

Article

## Pseudo-cyclic Face-to-face Rigid Structure Caused by the Intramolecular Ion Pair Effect

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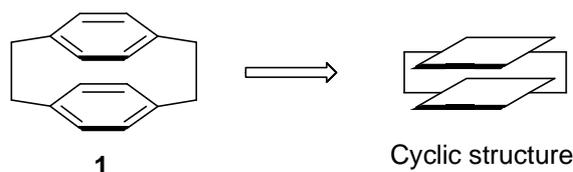
**Abstract:** Six 3-methylpyridine zwitterions and six quinoline zwitterions were synthesized through the reaction of 4-hydroxycoumarins, *p*-benzoquinone and the corresponding *N*-aromatics. The novel pseudo-cyclic face-to-face rigid structure of the zwitterion was elucidated by <sup>1</sup>H-NMR at different temperatures, and assumed to be caused by both the intramolecular ion pair attraction and the steric interaction.

**Keywords:** 4-Hydroxycoumarins; Zwitterion; Molecular structure.

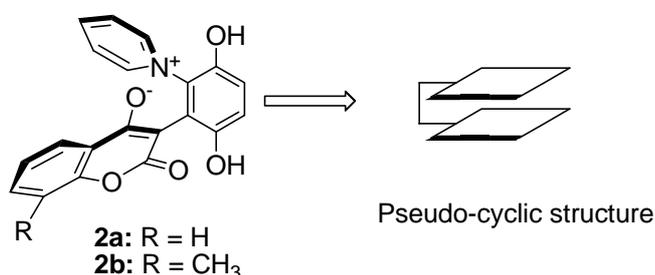
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### 1. Introduction

Recently, the compounds with cyclic structures derived from the [2.2] paracyclophane backbone **1** (Figure 1) have stimulated considerable interest due to their special properties and applications. 4,12-Bis(diphenylphosphino)-[2.2]-paracyclophane was shown to be an excellent transition metal ligand for the catalytic asymmetric hydrogenation of carbonyl groups [1-4]. The bridge-fluorinated paracyclophanes display intriguing chemical reactivity [5-7] and commercial applications [8-9]. The bridging ligands derived from paracyclophane have afforded the opportunity to investigate the role of  $\pi$ -stacking interactions in mediating electronic communication, as charge-transport was observed in double-stranded DNA [10-12]. It is believed that the cyclic face-to-face rigid structure of the paracyclophane moiety plays an important role in properties of these derivatives.

**Figure 1.** The structure of [2.2] paracyclophane.

In a recent communication [13], we reported the synthesis of zwitterionic 4-hydroxycoumarin derivatives. We now describe the novel pseudo-cyclic face-to-face rigid structures of these zwitterions (Figure 2).

**Figure 2.** The zwitterion structures.

## 2. Results and Discussion

The zwitterionic 4-hydroxycoumarin derivatives are composed of hydroquinone, pyridine and 4-hydroxycoumarin planes. The pyridine and 4-hydroxycoumarin planes are joined to the hydroquinone core to form the pseudo-cyclic face-to-face structure (Figure 2).

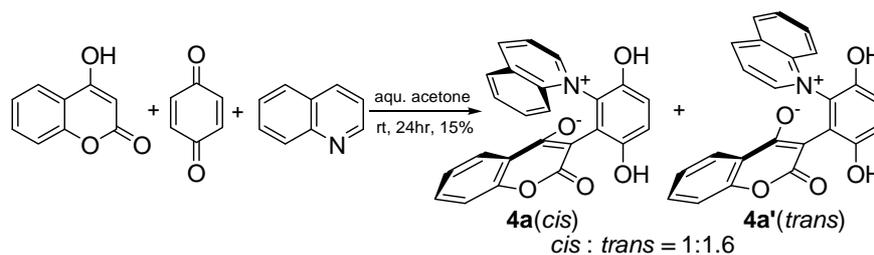
The different <sup>1</sup>H-NMR shifts of the two  $\alpha$ -protons located on the pyridine ring of **2b** [13] indicated that the pyridine plane cannot rotate freely at room temperature, as it is known that if the pyridine ring can rotate freely, the two  $\alpha$ -protons do not give separate <sup>1</sup>H-NMR signals. Moreover, when *N*-heterocyclic aromatics such as 3-methylpyridine and quinoline (which lack a C<sub>2</sub>-symmetric axis through the nitrogen atom) were treated with 4-hydroxycoumarins and *p*-benzoquinone, both *cis* and *trans* products were obtained, due to the restricted rotation about the C-N bond. The results of these reactions are summarized in Tables 1 and 2.

These *cis* and *trans* products could not be separated by silica gel column chromatography. The assignment of the respective stereochemistry and their isomer ratios could however be established from the <sup>1</sup>H-NMR spectra. For the 3-methylpyridinium zwitterion **3a**, the  $\alpha$ -proton next to the methyl group on the pyridine ring was predicted to only show a single peak in the aromatic region (Figure 3). The appearance of the two aromatic singlets, at  $\delta$  8.92 and 8.51 ppm, respectively, implied that both *cis* and *trans* isomers might be generated. Furthermore, the two aromatic singlets had a total integrated area equal to 1H, consistent with a mixture of the two isomers. The peak at  $\delta$  8.92 was attributed to the  $\alpha$ -proton (H2) adjacent to the methyl group of *cis* isomer, in which H2 was further away from the shielding region of the oxyanion, and came at low fields relative to H2' of the *trans* isomer. Thus the area ratio of 1.3:1 of the two aromatic singlets represents the *cis* and *trans* isomer ratio.

**Table 1.** The synthesis of 3-methylpyridinium zwitterions.

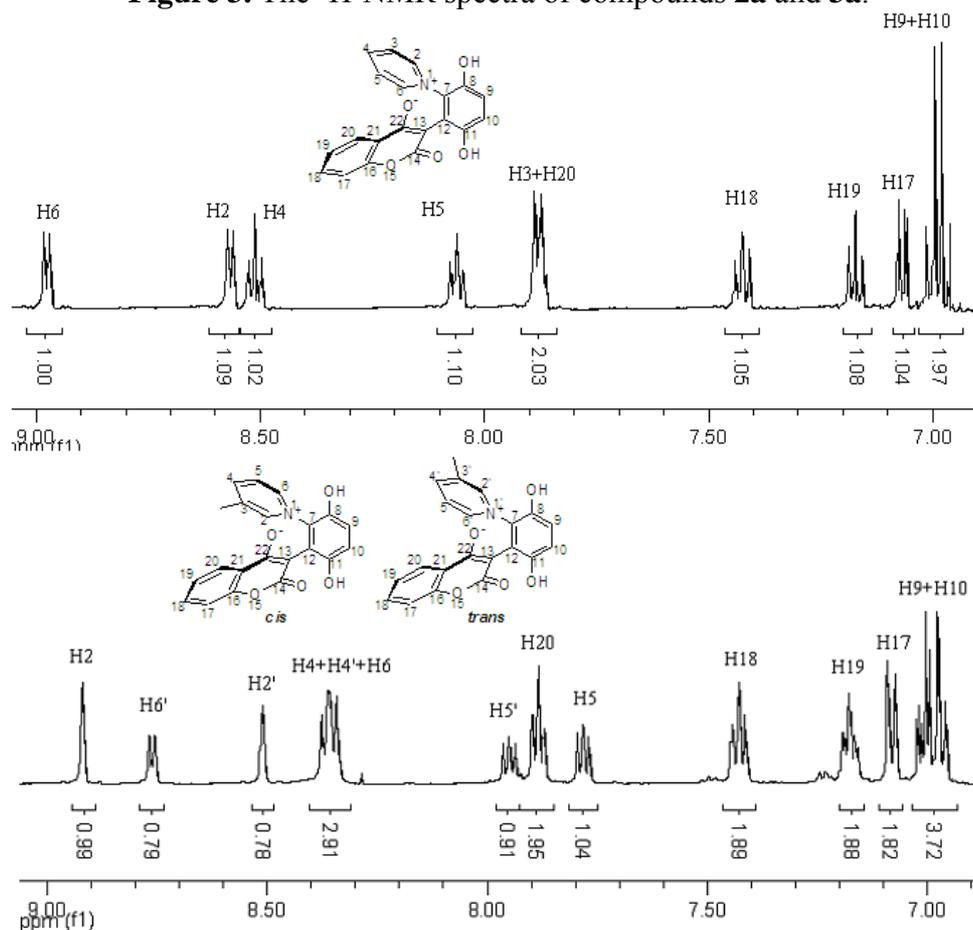
Entry	4-HCs	Yield(%) <sup>a</sup>	Product	Cis/Trans <sup>b</sup>
			 <b>3a(cis)</b> <b>3a'(trans)</b> <i>cis</i> : <i>trans</i> = 1.3:1	
1		35	 <b>3b(cis)</b> <b>3b'(trans)</b>	1.3:1
2		29	 <b>3c(cis)</b> <b>3c'(trans)</b>	1.2:1
3		42	 <b>3d(cis)</b> <b>3d'(trans)</b>	1.3:1
4		37	 <b>3e(cis)</b> <b>3e'(trans)</b>	1.1:1
5		31	 <b>3f(cis)</b> <b>3f'(trans)</b>	1.1:1

<sup>a</sup>Isolated. <sup>b</sup>Determined by <sup>1</sup>H-NMR

**Table 2.** The synthesis of quinolinium zwitterions.

Entry	4-HCs	Yield(%) <sup>a</sup>	Product	<i>Cis/Trans</i> <sup>b</sup>
1		12		1:1.3
2		9		1:1.4
3		16		1:1.7
4		13		1:1.3
5		12		1:1.5

<sup>a</sup>Isolated yield. <sup>b</sup>Determined by <sup>1</sup>H-NMR

**Figure 3.** The  $^1\text{H-NMR}$  spectra of compounds **2a** and **3a**.

The chemical shifts and the integration of the peaks of the  $^1\text{H-NMR}$  spectrum did not change even when the sample of **2b** and **4a** was warmed. (Figures 4 and 5.) This showed that the zwitterionic 4-hydroxycoumarin derivatives were very stable. However, pyridium zwitterions are generally considered to be reactive species and unstable [14]. The characteristic features of the  $^1\text{H-NMR}$  spectra of the zwitterions at different temperatures indicated that the zwitterionic 4-hydroxycoumarin derivatives possessed a rigid backbone containing two defined face-to-face planes, just likes [2.2] paracyclophanes do. However, [2.2] paracyclophane is a macrocyclic ring, and the zwitterions just were pseudo-cyclic.

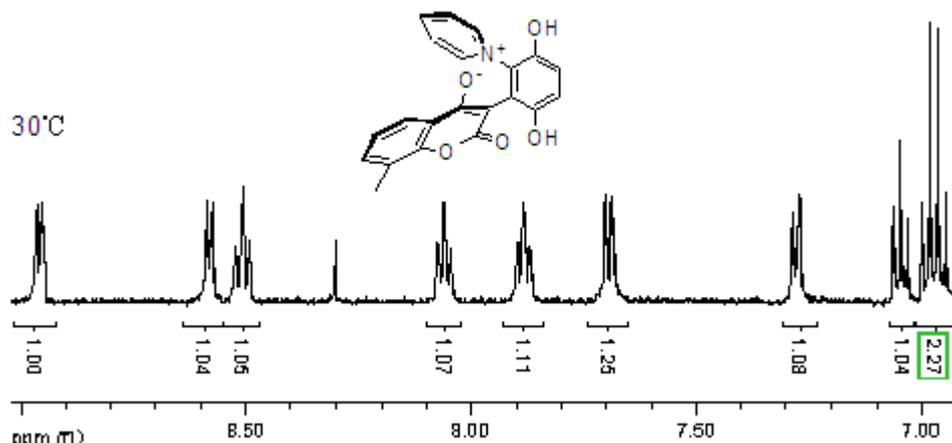
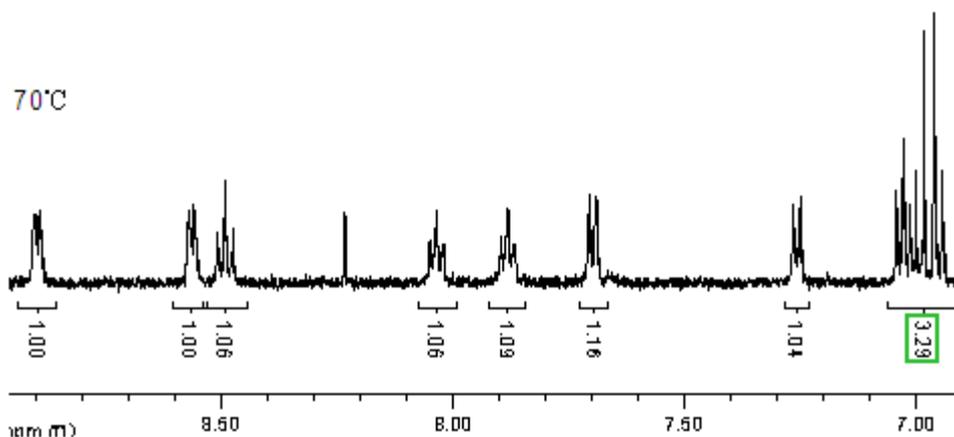
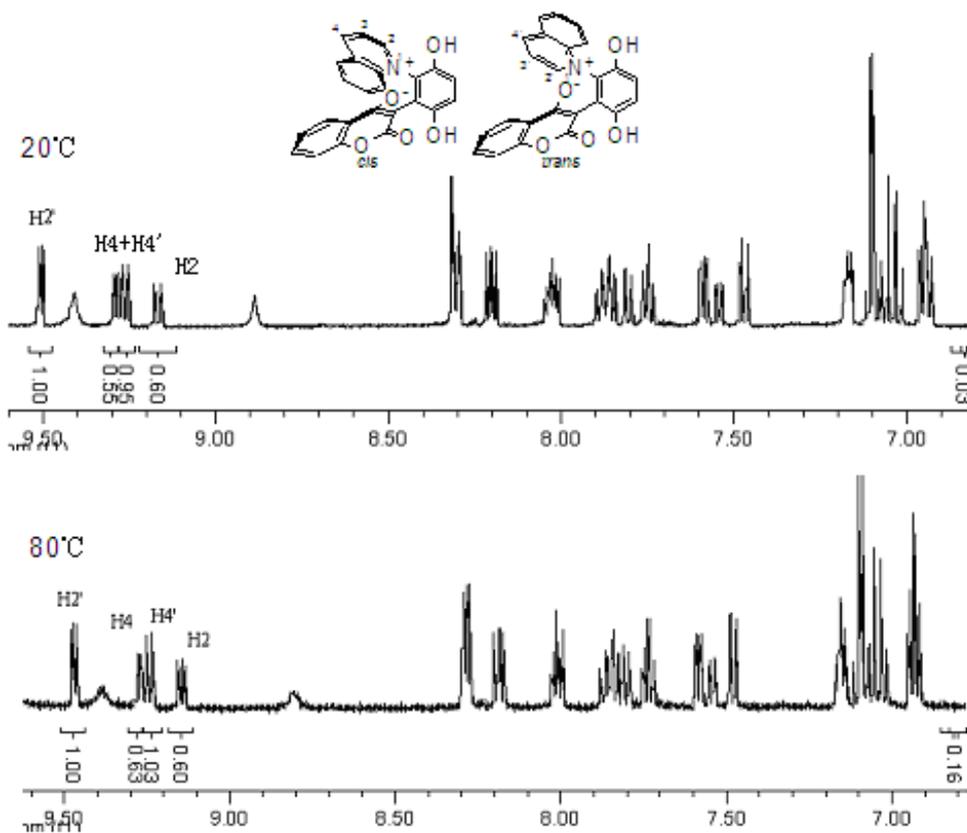
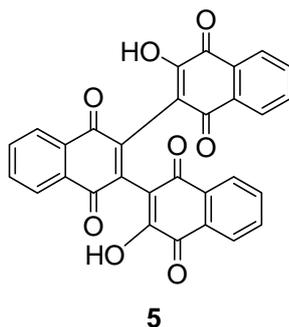
**Figure 4.** The  $^1\text{H-NMR}$  spectra of compound **2b** at 30 °C and 70 °C.

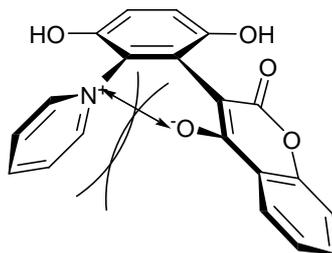
Figure 4. Cont.

Figure 5. The  $^1\text{H-NMR}$  spectra of compound **4a** at 30 °C and 80 °C.

Emadi *et al.* [15] have reported a trimeric compound **5** (Figure 6), with structural features similar to those of zwitterionic 4-hydroxycoumarin derivatives. In compound **5** the presence of conjugation between the naphthoquinone and the two (2-hydroxynaphthoquinone) subunits was suggested. This conjugation implied that the subunit could rotate along the bond joining the subunit to the quinone core and a rigid structure wasn't generated.

**Figure 6.** The structure of compound 5.

The face-to-face rigid backbone of the zwitterions was assumed to be caused by both the intramolecular ion pair attraction and the steric interaction (Figure 7). The ion pair attraction made the 4-hydroxycoumarin ring tilt toward the pyridine ring until the equilibration between the ion pair attraction and the steric interaction was reached and the rings could remain stable at a certain angle. Conversely, the tilted 4-hydroxycoumarin ring constrained the pyridine from rotating freely through steric interactions.

**Figure 7.** The intramolecular ion pair attraction and steric interaction of the zwitterion.

### 3. Experimental

#### 3.1. General

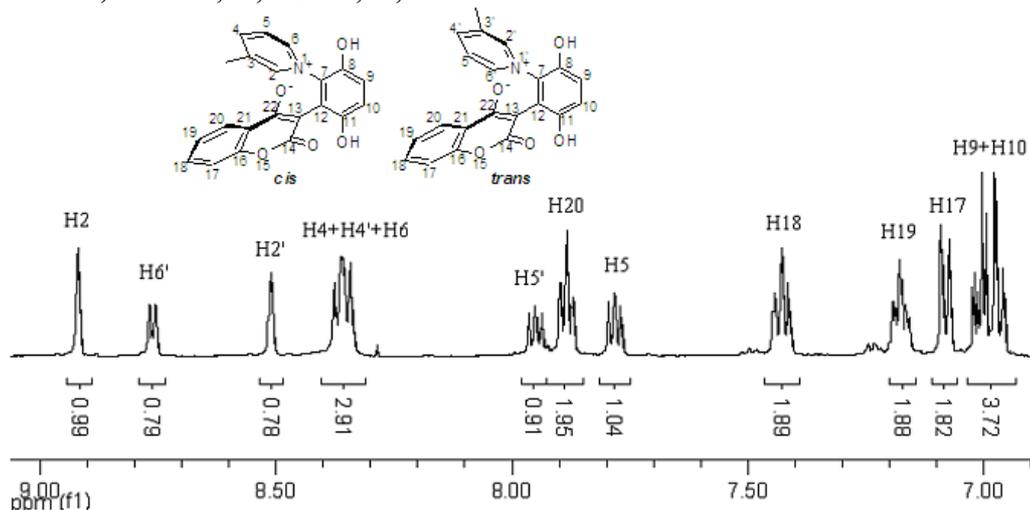
<sup>1</sup>H-NMR spectra were measured at room temperature (except for the temperature dependence studies) on a Varian UNITY INOVA 500 MHz spectrometer using TMS as an internal standard. For the electrospray (ESI) MS analysis, a Finnigan LCQ Deca XP ion trap mass spectrometer equipped with a Microsoft Windows NT data system and an ESI interface was used. Elementary analysis was recorded on an Elementar Vario EL elementary analysis device. IR spectra were recorded on a Bruker TENSOR 37 spectrophotometer.

#### 3.2. General procedure: synthesis of 4-hydroxycoumarin zwitterions

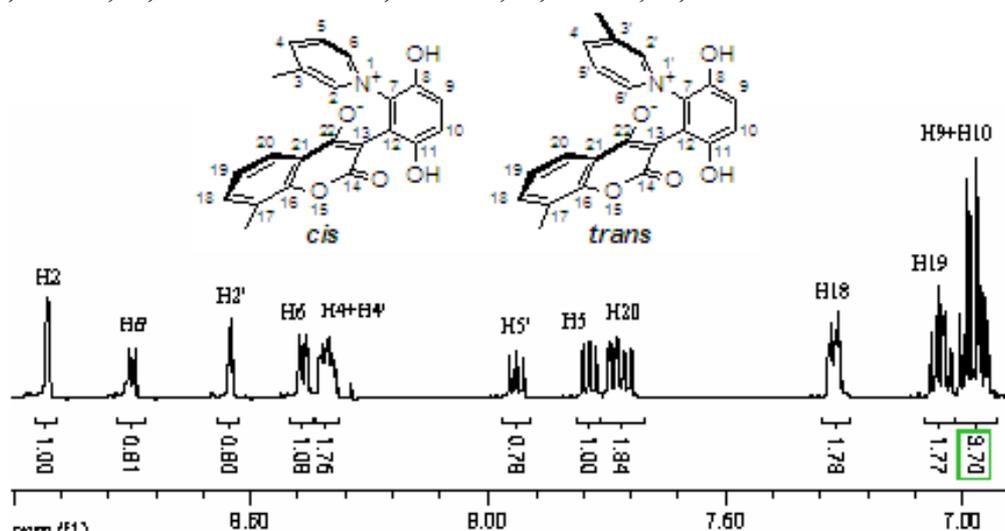
A mixture of 4-hydroxycoumarin (5 mmol), *p*-benzoquinone (1.08 g, 10 mmol) and the appropriate *N*-heterocyclic aromatic (10 mmol) was magnetically stirred in aqueous acetone (30 mL, v:v = 1:1) at room temperature for 24 h. The reaction mixture was filtered to afford a brown crude product which

was purified by column chromatography (silica gel, methanol-chloroform = 1:10) to give yellow compounds.

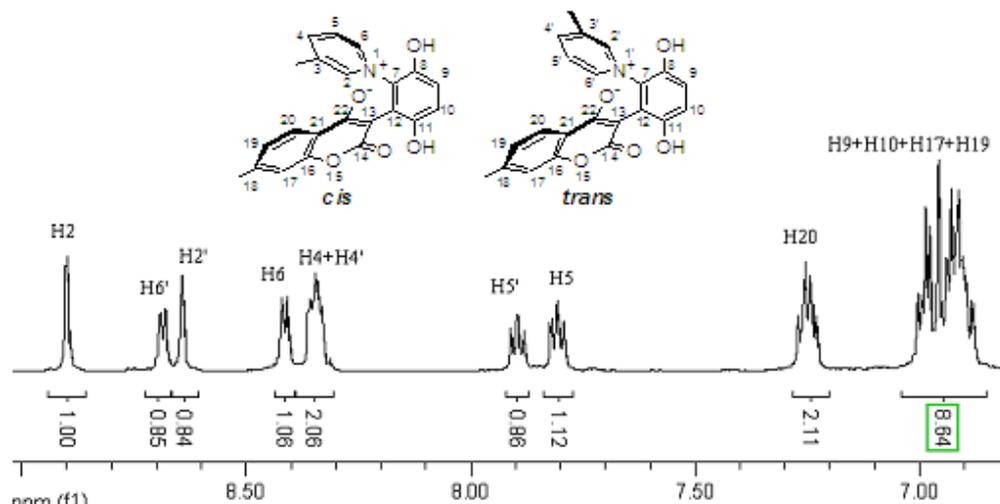
*Cis and trans 3-(3,6-Dihydroxy-2-(3-methylpyridinium-1-yl)phenyl)-2-oxo-2H-chromen-4-olate (3a and 3a')*: yield 39%; **3a:3a'** = 1.3:1;  $^1\text{H-NMR}$  (DMSO- $d_6$ )  $\delta$  2.25 (3H, s) ppm; IR: 3404, 3060, 1649, 1597, 1505, 1445  $\text{cm}^{-1}$ ; ESI-MS ( $m/e$ ): 360 (M-1) $^-$ ; Anal. Calcd. for  $\text{C}_{21}\text{H}_{15}\text{NO}_5$ : C, 69.80%; H, 4.18%; N, 3.88%. Found: C, 69.47%; H, 4.35%; N, 4.02%.



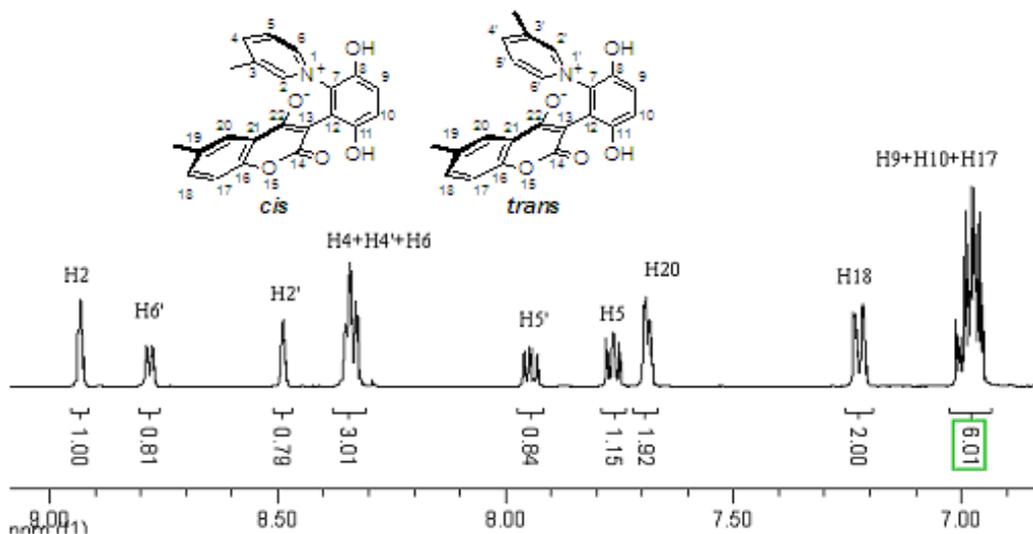
*Cis and trans 3-(3,6-dihydroxy-2-(3-methylpyridinium-1-yl)phenyl)-8-methyl-2-oxo-2H-chromen-4-olate (3b and 3b')*: yield 35%, **3b:3b'** = 1.3:1;  $^1\text{H-NMR}$  (DMSO- $d_6$ )  $\delta$  2.25 (3H, s), 2.21 (3H, s) ppm; IR: 3062, 1620, 1504, 1424, 1335, 1278  $\text{cm}^{-1}$ ; ESI-MS ( $m/e$ ): 374 (M-1) $^-$ ; Anal. Calcd. for  $\text{C}_{22}\text{H}_{17}\text{NO}_5$ : C, 70.39%; H, 4.56%; N, 3.73%. Found: C, 69.56%; H, 4.73%; N, 3.95%.



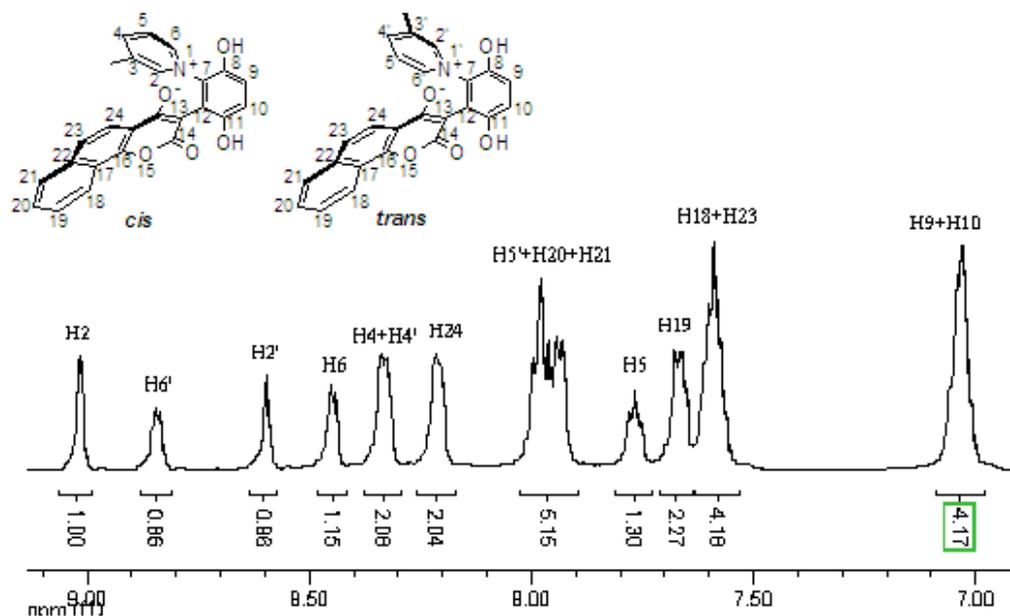
*Cis and trans 3-(3,6-dihydroxy-2-(3-methylpyridinium-1-yl)phenyl)-7-methyl-2-oxo-2H-chromen-4-olate (3c and 3c')*: yield 29%; **3c:3c'** = 1.2:1;  $^1\text{H-NMR}$  (DMSO- $d_6$ )  $\delta$  2.67 (3H, s), 2.29 (3H, s) ppm; IR: 2924, 1603, 1501, 1434, 1272  $\text{cm}^{-1}$ ; ESI-MS ( $m/e$ ): 374 (M-1) $^-$ ; Anal. Calcd. for  $\text{C}_{22}\text{H}_{17}\text{NO}_5$ : C, 70.39%; H, 4.56%; N, 3.73%. Found: C, 70.15%; H, 4.81%; N, 3.87%.



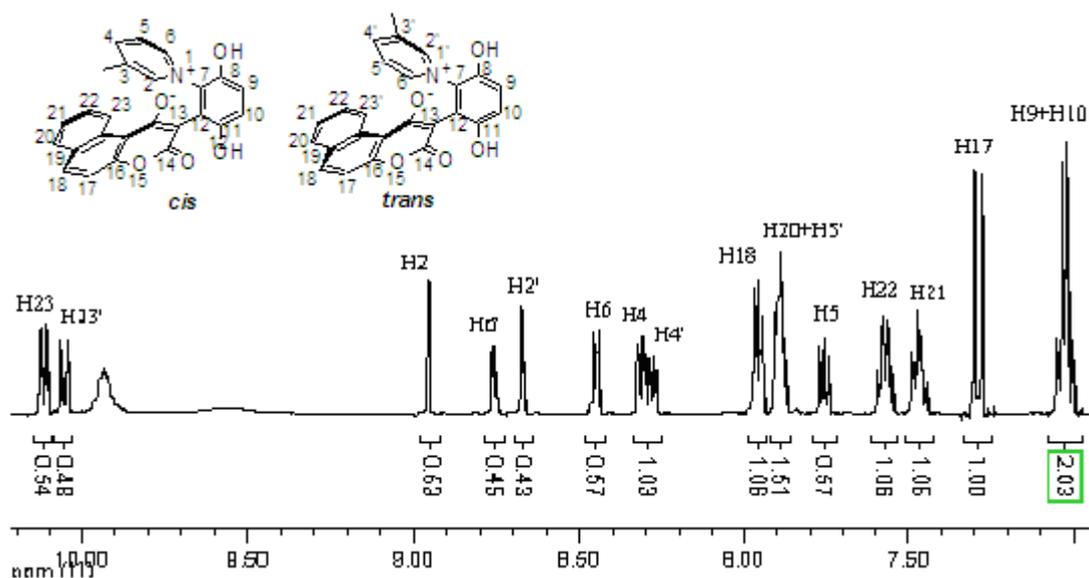
*Cis* and *trans* 3-(3,6-dihydroxy-2-(3-methylpyridinium-1-yl)phenyl)-6-methyl-2-oxo-2H-chromen-4-olate (**3d** and **3d'**): yield 42%; **3d**:**3d'** = 1.3:1;  $^1\text{H-NMR}$  (DMSO- $d_6$ )  $\delta$  2.32 (3H, s), 2.24 (3H, s) ppm; IR: 3394, 1641, 1504, 1512, 1270  $\text{cm}^{-1}$ ; ESI-MS ( $m/e$ ): 374 (M-1) $^-$ ; Anal. Calcd. for  $\text{C}_{22}\text{H}_{17}\text{NO}_5$ : C, 70.39%; H, 4.56%; N, 3.73%. Found: C, 70.22%; H, 4.63%; N, 3.81%.



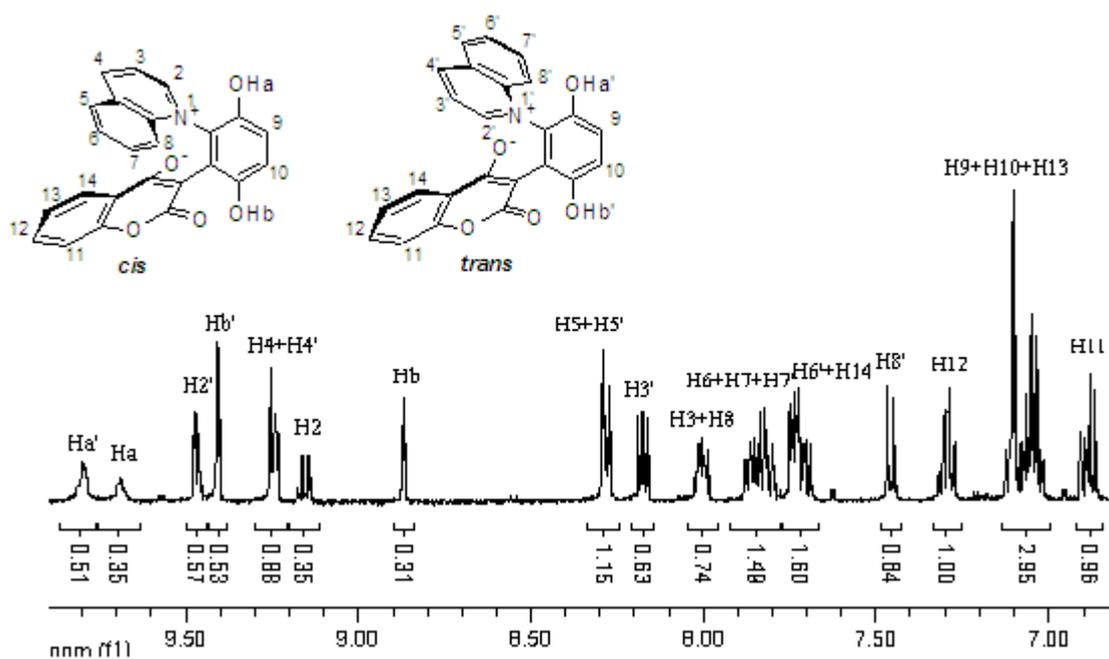
*Cis* and *trans* 3-(3,6-dihydroxy-2-(3-methylpyridinium-1-yl)phenyl)-2-oxo-2H-benzo[h]chromen-4-olate (**3e** and **3e'**): yield 37%; **3e**:**3e'** = 1.1:1;  $^1\text{H-NMR}$  (DMSO- $d_6$ )  $\delta$  2.22 (3H, s) ppm; IR: 3068, 1638, 1478, 1271  $\text{cm}^{-1}$ ; ESI-MS ( $m/e$ ): 410 (M-1) $^-$ ; Anal. Calcd. for  $\text{C}_{25}\text{H}_{17}\text{NO}_5$ : C, 72.99%; H, 4.16%; N, 3.40%. Found: C, 72.67%; H, 4.57%; N, 3.76%.



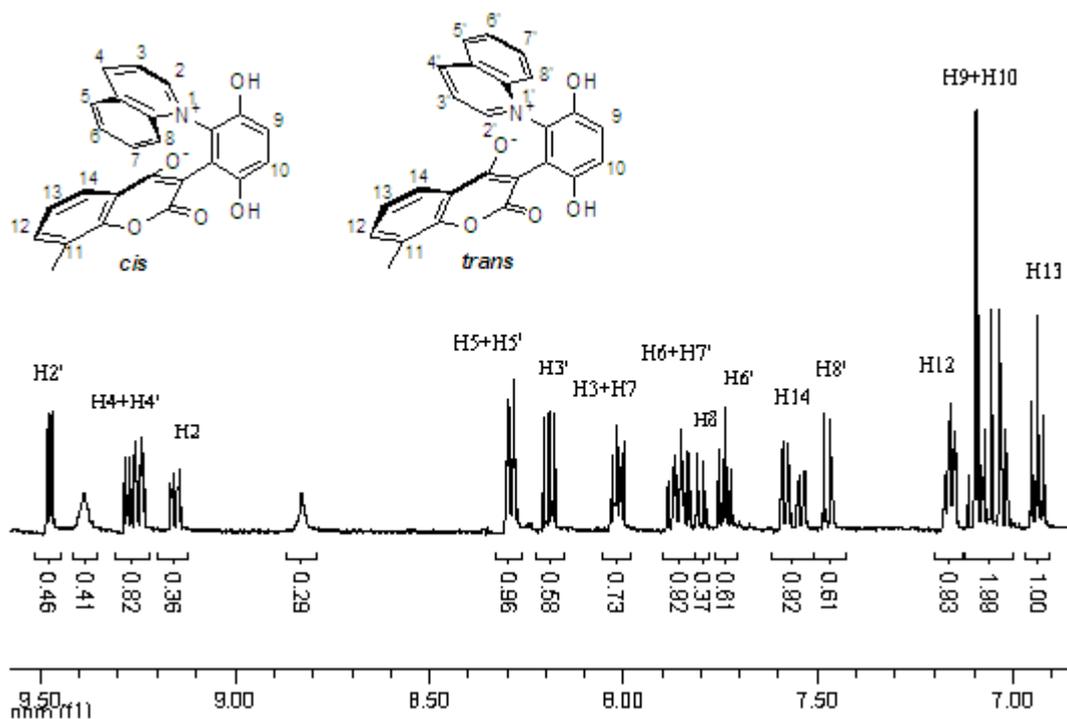
*Cis and trans 2-(3,6-dihydroxy-2-(3-methylpyridinium-1-yl)phenyl)-3-oxo-3H-benzo[f]chromen-1-olate (3f and 3f')*: yield 31%; **3f:3f'** = 1.1:1;  $^1\text{H-NMR}$  (DMSO- $d_6$ )  $\delta$  2.24 (3H, s) ppm; IR: 3059, 1632, 1507, 1266  $\text{cm}^{-1}$ ; ESI-MS ( $m/e$ ): 410 (M-1); Anal. Calcd for  $\text{C}_{25}\text{H}_{17}\text{NO}_5$ : C, 72.99%; H, 4.16%; N, 3.40%. Found: C, 72.63%; H, 4.51%; N, 3.69%.



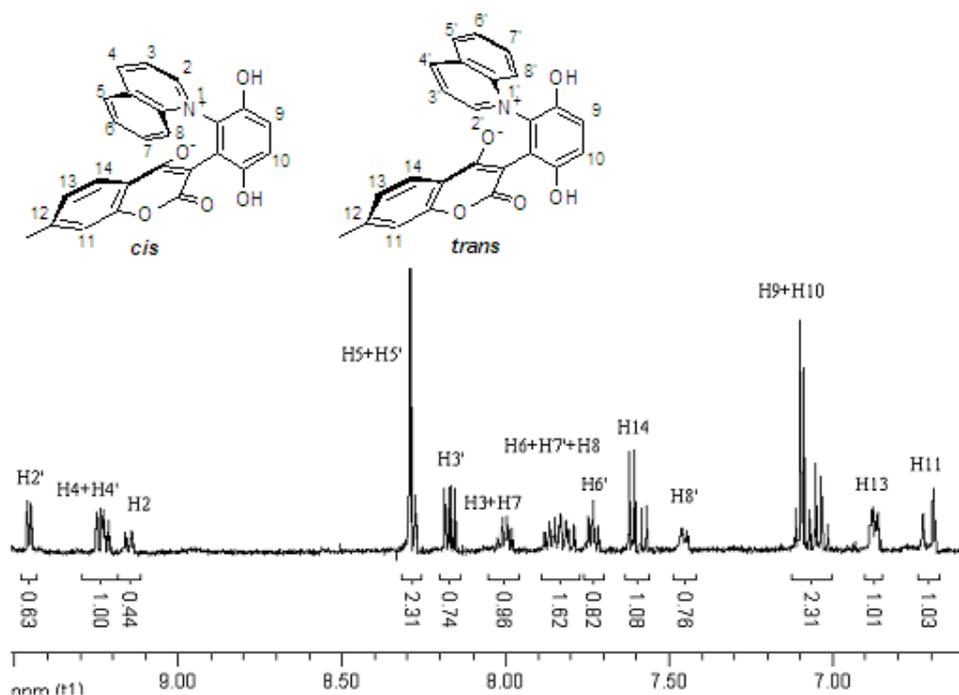
*Cis and trans 3-(3,6-dihydroxy-2-(quinolinium-1-yl)phenyl)-2-oxo-2H-chromen-4-olate (4a and 4a')*: yield 15%, **4a(cis):4a'(trans)** = 1:1.6; IR: 3093, 1639, 1513, 1274  $\text{cm}^{-1}$ ; ESI-MS ( $m/e$ ): 396 (M-1); Anal. Calcd for  $\text{C}_{24}\text{H}_{15}\text{NO}_5$ : C, 72.54%; H, 3.80%; N, 3.52%. Found: C, 72.55%; H, 3.91%; N, 3.65%.



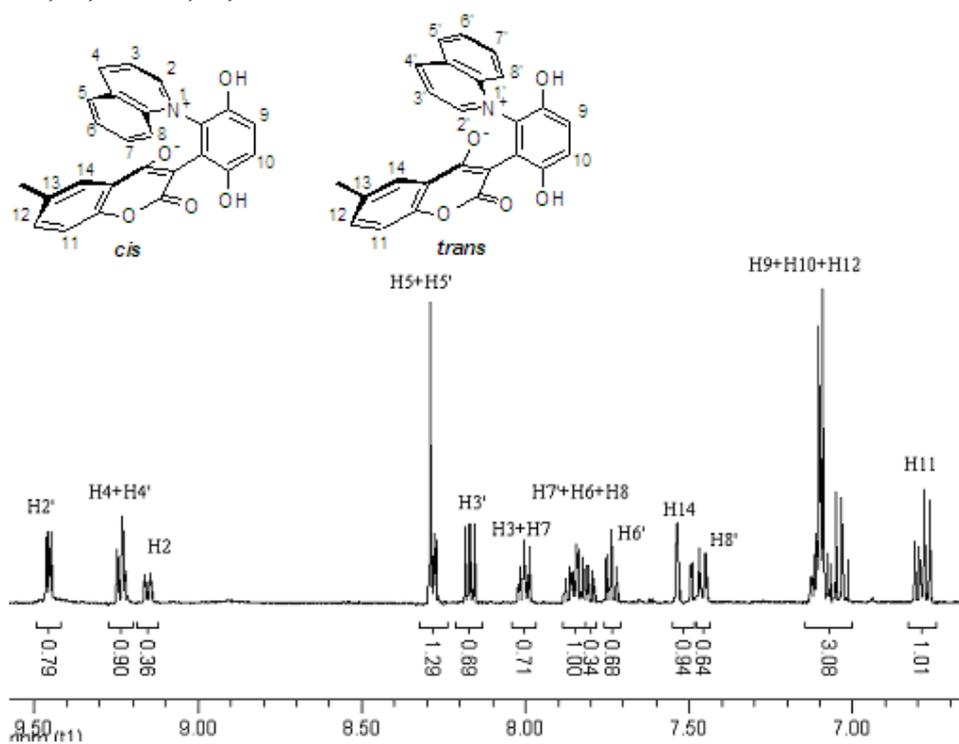
*Cis* and *trans* 3-(3,6-dihydroxy-2-(quinolinium-1-yl)phenyl)-8-methyl-2-oxo-2H-chromen-4-olate (**4b** and **4b'**): yield 12%; **4b**(*cis*):**4b'**(*trans*) = 1:1.3;  $^1\text{H-NMR}$  (DMSO- $d_6$ )  $\delta$  9.39 (0.56H, s), 8.83 (0.44H, br), 2.10 (3H, s) ppm; IR: 3391, 1635, 1516, 1274  $\text{cm}^{-1}$ ; ESI-MS ( $m/e$ ): 410 (M-1) $^-$ ; Anal. Calcd for  $\text{C}_{25}\text{H}_{17}\text{NO}_5$ : C, 72.99%; H, 4.16%; N, 3.40%. Found: C, 72.74%; H, 4.32%; N, 3.55%.



*Cis* and *trans* 3-(3,6-dihydroxy-2-(quinolinium-1-yl)phenyl)-7-methyl-2-oxo-2H-chromen-4-olate (**4c** and **4c'**): yield 9%; **4c**(*cis*):**4c'**(*trans*) = 1:1.4;  $^1\text{H-NMR}$  (DMSO- $d_6$ )  $\delta$  2.24 (3H, s) ppm; IR: 3432, 1605, 1508  $\text{cm}^{-1}$ ; ESI-MS ( $m/e$ ): 410 (M-1) $^-$ ; Anal. Calcd. for  $\text{C}_{25}\text{H}_{17}\text{NO}_5$ : C, 72.99%; H, 4.16%; N, 3.40%. Found: C, 72.77%; H, 4.33%; N, 3.46%.

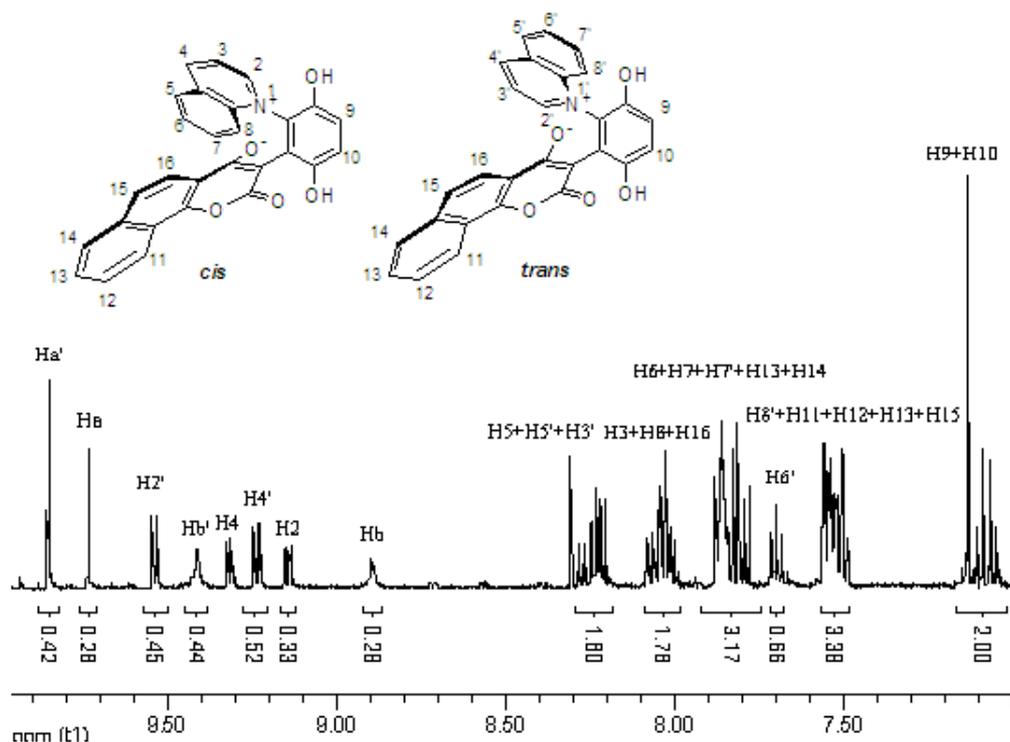


*Cis and trans 3-(3,6-dihydroxy-2-(quinolinium-1-yl)phenyl)-6-methyl-2-oxo-2H-chromen-4-olate (4d and 4d')*: yield 16%, **4d:4d'** = 1:1.7,  $^1\text{H-NMR}$  ( $\text{DMSO-}d_6$ )  $\delta$  2.25 (3H, s) ppm; IR: 3366, 1641, 1512, 1277  $\text{cm}^{-1}$ ; ESI-MS ( $m/e$ ): 410 (M-1) $^-$ ; Anal. Calcd. for  $\text{C}_{25}\text{H}_{17}\text{NO}_5$ : C, 72.99%; H, 4.16%; N, 3.40%. Found: C, 72.83%; H, 4.26%; N, 3.43%.

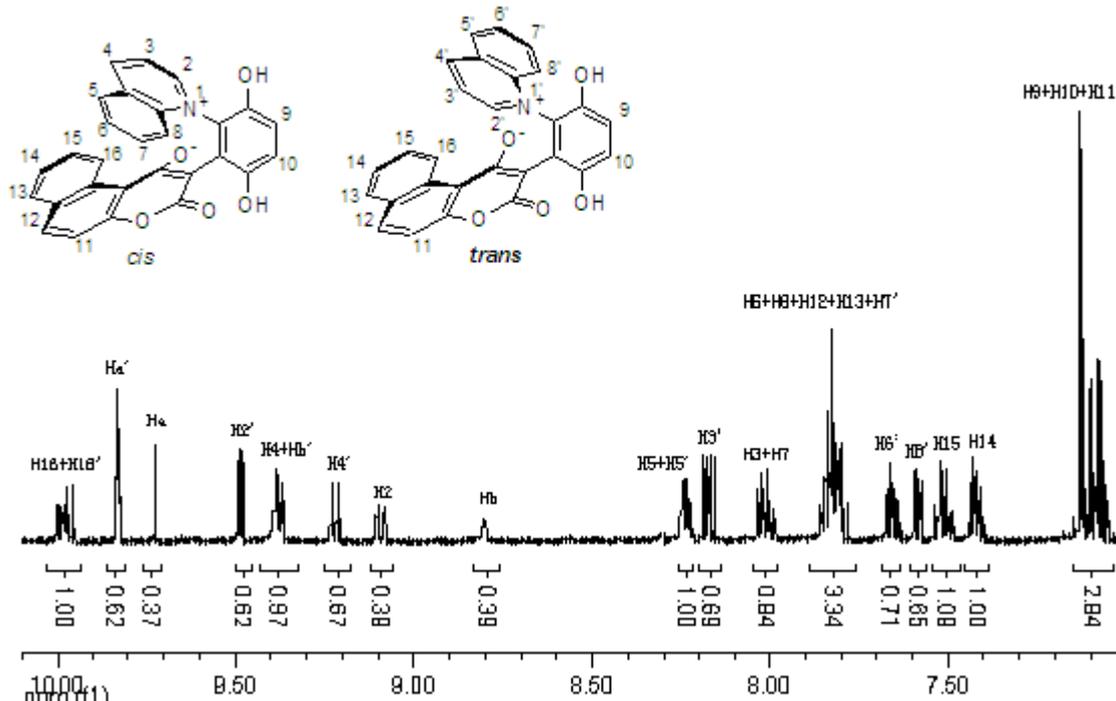


*Cis and trans 3-(3,6-dihydroxy-2-(quinolinium-1-yl)phenyl)-2-oxo-2H-benzo[h]chromen-4-olate (4e and 4e')*: yield 13%; **4e:4e'** = 1.3:1; IR: 3090, 1638, 1578, 1524, 1272  $\text{cm}^{-1}$ ; ESI-MS ( $m/e$ ): 410 (M-1) $^-$ ;

Anal. Calcd. for  $C_{28}H_{17}NO_5$ : C, 75.16%; H, 3.83%; N, 3.13%. Found: C, 75.06%; H, 3.93%; N, 3.28%.



*Cis* and *trans* 2-(3,6-dihydroxy-2-(quinolinium-1-yl)phenyl)-3-oxo-3H-benzo[f]chromen-1-olate (**4f** and **4f'**): yield 12%, **4f**:**4f'** = 1:1.5; IR: 3094, 1629, 1512, 1270  $cm^{-1}$ ; ESI-MS ( $m/e$ ): 410 ( $M-1$ ); Anal. Calcd for  $C_{28}H_{17}NO_5$ : C, 75.16%; H, 3.83%; N, 3.13%. Found: C, 75.31%; H, 3.98%; N, 3.24%.



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## References and Notes

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*Sample Availability:* Samples of the compounds are available from the authors.

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