Preparation of Diaza Dioxa Dithia Crown *p-tert*-Butylcalix[4]arene by S-Alkylation Reactions: Use of Metallo-Calix[4]arene Complexes as Reaction Templates

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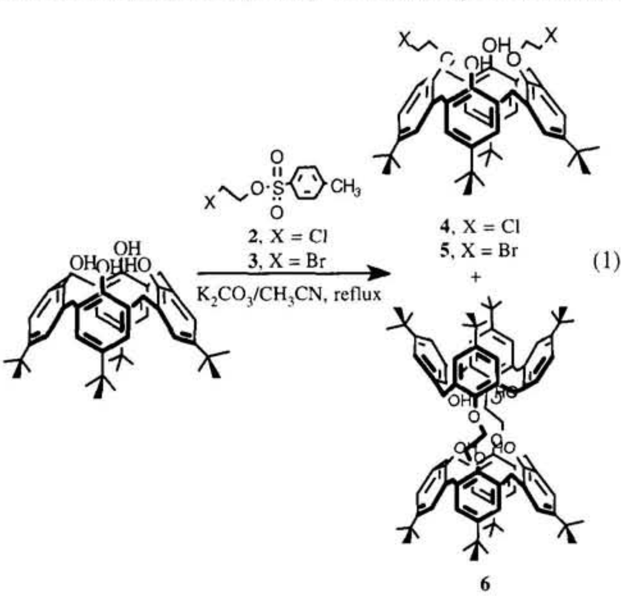
New nickel-thiolato-calix[4]arene complexes were produced by mean of metal-template synthesis employing S-alkylation of a nickel thiolato complex with a dichloroethyl- or a dibromoethyl-calix[4]arene derivative. Demetallation of a nickel-thiolato-calix[4]arene complex resulted in a *p-tert*-butylcalix[4]arene derivative containing two N-, two O- and two S-donors.

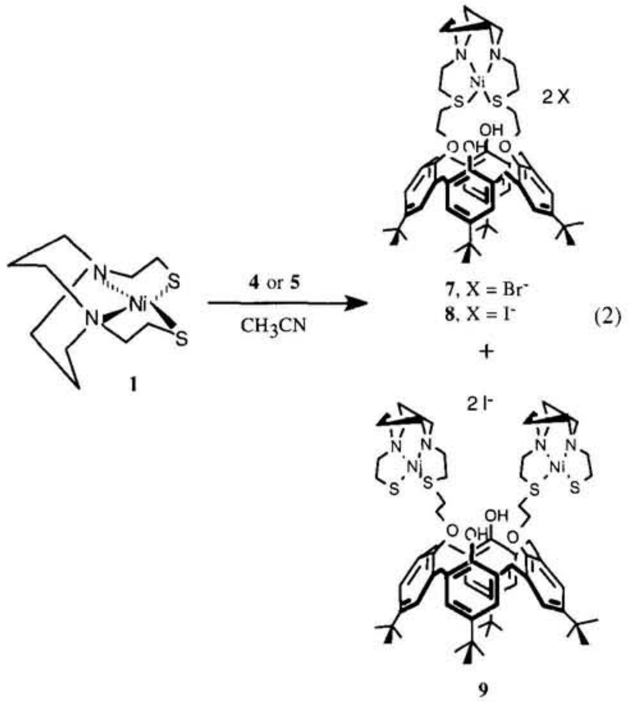
Reports of closed-ring crown ether type derivatives of calix[4]arenes which possess sulfur donors are quite rare compared to those containing nitrogen and oxygen donors.[1] This scarcity may stem from the difficulty in handling the mercaptan ligands due to their facile oxidizability to disulfide or polymerization. One way to overcome this obstacle is to use a metal thiolate complex as template for synthesizing macrocyclic compounds containing sulfur donors usually by S-alkylation reaction. Classic examples of this method were described by Busch et al.[2]

A well-known square planar nickel(II) thiolate, (bme-daco)Ni or **1**, containing two nitrogen and two sulfur donors synthesized by the Darensbourg group has been demonstrated its versatility as a bidentate metallo-thiolate ligand.[3] The available lone pairs on the thiolate sulfurs of **1** can also act as nucleophiles towards alkyl halides to produce a number of macrocyclic nickel complexes which possess interesting $Ni^{II/I}$ redox potential.[4]

We would like to prepare a calix[4]arene derivative containing a macrocyclic N-, O- and S- donors by modifying the lower rim OH moiety. On this account we employ **1** as a precursor for N- and S-atom donors and a nucleophile, and dichloroethyl-calix[4]arene (**4**) or dibromoethyl-calix[4]arene (**5**) as a precursor for an O-atom donor and alkylating agent. The synthetic methodology for **4** and **5** is represented by equation 1. Chloroethyl tosylate (**2**) and bromoethyl tosylate (**3**) were prepared from the reaction of 2-chloroethanol and 2-bromoethanol, respectively, with *p*-toluenesulfonylchloride in the presence of triethylamine and a catalytic amount of 4-dimethylaminopyridine (DMAP). The nucleophilic substitution reaction between *p-tert*-butylcalix[4] arene and **2** (2 equivalence) in acetonitrile in the presence of K_2CO_3 then yielded the dichloroethyl-calix[4]arene precursor (**4**) which could be readily separated from the reaction mixture by precipitating with methanol (67%). However, the similar reaction of the bromo substituent **3** (2 equivalence) with *p-tert*-butylcalix[4]arene gave a mixture of products which were separated on a silica gel column. Using a 40% mixture of hexane/methylene chloride as eluant gave in order dibromoethyl-calix[4]arene (**5**) and calix[4]arene dimer (**6**) in 23% and 41% yield, respectively. ^1H NMR spectra and elemental analysis results of compounds **4**-**6** agree with the proposed structures.[5]

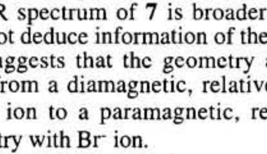
The alkylation reactions of the metallo nucleophile **1** with **4** and **5** are shown in equation 2. Under a nitrogen atmosphere, dropwise addition of purple acetonitrile solution of **1** into a mixture of **4** and NaI gradually shifted the color of the solution to dark red upon stirring at reflux for 48 h. The mixture was then separated on a silica gel column. Elution with a mixture of 15% $MeOH/CH_2Cl_2$ gave in order the yellowish green Ni-calix[4]arene complex (**8**) in 11% yield, a unidentified green complex[6] and the bisNi-calix[4]arene complex (**9**) in 35% yield. The distribution of the products depends largely on the concentration of reagents. Increasing the concentration enhanced the yield of **9** and lowered that of **8**. On the other hand, a reaction of **1** with **5** resulted in higher yield (18%) of the green Ni-calix[4]arene complex (**7**). All reactions presented in equation 2 yielded the trimetallic complex which adhered on silica gel as a by-product.[7]





Complexes **8** and **9** were characterized by ^{1}H NMR and MALDI-TOF MS.[8] Due to the paramagnetic contribution from the nickel centers in these complexes their ^{1}H NMR spectrum were broad in ~2-4 ppm region where signals of the protons from component **1** should appear. Nevertheless, some characteristic of the complexes can be deduced when compared the integral ratio of proton signals of calix[4]arene aromatic protons with overall proton signals appearing between 2-4 ppm which belong to the segment of **1**, the methylene bridges between the phenolic units and the ethano bridges on the lower rim of calix[4]arene. For **8**, the ^{1}H NMR spectrum shows two intense signals due to the protons of *tert*-butyl moieties and an AB system in the region of 3-4 ppm suggesting the cone conformation of the complex. The integral ratio of the signals of aromatic protons of the calix[4]arene component and the proton signals in 1.93-4.30 ppm region is 8:36 indicating the 1:1 proportion structure **8**. MALDI-TOF MS of **8** shows a molecular ion peak at 935.5 m/z which corresponds to its molecular mass when stripped off NiI_2. This is not unusual since the thioether is a worse donor than the thiolate and suggests that the complex can readily lose the nickel ion to produce a free ligand. ^{1}H NMR spectrum of **9** shows that the integral ratio of the aromatic protons of calix[4]arene to the protons signals in 1.48-4.40 ppm region is 8:56 indicating the 1:2 ratio structure **9**. MALDI-TOF MS of **9** gives two molecular ion peaks at 1412.1 and 1227.2 m/z corresponding to the $[C_{68}H_{102}O_4N_4S_4Ni_2I]^+$ ion and the $[C_{68}H_{103}O_4N_4S_4NiI]^+$ ion, respectively. These results thus agree with the proposed structures of **8** and **9**. We have tried to characterize **8** and **9** by elemental analysis, but the results are unacceptable probably due to mixed counter ions (Cl^- and I^-) in these two complexes (this stems from the preparation procedure which involved both Cl^- and I^- ions). However, the elemental analysis result of complex **7** that undoubtedly contains two Br^- counter ions agrees with the proposed structure accompanied with 2 water molecules.[9] In addition, ^{1}H NMR spectrum of **7** is broader than analogue **8**. Although we cannot deduce information of the solution structure of **8**, the result suggests that the geometry around the nickel center may alter from a diamagnetic, relatively square planar, geometry with I^- ion to a paramagnetic, relatively distorted tetrahedral, geometry with Br^- ion.

The nickel ion can be readily removed from the Ni-calix[4]arene complex (**8**). Upon addition of excess KCN into an acetonitrile solution of **8** resulted in immediate decolorization of the yellowish green solution. Separation of the free ligand from water-soluble inorganic products can be accomplished by CH_2Cl_2/H_2O extraction which yielded slightly yellow solid in the organic layer (92%). The solid was also very soluble in CH_3OH.



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^{1}H NMR spectrum of the solid is consistent with the free ligand structure (**10**).[10] The ligand contains two N-, two O- and two S-donors in a crown ether configuration suitable for further complexation studies.[11]

Unfortunately, preparative procedure for **1** is quite complicate and expensive.[12] We are, therefore, currently trying a less expensive nickel thiolates such as Busch's nickel Schiff base complexes to further investigate this reaction.

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References and Notes

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[5] **4**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.95 (s, 18H), 1.30 (s, 18H), 3.41 and 4.30 (dd, 8H, J = 13 Hz), 4.00 (t, 4H, J = 6 Hz), 4.30 (t, 4H, J = 6 Hz), 6.78 (s, 4H), 7.00 (s, 2H), 7.07 (s, 4H). Anal. Calcd. for $C_{44}H_{62}O_4Cl_2$: C, 74.49; H, 8.07%. Found: C, 74.57; H, 7.90%. **5**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.94 (s, 18H), 1.28 (s, 18H), 4.32 and 3.32 (dd, 8H, J = 13 Hz), 3.83 (t, 4H, J = 6 Hz), 4.27 (t, 4H, J = 6 Hz), 6.78 (s, 4H), 6.93 (s, 2H), 7.05 (s, 4H). Anal. Calcd. for $C_{44}H_{62}O_4Br_2$: C, 66.82; H, 7.24%. Found: C, 66.99; H, 7.19%. **6**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.98 (s, 36H), 1.25 (s, 36H), 3.36 and 4.51 (dd, 16H, J = 13 Hz), 4.60 (s, 8H), 6.85 (s, 8H), 7.00 (s, 8H), 7.63 (s, 4H). Anal. Calcd. for $C_{92}H_{116}O_8$: C, 81.86; H, 8.66%. Found: C, 81.86; H, 8.86%.

[6] MALDI-TOF MS shows a molecular ion peak at 1026.0 m/z which is close to the molecular mass of the one arm substituted complex $[C_{58}H_{82}O_4N_2S_2NiCl]^+$ (MW = 1029.56 g/mol). However, we don't have other evidence to support the MS result since the ^{1}H NMR spectrum is too broad to deduce any information from it.

[7] This nickel trimetallic complex composes of two units of **1** that acts as a bidentate ligand using S-donor to coordinate another Ni^{2+} ion in a square planar fashion. This complex is found in almost every reaction of **1**. See references 3 and 4.

[8] **8**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.87 (s, 18H), 1.29 (s, 18H), 1.93 (br m, 4H), 2.13 (br m, 4H), 3.20 and 4.30 (dd, 8H, J = 13 Hz), 3.54 (br, 8H), 3.63 (br, 2H), 3.80 (br, 2H), 4.05 (br m, 8H), 6.70 (s, 4H), 6.82 (s, 2H), 7.04 (s, 4H). MS (MALDI-TOF): 935.5 m/z ($[\mathbf{M}\text{-}NiI_2]^+$). UV-vis ($\lambda_{max}$): 281 nm. **9**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.82 (s, 18H), 1.36 (s, 18H), 1.48-4.40 (br, 56H), 5.77 (s, 2H), 6.60 (s, 4H), 7.10 (s, 4H). MS (MALDI-TOF): 1412.1 m/z ($[\mathbf{M}\text{-}I]^+$) and 1227.2 m/z ($[\mathbf{M}\text{-}NiI_2]^+$). UV-vis ($\lambda_{max}$): 244 nm.

[9] **7** can be crystallized by adding hexane into its CH_2Cl_2 solution. CH_2Cl_2 was then allowed to evaporate slowly to give green microcrystals of **7**•$2H_2O$. Anal Calcd. for $C_{58}H_{82}O_4S_2N_2Br_2Ni{\bullet}2H_2O$ (**7**•$2H_2O$): C, 58.54; H, 7.28; N, 2.35%. Found: C, 58.08; H, 7.05; N, 2.22%.

[10] **10**: ^{1}H NMR (200 MHz, CD_3OD) δ 0.96 (s, 18H), 1.31 (s, 18H), 1.68 (m, 4H), 2.8 (m, 8H), 2.96 (m, 4H), 3.15 (m, 4H), 3.30 and 4.13 (dd, 8H, J = 13 Hz), 4.00 (m, 2H), 4.32 (m, 6H), 6.77 (s, 4H), 6.93 (s, 2H), 7.03 (s, 4H).

[11] The N_2S_2 component can accommodate many transition metal ions such as Fe(II), Co(II), Ni(II), Cu(II), Zn(II), Pd(II), and Cd(II); T. Tuntulani, Ph.D. Thesis (1995), Texas A&M University, College Station, Texas.

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