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Dedicated to Full Member of the Russian Academy of Sciences I.P. Beletskaya on her jubilee

Benzoid–Quinoid Tautomerism of Schiff Bases and Their Structural Analogs: LV.* Crown-Containing *N*-Phenylimines Derived from *ortho*-Hydroxycarbaldehydes of the Coumarin Series

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Abstract—Schiff bases were synthesized from 3-hydroxy-6-oxo-6*H*-benzo[*c*]chromene-4-carbaldehyde, 5-hydroxy-4,7-dimethyl-2-oxo-2*H*-chromene-6-carbaldehyde, 6,7-dihydroxy-4-methyl-2-oxo-2*H*-chromene-8-carbaldehyde, 5,7-dihydroxy-4-methyl-2-oxo-2*H*-chromene-6,8-dicarbaldehyde, and 5-hydroxy-4,7-dimethyl-2-oxo-2*H*-chromene-6,8-dicarbaldehyde and (^{15}N)aniline or aminobenzo-15-crown-5 (2,3,5,6,8,9,11,12-octahydrobenzo[*b*][1,4,7,10,13]pentaoxacyclopentadecin-15-amine), and tautomeric equilibrium between the hydroxy enimino and keto enamino forms of the 4- and 8-iminomethyl derivatives in solution was revealed by ^{1}H NMR and electronic spectroscopy. Addition of alkaline earth cations to their solutions in acetonitrile displaced the tautomeric equilibrium toward the hydroxy enimino structure due to complex formation with the crown ether fragment.

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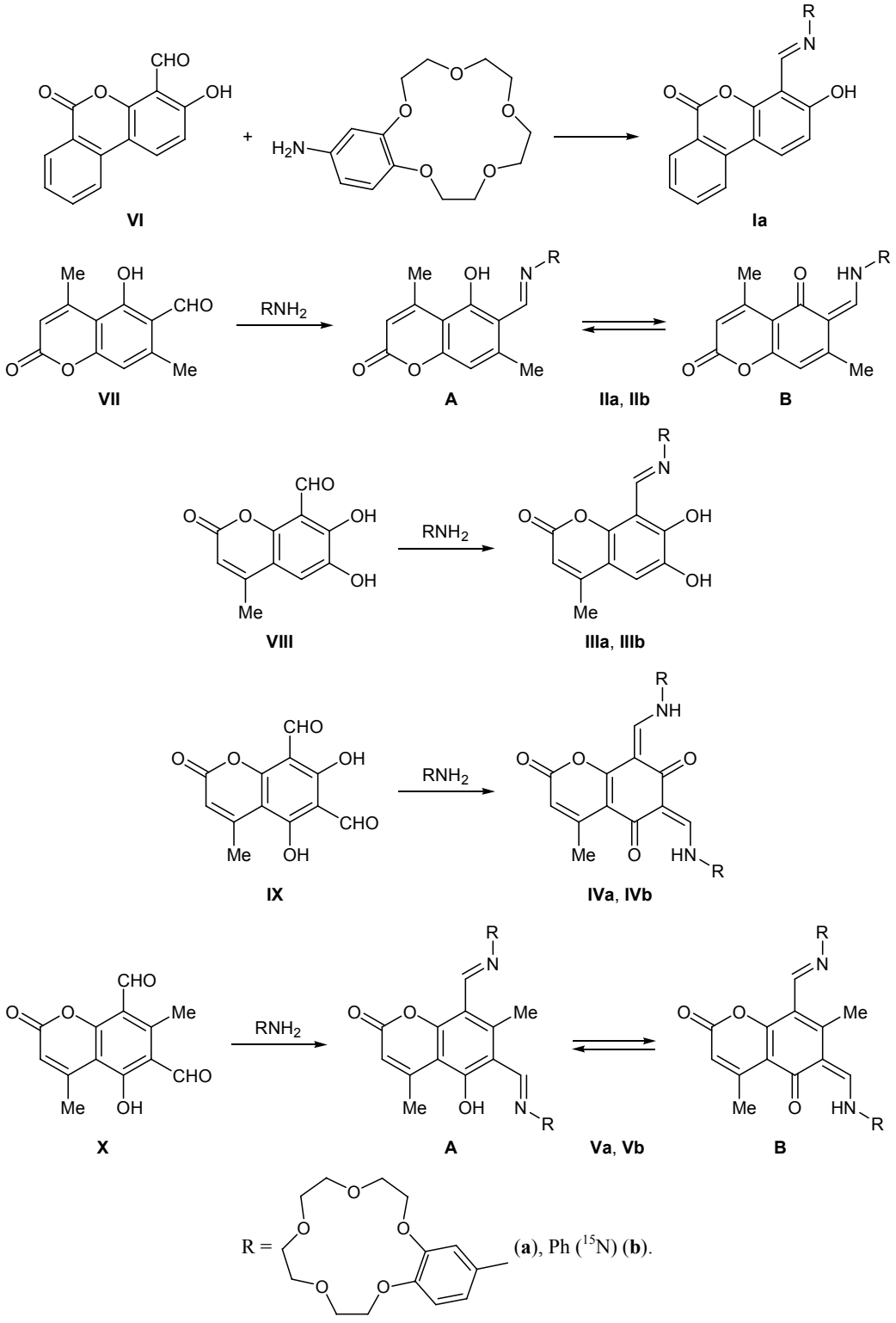
We previously synthesized potentially tautomeric crown-containing Schiff bases from aldehydes of the benzo[*b*]furan [1–7] and benzo[*h*]coumarin series [8], and the products were found to be capable of detecting alkali and alkaline earth metal cations. With a view to obtain new tautomeric chemosensors, in the present work we synthesized crown-containing Schiff bases **Ia**–**Va** by condensation of 3-hydroxy-6-oxo-6*H*-benzo[*c*]chromene-4-carbaldehyde (**VI**), 5-hydroxy-4,7-dimethyl-2-oxo-2*H*-chromene-6-carbaldehyde (**VII**), 6,7-dihydroxy-4-methyl-2-oxo-2*H*-chromene-8-carbaldehyde (**VIII**), 5,7-dihydroxy-4-methyl-2-oxo-2*H*-chromene-6,8-dicarbaldehyde (**X**), and 5-hydroxy-4,7-dimethyl-2-oxo-2*H*-chromene-6,8-dicarbaldehyde (**X**) with aminobenzo-15-crown-5 (2,3,5,6,8,9,11,12-octahydrobenzo[*b*][1,4,7,10,13]pentaoxacyclopentadecin-15-amine) in propan-2-ol; in addition, model ^{15}N-labeled Schiff bases **IIb**–**Vb** were prepared from aldehydes **VII**–**X** and (^{15}N)aniline (Scheme 1). Compounds **VI**–**VI** and **X** were synthesized according to the procedures reported in [9–11], and the synthesis of **IX** is described in Experimental.

The IR spectra of **I**–**V** contained absorption bands at 1700–1750 cm^{-1} due to stretching vibrations of the lactone carbonyl group. In the ^{1}H NMR spectra of these compounds in $CDCl_3$ we observed signals from methyl groups on the chromene ring system (δ 2.35–2.82 ppm), methylene protons in the crown ether fragment (δ 3.55–4.30 ppm), aromatic protons (δ 6.02–8.36 ppm), azomethine proton CH=N (δ 8.65–9.33 ppm), and OH and NH protons (δ 13.10–15.15 ppm). Schiff bases **I** and **IIIa** displayed in the ^{1}H NMR spectra signals from the CH=N and exchangeable (OH) protons as sharp singlets, indicating

* For communication LIV, see [1].

Scheme 1.



the presence in solution of hydroxy enimino structure **A** as predominating tautomer. In the spectrum of **IVa**, these signals were split into doublets with a coupling constant J of ~13.0 Hz due to the presence of keto enamine tautomer **B**. In addition, all other signals were doubled; in keeping with published data [12], this is the result of *Z/E* isomerization about the exocyclic C=C bond (isomer ratio 2:1). The coupling constant

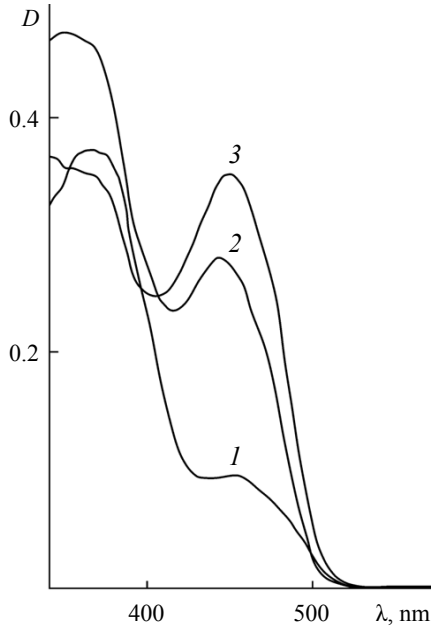


Fig. 1. Electronic absorption spectra of compound **IIa** in (*1*) toluene, (*2*) acetonitrile, and (*3*) DMSO; $c = 2.5 \times 10^{-5}$ M.

J = 7.6 Hz in the spectrum of **Va** corresponds to tautomeric equilibrium **A** ⇌ **B** where the fraction of keto enamine tautomer **B** is 58% [13].

In order to estimate the state of the tautomeric equilibrium more accurately, we analyzed the NMR spectra of ^{15}N-labeled compounds **IIb**–**Vb**. The

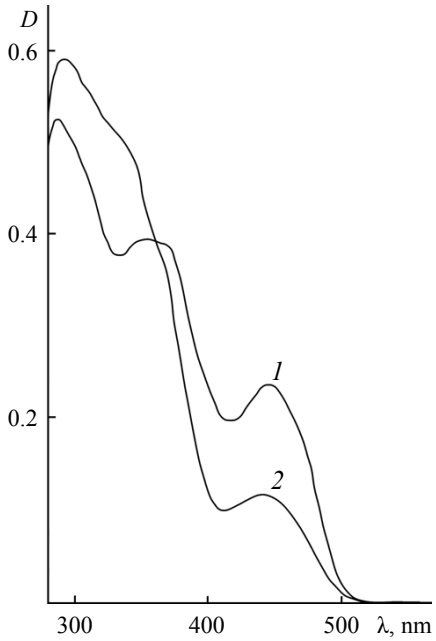


Fig. 2. Electronic absorption spectra of compound **IIa** in acetonitrile ($c = 2.0 \times 10^{-5}$ M) (*1*) before and (*2*) after addition of $Mg(ClO_4)_2$, $c = 2.5 \times 10^{-4}$ M.

^{1}H NMR spectrum of **IIIb** showed no coupling of the exchangeable proton with ^{15}N nucleus, which should be observed for the keto enamine tautomer **B**; this means that compound **IIIb** exists exclusively as hydroxy enimine structure **A** [14, 15]. By contrast, the spectrum of **IVb** contained doublets of doublets from the CH and NH protons, J(H–^{15}N) ≈ 90 Hz, indicating its keto enamine structure **B** [14, 15]. The coupling constants J(H–^{15}N) in the spectra of **IIb** and **Vb** were equal to 39.0 and 32.5 Hz, which correspond, respectively, to 43 and 36% fractions of tautomer **B**.

The electronic absorption spectra of crown-containing Schiff bases **Ia**–**IIIa** and **Va** were characterized by the presence of broad bands arising from hydroxy enimine tautomer **A** in the region λ 350–390 nm. Compounds **IIa** and **Va** also displayed a long-wave maximum at λ 480–500 nm due to keto enamine **B**; i.e., there is equilibrium **A** ⇌ **B** (Scheme 1). The fraction of tautomer **B** increases with rise in solvent polarity in the series toluene < acetonitrile < DMSO (Fig. 1). In the electronic absorption spectrum of **IVa** we observed only one absorption band with its maximum at about λ 420 nm, which is typical of quinoid structure **B**.

The crown ether fragment in Schiff bases **Ia**–**Va** is capable of coordinating cations of an appropriate size [3]. Addition of alkaline earth metal salts to solutions of Schiff bases **IIa** and **Va** in acetonitrile led to reduction of the fraction of keto enamine tautomer **B** and simultaneous increase of the fraction of structure **A** in the series $Mg^{2+} > Ba^{2+} > Ca^{2+}$ (Fig. 2). The electronic absorption spectra of compounds **I**, **III**, and **IV** existing as a single tautomer almost did not change in the presence of alkaline earth cations.

Thus, tautomeric crown-containing Schiff bases derived from *ortho*-hydroxycarbaldehydes of the coumarin series exhibit ionochromic behavior related to displacement of the hydroxy enimine–keto enamine equilibrium toward the hydroxy enimine tautomer.

EXPERIMENTAL

The ^{1}H NMR spectra were recorded on a Varian Unity-300 spectrometer (300 MHz) at 20°C using the residual solvent signal ($CHCl_3$, δ 7.25 ppm; DMSO-d_5, δ 2.49 ppm) as reference. The IR spectra were measured on a Varian Excalibur spectrometer with Fourier transform. The electronic absorption spectra were recorded on a Varian Cary 100 spectrophotometer.

3-Hydroxy-6-oxo-6*H*-benzo[*c*]chromene-4-carbaldehyde (**VI**) [9], 5-hydroxy-4,7-dimethyl-2-oxo-2*H*-

chromene-6-carbaldehyde (**VII**) and 5-hydroxy-4,7-dimethyl-2-oxo-2*H*-chromene-6,8-dicarbaldehyde (**X**) [10], and 6,7-dihydroxy-4-methyl-2-oxo-2*H*-chromene-8-carbaldehyde (**VIII**) [11] were synthesized according to known methods.

5,7-Dihydroxy-4-methyl-2-oxo-2*H*-chromene-6,8-dicarbaldehyde (IX). A mixture of 5.76 g (30 mmol) of 4-methyl-5,7-dihydroxycoumarin, 7.38 g (60 mmol) of *p*-anisidine, and 4.5 ml of triethyl orthoformate was heated for 5 h at 170°C. The dark yellow precipitate was filtered off and dissolved in 250 ml of acetic acid, 200 ml of 15% aqueous HCl was added, and the mixture was heated for 20 min under reflux, cooled, and diluted with 500 ml of water. The precipitate was filtered off, dried, and recrystallized from acetic acid. The product was dissolved in acetone and purified by column chromatography on silica gel using acetone as eluent. Yield 35%, mp 168–170°C. IR spectrum, ν, cm^{-1}: 1740, 1700, 1695. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.61 s (3H, CH_3), 6.05 s (1H, 3-H), 10.28 s (1H, CHO), 10.34 s (1H, CHO), 13.73 s (1H, OH), 14.45 s (1H, OH). Found, %: C 58.15; H 3.64. $C_{12}H_8O_6$. Calculated, %: C 58.07; H 3.25.

Schiff bases I–V (*general procedure*). A mixture of 4 mmol of aldehyde **VI**–**X** and 4 mmol of aminobenzo-15-crown-5 or (^{15}N)aniline in propan-2-ol was heated for 5 h under reflux. The precipitate was filtered off and recrystallized from DMF or DMF–propan-2-ol (1:1) (**IVa**, **IVb**, **Va**).

3-Hydroxy-4-[(2,3,5,6,8,9,11,12-octahydrobenzo[*b*][1,4,7,10,13]pentaoxacyclopentadecin-15-yl)iminomethyl]-6*H*-benzo[*c*]chromen-6-one (Ia). Yield 56%, mp 218–220°C. IR spectrum, ν, cm^{-1}: 1738, 1620. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 3.68–4.23 m (16H, CH_2O), 6.89–8.36 m (9H, H_{arom}), 9.33 s (1H, N=CH), 15.15 s (1H, OH). Found, %: C 76.40; H 4.65; N 4.20. $C_{28}H_{27}NO_8$. Calculated, %: C 66.53; H 5.38; N 2.77.

5-Hydroxy-4,7-dimethyl-6-[(2,3,5,6,8,9,11,12-octahydrobenzo[*b*][1,4,7,10,13]pentaoxacyclopentadecin-15-yl)iminomethyl]-2*H*-chromen-2-one (IIa). Yield 43%, mp 215–217°C. IR spectrum, ν, cm^{-1}: 1720, 1610. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.52 s (3H, CH_3), 2.71 s (3H, CH_3), 3.63–4.25 m (16H, CH_2O), 6.02–6.97 m (5H, H_{arom}), 8.71 s (1H, N=CH), 16.47 s (1H, OH). Found, %: C 64.65; H 6.35; N 2.41. $C_{26}H_{29}NO_8$. Calculated, %: C 64.59; H 6.05; N 2.90.

5-Hydroxy-4,7-dimethyl-6-[(^{15}N)phenyliminomethyl]-2*H*-chromen-2-one (IIb). Yield 55%, mp 222–224°C. IR spectrum, ν, cm^{-1}: 1730, 1600. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.60 s (3H, CH_3), 2.72 s (3H, CH_3), 7.03–7.51 m (7H, H_{arom}), 9.00 d (1H, N=CH, J_{HH} = 4.4 Hz), 16.51 d.d [1H, OH, J_{HH} = 4.4, $J(H-^{15}N)$ = 39.0 Hz]. Found, %: C 73.25; H 6.03; N 5.11. $C_{18}H_{15}NO_3$. Calculated, %: C 73.49; H 6.12; N 5.10.

6,7-Dihydroxy-4-methyl-8-[(2,3,5,6,8,9,11,12-octahydrobenzo[*b*][1,4,7,10,13]pentaoxacyclopentadecin-15-yl)iminomethyl]-2*H*-chromen-2-one (IIIa). Yield 64%, mp 188–190°C. IR spectrum, ν, cm^{-1}: 3300, 1700, 1630. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.35 s (3H, CH_3), 3.84–4.30 m (16H, CH_2O), 6.06 s (1H, 3-H), 6.54 br.s (1H, OH), 6.95–7.02 m (4H, H_{arom}), 9.08 s (1H, N=CH), 15.75 br.s (1H, OH). Found, %: C 61.85; H 5.29; N 2.85. $C_{24}H_{24}NO_9$. Calculated, %: C 61.27; H 5.14; N 2.98.

6,7-Dihydroxy-4-methyl-8-[(^{15}N)phenyliminomethyl]-2*H*-chromen-2-one (IIIb). Yield 57%, mp 230–232°C. IR spectrum, ν, cm^{-1}: 3300, 1710, 1640. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.36 s (3H, CH_3), 6.07 s (1H, 3-H), 6.59 br.s (1H, OH), 7.03–7.58 m (6H, H_{arom}), 9.20 s (1H, N=CH), 15.25 br.s (1H, OH). Found, %: C 68.45; H 4.29; N 4.85. $C_{17}H_{13}NO_4$. Calculated, %: C 68.92; H 4.39; N 4.73.

(*Z*,*E*)-4-Methyl-6,8-bis[(2,3,5,6,8,9,11,12-octahydrobenzo[*b*][1,4,7,10,13]pentaoxacyclopentadecin-15-yl)aminomethylidene]-2*H*-chromene-2,5,7(6*H*,8*H*)-trione (IVa). Yield 36%, mp 134–136°C. IR spectrum, ν, cm^{-1}: 1747, 1645, 1622, 1600. ^1H NMR spectrum (DMSO-d_6), δ, ppm: *Z* isomer: 2.49 s (3H, CH_3), 3.55–4.17 m (32H, CH_2O), 5.80 s (1H, 3-H), 6.92–7.18 m (6H, H_{arom}), 8.52 d (1H, CHN, *J* = 12.6 Hz), 8.71 d (1H, CHN, *J* = 13.2 Hz), 13.57 d (1H, NH, *J* = 13.2 Hz), 14.21 d (1H, NH, *J* = 12.6 Hz); *E* isomer: 2.55 s (3H, CH_3), 3.55–4.17 m (32H, CH_2O), 5.80 s (1H, 3-H), 6.92–7.18 m (6H, H_{arom}), 8.43 d (1H, CHN, *J* = 13.0 Hz), 8.65 d (1H, CHN, *J* = 13.8 Hz), 13.14 d (1H, NH, *J* = 13.8 Hz), 13.29 d (1H, NH, *J* = 13.0 Hz). Isomer ratio *Z*/*E* ~2:1. Found, %: C 61.50; H 5.48; N 4.01. $C_{40}H_{46}N_2O_{14}$. Calculated, %: C 61.69; H 5.95; N 3.60.

4-Methyl-6,8-bis{(^{15}N)phenylamino]methylidene}-2*H*-chromene-2,5,7(6*H*,8*H*)-trione (IVb). Yield 45%, mp 256–258°C. IR spectrum, ν, cm^{-1}: 1744, 1645, 1608. ^1H NMR spectrum (DMSO-d_6), δ, ppm: *Z* isomer: 2.65 s (3H, CH_3), 5.82 s (1H, 3-H), 7.19–7.50 m (10H, H_{arom}), 8.60–8.95 m (2H, CHN), 13.59 d.d and 13.94 d.d [1H, NH, J_{HH} = 13.0, $J(H-^{15}N)$ = 89.5 Hz], 13.82 d.d and 14.17 d.d [1H,

NH, J_{HH} = 12.7, J(H–^{15}N) = 89.7 Hz]; *E* isomer: 2.62 s (3H, CH_3), 5.83 s (1H, 3-H), 7.19–7.50 m (10H, H_{arom}), 8.60–8.95 m (2H, CHN), 13.10 d.d and 13.46 d.d [1H, NH, J_{HH} = 13.5, J(H–^{15}N) = 90.0 Hz], 13.20 d.d and 13.57 d.d [1H, NH, J_{HH} = 13.0, J(H–^{15}N) = 90.5 Hz]. Isomer ratio *Z*/*E* ~5:2. Found, %: C 75.50; H 5.15; N 7.39. $C_{25}H_{20}N_2O_3$. Calculated, %: C 75.38; H 5.02; N 7.54.

5-Hydroxy-4,7-dimethyl-6,8-bis-[(2,3,5,6,8,9,11,12-octahydrobenzo[*b*][1,4,7,10,13]-pentaoxacyclopentadecin-15-yl)iminomethyl]-2*H*-chromen-2-one (Va). Yield 25%, mp 145–147°C. IR spectrum, ν, cm^{-1}: 1750, 1670, 1615. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.71 s (3H, CH_3), 2.82 s (3H, CH_3), 3.61–4.22 m (32H, CH_2O), 6.05 s (1H, 3-H), 6.82–6.97 m (6H, H_{arom}), 8.84 d (1H, CH=N, J = 7.80 Hz), 8.94 s (1H, CH=N), 17.33 d (1H, CNH, J = 7.6 Hz). Found, %: C 62.65; H 6.35; N 3.61. $C_{45}H_{58}N_2O_{15}$. Calculated, %: C 62.34; H 6.74; N 3.23.

5-Hydroxy-4,7-dimethyl-6,8-bis[(*^{15}*N)phenyliminomethyl]-2*H*-chromen-2-one (Vb). Yield 38%, mp 198–200°C. IR spectrum, ν, cm^{-1}: 1740, 1670, 1610. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.50 s (3H, CH_3), 2.70 s (3H, CH_3), 6.01 s (1H, 3-H), 7.23–7.52 m (10H, H_{arom}), 8.72–8.80 m (2H, CH=N), 16.26 d.d [1H, OH, J_{HH} = 4.74, J(H–^{15}N) = 32.5 Hz]. Found, %: C 75.55; H 4.92; N 7.50. $C_{25}H_{20}N_2O_3$. Calculated, %: C 75.39; H 5.02; N 7.53.

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