Synthesis of doubly azacrowned thiacalixarenes

Yan Jin, Xiong Li, Shuling Gong and Yuanyin Chen*

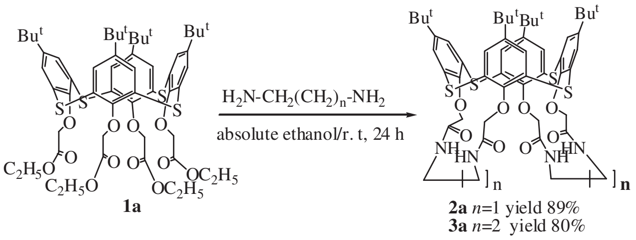
Department of Chemistry, Wuhan University, Wuhan 430072, China

Under selected conditions, 1,2:3,4-doubly crowned *p-tert*-butyl-thiacalix[4]arene in cone conformation and 1,3:2,4-doubly crowned *p-tert*-butyl-thiacalix[4]arene in 1,3-alternate conformation were obtained through aminolysis in high to good yield, respectively.

Keywords: calixarene, thiacalixarene, crown, aminolysis

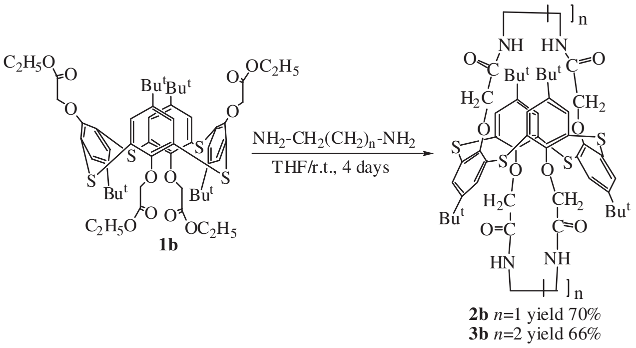
Thiacalixarene is a new member of calixarene family in which epithio groups replaced the methylene bridges of traditional calixarenes. When they were accessible in multi-grams scale by a simple synthetic procedures,[1] thiacalixarenes became attractive candidates as molecular platforms for constructing more sophisticated host molecules. A number of derivatives of thiacalix[4]arenes have been synthesised.[2,3] Among them, it is mentioned that *p-tert*-butyl-tetrakis[(ethoxycarbonyl)methoxy]thiacalix[4]arene could be synthesised easily in definite, desired conformation.[4] In calixarene chemistry, it is known that a number of nitrogenous calixarene derivatives can be synthesised from ester-containing calixarene via aminolysis including substituted amides,[5–7] amides bridged calixarenes,[8,9] *etc*. Aminolysis can be also provided a route to incorporate amino acid or polypeptide residues.[10,11] Such nitrogenous calixarenes may show better complexation ability towards transitional metal ions. Here we report the research on doubly azacrowned *p-tert*-butyl-thiacalix[4]arenes which could be synthesised under selected conditions.

p-tert-butyl-tetrakis[(ethoxycarbonyl)methoxyl]thiacalix[4]arene **1a** (cone) and **1b** (1,3-alternate) were synthesised according to the literature.[4] The aminolysis was very sensitive to reaction conditions. When ethylenediamine or propylenediamine reacted with **1a** in a molar ratio of 20:1 in absolute ethanol at reflux temperature for 24 h, corresponding 1,2:3,4-doubly crowned *p-tert*-butyl-thiacalix[4]arene with conic conformation were obtained in high yields as shown in Scheme 1.



Scheme 1

If **1b** reacted with ethylenediamine or propylenediamine in a molar ratio of 20:1 in THF at reflux temperature for 24 h, only very complicated products were obtained and no product with defined structure could be separated. However, changing molar ratio to 100:1 and carrying out the reaction at room temperature and lengthening reaction time to 4 days, 1,3:2,4-doubly crowned *p-tert*-butyl-thiacalix[4]arene with 1,3-*alt*-conformation could be obtained in good yields as shown in Scheme 2.



Scheme 2

In comparison with the ^{1}H NMR spectra of **2a** with that of **2b,** it is remarkable that the signals of the *tert*-butyl protons appeared as a singlet at 1.12 ppm in **2a** and at 1.32 ppm for **2b** indicating both with high symmetry and existed in conic or 1,3-*alt* conformation. The resonance signals of OCH_2CO appeared at higher field for **2a** (4.00–4.04 ppm) compared with that for **2b** (4.40 ppm) indicates **2b** existing in 1,3-alt-conformation. This is attributed to the shielding effect of two adjacent phenyls in 1,3-*alt*-conformation. The conclusion can be further proved by comparison with the resonance signals at δ1.12 ppm and 4.00–4.04 ppm (*t*-butyl and OCH_2CO) for **2a** and 1.32, 4.40 ppm for **2b** with corresponding resonance signals at 1.08, 5.17 ppm for conic *p-tert*-butyl-tetrakis[(ethoxycarbonyl)methoxy]thiacalix[4]arene **1a** and 1.24, 4.61 ppm for 1,3-alt-*p-tert*-butyl-tetrakis[(ethoxycarbonyl)methoxy]thiacalix[4]arene **1b**. Besides, all the patterns for *tert*-butyl, $-CH_2CO-$ and phenyl protons of **2a** show good comparability to the 1,2:3,4-doubly crowned calix[4]arene[5a] which is in conic conformation. The patterns for *tert*-butyl and phenyl protons of **2b** are also similar to those of 1,3-alternate thiacalix[4]arene-biscrowns-4,-5, and -6 which synthesised by reacting thiacalix[4]arene with tri-, tetra-, and pentaethylene glycol ditosylates[12–14]. So It can be concluded that the product **2a** is a conic 1,2:3,4-doubly crowned *p-tert*-butylthiacalix[4]arene, and **2b** is a 1,3-*alt* one. The conformation of **3a** and **3b** can be deduced similarly.

Experimental

Melting points were determined on a Gallenkamp melting point apparatus and were uncorrected. ^{1}H NMR spectra were measured on Varian Mercury VX300 instrument using TMS as internal standard. Elemental analyses were carried out on a Carlo-Erba 1106 elemental analyzer. ESI-MS were recorded on VG ZAB-HS instrument. The reaction was carried out under an argon atmosphere. Yields refer to isolated pure products.

Synthesis of 5,11,17,23-tert-butyl-25,26: 27,28-bis[oxy(2,7-dioxo-3,6-diazaoctamethylene)oxy]-2,8,14,20-tetrathiacalix[4]arene (**2a**): A mixture of 0.53 g (0.5 mmol) of **1a**, 50 ml of absolute ethanol and 10 mmol diamine was stirred under reflux for 24 h. After recrystallisation from $CHCl_3/C_2H_5OH$(V/V, 1:2), **2a** was obtained as colourless crystal in 89% yield.

Yield. 89%, m.p. >290°C, ^{1}H NMR (300Hz, $CDCl_3$): δ (ppm) 1.12 (s, 36H, *t*-Bu), 3.45–3.56 (broad m, 4H, NCH_2CH_2N), 3.68–3.79 (broad m, 4H, NCH_2CH_2N), 4.00–4.04 (d, 4H, *J*=13.5Hz, OCH_2CO), 5.16–5.20 (d, 4H, *J*=13.5Hz, OCH_2CO), 7.24–7.36 (d, 8H, ArH), 7.85 (s, 4H, CONH), ESI-MS(+): 1000.3 $[M]^+$, Anal. calcd.

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* Correspondent. E-mail: yychen@whu.edu.cn

For. $C_{52}H_{64}N_4S_4O_8$: C, 62.37; H, 6.44; N 5.60; S 12.81; Found C, 62.29; H, 6.35; N 5.51; S 12.74.

Synthesis of 5,11,17,23-tert-butyl-25,26: 27,28-bis[oxy(2,7-dioxo-3,6-diazanonamethylene)oxy]-2,8,14,20-tetrathiacalix[4]arene (**3a**): Compound **3a** was synthesised according to the procedure mentioned above in 80% yield.

Yield. 80%, m.p. >290°C, ^{1}H NMR (300Hz, $CDCl_3$): δ (ppm) 1.12 (s, 36H, *t*-Bu), 1.72–1.85 (broad m, 4H, $NCH_2CH_2CH_2N$), 3.51–3.65 (broad m, 8H, $NCH_2CH_2CH_2N$), 4.15 (d, 4H, OCH_2CO), 5.07 (d, 4H, OCH_2CO), 7.26–7.37 (d, 8H, ArH), 7.93 (s, 4H, CONH), ESI-MS(+): 1028.7 [M] +, Anal. calcd. For. $C_{54}H_{68}N_4S_4O_8$: C, 63.01; H, 6.66; N 5.44; S 12.46; Found C, 62.90; H, 6.58; N 5.39; S 12.37.

Synthesis of 5,11,17,23-tert-butyl-25,27: 26,28-bis[oxy(2,7-dioxo-3,6-diazaoctamethylene)oxy]-2,8,14, 20-tetrathiacalix[4]arene (**2b**): A mixture of 0.53 g (0.5 mmol) of **1b**, 50 mmol diamine in 25 ml of THF was stirred for 4 days at room temperature. The work-up was the same as described above. **2b** were obtained in 70% yield.

Yield. 70%, m.p. >290°C ^{1}H NMR (300Hz, $CDCl_3$): δ (ppm) 1.28 (s, 36H, *t*-Bu), 3.04 (broad m, 8H, NCH_2CH_2N), 4.40 (s, 8H, OCH_2CO), 5.45 (s, 4H, CONH), 7.40 (s, 8H, ArH), ESI-MS(+): 1000.3 [M] +, Anal. calcd. For. $C_{52}H_{64}N_4S_4O_8$: C, 62.37; H, 6.44; N 5.60; S 12.81; Found C, 62.30; H, 6.34; N 5.52; S 12.76.

Synthesis of 5,11,17,23-tert-butyl-25,27: 26,28-bis[oxy(2,7-dioxo-3,6-diazanonamethylene)oxy]-2,8,14,20-tetrathiacalix[4]arene (**3b**): Compound **3b** was synthesised according to the procedure mentioned above in 66% yield.

Yield. 66%, m.p. >290°C, ^{1}H NMR (300Hz, $CDCl_3$): δ (ppm) 1.27 (s, 36H, *t*-Bu), 1.69–1.74 (broad m, 4H, $NHCH_2CH_2CH_2NH$), 2.71–2.75 (broad m, 8H, $NHCH_2CH_2CH_2NH$), 4.10 (s, 8H, OCH_2CO), 5.50 (m, 4H, CONH), 7.54 (s, 8H, ArH), ESI-MS(+): 1028.6 [M]$^+$, Anal. calcd. For. $C_{54}H_{68}N_4S_4O_8$: C, 63.01; H, 6.66; N 5.44; S 12.46; Found C, 62.88; H, 6.60; N 5.37; S 12.40.

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