Synthesis of straight arm chains substituted dibenzo-21-crown-7 derivatives

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A series of straight arm chains substituted dibenzo-21-crown-7 derivatives **2a–c**, **3a–c**, and **5a–c** have been synthesised by the Huang Minlon method or reduction with sodium borohydride from the corresponding dibenzo-21-crown-7 bridged diketones **1a–c** and **4a–c**, which were obtained by diacylation of dibenzo-21-crown-7 with excessive mono- or dicarboxylic acids in the presence of polyphosphoric acid. All new compounds were characterised by IR, MS, ^{1}H NMR and elemental analysis.

Keywords: synthesis, dibenzo-21-crown-7, derivatives

Introduction

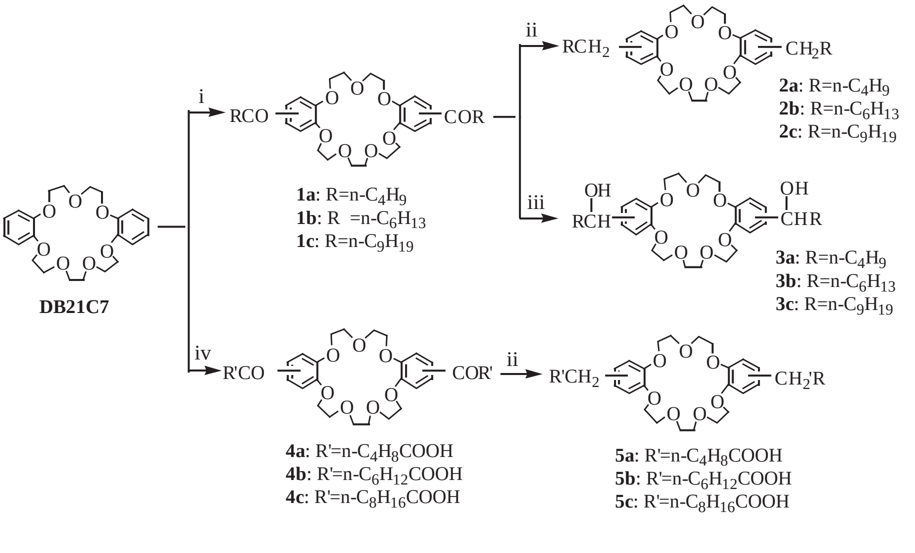
Crown compounds have attracted considerable interest as important complexants for various metal ions in coordination chemistry, analytical chemistry and radiochemistry.[1–3] Among them, dibenzo-crown ethers were one of the most early and common species,[4] but the low lipophilicity and poor coordinative capacity limited their sphere of application. It was known that the solubility of dibenzo-crown ethers in organic solvents could be much improved by appending alkyl substituents to their aromatic rings.[5] The alkyl substituted derivatives of dibenzo-18-crown-6 have been reported long ago,[6,7] and we also reported a series of dibenzo-18-crown-6 with long-chain dihydroxamic acids as side arms[8] previously. However, there were few studies on alkyl substituted dibenzo-crown ethers possessing larger cavity size, such as dibenzo-21-crown-7 (DB21C7), which could coordinate with metal ions possessing larger diameter. In recent years, special attentions have been paid to these crown ethers, for they have high selectivity for cesium cation.[9,10] The first alkylated dibenzo-21-crown-7, bis[4(or 5)-*tert*-butylbenzo]-21-crown-7, was synthesised by McDowell,[11] and then bis[4(or 5)-*tert*-octylbenzo]-21-crown-7 was also prepared [12], but no straight arm chains substituted dibenzo-21-crown-7 has been reported yet. In order to investigate the effect of side arms which containing different length polymethylene chains and certain functional groups (such as –OH or -COOH) on lipophilicity and coordinative capacity of the parent DB21C7, we designed and synthesised dibenzo-21-crown-7 derivatives **2a–c**, **3a–c** and **5a–c** (Scheme 1), and anticipated that they could be used in the field of ionic extraction, liquid membrane transport and disposal of nuclear wastes containing ^{137}Cs.

In the diacylation of DB21C7, we found the yields of **4a–c** were lower than that of **1a–c** because of the polymerisation accompanying the formation of **4a–c**, but if at least four fold excess of the dicarboxylic acid was added the polymer was reduced to a low level.

When **1a–c** and **4a–c** were reduced with Huang Minlon method, the experimental conditions (reaction temperature 150°C, time 3h) were more mild comparing with the reduction of common ketone [13], it may be due to the phase transfer catalysis of the dibenzo-21-crown-7-bridged diketone **1a–c** and **4a–c** which were also used as reacting substance here.

Experimental

General methods and materials: Melting points were taken on a micro-melting aPPAratus and uncorrected. IR spectra were recorded with a Nicolet-1705X IR spectrophotometer and frequencies reported in cm^{-1}. ^{1}H NMR spectra were obtained with a Bruker AC-E200, and chemical shifts in p.p.m. were reported relative to tetramethylsilane. Mass spectra data were measured in a Finnigan MAT 95 spectrometer. Elemental analyses were performed with a Carlo



i). $CH_3(CH_2)_nCO_2H$, PPA ii). H_2NNH_2 , KOH , $HO(CH_2)_2O(CH_2)_2O(CH_2)_2OH$
iii). $NaBH_4$, C_2H_5OH iv). $HO_2C(CH_2)_nCO_2H$, PPA

Scheme 1

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Erba 1106 instrument. Column Chromatography was carried out using silica gel (60H, Qingdao, China). The following compounds were prepared according to the literature: dibenzo-21-crown-7 (DB21C7),[4] polyphosphoric acid (PPA). [14]All reagents, unless otherwise indicated, were of analytical grade and were used without further purification.

General procedure for the preparation of dibenzo-21-crown-7-bridged diketones **1a–c.**

A mixture of DB21C7 (5mmol) and monocarboxylic acid (20mmol) in PPA (20ml) was vigorous stirred at 85°C for 4h. To the cooled reaction mixture was slowly added warm water (60ml) to hydrolysis excess PPA, and then filtered. After washing with water, the solid was crystallised from ethanol.

1a: Yellow solid. Yield 83.5%. M.p.62–65°C; IR(KBr): ν_{max}/cm^{-1} 2928, 2857, 1672, 1590, 1516, 1275, 1142, 1050; ^{1}H NMR(CDCl$_3$): δ 7.80–6.61(m, 6H, ArH), 4.82–3.63(m, 20H, OCH$_2$), 3.14–2.75 (t, J=6.6Hz, 4H, ArCOCH$_2$), 1.72–1.26(m, 8H, CH$_2$), 0.97–0.92 (t, J=6.6Hz, 6H, CH$_3$); Anal. Calcd for C$_{32}$H$_{44}$O$_9$: C 67.13, H 7.69. Found: C 67.02, H 7.73; MS (m/z): 572(M$^+$).

1b: Yellow solid. Yield 87.2%. M.p.60–64°C; IR(KBr): ν_{max}/cm^{-1} 2930, 2843, 1674, 1584, 1516, 1270, 1146, 1054; ^{1}H NMR(CDCl$_3$): δ 7.83–6.67(m, 6H, ArH), 4.76–3.50(m, 20H, OCH$_2$), 3.17–2.70 (t, J=6.5Hz, 4H, ArCOCH$_2$), 1.67–1.22(m, 16H, CH$_2$), 0.96–0.90 (t, J=6.6Hz, 6H, CH$_3$); Anal. Calcd for C$_{36}$H$_{52}$O$_9$: C 68.79, H 8.28. Found: C 68.67, H 8.41; MS (m/z): 629(M$^+$+1).

1c: Yellow solid. Yield 89.5%. M.p.65–69°C; IR(KBr): ν_{max}/cm^{-1} 2924, 2853, 1675, 1594, 1517, 1272, 1147, 1052; ^{1}H NMR(CDCl$_3$): δ 7.70–6.62(m, 6H, ArH), 4.75–3.53(m, 20H, OCH$_2$), 3.25–2.78 (t, J=6.6Hz, 4H, ArCOCH$_2$), 1.74–1.23(m, 28H, CH$_2$), 0.99–0.95 (t, J=6.6Hz, 6H, CH$_3$); Anal. Calcd for C$_{42}$H$_{64}$O$_9$: C 70.79, H 8.99. Found: C 70.85, H 8.83; MS (m/z): 713(M$^+$+1).

General procedure for the preparation of di-n-alkyl substituted dibenzo-21-crown-7 **2a–c**

A mixture of **1** (1.7mmol), 85% hydrazine hydrate (7.3ml) and triethylene glycol (9.2ml) was refluxed for 1h. The excess hydrazine hydrate was removed and KOH (0.92g) was added. When the temperature rose to 150°C, the mixture was refluxed for additional 3h, cooled, poured into 6N hydrochloric acid (20ml) and filtered. The precipitate was dissolved in CHCl$_3$ and chromatographed on a silica gel column with acetone/chloroform (1:1) as an eluent. The pure product as white solid was obtained by crystallisation from ethanol.

2a: White solid. Yield 67.5%. M.p.52–55°C; IR(KBr): ν_{max}/cm^{-1} 2928, 2851, 1589, 1512, 1267, 1139, 1057; ^{1}H NMR(CDCl$_3$): δ 6.85–6.70(m, 6H, ArH), 4.15–3.86(m, 20H, OCH$_2$), 2.55–2.48(t, J=7.5Hz, 4H, ArCH$_2$), 1.76–1.30(m, 12H, CH$_2$), 0.91–0.85(t, J=6.20Hz, 6H, CH$_3$); Anal. Calcd for C$_{32}$H$_{48}$O$_7$: C 70.59, H 8.82. Found: C 70.39, H 8.85; MS(m/z): 545(M$^+$+1).

2b: White solid. Yield 62.3%. M.p.57–61°C; IR(KBr): ν_{max}/cm^{-1} 2934, 2850, 1590, 1508, 1271, 1133, 1050; ^{1}H NMR(CDCl$_3$): δ 6.89–6.59(m, 6H, ArH), 4.26–3.78(m, 20H, OCH$_2$), 2.55–2.48(t, J=7.6Hz, 4H, ArCH$_2$), 1.70–1.30(m, 20H, CH$_2$), 0.93–0.87(t, J=6.4Hz, 6H, CH$_3$); Anal. Calcd for C$_{36}$H$_{56}$O$_7$: C 72.00, H 9.33. Found: C 71.87, H 9.41; MS(m/z): 601(M$^+$+1).

2c: White solid. Yield 70.6%. M.p.63–68°C; IR(KBr): ν_{max}/cm^{-1} 2932, 2854, 1594, 1513, 1274, 1135, 1056; ^{1}H NMR(CDCl$_3$): δ 6.84–6.51(m, 6H, ArH), 4.20–3.79(m, 20H, OCH$_2$), 2.53–2.44(t, J=7.5Hz, 4H, ArCH$_2$), 1.73–1.28(m, 32H, CH$_2$), 0.95–0.86(t, J=6.6Hz, 6H, CH$_3$); Anal. Calcd for C$_{42}$H$_{68}$O$_7$: C 73.68, H 9.94. Found: C 73.79, H 9.81; MS(m/z): 684(M$^+$).

General procedure for the preparation of dibenzo-21-crown-7-bridged dialkanols **3a–c**

To a well-stirred suspension of **1** (2.6mmol) in ethanol (24ml), powdered sodium borohydride (10 mmol) was added carefully. After stirring for 3h at room temperature, the solution was poured into water (20ml), neutralised with dilute H$_2$SO$_4$, filtered, and extracted with CHCl$_3$ (3×20ml). After washing with water and drying with MgSO$_4$, the CHCl$_3$ was evaporated and the residue was allowed to crystallised from ethanol to give the pure product.

3a: White solid. Yield 68.2%. M.p.94–98°C; IR(KBr): ν_{max}/cm^{-1} 3413, 2930, 2860, 1592, 1510, 1264, 1138, 1056; ^{1}H NMR(CDCl$_3$): δ6.92–6.80(m, 6H, ArH), 4.59–4.49(t, J=6.2, 2H, ArCH), 4.20–3.88(m, 20H, OCH$_2$), 2.25(s, 2H, OH, D$_2$O exchangeable), 1.83–1.18(m, 12H, CH$_2$), 0.94–0.85(t, J=6.1Hz, 6H, CH$_3$); Anal. Calcd for C$_{32}$H$_{48}$O$_9$: C 66.67, H 8.33. Found: C 66.59, H 8.40; MS (m/z): 576(M$^+$).

3b: White solid. Yield 70.0%. M.p.96–98°C; IR(KBr): ν_{max}/cm^{-1} 3406, 2928, 2843, 1591, 1515, 1270, 1141, 1051; ^{1}H NMR(CDCl$_3$): δ6.88–6.78(m, 6H, ArH), 4.57–4.50(t, J=6.2, 2H, ArCH), 4.17–3.81(m, 20H, OCH$_2$), 2.31(s, 2H, OH, D$_2$O exchangeable), 1.82–1.27(m, 20H, CH$_2$), 0.92–0.87(t, J=6.2Hz, 6H, CH$_3$); Anal. Calcd for C$_{36}$H$_{56}$O$_9$: C 68.35, H 8.86. Found: C 68.41, H 8.82; MS(m/z): 633(M$^+$+1).

3c: White solid. Yield 76.8%. M.p.95–99°C; IR(KBr): ν_{max}/cm^{-1} 3411, 2921, 2857, 1594, 1512, 1260, 1140, 1058; ^{1}H NMR(CDCl$_3$): δ6.93–6.80(m, 6H, ArH), 4.60–4.54(t, J=6.3, 2H, ArCH), 4.19–3.86(m, 20H, OCH$_2$), 2.17(s, 2H, OH, D$_2$O exchangeable), 1.79–1.24(m, 32H, CH$_2$), 0.90–0.84(t, J=6.1Hz, 6H, CH$_3$); Anal. Calcd for C$_{42}$H$_{68}$O$_9$: C 70.39, H 9.50. Found: C 70.45, H 9.42; MS (m/z): 716(M$^+$).

General procedure for the preparation of dibenzo-21-crown-7-bridged diketonic acids **4a–c**

A mixture of DB21C7 (5mmol) and dicarboxylic acid (20mmol) in PPA (20ml) was vigorous stirred at 75–80°C for 0.5h. To the cooled reaction mixture was slowly added warm water (60ml) to hydrolysis excess PPA, and then filtered. After washing with water, the precipitate was dissolved in CHCl$_3$ (20ml), dried with MgSO$_4$, filtered, and evaporated to dryness. The residue was treated as follow different method to afford pure sample.

4a: The residue stated above was chromatographed on a silica gel column with acetone/chloroform (1:1) as an eluent. The product was crystallised from methanol as light red solid. Yield 57.3%. M.p.82–87°C; IR(KBr): ν_{max}/cm^{-1} 3442, 2937, 2860, 1721, 1679, 1591, 1515, 1271, 1127, 1052; ^{1}H NMR(CDCl$_3$): δ 8.10(bs, 2H, CO$_2$H, D$_2$O exchangeable), 7.56–6.80(m, 6H, ArH), 4.20–3.65(m, 20H, OCH$_2$), 2.92–2.83(t, J=6.8, 4H, ArCOCH$_2$), 2.36–2.28(t, J=7.2, 4H, CH$_2$CO$_2$), 1.69–1.34(m, 8H, CH$_2$); Anal. Calcd for C$_{34}$H$_{44}$O$_{13}$: C 61.82, H 6.67. Found: C 61.89, H 6.56; MS(m/z): 660(M$^+$).

4b: The residual solid was recrystallised from methanol as white solid. Yield 73.5%. M.p.82–85°C; IR(KBr): ν_{max}/cm^{-1} 3436, 2934, 2845, 1710, 1678, 1592, 1516, 1268, 1128, 1058; ^{1}H NMR(CDCl$_3$): δ 8.07(bs, 2H, CO$_2$H, D$_2$O exchangeable), 7.55–6.84(m, 6H, ArH), 4.22–3.66(m, 20H, OCH$_2$), 2.93–2.86(t, J=6.9, 4H, ArCOCH$_2$), 2.38–2.31(t, J=7.2, 4H, CH$_2$CO$_2$), 1.71–1.38(m, 16H, CH$_2$); Anal. Calcd for C$_{38}$H$_{52}$O$_{13}$: C 63.69, H 7.26. Found: C 63.59, H 7.32; MS(m/z): 717(M$^+$+1).

4c: The residual solid was crystallised from methanol as white solid. Yield 71.6%. M.p.83–87°C; IR(KBr): ν_{max}/cm^{-1} 3423, 2930, 2840, 1719, 1676, 1592, 1514, 1268, 1128, 1056; ^{1}H NMR(CDCl$_3$): δ 8.02 (bs, 2H, CO$_2$H, D$_2$O exchangeable), 7.50–6.86(m, 6H, ArH), 4.28–3.72(m, 20H, OCH$_2$), 2.95–2.83(t, J=6.9, 4H, ArCOCH$_2$), 2.34–2.25 (t, J=7.2, 4H, CH$_2$CO$_2$), 1.73–1.36(m, 24H, CH$_2$); Anal. Calcd for C$_{42}$H$_{60}$O$_{13}$: C 65.28, H 7.77. Found: C 63.39, H 7.71; MS(m/z): 772(M$^+$).

General procedure for the preparation of dibenzo-21-crown-7-bridged dialkanoic Acids **5a–c**

A mixture of **4** (3.6mmol), 85% hydrazine hydrate (15ml) and triethylene glycol (19ml) was refluxed for 1h. The excess hydrazine hydrate was removed and KOH (1.9g) was added. When the temperature rose to 150°C, the mixture was refluxed for additional 3h, cooled, poured into 6N hydrochloric acid (50ml), and extracted with benzene (3×50ml). After washing with water, the benzene was removed by evaporation. The residue was chromatographed on a silica gel column using acetone/chloroform (1:1) as an eluent to give the desired product.

5a: Oil, yield 58.2%. IR(KBr): ν_{max}/cm^{-1} 3413, 2932, 2864, 1708, 1592, 1513, 1282, 1130, 1056; ^{1}H NMR(CDCl$_3$): δ 7.52(bs, 2H, CO$_2$H, D$_2$O exchangeable), 6.88–6.67(m, 6H, ArH), 4.14–3.39(m, 20H, OCH$_2$), 2.54–2.47(t, J=7.0, 4H, ArCH$_2$), 2.32–2.25(t, J=7.0, 4H, CH$_2$CO$_2$), 1.69–1.16(m, 12H, CH$_2$); Anal. Calcd for C$_{34}$H$_{48}$O$_{11}$: C 64.56, H 7.59. Found: C 64.47, H 7.50; MS(m/z): 633(M$^+$+1).

5b: Oil, yield 54.7%. IR(KBr): ν_{max}/cm^{-1} 3445, 2927, 2850, 1715, 1590, 1513, 1285, 1138, 1057; ^{1}H NMR(CDCl$_3$): δ 7.75(bs, 2H, CO$_2$H, D$_2$O exchangeable), 6.87–6.58(m, 6H, ArH), 4.24–3.77(m, 20H, OCH$_2$), 2.53–2.46(t, J=7.6, 4H, ArCH$_2$), 2.38–2.30(t, J=7.3, 4H, CH$_2$CO$_2$), 1.57–1.32(m, 20H, CH$_2$); Anal. Calcd for C$_{38}$H$_{56}$O$_{11}$: C 66.28, H 8.14. Found: C 66.37, H 8.06; MS(m/z): 688(M$^+$).

5c: oil, yield 61.3%. IR(KBr): ν_{max}/cm^{-1} 3427, 2928, 2864, 1712, 1594, 1512, 1268, 1134, 1056; ^{1}H NMR(CDCl$_3$): δ 7.63(bs, 2H, CO$_2$H, D$_2$O exchangeable), 6.84–6.63(m, 6H, ArH), 4.22–3.73 (m, 20H, OCH$_2$), 2.51–2.42(t, J=7.5, 4H, ArCH$_2$), 2.35–2.27(t, J=7.2, 4H, CH$_2$CO$_2$), 1.60–1.34(m, 28H, CH$_2$); Anal. Calcd for C$_{42}$H$_{64}$O$_{11}$: C 66.74, H 8.60. Found: C 66.83, H 8.58; MS(m/z): 745(M$^+$+1).

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