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SUPPORTING INFORMATION

Title: Efficient Synthesis of a Variety of New Functionalized Oxacalixarenes by Ullmann Coupling Reactions
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Experimental Section

General Remarks: All manipulations of air- and /–or water-sensitive reactions were performed under an atmosphere of oxygen-free, dry dinitrogen using standard Schlenk-line techniques. ^{1}H NMR spectra were recorded at 400 MHz and ^{13}C NMR spectra were recorded at 100 MHz on Bruker instruments. ^{1}H and ^{13}C NMR chemical shifts are reported as δ values in ppm relative to residual solvent: $CDCl_3$ (7.26 ppm). Carbon NMR spectra were recorded in ppm relative to the solvent signals: $CDCl_3$ (77.23 ppm). Elemental analyses were performed using a Heraeus CHN-O-RAPID instrument. The high resolution FAB-mass spectra and EI-mass spectra were obtained using a JEOL JMS-SX/SX 102A instrument.

Materials: All commercial reagents were used as received with the following exceptions: Solvents were dried by heating under refluxing for at least 24 h over CaH_2 (DMF, N-methyl-2-pyrrolidine or pyridine,) and sodium/benzophenone (dioxane), and freshly distilled prior to use. Liquid chromatography was performed using forced flow (flash chromatography) of the indicated solvent system on silica gel (200-300 mesh).

General Synthetic Procedures

Synthesis of 3, 5-dibromo-4-nitrotoluene 1 [1]: 2,6-Dibromo-4-methylaniline (25.0 g, 94.4 mmol) and 3-chloroperoxybenzoic acid (73.0 g, 326 mmol) were dissolved in CH_2Cl_2 (700 mL). The solution was heated under reflux for 2 hours, and then cooled to room temperature. The precipitate (3-chlorobenzoic acid) was filtered off. The solution was extracted with 1 M aqueous KOH (1000 mL) until 3-chloroperoxybenzoic acid could not be detected by TLC (silica gel, $CHCl_3$). The solvent was removed and the obtained 2, 6-dibromonitroso-4-toulene was recrystallized from hexane to get a pale yellow solid (20. 6g, 79%).

To the suspension of glacial acetic acid (500 mL) and 2, 6-dibromonitroso-4-toulene (20.6 g, 73.9 mmol) was added a solution of H_2O_2 (a mixture of 210 mL of a 31.1 % solution in water and 200 mL of glacial acetic acid) at room temperature. HNO_3 (69.3%,13.9 mL) was then added. The mixture was heated in an oil bath at 90 ºC until the color of the solution turned to orange (3 hours). Water (1000 mL) was added, the formed solid was separated. The crude product was recrystallized from hexane to get a lightly yellow crystals (16.6 g, 76 %).^{1}H NMR (400 MHz, $CDCl_3$, 25 ºC): δ = 2.40 (s, 3H), 7.44 (s, 2H).

Synthesis of 2,6-difluoro-4-nitrobenzene 7 [1]: 2,6-Difluoroaniline (2.4 g, 2 mL, 18.6 mmol) and 3-chloroperoxybenzoic acid (18.6 g, 83.0 mmol) were dissolved in CH_2Cl_2 (130 mL). The solution was heated under reflux for 2 hours, and then cooled to room temperature. The precipitate (3-chlorobenzoic acid) was filtered off. The solution was extracted with 1 M aqueous KOH (186 mL) until 3-chloroperoxybenzoic acid could not be detected by TLC (silica gel, $CHCl_3$). The solvent was removed to afford 2, 6-difluoronitrosobenzene.

To the solution of 2, 6-difluoronitrosobenzene in glacial acetic acid (80 mL) was added a solution of H_2O_2 (a mixture of 50 mL of a 31.1 % solution in water and 50 mL of glacial acetic acid) at room temperature. HNO_3 (69.3%, 3.3 mL) was then added. The mixture was heated in an oil bath at 90 ºC until the color of the solution turned to orange (2 hours). After water (250 mL) was added, the mixture was extracted with CH_2Cl_2 (2 x 100 mL). The combined extracts were washed with aqueous Na_2CO_3, dried over Na_2SO_4 and concentrated, affording as a yellow oil (2.45 g, 82.9%). ^1H NMR (400 MHz, $CDCl_3$, 25 ºC): $\delta = 7.10$ (m, 2H), 7.49 (m, 1H).

General Ullmann ether reactions: A mixture of dihydroxy aromatic derivative (resorcinol or 2,7-dihydroxynaphthalene, 3.39 mmol), aryl dibromide (3,5-dibromo-4-nitrotoluene or 2,6-dibromonitrobenzene, 3.39 mmol), copper salt (0.2 mmol or 1 equiv), 0.4 mmol of *N*,*N*-dimethylglycine and 6.78 mmol of Cs_2CO_3 in 220 mL of solvent (dioxane or pyridine) was heated at 100-140 ^oC under nitrogen atmosphere for 1 day. The solvent was concentrated under vacuum to give a brown solid, which could be purified by chromatography on silica gel using $CHCl_3$ as eluent to afford a white solid.

Oxacalix[4]arene **3**: ^1H NMR (400 MHz, $CDCl_3$, 25 ºC): $\delta = 2.33$ (s, 6H), 5.28 (t, $J = 2.4$ Hz, 2H), 6.85 (m, 8H), 7.28 (t, $J = 6.6$ Hz, 2H). ^{13}C NMR (100.62 MHz, $CDCl_3$, 25 ºC): $\delta = 156.4$, 150.2, 143.4, 127.9, 123.0, 110.3, 109.9, 106.1, 24.1. HRMS (FAB): calcd. for $[C_{26}H_{18}N_2O_8Na]$ ($[M+Na]^+$) 509.0961; found 509.0970. $C_{26}H_{18}N_2O_8$(486.1): C 64.20, H 3.73, N 5.76; found C 64.10, H 3.81, N 5.61.

Oxacalix[4]arene **6:** ^1H NMR (400 MHz, $CDCl_3$, 25 ºC): $\delta = 6.51$ (d, $J = 2.5$ Hz, 4H), 7.26 (m, 8H), 7.71 (d, $J = 8.8$ Hz, 2H), 7.77 (d, $J = 9.0$ Hz, 4H); ^{13}C NMR (100.62 MHz, $CDCl_3$, 25 ºC): $\delta = 153.4$, 149.9, 135.0, 134.2, 129.4, 126.4,124.1, 115.5, 114.8, 107.4. HRMS (FAB): calcd. for $[C_{32}H_{18}N_2O_8Na]$ ($[M+Na]^+$) 581.0961; found 581.0970. $C_{32}H_{18}N_2O_8$ (558.1): C 68.82, H 3.25, N 5.02; found C 68.70; H 3.40; N 4.93.

Synthesis of the large, fully aromatic crown ether 8: A mixture of resorcinol (3.14 mmol), 2,6-difluoronitrobenzne (3.14 mmol), CuI (6.28 mmol) and K_2CO_3 (6.28 mmol) in 250 mL of pyridine was heated under reflux for 1 day. The solid was filtered off and the filtrate was concentrated under vacuum to give a brown a solid, which could be purified by chromatography on silica gel using $CHCl_3$: hexanes = 8: 2 as eluent to afford a white solid.

Oxacalix[6]arene **8:** 0.18 g, 25 %. ^{1}H NMR (400 MHz, $CDCl_3$, 25 ºC): δ 6.51 (t, *J* = 2.0 Hz, 3H), 6.67 (d, *J* = 8.5 Hz, 6H), 7.06 (2d, *J* = 1.9, 2.0 Hz, 6H), 7.30 (t, *J* = 8.6 Hz, 2H), 7.44 (t, *J* = 8.8 Hz, 4H). ^{13}C NMR (100.62 MHz, $CDCl_3$, 25 ºC): δ = 156.3, 148.9, 134.0, 127.5, 125.8, 111.1, 109.8, 106.1. HRMS (FAB): calcd. for [$C_{36}H_{21}N_3O_{12}Na$] ($[M+Na]^+$) 710.1023; found 710.1029. $C_{36}H_{21}N_3O_{12}$ (687.1): C 62.89, H 3.08, N 6.11; found C 62.77; H 3.19, N 6.03.

Hydrogenation of the NO_2 groups of aromatic crown ether 10: In the presence of 10% of Pd/C (5%), the oxacalix[4]arene **3**（500 mg, 1.03 mmol）was hydrogenated in 10 mL of DMF at 1 atm to afford the aromatic crown ether **10** as a pale yellow solid (395 mg, 90%). ^{1}H NMR (400 MHz, $CDCl_3$, 25 ºC): δ = 2.31 (s, 6H), 3.54 (br s, 4H), 5.56 (s, 2H), 6.25 (s, 4H), 6.80 (d, *J* = 7.0 Hz, 4H), 7.21 (t, *J* = 7.0 Hz, 2H). ^{13}C NMR (100.62 MHz, $CDCl_3$, 25 ºC): δ = 156.3, 138.9, 128.0, 127.1, 121.9, 106.1, 110.3, 109.9, 24.5. HRMS (FAB) calcd. for [$C_{26}H_{22}N_2O_4Na$] ($[M+Na]^+$): 449.1477; found: 449.1470. $C_{26}H_{22}N_2O_4$ (426.2): C 73.23, H 5.20, N 6.57; found: C 73.13, H 5.29, N 6.48.

References

[1] D. Shen, S. Diele, G. Pelzl, I.Wirthb, C.Tschierske, *J. Mater. Chem.* **1999**, *9*, 661-672.