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ORIGINAL ARTICLE

Regioselective synthesis of calix[4]arene 1,3-di- and monosubstituted sulfur-containing Schiff bases

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Abstract Regioselective alkylations of *p-tert*-butylcalix[4]arene with 3-methoxy-4-ω-chloroalkoxy-benzaldehydes in the system of K_2CO_3/KI/CH_3CN efficiently produce 1,3-di- and monosubstituted aldehydes according to the length of alkyl chains in alkylating reagent, which provides a versatile protocol for preparing calixarene 1,3-di- and sulfur-containing Schiff bases.

Keywords Calixarene · Alkylation · Dithiocarbazate · Schiff base · Crystal structure

Introduction

Calixarenes, which are macrocyclic compounds available in a variety ring sizes, are of particular interest as inclusion hosts, selective receptors, molecular sensors, and novel building blocks for supramolecular chemistry [1–5]. Owing to its pro-organized structure, calix[4]arene is currently a popular molecular platform for designing highly selective receptors. For these purpose numerous functional groups have been introduced on the upper or lower rim of calix[4]arene [6–10]. In spite of numerous efficient methods for chemical modification of calixarenes, the region- and stereoselective introduction of functional groups, however, continues to be a challenge to the synthetic chemist. The regioselective substitution of calix[4]arenes at the lower rim is mainly due to the different acidities of the phenolic hydroxyl groups. While 1,3-bridged or tetrasubstituted functionalization may be considered as one of the standard reactions in calix[4]arene chemistry [6, 11, 12], only a few examples of monofunctionalization are known [13, 14]. Direct alkylation of *p-tert*-butyl calix[4]arene with alkyl halides in the presence of one equivalent of the base (NaOMe [15], K_2CO_3, CsF [16], NaH [17], $(Bu_3Sn)_2O$ [18]) is less selective and gives the complicated mixture of monoalkoxycalixarenes with considerable amounts of deeper alkylation products and unreactive starting *p-tert*-butylcalixarene. Several indirect synthetic methods of monoalkoxy *p-tert*-butylcalixarenes involve preliminary protection of three hydroxyl groups of tetrahydroxycalixarene [19, 20], or selective dealkylation of di- or tetraalkoxycalixarenes with iodotrimethylsilane [21]. However, these methods are preparatively inconvenient. Now we report the selective preparation of functional *p-tert*-calix[4]arene 1,3-di-aldehyde and monoaldehyde derivatives by direct alkylation reaction as well as the synthesis of sulfur-containing Schiff bases in a very efficient procedure.

Experiment section

All reagents and solvents were commercial available with analytical grade and used as received. Further purification and drying by standard method were employed and distilled prior to use when necessary. All evaporations of organic solvents were carried out with a rotary evaporator in conjunction with a water aspirator. *p-tert*-Butylcalix[4]arene, [22] *S*-methyl and *S*-benzyldithiocarbazate [23–25] were prepared according to the published methods. Melting points were taken on a hot-plate microscope apparatus and are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded with a Bruker AV-600 spectrometer. IR spectra were obtained on a Bruker Tensor27 spectrometer (KBr disc). Elemental analyses were obtained on PE 2400 instrument.

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X-ray data were collected on a Bruker Smart APEX-2 CCD diffractometer.

The general procedure for preparation of calixarene aldehydes **3a–b** and **4a**

A suspension of *p-tert*-butylcalix[4]arene **1** (6.0 mmol, 4.00 g) and anhydrous potassium carbonate (48.0 mmol, 6.6 g), potassium iodide (2.4 g, 14.0 mmol) in dry acetonitrile (150 mL) was heated to refluxing under nitrogen for 2 h. Then 3-methoxy-4-(chloroalkoxy)benzaldehyde **2a–b** (14.0 mmol) was added. The reaction mixture was refluxed for 4 days. After removal of larger portion of acetonitrile, the residue was put in large portion of water. The resulting precipitates were collected by filtration and recrystallized from a mixture of chloroform and ethanol to give pure solid product for analysis.

3a ($n = 2$, *R*=CH_3, *p*-CHO): white solid, Yield: 18%, m.p. 110–115 °C, ^{1}H NMR($CDCl_3$, 600 MHz)δ: 9.82 (s, 2H, CHO), 7.39 (br, 2H, ArH), 7.30 (br, 2H, ArOH), 7.06 (s, 4H, ArH), 7.03 (br, 2H, ArH), 6.97 (br, 2H, ArH), 6.73 (s, 4H, ArH), 4.46 (br, 4H, OCH_2), 4.40 (d, $J = 13.2$ Hz, 4H, $ArCH_2Ar$), 4.33 (br, 4H, OCH_2), 3.64 (s, 6H, OCH_3), 3.28 (d, $J = 13.2$ Hz, 4H, $ArCH_2Ar$), 1.31 (s, 18H, CH_3), 0.92 (s, 18H, CH_3); IR (KBr, cm^{-1}) υ: 3449 (m), 2958 (s), 2870 (m), 1687 (s), 1591 (s), 1511 (s), 1474 (s), 1271 (vs), 1201 (s), 1131 (s), 1037 (m). Anal Calcd for $C_{64}H_{76}O_{10}$: C, 76.46; H, 7.62; Found: C, 76.28; H 7.85.

3b ($n = 3$, R=CH_3, *p*-CHO): white solid, Yield: 79%, m.p. 82–85 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ: 9.80 (s, 2H, CHO), 7.59 (s, 2H, ArH), 7.42 (d, $J = 7.8$ Hz, 2H, ArH), 7.35 (s, 2H, ArOH), 7.12 (d, $J = 7.8$ Hz, 2H, ArH), 7.03 (s, 4H, ArH), 6.84 (s, 4H, ArH), 4.51 (br, 4H, OCH_2), 4.21 (d, $J = 12.0$ Hz, 4H, $ArCH_2Ar$), 4.14 (br, 4H, OCH_2), 3.86 (s, 6H, OCH_3), 3.31 (d, $J = 12.0$ Hz, 4H, $ArCH_2Ar$), 2.25–2.46 (m, 4H, CH_2), 1.27 (s, 18H, CH_3), 0.99 (s, 18H, CH_3); ^{13}C NMR ($CDCl_3$, 150 MHz) δ: 190.9, 154.0, 150.5, 149.4, 147.3, 141.8, 132.6, 130.1, 127.7, 126.8, 125.6, 125.1, 111.9, 109.3, 72.4, 65.8, 55.9, 34.0, 33.9, 31.7, 31.6, 31.0, 29.8; IR (KBr, cm^{-1}) υ: 2958 (s), 2870 (m), 1687 (s), 1591 (s), 1511 (s), 1474 (s), 1271 (vs), 1201 (s), 1131 (s), 1037 (m). Anal Calcd for $C_{66}H_{80}O_{10}$: C, 76.71; H, 7.80; Found: C, 76.51; H 7.47.

4a ($n = 2$, R=CH_3, *p*-CHO): The same reaction procedure was used by using 1:1.2 ratio of *p-tert*-butylcalix[4]arene (6.0 mmol, 4.00 g) **1** to 3-methoxy-4-(chloroethoxy)benzaldehyde **2a** to give white solid of **4a**: Yield: 77%, m.p. 115–118 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ: 9.89 (s, 1H, CHO), 9.16, 9.17 (s, s, 2H, ArOH), 7.51 (d, $J = 7.8$ Hz, 2H, ArH), 7.42 (s, 1H, ArOH), 7.18 (d, $J = 7.8$ Hz, 2H, ArH), 7.12 (s, 2H, ArH), 7.07 (s, 2H, ArH), 7.06 (s, H, ArH), 7.02 (s, 2H, ArH), 6.98 (s, 2H, ArH), 4.71 (s, 2H, OCH_2), 4.59 (s, 2H, OCH_2), 4.55 (d, $J = 12.0$ Hz, 2H, $ArCH_2Ar$), 4.14 (d, $J = 12.0$ Hz, 2H, $ArCH_2Ar$), 3.71 (s, 3H, OCH_3), 3.44 (d, $J = 12.0$ Hz, 2H, $ArCH_2Ar$), 3.38 (d, $J = 12.0$, 2H, $ArCH_2Ar$), 1.20 (s, 36H, CH_3); ^{13}C NMR ($CDCl_3$, 150 MHz) δ: 191.1, 153.5, 150.4, 149.1, 148.3, 147.5, 144.0, 143.4, 133.8, 130.8, 128.3, 128.1, 127.8, 127.6, 126.6, 126.5, 125.9, 125.6, 125.5, 116.4, 112.2, 109.3, 74.0, 67.8, 55.8, 34.3, 34.0, 32.7, 31.9, 31.5, 31.3; IR (KBr) υ: 2959 (s), 1692 (s), 1600v (s), 1478 (m), 1307 (m), 1257 (s), 1210 (m), 1162 (m), 1114 (w), 1059 (w), 832 (w). Anal Calcd for $C_{54}H_{66}O_7$: C, 76.56; H, 8.33; Found: C, 76.79; H 8.57.

General procedure of preparation of sulfur-containing Schiff bases **5a–d**

To a methanol solution (50 mL) of **3a–b** (1.0 mmol) was added *S*-methyldithiocarbazate or *S*-benzyldithiocarbazate (2.2 mmol) and one drop of concentrated hydrochloric acid. The mixture was stirred at room temperature for about 2 days. The resulting precipitate was filtrated out and recrystallized from chloroform and ethanol to give **5a–d**:

5a ($n = 2$, R=OCH_3, *p*-CHO, R′=H): yellow solid, 69%, m.p. 160–168 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ: 10.89 (s, 2H, NH), 7.77 (s, 2H, CH=N), 7.68 (br, 2H, ArH), 7.37 (s, 2H, ArOH), 7.15 (s, 2H, ArH), 7.06 (s, 2H, ArH), 7.03 (s, 2H, ArH), 6.97 (br, 2H, ArH), 6.86–6.80 (m, 4H, ArH), 4.36 (br, 4H, OCH_2), 4.30 (d, $J = 13.2$ Hz, 4H, $ArCH_2Ar$), 4.21 (br, 4H, OCH_2), 3.91 (s, 6H, OCH_3), 3.23 (d, $J = 13.2$ Hz, 4H, $ArCH_2Ar$), 2.67 (s, 6H, SCH_3), 1.14 (s, 18H, CH_3), 1.03 (s, 18H, CH_3); IR (KBr, cm^{-1}) ν: 3382 (s), 3415 (s), 2956 (s), 2866 (w), 1617 (vs), 1508 (s), 1454 (s), 1404 (vs), 1276 (vs), 1196 (m), 1137 (m), 1032 (m); Anal Calcd for $C_{68}H_{84}N_4S_4O_8$: C, 67.31; H, 6.98; N, 4.62; Found: C, 67.05; H 7.22; N, 4.69.

5b ($n = 3$, R=OCH_3, *p*-CHO, R′=H): yellow solid, 65%, m.p. 140–145 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ: 10.58 (s, 2H, NH), 7.70 (s, 2H, CH=N), 7.69 (d, $J = 7.8$ Hz, 2H, ArH), 7.32 (s, 2H, ArOH), 7.06 (s, 2H, ArH), 7.05 (s, 4H, ArH), 6.94 (d, $J = 7.8$ Hz, 2H, ArH), 6.86 (s, 4H, ArH), 4.36 (s, 4H, OCH_2), 4.26 (d, $J = 12.0$ Hz, 4H, $ArCH_2Ar$), 4.13 (s, 4H, OCH_2), 3.90 (s, 6H, OCH_3), 3.34 (d, $J = 12.0$ Hz, 4H, $ArCH_2Ar$), 2.66 (s, 6H, SCH_3), 2.43 (s, 4H, CH_2), 1.28 (s, 18H, CH_3, 1.00 (s, 18H, CH_3); ^{13}C NMR ($CDCl_3$, 150 MHz) δ: 199.2, 151.2, 150.6, 149.6, 149.4, 147.2, 145.8, 141.7, 132.7, 127.7, 125.6, 125.1, 123.5, 112.2, 108.6, 72.7, 65.7, 56.0, 34.0, 31.7, 31.1, 29.8, 17.7; IR (KBr, cm^{-1}) υ: 3382 (m), 2958 (vs), 2870 (m), 1600 (m), 1483 (vs), 1361 (m), 1268 (vs), 1235 (s), 1201 (s), 1133 (m), 1099 (m), 1045 (s). Anal Calcd for $C_{70}H_{88}N_4S_4O_8$: C, 67.72; H, 6.98; N, 4.51; Found: C, 67.87; H 6.90; N, 4.34.

5c ($n = 2$, R=OCH_3, *p*-CHO, R′=Ph): yellow solid, 60%, m.p. 195–200 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ: 10.56 (s, 2H, NH), 7.70 (s, 2H, CH=N), 7.58 (s, 2H, ArOH), 7.46 (t, $J = 7.2$ Hz, 6H, ArH), 7.30 (t, $J = 7.2$ Hz,

6H, ArH), 7.06 (br, 8H, ArH), 6.90 (s, 4H, ArH), 4.52 (s, 4H, SCH_2), 4.38 (d, $J = 6.0$ Hz, 4H, OCH_2), 4.32 (d, $J = 13.2$ Hz, 4H, $ArCH_2Ar$), 4.12 (d, $J = 6.0$ Hz, 4H, OCH_2), 3.80 (s, 6H, OCH_3), 3.30 (d, $J = 13.2$ Hz, 4H, $ArCH_2Ar$), 1.30 (s, 18H, CH_3), 0.99 (s, 18H, CH_3); IR (KBr, cm^{-1}) υ: 3143 (s), 2957 (vs), 2870 (m), 1598 (s), 1479 (s), 1402 (s), 1270 (vs), 1199 (m), 1136 (m), 1033 (m). Anal Calcd for $C_{80}H_{92}N_4S_4O_8$: C, 70.34; H, 6.79; N, 4.10; Found: C, 70.32; H 6.90; N, 3.75.

5d ($n = 3$, R=OCH_3, *p*-CHO, R′=Ph): yellow solid, 62%, m.p. 138–146 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ: 10.60 (s, 2H, NH), 7.72 (s, 2H, CH=N), 7.61 (s, 2H, ArOH), 7.45 (t, $J = 7.2$ Hz, 6H, ArH), 7.34 (t, $J = 7.2$ Hz, 6H, ArH), 7.06 (s, 8H, ArH), 6.87 (s, 4H, ArH), 4.58 (s, 4H, SCH_2), 4.33 (d, $J = 6.0$ Hz, 4H, OCH_2), 4.25 (d, $J = 13.2$ Hz, 4H, $ArCH_2Ar$), 4.12 (d, $J = 6.0$ Hz, 4H, OCH_2), 3.84 (s, 6H, OCH_3), 3.32 (d, $J = 13.2$ Hz, 4H, $ArCH_2Ar$), 2.43–2.41 (m, 4H, CH_2), 1.29 (s, 18H, CH_3), 1.02 (s, 18H, CH_3); ^{13}C NMR ($CDCl_3$, 150 MHz) δ: 196.9, 150.8, 150.1, 149.1, 148.9, 146.6, 145.5, 141.1, 135.8, 132.2, 129.0, 128.1, 127.2, 127.0, 125.5, 125.1, 124.6, 123.1, 111.7, 108.2, 72.2, 65.1, 55.5, 38.9, 33.5, 33.3, 31.2, 30.9, 30.8, 30.6, 29.3; IR (KBr, cm^{-1}) υ: 2956 (s), 2869 (m), 1597 (m), 1481 (s), 1269 (vs), 1201 (m), 1132 (m), 1037 (m). Anal Calcd for $C_{82}H_{96}N_4S_4O_8$: C, 70.67; H, 6.94; N, 4.02; Found: C, 70.88; H 7.24; N, 3.81.

General procedure of preparation of sulfur-containing Schiff bases **6a–b**

To a methanol solution (50 mL) of **4a** (1.0 mmol) was added *S*-methyl or *S*-benzyldithiocarbazate (1.2 mmol) and one drop of concentrated hydrochloric acid. The mixture was stirred at room temperature for about 2 days. The resulting precipitate was filtrated out and recrystallized from chloroform and ethanol to give **6a–b**:

6a (R′=H): yellow solid, 75%, m.p. 188–194 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ: 10.30 (s, 1H, NH), 10.11 (s, 1H, OH), 9.30 (s, 2H, OH), 7.80 (s, 1H, CH=N), 7.38 (s, 1H, ArH), 7.20 (d, $J = 8.4$ Hz, 1H, ArH), 7.10 (s, 2H, ArH), 7.09 (d, $J = 8.4$ Hz, 1H, ArH), 7.02 (s, 2H, ArH), 6.97 (s, 2H, ArH), 4.66 (s, 2H, OCH_2), 4.57 (s, 2H, OCH_2), 4.56 (d, $J = 13.2$ Hz, 2H, $ArCH_2Ar$), 4.18 (d, $J = 13.2$ Hz, 2H, $ArCH_2Ar$), 3.73 (s, 3H, OCH_3), 3.42 (d, $J = 13.2$ Hz, 2H, $ArCH_2Ar$), 3.39 (d, $J = 13.2$ Hz, 2H, $ArCH_2Ar$), 2.66 (s, 3H, SCH_3), 1.21 (s, 30H, CH_3), 1.20 (s, 6H, CH_3); ^{13}C NMR ($CDCl_3$, 150 MHz) δ: 199.2, 150.3, 149.8, 148.7, 147.9, 147.8, 143.1, 142.6, 133.1, 127.7, 127.6, 127.0, 126.1, 125.2, 122.6, 112.6, 108.3, 73.7, 67.3, 55.2, 33.8, 33.5, 33.4, 32.5, 31.6, 31.0, 17.2; IR (KBr, cm^{-1}) υ: 3284 (m), 3128 (m), 2959 (vs), 2870 (m), 1597 (m), 1484 (vs), 1403 (m), 1270 (vs), 1201 (s), 1135 (m), 1100 (m), 1045 (m). Anal Calcd for $C_{56}H_{70}N_2S_2O_6$: C, 72.23; H, 7.58; N, 3.01; Found: C, 72.44; H 7.87; N, 2.71.

6b (R′=Ph): yellow solid, 56%, m.p. 140–144 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ: 10.19 (s, 1H, NH), 10.15 (s, 1H, OH), 10.07 (s, 1H, OH),8.63 (s, 1H, CH=N), 7.77 (s, 1H, OH), 7.44 (d, $J = 13.8$ Hz, 1H, ArH), 7.34 (t, $J = 13.2$ Hz, 1H, ArH), 7.18 (d, $J = 13.8$ Hz, 1H, ArH), 7.10 (br, 2H, ArH), 7.06 (br, 2H, ArH), 7.02 (s, 2H, ArH), 6.96 (s, 2H, ArH), 4.67–4.68 (m, 2H, $ArCH_2Ar$), 4.57–4.54 (m, 4H, $ArCH_2Ar$, OCH_2), 4.20–4.15 (m, 2H, OCH_2), 3.66 (s, 3H, OCH_3), 3.44–3.37 (m, 4H, $ArCH_2Ar$), 1.21 (s, 27H, CH_3), 1.20 (s, 9H, CH_3); ^{13}C NMR ($CDCl_3$, 150 MHz) δ: 197.5, 160.9, 150.4, 149.8, 148.7, 147.9, 147.8, 147.3, 143.0, 142.5, 133.1, 129.0, 128.1, 127.7, 127.0, 126.9, 126.1, 125.2, 125.1, 122.7, 112.5, 73.7, 67.2, 55.3, 39.0, 33.7, 33.5, 33.4, 32.5, 31.6, 31.0, 30.8; IR (KBr, cm^{-1}) υ: 3553 (s), 3477 (vs), 3415 (vs), 2958 (s), 1618 (m), 1485 (s), 1269 (s), 1201 (m), 1040 (m). Anal Calcd for $C_{62}H_{74}N_2S_2O_6$: C, 73.93; H, 7.41; N, 2.78; Found: C, 734.21; H 7.65; N, 2.69.

Results and discussion

The alkylation reaction was carried out by refluxing *p-tert*-calix[4]arene **1** with 3-methoxy-4-(2-chloroethoxy)benzaldehyde **2a** with molar ratio of 1:2.2 in the system of K_2CO_3/KI/CH_3CN for 4 days. Under this condition the reaction mainly stopped at monosubstitution stage and could go further. After column chromatography 18% of 1,3-dialdehyde **3a** and 50% of monoaldehyde **4a** can be isolated. The yield of 1.3-dialdehyde **3a** could not be increased by prolonging the reaction time or adding more alkylating reagent in the reaction. On the other hand by using the 1:1.2 molar ratio of reactants, monoalkylated product **4a** can be prepared in very satisfied yield (77%) with very high purity. In such case pure monoaldehyde **4a** could be gotten by merely crystallization from ethanol and no need further purification with LC. Under similar reaction conditions *p-tert*-calix[4]arene **1** was alkylated with 3-methoxy-4-(3-chloropropoxy)benzaldehyde **2b** with molar ratio of 1:2.2 in the system of K_2CO_3/KI/CH_3CN at refluxing for 4 days, 1,3-disubstituted aldehyde derivative **3b** can be prepared in excellent yield (79%) and nearly no monosubstituted product was found in this reaction. In the literature the reactive aldehyde function has been introduced into calixarene at upper rim [26, 27] or lower rim [28–33] with several kinds of methodology. Here calix[4]arene 1,3-disubstituted- and monosubstituted aldehyde derivatives can be efficiently prepared by regioselective alkylation reaction with different alkylating reagents. This great difference in the reactivity and in the outcome of the reaction seems due to the length of alkyl chain in alkylating reagent (Scheme 1).

^{1}H NMR spectra of **3a** and **3b** display two doublet at about 4.40 and 3.30 ppm with coupling constant of more than 12 Hz, which are characteristic peaks of the axial and equatorial protons of bridging methylene groups in 1,3-disubstituted calixarene. Two singlets with 1:1 ratio for *t*-butyl groups at 1.27 and 0.99 also suggest calixarene in *cone* conformation. In ^{1}H NMR spectra of **4a** four doublet peaks at 4.55, 4.14 3.44 and 3.38 ppm for the bridging methylene groups clearly indicate there are two kinds of methylene groups in the molecule and only one phenolic hydroxyl group is alkylated. The dialkylated and mono-alkylated calixarene structures were confirmed by the X-ray diffraction determination of single crystals of **3b** and **4a**. The perspective views with the same atomic numbering scheme are shown in Figs. 1 and 2, respectively. The crystal data and refinement details are given in Table 1. It is clearly seen that two molecules have similar structural pattern with calix[4]arene core remaining in *cone* conformation. In molecules of **3b** the steric interaction of the two bulky bisphenol units without substituent causes the two bisphenol substituted aryl rings to be oriented perpendicular to the plane of the methylene bridge carbon atoms. The other two aryl rings are more inclined. The two pendant arms of *O*-alkoxyaldehyde stretch equivalently outside and the whole molecule is in nearly centrosymmetric manner.

Compound **3a–b** and **4a** have one or two reactive functional aldehyde groups and remain two or three phenolic groups, which provide great possibility for further modification and introduction of other functional motifs into calix[4]arene. To illustrate the advantages of this method, we carried out the condensation reactions of **3a–b** and **4a** with *S*-methyl and *S*-benzyldithiocarbazate. Because condensation products of *S*-alkyldithiocarbazates with carbonyl compounds are special kinds of sulfur-containing Schiff bases, The synthesis and application study of them in metal complexation, biochemical and pharmacological activity have been under study for many years [23–25, 34–42].

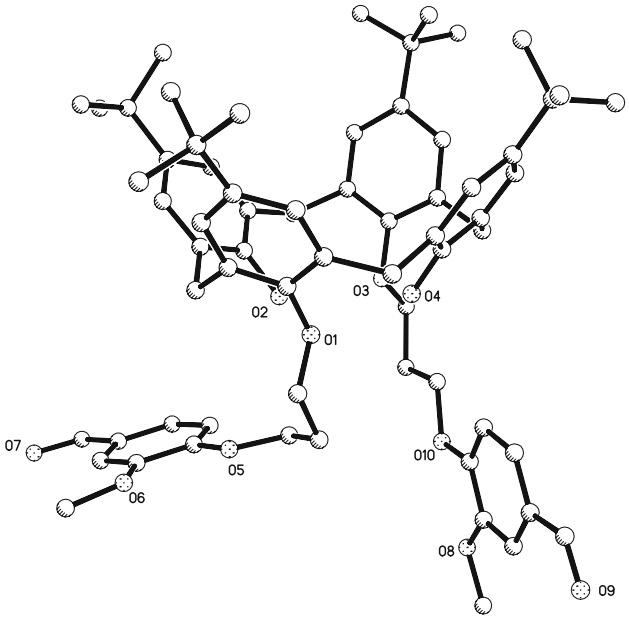
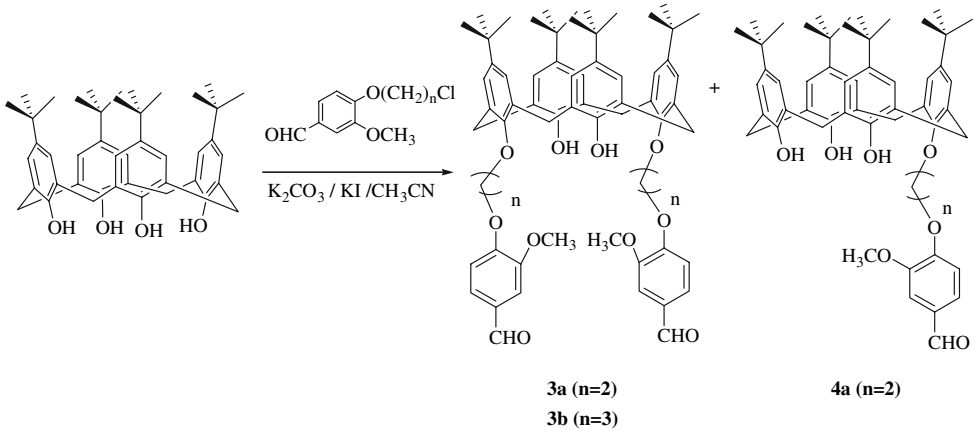


Fig. 1 Molecular structure of **3b** in crystal

Introduction of dithiocarbazate into calixarene core will provides potential sulfur-containing products and these compounds are potential candidates for sensors and coordinating ligands of metal complexes [43]. In the presence of concentrated hydrochloric acid as catalyst the mixture of calixarene aldehydes and *S*-methyl or *S*-benzyldithiocarbazate in ethanol was stirred at room temperature for 2 days, the corresponding calix[4]arene 1,3-di- and mono sulfur-containing Schiff bases **5a–d** and **6a–b** were prepared efficiently as yellow solids in satisfied yields (56–75%) (Schemes 2 and 3).

The structure of calix[4]arene 1,3-dischiff bases **5a–d** and monoschiff bases **6a–b** were fully characterized by ^{1}H and ^{13}C NMR, IR spectra and elemental analysis. In ^{1}H NMR spectra of **5a–d** a pair of doublets at about 3.30 and

Scheme 1 Synthesis of calix[4]arene 1,3-dialdehydes and monoaldehyde



3a (n=2)
3b (n=3)

4a (n=2)

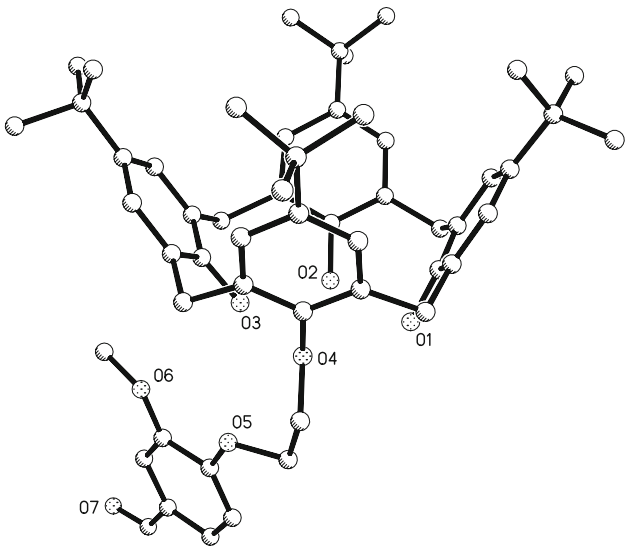


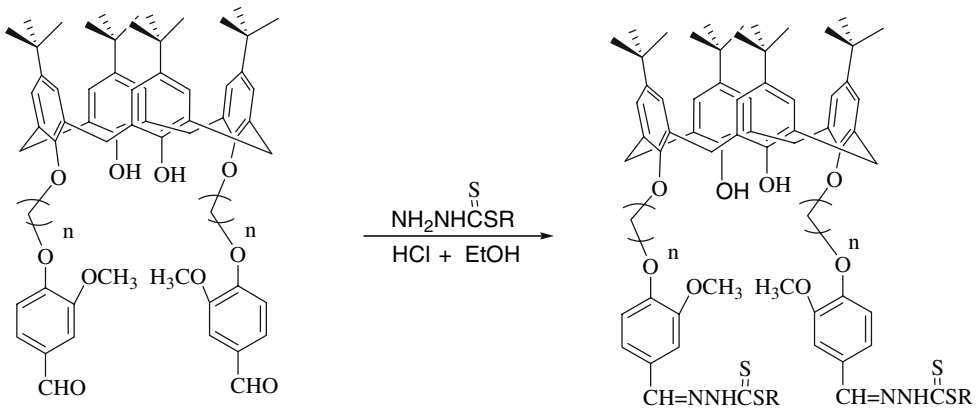
Fig. 2 Molecular structure of **4a** in crystal

4.30 ppm with coupling constant of more than 12 Hz for the axial and equatorial protons of bridging methylene groups means that calixarenes are 1,3-disubstituted and exist in *cone* conformation. The 1,3-disubstitution at the lower rim was also confirmed by the appearance of one singlet at about 7.30–7.90 ppm for the phenolic protons on calix[4]-arene core and two singlets at about 1.00 and 1.20 ppm for the *tert*-butyl groups on the upper rim with the actual positions of the signals dependant on the substituent attached. The formation of the Schiff bases was further determined by one signal of CH=N group at a range of 7.70–8.60 ppm and one singlet of NH group at a range of 9.90–10.90 ppm. In ^{1}H NMR spectra of **6a**–**b** the two peaks for phenolic hydroxyl groups and several mixed peaks for the bridging methylene groups clearly shows that the calixarene is monosubstituted. In the IR spectra of Schiff bases the disappearance of stronger carbonyl group at 1690 cm^{-1} indicates that all aldehyde groups in **3a**–**b** and **4a** have been

Table 1 Crystal data and structure refinement details of compounds

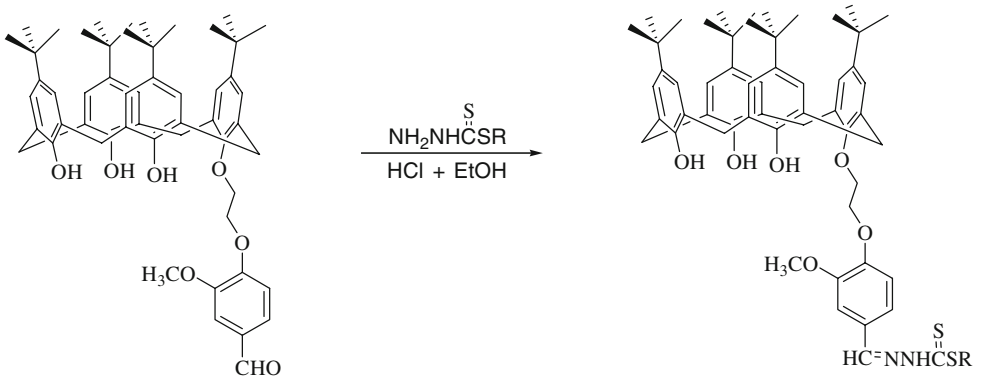
	3b	**4a**
Molecular formula	$C_{66}H_{80}O_{10}$,H_2O,CH_4O	$C_{55}H_{70}O_8$
Formula weight	1083.36	859.11
T/K	296	296
Wavelength/nm	0.71073	0.71073
Crystal system	Triclinic	Triclinic
Space group	*P*-1 (No. 2)	*P*-1 (No. 2)
a/Å	12.172 (3)	11.781 (3)
b/Å	13.124 (3)	13.544 (3)
c/Å	20.682 (5)	18.455 (4)
β (°)	90.026 (3)	80.850 (3)
	99.352 (3)	74.043 (3)
	95.704 (3)	66.862 (3)
V (nm^3)	3243.3 (13)	2599.4 (11)
Z	2	2
F(000)	1168	928
D_{calc} (g/cm^3)	1.109	1.098
Absorption Coefficient (mm^{-1})	0.075	0.072
θ range/(°)	1.6–25.0	1.95–25.01
Limiting indices	$-14 \le h \le 14, -14 \le k \le 15, -24 \le l \le 24$	$-13 \le h \le 14, -14 \le k \le 16, -21 \le l \le 21$
Reflections collected/unique	23597/11366[R(int) = 0.067]	18929/9092 [R(int) = 0.067]
Completeness to theta	99.3%	99.3%
Data/restraints/parameters	11366/2/724	9092/1/586
Refinement method	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2
Final R indices[$I > 2\sigma(I)$]	$R_1 = 0.0849$, $wR_2 = 0.2359$	$R_1 = 0.0798$, $wR_2 = 0.2154$
R indices (all data)	$R_1 = 0.2156$, $wR_2 = 0.3322$	$R_1 = 0.2156$, $wR_2 \setminus 0.3051$
Goodness-of-fit on F^2	1.001	0.984
Largest diff. peak and hole/(e · nm^{-3} × 10^{-3})	0.764 and −0.366	0.402 and −0.206

Scheme 2 Synthesis of calix[4]arene 1,3-dischiff bases



5a: n = 2, R = CH_3; **5b**: n = 3, R = CH_3; **5c**: n = 2, R = CH_2Ph; **5d**: n = 3, R = CH_2Ph

Scheme 3 Synthesis of calix[4]arene monoschiff bases



6a: R = CH_3 ; **6b**: R = CH_2Ph

transformed into imine groups, which show middle strong absorption at about 1600 cm^{-1} (Scheme 3).

In conclusion, we have demonstrated the selective di- and monoalkylation of *p-tert*-butylcalix[4]arene with chloroalkyl vanillin under normal alkylation protocol, thus opening a simple access to calixarene derivatives with reactive a functional aldehyde groups which are not available by other methods. Furthermore, the useful *S*-alkyldithiocarbazate has also been introduced into calixarene chemistry. The complexation study of these potential ligands is on the way.

Supplementary material

Single crystal X-ray diffraction data are deposited with CCDC (Deposition numbers **3b**: 693350; **4a**: 693348).

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