http://dx.doi.org/10.5012/bkcs.2012.33.5.1

Supporting Information

Inclusion Extraction of Alkali Metals by Emulsion Liquid Membranes and Nano-baskets of *p-tert*-calix[4]arene bearing Di-[N-(X)sulfonyl Carboxamide] and Di-(1-propoxy) in *ortho*-cone Conformation

Bahram Mokhtari and Kobra Pourabdollah*

Department of Chemical Engineering, Shahreza Branch, Islamic Azad University, Shahreza, Iran
*Islamic Azad University, Pasdaran st., Shahreza, Isfahan Province, Iran. *E-mail: pourabdollah@iaush.ac.ir*
Received December 20, 2011, Accepted January 1, 2012

In the present work, the synthesis of four derivatives of *p-tert*-calix[4]arene bearing di-[*N*-(X)sulfonyl carboxamide] and di-(1-propoxy) in ortho-cone conformation and the preparation of its bonded silica stationary phase were described [X= Phenyl (**01**), *p*-CH_3Phenyl (**02**), *p*-OHPhenyl (**03**), *p*-NO_2Phenyl (**04**)]. A new method for determination of clenbuterol in the livestock meat samples was set up by using the new calix[4]arene-based column. The chromatographic performance using clenbuterol as well as the influence of methanol content (in mobile phase) on the chromatographic behavior of the solutes was investigated. Figure 1 shows the expanded chemical structure of derivatives **01-04**.

2. Synthesis of *ortho*-cone Conformers (01-04)

2.1. Instruments and Apparatus

Elemental analysis was performed with a Flash EA 1112 elemental analyzer. ^{1}H NMR spectrum was recorded with a Bruker 400 MHz spectrometer in $CDCl_3$. IR spectra were recorded with a Bruker Vector 22 instrument.

2.2. Synthesis of Intermediates

5,11,17,23-tetrakis(1,1-dimethylethyl)-25,26-dihydroxy-27,28-di(1-propoxy)calix[4]arene has been synthesized by the procedure, which is reported here. 7.00 g (10.80 mmol) *p-tert*-butylcalix[4]arene was added to a solution of DMSO (50 mL) and 40% aqueous NaOH (7.06 mL, 100.00 mmol). After that, the mixture was warmed to 50 ºC and 9.20 g (43.00 mmol) PrOTs was added. The mixture was stirred for 24 h at 70 ºC. After cooling to room temperature, the reaction mixture was poured into a 5% aqueous HCl solution (100 mL). The crude product was extracted with dichloromethane and the solution was dried over $MgSO_4$. The dichloromethane was evaporated *in vacuo* and the residue was washed with MeOH to give 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,26-dihydroxy-27,28-di(1-propoxy)calix[4]arene (6.31 g, 88%) with mp 168-170 °C.

A mixture of THF (32 mL) and NaH (0.56 g, 22.19 mmol) was stirred and a solution of THF (25 mL) and 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,26-dihydroxy-27,28-di(1-propoxy)calix[4]arene (2.75 g, 3.70 mmol) was added dropwise. The solution was stirred at room temperature under nitrogen for 3 h, and then ethyl bromoacetate (2.4 mL, 22.19 mmol) was added. The reaction mixture was refluxed for 24 h and was quenched with 25 mL of 5% aqueous HCl. After evaporating the THF *in vacuo*, the residue was allowed to cool to room temperature. The residue was washed with 5% HCl (150 mL) and dichloromethane was used to extract 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,26-bis[(ethoxycarbonyl)methoxy]-27,28-di(1-propoxy)calix[4]arene. The organic layer was washed with water, dried over $MgSO_4$, and evaporated *in vacuo*. The crude product was recrystallized from MeOH to obtain 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,26-bis[(ethoxycarbonyl)methoxy]-27,28-di(1-propoxy)calix[4]arene (2.72 g, 78%) as a white solid with mp 78-80 ºC.

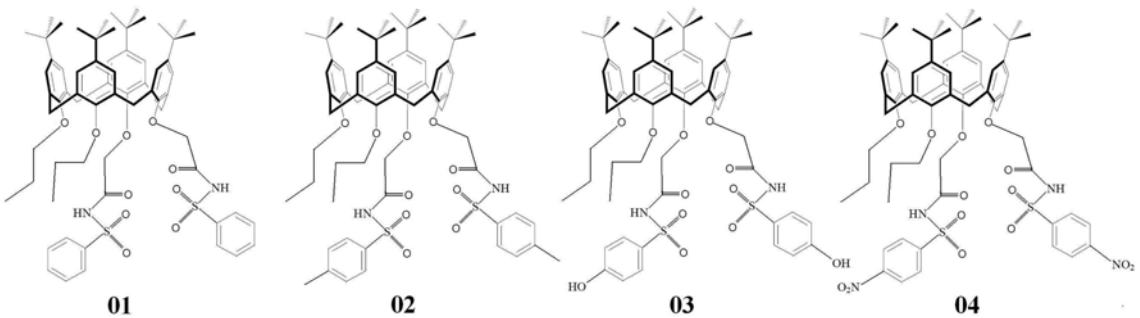

Figure 1. Chemical structure of derivatives **01-04**.

A solution of 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,26-bis[(ethoxycarbonyl)methoxy]-27,28-di(1-propoxy)-calix[4]arene (3.54 mmol), 10% aqueous Me_4NOH (75 mL), and THF (75 mL) was refluxed for 24 h. The reaction mixture was cooled to room temperature and was stirred with 6 N HCl (30 mL) for 2 h. After evaporating the THF *in vacuo*, a white precipitate was filtered and dissolved in CH_2Cl_2 (75 mL). The aqueous filtrate was extracted with CH_2Cl_2 (2 × 75 mL). The combined organic layers were washed with 6 N aqueous HCl until pH=1 and dried over $MgSO_4$. The dichloromethane was evaporated *in vacuo* to give 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,26-bis-(carboxymethoxy)-27,28-di(1-propoxy)calix[4]arene (3.40 g, 96% yield) as a white solid with mp 169-171 ºC.

2.3. Synthesis of 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,26-bis(*N*-phenylsulfonyl carbamoylmethoxy)-27,28-di(1-propoxy)calix[4]arene (01)

A solution of 5,11,17,23-tetrakis(1,1-dimethylethyl)-25, 26-bis(chlorocarboxymethoxy)-27,28-di(1-propoxy)calix[4]-arene in THF (10 mL) was added to a mixture containing NaH (0.58 g, 24.0 mmol) and 9.50 mmol of phenyl sulfonamide in 100 mL THF, and the mixture was stirred under nitrogen for 6 hr at room temperature. Then 2 mL H_2O was added to decompose the excess NaH and the THF was evaporated *in vacuo* and 200 mL CH_2Cl_2 was added to the residue. The organic layer was washed with 200 mL 1 N HCl and water, and was dried over $MgSO_4$ and was evaporated *in vacuo* to give the crude di-ionizable calix[4]arene. After purification, the product was dissolved in CH_2Cl_2, washed with 10% aqueous HCl and water, and dried over $MgSO_4$. The solution was evaporated *in vacuo* to give the derivative **01**. The product **01** was obtained in 90% yield after chromatography on silica gel with CH_2Cl_2–MeOH (80:1) as eluent. White solid; mp 130-142 ºC; ν_{max} (film)/cm^{-1}: 3240 (NH), 1724 (C=O), 1360 and 1188 (S=O); ^{1}H NMR ($CDCl_3$) δ 0.96 (br s, 18H), 1.24 (br s, 18H), 2.00-4.28 (br m, 26H), 6.22-7.32 (br m, 8H), 7.68 (t, *J* = 7.52, 4H), 7.82 (t, *J* = 7.42, 2H), 7.98 (d, *J* = 7.52, 4H), 9.32 (br s, 2H); ^{13}C NMR ($CDCl_3$): δ_C 171.20, 171.00, 155.68, 153.70, 144.50, 138.12, 133.90, 132.60, 129.02, 128.20, 125.80, 72.88, 60.22, 33.88, 33.12, 33.14, 31.82, 31.04, 25.30; Anal. Calc. $C_{66}H_{82}N_2O_{10}S_2$: C, 70.30; H, 7.36; N, 2.42 Found: C, 70.20; H, 7.28; N, 2.52.

2.4. Synthesis of 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,26-bis[*N*-(4-methylphenyl)sulfonyl carbamoylmethoxy]-27,28-di(1-propoxy)calix[4]arene (02)

2.40 mmol 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,26-bis(chlorocarboxymethoxy)-27,28-di(1-propoxy)calix[4]-arene was dried by benzene-azeotropic distillation. 24.0 mmol (3.04 g) oxalyl chloride was added and the reaction mixture was refluxed for 4 h under nitrogen atmosphere. The solvent was removed *in vacuo* to provide the corresponding acid chloride. A solution of the acid chloride in 10 mL THF was added to a mixture of 9.60 mmol (*p*-methyl)phenyl sulfonamide and 0.58 g NaH (24.0 mmol) in 100 mL THF, and the mixture was stirred under nitrogen for 4 h at room temperature. H_2O (2 mL) was added to decompose the excess NaH. The THF was evaporated *in vacuo* and 200 mL CH_2Cl_2 was added to the residue. The organic layer was washed with 200 mL HCl (1N) and water, dried over $MgSO_4$ and evaporated *in vacuo* to give the di-ionizable calix[4]-arene. After purification, the product was dissolved in CH_2Cl_2, washed with 10% aqueous HCl and water and dried over $MgSO_4$. The solution was evaporated *in vacuo* to give the product **02**, which was obtained in 88% yield after chromatography on silica gel with CH_2Cl_2–MeOH (80:1) as eluent. White solid; mp 148-154 ºC; ν_{max} (film)/cm^{-1}: 3254 (NH), 1720 (C=O), 1342 and 1188 (S=O); ^{1}H NMR ($CDCl_3$): δ 0.98 (br s, 18H), 1.24 (br s, 18H), 2.08-4.16 (br m, 32H), 6.50-7.10 (br m, 8H), 8.22 (d, J=4.76, 4H), 8.32 (d, J=4.68, 4H), 9.38 (br s, 2H); ^{13}C NMR ($CDCl_3$): δ_C 174.42, 170.62, 152.62, 150.82, 144.42,143.68, 134.26, 132.48, 129.32, 125.84, 124.66, 34.24, 33.42, 33.12, 31.28, 31.04, 25.26, 21.28; Anal. Calcd. $C_{68}H_{86}N_2O_{10}S_2$·0.1 CH_2Cl_2: C, 65.12; H, 7.38; N, 4.52 Found: C, 65.24; H, 7.28; N, 4.62.

2.5. Synthesis of 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,26-bis[*N*-(4-hydroxyphenyl)sulfonyl carbamoylmethoxy]-27,28-di(1-propoxy)calix[4]arene (03)

2.40 mmol 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,26-bis(chlorocarboxymethoxy)-27,28-di(1-propoxy)calix[4]arene was dried by benzene-azeotropic distillation. 24.0 mmol (3.04 g) oxalyl chloride was added and the reaction mixture was refluxed for 5 h under nitrogen atmosphere. The solvent was removed *in vacuo* to provide the corresponding acid chloride. A solution of the acid chloride in 10 mL THF was added to a mixture of 9.60 mmol (4-hydroxy)phenyl sulfonamide and 0.58 g NaH (24.0 mmol) in 100 mL THF, and the mixture was stirred under nitrogen at room temperature for 4 h. Then, 2 mL H_2O was added to decompose the excess NaH. The THF was evaporated *in vacuo* and 200 ml CH_2Cl_2 was added to the residue. The organic layer was washed with 200 mL HCl (1 N) and water, dried over $MgSO_4$ and evaporated *in vacuo* to give the crude di-ionizable calix[4]arene. After purification, the product was dissolved in CH_2Cl_2, washed with 10% aqueous HCl and water and dried over $MgSO_4$. The solution was evaporated *in vacuo* to give the product **03**. Derivative **03** was obtained in 84% yield after chromatography on silica gel with CH_2Cl_2–MeOH (80:1) as eluent. White solid; mp 170-176 ºC; ν_{max} (film)/cm^{-1}: 3238 (NH), 1724 (C=O), 1362 and 1168 (S=O); ^{1}H NMR ($CDCl_3$): δ 0.96 (br s, 18H), 1.24 (br s, 18H), 2.08-4.04 (br m, 26H), 6.38-7.46 (br m, 8H), 7.62 (t, *J* = 7.76, 4H), 8.02 (d, *J* = 7.42, 4H), 8.54 (t, J=7.30, 2H), 9.44 (br s, 2H); ^{13}C NMR ($CDCl_3$): δ_C 171.38, 171.02, 155.06, 153.72, 144.18, 138.96, 133.32, 132.44, 129.20, 128.34, 125.28, 73.06, 60.08, 34.28, 33.96, 33.42, 31.14, 31.06, 22.27; Anal. Calc. $C_{66}H_{82}N_2O_{12}S_2$: C, 70.66; H, 7.42; N, 2.44 Found: C, 70.28; H, 7.32; N, 2.40.

2.6. Synthesis of 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,26-bis[*N*-(4-nitrophenyl)sulfonyl carbamoylmethoxy]-27,28-di(1-propoxy)calix[4]arene (04)

2.40 mmol 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,26-bis(chlorocarboxymethoxy)-27,28-di(1-propoxy)calix[4]-arene was dried by benzene-azeotropic distillation. 3.04 g (24.0 mmol) oxalyl chloride was added and the reaction mixture was refluxed for 7 h under nitrogen atmosphere. The solvent was removed *in vacuo* to provide the corresponding acid chloride. A solution of the acid chloride in 10 ml THF was added to a mixture of 12.20 mmol (4-nitro)phenyl sulfonamide and 28.8 mmol NaH (0.70 g) in 100 mL THF, and the mixture was stirred under nitrogen at room temperature for 6 h. Then, 2 mL H_2O was added to decompose the excess NaH. The THF was evaporated *in vacuo* and 200 mL CH_2Cl_2 was added to the residue. The organic layer was washed with 1 N HCl (200 mL) and water, dried over $MgSO_4$ and evaporated *in vacuo* to give the crude di-ionizable calix[4]arene. After purification, the product was dissolved in CH_2Cl_2, washed with 10% aqueous HCl and water and dried over $MgSO_4$. The solution was evaporated *in vacuo* to give the product **04**, which was obtained in 68% yield after chromatography on silica gel with CH_2Cl_2–MeOH (80:1) as eluent. Yellow solid; mp 174-176 ºC; ν_{max} (film)/cm^{-1}: 3232 (NH), 1704 (C=O), 1358 and 1196 (S=O); ^{1}H NMR ($CDCl_3$): δ 0.96 (br s, 18H), 1.24 (br s, 18H), 2.10-4.02 (br m, 26H), 6.32-7.48 (br m, 8H), 7.44 (t, J = 7.08, 4H), 8.26 (d, J = 7.38, 4H), 9.42 (br s, 2H); ^{13}C NMR ($CDCl_3$): δ_C 171.02, 171.24, 155.62, 153.24, 144.28, 138.82, 133.38, 132.66, 129.04, 128.48, 125.24, 73.20, 60.15, 34.40, 33.28, 33.00, 31.38, 31.10, 20.14; Anal. Calc. $C_{66}H_{80}N_4O_{14}S_2$: C, 70.16; H, 7.18; N, 4.48 Found: C, 70.26; H, 7.24; N, 4.52.