

# Synthesis, X-ray structure, and binding properties of a new fluorescent molecular clip derived from diethoxycarbonyl glycoluril

Sheng-Li Hu, Guo-Dong Yin, Yu-Zhou Wang, and An-Xin Wu

**Abstract:** A new fluorescent molecule clip derived from diethoxycarbonyl glycoluril with two 2,5-diphenyl-furan side-walls was designed and synthesized. Its structure and conformation was confirmed by single-crystal X-ray diffraction. Its binding properties, investigated by fluorescence spectroscopy, showed that it can selectively bind  $\text{Fe}^{3+}$  with fluorescence quenching.

*Key words:* diethoxycarbonyl glycoluril, molecular clip, fluorescence, Fe(III).

**Résumé :** On a développé une méthode de synthèse pour une nouvelle pince moléculaire fluorescente qui est dérivée du diéthoxycarboxylglycoluril et qui comporte deux 2,5-diphénylfuranes comme murs latéraux. On a confirmé sa structure et sa conformation sur la base de la diffraction des rayons X par un cristal unique. Ses propriétés de fixation étudiées par spectroscopie de fluorescence montrent qu'elle peut se fixer sélectivement avec le  $\text{Fe}^{3+}$  avec désactivation de la fluorescence.

*Mots-clés :* diéthoxycarboxylglycoluril, pince moléculaire, fluorescence, Fe(III).

[Traduit par la Rédaction]

## Introduction

Development of fluorescent chemosensors, capable of recognizing metal ions, anions, and neutral molecules, is of interest because of their high sensitivity and low-cost instrumentation (1). In general, fluorescence chemosensors are composed of two covalently linked components: a recognition site that binds the target substance and a transducer (fluorophore) that signals the binding (2–4).

Glycoluril is an important building block for supramolecular chemistry, and its derivatives have been used as the basis for molecular clips (5), molecular capsules (6), anion-binding receptors (7), xerogels (8), and the cucurbit[*n*]uril (CB[*n*]) family (9). However, few studies have been carried out to explore its utilization as a platform for the synthesis of fluorescent chemosensors for ionic guest in recent years (10).

In the previous work, we had reported a pair of molecular clips derived from diethoxycarbonyl glycoluril with two 1,2-dihydro-indazol-3-one moieties as sidewall and developed their function as selective fluorescent chemosensors for  $\text{Fe}^{3+}$

(11). In continuing our research to develop new fluorescent chemosensors based on glycoluril, we designed a new molecular clip **5**, which has two 2,5-diphenyl-furan fluorescent moieties used as the signaling subunit in its two sidewalls and two carbonyl oxygen atoms of glycoluril ring used as the potential binding sites in its cavity. We assume that such crown-ether derivatives can be used as a fluorescent chemosensor for alkali or alkaline earth metal cations. In this paper, we report its synthesis, X-ray structure, and binding study with different metal ions. Interestingly, the new fluorescent clip molecule **5** also exhibited selective recognition to  $\text{Fe}^{3+}$  over the other tested metals ions, including alkali and alkaline earth metal cations. This experimental result shows that the two polarized carbonyl groups oxygen atoms of glycoluril ring may be an effective recognition position for  $\text{Fe}^{3+}$ .

## Results and discussion

Fluorescent molecule clip **5** was prepared by reacting diethoxycarbonyl glycoluril (**3**) with 3,4-bis-bromomethyl-2,5-diphenyl-furan (**4**) using *t*-BuOK as base in anhyd. DMSO (Scheme 1), and the product was further characterized by NMR spectra. The  $^1\text{H}$  NMR spectrum of **5** in  $\text{CDCl}_3$  shows two pairs of well-defined doublets with equal intensity for the protons of methylene at  $\delta = 5.28$  ppm ( $J = 16.0$  Hz) and  $\delta = 4.36$  ppm ( $J = 16.0$  Hz), indicating that the molecules possess good symmetry and the four bridging methylenes have the same chemical environment. The IR and MS spectra for the product are in good agreement with the title compound. In addition, its structure and conformation were confirmed by single-crystal X-ray diffraction, as

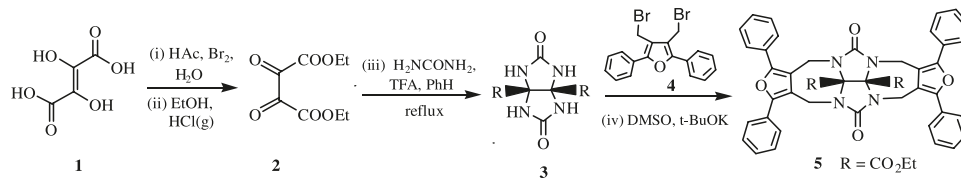
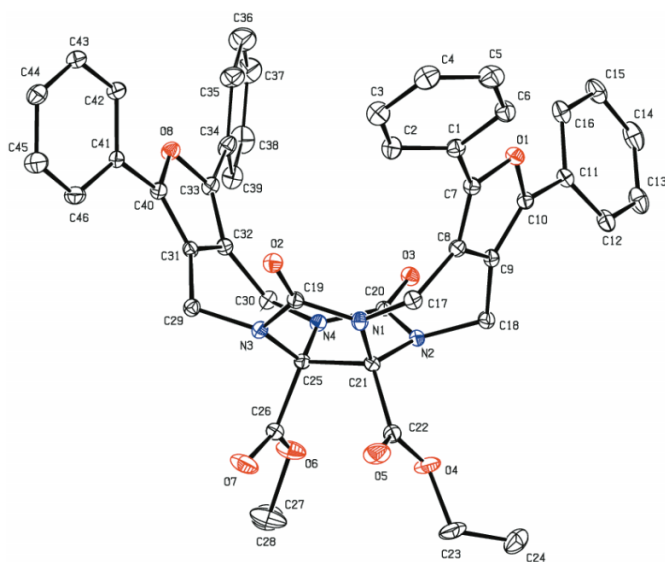
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Scheme 1. Synthesis of molecular clip **5**.Fig. 1. X-ray crystal structure of compound **5**. Hydrogen atoms and minor components are omitted for clarity.

shown in Fig. 1. Its crystal data and details of structure determinations were summarized in Table 1.

The crystal structure of **5** clearly reveals that it has well-defined geometry because of the rigidity that the fused rings confer on the molecule. However, two phenyl rings of the sidewall are twisted away from the furan ring. The phenyl ring (C1–C6) and phenyl ring (C11–C16) form dihedral angles of 41.47° and 35.40°, respectively, with the furan ring (O1–C10). The phenyl ring (C34–C39) and phenyl ring (C41–C46) form dihedral angles of 34.31° and 28.33°, respectively, with the (O8–C40) furan ring. The dihedral angle between them is 34.76°. The dihedral angle between two furan rings is 38.61°, and the distance between the centroids of two furan rings is 6.603 Å. The distances between the two oxygen atoms (O1–O8) of two furan rings and two carbonyl oxygen atoms (O2–O3) of glycoluril ring amount to 7.494 Å and 5.722 Å, respectively.

The binding properties of the clip molecule **5** with various metal ions were investigated through fluorescence-spectroscopy titration experiments. Changes of the fluorescence properties of  $1 \times 10^{-5}$  mol/L of **5** in DMF/CH<sub>3</sub>OH (50:1, v/v) solution caused by 15 equiv. of various metal ions (K<sup>+</sup>, Na<sup>+</sup>, Mg<sup>2+</sup>, Hg<sup>2+</sup>, Cd<sup>2+</sup>, Fe<sup>3+</sup>, Zn<sup>2+</sup>, Co<sup>2+</sup>, Ni<sup>2+</sup>, Cu<sup>2+</sup>, Pb<sup>2+</sup>, Cr<sup>3+</sup>, and Mn<sup>2+</sup>) were measured once their emission intensity were constant. The result showed that Fe<sup>3+</sup> produced significant quenching in the fluorescent emission of **5**; the other tested metals only show relatively insignificant

Table 1. Crystal structure data for **5**.

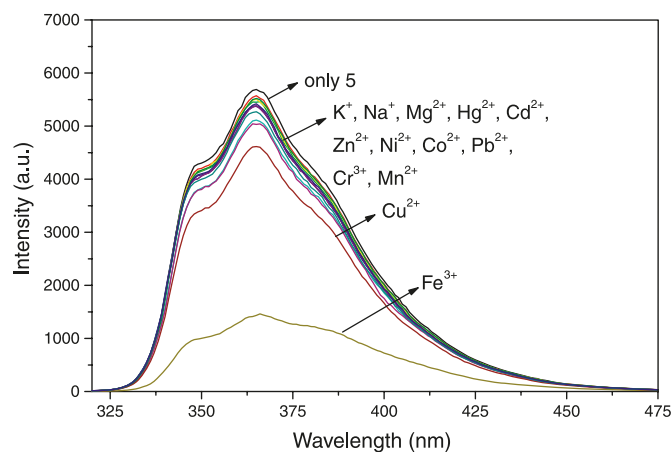
Empirical formula	C <sub>46</sub> H <sub>38</sub> N <sub>4</sub> O <sub>8</sub>
Formula mass	774.80
Temperature (K)	294(2)
Wavelength (Å)	0.71073
Crystal system	Monoclinic
Space group	<i>P</i> 2(1)/ <i>n</i>
<i>a</i> (Å)	12.7623(9)
<i>b</i> (Å)	11.5771(8)
<i>c</i> (Å)	26.5023(19)
$\alpha$	90°
$\beta$	96.1500(10)°
$\gamma$	90°
<i>V</i> (Å <sup>3</sup> )	3893.2(5)
<i>Z</i>	4
Density <sub>calcd.</sub> (Mg/m <sup>3</sup> )	1.322
Index ranges	−15 ≤ <i>h</i> ≤ 15, −13 ≤ <i>k</i> ≤ 13, −31 ≤ <i>l</i> ≤ 31
<i>F</i> (000)	1624
Crystal size	0.20 mm × 0.10 mm × 0.04 mm
$\theta$ range for data collection	1.55–25.00°
Reflections collected	33604
Independent reflections	6862 [ <i>R</i> <sub>(int)</sub> = 0.1084]
Data, restraints, parameters	6862, 0, 526
Goodness-of-fit on <i>F</i> <sup>2</sup>	1.000
Absorption correction	None
>2 $\sigma$ ( <i>I</i> )	3472
Final <i>R</i> indices ( <i>I</i> > 2 $\sigma$ ( <i>I</i> ))	<i>R</i> <sub>1</sub> = 0.0761, <i>wR</i> <sub>2</sub> = 0.1782
<i>R</i> indices (all data)	<i>R</i> <sub>1</sub> = 0.1563, <i>wR</i> <sub>2</sub> = 0.2090
Largest diff. peak and hole (e Å <sup>−3</sup> )	0.312 and −0.246

changes (Fig. 2). So, it can be concluded that **5** has higher selectivity for the recognition of Fe<sup>3+</sup>.

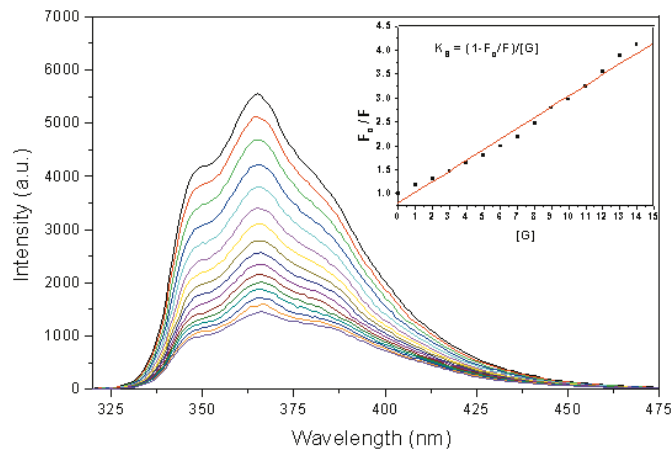
The sensitivity of the fluorescence emission response of **5** towards Fe<sup>3+</sup> was also examined under the same conditions with various Fe<sup>3+</sup> concentrations (Fig. 3). The fluorescence intensity ( $\lambda_{\text{em}} = 365$  nm) of **5** was decreased continually upon addition of Fe<sup>3+</sup> with no significant change in the position of the emission maxima. When the concentration of Fe<sup>3+</sup> increased to 15 equiv., the fluorescence intensity of **5** was reduced to 24% of the initial one. From the Stern–Volmer plot (the fluorescence quenching followed the Stern–Volmer equation) (12), host **5** formed 1:1 stoichiometry complex with Fe<sup>3+</sup>, and the association constant was estimated  $2.24 \times 10^4$ .

Actually, quenching of electronically excited state of aromatic hydrocarbons by Fe<sup>3+</sup> chelates is a known

**Fig. 2.** Fluorescence emission changes of **5** ( $1 \times 10^{-5}$  mol/L) in DMF–MeOH (50:1 v/v) in the presence of  $15 \times 10^{-5}$  mol/L various metal ions (excitation at 305 nm).



**Fig. 3.** Fluorescence emission spectra (excitation at 305 nm) of **5** ( $1 \times 10^{-5}$  mol/L) in DMF–MeOH (50:1 v/v) in the presence of  $Fe(H_2O)_6Cl_3$ . The concentration of  $Fe^{3+}$ : 0, 1.0, 2.0, 3.0, 4.0, 5.0, 6.0, 7.0, 8.0, 9.0, 10.0, 11.0, 12.0, 13.0, 14.0, and  $15 \times 10^{-5}$  mol/L. Inset: Stern–Volmer plot of the emission data.



phenomenon that has been the subject of extensive investigations. It has been suggested that two main pathways could account for the efficient radiationless deactivation of the singlet excited state, i.e., electron transfer from the excited aromatic chromophore to the metal and (or) energy transfer from the excited aromatic chromophore to low-lying metal-centered energy states (13). Such processes could be particularly effective in the complex of **5** with  $Fe^{3+}$ , due probably to the fact that the chelated metal cation is held very close to two excited 2,5-diphenyl-furan chromophores. Additionally, because molecular clip **5** has different sidewalls but same binding properties compared with previously reported molecular clips (11), we may draw a conclusion that the two polarized carbonyl groups of the glycoluril ring play a crucial role in the recognition of  $Fe^{3+}$ .

## Conclusion

A new fluorescent molecule clip **5** derived from diethoxycarbonyl glycoluril with two 2,5-diphenyl-furan sidewalls was designed and synthesized. Its binding properties, investigated by fluorescence spectroscopy, showed that it can selectively bind  $Fe^{3+}$  with fluorescence quenching.

## Experimental

### General

Melting point was determined on an XT4A Meltemp apparatus and is uncorrected. IR was recorded on a Perkin–Elmer PE–983 infrared spectrometer as KBr pellets with absorption in  $cm^{-1}$ . NMR was recorded in  $CDCl_3$  on a Varian Mercury 400 spectrometer. MS was measured on a Finnigan Trace MS spectrometer. Fluorescence spectra were determined on a Hitachi F-4500.

### Synthesis

Diethoxycarbonyl glycoluril **3** (14) and 3,4-bis-bromomethyl-2,5-diphenyl-furan **4** (15) were synthesized according to the previously reported procedures.

Compound **3** (0.72 g, 2.5 mmol) was dissolved in anhyd. DMSO (50 mL) under  $N_2$ , and *t*-BuOK (1.12 g, 10.0 mol) was added. After stirring for 15 min, compound **4** (2.22 g, 5.5 mmol) was added in one portion, and stirring was continued for 3 h. The reaction mixture was poured into 0.1 N HCl (500 mL) and extracted with EtOAc ( $3 \times 200$  mL). The extracts were washed with brine ( $2 \times 150$  mL) and dried over anhyd.  $MgSO_4$ . After filtration and rotary evaporation, the residue was purified by flash chromatography ( $SiO_2$ ,  $CHCl_3/MeOH$ , 50:1) to give compound **5** (0.31 g, 40%) as a white solid. Mp > 300 °C. IR (KBr,  $cm^{-1}$ ): 3059, 2983 w, 2898 w, 1758 s, 1722 s, 1653 w, 1464 s, 1428 s, 1255 s, 910 s, 764 s, 695 s.  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$ : 7.75–7.74 (m, 8H), 7.50–7.35 (m, 8H), 7.32–7.31 (m, 4H), 5.28 (d,  $J = 16.0$  Hz, 4H), 4.36 (d,  $J = 16.0$  Hz, 4H), 4.28 (q,  $J = 7.2$  Hz, 4H), 1.30 (t,  $J = 7.2$  Hz, 6H).  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$ : 165.5, 156.1, 148.7, 130.0, 128.8, 128.1, 126.8, 118.7, 81.3, 63.6, 37.4, 14.0. EI-MS  $m/z$ : 774.0, 778 [ $M + 4H$ ] $^{4+}$ .

### X-ray crystallography

A single crystal suitable for X-ray crystallographic analysis was obtained from a slow evaporation of the dichloromethane and methanol solution. Crystallographic measurement of compound **5** was carried out using a Bruker SMART CCD diffractometer. The SMART (version 5.628) program was used for collecting data frames, and SAINT Plus (version 6.45) was used for integration of the intensity of reflections and scaling. SADABS was used for absorption correction (16). The structure was solved by direct methods using the program SHELXS-97 and refined by full-matrix least-squares against all  $F^2$  data using Bruker SHELXTL (17). The phenyl ring (C34–C39) was found to be disordered over two orientations; the site-occupancy factor for the two orientations were refined giving 0.67(8) and 0.33(8) for the major and minor components, respectively. All non-H atoms

were refined anisotropically. Hydrogen atoms were constrained to the ideal geometries.<sup>3</sup>

### Binding studies

The solvents for the fluorescence measurement were all of spectroscopic grade. Stock solutions of compound **5** was prepared by dissolution in DMF/MeOH (50:1, v/v) ( $1.0 \times 10^{-5}$  mol/L). The solutions of metal ions were prepared from  $\text{Pb}(\text{NO}_3)_2$  and the chlorides of  $\text{K}^+$ ,  $\text{Na}^+$ ,  $\text{Mg}^{2+}$ ,  $\text{Hg}^{2+}$ ,  $\text{Cd}^{2+}$ ,  $\text{Fe}^{3+}$ ,  $\text{Cu}^{2+}$ ,  $\text{Zn}^{2+}$ ,  $\text{Co}^{2+}$ ,  $\text{Ni}^{2+}$ ,  $\text{Pb}^{2+}$ ,  $\text{Cr}^{3+}$ , and  $\text{Mn}^{2+}$ , respectively, and were dissolved in methanol ( $3.0 \times 10^{-3}$  mol/L). Fluorescence titration was performed by filling 3 mL solution of **5** in a quartz cell of 1 cm optical path length and adding different stock solutions of cations into the quartz cell portionwise using a micro-syringe each time. Both excitation and emission bands were set at 5 nm.

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<sup>3</sup>Supplementary data for this article are available on the journal Web site ([canjchem.nrc.ca](http://canjchem.nrc.ca)) or may be purchased from the Depository of Unpublished Data, Document Delivery, CISTI, National Research Council Canada, Ottawa, ON K1A 0R6, Canada. DUD 3758. For more information on obtaining material, refer to [cisti-icist.nrc-cnrc.gc.ca/irm/unpub\\_e.shtml](http://cisti-icist.nrc-cnrc.gc.ca/irm/unpub_e.shtml). CCDC 668714 contains the crystallographic data for this manuscript. These data can be obtained, free of charge, via [www.ccdc.cam.ac.uk/conts/retrieving.html](http://www.ccdc.cam.ac.uk/conts/retrieving.html) (Or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax +44 1223 336033; or [deposit@ccdc.cam.ac.uk](mailto:deposit@ccdc.cam.ac.uk)).