# Amphiphilic O – functionalized calix[4]resocinarenes with tunable structural behavior

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## Contents

## General Remarks

NMR spectra were recorded on a «Bruker AVANCE 600» spectrometer. The operating frequency of the spectrometer was 600.13 ($^1$H) and 150 MHz ($^{13}$C). The 5 mm inverse probe with Z-gradient coil was used. Spectra were recorded at a temperature of 303 K. Chemical shifts are given on the δ-scale relative to residual signal of the solvent (DMSO δ($^1$H)=2.50 ppm, δ($^{13}$C)=39.5 ppm).

IR spectra were recorded on a Vector 22 Fourier spectrometer (Bruker, Germany) in the range 400-4000 cm$^{-1}$. Crystalline samples were studied in the form of an emulsion of liquid paraffin and in KBr tablets. For these types of calix[4]resorcinarenes the most suitable mass spectrometry method is MALDI, with the accuracy of ±0.2. The matrix-assisted laser desorption/ionization (MALDI) MS analysis was performed on an Ultraflex-III TOF/TOF mass spectrometer «Bruker Daltonics» (Germany) equipped with Nd:YAG laser (λ 335 nm). The mass spectrometer was operated in the positive linear mode; p-NA was used as the matrix. Elemental analyzes were performed on a Carlo Erba elemental analyzer EA 1108. The reaction mixtures were analyzed by TLC on Silufol UV-254 plate sand visualized by UV light.

All aldehydes were purchased from Acros Organics and used without further purification unless otherwise stated. Anhydrous ethyl alcohol was purified by distillation from CaO. 1,3-bis(2-hydroxyethoxy)benzene was synthesized according to literature procedure.[1]

## Experimental Procedures

**Syntheses of O – functionalized calix[4]resorcinarenes.** Basic compounds for the synthesis of O-functionalized calix[4]resorcinarenes are calix[4]resorcinarenes with hydroxyalkyl groups at the upper rim of the molecule. The syntheses of these compounds have previously been carried out by acid-catalyzed condensation of 1,3-bis(2-hydroxyethoxy) benzene with aliphatic aldehydes. Syntheses of octa-2-hydroxyethyl calix[4]resorcinarenes **3a**, **3b**, **3c** were obtained by.[2] We have circulated a new method of synthesis of O-functionalized calix[4]resorcinarenes to other members of the homologous series of aldehydes.

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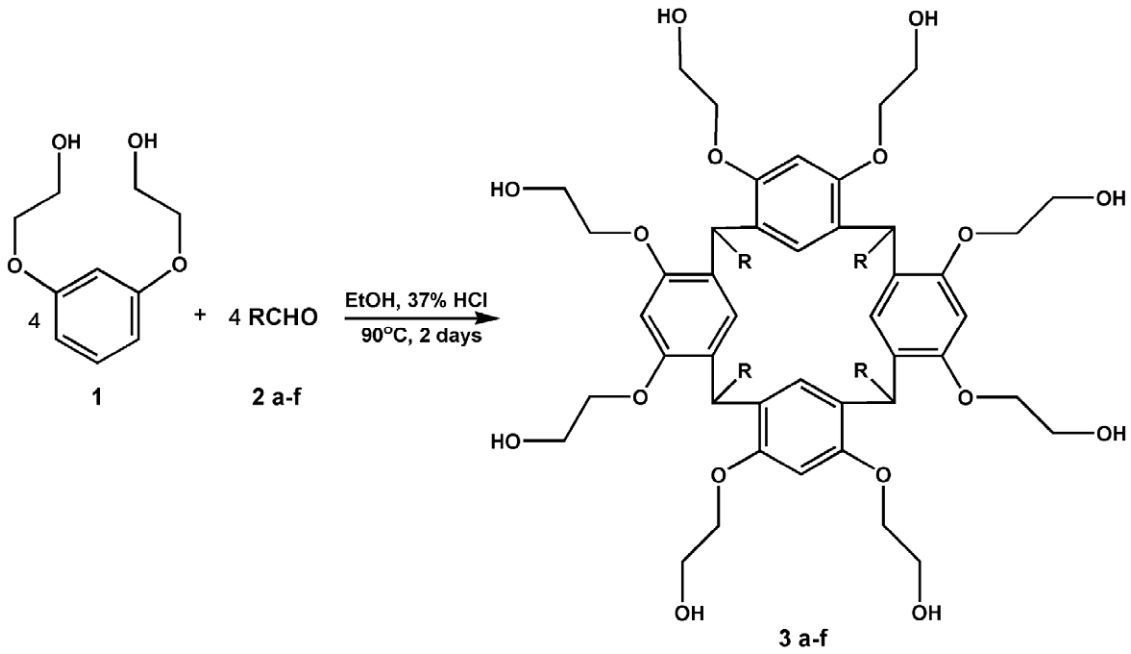
[1] Ashton, P. R; Chemin, A.; Claessens, C. G.; Menzer, S.; Stoddart, J. F.; White, A. J. P.; Williams, D. J. *Eur. J. Org. Chem.,* **1998**, *6*, 969-981.

[2] Kasymova, E. M.; Kaypov A. R.; Burilov, A. R; Pudovik, M. A.; Khabikher, V. D.; Konovalov, A. I. *Russ. J. Gen. Chem*. **2007**, *77*, 1472-1473.

Derivatives **3 d-f** with the lower rim functionalized by octyl, nonyl and undecyl chains (Scheme 1) were obtained by reaction of 1,3-bis(2-hydroxyethoxy)benzene **1** with aliphatic aldehydes **2**. It is shown that the yield of cyclization increases with the length of the alkyl substituents on the lower rim of calixarene matrix.




**Scheme 1.** Synthesis of the calix[4]resorcinarenes **3 a-f** with R=$C_2H_5$ (a); n-$C_5H_{11}$ (b); n-$C_7H_{15}$ (c); n-$C_8H_{17}$(d); n-$C_9H_{19}$ (e); n-$C_{11}H_{23}$ (f).

General procedure for synthesis of **3 a-f**: A mixture of 1,3-bis(2-hydroxyethoxy)benzene (**1**) (1.0 g, 5.05 mmol), ethanol (1.5 mL), 37% HCl (2 mL) and corresponding aliphatic aldehydes **2a-f** (5.05 mmol) was kept at 90 °C for 2 days. After cooling the reaction mixture, the white precipitate was deposited, washed successively with methanol and water and dried to constant weight in the vacuum to get powdered compounds **3 a-f**.

***4,6,10,12,16,18,22,24*-octakis(2'-hydroxyethoxy)-*2,8,14,20*-tetraethylcyclopenta[*19.3.1.1*$^{3,7}$.*1*$^{9,13}$.*1*$^{15,19}$]octacoza-*1(25),3,5,7(28),9,11,13(27),15,17,19(26),21,23*-dodecaene (3a)**: 37% yield, m.p. >330 °C. (decomp.); $^1$H NMR (600 MHz, DMSO-$d_6$, 303 K): δ=6.84 (s, ArH, 4H), 6.44 (s, ArH, 4H), 4.64 c (s, OH, 8H), 4.51 (t, CH, *J*=7.0 Hz, 4H), 3.86 (br.m, $OCH_2$, 16H), 3.66 (br.m, $C\underline{H_2}OH$, 16H), 1.59 (m, $CH_2$, 8H), 0.62 ppm (t, $CH_3$, *J*=6.97 Hz, 12H); $^{13}$C NMR (150 MHz, DMSO-$d_6$, 303 K): δ=154.4, 125.7, 125.5, 98.0, 70.1, 59.8, 34.5, 28.3, 11.9 ppm; IR (KBr): ν̃=3408, 1610, 1584, cm$^{-1}$; MS (MALDI-TOF): *m/z* calcd for $C_{52}H_{72}O_{16}$: $[M+Na]^+$ 975.38, $[M+K]^+$ 991.44; found:

$[M+Na]^+$ 975.18, $[M+K]^+$ 991.38; elemental analysis calcd (%) for $C_{52}H_{72}O_{16}$: C 65.53, H 7.61; found: C 65.51, H 7.59.

***4,6,10,12,16,18,22,24*-octakis(2'-hydroxyethoxy)-*2,8,14,20*-tetrapentylcyclopenta[*19.3.1.1*$^{3,7}$.*1*$^{9,13}$.*1*$^{15,19}$]octacoza-*1(25),3,5,7(28),9,11,13(27),15,17,19(26),21,23*-dodecaene (3b)**: 87% yield, m.p. 257 °C; $^1$H NMR (600 MHz, DMSO-$d_6$, 303 K): δ=6.69 (s, ArH, 4H), 6.41 (s, ArH, 4H), 4.62 (s, OH, 8H), 4.54 (t, CH, *J*=7.0 Hz, 4H), 3.72, 3.84 (br., $OCH_2$, 16H), 3.58 (br.m., $C\underline{H_2}OH$, 16H), 1.70 (m, $CH_2$, 8H), 1.22 (m, $(CH_2)_3CH$, 24H), 0.80 ppm (t, $CH_3$, *J*=6.97 Hz, 12H); $^{13}$C NMR (150 MHz, DMSO-$d_6$, 303 K): δ=155.0, 125.9, 125.7, 99.4, 70.6, 60.2, 35.4, 34.1, 31.8, 27.4, 22.4, 14.2 ppm; IR (Nujol): ν̃=3345, 1609, 1584 cm$^{-1}$; MS (MALDI-TOF): *m/z* calcd for $C_{64}H_{96}O_{16}$: $[M+Na]^+$ 1143.66, $[M+K]^+$ 1159.63; found: $[M+Na]^+$ 1143.77, $[M+K]^+$ 1159.75; elemental analysis calcd (%) for $C_{64}H_{96}O_{16}$: C 68.53, H 8.63; found: C 68.39, H 8.45.

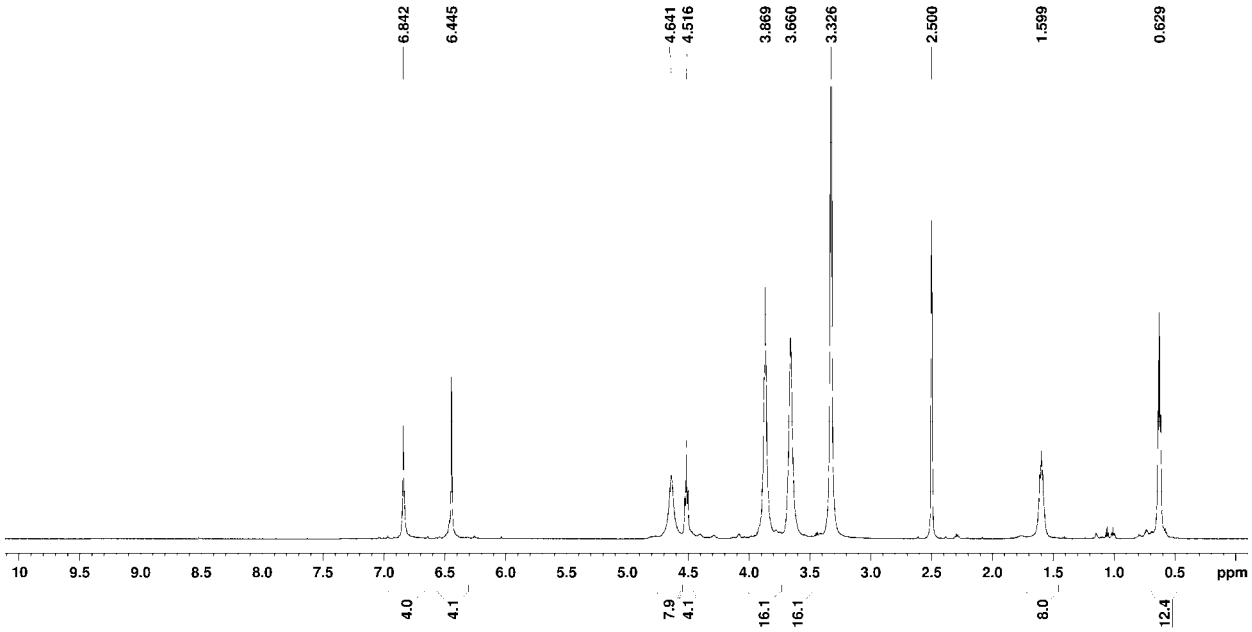
***4,6,10,12,16,18,22,24*-octakis(2'-hydroxyethoxy)-*2,8,14,20*-tetraheptylcyclopenta[*19.3.1.1*$^{3,7}$.*1*$^{9,13}$.*1*$^{15,19}$]octacoza-*1(25),3,5,7(28),9,11,13(27),15,17,19(26),21,23*-dodecaene (3c)**: 80% yield, m.p. 230°C; $^1$H NMR (600 MHz, DMSO-$d_6$, 303 K): δ=6.70 (br.s, ArH, 4H), 6.41 (s, ArH, 4H), 4.63 (s, OH, 8H), 4.56 (t, CH, *J*=7.0 Hz, 4H), 3.74, 3.84 (br.m, $OCH_2$, 16H), 3.60 (br.m, $C\underline{H_2}OH$, 16H), 1.70 (m, $CH_2$, 8H), 1.18 (m, $(CH_2)_5$, 40H), 0.81 ppm (t, $CH_3$, *J*=6.97 Hz, 12H); $^{13}$C NMR (150 MHz, DMSO-$d_6$, 303 K): δ=154.6, 125.5, 125.3, 98.9, 70.2, 59.9, 35.2, 33.7, 31.3, 29.2, 28.7, 27.3, 22.0, 13.8 ppm; IR (KBr): ν̃=3365, 1610,1584 cm$^{-1}$. MS (MALDI-TOF): m/z calcd for $C_{72}H_{112}O_{16}$: $[M+Na]^+$ 1255.78, $[M+K]^+$ 1271.76; found: $[M+Na]^+$ 1255.68, $[M+K]^+$ 1271.84; elemental analysis calcd (%) for $C_{72}H_{112}O_{16}$: C 70.10, H 9.15; found: C 69.95, H 9.12.

***4,6,10,12,16,18,22,24*-octakis(2'-hydroxyethoxy)-*2,8,14,20*-tetraoctylcyclopenta[*19.3.1.1*$^{3,7}$.*1*$^{9,13}$.*1*$^{15,19}$]-octacoza-*1(25),3,5,7(28),9,11,13(27),15,17,19(26),21,23*-dodecaene (3d)**: 78% yield, m.p. 223 °C; $^1$H NMR (600 MHz, DMSO-$d_6$, 303 K): δ=6.70 (br.s, ArH, 4H), 6.41 (s, ArH, 4H), 4.63 (s, OH, 8H), 4.56 (t, CH, *J* = 7.00 Hz, 4H), 3.74, 3.84 (br.m., $OCH_2$, 16H), 3.60 (br.m, $C\underline{H_2}OH$, 16H), 1.68 (br.m, $CH_2$, 8H), 1.17 (m, $(CH_2)_6$, 48H), 0.81 ppm (t, $CH_3$, *J* = 6.83 Hz, 12H); $^{13}$C NMR (150 MHz, DMSO-$d_6$, 303 K): δ=154.6, 125.6, 125.2, 98.8, 70.2, 59.9, 35.3, 33.7, 31.3, 29.4, 29.0, 28.8, 27.3, 22.1, 13.8 ppm; IR (Nujol): ν̃=3347, 1609, 1584 cm$^{-1}$; MS (MALDI-TOF): m/z calcd for $C_{76}H_{120}O_{16}$: $[M+Na]^+$ 1311.85, $[M+K]^+$ 1327.82; found: $[M+Na]^+$ 1311.77, $[M+K]^+$ 1327.75; elemental analysis calcd (%) for $C_{76}H_{120}O_{16}$: C 70.76, H 9.38; found: C 70.62, H 9.27.

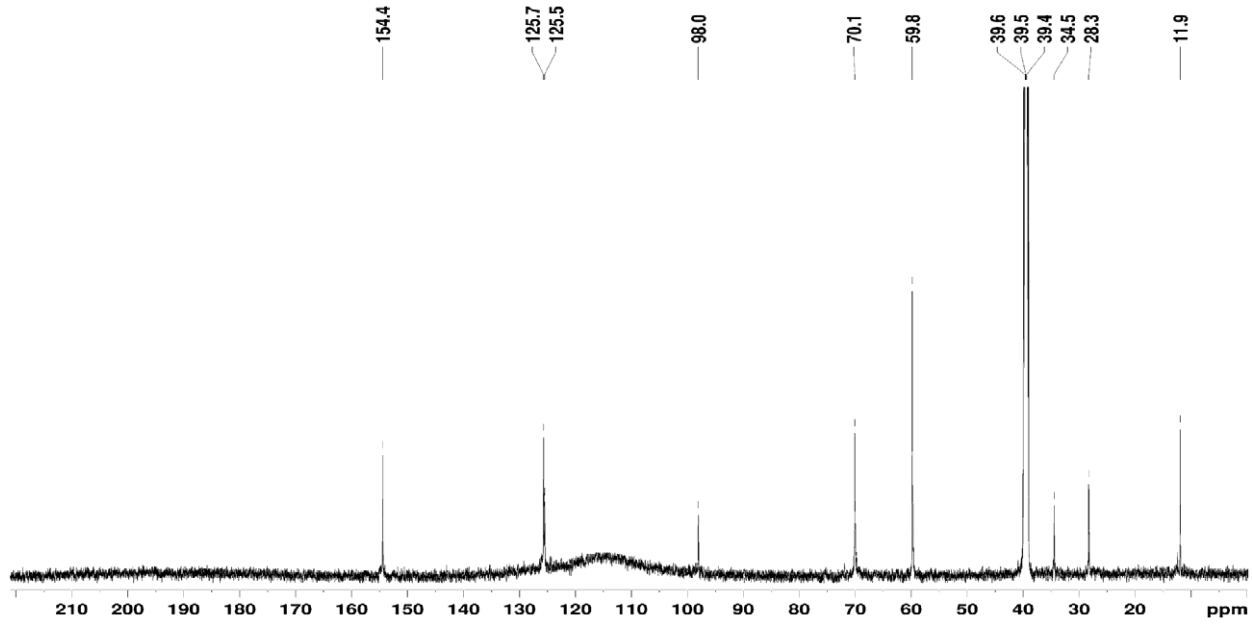
***4,6,10,12,16,18,22,24*-octakis(2'-hydroxyethoxy)-*2,8,14,20*-tetranonylcyclopenta*[19.3.1.1$^{3,7}$.1$^{9,13}$.1$^{15,19}$]*-octacoza-*1(25),3,5,7(28),9,11,13(27),15,17,19(26),21,23*-dodecaene (3e)**: 85% yield, m.p. 195 $^{o}$C, $^{1}$H NMR (600 MHz, DMSO-$d_6$, 303 K): δ=6.70 (br.s, ArH, 4H), 6.40 (s, ArH, 4H), 4.63 (s, OH, 8H), 4.56 (t, CH, *J*=7.00 Hz, 4H), 3.74, 3.83 (br.m, $OCH_2$, 16H), 3.61 (br.m, $C\underline{H_2}OH$, 16H), 1.68 (m, $CH_2$, 8H), 1.16 (m, $(CH_2)_7$, 56H), 0.80 ppm (t, $CH_3$, *J* = 6.98 Hz, 12H); $^{13}$C NMR (150 MHz, DMSO-$d_6$, 303 K): δ=154.6, 125.6, 125.2, 98.8, 70.2, 59.9, 35.3, 33.6, 31.3, 29.4, 29.1, 28.7, 27.3, 22.1, 13.8 ppm; IR (Nujol): ν̃=3339, 1609, 1584 cm$^{-1}$; MS (MALDI-TOF): m/z calcd for $C_{80}H_{128}O_{16}$: $[M+Na]^+$ 1367.91, $[M+K]^+$ 1384.02; found: $[M+Na]^+$ 1367.96, $[M+K]^+$ 1384.10; elemental analysis calcd (%) for $C_{80}H_{128}O_{16}$: C 71.38, H 9.59; found: C 71.26, H 9.60.

***4,6,10,12,16,18,22,24*-octakis(2'-hydroxyethoxy)-*2,8,14,20*-tetraundecylcyclopenta*[19.3.1.1$^{3,7}$.1$^{9,13}$.1$^{15,19}$]*-octacoza-*1(25),3,5,7(28),9,11,13(27),15,17,19(26),21,23*-dodecaene (3f)**: 87% yield, m.p. 180 $^{o}$C; $^{1}$H NMR (600 MHz, DMSO-$d_6$, 303 K): δ=6.70 (br.s, ArH, 4H), 6.39 (s, ArH, 4H), 4.62 (br.s, OH, 8H), 4.54 (t, CH, *J*=7.0 Hz, 4H), 3.73, 3.82 (br.m, $OC\underline{H_2}$, 16H,), 3.60 (br.m, $C\underline{H_2}OH$, 16H), 1.67 (m, $CH_2$, 8H), 1.15 (m, 72H, $(CH_2)_9$), 0.78 ppm (t, $CH_3$, *J*=7.00 Hz, 12H); $^{13}$C NMR (150 MHz, DMSO-$d_6$, 303 K): δ=154.6, 125.6, 125.1, 98.7, 70.2, 59.8, 35.4, 33.6, 31.3, 29.5, 29.2, 29.1, 28.7, 27.3, 22.1, 13.7 ppm; IR (Nujol): ν̃=3332, 1610, 1584 cm$^{-1}$; MS (MALDI-TOF): m/z calcd for $C_{88}H_{144}O_{16}$: $[M+Na]^+$ 1480.04, $[M+K]^+$ 1496.01; found: $[M+Na]^+$ 1480.20, $[M+K]^+$ 1496.17; elemental analysis calcd (%) for $C_{88}H_{144}O_{16}$: C 72.49, H 9.95; found: C 72.35, H 9.91.

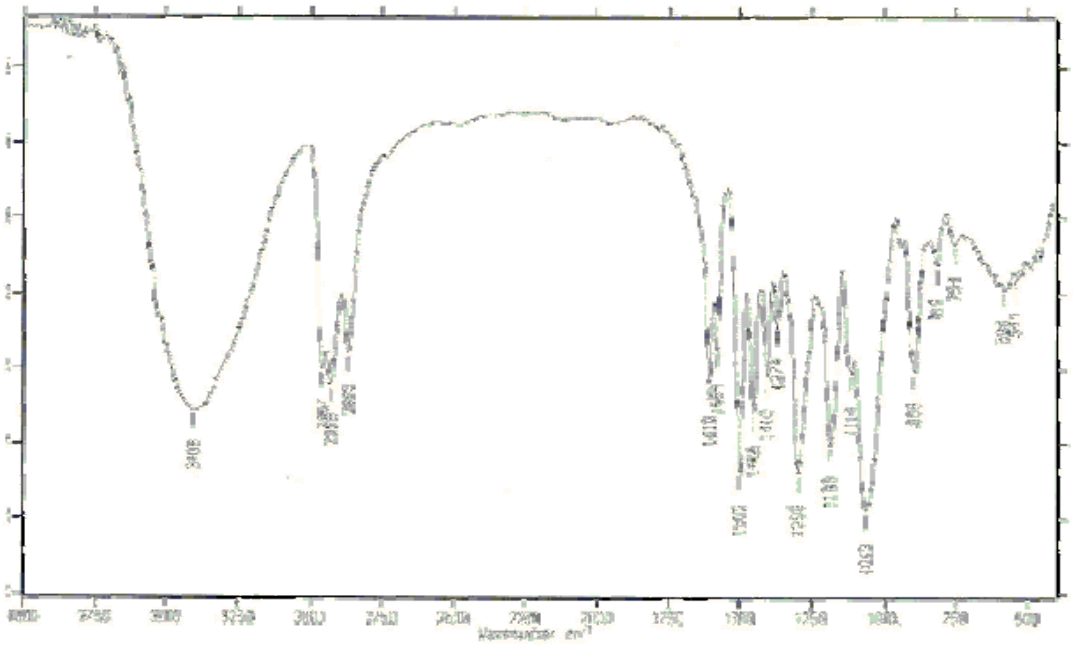
**Spectral Data**



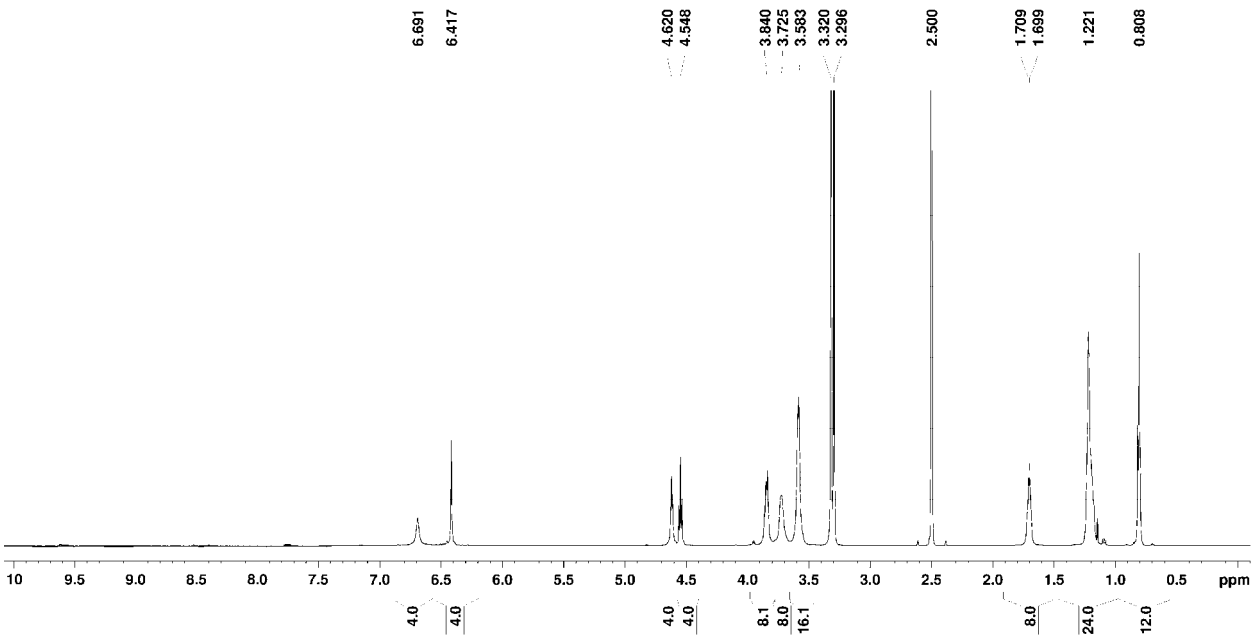

$^{1}$H NMR spectrum (600 MHz, DMSO-$d_6$, 303K, 60 mM) of **3a**.



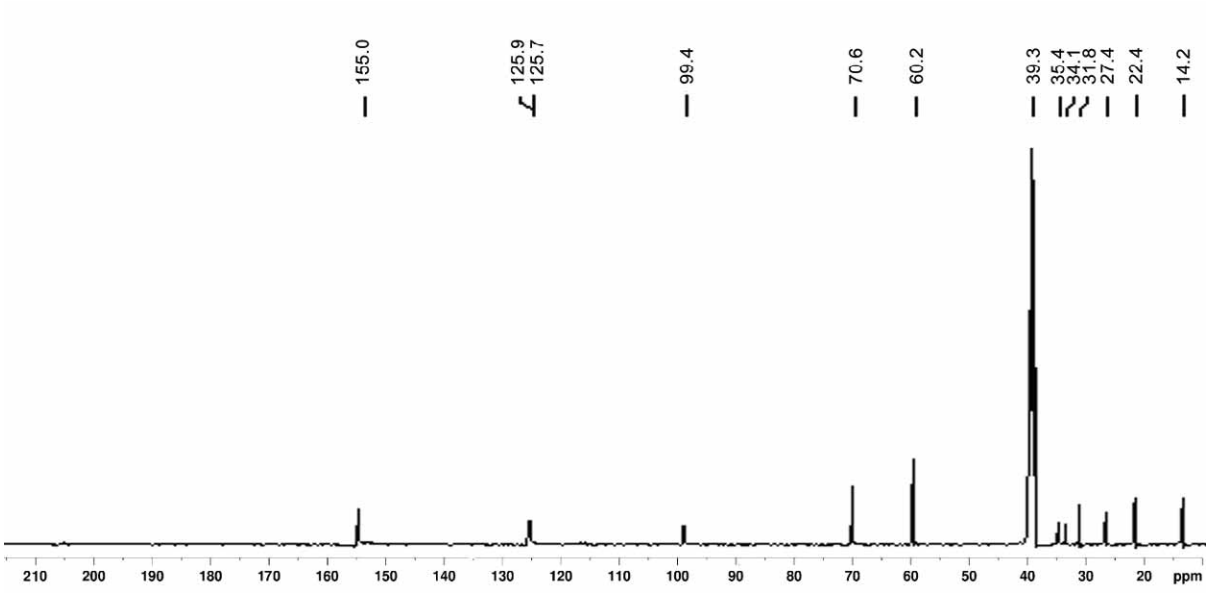

$^{13}$C NMR spectrum (150 MHz, DMSO-$d_6$, 303K, 60 mM) of **3a**.



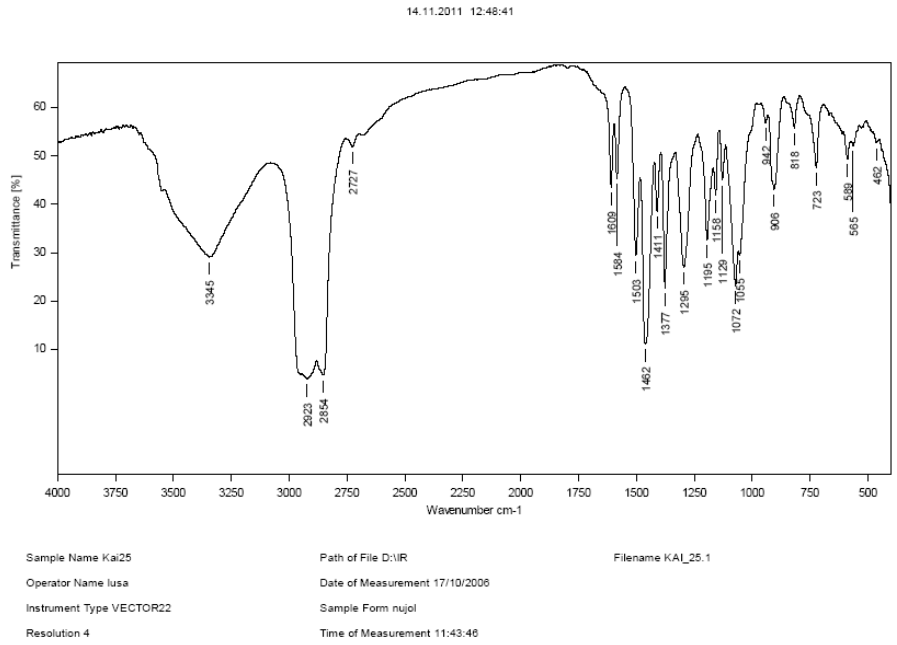
IR spectrum of **3a**.



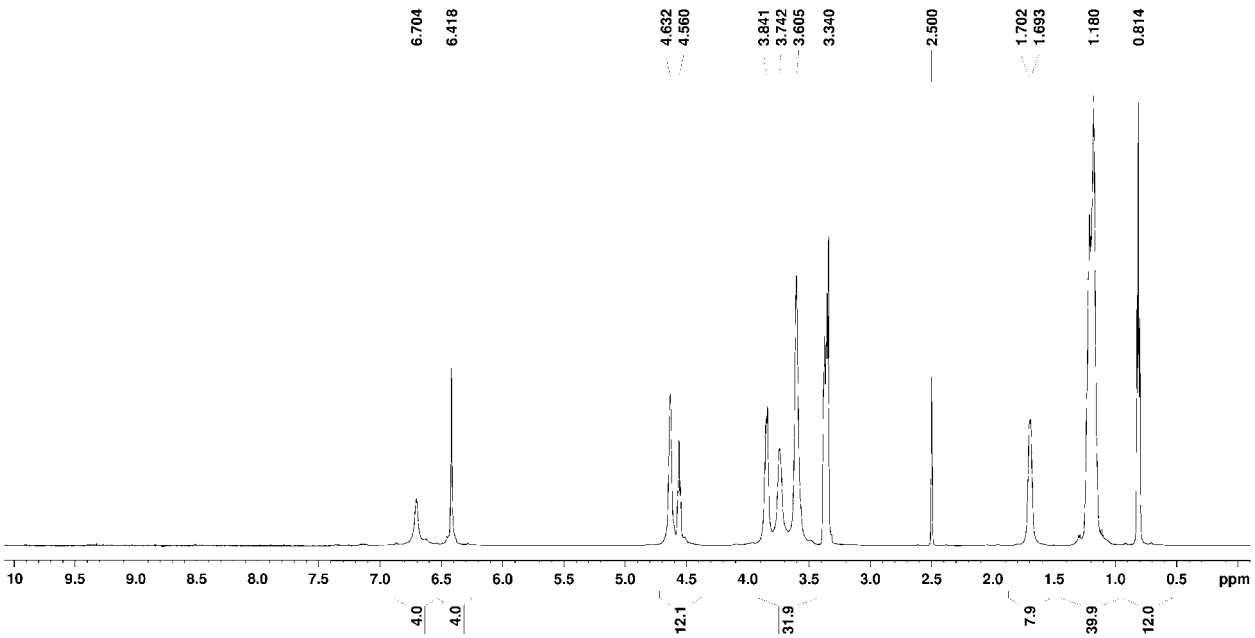

$^{1}$H NMR spectrum (600 MHz, DMSO-$d_6$, 303K, 60 mM) of **3b**.



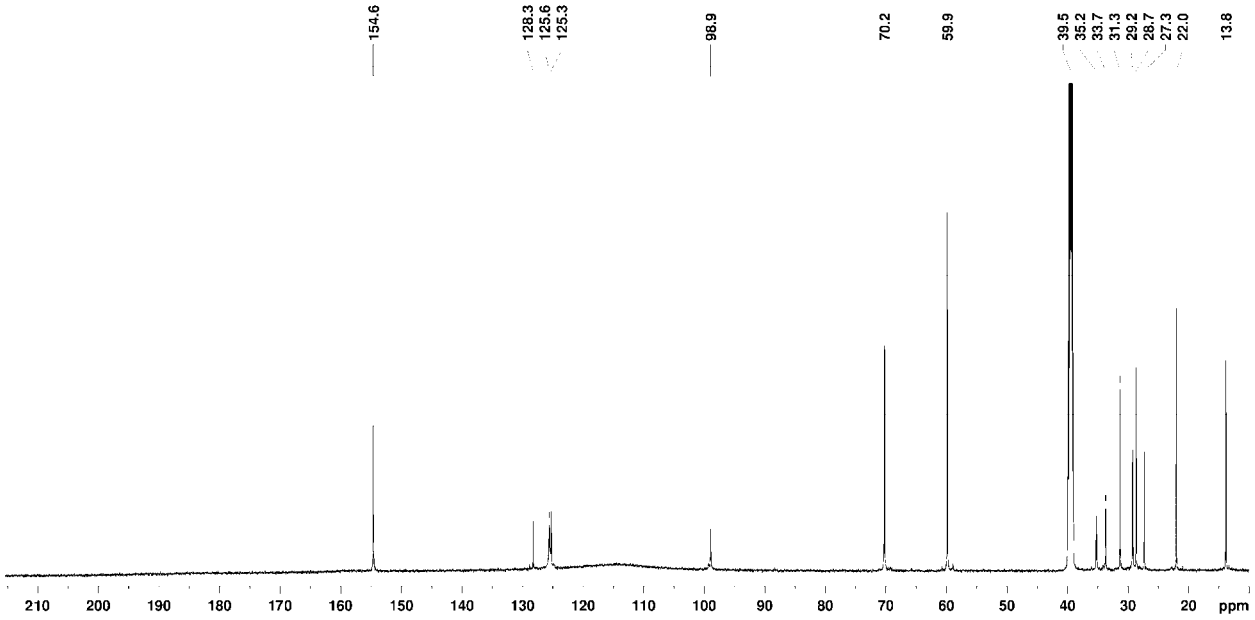

$^{13}$C NMR spectrum (150 MHz, DMSO-$d_6$, 303K, 60 mM) of **3b**.



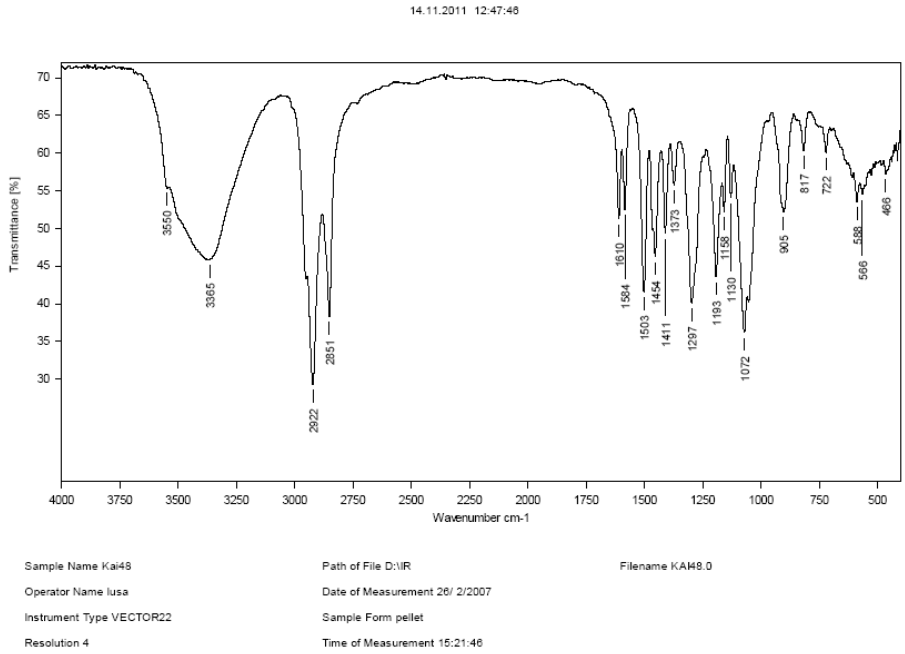

IR spectrum of **3b**.



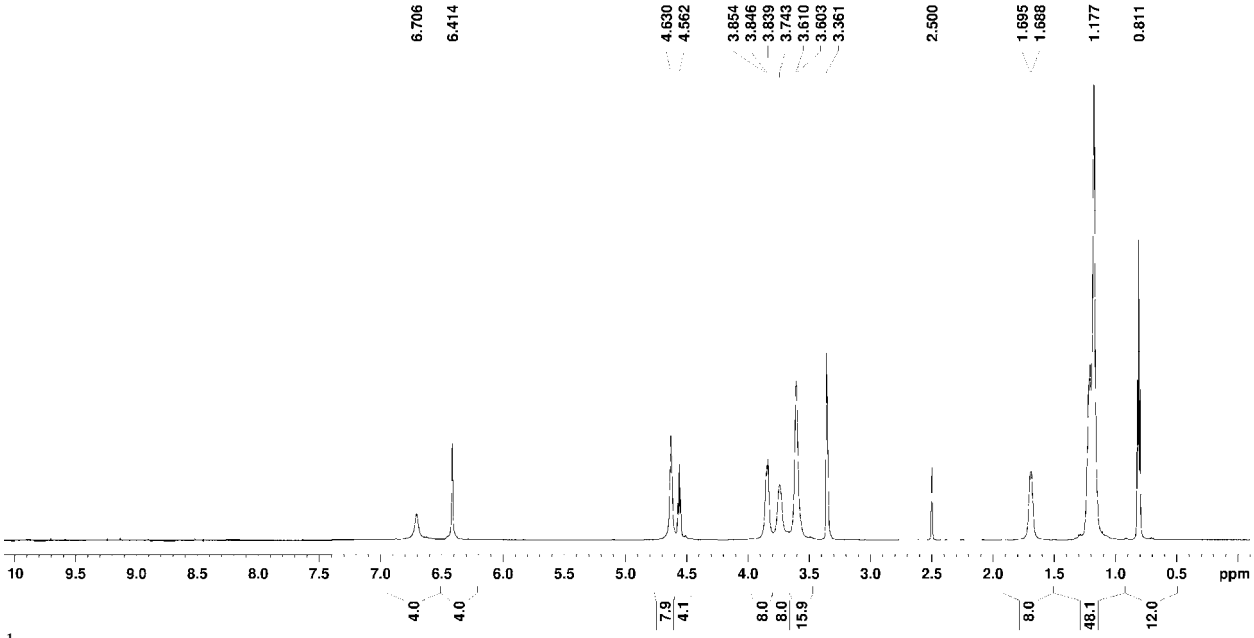

$^{1}$H NMR spectrum (600 MHz, DMSO-$d_6$, 303K, 60 mM) of **3c**.



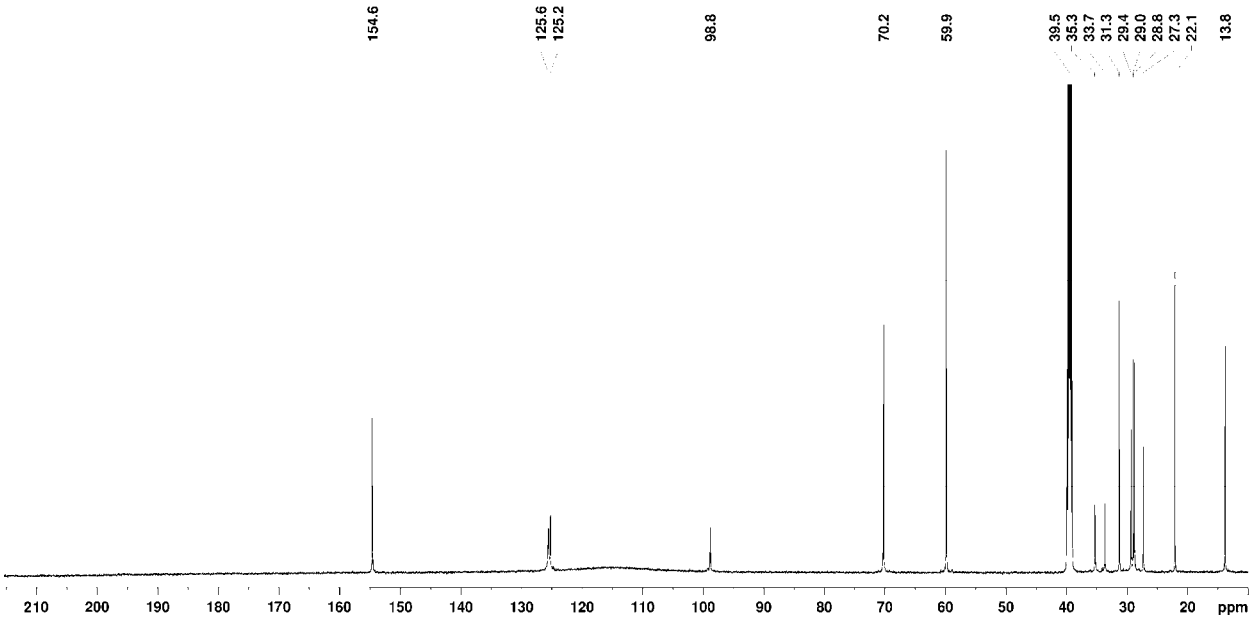

$^{13}$C NMR spectrum (150 MHz, DMSO-$d_6$, 303K, 60 mM) of **3c**.



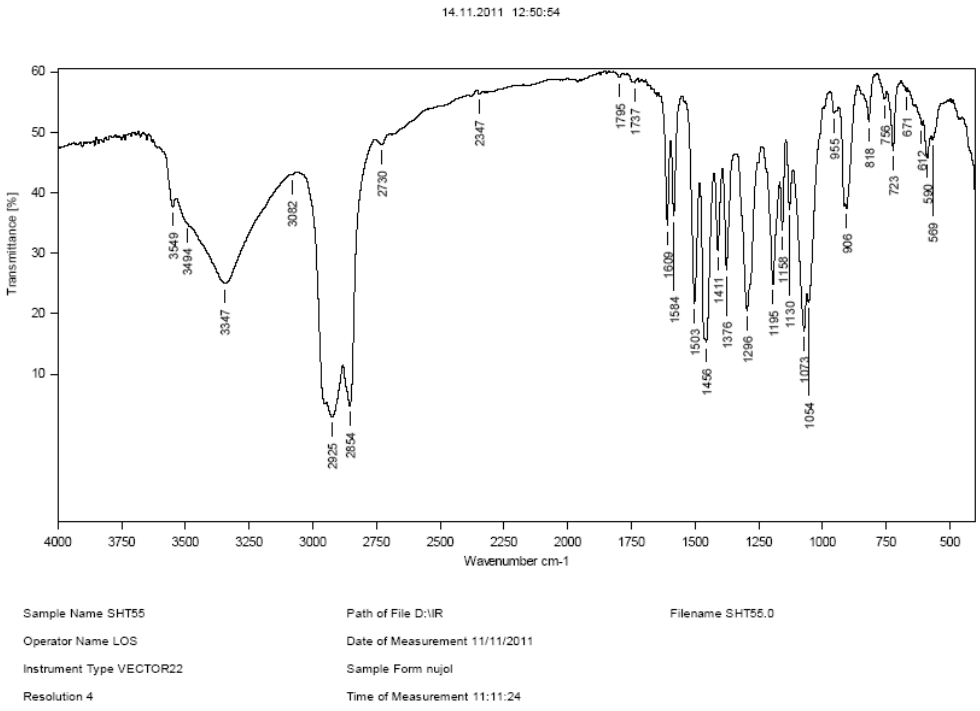

IR spectrum of **3c.**



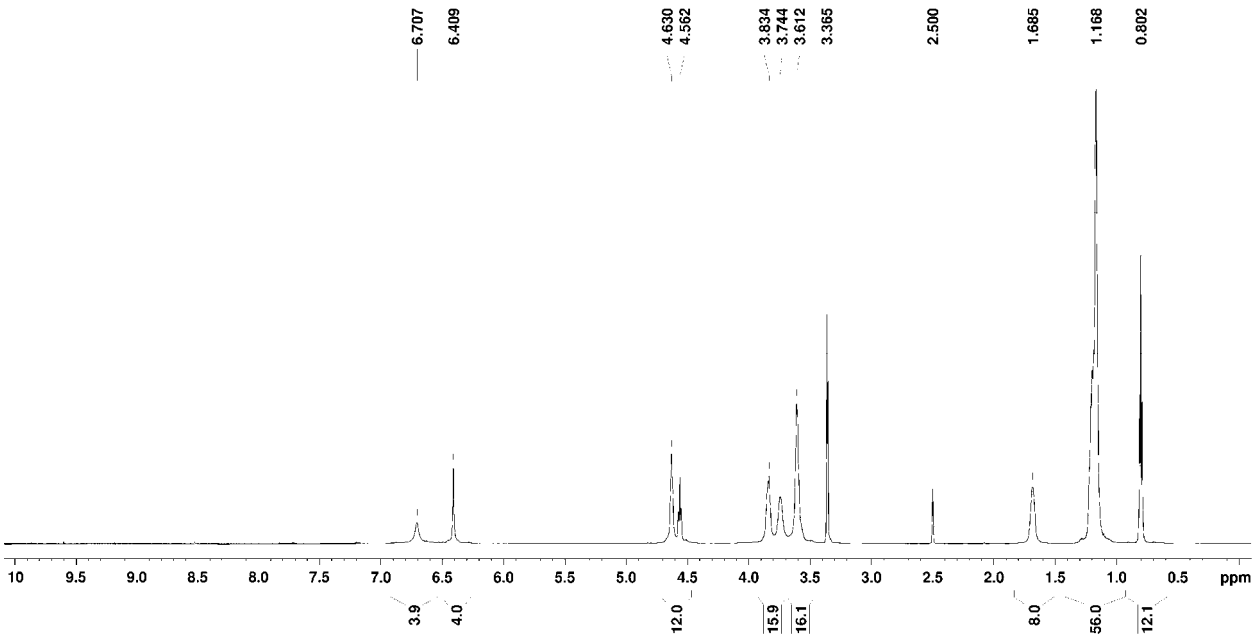

$^{1}$H NMR spectrum (600 MHz, DMSO-$d_6$, 303K, 60 mM) of **3d**.



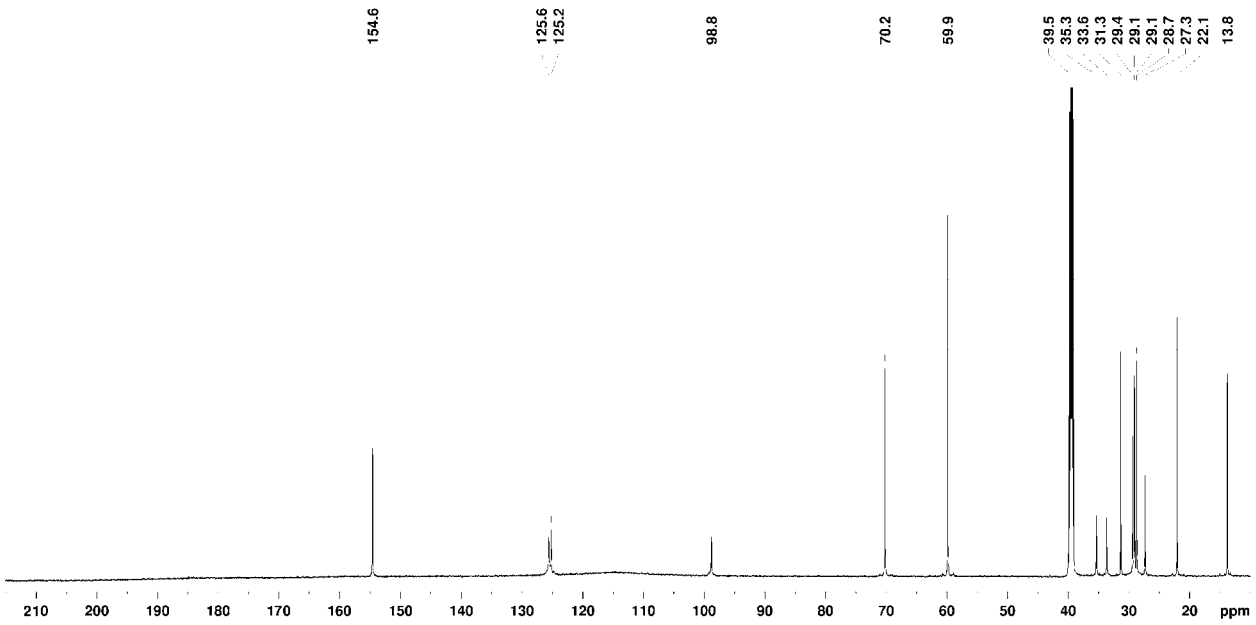

$^{13}$C NMR spectrum (150 MHz, DMSO-$d_6$, 303K, 60 mM) of **3d**.



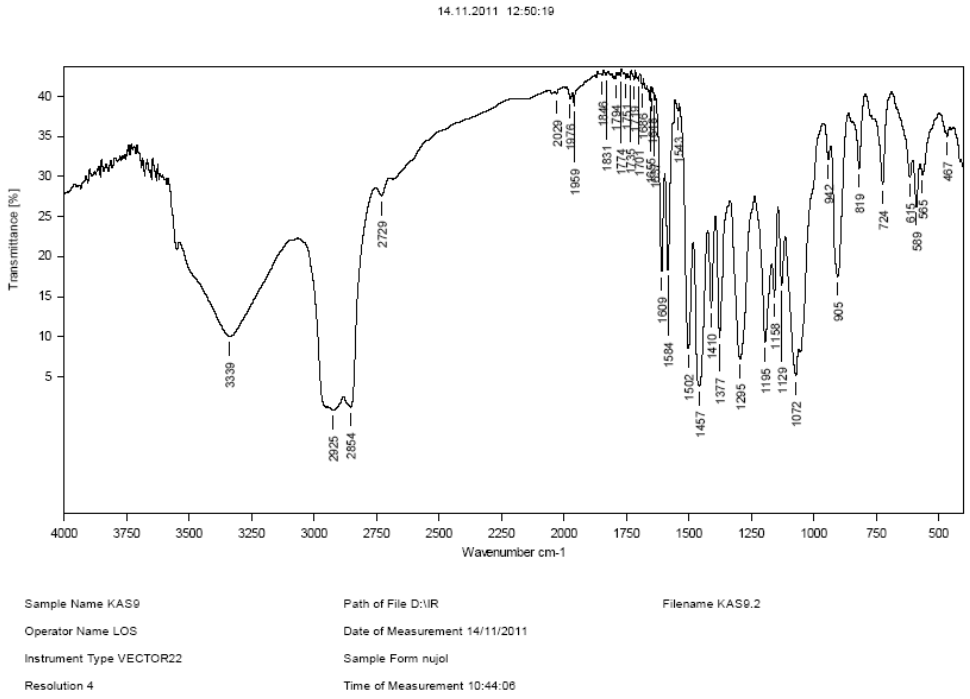

IR spectrum of **3d**.



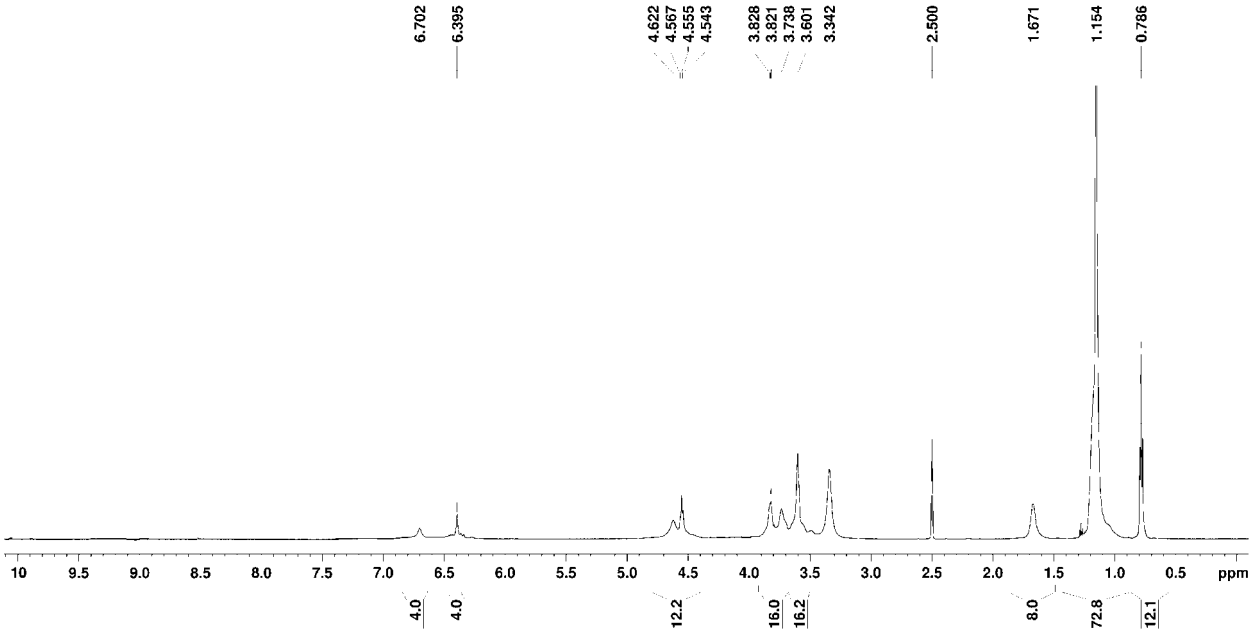

$^{1}$H NMR spectrum (600 MHz, DMSO-$d_6$, 303K, 60 mM) of **3e**.



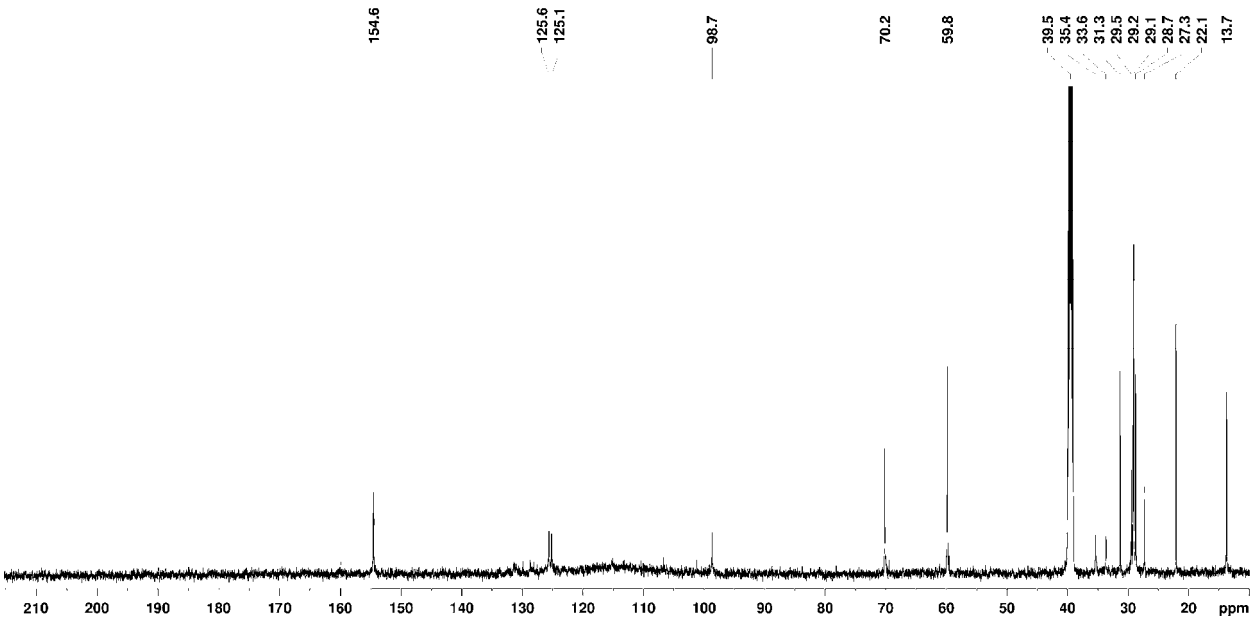

$^{13}$C NMR spectrum (150 MHz, DMSO-$d_6$, 303K, 60 mM) of **3e**.



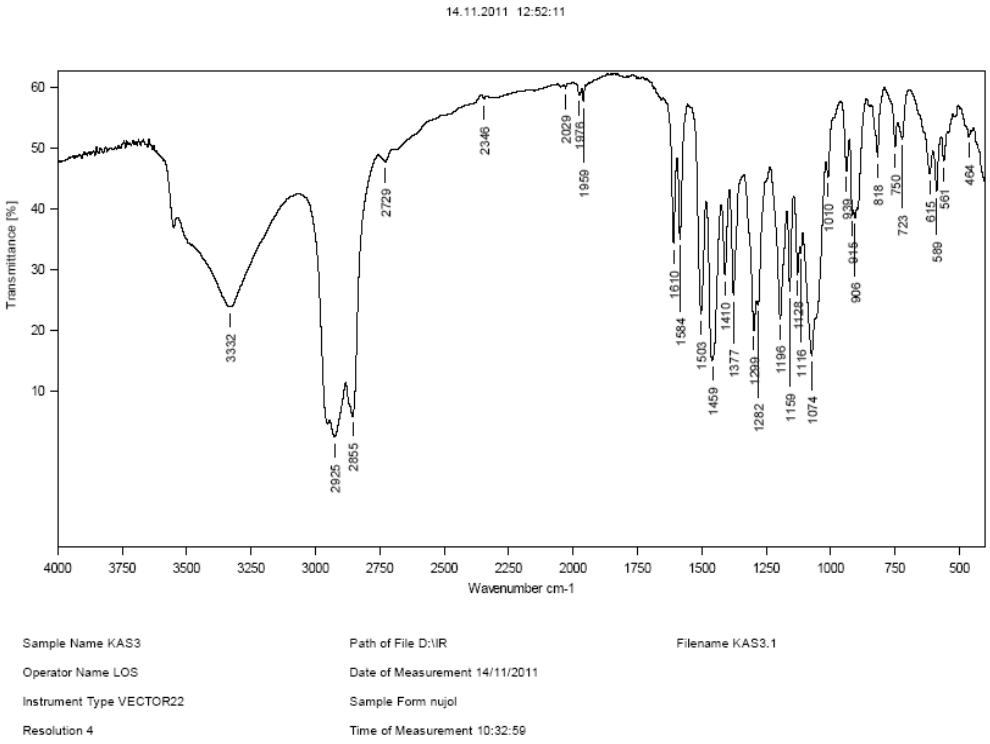

IR spectrum of **3e.**




$^{1}$H NMR spectrum (600 MHz, DMSO-$d_6$, 303K, 60 mM) of **3f**.




$^{13}$C NMR spectrum (150 MHz, DMSO-$d_6$, 303K, 60 mM) of **3f**.




IR spectrum of **3f.**

**Fluorescence data**

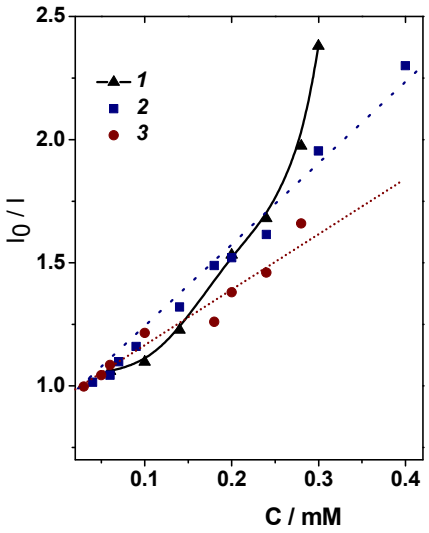



**Figure S1**. Dependence of the intensity ratio ($I_0/I$) for pyrene in the absence ($I_0$) and in the presence of the **3a** (1), **3**b (2), **3f** (3) (I) on their concentration in water-DMF (50% vol) solutions.

The Stern-Volmer dependence for **3b** has linear character and can be described by eq.(S1)[3] :

$$I_0/I_I = 1 + K \times C_{CR} \quad \text{(S1)},$$

here K – Stern-Volmer constant equal to 2908 ± 134 $M^{-1}$ (r = 0.991).

For macrocycles **3a** and **3b**, dependences are close to linear plots however some deviation to Y axis occurs with the surfactant concentration (Figure S1). This probably indicates that admixed quenching mechanism contributes, with eq.(S2) realized:

$$I_0/I_I = (1 + K_D C_{CR})( 1 + K_S C_{CR} ) \quad \text{(S2)},$$

here $K_D$ and $K_S$ are quenching constants characterized dynamic and static quenching mechanism.

At the same time, upon the linearization in $(I_0/I_I - 1)/C_{CR}$ vs. $C_{CR}$ coordinates (the modified form of eq.S2) correlation coefficients of 0.975 and 0.952 for **3a** and **3f** respectively are obtained, which is close or even higher as compared to those for eq.S1. This indicates that the single mechanism is predominantly contributes to the fluorescence quenching, which is characterized by the quenching constants of 2902 ± 401 $M^{-1}$ and 2278 ± 257 $M^{-1}$ for **3a** and **3f** respectively.

[3] J. R. Lakowicz, In *Principles of fluorescence spectroscopy*, 3rd Ed.; Springer: Berlin Heidelberg New York, **2006**, 954 p.

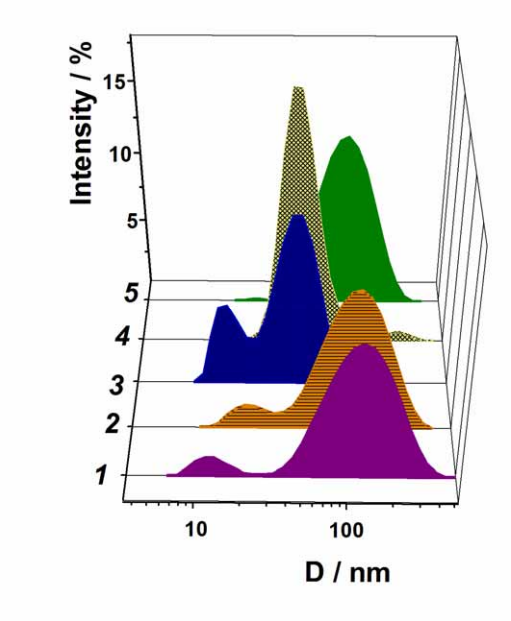



**Figure S2.** Analysis of the size (D, nm) distribution of **3f** particles in water- organic solutions using the intensity parameter; 25 $^{0}$C: (1) water-DMF (30 % vol), C=0.1 mM; (2) water -DMF (30 % vol), C=0.2 mM; (3) water -DMSO (30 % vol), C=0.1 mM; (4) water -DMSO (50 % vol), C=0.1 mM; (5) water –THF (5 % vol), C=0.1 mM.

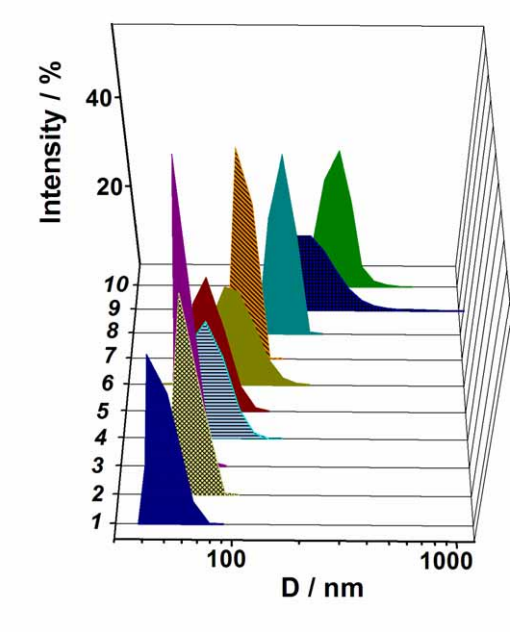



**Figure S3.** Analysis of the size (D, nm) distribution of **3e** particles in water-THF (5% vol) solutions using the intensity parameter; 25 $^{0}$C: (1)- 0.006 mM; (2) 0.008 mM; (3) 0.01 mM; (4) 0.02 mM; (5) 0.04 mM; (6) 0.06 mM; (7) 0.08 mM; (8) 0.1 mM; (9) 0.2 mM; (10) 0.3 mM.

**Table S1.** The distribution of sizes (diameter, nm) of **3b** and **3e** aggregates in terms of number of particles and polydispersity index of the system in water-THF (5% vol) solutions.

| Concentration (mM) | Diameter (nm) | | Polydispersity index | |
|---|---|---|---|---|
| | **3b** | **3e** | **3b** | **3e** |
| 0.006 | - | 51 | - | 0.1 |
| 0.008 | - | 68 | - | 0.14 |
| 0.01 | 295 | 68 | 0.11-0.20 | 0.2 |
| 0.02 | 342 | 78 | 0.1-0.16 | 0.1-0.15 |
| 0,03 | 531 | - | 0.27-0.34 | - |
| 0.04 | 459 | 78 | 0.27-0.34 | 0.1-0.2 |
| 0.06 | - | 91 | - | 0.1 |
| 0.08 | - | 106 | - | 0.12-0.2 |
| 0.1 | 142 | 164 | 0.17-0.22 | 0.18-0.15 |
| 0.2 | 190 | 220 | 0.23-0.29 | 0.15-0.19 |
| 0.3 | 295 | 255 | 0.32-0.46 | 0.23-0.28 |

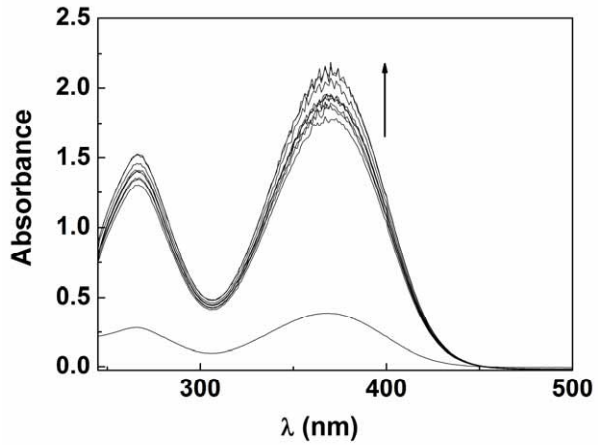



**Figure S4.** Absorption spectra of nitrofurantoin ($5.0\times10^{-3}$ M) in water (the lower line) and **3b** water-DMF (30% vol) solutions; 25 $^{0}$C (the upper arrow indicate the increase of the CR concentration within the range of 0.02 to 0.3 mM).