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SYNTHESIS OF ESTER DERIVATIVES OF CALIX[N]ARENE

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ABSTRACT. The synthesis of *p-tert*-butyl calix[n]arene derivatives with two and four, as well as, four and six (ethoxycarbonyl)methoxy groups at the lower rim is reported. The selective alkylation of the parent calix[n]arenes is performed in organic solvents, with ethyl bromoacetate in the presence of potassium carbonate or sodium hydride as a base. UV-Vis, FTIR, ^{1}H-NMR investigations confirmed the formation of the ester derivatives of calix[n]arene with variable number of ester groups at the narrow rim.

Keywords: Calix[n]arene, selective O-alkylation, ethyl bromoacetate

INTRODUCTION

A dedicated class of [1n] metacyclophanes generally designed as calixarene are nowadays receiving an increasing attention in the field of supramolecular chemistry because of their simple synthesis, easy modification (functionalisation) and unique properties [1, 2]. It is well known that calixarene derivatives containing oxygen donor groups, acid, ester or keto, linked at the phenolic oxygen at the narrow rim, exhibit excellent properties as neutral receptors for metallic ions [3-16]. Many recent works have been focussed on the utilisation of calixarene derivatives as prospective ionophores for ion selective electrodes, optical sensors or colorimetric reagents for use in the determination of clinically important species [17].

Our earlier findings on the synthesis of calix[n]arene for sequestration of rare earth and precious ions revealed that derivatives having three 2-butenyl (crotyl) groups at the narrow rim show good extraction ability for europium and palladium ions [18]. Good results we also obtained with organo-phosphorus and/or crotyl functionalised calix[6]arene [19,20].

Aiming to develop new ionophores or cation extraction reagents based on calixarene derivatives, a variable number of oxygen donor groups e.g. ester groups was grafted on the parent *p-tert*-butyl calix[6,8]arenes.

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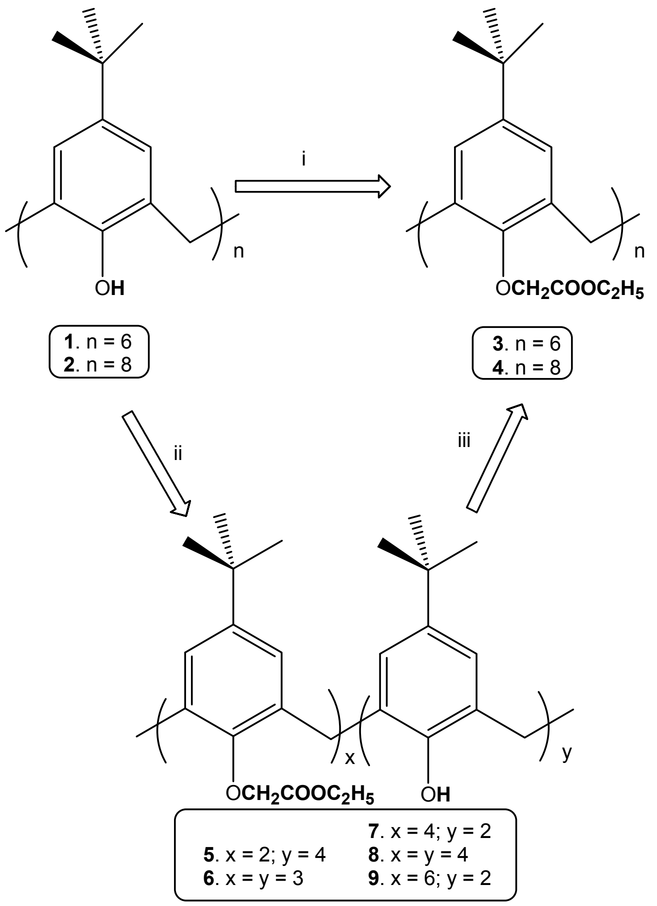
Due to the presence of the *p*-electrons of the ester groups, these derivatives are of practical interest for rare earth and precious metal sequestration.

Herein we present our study referring to the synthesis and characterization of new derivatives of *p-tert*-butyl calix[6]arene and *p-tert*-butyl calix[8]arene with two and four, as well as, four and six (ethoxycarbonyl)methoxy groups. We previously reported the synthesis of some other ester derivatives [25-27] in this class of compounds.

RESULTS AND DISCUSSION

The chemistry we followed is shown in scheme 1 (depicted).



i: $BrCH_2COOC_2H_5$, K_2CO_3, Acetone , reflux, 18h
ii and **iii**: $BrCH_2COOC_2H_5$, NaH, THF/DMF, reflux, 20h

Scheme 1

Thus, the parent calix[n]arenes were O-alkylated with ethyl bromoacetate in alkaline conditions in order to prepare derivatives with two-to-eight [(ethoxycarbonyl)methoxy] groups grafted at the narrow rim.

Reaction of *p-tert*-butyl calix[n]arene (**1-2**) in the presence of K_2CO_3 or NaH as a base, with the required amount of ethyl bromoacetate in organic solvents or mixture of them, yielded calix[n]arene ester derivatives with two (**5**), three (**6**), tetra (**7,8**), hexa (**3,9**) and octa (**4**) ester groups respectively.

UV-Vis, FTIR and ^{1}H-NMR investigations confirmed the formation of the desired O-functionalised calix[n]arene.

^{1}H-NMR spectra

The ^{1}H-NMR spectra of calixarene contain several broad bands which are characteristic for the conformational flexibility of calix[6]- and calix[8]arene derivatives. Indeed, the ^{1}H-NMR spectra showed the expected differences between the chemical shifts of the parent calixarene and their derivatives. The position of the singlet belonging to the phenolic OH groups varies with the ring size of the calixarene. Thus the chemical shifts of OH groups appeared at 10.55 ppm for compound **1**, and 9.86 ppm for compound **2**, whereas calixarene derivatives **5** and **7-9** showed the chemical shifts at: 7.11 (**5**), 7.11 (**7**), 7.10 (**8**) and 7.06 (**9**) ppm.

Table 1 collects the relevant ^{1}H-NMR data of calixarene derivatives.

Table 1. Selected ^{1}H-NMR data of compounds **5,7-9** in comparison with the parent calixarenes **1, 2**

	$C(C\underline{H}_3)_3$	**$O\text{-}CH_2\text{-}\underline{CH_3}$**	**$O\text{-}\underline{CH_2}\text{-}CH_3$**	**$ArCH_2Ar$**	**$O\text{-}\underline{CH_2}\text{-}CO$**	**$Ar\underline{H}$**	**$ArO\underline{H}$**
1	1.27,s	-	-	3.78,bs	-	7.16,s	10.55,s
2	1.26,s	-	-	3.53,d; 4.39,d	-	7.17,s	9.86,s
5	0.87,s; 1.19,s	1.24,t	4.06-4.20,m	3.48,bs	4.49,s	6.99,s; 7.04,s	7.11,s
7	1.15,s; 1.20,s	1.17,t	4.06 – 4.12,m		4.47,s	6.84,s; 6.90,s	7.11,s
8	0.93s; 1.04,s	1.02,t	3.64 – 4.07,m			6.83,s; 6.87,s	7.10,s
9	1.02,s; 1.18,s	0.94,t	3.93 – 4.37,m		4.61,s	6.83,s; 6.86,s	7.06, s

FTIR spectra

FTIR spectra of the parent calixarene showed the stretching vibration of the phenol group at 3149 (**1**) and 3244 (**2**) cm^{-1}, respectively, in agreement with literature data [2]. By functionalisation at the narrow rim, the strong circular hydrogen bonding was supressed and derivatives **5-9** show the OH vibrations to be shifted at 3423 (**5**), 3448 (**7**), 3448 (**8**) 3438 (**9**) cm^{-1}, close to the OH stretching in isolated phenolic OH.

The stretching vibration arising from carbonyl group were observed as two strong bands at 1762, 1740 (**5**), 1759, 1735 (**7**), 1759, 1730 (**8**), and 1760, 1738 (**9**) cm^{-1}, respectively. The presence of two $\nu_{C=O}$ bands in the IR spectra suggests that two different carbonyl groups exist in these calixarene under different environments [28].

A relevant example is shown in Figure 1.

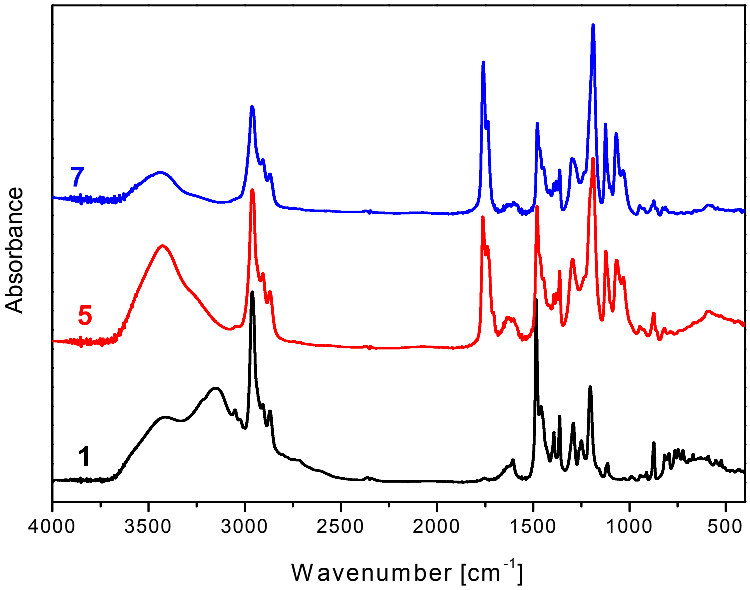


Figure 1. FTIR spectra of compounds **1** (parent calix[6]arene), **5** (diester derivative) and **7** (tetraester derivative)

UV-VIS spectra

The functionalisation of parent calixarene **1, 2** induced significant changes in the UV-Vis absorption spectra allowing pertinent analysis of the resulting ester derivatives (Figure 2). absorption maxima at about 280 and 288 nm in the UV region. The

According to literature [2], such cyclic oligomers have a pair of absorption ratio of these two maxima is a function of the ring size.

The starting calixarene revealed the specific absorption bands at 280, 288 (**1**), and 283, 291 (**2**) nm, respectively. In parallel with the increase of the number of phenolic rings, the shift of the maxima toward longer wavelengths as well as the rise of the band ratios were noticed.

The specific UV absorptions of our O-functionalised calixarene appeared at 278, 286 (sh) (**5**), 273, 279 (**7**), 273, 278, 289 (sh) (**8**) and 270, 278 (**9**). For comparison, the complete O-alkylation of calix[8]arenes (**4**) is also presented, showing the specific absorption bands at 271 and 279 nm, respectively.

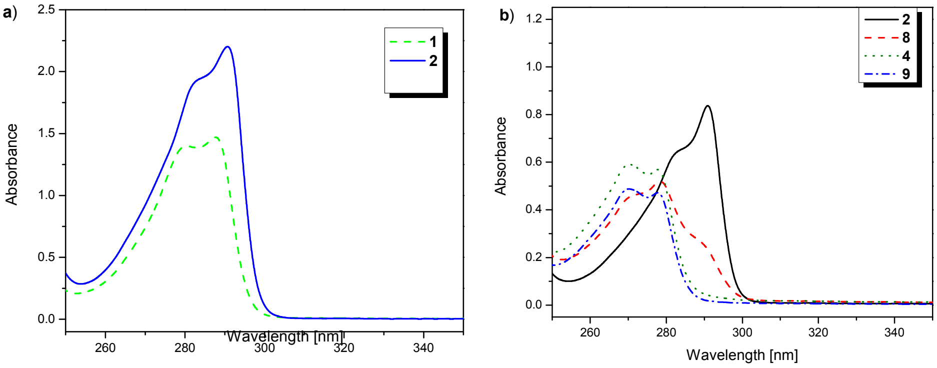


Figure 2. UV-vis absorption spectra of *p-tert*-butyl calix[n]arene and their derivatives ($CHCl_3$ solution;$1x10^{-4}$M): a) **1** (calix[6]arenes), **2** (calix[8]arenes); b) **4** (octaester derivative), **8**(tetraester derivative), **9** (hexaester derivative) and **2**(calix[8]arenes; $0.322x10^{-4}$M).

One note that the ester functionalisation brings about a new absorption band at shorter wavelength that increases in intensity with the number of grafted ester groups. The decrease of the absorption energy with the increasing of number of phenolic rings is also evident.

The ester calix[n]arene derivatives were tested as extracting reagent for precious metal and rare earth ions. Extraction was performed at pH= 2-3, from $1x10^{-3}$ M aqueous solution of $PdCl_2/Eu(NO_3)_3$, using $1x10^{-3}$ M solution of calixarene in $CHCl_3$. Relative high ability for the sequestration of divalent palladium was found, especially, for half substituted calix[6]arene or calix[8]arene. For instance, the extraction yield was ~53% for compound **6** and ~35% for compound **3**. The extraction capability for trivalent europium ions was low for all the ester calix[n]arene derivatives.

CONCLUSIONS

Calix[n]arene [n=6,8] derivatives comprising bi-, tetra-, hexa- and octa (ethoxycarbonyl)methoxy groups were obtained by O-alkylation of calix[n]arene with variable amounts of ethyl bromoacetate. Their structure was confirmed by spectroscopic investigations (UV-Vis, FTIR, ^{1}H-NMR).

Ester calix[n]arene derivatives with variable number of oxygen donor groups e.g. ester linked at the narrow rim, showed ability for the extraction of precious metal ions e.g. palladium from aqueous medium.

EXPERIMENTAL SECTION

All reactions were performed under nitrogen atmosphere using oven-dried glassware. Reagents were purchased from commercial suppliers and were used without further purification. All solvents were dried over standard drying agents and distilled prior to use. Reactions were monitored by TLC on Kiselgell 60 F_{254} plates with detection by UV or Iodine.

Melting points were determined with POINT METER KSP II apparatus in a sealed capillary and are uncorrected values. ^1H-NMR spectra were recorded on VARIAN GEMINI 300 S (300 MHz) spectrometer. Deuterated chloroform was used as solvent and TMS as references. IR spectra were recorded on FTIR (JASCO) 610 and UV-Vis spectra on UNICAM UV 4 spectrometers. Elemental analysis (E.A.) was performed with a Vario EL analyser.

The starting calixarenes **1** and **2** were synthesised according to literature [21-23].

Reaction of *p-tert*-butyl calix[n]arene **1** or **2** with the required amount of ethyl bromoacetate was performed in the presence of K_2CO_3 or NaH as a base, using THF/DMF or acetone as solvent (Scheme 1). *p-tert*- butyl calix[n]arene derivatives containing two (**5**), three (**6**), tetra (**7, 8**), hexa (**3, 9**) and octa (**4**) ester groups were isolated and recrystallised from dichloromethane-ethanol mixture. The synthesis of compounds **3** and **4** [24] and **6** [25] was carried out according to literature.

The preparation yield was 81%(**3**), 61%(**4**), 62%(**5**), 38%(**6**), 72%(**7**), 71%(**8**) and 49%(**9**).

The main characteristics of the new synthesised calixarenes derivatives are presented bellow. For the 1H chemical shifts, see Table 1.

5,11,17,23,29,35-hexa-*tert*-butyl-bis[(ethoxycarbonyl)methoxy]-tetrahydroxy-calix[6]arene (5)

M.p.=221°C
M.W. calcd. for $C_{74}H_{96}O_{10}$=1144
E.A: Calcd: C=77.59; H=8.45 ; *Found:* C=77.90; H=8.21
UV-Vis: [$CHCl_3$; λ_{max} (nm)/$\varepsilon(M^{-1}cm^{-1})$]=278/6373; 286/5000
FTIR: ($\nu_{max.}$, KBr, cm^{-1}): $\nu_{C=O}$=1740, 1762; ν_{OH}=3423

5,11,17,23,29,35-hexa-*tert*-butyl-tetrakis[(ethoxycarbonyl)methoxy]-dihydroxy-calix[6]arene (7)

M.p.=261°C
M.W. calcd. for $C_{82}H_{108}O_{14}$=1316
E.A.: Calcd: C=74.74; H=8.26 ; *Found:* C=74.90; H=8.21
UV-Vis: [$CHCl_3$; λ_{max} (nm)/$\varepsilon(M^{-1}cm^{-1})$]=273/5880; 279/5697
FTIR: ($\nu_{max.}$, KBr, cm^{-1}): $\nu_{C=O}$=1759, 1735; ν_{OH}=3448

5,11,17,23,29,35,41,47-octa-*tert*-butyl -tetrakis-((ethoxycarbonyl)methoxy)- tetrahydroxy-calix[8]arene (8)

M.p.=195°C
M.W. calcd. for: $C_{104}H_{136}O_{16}$=1640
E.A.: Calcd: C=76.06; H=8.35; *Found:* C=74.90; H=8.21
UV-Vis: [$CHCl_3$; λ_{max} (nm)/$\varepsilon(M^{-1}cm^{-1})$]=273/4680; 278/5210;289(sh)/2670
FTIR: ($\nu_{max.}$, KBr, cm^{-1}): $\nu_{C=O}$=1759, 1730; ν_{OH}=3448

5,11,17,23,29,35,41,47-octa- ***tert*****-butyl -hexakis-((ethoxycarbonyl)methoxy)- dihydroxy-calix[8]arene (9)**
M.p.=216°C
M.W. calcd for: $C_{112}H_{148}O_{20}$=1812
E.A. Calcd: C=74.14; H=8,22; *Found:* C=74.60; H=8.45
UV-Vis: [$CHCl_3$; λ_{max} (nm)/$\varepsilon(M^{-1}cm^{-1})$]=270/4900; 278/4760
FTIR: ($\nu_{max.}$, KBr, cm^{-1}): $\nu_{C=O}$=1760, 1738; ν_{OH}=3438

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