Synthesis, crystal structure, binding properies of a noncyclic crown-type receptor derived from diethoxycarbonyl glycoluril

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A novel noncyclic crown-type diethoxycarbonyl glycoluril derivative receptor was synthesised and its crystal structure was obtained. The study of its binding behaviour towards neutral guests showed that it can bind hydroquinone, resorcinol and catechol.

Keywords: noncyclic crown-type, crystal structure, binding properies

There has been much interest in synthetic macrocyclic polyethers in recent years because of their ability to selectively complex both metal[1] and organic ammonium[2-6] cations. The basic molecular frame of ordinary crown ether molecules consists of a ring of several oxygen atoms connected by ethylene groups. Various modifications[7,8] have been made to the basic crown ether structure in an attempt to enhance the selectivity of these ligands and the stabilities of complexes formed. In this paper, we describe the synthesis of a new class of modified crown-type analogue containing heterocyclic residues (Scheme 1). This main structural pattern was altered in order to construct a rigid crown-type analogue and study its binding ability for neutral guests.

The crystal structure of **5** is showed in Fig. 1. As can be seen compound **5** is similar to Nolte's molecular clips,[9-12] but has a larger cavity. Hence these molecules are potential synthetic receptors for some neutral molecules through π–π stacking and hydrogen bond interactions.

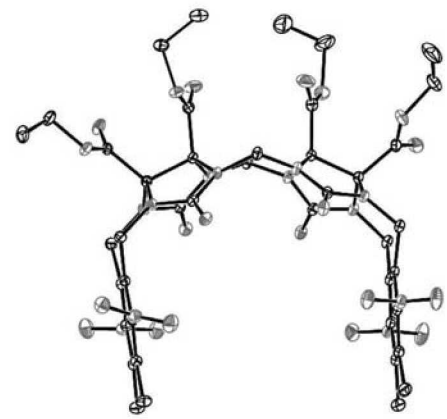
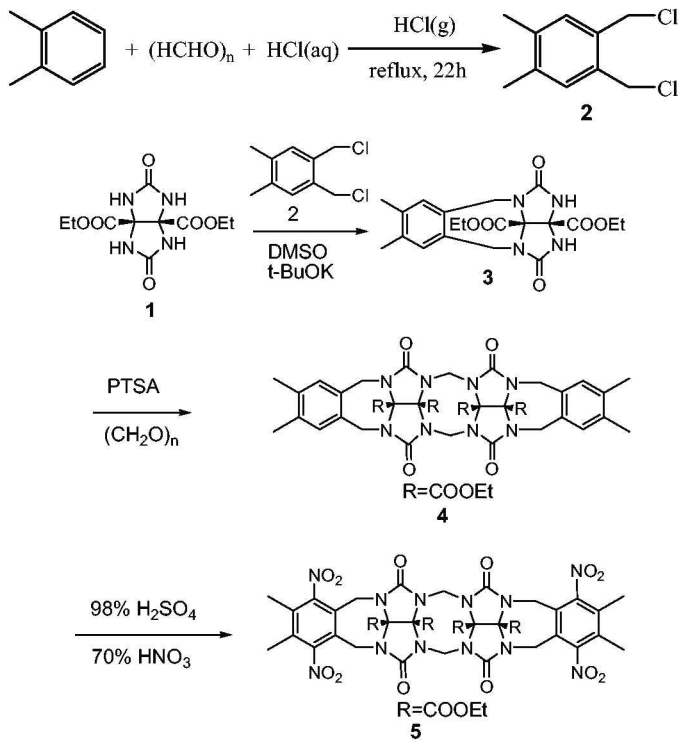


Fig. 1 Molecular structure of compound **5**.



Scheme 1 Synthetic routes of the open chain crown ether analogue.

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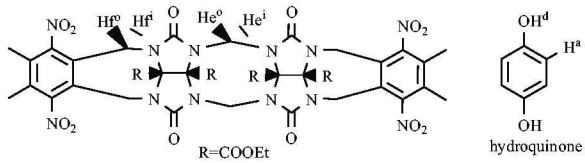

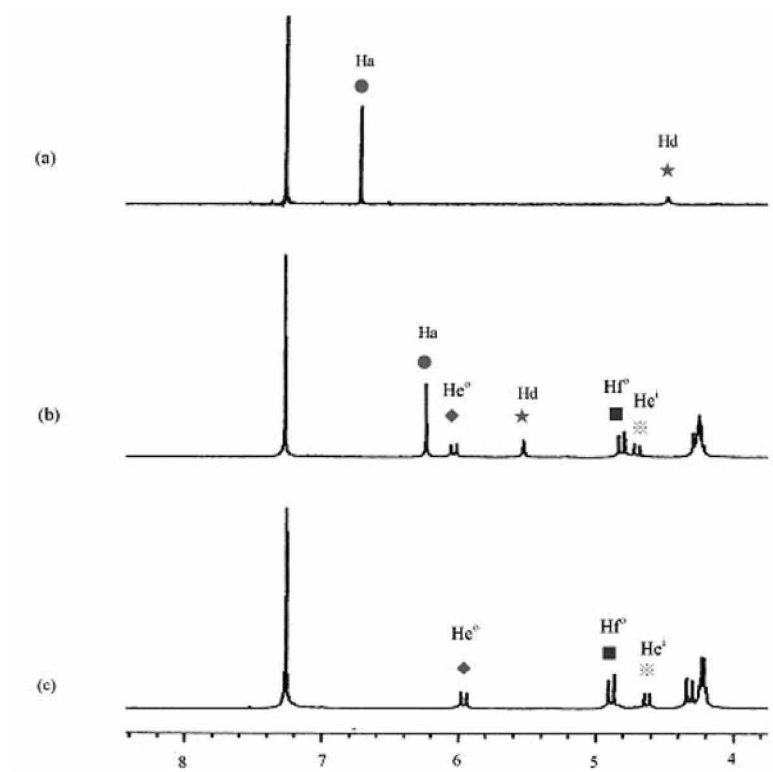

Fig. 2 Partial ^{1}H NMR spectra (400 MHz, $CDCl_3$, 298K) of (a) free guest hydroquinone; (b) The mixture of host **5** and guest hydroquinone (1:1); (c) Free host **5**.

The binding properties of **5** was studied with the aid of ^{1}H NMR. It was found that addition of hydroquinone to the solution of **5** caused the NMR signals of the aromatic protons of the guest to shift upfield as shown in Fig. 2, whereas the proton signals of the OH groups moved downfield, and the signals of methylene-bridged proton of the host Hf^o also shifts upfield. But the protons of He^i, He^o are shifted downfield. These shifts indicate that complexes are formed involving hydrogen bonds between the OH groups of the guest and the carbonyl groups of the host. Furthermore, they suggest that the aromatic moiety of the guest is wedged in between the walls of the cavity. Only one signal was observed for the free and bound forms of host and guest, implying that the exchange process is fast on the NMR time scale.

IR spectroscopy was also used to investigate hydrogen bonding between hosts and guests (Fig. 3). The host carbonyl stretching vibration band is influenced by hydrogen bonding by the guest. The IR spectra of compounds **5** mixed with hydroquinone shows that ν C=O splits into two bands (1759 and 1744 cm^{-1})

It can also bind metal ions through coordination with oxygen atom. Further studies are in progress on selectively binding guest molecules.

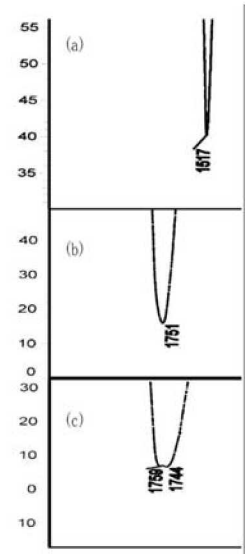

Fig. 3 The IR spectra of (a) free guest hydroquinone; (b) Free host **5**; (c) The mixture of host **5** and guest hydroquinone (1:1).

Experimental

General

All reagents obtained from commercial sources, were of AR grade. Melting points were determined with XT4A micromelting point apparatus and were uncorrected. NMR spectra were recorded on a Mercury Plus-400 spectrometer with TMS as internal reference and $CDCl_3$ as solvent. IR spectra were recorded on a Perkin–Elmer PE–983 IR spectrometer as KBr pellets with absorption in cm^{-1}. MS were obtained with Finnigan Trace MS instrument using EI method. Elemental analyses were carried out on a Vario EL III instrument. Fluorescence spectra were determined on a Hitachi F-4500.

Synthesis

The compound **5** was synthesised according to Scheme 1. To a solution of glycoluril **1** (20 mmol) in anh.DMSO (80 mL) under Ar was added *t*-BuOK (40 mmol), After stirring for 13 min, 1, 2-bis(chloromethyl)-4,5-dimethylbenzene **2**[13] (10 mmol) was added in one portion and stirring was continued for 3 h. The mixture was poured into 0.1M HCl (1 L) and extracted with EtOAC (3 × 400 mL). The extracts was washed with brine (2 × 300 mL) and dried over anh. $MgSO_4$. Filtration and rotary evaporation gave a white solid **3** which was purified by flash chromatography (25:1, chloroform/methanol). A mixture of PTSA (12 mmol) in $ClCH_2CH_2Cl$ (75 mL) was heated under Ar at reflux for 30 min, under a soxlhet apparatus filled with molecular sieves (4 Å). Compound **3** (3 mmol) and paraformaldehyde (9 mmol) were added and the reflux was continued for 12 h. The reaction mixture was diluted with $CHCl_3$, washed with sat. Na_2CO_3, dried over anh. $MgSO_4$, and concentrated. Flash Chromatography (SiO_2, $CHCl_3/CH_3CN$, 20:1) yielded **4** (61%) as a white solid. Compound **4** (0.1 mmol), dissolved in $CHCl_3$ (5 mL), was floated over conc. sulfuric acid (1.0 mL). The mixture was cooled with ice, and fuming nitric acid (1.0 mL) was added drop by drop from a funnel while the mixture was rapidly stirred mechanically. Then the reaction was continued for 0.5 h at room temperature. The reaction mixture was diluted with $CHCl_3$, washed with sat. Na_2CO_3, dried over anh. $MgSO_4$, and concentrated. Yield **5** (76%) as a white solid.[14]

3: M.p. 235–236 °C ^{1}H NMR(400 MHz, DMSO-d_6) δ(ppm): 8.40(s, 2H, NH), 7.02(s, 2H, ArH), 4.51(d, J = 15.8 Hz, 2H, NCH_2), 4.35(d, J = 15.8 Hz, 2H, NCH_2), 4.22(q, J = 7.1 Hz, 2H, OCH_2), 4.12(q, J = 7.1 Hz, 2H, OCH_2), 2.15(s,6H, $ArCH_3$), 1.22(t, J = 7.1 Hz, 3H, CH_2CH_3), 1.19(t, J = 7.1 Hz, 3H, CH_2CH_3).

4: Mp > 300 °C; ^{1}H NMR(400 MHz, DMSO-d_6) δ(ppm): 7.00 (s, 4H, ArH), 5.77(d, J = 16.0 Hz, 2H, NCH_2N), 4.55(d, J = 16.0, 4H, NCH_2), 4.47(d, J = 16.0, 2H), 4.42(d, J = 16.0, 4H), 4.24–4.16(m, 8H, OCH_2), 2.09(s, 12H, $ArCH_3$), 1.23(t, J = 7.1 Hz, 6H, CH_2CH_3), 1.18(t, J = 7.1 Hz, 6H, CH_2CH_3).

5: IR (KBr, cm^{-1}): 2985w, 1751 s, 1538 s, 1455 m, 1369 m, 1255 s, 918 m; ^{1}H NMR (400 MHz, $CDCl_3$) δ(ppm): 5.96(d, J = 16.4 Hz, 2H), 4.89(d, J = 16.8 Hz, 4H,), 4.63(d, J = 16.4 Hz, 2H), 4.32 (d, J = 16.8 Hz, 4H), 4.25–4.20(m, 8H), 2.18(s, 12H), 1.32–1.26 (m, 12H); ^{13}C NMR (100 MHz, DMSO-d_6) δ(ppm): 164.2, 163.5, 153.5, 151.0, 130.9, 127.6, 78.9, 78.1, 64.7, 64.3, 47.5, 14.8, 13.5, 13.4; MS: *m/z* 1075.8[M + K]$^+$, 1059.7[M + Na]$^+$, 1038.1[M + H]$^+$, $C_{42}H_{44}N_{12}O_{20}$, Calcd 1036.87.

Binding studies: ^{1}H NMR The ^{1}H NMR spectra was performed at 298K in $CDCl_3$. The concentration of the host and the guest is 2×10^{-3} mmol L^{-1}, respectively and the mixture of the host and the guest is 2×10^{-3} mmol L^{-1}.

X-ray diffraction study of **5**

Crystals were obtained by slow evaporation from chloroform-methanol solution (20:1 v/v). A colourless crystal of the title compound **5** having approximate dimensions of 0.30 × 0.20 × 0.20 was mounted on a glass fiber in a random orientation at 295(2) K. The determination of unit cell and the data collection were performed with MoKα radiation (λ = 0.71073 Å) on a Bruker Smart Apex-CCD diffactometer with a ψ–ω scan mode. A total of 25286 reflections were collected in the range of 11.85 to 25.00° at room temperature, and 8952 were independent (R_{int} = 0.0304), of which 2360 observed reflections with $I>2\sigma(I)$ were used in the structure determination and refinements. The structure was solved by direct methods with SHELXS-97 program and expanded by Fourier technique. The non-hydrogen atoms were refined anisotropically, and the hydrogen atoms were placed using theoretical calculations. A full-matrix least-squares refinement gave the final $R^1 = 0.0633$, $wR^2 = 0.1744$ [$W = 1/[\sigma^2 (Fo^2) + (0.1036P)^2 + 1.2522P]$ where $P = (Fo^2 + 2Fc^2)/3$, $(\Delta/\sigma)_{max} = 0.000$, S = 1.070, (Δρ)max = 0.530, (Δρ)min = -0.486 e/Å^3. All calculations were performed on a PC with SHELXS-97 program. *Crystal data*: C_{44} H_{48} Cl_2 N_{12} O_{20}, M = 1135.84, Monoclinic, space group P2 (1)/c, a = 14.0878(9) Å, b = 16.4678(10) Å, c = 22.3064(13) Å, α = 90.00°, β = 95.820(10)°, γ = 90.00°, V = 5102.8(5) Å^3, Z = 4, ρCalcd = 1.479 g cm^{-3}, μ = 0.218 mm^{-1}. The crystallographic data have been deposited with Cambridge Crystallographic Data Centre No. CCDC 625796.

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