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Tetrahedron Letters 47 (2006) 3443–3446

Tetrahedron Letters

Di-ionizable *p-tert*-butylcalix[4]arene-1,2-crown-4 ligands: synthesis and high divalent metal ion extraction selectivity

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Received 15 January 2006; revised 7 March 2006; accepted 9 March 2006
Available online 30 March 2006

Abstract—Di-ionizable *p-tert*-butylcalix[4]arene-1,2-crown-4 ethers in the cone conformation are synthesized with their conformation and regioselectivity verified by NMR spectroscopy. The new ligands are efficient extractants with high selectivity for Ba^{2+} in competitive solvent extraction of alkaline earth metal cations from aqueous solutions into chloroform.

Calix[4]arene is an important scaffold for the construction of new metal ion receptors. Introduction of a polyether loop on the lower rim of calix[4]arene not only increases the cation binding ability of the parent calix[4]arene, but allows control of the selectivity through modulation of the crown ether ring size.[1]

Two types of polyether chain bridging on the lower rim of a calix[4]arene molecule are possible: 1,3-bridging of distal phenolic units and 1,2-bridging of proximal phenolic units. To date, the study of calix[4]arene-crown compounds has been heavily focused on the 1,3-bridged isomers. This type of ligand was found to exhibit high binding affinity and selectivity in alkali and alkaline earth metal cation extractions.[2] In contrast, research on 1,2-bridged calix[4]crowns lags far behind. Reported examples are sparse. From the limited available information, 1,2-bridged ligands are expected to exhibit poor binding ability and selectivity toward metal cations.[3]

Earlier work has shown that incorporation of a pendant proton-ionizable group into calix[4]arenes can dramatically enhance their metal ion extraction efficiency compared with non-ionizable analogues. The ionized group not only participates in cooperative metal ion coordination, but also eliminates the need to transfer aqueous phase anions into the organic phase during extraction by operating in a cation-exchange mode with the metal cation.[4]

We now report the preparation of five di-ionizable *p-tert*-butylcalix[4]arene-1,2-crown-4 compounds in the cone conformation and evaluation of their alkaline earth metal cation extraction abilities.

p-tert-Butylcalix[4]arene-1,2-crown-4 (**1**) was synthesized by a reported method[3c] and reacted with ethyl bromoacetate and NaH in THF for 48 h to give diester **2** in 70% yield (Scheme 1). Hydrolysis of diester **2** with tetramethylammonium hydroxide in aqueous THF gave diacid **3** in nearly quantitative yield. Di-acid **3** was converted into the corresponding di(acid chloride) by reaction with oxalyl chloride in benzene at 50–55 °C for 12 h. Formation of the di(acid chloride) was verified by IR spectroscopy with the appearance of a strong carbonyl group absorption at 1810 cm^{-1} and disappearance of the carbonyl group absorption for **3** at 1748 cm^{-1}. The di(acid chloride) was reacted with appropriate sulfonamide anions to afford cone, di-ionizable *p-tert*-butylcalix[4]arene-1,2-crown-4 compounds **4**–**7** in 42–85% yields.[5,6]

The conformation and regioselectivity of **3**–**7** were verified by NMR spectroscopy. For example, for compound **5**[7] there are no peaks between 36 and 40 ppm in the ^{13}C NMR spectrum, revealing that all four benzene rings have *syn*-arrangements.[8] In the ^{1}H NMR spectrum, the bridging methylene protons of the calix[4]arene framework are split into three pairs of doublets with relative integrations of 1, 1 and 2, marked as 2, 3, 4

Keywords: Calixarene; Crown ether; Solvent extraction; Alkaline earth metal cations.

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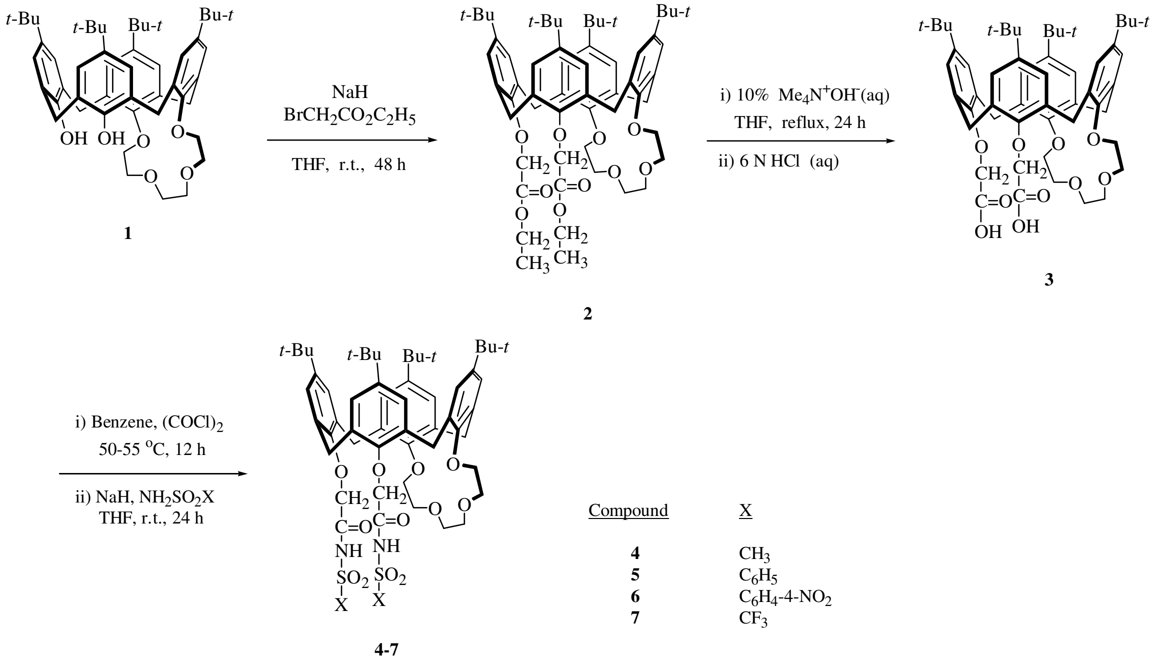
doi:10.1016/j.tetlet.2006.03.060



1

2

3

4-7

Compound	X
4	CH_3
5	C_6H_5
6	C_6H_4-4-NO_2
7	CF_3

Scheme 1. Synthesis of di-ionizable *p-tert*-butylcalix[4]arene-1,2-crown-4 ethers **3**–**7**.

(axial) and 2′, 3′, 4′ (equatorial) in Figure 1. These absorptions are correlated with each other, which demonstrates that the polyether ring is attached to the calix[4]arene scaffold through proximate phenolic oxygens. The correlated peaks are separated by more than 1 ppm, which verifies that the calix[4]arene molecule is in the cone conformation.[3f,8] The two methylene protons in the ionizable side arms ($–OCH_2C(O)–$), marked as 1 and 1′ in Figure 1, are diastereotopic. They are correlated with each other.

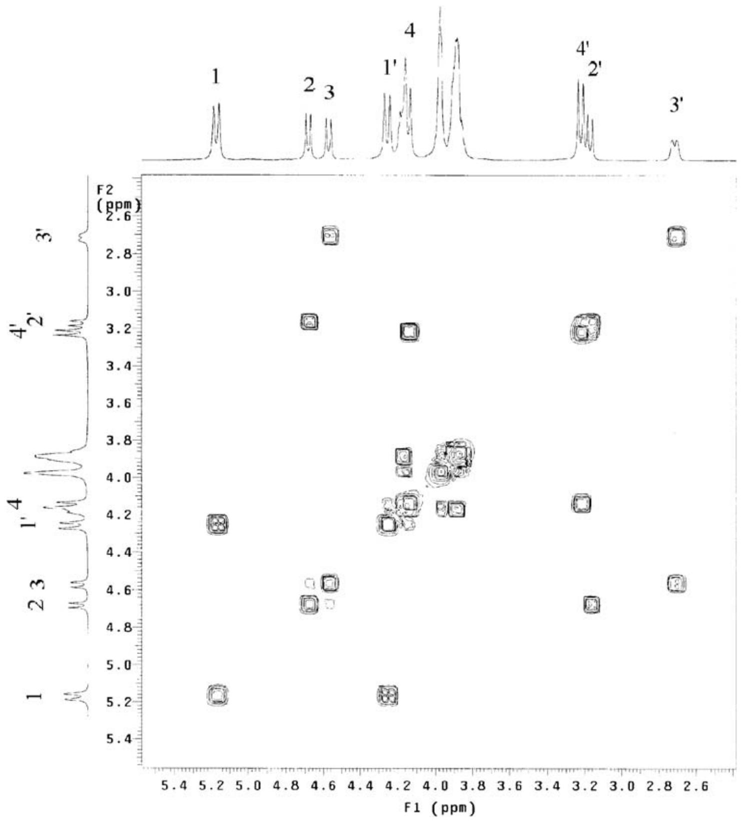


Figure 1. $^1H–^1H$ COSY spectrum for compound **5**.