

Ambident Chemosensors Based on Benzo[*h*]chromen-2-one

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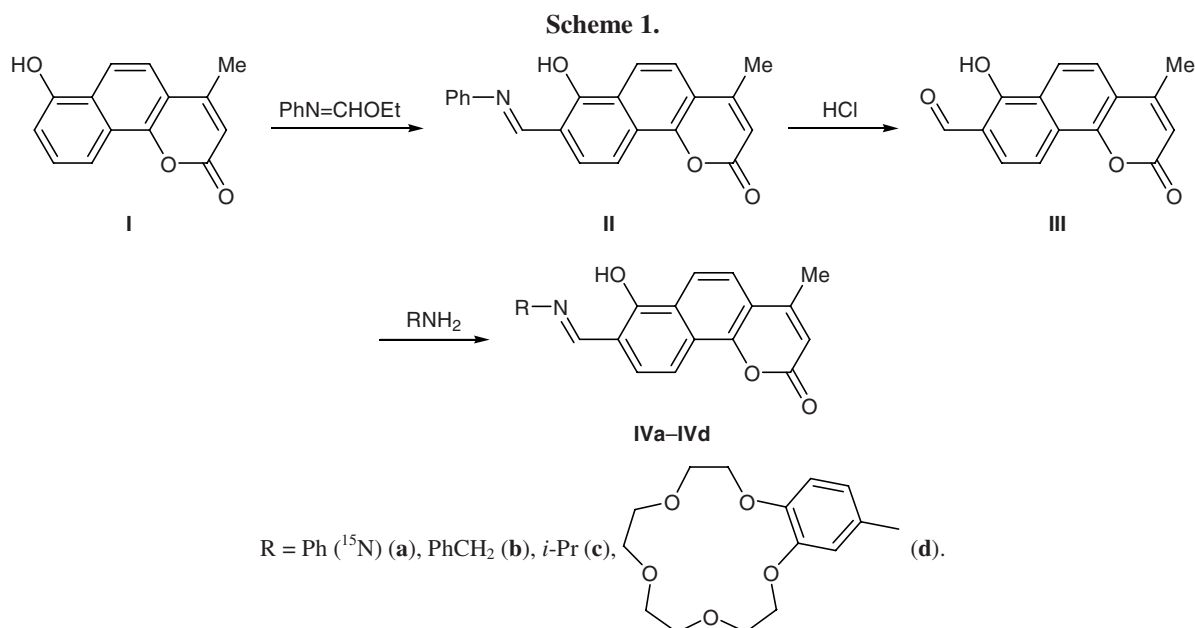
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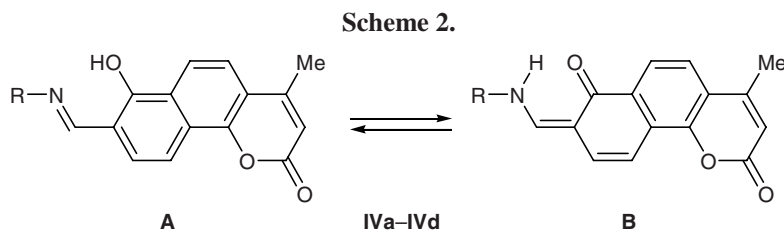
Abstract—Schiff bases derived from 7-hydroxy-4-methyl-2-oxobenzo[*h*]chromene-8-carbaldehyde in solution exist as equilibrium mixtures of benzoid and quinoid tautomers. The fraction of the quinoid tautomer increases with rise in solvent polarity. The Schiff base containing a benzo-15-crown-5 fragment on the nitrogen atom was shown to be a new ambident chemosensor capable of selectively binding transition metal cations via reaction at the *o*-hydroxyaldehyde imine fragment and alkaline-earth metals via host–guest interaction with the crown ether moiety. This compound exhibits a pronounced sensor activity toward Mg²⁺ and Ba²⁺ ions and is a selective naked-eye fluorescent chemosensor for Cu²⁺ and Co²⁺ ions.

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Chemosensors are abiotic systems including a receptor fragment which is capable of selectively interacting with a substrate, a signaling fragment, and a linker connecting them [1–3]. If a fluorescent signaling fragment is present, bridging moiety may be lacking, and sensor properties originate as a rule from the CHEQ effect (Chelation Enhanced Fluorescence Quenching) [4]. Most frequently, crown ether [5–7]

and *o*-hydroxyaldehyde imine [8, 9] receptors are used. However, only a few data are available on compounds having both these fragments in a single molecule [10–13], while their combination with a fluorophoric heterocyclic signaling system is almost unknown. With a view to obtain ambident CHEQ chemosensors capable of selectively interacting with both alkaline-earth and transition metals, in the present work we made





an attempt to synthesize benzo[*h*]chromen-2-one derivatives containing an *o*-hydroxyaldehyde moiety in the naphthalene fragment. This work continues our studies on the design of *ortho*- and *peri*-fused heterocyclic systems on the basis of naphthalene-1,5-diol [14].

The reaction of previously reported 7-hydroxy-4-methylbenzo[*h*]chromen-2-one (**I**) [15] with ethyl *N*-phenylformimidate turned out to be the most successful for the introduction of an aldehyde functionality into the *ortho* position with respect to the hydroxy group. We thus obtained Schiff base **II** in 83% yield, and acid hydrolysis of **II** smoothly afforded aldehyde **III**. Condensation of **III** with primary amines gave the corresponding Schiff bases **IVa-IVd** (Scheme 1).

In the ^1H NMR spectrum of *o*-hydroxyaldehyde **III**, signals from protons in the formyl and hydroxy groups appeared as sharp singlets at 10.1 and 12.6 ppm. Therefore, we presumed that compound **III** in CDCl_3 at room temperature exists exclusively in the hydroxyaldehyde form. Schiff bases **IVa-IVd** in solution give rise to equilibrium between the benzoid (**A**) and quinoid (**B**) tautomers that absorb at λ 420 and 490 nm, respectively [16–18] (Scheme 2). The fraction of the quinoid form decreases as the solvent polarity rises (Fig. 1). The effect of the substituent on the nitrogen atom changes depending on the solvent nature. In non-polar solvents, the fraction of the quinoid tautomer increases in the series $\text{Ph} < \text{PhCH}_2 < \text{Me}_2\text{CH}$, whereas the reverse order is observed in polar solvents (e.g., in DMSO).

The NH and CH protons in crown ether-containing derivative **IVd** resonate in the ^1H NMR spectrum as broadened singlets, indicating fast proton exchange [19]. ^{15}N -Labeled Schiff base **IVa** in dimethyl sulfoxide characteristically displayed splitting of the labile proton due to coupling with ^{15}N ($J = 50.1$ Hz), which corresponded to an **A/B** ratio of 44:56 [20, 21]. On the basis of the electronic absorption and ^1H NMR spectra we calculated the molar absorption coefficient for the quinoid tautomer ($\epsilon_{\text{B}} = 2.63 \times 10^4 \text{ l mol}^{-1} \text{ cm}^{-1}$) and parameters of tautomeric equilibria for Schiff bases **IVa-IVd** assuming that the coefficient ϵ_{B} weakly depends on the solvent and substituent nature (see table) [17].

Reactions of crown ether derivative **IVd** with alkali and alkaline-earth metal cations are accompanied by considerable displacement of tautomeric equilibrium toward benzoid complexes **V** (Scheme 3), as was reported previously for Schiff bases of the benzofuran series [22, 23]. The intensity of the absorption maximum at λ 480 nm (corresponding to the quinoid tautomer) in the electronic spectra decreases by ~15% for alkali metals and 25% for alkaline-earth metals. Addition of a transition metal acetate to a solution of **IVd** in dimethyl sulfoxide induces a blue shift of the long-wave absorption maximum ($\Delta\lambda \approx 10\text{--}30$ nm) as a result of formation of chelates **VI** (Scheme 3) [24].

Crown ether-containing Schiff base **IVd** showed a high sensitivity for copper(II) and cobalt(II) ions. Acetonitrile and dimethyl sulfoxide solutions of **IVd** exhibit strong fluorescence with its maximum at λ 530 nm upon excitation at λ_{excit} 480 nm. Addition of

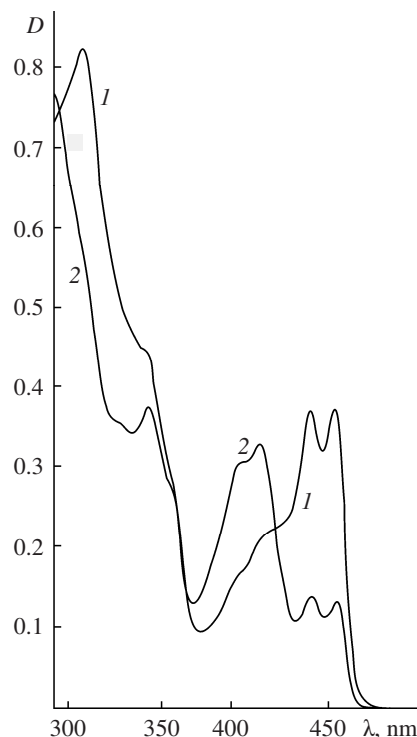


Fig. 1. Electronic absorption spectra of Schiff base **IVa** in (1) DMSO and (2) toluene; $c = 2.5 \times 10^{-5}$ M.

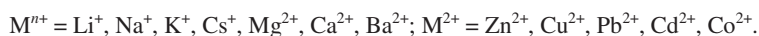
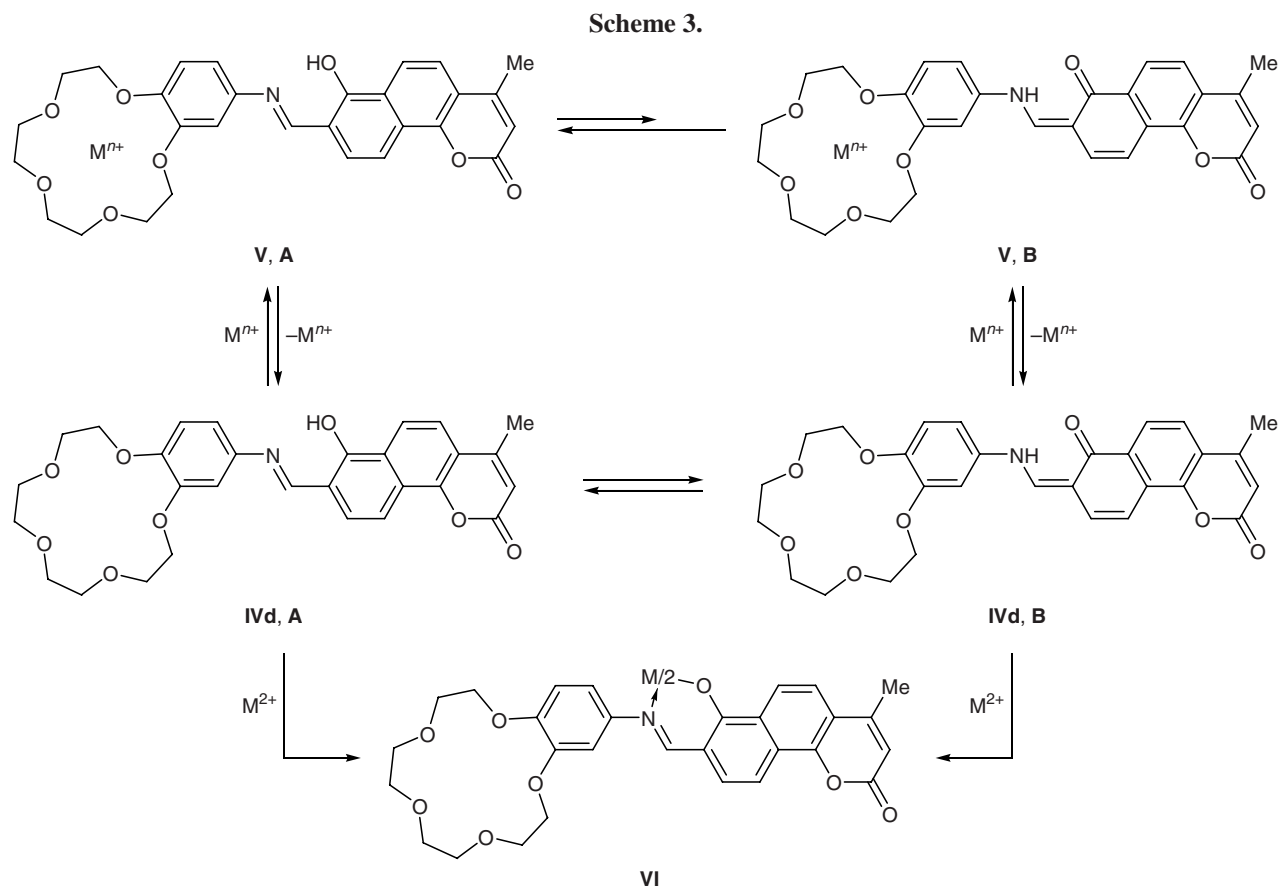
Spectral parameters of Schiff bases **IVa–IVd** and parameters of the tautomeric equilibrium **A** \rightleftharpoons **B**

Compound no.	Solvent	Electronic absorption spectrum, λ_{\max} , nm ($\epsilon \times 10^{-4}$, $l \text{ mol}^{-1} \text{ cm}^{-1}$)	Fraction of tautomer B , %	K^0 ($[\mathbf{B}]/[\mathbf{A}]$)	ΔG_{293}^0 , kJ/mol
IVa	Toluene	342 (1.52), 425 (1.33), 477 (0.56), 510 (0.54)	19.8	0.247	3.4
	DMSO	307 (3.28), 477 (1.48), 508 (1.52)	56.3	1.288	-0.6
IVb	Toluene	390 (0.68), 412 (0.80), 453 (0.60), 476 (0.60)	22.8	0.295	3.0
	DMSO	299 (4.48), 453 (1.32), 476 (1.32)	50.2	1.008	-0.02
IVc	Toluene	298 (2.96), 390 (0.64), 412 (0.76), 453 (0.80), 478 (0.80)	30.4	0.437	2.0
	DMSO	298 (4.20), 450 (1.20), 475 (1.20)	45.6	0.838	0.4
IVd	Toluene	357 (1.20), 425 (1.88), 483 (0.56), 514 (0.54)	19.8	0.247	3.4
	DMSO	450 (1.10), 480 (1.20), 510 (0.88)	33.5	0.504	1.7

copper(II) or cobalt(II) acetate leads to a pronounced CHEQ effect: the fluorescence intensity decreases by a factor of 39 and 33, respectively, without appreciable shift of the emission maximum (Fig. 2). The change in the emission intensity is readily detected visually, so that Schiff base **IVd** may be used as naked-eye sensor for qualitative express analysis of Cu(II) and Co(II) ions in solution. Reactions of **IVd** with alkali and alkaline-earth metal cations are accompanied

by considerably weaker variations in the fluorescence intensity. Addition of magnesium or barium perchlorate to a solution of chemosensor **IVd** in acetonitrile induces fluorescence quenching by a factor of 3.4 or 2.9, respectively (Fig. 3). Nevertheless, this effect is sufficient to detect Mg^{2+} and Ba^{2+} ions in solution.

Thus we have synthesized a novel ambident fluorescent chemosensor capable of selectively binding different metal ions, transition metal cations (due to



the presence of *o*-hydroxyaldehyde imine fragment), and alkaline-earth metal ions (due to crown ether receptor). Crown ether-containing Schiff base **IVd** is characterized by pronounced sensitivity for Mg²⁺ and Ba²⁺ ions and is an efficient selective naked-eye fluorescent chemosensor for Cu²⁺ and Co²⁺ ions.

EXPERIMENTAL

The ¹H NMR spectra were recorded on a Varian Unity-300 spectrometer at 300 MHz using the residual solvent signal as reference (CHCl₃, δ 7.25 ppm; DMSO, δ 2.50 ppm). The electronic absorption spectra were measured on a Specord M-40 spectrophotometer, and the luminescence spectra, on a Hitachi 650-60 spectrofluorimeter. The IR spectra were obtained on a Specord 75IR instrument from samples dispersed in mineral oil.

7-Hydroxy-4-methyl-8-(phenyliminomethyl)-benzo[*h*]chromen-2-one (II). A mixture of 0.45 g (2 mmol) of 7-hydroxy-4-methylbenzo[*h*]chromen-2-one [15] and 0.6 ml of ethyl *N*-phenylformimidate in 5–7 ml of *o*-dichlorobenzene was heated for 2 h under reflux. The mixture was cooled, and the yellow–orange precipitate (0.45 g) was filtered off and washed with petroleum ether. The filtrate was diluted with petroleum ether to isolate an additional portion (0.1 g) of the product. Overall yield 0.55 g (83%), mp 266–267°C (from DMF). IR spectrum, ν, cm⁻¹: 3447, 1714, 1640, 1620. ¹H NMR spectrum (CDCl₃), δ, ppm: 2.61 s (3H, 4-CH₃), 6.42 s (1H, 3-H), 7.28–7.52 m (6H, H_{arom}), 7.64 d (1H, 10-H, *J*_{9,10} = 8.7 Hz), 7.80 d (1H, 5-H, *J*_{5,6} = 8.9 Hz), 8.36 d (1H, 9-H, *J*_{9,10} = 8.7 Hz), 8.58 d (1H, N=CH, *J*_{CH,NH} = 5.3 Hz), 15.20 br.s (1H, N···H···O). Found, %: C 76.77; H 4.34; N 4.57. C₂₁H₁₅NO₃. Calculated, %: C 76.59; H 4.55; N 4.25.

7-Hydroxy-4-methyl-2-oxobenzo[*h*]chromene-8-carbaldehyde (III). Dilute hydrochloric acid (1:1), 3–5 ml, was added to 0.3 g (0.9 mmol) of Schiff base **II** in 50 ml of dioxane, and the mixture was heated for 30 min on a boiling water bath. The mixture was cooled and diluted with water, and the precipitate was filtered off. Yield 0.23 g (76%), mp 290–292°C (decomp.; from DMF). IR spectrum, ν, cm⁻¹: 3100, 1700, 1680, 1630, 1600. ¹H NMR spectrum (CDCl₃), δ, ppm: 2.61 s (3H, 4-CH₃), 6.50 s (1H, 3-H), 7.72 d (2H, 6-H, 10-H, *J*_{5,6} = *J*_{9,10} = 8.9 Hz), 8.11 d (1H, 5-H, *J*_{5,6} = 8.9 Hz), 8.31 d (1H, 9-H, *J*_{9,10} = 8.9 Hz), 10.10 s (1H, CHO), 12.60 s (1H, OH). Found, %: C 70.57; H 4.27. C₁₅H₁₀O₄. Calculated, %: C 70.86; H 3.93.

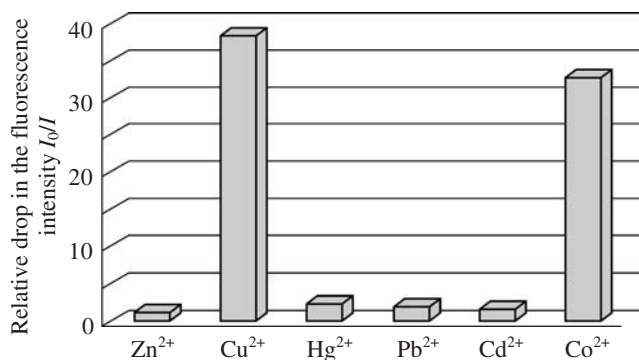


Fig. 2. Relative changes in the fluorescence intensity of Schiff base **IVd** in DMSO ($c = 2.5 \times 10^{-5}$ M) upon addition of transition metal ions ($c = 2.5 \times 10^{-4}$ M).

7-Hydroxy-4-methyl-8-[phenyl(¹⁵N)iminomethyl]benzo[*h*]chromen-2-one (IVa). A mixture of 0.1 g (0.4 mmol) of *o*-hydroxyaldehyde **III** and 0.04 ml (0.4 mmol) of (¹⁵N)aniline in 5 ml of dioxane was heated for 30 min under reflux. The precipitate was filtered off, recrystallized from dimethylformamide, washed with alcohol, and dried in air. Yield 0.065 g (50%), mp 265–267°C. IR spectrum, ν, cm⁻¹: 3390, 1714, 1620, 1590. ¹H NMR spectrum, δ, ppm: in CDCl₃: 2.58 s (3H, 4-CH₃), 6.42 s (1H, 3-H), 7.28–7.52 m (6H, H_{arom}), 7.63 d (1H, 10-H, *J*_{9,10} = 8.7 Hz), 7.80 d (1H, 5-H, *J*_{5,6} = 9.0 Hz), 8.35 d (1H, 9-H, *J*_{9,10} = 8.7 Hz), 8.57 d (1H, ¹⁵N=CH, *J*_{CH,NH} = 1.7 Hz), 15.20 br.s (1H, ¹⁵N···H···O); in DMSO-*d*₆: 2.56 s (3H, 4-CH₃), 6.55 s (1H, 3-H), 7.27–7.64 m (6H, H_{arom}), 7.78 d (1H, 10-H, *J*_{9,10} = 8.6 Hz), 8.24 d (1H, 9-H, *J*_{9,10} = 8.6 Hz), 9.10 d (1H, ¹⁵N=CH, *J*_{CH,NH} = 6.9 Hz), 15.21 d (1H, ¹⁵N···H···O, ¹*J*_{NH} = 50.1 Hz). Found, %: C 76.67; H 4.34; N 4.57. C₂₁H₁₅NO₃. Calculated, %: C 76.36; H 4.54; N 4.54.

8-Benzyliminomethyl-7-hydroxy-4-methylbenzo[*h*]chromen-2-one (IVb). A mixture of 0.1 g (0.4 mmol) of *o*-hydroxyaldehyde **III**, 3 ml of dioxane,

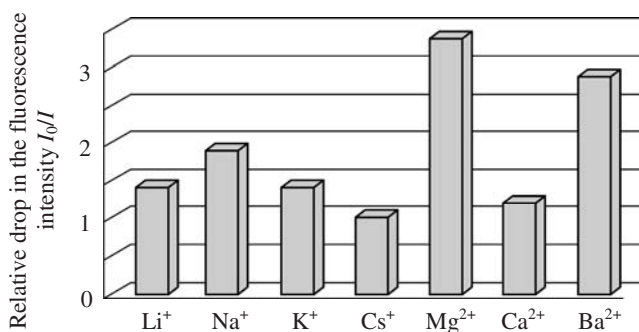


Fig. 3. Relative changes in the fluorescence intensity of Schiff base **IVd** in acetonitrile ($c = 2.5 \times 10^{-5}$ M) upon addition of alkali and alkaline-earth metal ions ($c = 2.5 \times 10^{-4}$ M).

and 3 ml of acetonitrile was heated to the boiling point. The hot solution was filtered from the undissolved material, 0.04 ml (~0.4 mmol) of benzylamine was added to the filtrate, and the mixture was heated under reflux until a solid began to separate (~10 min). The mixture was cooled, and the precipitate, 0.08 g (~60%), was filtered off and purified by column chromatography on Silokhrom using chloroform as eluent. Yield 0.065 g (48%), mp 216–217°C. IR spectrum, ν , cm^{-1} : 3420, 1727, 1633, 1620. ^1H NMR spectrum (DMSO- d_6), δ , ppm: 2.49 s (3H, 4- CH_3), 4.84 s (2H, NCH_2), 6.53 s (1H, 3-H), 7.16 d (1H, 6-H, $J_{5,6} = 9.0$ Hz), 7.30 d (1H, 5-H, $J_{5,6} = 9.0$ Hz), 7.32–7.46 m (5H, H_{arom}), 7.66 d (1H, 10-H, $J_{9,10} = 8.6$ Hz), 8.18 d (1H, 9-H, $J_{9,10} = 8.6$ Hz), 8.54 d (1H, $\text{N}=\text{CH}$, $J_{\text{CH,NH}} = 6.5$ Hz), 13.57 br.s (1H, $\text{N}\cdots\text{H}\cdots\text{O}$). Found, %: C 76.65; H 5.34; N 4.44. $\text{C}_{22}\text{H}_{17}\text{NO}_3$. Calculated, %: C 76.97; H 4.96; N 4.08.

7-Hydroxy-8-isopropyliminomethyl-4-methylbenzo[h]chromen-2-one (IVc). A mixture of 0.06 g (0.2 mmol) of *o*-hydroxyaldehyde **III** and 0.02 ml (0.2 mmol) of isopropylamine in 10 ml of alcohol was heated for 10 min under reflux. The mixture was cooled and diluted with water, the precipitate (0.04 g) was filtered off, and most part of the filtrate was evaporated to isolate an additional portion (0.02 g) of the product. The fractions were combined and purified by chromatography on aluminum oxide using chloroform as eluent. Yield 0.05 g (50%), mp 207–208°C. IR spectrum, ν , cm^{-1} : 3434, 1727, 1640, 1607. ^1H NMR spectrum (DMSO- d_6), δ , ppm: 1.33 d [6H, $\text{CH}(\text{CH}_3)_2$, $J = 4.0$ Hz], 2.47 s (3H, 4- CH_3), 3.90 m [1H, $\text{CH}(\text{CH}_3)_2$, $J = 4.0$ Hz], 6.51 s (1H, 3-H), 7.12 d (1H, 6-H, $J_{5,6} = 9.0$ Hz), 7.30 d (1H, 5-H, $J_{5,6} = 9.0$ Hz), 7.67 d (1H, 10-H, $J_{9,10} = 8.7$ Hz), 8.20 d (1H, 9-H, $J_{9,10} = 8.7$ Hz), 8.46 d (1H, $\text{N}=\text{CH}$, $J_{\text{CH,NH}} = 6.5$ Hz), 13.50 br.s (1H, $\text{N}\cdots\text{H}\cdots\text{O}$). Found, %: C 73.57; H 5.55; N 4.49. $\text{C}_{18}\text{H}_{17}\text{NO}_3$. Calculated, %: C 73.22; H 5.76; N 4.75.

7-Hydroxy-8-[3,4-(3,6,9-trioxaundecane-1,11-dioxy)phenyliminomethyl]-4-methylbenzo[h]chromen-2-one (IVd). A solution of 0.025 g (1 mmol) of *o*-hydroxyaldehyde **III** and 0.028 g (1 mmol) of 4-aminobenzo-15-crown-5 in 10 ml of dioxane was heated for 30 min. The precipitate was filtered off, recrystallized from dimethylformamide, washed with alcohol, and dried in air. Yield 0.033 g (63%), mp 242–243°C. IR spectrum, ν , cm^{-1} : 3450, 1700, 1620, 1560, 1500. ^1H NMR spectrum (CDCl_3), δ , ppm: 2.57 s (3H, CH_3), 3.70–4.24 m (16H, CH_2O), 6.41 s (1H, 3-H),

6.83–6.98 m (3H, H_{arom}), 7.40 d (1H, 6-H, $J_{5,6} = 8.9$ Hz), 7.61 d (1H, 5-H, $J_{5,6} = 8.9$ Hz), 7.81 d (1H, 10-H, $J_{9,10} = 8.9$ Hz), 8.33 d (1H, 9-H, $J_{9,10} = 8.9$ Hz), 8.55 s (1H, $=\text{CH}$), 15.27 br.s (1H, OH). Found, %: C 66.70; H 6.07; N 2.58. $\text{C}_{29}\text{H}_{31}\text{NO}_8$. Calculated, %: C 66.78; H 5.99; N 2.69.

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