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New fluorogenic chemosensors derived from benzimidazole

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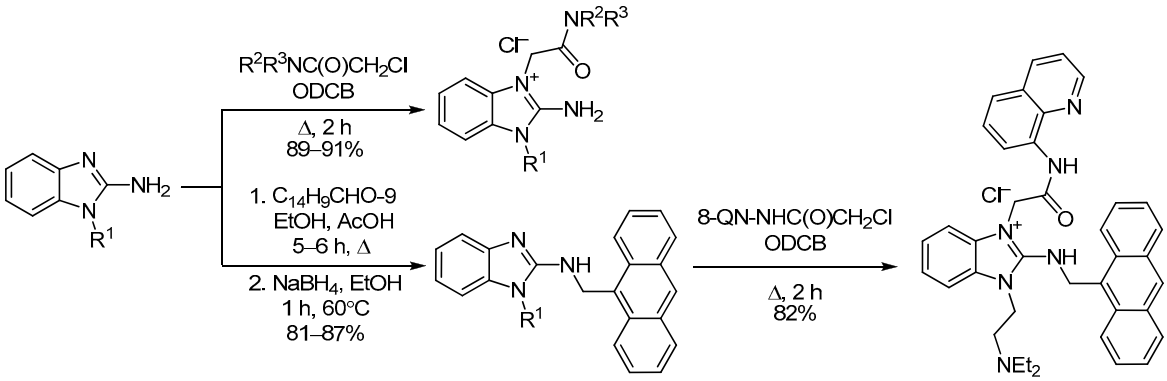


We report the synthesis of new 1-substituted *N*-(anthracen-9-ylmethyl)-1*H*-benzimidazol-2-amines and 1,2,3-trisubstituted 1*H*-benzimidazolium chlorides containing anthracene fluorophores. Benzimidazol-2-amine derivatives exhibited high chemosensing activity toward H^+ cations, but in neutral media – toward Zn^{2+} and Cd^{2+} cations. The quinoline-containing benzimidazolium chloride showed fluorogenic sensor properties toward F^- and CN^- anions.

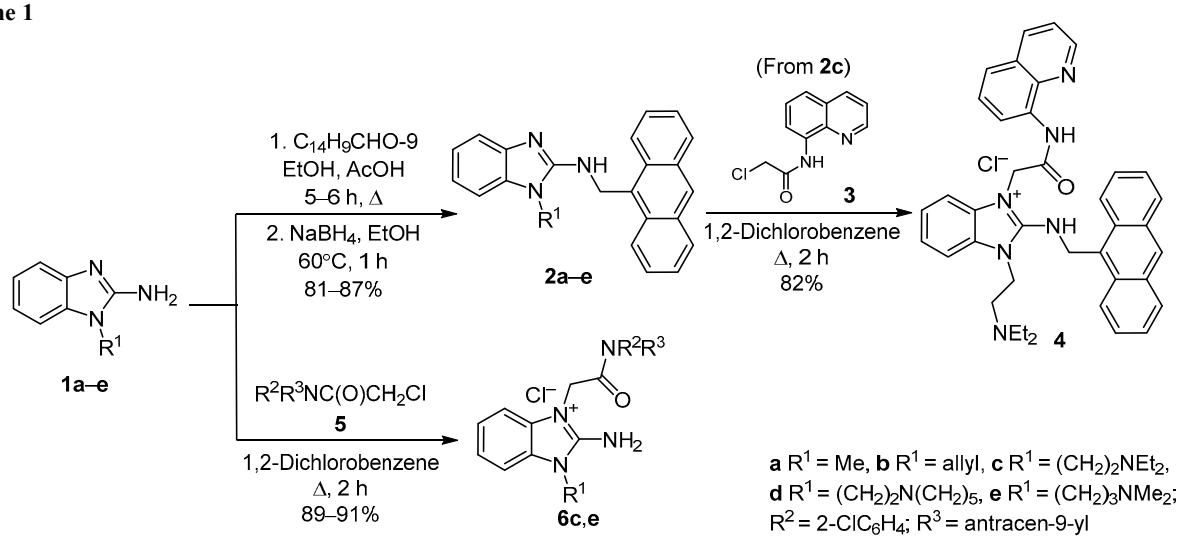
Keywords: amides, anthracene, benzimidazole, anions, cations, chemosensors, fluorescence, quaternary salts.

Organic chemosensors represent molecular or supramolecular systems that can be used for collecting information about the qualitative and quantitative content of specific ions or molecules in studied samples.[1] Chemosensors are commonly used in biology, medical diagnostics, and for environmental monitoring applications.[2] Fluorescent ionochromic compounds are superior to different types of chemosensors (colorimetric, potentiometric, and others) due to their high sensitivity, universal applicability, convenience of analytical procedures, suitability for simultaneous determination of a set of spectral parameters for the analytes in question (intensity, batho- and hypsochromic shifts of spectral bands, quantum yield and half-life of fluorescence).

One of the most commonly used building blocks for the construction of biologically active molecules and drugs is the benzimidazole system,[3] which is also a structural feature present in various ligand systems, fluorogenic and chromogenic chemosensors,[4] materials for OLED devices,[5] and palladium-containing catalysts of cross-coupling reactions.[6] The presence of electron-donating pyridine nitrogen atom with the ability to form complexes, and the possibility of structural modifications involving several active centers offer a range of possibilities for using benzimidazole ring systems as a basis for the design of effective chemosensor systems.[7] Previously we have demonstrated the possibilities for using derivatives of benzimidazol-2-amine and its hydrogenated analog as effective receptors for H^+ and Zn^{2+} cations, F^- anions, while employing anthracene system in the role of a fluorophore.[8]

The goal of this work was to synthesize and study a new series of chemosensors containing receptor moieties based on the highly basic 1-alkyl- and 1-(dialkylamino)-alkyl-1*H*-benzimidazol-2-amines, as well as the respective quaternary salts. Condensation of benz-imidazoles **1a**–**e** with anthracene-9-carbaldehyde and reduction of the formed imines with $NaBH_4$ in EtOH allowed to obtain the amines **2a**–**e** (Scheme 1). The formation of amines **2a**–**e** was accompanied by the appearance of a signal in ^{1}H NMR spectra due to the CH_2 group protons (a doublet in the region of 5.51–5.68 ppm) and also the anthracene system protons. Compound **2c** was modified by the introduction of an additional chelating group derived from 8-amino-quinoline, resulting in salt **4**, which contained several

Scheme 1



potential coordination sites: a charged aminobenzimidazole system, a quinoline moiety, as well as the 2-diethylaminoethyl and amide groups. The anthracene fluorophore was also introduced into the molecular structure by combining the starting benzimidazole amines **1c**,**e** with *N*-(anthracen-9-ylmethyl)-2-chloro-*N*-(2-chlorophenyl)acetamide (**5**). The anthryl fluorophore and receptor in the obtained products (salts **6c**,**e**) were linked by an acetamide bridge. Quaternization of the amines **1c**,**e** and **2c** was accompanied by the appearance of characteristic additional ^{1}H NMR signals due to the protons belonging to the aromatic rings and CH_2CO groups.

The investigation of compounds **2a**,**b** as potential chemosensors demonstrated their high sensitivity toward hydrogen ions. Amines **2a**,**b** upon excitation with light at λ_{exc} 350 nm in acetonitrile solution exhibited anthracene type fluorescence (three separate peaks in the region of 390–440 nm and a shoulder at 460–470 nm), the intensity of which was substantially diminished as a consequence of the photoinduced electron transfer (PET) effect.[1e,g] The addition of trifluoroacetic acid to acetonitrile solutions of these compounds prevented the aforementioned effect and led to 45-fold and 75-fold increase of the relative intensity of fluorescence, respectively (Fig. 1).

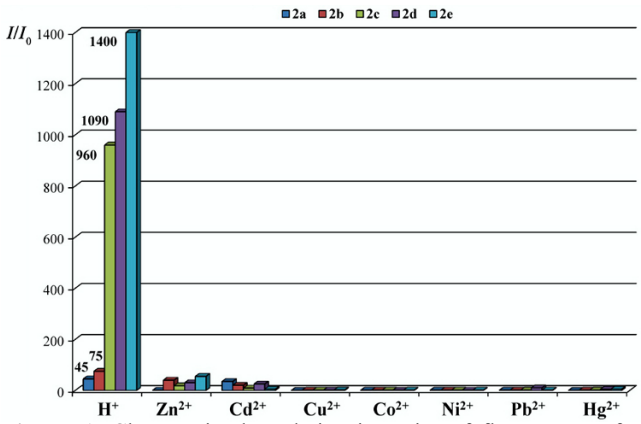


Figure 1. Changes in the relative intensity of fluorescence for compounds **2a**–**e** (c 5 × 10^{-6} M) in acetonitrile upon the addition of various cations (c 2.5 × 10^{-5} M), λ_{exc} 350 nm, λ_{obs} 415 nm.

The presence of dialkylaminoalkyl substituent in benzimidazole ring of compounds **2c**–**e** is expected to increase the quenching of initial fluorescence due to the electron density transfer from the nitrogen atom of dialkylamino group to the anthracene system (synergistic PET effect, Fig. 2).[1e,g]

Such compounds, as a rule, show increased sensitivity to the pH value of the solution. The addition of trifluoroacetic acid to acetonitrile solutions of amines **2c**–**e** led to a sharp increase of fluorescence intensity of such solutions by 960, 1090, and 1400[8e] times, respectively (Fig. 1). The increase of sensitivity to the pH value of solution when switching from the diethylamine derivative **2c** to the piperidine derivative **2d** was symbatic with the basicity values of the respective dialkylamines (diethylamine pK_a 10.98, piperidine pK_a 11.22).[9]

In order to study the influence of dialkylaminoalkyl substituents on the chemosensor properties of compounds **2c**–**e**, we performed a quantum-chemical study of the structure and stability of compound **2d** and its conjugated acids. In contrast to the amines **2a**,**b** containing methyl and allyl groups, the molecule of 2-piperidinoethyl derivative **2d** contains two competing highly basic sites that can be protonated – the nitrogen atoms of benzimidazole and piperidine rings. The anthryl (signal) and heterocyclic (receptor of analytes) moieties of the molecule **2d**, which

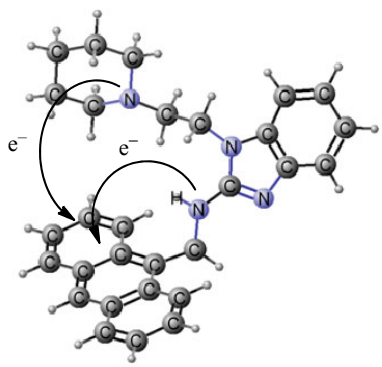


Figure 2. Scheme of the possible PET effect for a molecule of amine **2d**.

were linked by a methylene bridge, were located in mutually perpendicular planes (Fig. 3). The nitrogen atom of NH group had a pyramidal configuration and existed in an sp^3-hybridized state.

According to energy calculations, the most favored was protonation at the pyridine nitrogen atom of imidazole ring with the formation of conjugated acid **2dA** (Fig. 3, Table 1). This process led to significant equalization of N–C bond lengths in the guanidine moiety, but did not affect the arrangement of signal and receptor moieties. The C–N distance was reduced from 1.379 to 1.334 Å, while the length of C=N bond increased from 1.314 to 1.355 Å, possibly indicating a change of bond order. Besides that, a substantial flattening was observed for the pyramidal nitrogen atom of the amino group. Protonation at the piperidine nitrogen atom, which led to the conjugated acid **2dB**, was less favorable by 13.7 kcal/mol (Table 1). The performed computational study confirmed that photo-induced electron transfer from the nitrogen atom of dialkyl-amino group to the anthracene system indeed had the dominant effect on the desired chemosensor properties.

Accounting for solvent effects led to a noticeably increased affinity of molecule **2d** toward protons (Table 1), which was in agreement with the previously published data.[10] The consideration of solvation effects substantially decreased the calculated energy difference between the conjugated acids **2dA** and **2dB**, practically to the level enabling a prototropic equilibrium between these species.

Compounds **2a**–**e** in neutral medium also exhibited a noticeable chemosensor activity toward Zn^{2+} and Cd^{2+} cations, in contrast to the cations of other d-block metals (Fig.1).

The benzimidazolium chlorides **4** and **6c**,**e**, featuring salt type structures, showed an entirely different set of chemo-sensor properties compared to the neutral molecules **2c**,**e**, for which, as was shown above, a significant chelation-enhanced fluorescence effect (CHEF effect) was caused by the interactions with cations.[1g] The quaternary salt **4** was substantially less sensitive toward hydrogen ions, while its interactions with Cu^{2+} and Hg^{2+} cations led to a very pronounced chelation-enhanced fluorescence quenching effect (CHEQ effect),[1g] and practically completely quenched the initial fluorescence (Table 2, Fig. 4*a*). The majority of the tested anions also exhibited the CHEQ effect, but in the case of CN^- and F^- anions it was accompanied by the appearance of new, broad long-wavelength emission bands in the region of 450 and 500 nm (Fig. 4*a*), which can be used for the detection of these ions.

Salts **6c**,**e** were found to have even lower sensitivity toward hydrogen ions. Metal cations also exerted only insignificant effects on the emission intensity, while Hg^{2+} ions showed a noticeable CHEF effect (Table 2, Fig. 4*b*). The interaction of anions with salts **6c**,**e** in all cases led to quenching of the initial fluorescence.

Thus, new fluorescent chemosensors on the basis of *N*-(anthracen-9-ylmethyl)-1*H*-benzimidazol-2-amines showed strong chemosensing performance toward H^+ cations, but in neutral media – also toward Zn^{2+} and Cd^{2+} cations. Quinoline-containing benzimidazolium chloride exhibited fluorogenic chemosensor properties toward F^- and CN^- anions.

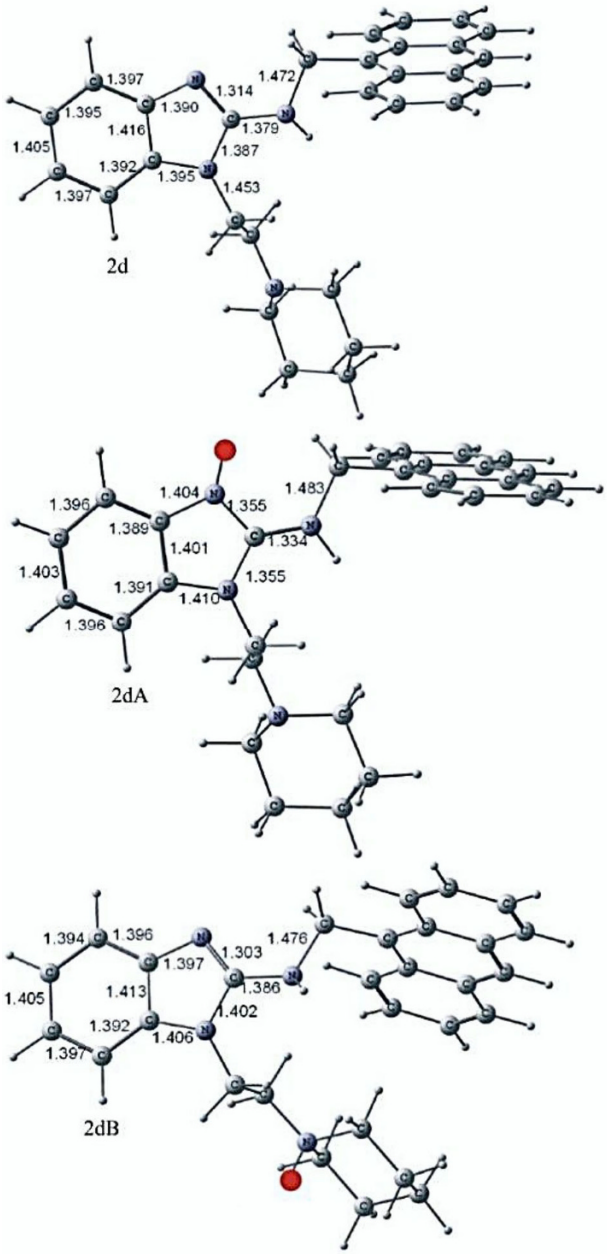


Figure 3. Geometric properties of structures **2d**, **2dA**, and **2dB**, calculated by the DFT method with B3LYP/6-31G(d,p) basis set. Bond lengths reported in Å.

Table 1. The total energy (E_{total}), proton affinity (PA), and energy difference between protonated forms (ΔE) in structures **2d**, **2dA**, and **2dB**, calculated by the DFT B3LYP/6-31G(d,p) method without/with accounting for solvent (MeCN) effects.

Structure	E_{total}, au	PA, kcal/mol	ΔE, kcal/mol
2d	−1342.236579	0.0	
2dA	−1342.647946	−258.1	0.0
2dB	−1342.626122	−244.4	13.7
2d*	−1342.244727	0.0	
2dA*	−1342.705237	−289.0	0.0
2dB*	−1342.697629	−284.2	4.8

* Accounting for the solvent effects (MeCN).

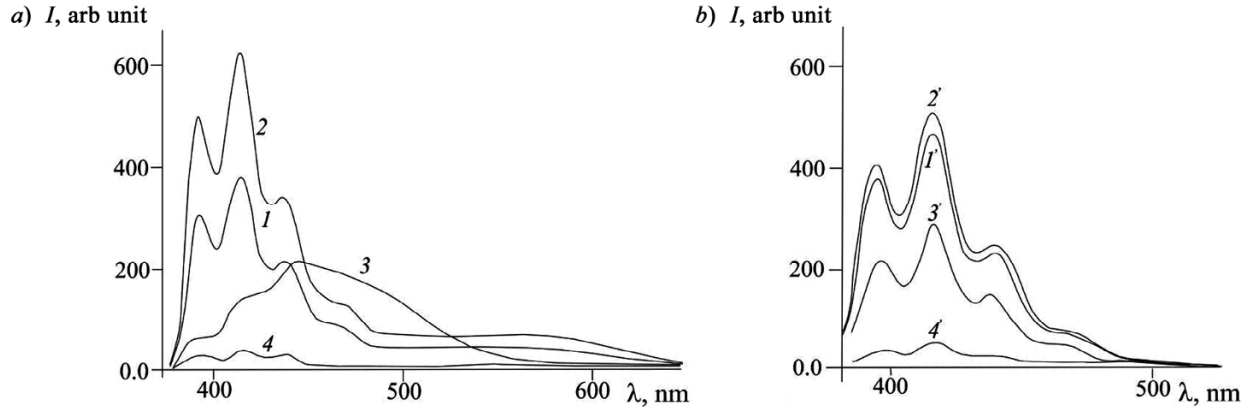


Figure 4. Fluorescence spectra for acetonitrile solutions (c 5 × 10^{-6} mol/l, λ_{excit} 350 nm) of salts **4** (*a*) and **6c** (*b*) before (graphs *1* and *1*') and after the addition of H^+ cations (graphs *2* and *2*'), Hg^{2+} (graphs *3* and *3*'), and CN^- anion (graphs *4* and *4*') (c 2.5 × 10^{-5} mol/l).

Table 2. Changes in relative intensity of fluorescence (I/I_0) for compounds **4** and **6c**,**e** in MeCN (c 5 × 10^{-6} mol/l)*

Compound	Cations						Anions			
	H^+	Mg^{2+}	Zn^{2+}	Cd^{2+}	Cu^{2+}	Hg^{2+}	F^-	$H_2PO_4^-$	CN^-	AcO^-
4	1.67	1.33	1.22	0.89	**0.09**	**0.09**	0.18	0.24	0.36	0.39
6c	1.11	1.06	1.05	0.97	0.99	**0.54**	0.04	0.06	0.06	0.06
6e	1.09	1.05	1.09	1.00	1.00	**0.61**	0.03	0.05	0.05	0.08

* After the addition of cations (c 2.5 × 10^{-5} mol/l) and anions (c 2.5 × 10^{-5} mol/l), λ_{excit} 350 nm, λ_{obs} 415 nm.

Experimental

IR spectra were recorded on a Varian Excalibur 3100 FT-IR instrument by the method of attenuated total reflectance using a ZnSe crystal. ^{1}H NMR spectra were acquired on Varian Unity 300 (300 MHz, compounds **2a**, **3**–**5**, **6c**,**e**) and Bruker Avance 600 (600 MHz, the rest of the compounds) spectrometers. ^{13}C NMR spectra were acqui-red on a Bruker Avance 600 spectrometer at 150 MHz. The solvents were $CDCl_3$ (for compounds **2a**, **3**, **5**) and DMSO-d_6 (for the rest of the compounds), while residual proton signals of $CHCl_3$ and DMSO were used as internal standards (^{1}H NMR signals at δ 7.26 ppm and 2.49 ppm, respectively). The fluorescence spectra were recorded on a Varian Cary Eclipse fluorescence spectrophotometer. Mass spectra were recorded on a Shimadzu GCMS-QP2010SE gas chromato-mass spectrometer with a system for direct introduction of sample into the ion source (EI, 70 eV). Elemental analysis was performed on an Analytik Jena multi EA 5000 instrument. Melting points were determined in glass capillaries using a PTP(M) apparatus. The reaction progress and purity of the obtained compounds were controlled by TLC (Silufol U-254 plates, $CHCl_3$ as eluent, visualization with iodine vapor in a moist chamber). Solutions were prepared by using spectral grade acetonitrile, perchlorates of d-block metals and tetrabutylammonium salts (Sigma-Aldrich). Amines **1a**–**e** were obtained according to published procedures,[15] while amine **2e** was obtained according to another literature method.[8e]

Synthesis of *N*-(anthracen-9-ylmethyl)-1*H*-benzimidazol-2-amines 2a–d (General method). Glacial acetic acid (2–3 drops) was added to a solution of anthracene-9-carbaldehyde (2.06 g, 10 mmol) and the respective 1*H*-benzimidazol-2-amine **1a**–**d** (10 mmol) in EtOH (60–70 ml), followed by refluxing of the mixture for 5–6 h. The reaction mixture was further stirred and heated at 50–60°C (in the case of precipitate formation, 5–10 ml of DMF was added) and treated over 15–20 min with $NaBH_4$ (1.30 g, 35 mmol). The solution was additionally stirred for another 1 h, then it was diluted with H_2O (100 ml) and the excess of $NaBH_4$ was neutralized by the addition of 2–3% AcOH. The mixture was cooled to 5°C and the obtained precipitate of amine **2a**–**d** was filtered off after 1.5–2 h, washed with cold H_2O and cold MeOH, and air-dried. The products were purified by crystallization from suitable solvents.

***N*-(Anthracen-9-ylmethyl)-1-methyl-1*H*-benzimidazol-2-amine (2a)**. Yield 2.9 g (87%), orange coarse-grained crystalline precipitate, mp 257–258°C (PhH). IR spectrum, ν, cm^{-1}: 3320 (NH), 1460 (C=C), 1360 (C–N). ^{1}H NMR spectrum, δ, ppm (J, Hz): 3.33 (3H, s, CH_3); 4.18 (1H, t, J = 4.5, NH); 5.68 (2H, d, J = 4.5, CH_2); 7.00–7.28 (3H, m, H Ar); 7.42–7.60 (4H, m, H Ar); 7.64 (1H, d, J = 7.7, H Ar); 8.06 (2H, d, J = 8.5, H Ar); 8.37 (2H, d, J = 8.5, H Ar); 8.51 (1H, s, H Ar). Mass spectrum, m/z (I_{rel}, %): 337 $[M]^+$ (21), 191 $[C_{14}H_9CH_2]^+$ (100). Found, %: C 81.80; H 5.72; N 12.48. $C_{23}H_{19}N_3$. Calculated, %: C 81.87; H 5.68; N 12.45.

1-Allyl-*N*-(anthracen-9-ylmethyl)-1*H*-benzimidazol-2-amine (2b). Yield 3.1 g (85%), light-yellow fibrous precipitate, mp 228–229°C (*n*-BuOH). IR spectrum, ν, cm^{-1}: 3335 (NH), 1465 (C=C), 1360 (C–N). ^{1}H NMR spectrum, δ, ppm (J, Hz): 4.56 (2H, d, J = 4.8, CH_2); 4.85 (1H, d, J = 17.3) and 4.96 (1H, d, J = 10.2, $=CH_2$); 5.54 (2H, d, J = 4.6, CH_2); 5.64–5.75 (1H, m, CH); 6.91 (1H, t, J = 7.5, H Ar); 6.96–7.03 (2H, m, H Ar, NH); 7.08 (1H, d, J = 7.6, H Ar); 7.36 (1H, d, J = 7.7, H Ar); 7.46–7.55 (4H, m, H Ar); 8.09 (2H, d, J = 8.4, H Ar); 8.42 (2H, d, J = 8.4, H Ar); 8.60 (1H, s, H Ar). ^{13}C NMR spectrum, δ, ppm: 39.5; 43.3; 107.8; 115.2; 116.0; 118.5; 120.4; 124.7; 125.1; 126.1; 127.2; 128.7; 130.0; 130.3; 131.1; 132.9; 134.7; 142.7; 154.5. Mass spectrum, m/z (I_{rel}, %): 363 $[M]^+$ (14), 191 $[C_{14}H_9CH_2]^+$ (100), 41 $[CH_2{=}CHCH_2]^+$ (38). Found, %: C 82.70; H 5.76; N 11.54. $C_{25}H_{21}N_3$. Calculated, %: C 82.62; H 5.82; N 11.56.

***N*-(Anthracen-9-ylmethyl)-1-[2-(diethylamino)ethyl]-1*H*-benzimidazol-2-amine (2c)**. Yield 3.6 g (85%), beige fine crystalline precipitate, mp 167–168°C (2-PrOH). IR spectrum, ν, cm^{-1}: 3325 (NH), 1460 (C=C). ^1H NMR spectrum, δ, ppm (*J*, Hz): 0.32 (6H, t, *J* = 7.7, $2CH_3$); 1.99 (4H, q, *J* = 7.7, $2CH_2$); 2.42 (2H, t, *J* = 4.6, CH_2); 3.86 (2H, t, *J* = 4.6, CH_2); 5.51 (2H, d, *J* = 5.4, CH_2); 6.92 (1H, t, *J* = 8.1, H Ar); 6.99 (1H, t, *J* = 8.1, H Ar); 7.13 (1H, d, *J* = 7.7, H Ar); 7.33 (1H, d, *J* = 7.7, H Ar); 7.47–7.56 (4H, m, H Ar); 7.62 (1H, t, *J* = 5.4, NH); 8.09 (2H, d, *J* = 8.2, H Ar); 8.41 (2H, d, *J* = 8.2, H Ar); 8.60 (1H, s, H Ar). ^{13}C NMR spectrum, δ, ppm: 10.6; 38.8; 39.5; 46.5; 52.4; 107.4; 115.3; 118.5; 120.2; 124.4; 125.1; 126.2; 127.3; 128.8; 130.0; 130.1; 131.1; 135.1; 142.6; 155.5. Mass spectrum, *m/z* (I_{rel}, %): 422 $[M]^+$ (6), 191 $[C_{14}H_9CH_2]^+$ (38), 86 $[Et_2NCH_2]^+$ (100). Found, %: C 79.52; H 7.20; N 13.28. $C_{28}H_{30}N_4$. Calculated, %: C 79.58; H 7.16; N 13.26.

***N*-(Anthracen-9-ylmethyl)-1-[2-(piperidin-1-yl)ethyl]-1*H*-benzimidazol-2-amine (2d)**. Yield 3.5 g (81%), light-yellow fine crystalline precipitate, mp 174–175°C (2-PrOH). IR spectrum, ν, cm^{-1}: 3320 (NH), 1460 (C=C), 1360 (C–N). ^1H NMR spectrum, δ, ppm (*J*, Hz): 0.10–0.20 (4H, m, $2CH_2$); 0.40–0.65 (2H, m, CH_2); 1.78–2.06 (4H, m, $2CH_2$); 2.36–2.52 (2H, m, CH_2); 3.77–3.93 (2H, m, CH_2); 5.67 (2H, d, *J* = 3.6, CH_2); 6.94–7.08 (2H, m, H Ar); 7.18 (1H, d, *J* = 7.7, H Ar); 7.38 (1H, d, *J* = 7.7, H Ar); 7.51–7.70 (5H, m, H Ar, NH); 8.11 (2H, d, *J* = 8.2, H Ar); 8.43 (2H, d, *J* = 8.2, H Ar); 8.63 (1H, s, H Ar). ^{13}C NMR spectrum, δ, ppm: 23.2; 24.2; 39.0; 39.9; 54.0; 58.2; 107.5; 115.2; 118.5; 120.3; 124.4; 125.1; 126.2; 127.4; 128.8; 129.8; 130.3; 131.1; 135.1; 142.6; 155.3. Mass spectrum, *m/z* (I_{rel}, %): 434 $[M]^+$ (7), 191 $[C_{14}H_9CH_2]^+$ (28), 98 $[(CH_2)_5NCH_2]^+$ (100). Found, %: C 80.10; H 6.98; N 12.92. $C_{29}H_{30}N_4$. Calculated, %: C 80.15; H 6.96; N 12.89.

2-Chloro-*N*-(quinolin-8-yl)acetamide (3). A solution of freshly distilled chloroacetyl chloride (5.7 ml, 72 mmol) in anhydrous toluene (25 ml) was added to a stirred solution of quinolin-8-amine (8.65 g, 60 mmol) in anhydrous toluene (50 ml) containing anhydrous pyridine (7.3 ml, 90 mmol). The obtained solution was refluxed for 1–1.5 h, cooled to 5°C, the obtained precipitate of pyridine hydrochloride was filtered and washed on filter with toluene (3×10 ml). The filtrate was washed with water (4×25 ml), dried over anhydrous Na_2SO_4, and evaporated at reduced pressure. The residue was recrystallized from 2-PrOH. Yield 9.5 g (72%), white fine crystalline precipitate, mp 133–134°C. IR spectrum, ν, cm^{-1}: 3174 (NH), 1674 (C=O), 1641 (C=N). ^1H NMR spectrum, δ, ppm (*J*, Hz): 4.31 (2H, s, CH_2); 7.40–7.63 (3H, m, H Ar); 8.17 (1H, d, *J* = 8.3, H Ar); 8.68–8.80 (1H, m, H Ar); 8.83–8.91 (1H, m, H Ar); 10.90 (1H, s, NH). Found, %: C 59.95; H 4.04; Cl 16.00; N 12.80. $C_{11}H_9ClN_2O$. Calculated, %: C 59.88; H 4.11; Cl 16.07; N 12.70.

***N*-(Anthracen-9-ylmethyl)-2-chloro-*N*-(2-chlorophenyl)-acetamide (5)**. Glacial acetic acid (0.1 ml) and 2-chloroaniline (3.5 ml, 33 mmol) were added to a solution of anthracene-9-carbaldehyde (6.20 g, 30 mmol) in *n*-BuOH (70 ml). The mixture was refluxed for 4 h, evaporated under reduced pressure to 20–25 ml volume, cooled to 10–15°C, and maintained at that temperature for 3–4 h. The precipitate that formed was filtered off, washed with EtOH, and air-dried. The obtained 1-(anthracen-9-ylmethyl)-*N*-(2-chlorophenyl)methanimine was recrystallized from toluene. Yield 8.7 g (92%), bright-yellow fibrous crystals, mp 178–179°C (toluene). IR spectrum, ν, cm^{-1}: 1628 (C=N). ^1H NMR spectrum, δ, ppm (*J*, Hz): 7.14–7.23 (2H, m, H Ar); 7.28–7.46 (2H, m, H Ar); 7.50–7.65 (4H, m, H Ar); 8.07 (2H, d, *J* = 8.4, H Ar); 8.64 (1H, s, H Ar); 8.77 (1H, d, *J* = 8.4, H Ar); 9.61 (1H, s, CH). Found, %: C 79.81; H 4.55; Cl 11.15; N 4.49. $C_{21}H_{14}ClN$. Calculated, %: C 79.87; H 4.47; Cl 11.22; N 4.44.

Sodium borohydride (1.90 g, 50 mmol) was gradually added to a stirred and heated (50–60°C) solution of 1-(anthracen-9-ylmethyl)-*N*-(2-chlorophenyl)methanimine (6.32 g, 20 mmol) in 2:1 mixture of EtOH–DMF (50 ml). The mixture was stirred at the same temperature for 1 h, then diluted with hot H_2O (200 ml), and the excess of borohydride was destroyed by adding dilute AcOH. The suspension was cooled to 5–10°C and maintained at that temperature for 4–5 h, the precipitate of *N*-(anthracen-9-ylmethyl)-2-chloroaniline was filtered off and recrystallized from *n*-BuOH. Yield 5.1 g (81%), yellow fine crystalline precipitate, mp 144–145°C. IR spectrum, ν, cm^{-1}: 3261 (NH), 1617 (NH). ^1H NMR spectrum, δ, ppm (*J*, Hz): 3.93 (1H, t, *J* = 5.2, NH); 5.14 (2H, d, *J* = 5.2, CH_2); 7.10–7.21 (2H, m, H Ar); 7.25–7.37 (2H, m, H Ar); 7.46–7.58 (4H, m, H Ar); 8.05 (2H, d, *J* = 9.0, H Ar); 8.20 (1H, d, *J* = 9.0, H Ar); 8.51 (1H, s, H Ar). Found, %: C 79.27; H 5.15; Cl 11.25; N 4.33. $C_{21}H_{16}ClN$. Calculated, %: C 79.36; H 5.07; Cl 11.16; N 4.41.

N-(Anthracen-9-ylmethyl)-2-chloroaniline (4.75 g, 15 mmol) was dissolved in anhydrous toluene (50 ml), then anhydrous pyridine (2.4 ml, 30 mmol) was added; the mixture was vigorously stirred and treated with a solution of freshly distilled chloroacetyl chloride (1.6 ml, 20 mmol) in anhydrous toluene (10 ml). The reaction mixture was refluxed for 2.5–3 h, then cooled to 5°C, the obtained precipitate of pyridine hydrochloride was filtered and washed on filter with toluene (2×5 ml). The filtrate was washed with water (2×20 ml), dried over anhydrous Na_2SO_4, and the solvent was removed at reduced pressure. The residue was recrystallized from *n*-BuOH, giving acetamide **5**. Yield 4.9 g (84%), pale-green coarse-grained crystalline precipitate, mp 157–159°C (*n*-BuOH). IR spectrum, ν, cm^{-1}: 1671 (C=O). ^1H NMR spectrum, δ, ppm (*J*, Hz): 4.07 (2H, s, CH_2); 6.11 (2H, s, CH_2); 7.12–7.25 (2H, m, H Ar); 7.30–7.41 (2H, m, H Ar); 7.50–7.63 (4H, m, H Ar); 8.07 (2H, d, *J* = 8.7, H Ar); 8.23 (2H, d, *J* = 8.7, H Ar); 8.55 (1H, s, H Ar). Found, %: C 70.15; H 4.41; Cl 17.89; N 3.50. $C_{23}H_{17}Cl_2NO$. Calculated, %: C 70.06; H 4.35; Cl 17.98; N 3.55.

Synthesis of acetamides 4, 6c,e (General method). The appropriate amine **1c**,**e**, or **2c** (3.0 mmol) was dissolved in 1,2-dichlorobenzene (10 ml), the solution was heated to 80–90°C and treated with *N*-(anthracen-9-ylmethyl)-2-chloro-*N*-(2-chlorophenyl)acetamide (**5**) (1.30 g, 3.3 mmol) in the case of amines **1c**,**e** or 2-chloro-*N*-(quinolin-8-yl)acetamide (**3**) in the case of amine **2c**. The obtained solution was refluxed for 2 h. The reaction mixture was then cooled,

the precipitate that formed was filtered off and thoroughly washed on filter with anhydrous acetone. The residue was recrystallized from a 4:1 mixture of *n*-BuOH–DMF.

2-[(Anthracen-9-ylmethyl)amino]-1-[2-(diethylamino)-ethyl]-3-[2-oxo-2-(quinolin-8-ylamino)ethyl]-1*H*-benzimidazol-3-ium chloride (4). Yield 1.6 g (82%), light-brown fine crystalline precipitate, mp >240°C (decomp.). IR spectrum, ν, cm^{-1}: 3321, 3212 (NH), 1686 (C=O), 1655 (C=N). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.83 (6H, t, *J* = 6.9, $2CH_3$); 2.65 (2H, t, *J* = 6.3, CH_2); 3.30 (4H, q, *J* = 6.9, $2CH_2$); 4.30 (2H, t, *J* = 6.3, CH_2); 5.41 (2H, s, CH_2); 5.84 (2H, d, *J* = 6.8, CH_2); 7.15–8.05 (13H, m, H Ar, NH); 8.21 (2H, d, *J* = 8.8, H Ar); 8.50 (2H, d, *J* = 8.8, H Ar); 8.74–8.83 (2H, m, H Ar); 8.85–8.92 (1H, m, H Ar); 11.53 (1H, s, NH). Found, %: C 72.90; H 6.04; Cl 5.60; N 13.00. $C_{39}H_{39}ClN_6O$. Calculated, %: C 72.82; H 6.11; Cl 5.51; N 13.07.

2-Amino-3-{2-[(anthracen-9-ylmethyl)(2-chlorophenyl)-amino]-2-oxoethyl}-1-[2-(diethylamino)ethyl]-1*H*-benzimidazol-3-ium chloride (6c). Yield 1.7 g (91%), bright-yellow crystals, mp >220°C (decomp.). IR spectrum, ν, cm^{-1}: 3310, 3194 (NH_2), 1683 (C=O), 1662 (C=N). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.87 (6H, t, *J* = 6.7, $2CH_3$); 2.72 (2H, t, *J* = 6.5, CH_2); 3.41 (4H, q, *J* = 6.7, $2CH_2$); 4.27 (2H, t, *J* = 6.5, CH_2); 4.55 (2H, s, CH_2); 6.15 (2H, s, CH_2); 7.05–7.87 (12H, m, H Ar); 8.14 (2H, d, *J* = 8.7, H Ar); 8.40 (2H, d, *J* = 8.7, H Ar); 8.68 (1H, s, H Ar); 9.88 (2H, s, NH_2). Found, %: C 68.92; H 6.03; Cl 11.37; N 11.25. $C_{36}H_{37}Cl_2N_5O$. Calculated, %: C 69.00; H 5.95; Cl 11.31; N 11.18.

2-Amino-3-{2-[(anthracen-9-ylmethyl)(2-chlorophenyl)-amino]-2-oxoethyl}-1-[3-(dimethylamino)propyl]-1*H*-benzimidazol-3-ium chloride (6e). Yield 1.6 g (89%), orange-red crystals, mp >200°C (decomp.). IR spectrum, ν, cm^{-1}: 3294, 3178 (NH_2), 1680 (C=O), 1652 (C=N). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.48 (6H, s, $2CH_3$); 1.58–1.73 (4H, m, $2CH_2$); 4.01 (2H, t, *J* = 6.5, CH_2); 4.65 (2H, s, CH_2); 6.08 (2H, d, *J* = 5.3, CH_2); 7.12–7.95 (12H, m, H Ar); 8.24 (2H, d, *J* = 8.5, H Ar); 8.48 (2H, d, *J* = 8.5, H Ar); 8.57 (1H, s, H Ar); 10.11 (2H, s, NH_2). Found, %: C 68.70; H 5.83; Cl 11.49; N 11.37. $C_{35}H_{35}Cl_2N_5O$. Calculated, %: C 68.62; H 5.76; Cl 11.57; N 11.43.

Quantum-chemical calculations were performed using the Gaussian 09 program[11] with a method based on the density functional theory, using B3LYP/6-31G(d,p) basis set.[12] In order to identify stationary points on the potential energy surface (PEC), full geometry optimization of the molecular structures was performed with calculation of force constants. The structures representing energy minima on PES were found by the steepest descent method (along gradient lines) from the saddle point to the adjacent stationary point (saddle point or minimum).[13] The solvent effects were accounted for by performing single-point geometry calculations based on optimization in gas phase, using the polarizable continuum model (IEFPCM).[14]

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