Tetrahedron 65 (2009) 5893–5898

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Di-ionizable *p-tert*-butylcalix[4]arene-1,3-crown-4 ligands: synthesis and alkaline earth metal cation extraction

Xiaodong Liu, Kazimierz Surowiec, Richard A. Bartsch *

Department of Chemistry and Biochemistry, Texas Tech University, Lubbock, TX 79409-1061, USA

ARTICLE INFO

Article history:
Received 5 May 2009
Received in revised form 29 May 2009
Accepted 2 June 2009
Available online 10 June 2009

Keywords:
Calixarenes
Crown ethers
Ionic recognition
Solvent extraction

ABSTRACT

A series of di-ionizable calix[4]arene-1,3-crown-4 compounds has been synthesized. The ionizable groups are oxyacetic acid and *N*-(X)sulfonyl oxyacetamide groups with X=methyl, phenyl, 4-nitrophenyl and trifluoromethyl, which 'tunes' the acidity of the latter. The efficiency and selectivity of these novel ligands are assessed with competitive solvent extractions of alkaline earth metal cations from aqueous solutions into chloroform. The results are compared with those reported previously for calix[4]arene-crown analogues with crown-6 and crown-5 rings.

1. Introduction

In calixarene-crown ethers, also called calixcrowns, a calixarene scaffold is combined with a crown ether unit connecting two phenolic oxygens of the former with a polyether chain.[1–6] Most common are calix[4]arene-1,3-crown compounds in which a calix[4]arene platform is connected with a polyether fragment that bridges two distal phenolic oxygens. The first example of this ligand family, *p-tert*-butylcalix[4]arene-1,3-crown-6, was reported by Ungaro and co-workers in 1983.[7] In calix[4]arene-crown compounds, depending on the synthetic conditions used, the bridging polyether unit can lock the calixarene framework in cone, partial cone, or 1,3-alternate conformations.

Of particular interest to our metal ion separations research program are calix[4]arene-crown compounds with two acidic pendant groups attached to the remaining phenolic oxygens. Such ligands provide efficient extraction of divalent metal ions from aqueous solutions into organic diluents.[8–17] The extraction proceeds by an ion-exchange mechanism to form an electroneutral di-ionized calixcrown-divalent metal ion complex in the organic phase, thereby avoiding the need for concomitant transfer of a hydrophilic anion from the aqueous phase.

The initial example of such a di-ionizable calixcrown compound, cone *p-tert*-butylcalix[4]arene-1,3-crown-5 dicarboxylic acid **2a** (Fig. 1) was reported by Ungaro and Pochini in 1984.[18]

Previously we reported the synthesis and alkaline earth metal ion extraction behavior of di-ionizable *p-tert*-butylcalix[4]arene-1,3-crown-6 ligands in the cone (**3a**–**e**), partial cone (**6a**–**e**), and 1,3-alternate (**9a**–**e**) conformations.[8] In these series, the pendant di-ionizable groups included oxyacetic acid groups and *N*-(X)sulfonyl oxyacetamide groups. In the latter, variation of the electron-withdrawing ability of X 'tunes' the acidity of the ligand. For competitive solvent extraction of four alkaline earth metal cation species from aqueous solutions into chloroform, the cone conformers **3a**–**e** exhibited very high Ba^{2+} selectivity with high extraction efficiency. In the cone conformation, one ionized group is positioned above and the other below a divalent metal ion complexed within the polyether cavity. For a given ionizable group, the extraction selectivity decreased in the order: cone>1,3-alternate>partial cone.

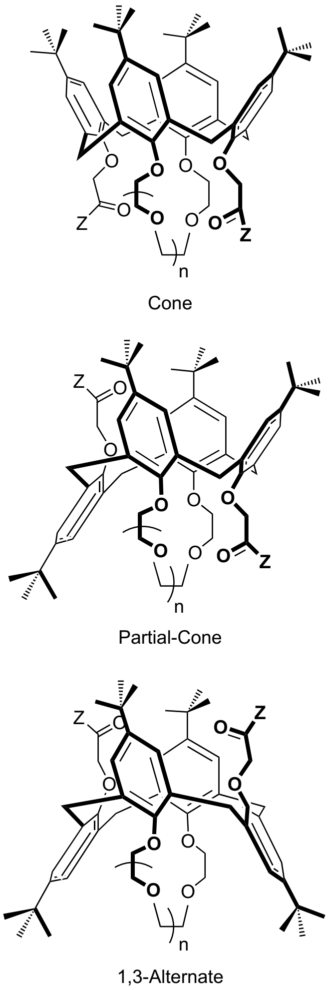
To probe the influence of decreasing the crown ether ring size, an analogous series of di-ionizable *p-tert*-butylcalix[4]arene-1,3-crown-5 ligands in the cone (**2a**–**e**), partial cone (**5a**–**e**), and 1,3-alternate (**8a**–**e**) conformations were prepared.[9] For competitive extraction of four alkaline earth metal cation species from aqueous solutions into chloroform by the dicarboxylic acid ligands **2a**, **5a**, and **8a**, the partial cone conformer **5a** was found to be the most effective extractant with a very high selectivity for Ba^{2+}. Of the three ligands, cone conformer **2a** gave the poorest extraction selectivity and extracted approximately the same amounts of Sr^{2+} and Ba^{2+}.

In light of this puzzling difference in alkaline earth metal cation extraction selectivity when the crown ring size was decreased from crown-6 to crown-5, we envisioned series of di-ionizable *p-tert*-

---

* Corresponding author. Tel.: +1 806 742 3069; fax: +1 806 742 1289.
E-mail address: richard.bartsch@ttu.edu (R.A. Bartsch).

0040-4020/$ – see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2009.06.004



	n
1	1
2	2
3	3
4	1
5	2
6	3
7	1
8	2
9	3

	Z
a	-OH
b	$-NHSO_2Me$
c	$-NHSO_2Ph$
d	$-NHSO_2C_6H_4$-4-NO_2
e	$-NHSO_2CF_3$

Figure 1. Structures of di-ionizable *p-tert*-butylcalix[4]arene-1,3-crown compounds.

butylcalix[4]arene-1,3-crown-4 ligands. We now report the results of these synthetic endeavors and the alkaline earth metal cation extraction behavior of the resultant ligands.

2. Results and discussion

2.1. Synthesis of new di-ionizable calix[4]arene-1,3-crown-4 ligands

The synthesis of cone di-ionizable *p-tert*-butylcalix[4]arene-1,3-crown-4 compounds **1a**–**e** was performed as depicted in Scheme 1. Using the procedure of Shinkai and co-workers,[19] *p-tert*-butylcalix[4]arene (**10**) was reacted with triethylene glycol ditosylate and Na_2CO_3 in MeCN to provide *p-tert*-butylcalix[4]arene-1,2-crown-4 (**11**). Reaction of **11** with NaH and ethyl bromoacetate in THF at room temperature gave the diester **12** in 80% yield. The diester was hydrolyzed with Me_4NOH in refluxing aqueous THF to produce di(carboxylic acid) **1a** in 99% yield. Treatment of **1a** with oxalyl chloride in refluxing benzene gave the corresponding di(acid chloride) **13**, which was reacted with the sodium salt forms of commercially available sulfonamides in THF to form ligands **1b**–**e** in 70–97% yields.

The cone conformation of di-ionizable *p-tert*-butylcalix[4]arene-1,3-crown-4 ligands **1a**–**e** was established by their ^1H and ^{13}C NMR spectra. There were no peaks between 35 and 40 ppm in the ^{13}C NMR spectra for the five compounds, showing that all four benzene rings have *syn* arrangements. In the ^1H NMR spectra, the methylene bridge ($ArCH_2Ar$) protons exhibited a typical AX pattern, that is two widely spaced doublets at δ 4.16–4.29 and 3.10–3.24 for the *exo*- and *endo*-geminal protons, respectively.

The envisioned synthetic route to di-ionizable *p-tert*-butylcalix[4]arene-1,3-crown-4 analogs **7a**–**e** in the 1,3-alternate conformations is presented in Scheme 2. Reaction of *p-tert*-butylcalix[4]arene-1,3-crown-4 with KH and ethyl bromoacetate in THF at room temperature gave an 80% yield of diester **14**. Hydrolysis with Me_4NOH in aqueous THF at reflux produced a near quantitative yield of di(carboxylic acid) **7a**. However, after heating di(carboxylic acid) **7a** with oxalyl chloride in benzene at reflux for 5 h there was no evidence (shift in the C═O absorption in the IR spectrum) for formation of di(acid chloride) **15**. Increasing the reaction time to 15 h gave the same result. Attention was then shifted to the use of thionyl chloride as reactant and solvent. It was found that heating **7a** in thionyl chloride (5 mL/g of **7a**) at reflux for 24 h gave a clean conversion into di(acid chloride) **15**, as shown by the shift of the C═O absorption from 1767 cm^{-1} to 1815 cm^{-1}. The attempt to convert the crude **15** into **7b** using the conditions that were successfully applied to the cone di(acid chloride) **13**, gave no reaction. Heating of the mixture of **15**, NaH, and $CH_3SO_2NH_2$ in THF at reflux for 24 and 48 h also produced no reaction. Likewise, substituting $CF_3SO_2NH_2$ for $CH_3SO_2NH_2$ gave no reaction. Apparently the flanking *tert*-butyl groups in the 1,3-alternate di(acid chloride) **15** provide steric hindrance to attack by $XSO_2NH^-Na^+$ at the carbonyl carbon.

The 1,3-alternate conformation of di(carboxylic acid) **7a** was verified by its ^1H and ^{13}C NMR spectra. Both the aromatic and *tert*-butyl protons gave two singlets that are closer together than those for the cone analogue **1a**. The methylene bridge ($ArCH_2Ar$) protons