point apparatus. FT-IR spectra were recorded on Bruker, Tensor 27 Infrared spectrometer. $^{1}$H-NMR spectra were recorded on a FT-NMR model Bruker, Avance II (500MHz) at 298 K with TMS as the internal reference. ESI-MS were recorded on micromassQuarter2 mass spectrometer.

3. Synthesis


$[\text{bis(ethoxycarbonyl)phenyl}-\text{octahydroxy tetrabenzenecyclooctaphanediyldibenoic acid}]$

The parent calix[4]resorcinarene (1) skeleton was synthesized by the acid catalyzed condensation reaction of resorcinol and 4-formylbenzoic acid. 5 mL hydrochloric acid in 15 mL aqueous solution of resorcinol (5 g, 0.045 mol) was
added to 15 mL solution of 4-formylbenzoic acid (6.83 g, 0.045 mol) in ethanol containing 5 mL of hydrochloric acid with constant stirring and then refluxed for 4–5 h at 75-80˚C. Buff coloured precipitates were obtained which were washed with cold ethanol and further recrystallized in DMF/ethanol mixture (Scheme 1).

**Scheme 1.** Formation of parent calix[4]resorcinarene (1)

### 3.1.1. Mechanism for the formation of parent calix[4]resorcinarene (1)

In acidic conditions, 4-formyl benzoic acid converts into carbocation which reacts with resorcinol to form a new carbocation D from which a water molecule gets removed. On reacting with new resorcinol unit, E gives a dimer. This dimer F on further reacting with 4-formylbenzoic acid, resorcinol and ethanol gives a linear trimer G with a removal of water molecule, which gives H on further treatment with resorcinol and 4-formylbenzoic acid. Finally, H gives calix[4]resorcinarene and higher oligomers on treatment with 4-formyl benzoic acid, resorcinol and ethanol with a removal of water molecule (**Scheme 2**).
Scheme 2. Synthetic mechanism of parent calix[4]resorcinarene (1)

[Tris(hydrazinecarbonyl)phenyl]-octahydroxy pentacyclo octacosa-dodecaen-yl]benzohydrazide

A mixture of 15 mL ethanolic solution of compound (1) (4.0 g, 3.9 mmol), \(N, N'\)-Dicyclohexylcarbodiimide (DCC) (3.2 g, 7.8 mmol) in 10 mL acetonitrile and hydrazine hydrate (20 mL, 80%) was refluxed for 24 h, at room temperature. Further the reaction mixture was dumped in water to ensure the removal of dicyclohexylurea (DCU). And pink colored solid precipitated out as pure compound CRTH (Scheme 2).

![Scheme 3. Formation of calix[4] resorcinarene tetrahydrazide (CRTH)](image)

3.2.2. Mechanism for the formation of calix[4]resorcinarene tetrahydrazide (CRTH)

The hydrogen of the carboxylic group attacks the nitrogen having lone pair of electrons so a carboxylate anion is formed at one end and at the other end a carbocation is formed at the DCC (A). This carbocation then attaches with the anion (B) by the removal of DCU as the by product and CRTH is synthesized (Scheme 4).
4. Results and discussion

4.1. Spectroscopic characterization

4.1.1. Parent calix[4]resorcinarene (Compound 1)

The macrocycle was fully characterized; its physical properties are presented in Table 1. The FT-IR, spectra of compound (1) showed a broad band at 3394 for OH group while the presence of acidic OH was confirmed by the presence of a small band at 2956 cm\(^{-1}\). The -C=O stretching for ester appeared at 1702 cm\(^{-1}\) and -C=O symmetrical stretching appeared at 1435 cm\(^{-1}\) (Figure 1). The peak at 1520 cm\(^{-1}\) appeared for CH\(_2\) coincide with CH\(_3\) confirmed the presence of ethyl group. \(^1\)H-NMR showed a peak at \(\delta\) 12.55 for (2H, Ar-COOH), 8.84 for (8H, Ar-
OH), 6-8 for (24H, Ar-H), 5.67 for (4H, Ar-CH), 4.24 for (4H, CH₂) and 1.41 for (6H, CH₃) (Figure 2). It may be noted that the mass spectra (ESI-MS) m/z value of compound (1) correspond to the (1022.9) (M-1) (Figure 3). ¹³C NMR (DMSO-d₆) of compound (1) displayed signal at 14.39 ppm for –CH₃, 41.0 ppm for bridge –CH, 65.15 ppm for -CH₂, 154.2 ppm for Ar-OH, 165.9 (COOC₂H₅) and 169.3 (C=O,COOH). Further ¹³C-NMR is shown in Figure 4. The detail of ¹³C characterization is summarised in Table 2. In the DEPT characterization of compound (1) the O-CH₂ peak appears at 65 ppm Figure 5.

4.1.2. Calix[4]resorcinarene tetrahydrazide(CRTH)

A new modified scheme has been developed for the synthesis of calix[4]resorcinarene tetrahydrazide. As in earlier reported methods the hydrazide functionalization requires tedious reaction steps [37]. The fully characterized parent calix[4]resorcinarene (1), upon reaction with hydrazine hydrate yielded calix[4]resorcinarene tetrahydrazide (2) in simple steps of reaction, which was further characterized by FT-IR, ¹H NMR, ESI-MS, ¹³C NMR and DEPT. The FT-IR peak at 3411 cm⁻¹, 3560 cm⁻¹ was assigned to –NH stretching and NH₂ group, respectively. The small peak of NH₂ subsides with a broad band of OH group at 3394 cm⁻¹. While the peak for acidic OH at 2956 cm⁻¹ has disappeared indicating the successful functionalization of NH-NH₂ group. The band at 1704 cm⁻¹ appears for -C=O stretching (amide group) while CN stretching appears at 1298 cm⁻¹. The peak for ethyl group at 1520 cm⁻¹ has also disappeared and a new peak appears at 1574 cm⁻¹ for amine group. ¹H NMR showed a peak between δ 8.5-9.5 for (12H, Ar-OH, NH) and 6-8 for (24H, Ar-H) 5.63 (4H, Ar-CH) and 3.87 for free terminal (8H, NH₂) (Figure 7). Mass
spectrometry (ESI-MS) 1023.5 (M⁺) is shown in Figure 8. ¹³C NMR (DMSO-d₆) of CRTH showed signal at 167.2 ppm for –C=O, and absence of signal around 14.39 ppm and 65.90 ppm indicated the absence of ester group, which confirmed the formation of hydrazide derivative of calix[4]resorcinarene. Also in DEPT characterization of CRTH no peak appears at 65 ppm indicating the absence of O-CH₂ group (Figure 9).

Table 1: Various physical properties of synthesized macrocyclic compounds

<table>
<thead>
<tr>
<th>Compound</th>
<th>Molecular formula</th>
<th>Molecular weight</th>
<th>M.P. °C</th>
<th>Colour</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>C₆H₄₈O₁₆</td>
<td>1022.9</td>
<td>&gt;300</td>
<td>Buff colour</td>
</tr>
<tr>
<td>CRTH</td>
<td>C₅₆H₄₈N₈O₁₂</td>
<td>1023.5</td>
<td>250</td>
<td>Light pink</td>
</tr>
</tbody>
</table>

Table 2: ¹³C-NMR spectral data for synthesized macrocyclic compounds

<table>
<thead>
<tr>
<th>Compound Code</th>
<th>¹³C-NMR (δ ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>14.1 (CH₃), 41(Bridge-C), 60.9 (CH₂), 104.6, 123.3, 127.7, 128.1, 130.4, 132.1, 147.7, 154.2 (C-Aromatic), 165.9 (COOCC₂H₅), 169.3 (C=0,COOH)</td>
</tr>
<tr>
<td>CRTH</td>
<td>41 (Bridge-C), 104.6, 123.3, 127.7, 128.3, 129.5, 132.1, 147.7, 154.2 (C-Aromatic), 167.2 (C=0,CONHNH₂)</td>
</tr>
</tbody>
</table>
Figure 1: FT-IR spectra of compound 1

Figure 2: $^1$H-NMR spectra of compound 1
Chapter 2

Figure 3: ESI-MS of compound 1

Figure 4: $^{13}$C of compound 1
Figure 5: $^{13}$C DEPT of compound 1

Figure 6: FT-IR spectra of compound CRTH
Figure 7: $^1$H-NMR spectra of compound CRTH

Figure 8: ESI-MS of compound CRTH
Figure 9: $^{13}$C of compound CRTH

Figure 10: $^{13}$C DEPT of compound CRTH
Conclusion

In recent times, organic synthesis with simple step and scheme is required in daily practice. With this in view, a simple, fast, efficient, economical approach has been developed for the formation of \((\text{bis(ethoxycarbonyl)phenyl}) - \text{octa hydroxyl tetrabenzenacyclo- octaphane diyl}) \text{ dibenzoic acid}\) and \([\text{Tris(hydrazinecarbonyl)phenyl]} - \text{octahydroxypentacyclo octacosa-dodecaenyl}]\text{benzohydrazide}\). One novel calix[4]resorcinarene tetrahydrazide derivative were synthesized for the synthesis of gold, silver and alloy metal nanoparticles. The structures of synthesized compounds were confirmed on the basis of FT-IR, $^1\text{H-NMR}$, ESI-MS, $^{13}\text{C-NMR}$ and DEPT spectroscopic techniques.
References


