

Synthesis of cobalt(II) complexes with *p*-tert-butylcalix[4]arene-supported dihydroxamic acids

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Four *p*-tert-butylcalix [4]arene supported dihydroxamic acids(**H₂L¹**–**H₂L⁴**) and their cobalt(II) complexes CoL² and CoL⁴ have been synthesised by condensation of hydroxylamine or N-substituted hydroxylamine with the calix [4]arene diacid chloride.

Keywords: calix [4]arene, dihydroxamic acid, synthesis, cobalt (II) complexes

Hydroxamic acids as weak proton donor have received increasing attention. Their synthesis,¹ photochemistry conformation,² ionisation and structure³ have been reported. In recent years, a number of reports have appeared on the applications of hydroxamic acids as enzyme inhibitors,⁴ artificial siderophore,⁵ synthetic nucleases,⁶ and chiral catalysts.⁷ Macrocyclic compound-tethered hydroxamic acid has been also reported.^{8–10} Previously, we reported the dioxygen affinities of cobalt(II) hydroxamates and biomimetic catalytic oxidation performance of transition-metal hydroxamates.^{11,12} In order to investigate the effects of calixarenes binding hydroxamic acid on some important performance of dihydroxamic acid, namely, ability for complexation with bivalent transition-metal ions and the dioxygen affinities of cobalt complexes, we designed and synthesised new *p*-tert-butylcalix[4]arene supported dihydroxamic acids **5a–5d** (**H₂L¹**–**H₂L⁴**) (Fig.1) and their cobalt (II) complexes CoL² and CoL⁴.

Experimental

Melting points were determined on a Yanaco MP-500 micro-melting point apparatus and were uncorrected. Infrared spectra were recorded on a Nicolet-1705X IR spectrometer (KBr, film). ¹H NMR spectra were recorded on a Bruker Avance-600 spectrometer using CDCl₃ as solvent and tetramethylsilane as internal standard. Mass spectra were obtained on a Finnigan LCQ-DECA spectrometer. The elemental analysis was performed on a Carlo Erba 1106 elemental analyzer. Compounds **2a**, **3a**, **4a** were prepared according to published procedure.¹³ Silica gel (60H for TLC, Qingdao, China) was used for flash column chromatography. All other reagents were of analytical grade and were used without further purification.

25,27-dihydroxy-26,28-bis(ethoxycarbonylbutyloxy)-5,11,17,23-p-tert-butylcalix[4]arene (2b): A mixture of *p*-tert-butylcalix[4]arene **1** (3.90 g, 6.0 mmol), potassium carbonate (0.84 g), and ethyl 5-bromovalerate (2.10 g, 10.0 mmol) in dry CH₃CN (240 ml) was stirred and heated under reflux for 24 h. The cooled solution was filtered, the filtrate was evaporated to a minimum volume. The residual mass was chromatographed (eluent: dichloromethane) to give the diester **2b** (3.28g, 60.5%) as white crystals, m.p. 180–182°C. IR ν_{\max} : 3414 (OH), 1732 (C=O), 1204 (Ar–O–C) cm⁻¹. ¹H NMR δ : 8.47 (2H, s, OH, D₂O exchange), 7.12 (4H, s, ArH), 6.92 (4H, s,

ArH), 4.62–4.59 (4H, q, *J* 6, CH₂ of Et), 4.28 (4H, m, OCH₂), 4.02 (4H, m, CH₂CO), 3.78 (4H, d, *J* 12.8, ArCH₂Ar), 3.40 (4H, d, *J* 12.9, ArCH₂Ar), 2.26–2.17 (8H, m, CH₂CH₂), 1.32 (6H, t, *J* 7, CH₃ of Et), 1.15 (18H, s, Bu^t), 1.05 (18H, s, Bu^t). ESI-MS *m/z*: 905 (M⁺+1). Anal. calcd for C₅₈H₈₀O₈: C 76.99, H 8.85; found C 76.71, H 8.99.

25, 27-dihydroxy-26, 28-bis(carboxybutyloxy)-5, 11, 17, 23-p-tert-butylcalix[4]arene (3b): A mixture of diester **2b** (2.10 g, 2.2 mmol) and 20% aq. sodium hydroxide (4 ml) in ethanol (60 ml) was stirred and heated under reflux for 12 h, then most of the ethanol was distilled off. The residue was diluted with cold water (50 ml) and 10% aq. hydrochloric acid was added with vigorous mixing until pH 1 was reached. The solid was then filtered off, washed with water and dried to afford the diacid **3b** (1.90 g, 96.5%) as white crystals, m.p. 256–258°C. IR ν_{\max} : 3413 (br. OH), 1710 (C=O), 1205 (Ar–O–C)cm⁻¹. ¹H NMR δ : 8.98 (2H, s, CO₂H, D₂O exchange), 8.51 (2H, s, OH, D₂O exchange), 7.15 (4H, s, ArH), 6.98 (4H, s, ArH), 4.25 (4H, m, OCH₂), 4.01 (4H, m, CH₂CO), 3.83 (4H, d, *J* 12.5, ArCH₂Ar), 3.38 (4H, d, *J* 12.6, ArCH₂Ar), 2.29–2.21 (8H, m, CH₂CH₂), 1.17 (18H, s, Bu^t), 1.03 (18H, s, Bu^t). ESI-MS *m/z*: 849 (M⁺+1). Anal. calcd for C₅₄H₇₂O₈: C 76.42, H 8.49; found C 76.65, H 8.31.

25, 27-dihydroxy-26, 28-bis(chloroformylbutyloxy)-5, 11, 17, 23-p-tert-butylcalix[4]arene (4b): A solution of the diacid **3b** (1.70 g, 20 mmol) in dry benzene (50 ml) containing thionyl chloride (1.8 ml) was heated under reflux and dinitrogen for 8h. Removal of the solvent and residual thionyl chloride under reduced pressure furnished the diacyl chloride **4b** as white solid (1.68 g, 94.9%). IR ν_{\max} : 3504 (OH), 1801 (C=O), 1779 (C=O), 1205 (Ar–O–C).

General method for synthesis 5a–5d (H₂L¹–H₂L⁴): To a stirred mixture of hydroxylamine or N-substituted hydroxylamine(20mmol) and NaHCO₃ (20 mmol) in dry THF (5 ml), a solution of diacyl chloride (10 mmol) in dry THF (10 ml) was added dropwise for 30 min under dinitrogen at 0°C. The mixture was stirred for 8 h. The solvent was distilled off under reduced pressure, then the residue was chromatographed (eluent: dichloromethane/diethyl ether=7:3) to give a pure sample.

25, 27-dihydroxy-26, 28-bis(N-hydroxycarbonylbutyloxy)-5, 11, 17, 23-p-tert-butylcalix[4]arene (5a) (H₂L¹): White crystals, 59.8% yield. m.p. >250°C. IR ν_{\max} : 3406 (OH), 3200 (OH), 1618 (C=O), 1204 (Ar–O–C), 908(N–O)cm⁻¹. ¹H NMR δ : 10.01(2H, s, OH, D₂O exchange), 8.55 (2H, s, OH, D₂O exchange), 7.10 (4H, s, ArH), 6.89 (4H, s, ArH), 4.61 (4H, s, COCH₂O), 4.21 (2H, s, NH), 3.82 (4H, d, *J* 13, ArCH₂Ar), 3.45 (4H, d, *J* 13, ArCH₂Ar), 1.22 (18H, s, Bu^t), 1.11(18H, s, Bu^t). ESI-MS *m/z*: 794 (M⁺). Anal. Calcd for C₄₈H₆₂N₂O₈: C 72.54, H 7.81, N 3.53; Found C 72.78, H 7.55, N 3.61.

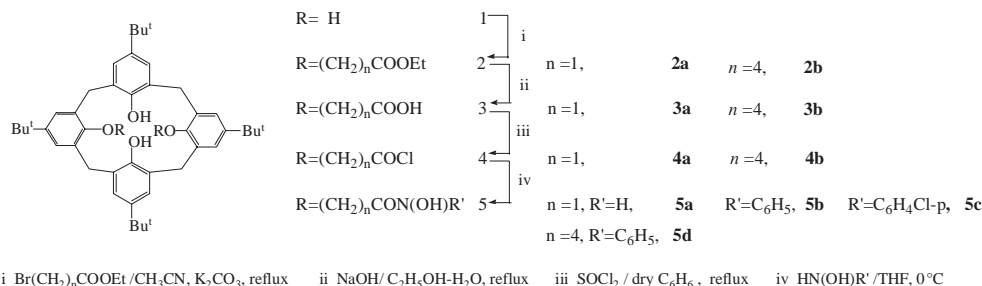


Fig.1 The synthesis and structure of calix[4]arene dihydroxamic acids

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25, 27-dihydroxy-26, 28-bis(*N*-hydroxy-*N*-phenylcarbamoylmethoxy)-5, 11, 17, 23-*p*-tert-butylcalix [4]arene (**5b**) (H_2L^2): White crystals, 61.7% yield. m.p.152–154°C. IR ν_{\max} :3395 (OH), 3210 (OH), 1654 (C=O), 1203 (Ar–O–C), 910 (N–O) cm^{-1} . ^1H NMR δ :9.94 (2H, s, OH, D_2O exchange), 8.55 (2H, s, OH, D_2O exchange), 7.61 (10H, m, ArH), 7.13 (4H, s, ArH), 7.02 (4H, s, ArH), 4.58 (4H, s, COCH_2O), 3.84 (4H, d, J 13, ArCH_2Ar), 3.44 (4H, d, J 13, ArCH_2Ar), 1.24 (18H, s, Bu^t), 1.09 (18H, s, Bu^t). ESI-MS m/z : 946(M^+). Anal. Calcd for $\text{C}_{60}\text{H}_{70}\text{N}_2\text{O}_8$: C 76.11, H 7.40, N 2.96; found C 76.30, H 7.32, N 2.93.

25, 27-dihydroxy-26, 28-bis(*N*-hydroxy-*N*-*p*-chlorophenyl-carbamoylmethoxy)-5, 11, 17, 23-*p*-tert-butylcalix[4]arene (**5c**) (H_2L^3): as white crystals, 68.4% yield. m.p. >250°C. IR ν_{\max} : 3422(OH), 3212 (OH), 1655 (C=O), 1204 (Ar–O–C), 908 (N–O) cm^{-1} . ^1H NMR δ :9.66 (2H, s, OH, D_2O exchange), 8.61 (2H, s, OH, D_2O exchange), 7.73 (8H, m, ArH), 7.10 (4H, s, ArH), 7.01 (4H, s, ArH), 4.65 (4H, s, COCH_2O), 3.83 (4H, d, J 13, ArCH_2Ar), 3.43 (4H, d, J 13, ArCH_2Ar), 1.21 (18H, s, Bu^t), 1.11 (18H, s, Bu^t). ESI-MS m/z :1015(M^+). Anal. Calcd for $\text{C}_{60}\text{H}_{68}\text{Cl}_2\text{N}_2\text{O}_8$: C 70.94, H 6.70, N 2.76; found C 71.23, H 6.65, N 2.88.

25, 27-dihydroxy-26, 28-bis(*N*-hydroxy-*N*-phenylcarbamoylbutyox)-5, 11, 17, 23-*p*-tert-butylcalix[4]arene (**5d**) (H_2L^4): White crystals, 63.3% yield. m.p.108–110°C. IR ν_{\max} :3402 (OH), 3276 (OH), 1638(C=O), 1202 (Ar–O–C), 915 (N–O) cm^{-1} . ^1H NMR δ : 9.99 (2H, s, OH, D_2O exchange), 8.64 (2H, s, OH, D_2O exchange), 7.68 (10H, m, ArH), 7.13 (4H, s, ArH), 7.01 (4H, s, ArH), 4.29 (4H, m, OCH_2), 4.06 (4H, m, CH_2CO), 3.84 (4H, d, J 13, ArCH_2Ar), 3.42 (4H, d, J 13, ArCH_2Ar), 2.31–2.19 (8H, m, CH_2CH_2), 1.23 (18H, s, Bu^t), 1.05 (18H, s, Bu^t). ESI-MS m/z : 1031 (M^+ +1). Anal. calcd for $\text{C}_{66}\text{H}_{82}\text{N}_2\text{O}_8$: C 76.89, H 7.96, N 2.72; found C 76.71, H 7.76, N 2.89.

General method for synthesis of cobalt (II) complexes with p-tert-butylcalix[4]arene supported dihydroxamic acids (CoL^1 – CoL^4): A solution of dihydroxamic acid ligand H_2L^1 – H_2L^4 (2.0 mmol) in EtOH (5 cm^3) was added to the solution of $\text{Co}(\text{OAc})_2 \cdot 4\text{H}_2\text{O}$ (2.1 mmol) in EtOH (50 cm^3) at 70°C. The pH of mixture was adjusted slowly from pH 7 to 8 with sodium acetate to precipitate solid. The mixture was kept at 70°C for 2h and then was filtered, washed with water and EtOH, dried in vacuum to give the cobalt (II) complexes.

CoL²: pink solid, 29.3% yield. m.p.>300°C. IR ν_{\max} : 1604 (C=O), 1203(Ar–O–C), 932 (N–O), 675 (Co–O) cm^{-1} . ESI-MS m/z : 1003 (M^+); Anal. Calcd for $\text{C}_{60}\text{H}_{68}\text{N}_2\text{O}_8\text{Co}$: C 71.78, H 6.78, N 2.79, Co 5.88; found C 71.57, H 6.92, N 2.93, Co 6.03. $\Lambda_m(\text{S}/\text{cm}^2/\text{mol}^{-1})$: 5.9.

CoL⁴: pink solid, 38.5% yield. m.p.>300°C. IR ν_{\max} : 1612 (C=O), 1204 (Ar–O–C), 926 (N–O), 668 (Co–O) cm^{-1} . ESI-MS m/z : 1087 (M^+); Anal. Calcd for $\text{C}_{66}\text{H}_{80}\text{N}_2\text{O}_8\text{Co}$: C 72.86, H 7.36, N 2.58, Co 5.43; found C 72.57, H 7.52, N 2.83, Co 5.12. $\Lambda_m(\text{S}/\text{cm}^2/\text{mol}^{-1})$: 5.4.

It is surprising that only H_2L^2 and H_2L^4 of all the ligands can smoothly complex with cobalt(II) ion, and the yield of complexes is relatively low. After concentrating the mixture solution, the cobalt (II) complexes CoL^1 and CoL^3 were not obtained. This fact may be due to the conformation of the ligand, which might be confirmed by further investigation.

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