596 **RESEARCH PAPER** SEPTEMBER, 596–599 JOURNAL OF CHEMICAL RESEARCH 2006

Syntheses and coordination properties of (thia)calix[4]arenes bearing single ω-quinolin-8-yl-oligooxyethylene pendant

Chun-Lei Zhang, Yan Jin, Shu-Ling Gong, Xiao-Feng Zhang and Yuan-Yin Chen*

Department of Chemistry, Wuhan University, Wuhan 430072, P. R. China

Four mono-quinolin-8-yl-substituted (thia)calix[4]arenes via oligooxyethylene spacers (**1a–b** and **2a–b**) were synthesised conveniently in one step. Their structures and conformations were characterised by ^{1}H NMR and ESI-MS spectra. Their coordination properties were studied by fluorescence spectra titration in CH_3CN. All of them can form stable 1:1 complex with Zn(II) and Mg(II) ions, respectively. The stability constants of thiacalix[4]arene (**2a** and **2b**) derivatives are higher than those of the calix[4]arene analog (**1a** and **1b**).

Keywords: calixarene, thiacalixarene, 8-hydroxyquinoline, oligooxyethylene, fluorescence

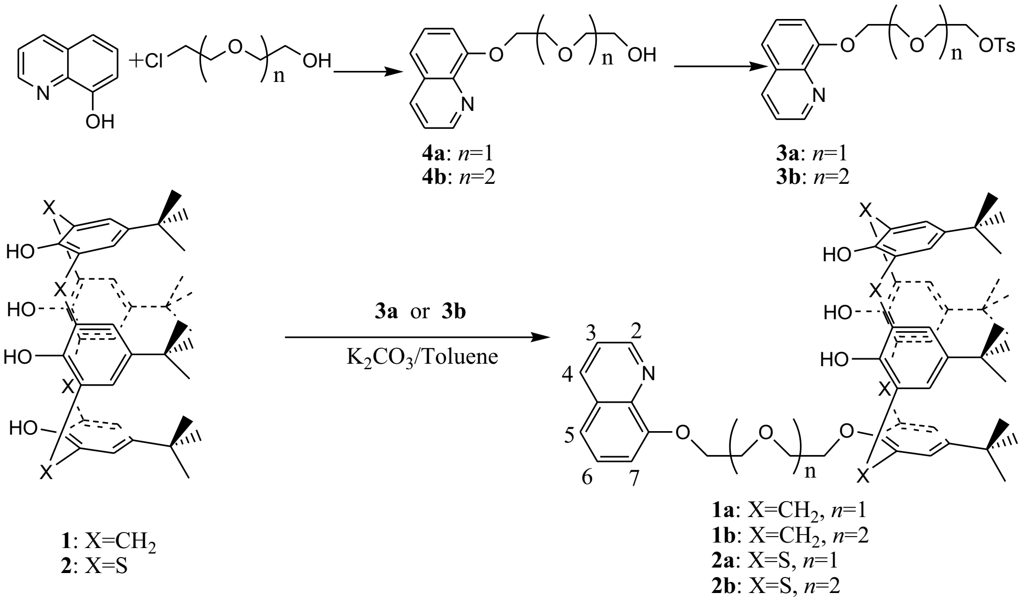
Thiacalixarene is a new member of calixarene family in which epithio groups replace the methylene bridges of traditional calixarene. Since *p-tert*-butylthiacalix[4]arene was accessible in multi-gram scale by a simple synthetic procedures,[1] thiacalixarenes along with calixarenes[2] have become attractive scaffolds for constructing more sophisticated host molecules.[3] Recently, fluorescent metal sensors based on calixarene[4] and thiacalixarene[5] derivatives have become the focus of much attention in supramolecular chemistry. Such compounds were constructed by introduction of fluorescent active moieties and ligands (such as oligooxyethylene[6]) onto the upper or lower rim of calixarenes or thiacalixarenes. As we all know, 8-hydroxyquinoline is one of the most extensively investigated luminescence moiety in the coordination chemistry[7] and has been used in metal ion detection,[8] chromatography,[9] organic light-emitting diodes (OLEDs).[10] To the best of our knowledge, very few quinolin-8-yloxy-containing calixarene derivatives have been reported in the literature until now. In 2000, Toma *et al.*[11] synthesised a bis(8-oxyquinoline) calix[4]arene, which exhibited luminescence and energy transfer properties. In 2003, Casnati et al.[12] synthesised calixarene derivative with a 8-alkoxyquinoline moiety and three diethylaminocarbonylmethyloxy liqands, which exhibited good complexation abilities towards metal cations. However, their synthetic procedures were in multi-steps and the types of hosts were strongly confined. Oligooxyethylene is a well known ligand used to complex metal ions. We thought if using ω-quinolin-8-yl-oligooxyethylenetosylate as reactant, the 8-quinolinyl and oligooxyethylene segment could be induced to calixarene or thiacalixarene directly and simultaneously, the residual hydroxyl can be further modified. We now report the results.

Results and discussion

Syntheses

In theory, there are two routes to construct fluorescent calixarene hosts possessing complexation ability towards metal cations. The first one is that fluorescent active moieties and ligands are introduced successively; the second one is that fluorescent active moiety which is possessing complexation ability is introduced to calixarene. We report here a modified route in which the fluorescent active moiety modified with oligooxyethylene segment is incorporated into calixarene in one step, *i.e.* using ω-quinolin-8-yl-oligooxyethylenetosylates (**3a** and **3b)** as reactants.

3a and **3b** were synthesised according to the literature.[13] We found that both of them could react with *p-tert*-butylcalix[4]arene (**1**) and *p-tert*-butylthiacalix[4]arene (**2**) to give the expected hosts in good yields (Scheme 1). Firstly, we designed K_2CO_3/acetone system, the raw material **1** or **2**



Scheme 1 Syntheses of **1a–b** and **2a–b**

---

* Correspondent. E-mail: yychen@whu.edu.cn

disappeared after seven days and the yield was about 50%. After much effort has been made, we found that K_2CO_3/toluene was preferable reaction system, the reaction time was shortened to 8–12 hours under refluxing and the yields were in the range 52.3–73.5%.

Structure and conformation analyses

The structures of **1a–b** and **2a–b** were characterised by ESI–MS spectra and ^{1}H NMR spectra. Take the ^{1}H NMR spectra of **1a** as an example, the signals of the *tert*-butyl protons appear as three singlets at 1.17, 1.19 and 1.21 ppm in a ratio of 1:2:1, and the signals of the **OH** protons appear as two singlets at 9.40 and 10.26 ppm in a ratio of 2:1, which indicate that **1a** is mono-substituted calix[4]arene. The result was further confirmed by the ESI-MS of **1a**. The structures of **1b**, **2a** and **2b** were deduced similarly.

Their conformations were also deduced from their ^{1}H NMR spectra. In the ^{1}H NMR spectra of **1a**, the present of two **AX** systems (4H each; δ = 3.35, 4.43 ppm, J = 13.2 Hz; δ = 3.36, 4.18 ppm, J = 13.8 Hz) for the methylene bridged $\mathbf{ArCH_2Ar}$ indicates that **1a** is locked in cone conformation.[14] **1b** is also conic according to the same method. The conic conformations of thiacalix[4]arene derivatives (**2a** and **2b**) could be deduced from the similarity of the signals of the *tert*-butyl protons with those of calix[4]arene analog. For **1a**, they appear at 1.17, 1.19 and 1.21 ppm, and for **1b**, 1.19, 1.20 and 1.22 ppm. The similar cases were observed for **2a** and **2b** (**2a**: 1.19, 1.20 and 1.22 ppm; **2b**: 1.18, 1.20 and 1.21 ppm).

Fluorescence spectra study

Due to its high sensitivity,[15] fluorescence spectra titration was carried out to investigate the stability constants[16] and the stoichiometries[17] of the four ligands (**1a–b** and **2a–b**) with Zn^{2+} and Mg^{2+} ions. The emission spectra (λ_{ex} = 322 nm) of **1a** and **2a** (In each case the concentration of the ligand is constant and equal to 0.1 mM) with various concentrations of $Zn(ClO_4)_2$ or $Mg(ClO_4)_2$ in acetonitrile are shown in Fig. 1. This shows that the fluorescence emission intensities of **1a** and **2a** at 394 nm gradually decrease upon the addition of Zn^{2+} ion, which indicates all of the four ligands can form complex with Zn^{2+} ion. 4 Equiv. of Zn^{2+} ion results in 31 nm (394–425 nm) red shift and 80% fluorescence quenching of ligand **1a**, while 3 Equiv. of Zn^{2+} ion results in 36 nm (394–430 nm) red shift and almost 100% fluorescence quenching of ligand **2a**, suggesting that the sulfur atoms in thiacalix[4]arene accelerate the fluorescence quenching. Similar fluorescence quenching phenomena were observed at 394 nm, but no obvious red shifts were found upon the addition of Mg^{2+} ion. The extent of fluorescence quenching of the four ligands results from the addition of Mg^{2+} ion is much lesser than that results from the addition of Zn^{2+} ion. Similar fluorescence spectra changes were observed about **1b** and **2b** with Zn^{2+} and Mg^{2+} ions.

Figure 2 shows the job plots for the four ligands (**1a–b** and **2a–b**) with Zn(II) in CH_3CN, respectively. It can be seen that the stoichiometries of the four ligands with Zn^{2+} ion are all 1:1. Similar job plots are observed for the four ligands with Mg^{2+} ion.

Binding constants

In a supramolecular system, when the ligand absorbs light or emits fluorescence but the cations do not, in a titration experiment, the concentration of the ligand is kept constant and the metal ions is gradually added. The absorption spectrum or fluorescence spectrum is recorded as a function of cation concentration. Changes in these spectra upon complexation allow us to determine the stability constant of the complexes.

For a 1:1 system, we can calculate the stability constant (K_s) by using the follow equation.[16]

$$Y = Y_0 + \frac{Y_{\lim} - Y_0}{2}\left\{1 + \frac{c_M}{c_L} + \frac{1}{K_s c_L} - \left[\left(1 + \frac{c_M}{c_L} + \frac{1}{K_s c_L}\right)^2 - 4\frac{c_M}{c_L}\right]^{1/2}\right\}$$

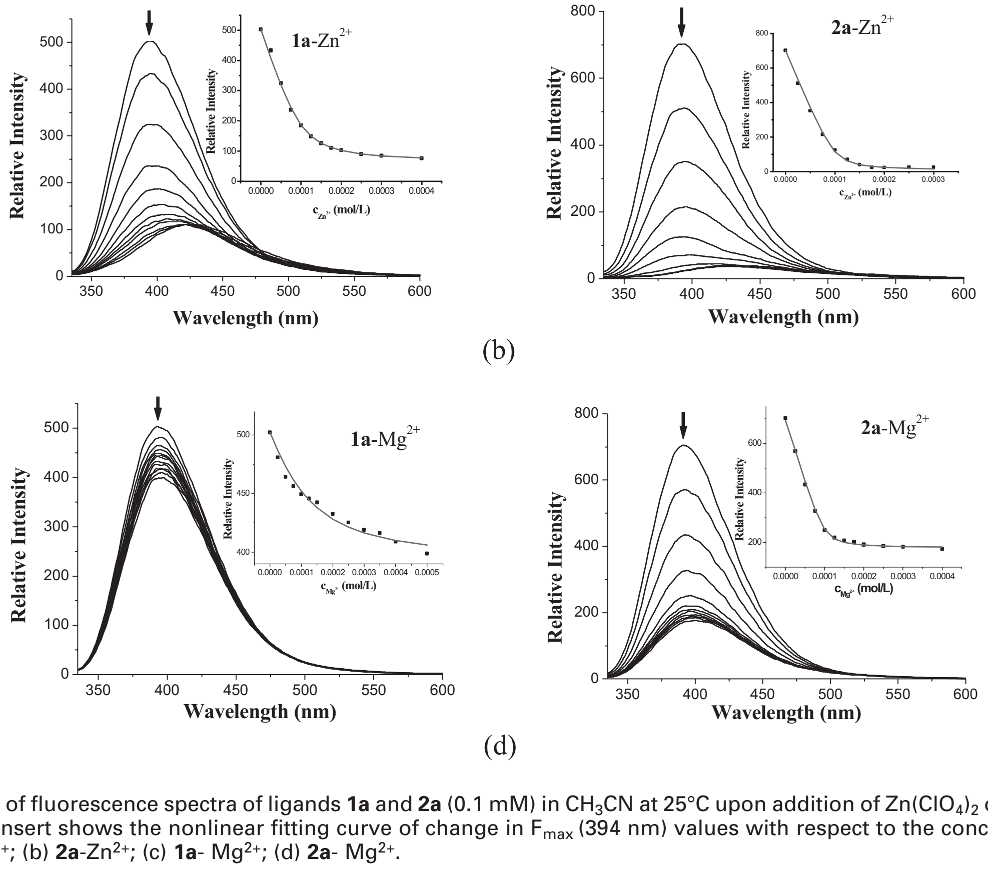


Fig. 1 The change of fluorescence spectra of ligands **1a** and **2a** (0.1 mM) in CH_3CN at 25°C upon addition of $Zn(ClO_4)_2$ or $Mg(ClO_4)_2$, λ_{ex} = 322 nm. The insert shows the nonlinear fitting curve of change in F_{max} (394 nm) values with respect to the concentrations of Zn^{2+} ion. (a) **1a**-Zn^{2+}; (b) **2a**-Zn^{2+}; (c) **1a**- Mg^{2+}; (d) **2a**- Mg^{2+}.

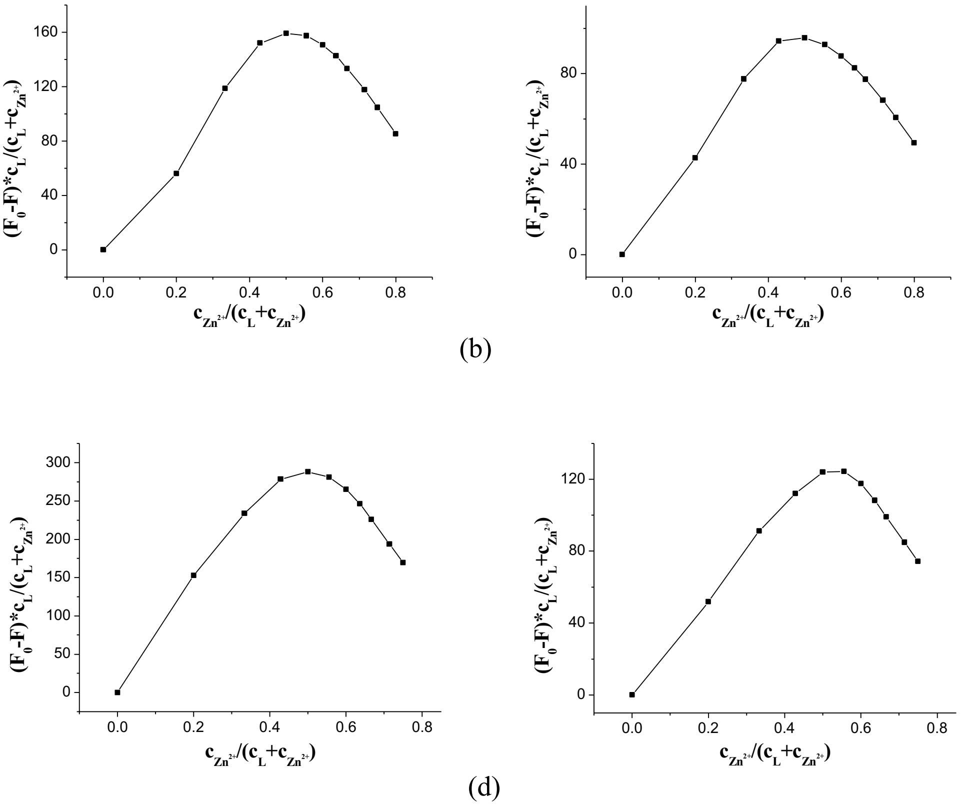


Fig. 2 Job plots for ligands (**1a–b** and **2a–b**) with Zn(II) titrated in CH_3CN, F_0 means the fluorescent value at 394 nm of free ligand, F means the fluorescent value at 394 nm of ligand with Zn(II) added. (a) ligand **1a**; (b) ligand **1b**; (c) ligand **2a**; (d) ligand **2b**.

Where Y represents the absorbance or the fluorescence intensity; Y_0 is the absorbance or the fluorescence intensity of the free ligand; Y_{lim} is the limiting value of Y; c_L and c_M are the corresponding total concentration of ligand and cation. According to the nonlinear least squares analysis of Y versus c_M, the stability constant (*K*s) can be obtained.

The stability constants of ligands **1a**–**b** and **2a**–**b** with Zn(II) and Mg(II) ions were calculated according to the nonlinear fitting method and listed in Table 1. This shows that the *K*s of thiacalix[4]arene derivatives (**2a** and **2b**) are higher than those of calix[4]arene analog (**1a** and **1b**) with Zn(II) or Mg(II) ions, especially with Mg(II) ion.

Conclusion

Four mono-quinolin-8-yl-substituted (thia)calix[4]arenes with oligooxyethylene spacers (**1a**–**b** and **2a**–**b**) were synthesised conveniently in one step. Their coordination properties were studied by fluorescence spectra titration in CH_3CN. All of them can form stable 1:1 complex with Zn(II) and Mg(II) ions, respectively. The stability constants of thiacalix[4]arene (**2a** and **2b**) derivative are higher than those of calix[4]arene analog (**1a** and **1b**).

Experimental

General

The melting points (uncorrected) were obtained from X6 microscopic melting point detector. The ^1H NMR was recorded at 300 MHz on Varian Mercury-VX300 spectrometer. The chemical shifts were recorded in parts per million (ppm) with TMS as the internal reference. Fluorescence spectra were obtained on a Shimadzu RF-5301 spectrometer. Elemental analyses were determined by Perkin–Elmer 204B elemental autoanalyser. ESI Mass spectra were determined using Finnigan LCQ Advantage mass spectrometer.

General procedure for the synthesis of compound **1a–b** *and* **2a–b**

A mixture of **1** or **2** (1.0 mmol) and **3a** or **3b** (1.2 mmol) and anhydrous K_2CO_3 (1.5 mmol) in dry toluene was stirred under refluxing for 12 hours to yield a red solution. The solvent was removed by rotary evaporation under reduced pressure. The resulting red mixture was treated with 40 ml pure water and then extracted with chloroform (30 ml × 3). The combined organic phases were dried over anhydrous Na_2SO_4, and filtered. After concentration in vacuum, the desired product was obtained by column chromatography on silica gel (chloroform/acetone = 100:1, V/V).

5,11,17,23-Tetra-tert-butyl-25,26,27-tri-hydroxy-28-[2-(2-(2-(quinolin-8-yloxy)ethoxy)ethoxy)]calix[4]arene (**1a**): 73.5%. M.p. 110–112°C ^1H NMR (300 MHz, TMS, $CDCl_3$) δ: 1.17 (s, 9H, $C(CH_3)_3$), 1.19 (s, 18H, $C(CH_3)_3$), 1.21 (s, 9H, $C(CH_3)_3$), 3.35 (d, J = 13.2 Hz, 2H, $ArCH_2Ar$), 3.36 (d, J = 13.8 Hz, 2H, $ArCH_2Ar$), 4.18

Table 1 Stability constant (*K*s) and correlation coefficients (*R*) of ligands **1a–b** and **2a–b** with Zn^{2+} and Mg^{2+} cations in CH_3CN

Ligands		Zn^{2+}	Mg^{2+}
1a	*K*s (M^{-1})	$(8.98 \pm 0.16^a) \times 10^4$	$(1.44 \pm 0.37^a) \times 10^4$
	R	0.9983	0.9865
1b	*K*s (M^{-1})	$(1.41 \pm 0.23^a) \times 10^5$	$(1.04 \pm 0.16^a) \times 10^4$
	R	0.9989	0.9937
2a	*K*s (M^{-1})	$(3.43 \pm 0.99^a) \times 10^5$	$(3.93 \pm 0.95^a) \times 10^5$
	R	0.9987	0.9992
2b	*K*s (M^{-1})	$(2.32 \pm 0.62^a) \times 10^5$	$(3.87 \pm 0.78^a) \times 10^5$
	R	0.9986	0.9994

[a] All error values were obtained by the results of non-linear fitting.

(d, *J* = 13.8 Hz, 2H, ArCH$_2$Ar), 4.25 (b, 2H, quiOCH$_2$CH$_2$OCH$_2$C*H*$_2$), 4.31–4.33 (m, 4H, quiOCH$_2$C*H*$_2$OC*H*$_2$CH$_2$), 4.43 (d, *J* = 13.2 Hz, ArCH$_2$Ar), 4.63 (t, *J* = 4.8 Hz, 2H, quiOCH$_2$), 6.93 (s, 2H, ArH), 6.97–7.00 (m, 1H, 7-CH), 7.01 (s, 4H, ArH), 7.05 (s, 2H, ArH), 7.37–7.43 (m, 3H, 3,5,6-CH), 8.18 (b, 1H, 4-CH), 8.98 (b, 1H, 2-CH), 9.40 (s, 2H, ArOH), 10.26 (s, 1H, ArOH); ESI-MS(+) *m/z*: 864.5 (M+H)$^+$. Anal. calcd. for $C_{57}H_{69}NO_6$(863.5): C, 79.22; H, 8.05; N, 1.62; Found: C, 79.33; H, 8.11; N, 1.54.

5,11,17,23-Tetra-tert-butyl-25,26,27-tri-hydroxy-28-[2-(2-(2-(2-(quinolin-8-yloxy)ethoxy)ethoxy)ethoxy)]calix[4]arene **(1b):** 62.1%. M.p. 104–106°C ^{1}H NMR (300 MHz, TMS, CDCl$_3$) δ: 1.19 (s, 9H, C(CH$_3$)$_3$), 1.20 (s, 18H, C(CH$_3$)$_3$), 1.22 (s, 9H, C(CH$_3$)$_3$), 3.38 (d, *J* = 12.6 Hz, 2H, ArCH$_2$Ar), 3.40 (d, *J* = 13.5 Hz, 2H, ArCH$_2$Ar), 3.90 (b, 4H, quiOCH$_2$CH$_2$OC*H*$_2$C*H*$_2$OCH$_2$CH$_2$), 4.10 (b, 4H, quiOCH$_2$C*H*$_2$OCH$_2$CH$_2$OC*H*$_2$CH$_2$), 4.25 (d, *J* = 13.5 Hz, 2H, ArCH$_2$Ar), 4.28–4.30 (m, 2H, quiOCH$_2$CH$_2$OCH$_2$CH$_2$OCH$_2$C*H*$_2$), 4.39 (t, *J* = 4.8 Hz, 2H, quiOCH$_2$), 4.46 (d, *J* = 12.6 Hz, 2H, ArCH$_2$Ar), 6.97 (s, 2H, ArH), 7.03 (s, 4H, ArH), 7.07 (s, 2H, ArH), 7.11 (b, 1H, 7-CH), 7.41–7.46 (m, 3H, 3,5,6-CH), 8.16 (d, *J* = 7.8 Hz, 1H, 4-CH), 8.97 (b, 1H, 2-CH), 9.41 (s, 2H, ArOH), 10.29 (s, 1H, ArOH); ESI-MS(-) *m/z*: 906.6(M-H)$^-$. Anal. calcd. for $C_{59}H_{73}NO_7$(907.5): C, 78.02; H, 8.10; N, 1.54; Found: C, 77.91; H, 8.15; N, 1.43.

5,11,17,23-Tetra-tert-butyl-25,26,27-tri-hydroxy-28-[2-(2-(2-(quinolin-8-yloxy)ethoxy)ethoxy)]-2,8,14,20-tetra-thiacalix[4]arene **(2a):** 63.5%. M.p. 98–100°C ^{1}H NMR (300 MHz, TMS, CDCl$_3$) δ: 1.19 (s, 9H, C(CH$_3$)$_3$), 1.20 (s, 18H, C(CH$_3$)$_3$), 1.22 (s, 9H, C(CH$_3$)$_3$), 4.34 (b, 2H, quiOCH$_2$CH$_2$OCH$_2$CH$_2$), 4.38 (b, 2H, quiOCH$_2$CH$_2$), 4.62 (b, 2H, quiOCH$_2$CH$_2$OCH$_2$CH$_2$), 4.75 (b, 2H, quiOCH$_2$), 7.17–7.19 (m, 1H, 7-CH), 7.37–7.47 (m, 3H, 3,5,6-CH), 7.52 (d, *J* = 2.4 Hz, 2H, ArH), 7.56 (d, *J* = 2.4 Hz, 2H, ArH), 7.58 (s, 2H, ArH), 7.64 (s, 2H, ArH), 8.25 (b, 1H, 4-CH), 9.08 (b, 1H, 2-CH), 9.61 (s, 2H, ArOH), 10.42 (s, 1H, ArOH); ESI-MS(+) *m/z*: 936.3(M+H)$^+$. Anal. calcd. for $C_{53}H_{61}NO_6S_4$(935.3): C, 67.99; H, 6.57; N, 1.50; Found: C, 67.81; H, 6.63; N, 1.48.

5,11,17,23-Tetra-tert-butyl-25,26,27-tri-hydroxy-28-[2-(2-(2-(2-(quinolin-8-yloxy)ethoxy)ethoxy)ethoxy)]-2,8,14,20-tetra-thiacalix[4]arene **(2b):** 52.3%. M.p. 83–85°C ^{1}H NMR (300 MHz, TMS, CDCl$_3$) δ: 1.18 (s, 9H, C(CH$_3$)$_3$), 1.20 (s, 18H, C(CH$_3$)$_3$), 1.21 (s, 9H, C(CH$_3$)$_3$), 3.92–3.97 (m, 4H, quiOCH$_2$CH$_2$OCH$_2$CH$_2$OCH$_2$CH$_2$), 4.18–4.20 (m, 4H, quiOCH$_2$CH$_2$OCH$_2$CH$_2$OCH$_2$CH$_2$), 4.48 (t, *J* = 5.1 Hz, 2H, quiOCH$_2$CH$_2$OCH$_2$CH$_2$OCH$_2$CH$_2$), 4.58 (t, *J* = 5.1 Hz, 2H, quiOCH$_2$), 7.16–7.19 (m, 1H, 7-CH), 7.37–7.50 (m, 3H, 3,5, 6-CH), 7.54 (s, 2H, ArH),7.58 (s, 4H, ArH), 7.62 (s, 2H, ArH), 8.22 (d, *J* = 8.7 Hz, 1H, 4-CH), 9.02 (b, 1H, 2-CH), 9.64 (s, 2H, ArOH), 10.52 (s, 1H, ArOH); ESI-MS(-) *m/z:* 978.4(M-H)$^-$. Anal. calcd. for $C_{55}H_{65}NO_7S_4$(979.4): C, 67.38; H, 6.68; N, 1.43; Found: C, 67.45; H, 6.62; N, 1.49.

This work was supported by the National Natural Science Foundation of China (No. 20272044).

Received 16 January 2006; accepted 16 June 2006
Paper 06/3741

References

1 H. Kumagai, M. Hasegawa, S. Miyanari, Y. Sugawa, Y. Sato, T. Hori, S. Ueda, H. Kamiyama and S. Miyano, *Tetrahedron Lett*., 1997, **38**, 3971.

2 Z. Asfari, V. Böhmer, J. Harrowfield and J. Vicens, *Calixarenes 2001*. Kluwer Academic publ. PO Box 173300 AA Dordrecht, Netherlands.

3 (a) P. Zlatušková, I. Stibor, M. Tkadlecová and P. Lhoták, *Tetrahedron,* 2004, **60***,* 11383; (b) S.K. Kim, J.K. Lee, S.H. Lee, M.S. Lim, S.W. Lee, W. Sim and J.S. Kim, *J. Org. Chem*., 2004, **69**, 2877; (c) Y. Jin, X. Li, S.L. Gong and Y.Y. Chen, *J. Chem., Res.,-S* 2005, **4**, 240.

4 (a) R. Métivier, I. Leray and B. Valeur, *Chem. Commun.,* 2003, **8**, 996; (b) M.J. Choi, M.Y. Kim and S.K. Chang, *Chem. Commun.,* 2001, **17**, 1664.

5 (a) M. Dudic, P. Lhotak, I. Stibor, H. Petrickova and K. Lang, *New J. Chem*., 2004, **28**, 85; (b) Y. Higuchi, M. Narita, T. Niimi, N. Ogawa, F. Hamada, H. Kumagai, N. Iki, S. Miyano and C. Kabuto, *Tetrahedron*, 2000, **56**, 4659.

6 Y. Tang, X.M. Gan, W.S. Liu, N. Tang, M.Y. Tan and K.B. Yu, *Polyhedron*, 1996, **15**, 2607.

7 C.H. Chen and J.M. Shi, *Coordin. Chem. Rev*., 1998, **171**, 161.

8 (a) R.T. Bronson, M. Montalti, L. Prodi, N. Zaccheroni, R.D. Lamb, N.K. Dalley, R.M. Izatt, J.S. Bradshaw and P.B. Savage, *Tetrahedron*, 2004, **60**, 11139; (b) G.M. Sawula, *Talanta*, 2004, **64**, 80.

9 C.A. Lucy and L.W. Ye, *J. Chromatogr., A* 1994, **671**, 121.

10 (a) C.W. Tang and S.A. Van Slyke, *Appl. Phys. Lett*., 1987, **51**, 913; (b) M.A. Baldo, D.F. Obrien, Y. You and A. Shoustikov, *Nature,* 1998, **395**, 151.

11 I.A. Bagatin and H.E. Toma, *New J. Chem*., 2000, **24**, 841.

12 A. Casnati, F. Sansone, A. Sartori, M. Prodi, N. Zaccheroni, F. Ugozzoli and R. Ungaro, *Eur. J. Org. Chem*., 2003, **8**, 1475.

13 C. Almansa, A. Moyano and F. Serratosa, *Tetrahedron,* 1991, **47**, 5867.

14 C.D. Gutsche and L.J. Bauer, *J. Am. Chem. Soc*., 1985, **107**, 6052.

15 L. Prodi, F. Bolletta, M. Montalti and N. Zaccheroni, *Coord. Chem. Rev*., 2000, **205**, 59.

16 B. Valeur (Ed.), *Molecular Fluorescence: Principles and Applications*, 2001, Wiley-VCH Verlag GmbH.

17 R. Nishiyabu and P. Anzenbacher, *Org. Lett.,* 2006, **8**, 359.