Polish J. Chem., **76**, 701–711 (2002) **ORGANIC CHEMISTRY**

Nitration of Calixcrown 6 Influence on Extracting Abilities. Use of Cesium Salts for Detection of Crown Ether Macrocycles with the Electrospray Ionization Mass Spectrometry Technique

by C.K. Jankowski[1,3*], J.F. Dozol[2], F. Allain[3], J.C. Tabet[7], R. Ungaro[4], A. Casnati[4], J. Vicens[5], A. Asfari[5] and J. Boivin[6]

[1]*Université de Moncton, Moncton, Canada*
[2]*CEA, DEN Cadarache/DED/SEP/LCD, France*
[3]*CEA, DEN Saclay/DPC/SCPA/LAS$_2$O, France*
[4]*Universita di Parma, 43100 Parma, Italy*
[5]*ECPM, URA 405 du CNRS, F-67008 Strasbourg, France*
[6]*ICSN,CNRS, 91198 - Gif sur Yvette, France*
[7]*LCSOB, URA 7613, Université P. et M. Curie, 76252, Paris, France*

(Received November 15th, 2001; revised manuscript January 21st, 2002)

Two organic synthetic reactions – mononitration and phosphorylation of crown-6 compounds were performed under Cs^+ cation monitoring *via in situ* complexation using electrospray ionization mass spectrometry (ESI-MS). Formation of Cs^+ complexes is a rapid analytical tool for characterization of complex reaction mixtures.

Key words: nitration of calix crown compounds, mononitration of calix arenes, Cs^+ spiking for detection of calix crown compounds *via* ESI, ESI of calix/crown compound

The use of calix[4]arenes in radioactive liquid waste treatment has been widely studied because of their capacity to selectively extract the cesium Cs^+ ion [1–7]. The extraction of radioactive ^{135}Cs and ^{137}Cs from highly concentrated nitric acid – sodium nitrate slurries remains an important technological problem. Calix[4]arene crown derivatives with one or two crowns of different size have been found to form stable complexes in solution. More recently, the electrospray mass spectrometry (ESI-MS) technique was used to study these complexes and together with molecular modelling (MD) enabled confirmation of the existence of these complexes in gas phase as well. For the calix[4]arene basic system, the attachment of one or two crown-6 ether units *via* 1,3 or 1,3 /2,4 links engenders important selectivity because the crown cavity is very well adapted to host the cesium ion [8,9]. In this note we would like to present the reverse application of the cationization of calixcrown compounds. Using in the ESI-MS, one can obtain an interesting detection tool for different crown compounds. In a similar manner, several slightly polar or non polar

---

[*] Author to whom all inquiries should be addressed: Christopher K. Jankowski, Département de chimie et biochimie, Université de Moncton, Moncton, NB E1A 3E9, Canada, e-mail: jankowc@umoncton.ca, FAX: 1 506 858 4541

compounds, *e.g.* terpenes, completely protected peptides or other difficult to protonate or to deprotonate natural products – could be analyzed by spiking the nebulizer spray with *e.g.* silver salts [10]. Such methods could have many applications in organic synthesis.

As examples, two applications in the synthesis of nitro calix[4]arene crowns obtained by irradiation of the calixcrown in presence of nitric acid and in the design of potential extractants based on phosphorylated crowns are presented. Finally, the mono or dinitrocalix[4]arene crown compounds are an interesting material for the alkylamino (or aminoalkyl) derivative synthesis. We have performed this reaction for two calix[4]arene crown compounds with one crown (MC-6) and two crowns (BC-6) respectively, studied the extracting abilities of these compounds and designed new crown esters for Cs^+ complexation. The identification of crown compounds as well as the reaction progress monitoring were performed using Cs^+ complexes detected under ESI monitoring.

The use of ESI-MS for semiquantitative analysis rised a question of the relationship between the liquid phase concentration of some species and their concentration measures in gas phase [11,12]. The straight application of ion intensities to estimate the liquid phase concentration of these compounds is impossible. However, the cross-comparison of the Cs^+ complexation intensities to the data obtained from LC, GC or column chromatography quantitation lead to an evaluation of the ESI as a semiquantitative tool. In order to estimate this in a case of nitration of calix[4]arene crown compounds both starting materials, MC-6 and BC-6, were used for calibration purpose and the results were compared to those obtained from flash-chromatography. In both cases, the ratios of *e.g.* MC-6 (or BC-6) and its corresponding nitro derivatives were within a 10% range (for instance 3 ± 0.3%) when Cs^+ complex detection was used under ESI. These results suggested that when such highly crowded (calix[4]arene, crown, iso-propoxyls) compounds are used, the nitration yield could be reasonably well estimated from the ESI data, especially when starting material and nitro derivatives maintained most of their structural features, has similar solubility (in acetonitrile) and the same complexation toward Cs^+ site.

The more formal calibration, using Cs^+ complex mixtures *e.g.* of two or more equimolar nitro compounds in this series, although more complicated, should also be attempted and after the appropriate dilution could further assert this methodology.

RESULTS AND DISCUSSION

Nitration of dialkoxycalix[4]crown (MC-6). The nitro calix[4]crown compounds are formed by calixcrown process of cesium removal from a radioactive waste containing nitric acid. As a result of either radical $^{\bullet}NO_2$ induced nitration because of the presence of residual radioactivity or aromatic substitution in 3M HNO_3 *via* NO_2^+ several nitration products can affect the extractant capacity of host substrate by blocking the cavity access for Cs^+ or by damaging the extractant recovery cycle.

Nitration of the 25,27-di-*iso*-propoxycalix[4]arene-crown-6 (MC-6) was studied under different reaction conditions (HNO_3/H_2SO_4, HNO_3/CH_3COOH and KNO_3/CF_3COOH) and different temperature. Although dinitro calix[4]arene ($(NO_2)_2$ MC-6) was formed under all these reaction conditions, the best yields were obtained with KNO_3/CF_3COOH (3 and 18 equivalents to respect with calixcrown) at room temperature. Under these experimental conditions, the dinitro derivative was obtained in 40% yield together with the trinitro compound ($(NO_2)_3$ MC-6) (3%), mononitro (NO_2-MC-6) (3%) and unreacted calix-crown-6 (MC-6) (40%) (Figs 1,3).

NMR spectroscopy studies have suggested that nitration occurs mainly in *para* to the isopropoxy rather than in *para* to the crown position. Strong NOE (Nuclear Overhauser Effect) contacts are present between the singlet of the protons of the nitrated aromatic nuclei and the signals of the protons on the polyether crown bridge. Interestingly, Molecular Modelling experiments show that the products formed are less stable than the corresponding dinitro compounds having nitro groups *para* to the crown ether moiety. However, is generally admitted that the aromatic substitution reactions, SE, are kinetically controlled.

Nitration of calix[4]bis-crown (BC-6). We have performed the calix[4]arene bis crown-6 (BC6) nitration using five soft procedures (a–e) leading to mononitration. The monitoring of this reaction with ESI-MS on Cs^+ spiked solution is fast and efficient methods for nitro compounds detection. The reaction with an excess of nitric acid can lead to tetranitro calix[4]crown compounds which, although formed under radiolytic condition, they are not major or only nitro compounds present in a real nuclear cycle.

The mononitration was carried out according to three modes at low temperature (–78°C) in a presence of acetic anhydride (method a) or trifluoroacetic anhydride (methods b–d). The post reaction mixtures were analyzed *via* ESI after one drop of CsCl molar solution spiking (methods a–e) and with KNO_3/CF_3COOH mixture (method f) with Cs^+(picrate chloride) spiking. It is assumed under these conditions that the nitrosyl acetate CH_3COONO_2 (or trifluoroacetate) is a reagent, which under these conditions released NO_2^+ producing substitution of the aromatic moiety, according to the phenolic ester activation pattern in *para* position [11,12].

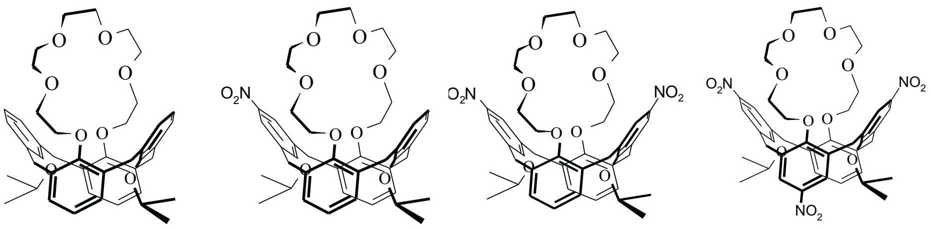
Using acetic anhydride (method a), tetranitro calix[4]arene bis crown-6 ($(NO_2)_4$ BC-6) was a sole product of nitration with a quantitative yield. The Cs^+ ion detection enabled to identify this product (ion at m/z 1141) together with approximately 1% of mononitro calix[4]arene bis crown-6 (NO_2 BC-6), ion at m/z 1006 and roughly the same amount of the starting material (detected from ion at m/z 961). The search for a clean mononitration was done, using methods b–e reaction conditions. With trifluoroacetic anhydride (method b), dinitro $(NO_2)_2$ BC-6 (ion at m/z 1051) was obtained as a major product (90%) (total yield 92%) together with 10% of starting BC-6; mononitro, trinitro $(NO_2)_3$ BC-6 (m/z 1096) and tetranitro $(NO_2)_4$ BC-6 were on trace level. The further modification of reaction conditions (method c, entirely at –78°C) leads to a two product mixture obtained with 52% yield, a ratio of mononitro (NO_2) BC-6 to dinitro $(NO_2)_2$ BC-6 55:45 as identified by corresponding Cs^+ ion complexes.

The remaining 48% of mixture was a starting material BC-6. Finally, in this series of reactions for BC-6, the mononitration only was achieved using diluted nitric acid at –78°C (method d) with 20% yield. The nitration with HNO_3 and acetic anhydride at 0–5°C (procedure e) leads to a mixture of 49% of nitro BC-6 derivatives (with mononitration as a main product at 25%).

The same reaction carried out with HNO_3 and trifluoroacetic acid at room temperature for MC-6, produced three nitro derivatives: dinitro MC-6 (40%), trinitro MC-6 (12%) and mononitro MC-6 at 3% only, the remaining 40% of unreacted MC-6 was recovered (method f).

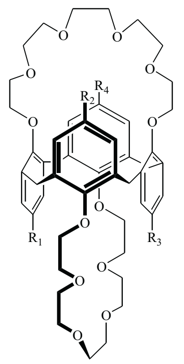
Consequently, the method c, applied to 1,3-diisopropoxy calix[4]arene crown-6 (MC-6) nitration, leads to obtaining of mixture of mononitro (NO_2) MC-6 (40%), dinitro $(NO_2)_2$ MC-6 (50%) together with small quantities of tetranitro $(NO_2)_4$ MC-6 (5%) starting MC-6 (5%) and traces of trinitro MC-6 (total yield of 70% of organic material recovery). The cationization was performed using Cs^+ spiking with two abundant ions at m/z 888 (NO_2 MC-6) and at m/z 933 ($(NO_2)_2$ MC-6) observed (Figs 2,4).

Under this detection method, we assumed that the stability of complexes calix[4]arene crown-Cs^+, for both MC and BC, and their nitro derivatives are similar.



MC-6 **NO_2-MC-6** **$(NO_2)_2$-MC-6** **$(NO_2)_3$-MC-6**

Figure 1. Di-isopropoxycalix[4]arene-mono-crown-6 (MC-6) and its nitro derivatives.



BC-6	$R_1 = R_2 = R_3 = R_4 = H$
NO_2 BC-6	$R_1 = NO_2$ $R_2 = R_3 = R_4 = H$
$(NO_2)_2$ BC-6	$R_1 = R_2 = NO_2$ $R_3 = R_4 = H$
$(NO_2)_3$ BC-6	$R_1 = R_2 = R_3 = NO_2$ $R_4 = H$
$(NO_2)_4$ BC-6	$R_1 = R_2 = R_3 = R_4 = NO_2$

Figure 2. Calix[4]arene-bis-crown-6 (BC-6) and its nitro derivatives.

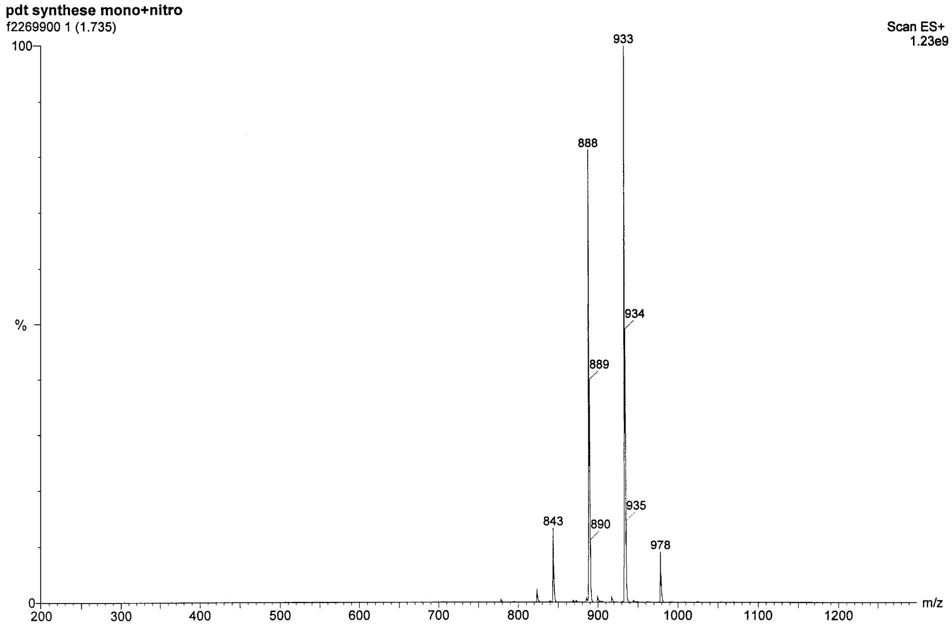


Figure 3. ESI-MS (+) spectrum of nitro-MC-6 derivatives (procedure e, without separation); m/z 843 (MC-6, starting material), 888 (NO_2-MC-6-Cs^+), 933 ((NO_2)$_2$-MC-6-Cs^+), 978 ((NO_2)$_3$-MC-6-Cs^+).

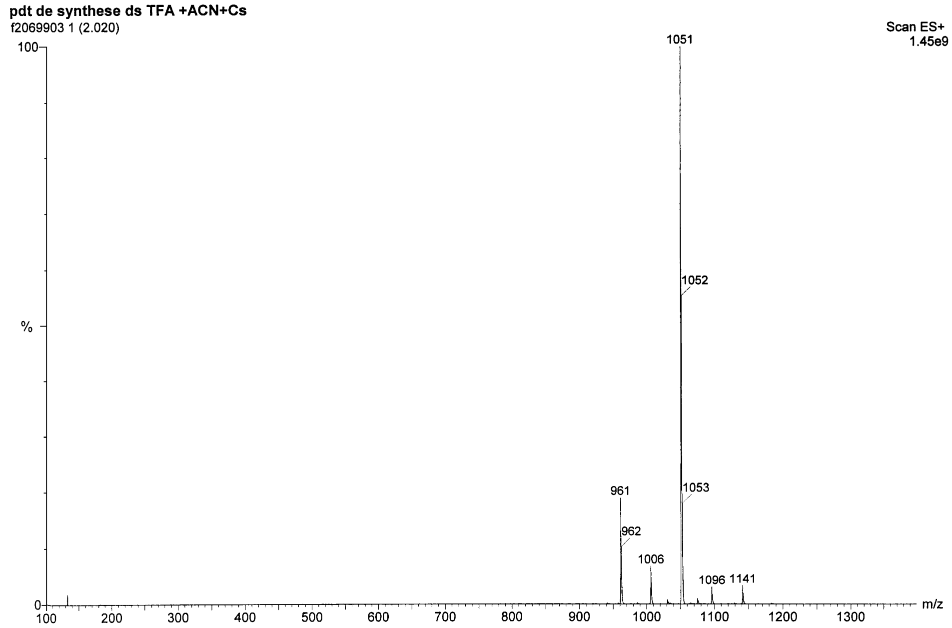


Figure 4. ESI-MS (+) spectrum of nitro-BC-6 derivatives (procedure b, without separation); m/z 961 (BC-6-Cs^+, starting material), 1006 ((NO_2)-BC-6-Cs^+), 1051 ((NO_2)$_2$-BC-6-Cs^+), 1096 ((NO_2)$_3$-BC-6-Cs^+), 1141 ((NO_2)$_4$-BC-6-Cs^+).

Crown ether phosphates (Phosphate ester crown ethers). Simultaneous presence of crown and phosphate functions on the same molecule offered an excellent receptor for cation species. The complexation of Cs$^+$ by crown-6, as well as its capacity to bind the neutral and solvent molecules can be used in a design of an analytic method for a follow-up of this cation species during extraction process. The presence of two or three crown-6 ether cycles attached to phosphate is also a simple way to complex more than one cation. The 2-(hydroxymethyl) 18-crown-6 phosphate synthesis was recently reported [13,14], the triester seems to be easily formed in the reaction of the alcohol with phosphorus oxychloride in pyridine. Although, we were not able to reproduce the reported yield or the purity of this reaction, the treatment of resulting crude mixture with Cs$^+$ leads to detection of triester Cs$^+$ ion at m/z 1059.4 and doubly charged triester Cs$_2^{2+}$ ions (m/z 596.2) but not the complex ion containing three Cs$^+$. Different ionic species enabled to identify a diester at m/z 651, protonated triester at m/z 927 and starting crown alcohol protonated or cationized with one Cs$^+$ (at m/z 295 and 427 respectively) as well as their pyridine adducts (Fig. 5).

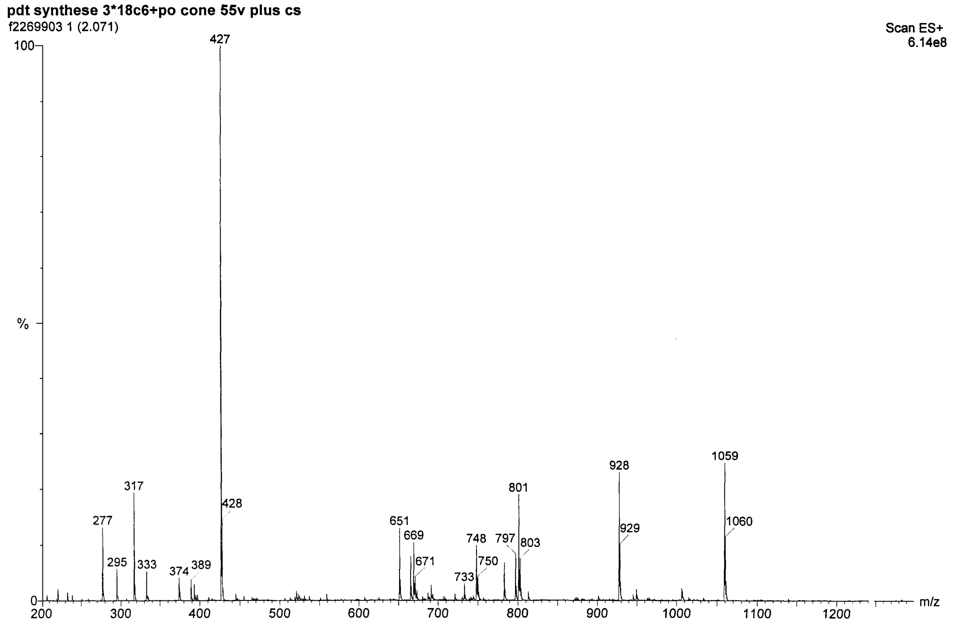


Figure 5. 2-(Hydroxymethyl) 18-crown-6 phosphates synthesis (Schroeder, Gierczyk method without separation); m/z 427 (starting alcohol - Cs$^+$), 651 (diester-H$_2$O-H$^+$), 7 (diester-H$_2$O-Cs$^+$), 927 (triester-H$^+$), 1059 (triester-Cs$^+$), 1006 (triester-H$^+$-pyridine).

The complexation of the triester by one or two cesium cations only was confirmed by molecular modelling. The third Cs$^+$ cation is immediately ejected when MD experiment was performed. The triscrown phosphate privileged one complexation only according to the octopus type stable conformation ((RO)$_3$ P=O geometry) (Fig. 6).

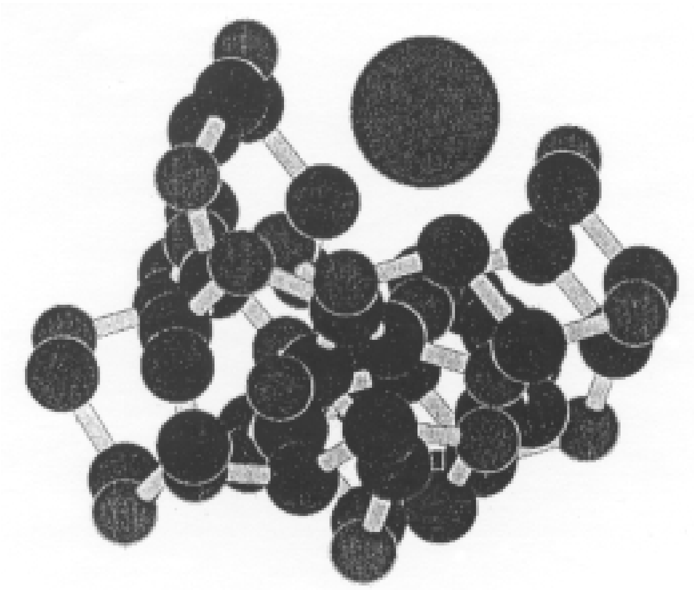


Figure 6. Complexation [2-(hydroxymethyl)-18-crown-6]yl phosphate by Cs^+ (modelling, HyperChem).

Influence of nitration of calixarenes on cesium extraction. Distribution coefficients of sodium and cesium insertion in crown substrate were also studied for some nitrated calixarenes and compared to that of starting **MC-6** and **BC-6**. As expected, the nitration has more effect on distribution coefficients of (NO_2) MC-6 than that (NO_2) BC-6, for the latter the cesium is simply located in the crown opposite to NO_2 [15] (Fig. 7). The steric hindrance of NO_2, which makes difficult the access of cation to the complexation site, is particularly evidenced by very low values of cesium distribution coefficients (D_M, see Experimental) obtained for $(NO_2)_2$ MC-6 and $(NO_2)_4$ BC-6 [16]. These D_M values were obtained in liquid-liquid extraction between the nitric phase and nitrophenylhexylether (NPHE) experiments using ^{22}Na and ^{137}Cs γ activity measurements. Both radioactive isotopes were used as spiking agents to evaluate this distribution coefficient for organic (NPHE) and aqueous nitric phases. The very low distribution coefficients of $(NO_2)_2$ MC-6 are explained by the nitration of benzene units in *para* to di-*iso*-propoxy position. In *para* to crown position, the decrease of extracting ability should be less marked.

Interested by the ESI induced cationization species presence, we have performed a series of MS-MS experiments observing also an important stability of pyridine insertion into the triester Cs^+ ion as well as a similar behavior of the diester Cs^+ ion and its pyridine insert analog, both present in post reaction mixture.

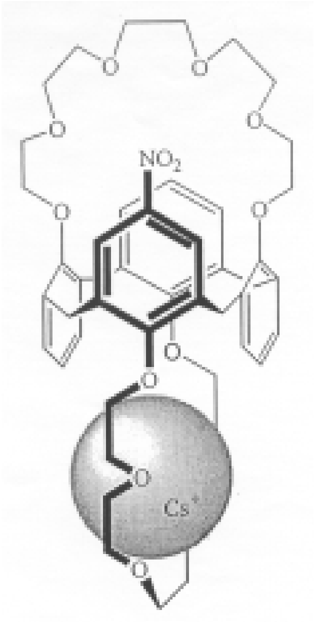


Figure 7. BC-6 complexation with Cs^+.

The cationization with Cs^+ under simple ESI-MS technique was found once more as being an efficient and fast tool for detection of several crown-6 compounds. It was possible, with a careful match between a cationic species and a crown cavity size, to monitor different organic synthetic reactions progress.

This technique enabled also to confirm some preliminary observations from the extraction and chromatographic experiments on the real life waste studies in progress in our laboratories.

Table. Cesium and sodium distribution coefficient of sodium and cesium insertion into host crown substrate D_M ($CsNO_3$ 5×10^{-4} M).

	HNO_3 (1M) $NaNO_3$		**$NaNO_3$ (4M) + HNO_3 (1M)**
	^{22}Na	**^{137}Cs**	**^{137}Cs**
MC-6	$< 10^{-3}$	28.5	18.5
(NO_2) MC-6	$< 10^{-3}$	1.05	0.65
(NO_2)$_2$ MC-6	$< 10^{-3}$	0.04	0.03
BC-6	$< 10^{-3}$	19.5	
(NO_2) BC-6	$< 10^{-3}$	8.5	6
(NO_2)$_4$ BC-6	$< 10^{-3}$	6×10^{-3}	$< 10^{-3}$

EXPERIMENTAL

The ESI (+) mass spectra were recorded on a triple quadrupole Quattro II(Micromass, UK). The sample was dissolved in acetonitrile, spiked with CsCl and introduced through a syringe pump (Harward Apparatus 11, Cambridge, MA, USA) at a rate of 10 μl/min. The ESI-MS was performed in the positive ion mode (+) and the tension of the capillary was maintained at 3 kV. The cone voltage was set first at *ca* 20 V and a skimmer voltage at 1.5 V. The ions detected were monitored over a mass range of m/z 100–1300 in 120 sec. At least 20 scans were averaged to obtain the reported spectra (available from CKJ, U. de Moncton, Moncton, Canada).

The semiquantitative analysis of spectra was performed using starting MC-6 and BC-6 compounds by comparing the results of flash-chromatography on crude mixtures, prior the separation of individual nitro compounds, with those obtained under Cs^+ spiking. The results obtained were within 10% range (*e.g.* for nitration of MC-6), the post reaction crude mixture showed (NO_2) MC-6 to MC-6 ratio of 42÷36 from ESI compared to 40÷40 using flash chromatography (with 10% of the material unaccounted for). This observation meant that no significant difference in relative ratio of nitro compounds was found using these two methods. This problem was discussed in a series of references quoted in this paper [11,12,15,17,18] as well as from our group works (using ERMS curves, solvent-cation affinity study and calibration of ESI spectra) [19,20].

Starting calixarenes mono crown and bis crown were respectively synthesized by Ungaro and Casnati [2] and by Vicens and Asfari [4]. Cesium derivatives were purchased from Johnson-Mattey Chemicals (Royster, UK). The ESI solvent acetonitrile, HPLC 99.8%, was purchased from Carlo Erba (France).

For some of these compounds, the CI (+) (CH_4, Finnigan MAT SSQ710) or FAB (+) mass spectra, were also recorded. The structure determination of most of nitro compounds were confirmed by NMR spectroscopy.

^{1}H NMR spectra were recorded on a Bruker 200 MHz or 300 MHz using TMS as internal standard, chemical shifts δ are expressed in ppm and coupling constant J in Hz. TLC were performed on precoated silica gel plates Merck 60 F_{254}. The molecular modelling was done using Hyper Chem II (Mm+). All calculated energy values for calix[4]arene crown compounds of this series are also available on request.

Nitration of MC-6. To a solution of MC-6 (0.800 mg, 1.12 mmol) in dry CH_2Cl_2 (15 mL), KNO_3 (0.341 mg, 3.37 mmol) was added and the mixture was stirred at room temperature under dry nitrogen atm for one hour. Upon addition of trifluoroacetic acid (TFA, 1.56 mL, 0.02 mol) the reaction mixture turns dark violet. After 24 hours the reaction was quenched with water (20 mL) and the organic layer separated. Dichloromethane was evaporated *in vacuo* and an orange solid residue was submitted to flash chromatography (SiO_2, hexane/ethyl acetate (3/2)). The $(NO_2)_2$ MC-6 was obtained in 40% yield together with $(NO_2)_3$ MC-6 (3%) and NO_2 MC-6 (3%), the starting MC-6 being at 40%.

Nitration of BC–6.

Procedure a. 10 mg of BC-6 in 0.5 mL of CH_2Cl_2 was stirred at –78°C. At this temperature, 0.04 mL of HNO_3 (conc.) was added, the mixture turned immediately brown. Slowly, the temperature was brought to 25°C and 0.05 mL of acetic anhydride was added, then reaction continued at –78°C for five minutes. The mixture was taken out of cooling bath and 2 mL of CH_2Cl_2 were added at room temperature. The dichloromethane solution was treated with an excess of triethylamine, extracted twice with 2 mL of CH_2Cl_2. The organic extracts were then washed with water, HCl 0.1 M, once more with water and saturated solution of NaCl. CH_2Cl_2 fraction was dried over anhydrous $MgSO_4$, producing after evaporation 12 mg of material analyzed by ESI. Total calix[4]arene products yield: quantitative, the major identified product $(NO_2)_4$ BC-6 99%.

Procedure b. Same as in a, except the use of trifluoroacetic anhydride instead of acetic anhydride. The persistent brown coloration was observed with the HCl 0.1 M work-up step. Yield: 9.3 mg of mixture analyzed by ESI. Major product $(NO_2)_2$ BC-6 (92%).

Procedure c. Reaction followed the same pathway that b but entirely at –78°C (except extraction and work-up). Yield: 5.3 mg (52% of nitro compounds, 48% of starting BC-6). Major products (NO_2) BC-6 55%, $(NO_2)_2$ BC-6 45%.

Procedure d. Reaction made entirely at –78°C with HNO_3 (3%) according to procedure b gave (NO_2) BC-6 (20%), and 80% of recovered BC-6 (starting material).

Procedure e. A mixture of BC-6 (0.828 g, 1 mmol), dichloromethane (40 mL) and acetic anhydride (20 mL) was placed in constant temperature at 0 and 5°C, then concentrated nitric acid (10 mL) was added. After 2.5 h, water and dichloromethane were added to stop the reaction. The organic layer was dried over $MgSO_4$, filtered and evaporated on rotary evaporator. The residue was chromatographed on a silica column using 80:20 dichloromethane – acetone as eluent to afford: NO_2 BC-6 (220 mg, 25%, R_f 0.39), $(NO_2)_2$ BC-6 (101 mg, 11%, R_f 0.54), $(NO_2)_3$ BC-6 (71 mg, 8%, R_f 0.71), $(NO_2)_4$ BC-6 (50 mg, 5%, R_f 0.79), and starting material BC-6 (423 mg, 51%, R_f 0.34).

Extraction. The β, γ emitters ^{22}Na, ^{137}Cs used for spiking the waste simulant were obtained from Amersham. The solvent nitro phenyl hexyl ether (NPHE), synthesized by Eras Labo (Isére, France), was used without further purification. Calixarenes were dissolved in NPHE at a concentration of 10^{-2} M in NPHE. Liquid-liquid experiments were performed by contacting for one hour the same volume of organic and aqueous nitric phases inside agitated tight tubes placed in a constant temperature enclosure (25 ± 0.2°C). Complete separation of phases was ensured by placing the tubes into a centrifuge for five minutes. Then aliquots of aqueous and organic were removed for analysis by γ spectrometry (Eurysis Measures). The measurement duration were adapted to obtain a reproducibility between ± 5%.

The distribution coefficients D_M were determined as the ratio of cation γ activity in the organic phase to γ cation activity in the aqueous phase [15,16].

$$D_M = \frac{\sum[\overline{M}]}{\sum[M]}$$

NMR General.

NO_2 MC-6 (11-Nitro-25,27-di-*iso*-propoxycalix[4]arene-26,28-crown-6). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.00 (s, 2H, NO_2ArH), 7.06 (d, 2H, ArH, J = 7.3 Hz), 7.04–6.99 (m, 4H, ArH), 6.81 (t, 3H, ArH, J = 7.3 Hz), 4.46–4.36 (m, 1H, $\mathrm{OC}H(\mathrm{CH_3})_2$), 4.25–4.17 (m, 1H, $\mathrm{OC}H(\mathrm{CH_3})_2$), 3.88 (d, 2H, ArCHAr, J = 15.6 Hz), 3.83 (d, 2H, ArCHAr, J = 15.8 Hz), 3.80 (d, 2H, ArCHAr, J = 15.6 Hz), 3.75 (d, 2H, ArCHAr, J = 15.8 Hz), 3.64 (s, 4H, OCH_2CH_2O), 3.61–3.44 (m, 12H, crown), 3.35–3.27 (m, 4H, crown), 0.95 (d, 6H, $\mathrm{OCH}(\mathrm{C}H_3)_2$, J = 6.1 Hz), 0.88 (d, 6H, $\mathrm{OCH}(\mathrm{C}H_3)_2$, J = 6.1 Hz); MS (PI-CI) m/z: 757 $(MH)^+$ 100%.

$(NO_2)_2$ MC-6 (11,23-Dinitro-25,27-di-*iso*-propoxycalix[4]arene-26,28-crown-6). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.00 (s, 4H, NO_2ArH), 7.04 (d, 4H, ArH, J = 7.5 Hz), 6.86 (t, 2H, ArH, J = 7.5 Hz), 4.43–4.37 (m, 2H, $\mathrm{C}H(\mathrm{CH_3})_2$), 3.91 (d, 4H, ArCHAr, J = 16.0 Hz), 3.83 (d, 4H, ArCHAr, J = 16.0 Hz), 3.59 (t, 4H, $\mathrm{ArOC}H_2\mathrm{CH_2O}$, J = 6.3 Hz), 3.56 (s, 4H, $\mathrm{OC}H_2\mathrm{C}H_2\mathrm{O}$), 3.53–3.45 (m, 8H, $\mathrm{ArOCH_2CH_2OC}H_2\mathrm{C}H_2\mathrm{O}$), 3.21 (t, 4H, $\mathrm{ArOCH_2C}H_2\mathrm{O}$, J = 6.3 Hz), 0.90 (d, 12 H, $\mathrm{CH}(\mathrm{C}H_3)_2$, J = 6.0 Hz); MS (PI-CI) m/z: 801 $(MH)^+$ 30%.

$(NO_2)_3$ MC-6 (5,11,23-Trinitro-25,27-di-*iso*-propoxycalix[4]arene-26,28-crown-6). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.04 (s, 4H, NO_2ArH), 8.02 (s, 2H, NO_2ArH), 7.05 (d, 2H, ArH, J = 7.5 Hz), 6.87 (t, 1H, ArH, J = 7.5 Hz), 4.47–4.41 (m, 2H, $\mathrm{OC}H(\mathrm{CH_3})_2$), 3.94–3.82 (m, 8H, $ArCH_2Ar$), 3.64 (t, 2H, $\mathrm{ArOC}H_2\mathrm{CH_2O}$, J = 5.6 Hz), 3.56–3.43 (m, 16H, OCH_2CH_2O), 3.21 (t, 2H, $\mathrm{ArOCH_2C}H_2\mathrm{O}$, J = 5.6 Hz), 1.01 (d, 6H, $\mathrm{CH}(\mathrm{C}H_3)_2$, J = 6.0 Hz), 0.93 (d, 6H, $\mathrm{CH}(\mathrm{C}H_3)_2$, J = 6.0 Hz); MS (PI-CI) m/z: 846 $(MH)^+$ 100%.

NO_2 BC-6: ^{1}H NMR (200 MHz, $CDCl_3$): δ 3.91 (m, 8H, O-CH_2), 3.42–3.54 (m, 8H, O-CH_2), 3.58–3.64 (m, 16H, O-CH_2), 3.65 (s, 4H, Ar-CH_2), 3.70 (s, 4H, Ar-CH_2), 3.82–3.96 (m, 8H, O-CH_2), 6.91 (m, 3H, H Ar), 7.12 (m, 6H, H Ar), 8.04 (s, 2H, NO_2-Ar H), m/z (PI-FAB) 814.5 (MH^+) [16].

$(NO_2)_2$ BC-6: ^{1}H NMR (200 MHz, $CDCl_3$): δ 3.25–3.91 (m, 48H, O-CH_2, Ar-CH_2), 6.89–6.97 (m, 2H, H Ar), 7.10–7.16 (m, 4H, H Ar), 8.04 (s, 4H, NO_2-Ar H), m/z (PI-FAB) 919.3 (MH^+).

$(NO_2)_3$ BC-6: ^{1}H NMR (200 MHz, $CDCl_3$): δ 3.25–3.95 (m, 48H, O-CH_2, Ar-CH_2), 6. 98 (t, J = 7 Hz, 1H, H Ar), 7.16 (d, J = 7 Hz, 2H, H Ar), 8.06 (s, 2H, H Ar), 8.08 (s, 4H, NO_2-Ar H), m/z (PI-FAB) 1005.6 $(M + Na + H_2O)^+$.

$(NO_2)_4$ BC-6 : ^{1}H NMR (200 MHz, $CDCl_3$): δ 3.39 (t, J = 6 Hz, 8H, O-CH_2), 3.49 (s, 16H, O-CH_2), 3.53 (s, 8H, Ar-CH_2), 3.74 (t, J = 6 Hz, 8H, O-CH_2), 3.97 (s, 8H, O-CH_2), 8.10 (s, 8H, NO_2-Ar H), m/z (PI-FAB) 1009.3 (MH^+).

Acknowledgments

The authors are indebted to H. Virelizier and C. Moulin, heads of LAMOG and LASSO Laboratories respectively, CEA, Saclay (France) for precious help in realizing this work and in development of the ESI methodology. Dr. V. Lamare (CEA, Cadarche, France) comments on the molecular modelling were greatly appreciated.

REFERENCES

1. Dozol J.F., Bohmer V., McKervey A., Lopez Calahorra F., Reinhoudt D., Schwing M.J., Ungaro R. and Wipff G., EUR 17615 EN (1995).
2. Casnati A., Pochini A., Ungaro R., Ugozzoli F., Arnaud F., Fanni S., Schwing M.-J., Egberink R.J.M., de Jong F. and Reinhoudt D.N., *J. Am. Chem. Soc*., **117**, 2767 (1995).
3. Ungaro R., Casnati A., Ugozzoli F., Pochini A., Dozol J.F., Hill C. and Rouquette H., *Angew, Chem. Int. Ed. Engl*., **33**, 1506 (1994).
4. Asfari Z., Bressot C., Vicens J., Hill C., Dozol J.F., Rouquette H., Eymard S., Lamare V. and Tournois B., *Anal. Chem*., **67**, 3133 (1995).
5. Hill C., Dozol J.F., Lamare V., Rouquette H., Eymard S., Tournois B., Vicens J., Asfari Z., Bressot C., Ungaro R. and Casnati A., *J. Incl. Phenom*., **19**, 399 (1994).
6. Haverlock T.J., Bonnesen P.V., Schleben R.A. and Moyer B.A., *Radiochim. Acta*, **76**, 103 (1997).
7. Bonnesen P.V., Delmau L.H., Myer B.A. and Leonard R.A., *Solvent Extr. Ion Exch*., **18**, 1107 (2000).
8. Lamare V., Dozol J.F., Ugozzoli F., Casnati A. and Ungaro R., *Eur. J. Org. Chem*., 1559 (1998).
9. Lamare V., Dozol J.F., Fuangswasdi S., Arnaud-Neu F., Thuery P., Nierlich M., Asfari Z. and Vicens J., *J. Chem. Soc., Perkin Trans. 2*, 271 (1999).
10. Bayer E., Gfrorer P. and Rentel C., *Angew. Chem. Int. Ed*., **38**, 992 (1999).
11. Allain F., Jankowski C.K., Tabet J.C., Moulin C. and Virelizier H., *Spectroscopy*, **14**, 127 (2000).
12. Allain F., Thèse, U de P et M Curie, Paris VI (2000), pp. A1-42.
13. Schroeder G. and Gierczyk B., *Polish J. Chem*., **71**, 754 (1997).
14. Krishnamohan Sharma C.V. and Clearfield A., *J. Am. Chem. Soc*., **122**, 1558 (2000).
15. Lamare V., Dozol J.F., Allain F., Virelizier H., Moulin C., Jankowski C. and Tabet J.-C., "Calixarenes Molecules for Separations" ACS Symposium Series 757, Chapitre 5, G. Lumetta, R.D. Rogers, A.S. Gopalan Eds, American Chemical Society, Washington DC, 2000, p. 56.
16. Dozol H., Asfari Z., Vicens J., Thuery P., Nierlich M. and Dozol J.F., *Tetrahedron Lett*., (accepted) (2001).
17. Young D.S., Hung H.-Y. and Liu L.K., *Rapid Commun. Mass Spectrom*., **11**, 769 (1997).
18. Kempen E.C. and Brodbelt J.S., *Anal. Chem*., **72**, 5411 (2000).
19. Lesage D., Virelizier H., Tabet J.C. and Jankowski C.K., *Rapid Commun. Mass Spectrom*., **15**, 1947 (2001).
20. Lesage D., Virelizier H., Tabet J.C. and Jankowski C.K., *Spectroscopy*, **13**, 275 (1997).