Aminomethylated calix[4]resorcinolarenes with NH groups on the upper rim of the molecule*

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The reaction of calix[4]resorcinolarenes with *N*,*N*-dimethylethylenediamine and aqueous CH_2O in a molar ratio of 1 : 5 : 5 affords calixarenes containing secondary amino groups arranged on the upper rim of the molecule. When the double amount (with respect to primary amine) of formalin is used (ratio of reactants 1 : 5 : 10), cavitands with four oxazinyl fragments are synthesized.

Key words: calix[4]resorcinolarenes, aminomethylation, oxazinyl fragments.

Increased interest of researchers in the chemistry of calixarenes has recently been evoked owing to the ability of these compounds to include and retain a wide scope of organic molecules and ions due to their cup-like shape. Therefore, the development of methods for calixarene functionalization[1—3] aimed at creating efficient complexing agents, extracting agents, and others is an urgent problem. Calix[4]resorcinolarenes, whose aromatic cycles have aminomethyl fragments in the *ortho*-positions to the hydroxyl groups, are of doubtless interest as starting spatially organized scaffolds. The first representative of this class of compounds was obtained using the Mannich reaction from calix[4]resorcinolarene, formaldehyde, and secondary amine.[4] The authors of this work also showed that the use of primary amines afforded a complex mixture of products. We succeeded in synthesizing for the first time (Scheme 1) aminomethylated derivatives of calix[4]resorcinolarenes with NH groups localized on the upper rim of the molecule (**2a**,**c**) by the introduction of *N*,*N*-dimethylethylenediamine into the Mannich reaction. In this case, the initial reactants (calixarene, primary amine, and formaldehyde) were used in a ratio of 1 : 5 : 5.

The structure of compounds **2a**,**c** was confirmed by the IR and ^{1}H NMR spectroscopic data, and their composition was determined by elemental analysis. Hydroxyl and secondary amino groups are presented in the IR spectrum by a broad band at 3200—3300 cm^{-1}. It is established that when the double amount of formaldehyde (with respect to primary amine) is used in this reaction (ratio of initial reactants 1 : 5 : 10), four oxazinyl fragments are formed on the upper rim of the molecule to produce cavitands (**3a—f**).

It should be noted that the yield of products **3a—f** is much higher (up to 95%) when the reaction is carried out in two stages: initially the ratio of reactants is 1 : 5 : 5, and then 5 equiv. of formaldehyde are added. Thus, we showed for the first time that formaldehyde can react with calixarenes **2**, whose secondary aminoalkyl groups are localized on the upper rim of the molecule.

Experimental

^{1}H NMR spectra were recorded on a Bruker WM-250 spectrometer (250 MHz) relatively to signals of residual protons of the solvent ($CDCl_3$). IR spectra of compounds were recorded on a UR-20 spectrometer as suspensions in Nujol in a frequency interval of 400—3600 cm^{-1}.

5,11,17,19-Tetrakis[2-(*N*,*N*-dimethylamino)ethylaminomethyl]-4,6,10,12,16,18,22,24-octahydroxy-2,8,14,20-tetramethylpentacyclo[19.3.1.1^{3,7}.1^{9,13}.1^{15,19}]octacosa-1(25),3,5,7(28),9,11,13(27),15,17,19(26),21,23-dodecaene (2a). *N*,*N*-Dimethylethylenediamine (1.80 g, 20 mmol) and 40% formalin (1.52 g, 20 mmol) were added to a solution of calixarene **1a** (2 g, 4 mmol) in a benzene—ethanol (1 : 1 vol/vol) mixture (30 mL). The reaction mixture was kept for 24 h at 20 °C. The solvent was removed *in vacuo* using an oil pump (80—100 °C, 0.04 Torr) until a constant weight. Compound **2a** was synthesized in 86% yield (3 g), >270 °C (with decomp.). Found (%): C, 65.46; H, 8.97; N, 12.09. $C_{52}H_{80}N_8O_8$. Calculated (%): C, 66.10; H, 8.47; N, 11.86. ^{1}H NMR ($CDCl_3$, 20 °C), δ: 1.70 (d, 12 H, $\underline{CH_3}CH$, J = 7.0 Hz); 2.12 (s, 24 H, $\underline{CH_3}N$); 2.35 (m, 8 H, $\underline{CH_2}N(CH_3)_2$); 2.72 (m, 8 H, $\underline{CH_2}CH_2N(CH_3)_2$); 4.01 (s, 8 H, $C_{arom}\underline{CH_2}NH$); 4.50 (q, 4 H, $CH_3\underline{CH}$, J = 7.0 Hz); 7.35 (s, 4 H, $C_6\underline{H}$); 7.40 (br.s, 8 H, OH).

5,11,17,19-Tetrakis[2-(*N*,*N*-dimethylamino)ethylaminomethyl]-2,8,14,20-tetrahexyl-4,6,10,12,16,18,22,24-

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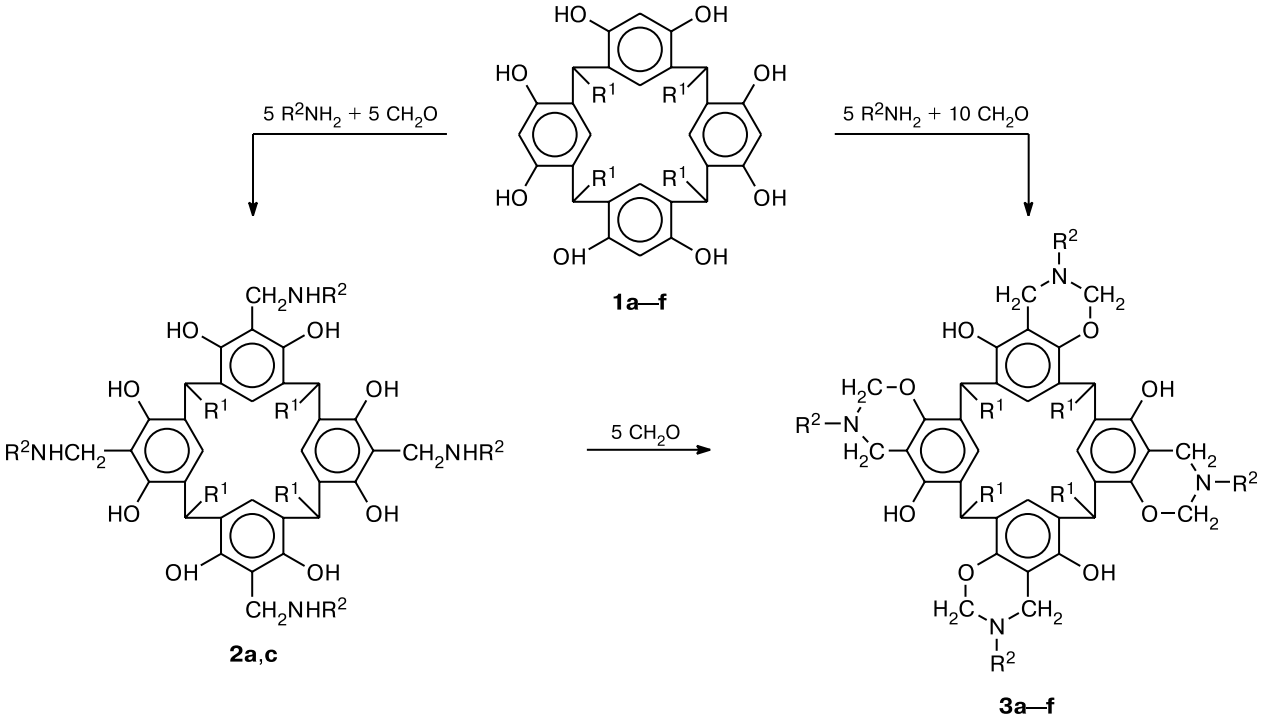
Scheme 1



1—3	a	b	c	d	e	f
R^1	Me	C_5H_{11}	C_6H_{13}	C_7H_{15}	C_9H_{19}	$C_{11}H_{23}$

2, **3**: $R^2 = CH_2CH_2NMe_2$

octahydroxypentacyclo[19.3.1.1^{3,7}.1^{9,13}.1^{15,19}]octacosa-1(25),3,5,7(28),9,11,13(27),15,17,19(26),21,23-dodecaene (2c) was synthesized similarly to compound **2a** from calixarene **1c** (2.0 g, 2.4 mmol), 40% formalin (0.91 g, 12 mmol), and *N*,*N*-dimethylethylenediamine (1.06 g, 2 mmol). The yield was 2.42 g (82%), m.p. >300 °C. Found (%): C, 60.24; H, 10.32; N, 9.02. $C_{52}H_{80}N_8O_8$. Calculated (%): C, 60.58; H, 9.80; N, 9.15. ^{1}H NMR ($CDCl_3$, 20 °C), δ: 0.86 (t, 12 H, $\underline{CH_3}CH_2$, J = 7.0 Hz); 1.25 (m, 32 H, $CH_3(\underline{CH_2})_4$); 2.10 (m, 8 H, $\underline{CH_2}CH$); 2.23 (s, 24 H, $\underline{CH_3}N$); 2.35 (m, 8 H, $\underline{CH_2}NMe_2$); 2.64 (m, 8 H, $\underline{CH_2}CH_2NMe_2$); 3.71—3.73 (m, 8 H, $C_{arom}\underline{CH_2}NH$); 4.24 (t, 4H, $\underline{CH}(CH_2)_5$, J = 6.9 Hz); 7.19 (s, 4 H, C_6H); 7.36 (s, 8 H, OH).

4,14,24,34-Tetrahydroxy-7,17,27,37-tetrakis(dimethylaminoethyl)-2,12,22,32-tetramethyl-9,19,29,39-tetraoxa-7,17,27,37-tetraazanonacyclo[31.7.1.1^{3,11}.1^{13,21}.1(41).3.5(10).11(44).13.1^{23,31}.0^{5,10}.0^{15,20}.0^{25,30}.0^{35,40}]tetratetraconta-15(20),21(43),23,25(30),31(42),33,35(41)-dodecaene (3a). A solution of calixarene **1a** (1 g, 1.83 mmol), *N*,*N*-dimethylethylenediamine (0.81 g, 9.2 mmol), and 20% formalin (2.75 g, 18.3 mmol) in a mixture of EtOH (5 mL) and benzene (5 mL) was heated for 8 h at the boiling temperature of the mixture. The solvent was removed, and the resulting precipitate was triply washed with benzene and dried at 60 °C (0.02 Torr) for 2 h. Compound **3a** was obtained in 80% yield (1.10 g), m.p. >300 °C (decomp.). Found (%): C, 67.38; H, 8.13; N, 10.80. $C_{56}H_{80}N_8O_8$. Calculated (%): C, 67.74; H, 8.06; N, 11.29. ^{1}H NMR ($CDCl_3$, 20 °C) δ: 1.72 (d, 12 H, $C\underline{H_3}CH$, J = 6.9 Hz); 2.23 (s, 24 H, $C\underline{H_3}N$); 2.41 (t, 8 H, $C\underline{H_2}N(CH_3)_2$, J = 6.5 Hz); 2.75 (t, 8 H, $C\underline{H_2}CH_2N(CH_3)_2$, J = 6.5 Hz); 3.87 (m, 8 H, $CC\underline{H_2}N$); 4.46 (q, 4 H, $CH_3C\underline{H}$, J = 7.0 Hz); 4.92 (m, 8 H, $OC\underline{H_2}N$); 7.1 (s, 4 H, C_6H); 7.81 (s, 4 H, OH).

4,14,24,34-Tetrahydroxy-7,17,27,37-tetrakis(dimethylaminoethyl)-2,12,22,32-tetrapentyl-9,19,29,39-tetraoxa-7,17,27,37-tetraazanonacyclo[31.7.1.1^{3,11}.1^{13,21}.1(41).3.5(10).11(44).13.1^{23,31}.0^{5,10}.0^{15,20}.0^{25,30}.0^{35,40}]tetratetraconta-15(20),21(43),23,25(30),31(42),33,35(41)-dodecaene (3b) was synthesized similarly to compound **3a** from calixarene **1b** (1 g, 1.3 mmol), 35% formalin (1.11 g, 13.2 mmol), and diamine (0.57 g, 6.5 mmol) in 85% yield (1.34 g), m.p. 105—110 °C. Found (%): C, 70.90; H, 9.44; N, 9.11. $C_{72}H_{112}N_8O_8$. Calculated (%): C, 71.05; H, 9.21; N, 9.21. ^{1}H NMR ($CDCl_3$, 20 °C), δ: 0.90 (t, 12 H, $C\underline{H_3}(CH_2)_4$, J = 6.9 Hz); 1.32 (m, 24 H, $CH_3(C\underline{H_2})_3$); 2.10 (m, 8 H, $\underline{CH_2}CH$); 2.23 (s, 24 H, $C\underline{H_3}N$); 2.43 (t, 8 H, $C\underline{H_2}N(CH_3)_2$, J = 6.5 Hz); 2.72 (t, 8 H, $C\underline{H_2}CH_2N(CH_3)_2$, J = 6.5 Hz); 3.88 (m, 8 H, $CC\underline{H_2}N$); 4.18 (t, 4 H, $C\underline{H}CH_2$, J = 6.9 Hz); 4.92 (m, 8 H, $OC\underline{H_2}N$,); 7.33 (s, 4 H, C_6H); 7.74 (s, 4 H, OH).

7,17,27,37-Tetrakis(dimethylaminoethyl)-2,12,22,32-tetrahexyl-4,14,24,34-tetrahydroxy-9,19,29,39-tetraoxa-7,17,27,37-tetraazanonacyclo[31.7.1.1^{3,11}.1^{13,21}.1(41).3.5(10).11(44).13.1^{23,31}.0^{5,10}.0^{15,20}.0^{25,30}.0^{35,40}]tetratetraconta-15(20),21(43),23,25(30),31(42),33,35(41)-dodecaene (3c) was synthesized similarly to compound **3a** from calixarene **1c** (0.2 g, 0.24 mmol), diamine (0.1 g, 1.2 mmol), and 35% formalin (0.2 g, 2.4 mmol) in 87% yield (0.26 g), m.p. >320 °C (decomp.).

Found (%): N, 9.22. $C_{76}H_{120}N_8O_8$. Calculated (%): N, 8.80. ^{1}H NMR ($CDCl_3$, 20 °C), δ: 0.85 (t, 12 H, $\underline{CH_3}(CH_2)_4$, J = 7.0 Hz); 1.23 (m, 32 H, $CH_3(\underline{CH_2})_4$); 2.17 (m, 8 H, $\underline{CH_2}CH$); 2.23 (s, 24 H, $\underline{CH_3}N$); 2.42 (t, 8 H, $\underline{CH_2}N(CH_3)_2$, J = 6.8 Hz); 2.77 (t, 8 H, $\underline{CH_2}CH_2NMe_2$, J = 6.8 Hz); 3.96 (m, 8 H, $C\underline{CH_2}N$); 4.23 (t, 4 H, $\underline{CH}CH_2$, J = 6.8 Hz); 4.91 (m, 8 H, $O\underline{CH_2}N$); 7.19 (s, 4 H, C_6H); 8.16 (s, 4 H, OH).

7,17,27,37-Tetrakis(dimethylaminoethyl)-2,12,22,32-tetraheptyl-4,14,24,34-tetrahydroxy-9,19,29,39-tetraoxa-7,17,27,37-tetraazanonacyclo[31.7.1.1^{3,11}.1^{13,21}.1(41).3.5(10).11(44).13.1^{23,31}.0^{5,10}.0^{15,20}.0^{25,30}.0^{35,40}]tetratetraconta-15(20),21(43),23,25(30),31(42),33,35(41)-dodecaene (3d) was synthesized similarly to compound **3a** from calixarene **1d** (0.5 g, 0.5 mmol), 35% formalin (0.48 g, 5.0 mmol), and diamine (0.25 g, 2.5 mmol) in 70% yield (0.51 g), m.p. 75 °C. Found (%): C, 71.76; H, 10.25; N, 8.00. $C_{80}H_{128}N_8O_8$. Calculated (%): C, 72.28; H, 9.63; N, 8.43. ^{1}H NMR ($CDCl_3$, 20 °C), δ: 0.86 (t, 12 H, $C\underline{H_3}(CH_2)_5$, J = 6.9 Hz); 1.26 (m, 40 H, $CH_3(C\underline{H_2})_5$); 2.13 (m, 8 H, $\underline{CH_2}CH$); 2.22 (s, 24 H, $C\underline{H_3}N$); 2.42 (t, 8 H, $CH_2C\underline{H_2}NMe)_2$, J = 6.8 Hz), 2.75 (t, 8 H, $C\underline{H_2}CH_2N(CH_3)_2$, J = 6.7 Hz); 3.87 (m, 8 H, $CC\underline{H_2}N$); 4.18 (t, 4 H, $C\underline{H}CH_2$, J = 7.0 Hz); 4.89 (m, 8 H, $OC\underline{H_2}N$); 7.33 (s, 4 H, C_6H); 7.74 (s, 4 H, OH).

7,17,27,37-Tetrakis(dimethylaminoethyl)-4,14,24,34-tetrahydroxy-2,12,22,32-tetranonyl-9,19,29,39-tetraoxa-7,17,27,37-tetraazanonacyclo[31.7.1.1^{3,11}.1^{13,21}.1(41).3.5(10).11(44).13.1^{23,31}.0^{5,10}.0^{15,20}.0^{25,30}.0^{35,40}]tetratetraconta-15(20),21(43),23,25(30),31(42),33,35(41)dodecaene (3e) was synthesized similarly to compound **3a** from calixarene **1e** (0.22 g, 0.3 mmol), 40% formalin (0.22 g, 3.0 mmol), and diamine (0.13 g, 1.5 mmol) in 80% yield (0.34 g), m.p. >320 °C (decomp.). Found (%): C, 72.62; H, 10.01; N, 7.63. $C_{88}H_{144}N_8O_8$. Calculated (%): C, 73.33; H, 10.00; N, 7.77. ^{1}H NMR ($CDCl_3$, 20 °C), δ: 0.88 (t, 12 H, $\underline{CH_3}(CH_2)_7$, J = 7.0 Hz); 1.23 (m, 56 H, $CH_3(\underline{CH_2})_7$); 2.14 (m, 8 H, $\underline{CH_2}CH$); 2.23 (s, 24 H, $\underline{CH_3}N$); 2.56 (m, 8 H, $\underline{CH_2}NMe_2$); 2.75 (m, 8 H, $\underline{CH_2}CH_2NMe_2$); 3.70 (m, 8 H, $C\underline{CH_2}N$); 4.19 (t, 4 H, $\underline{CH}CH_2$, J = 7.0 Hz); 4.92 (m, 8 H, $O\underline{CH_2}N$); 7.17 (s, 4 H, C_6H); 7.75 (s, 4 H, OH).

7,17,27,37-Tetrakis(dimethylaminoethyl)-4,14,24,34-tetrahydroxy-2,12,22,32-tetraundecyl-9,19,29,39-tetraoxa-7,17,27,37-tetraazanonacyclo[31.7.1.1.^{3,11}1.^{13,21}1(41).3.5(10).11(44).13.1^{23,31}.0^{5,10}.0^{15,20}.0^{25,30}.0^{35,40}]tetratetraconta-15(20),21(43),23,25(30),31(42),33,35(41)dodecaene (3f) was synthesized similarly to compound **3a** from calixarene **1f** (1.0 g, 0.9 mmol), 20% formalin (0.67 g, 9.0 mmol), and diamine (0.39 g, 4.5 mmol) in 29% yield (0.4 g), m.p. >330 °C (decomp.). Found (%): C, 74.41; H, 10.05; N, 7.11. $C_{96}H_{160}N_8O_8$. Calculated (%): C, 74.22; H, 10.31; N, 7.21. ^{1}H NMR ($CDCl_3$, 20 °C), δ: 0.88 (m, 12 H, $\underline{CH_3}(CH_2)_9$); 1.26 (m, 72 H, $CH_3(\underline{CH_2})_9$); 2.13 (m, 8 H, $\underline{CH_2}CH$); 2.23 (s, 24 H, $\underline{CH_3}N$); 2.41 (m, 8 H, $\underline{CH_2}NMe_2$); 2.72 (m, 8 H, $\underline{CH_2}CH_2NMe_2$); 3.99 (m, 8 H, $C\underline{CH_2}N$); 4.21 (t, 4 H, $\underline{CH}CH_2$, J = 7.0 Hz); 4.93 (m, 8 H, $O\underline{CH_2}N$); 7.18 (s, 4 H, C_6H); 7.36 (s, 4 H, OH).

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