Dual reactivity of diazonium salts derived from 1-amino-2-ethynyl-9,10-anthraquinones

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Diazotization of vicinal 1-amino-2-ethynyl-4-R-9,10-anthraquinones followed by a reaction with NaN_3 gave 5-hydroxy-3-R-1*H*-naphtho[2,3-*g*]indazole-6,11-diones or 3-ethynyl-5-R-6*H*-anthra[1,9-*cd*]isoxazol-6-ones, depending on the substituents at the triply bonded C atom and in position 4 of the anthraquinone framework.

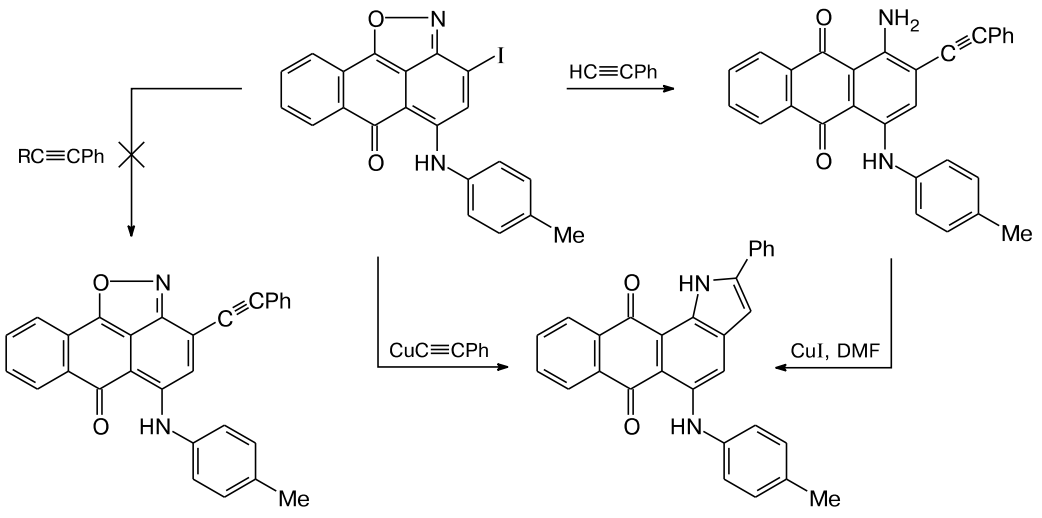
Key words: diazotization, heterocyclization, naphthoindazoles, anthraisoxazoles.

Preparation of hybrid molecules combining two (or more) structural elements is one of the leading trends in modern organic chemistry. Such natural and synthetic conjugates often exhibit high biological activity. Ethynyl fragments are common structural elements in such compounds since many natural metabolites with a triple bond show high antitumor activity.[1—3] In addition, high cytotoxicity against various types of tumors has been found[4] in fused anthraquinonoid rings capable of being inserted into the DNA chain. It has been demonstrated that compounds combining ethynyl and anthraquinone fragments are promising for these purposes.[5,6]

Earlier,[7] our attempted synthesis of ethynylisoxazolanthrones from appropriate 3-haloisoxazolanthrones and 1-alkynes or their copper salts has failed. Instead of the expected products, we obtained 1-amino-2-(phenylethynyl)-9,10-anthraquinones in reactions with HC≡CPh for the cross-coupling is accompanied by ring opening and naphtho[2,3-*g*]indole-6,11-diones in reactions with CuC≡CPh because of recyclization of an intermediate amine (Scheme 1).

The recently proposed[8] synthetic route to the target alkynylisoxazoles involves the preparation of vicinal 1-amino-2-ethynyl-9,10-anthraquinones, their diazotiza-

Scheme 1



R = Cu or H

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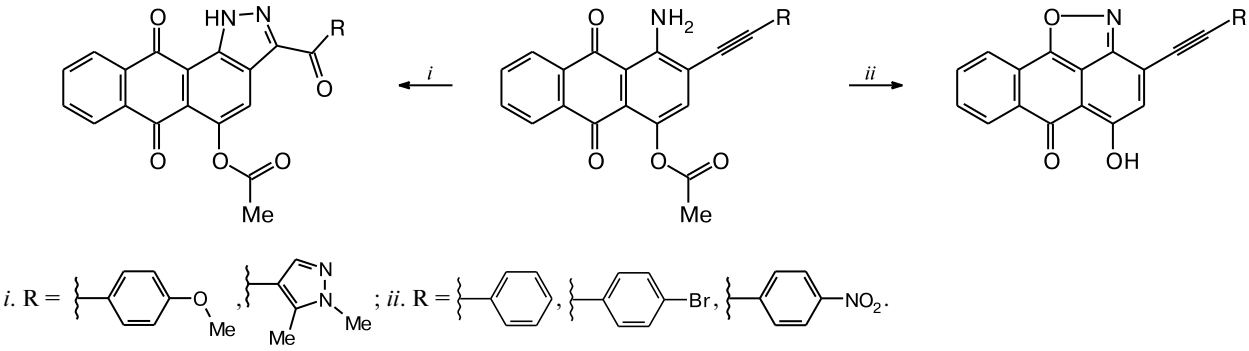
Scheme 2



tion, and closure of the isoxazole ring (Scheme 2). However, this reaction can also follow two pathways, depending on the substituent at the triply bonded C atom. When the substituent is an electron acceptor, the reaction follows pathway (*ii*) leading to the target ethynylisoxazoles, while the presence of an electron donor favors the formation of fused anthrapyrazoles (pathway *i*).

As a next step in our investigations, as well as for revealing general features and/or limitations of these reactions, we synthesized a number of the starting vicinal 1-amino-2-ethynyl-9,10-anthraquinones in which the ethynyl fragment bears an electron-withdrawing, electron-donating, or no substituent at all (Scheme 3). In addition, the substituent in position 4 of the anthraquinone framework was also varied (NHAr, OH) in the starting compounds.

Prepared 1-amino-4-hydroxy-2-[(trimethylsilyl)ethynyl]-9,10-anthraquinone (**1**) was decomposed with K_2CO_3 in methanol to 2-ethynyl-9,10-anthraquinone **2b**. Since the substrates with the protected OH group (**3a**—**c**) proved to undergo smoother diazotization than amines **2a**—**c**, the hydroxyl group in the latter was selectively protected by acylation with Ac_2O in pyridine prior to diazotization.[9]

Diazotization of aminoanthraquinones **3a**,**b** with nitrosylsulfuric acid for 15 min gave diazonium salts, which were treated with a solution of NaN_3 at room temperature and kept for 5 h. The yields of crude 1-azido-9,10-anthraquinones **4a**,**b** were 88 and 91%, respectively (Scheme 4).

The crude azides were employed in further transformations, regardless of some content of isoxazolanthrone as a result of N_2 elimination and O—N bond formation.

Scheme 3

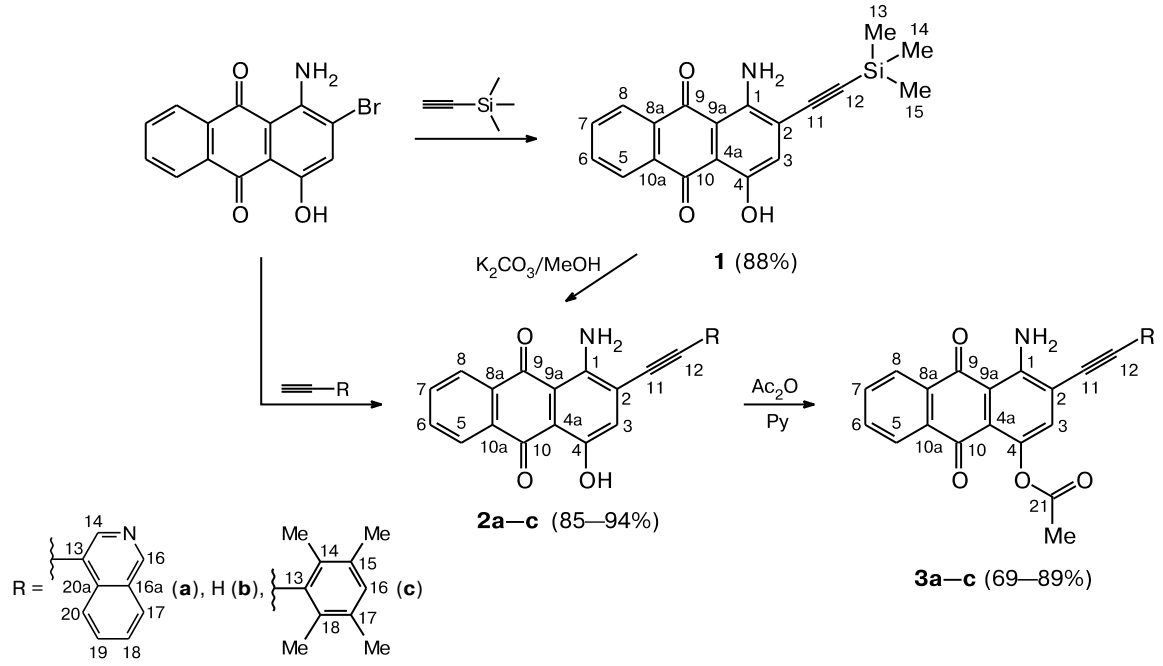
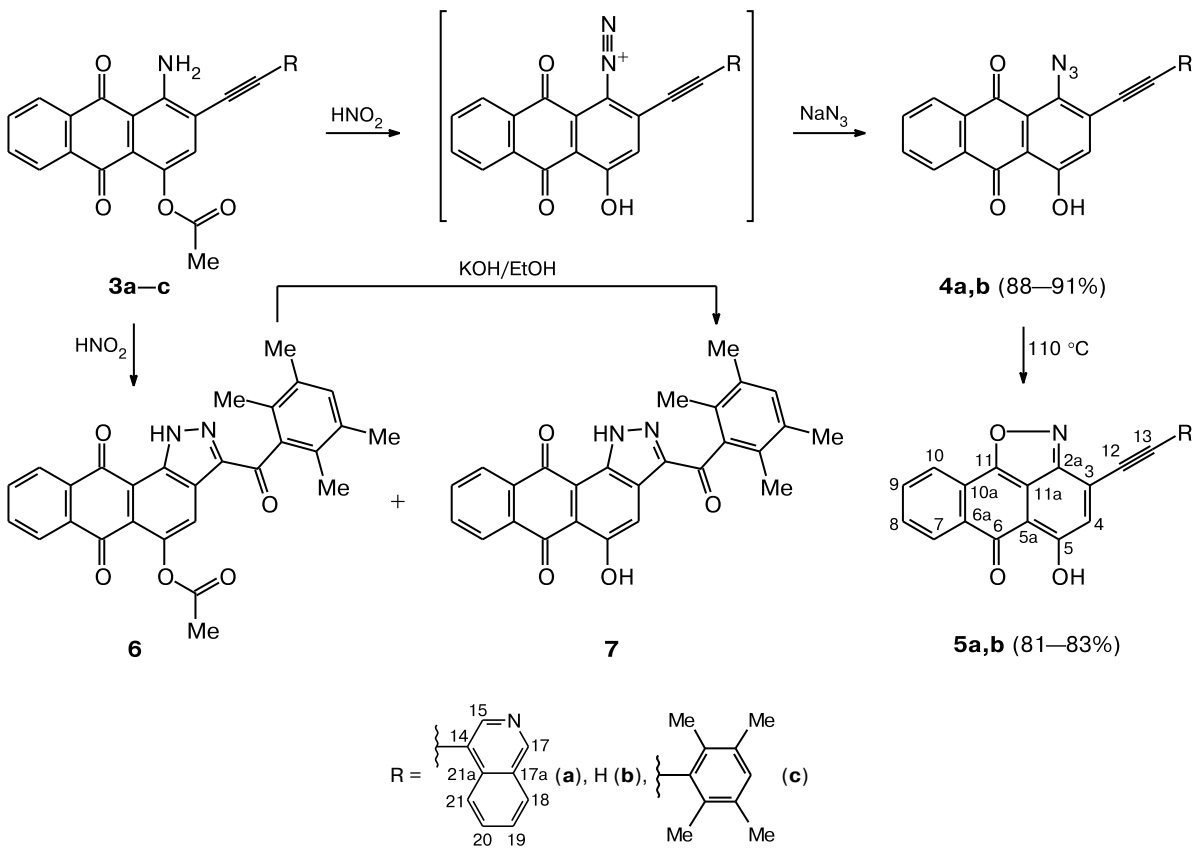


Схема 4



Attempted purification of these compounds only increased the amount of the cyclization products. Note that the acyl protection was removed from the hydroxyl group during the diazotization.

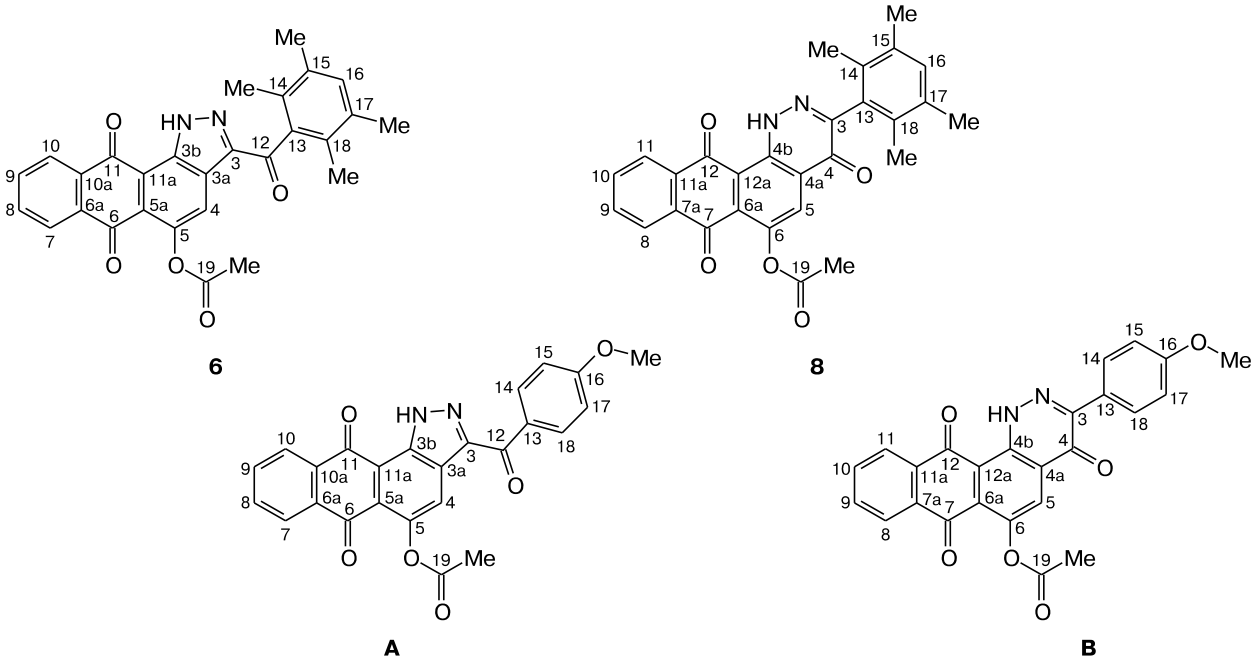
Cyclization of vicinal ethynyl-containing azides **4a**,**b** was carried out in boiling toluene for 0.5—3 h; the yields of the target ethynylisoxazolanthrones **5a** and **5b** were 81 and 83%, respectively. Therefore, the reaction involves the azido and carbonyl groups of 9,10-anthraquinones, the alkynyl substituent in position 2 remaining intact.

The diazotization of aminoanthraquinone **3c** containing an electron-donating group at the triple bond occurred in a different way, giving cyclization products **6** and **7** (10 : 1, ^{1}H NMR) rather than diazonium salts. Free phenol **7** is formed by partial deacylation of *O*-acetyl derivative **6**. The overall yield of compound **6** (as if no deacylation occurred) was 80% (see Scheme 4). Hydrolysis of the mixture of compounds **6** and **7** with KOH in ethanol gave phenol **7** in the individual state (76% yield).

Since vicinal ethynyl-containing diazonium salts can undergo cyclization according to both the 5-*exo*-*dig* and 6-*endo*-*dig* patterns,[8,10] we used calculational and experimental methods to prove the structure of compound **6**.

Earlier,[8] we have demonstrated that methoxy derivative **A**, a product of a similar diazotization—cyclization sequence and a close structural analog to compound **6**, contains a five-membered fused heterocycle rather than a six-membered ring as in structure **B**. This conclusion was drawn from the HMBC spectra revealing couplings between the C(12) atom and the H(14) and H(18) protons but no coupling between the C(12) atom and the H(4) proton.[8] For structure **B** containing a new six-membered ring formed, the reverse spectral pattern would be very likely, with the C(4) atom coupling with the H(5) proton but not coupling with the H(14) and H(18) protons.

Since the chemical shifts of analogous signals in the ^{1}H and ^{13}C NMR spectra of compounds **6** and **A** have close values and the structure of derivative **A** is proved, we concluded that the cyclization of the diazonium salt derived from amine **3c** leads to a five-membered rather than six-membered ring. Otherwise, greater differences between the corresponding chemical shifts could be expected. This conclusion was confirmed by DFT/PBE/λ22 quantum chemical calculations[11—14] of the ^{13}C and ^{1}H NMR chemical shifts. The calculated δ value for C(12) (201.63) in compound **6** containing the five-membered ring agrees



6 **8** **A** **B**

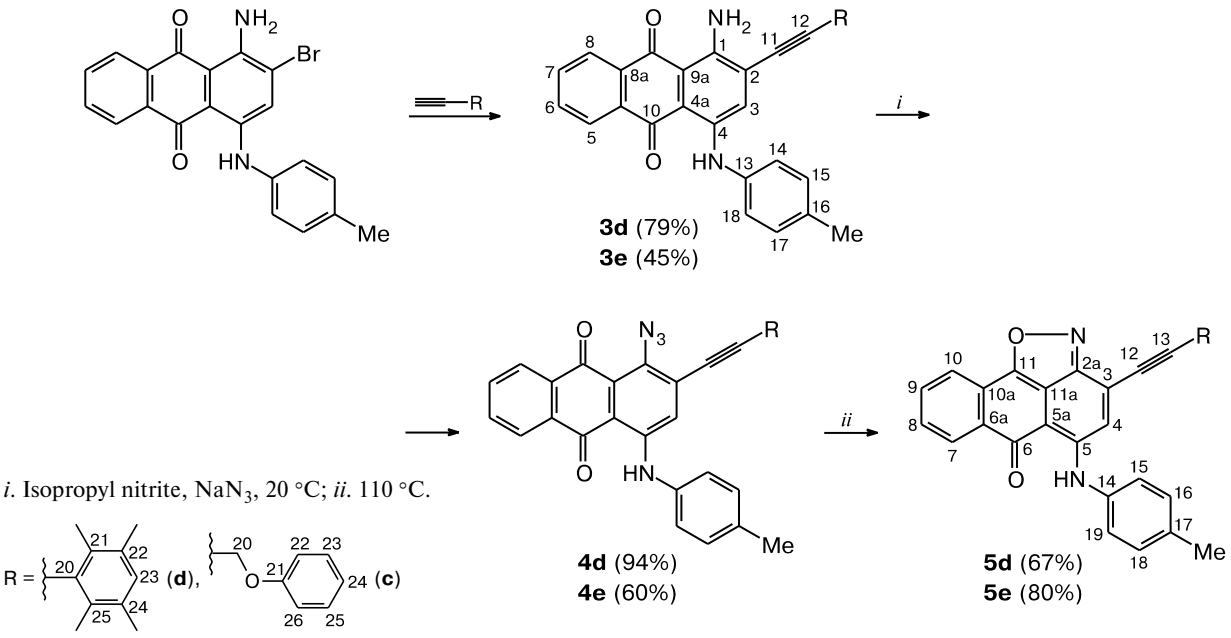
well with experimental data (δ 195.83). This value differs substantially from δ 166.55 for C(4) in plausible structure **8** with the six-membered ring.

To find out whether the outcome of the diazotization depends on the substituent in position 4 of the anthraquinone framework, we diazotized a *p*-toluidine analog (**3d**) of the durene derivative **3c**.

Diazotization of *p*-toluidine-containing derivatives with nitrosylsulfuric acid was accompanied by the formation of by-products, with decreasing yields of the target products. Earlier,[8] it has been noted that the diazotizating agent influences the reaction time, the reaction pathway remaining unchanged. That is why we carried out the diazotization with isopropyl nitrite at 50 °C for 2 h (Scheme 5). Treatment of a solution of the corresponding diazonium salt with NaN_3 gave 1-azidoanthraquinone **4d** in 94% yield.

A room-temperature reaction of isopropyl nitrite in glacial AcOH with amine **3e** for 1 h produced a solution of

Scheme 5



3d (79%)
3e (45%)
4d (94%)
4e (60%)
5d (67%)
5e (80%)

i. Isopropyl nitrite, NaN_3, 20 °C; *ii*. 110 °C.

R = (**d**), (**c**)

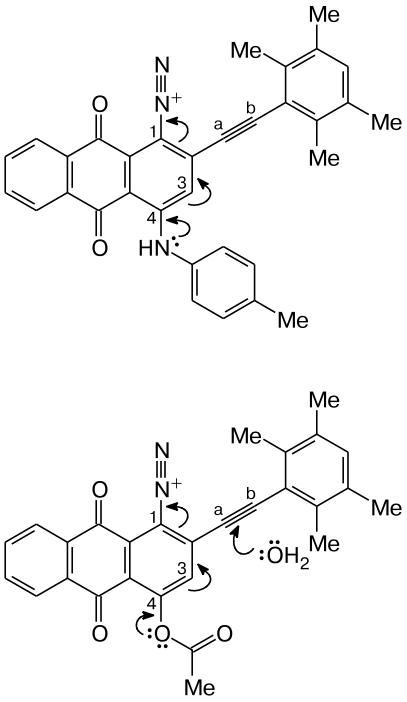


Fig. 1. Effect of the electron-donating substituent on the electron density of the alkyne fragment.

the corresponding diazonium salt, which was treated with excess NaN_3. The yield of 1-azidoanthraquinone **4e** was 60%. The IR spectra of the compounds obtained contain bands at 1624—1628 and 1660—1662 cm^{-1} (C=O). The bands due to N_3 and C≡C are unresolved for **4e** (2027—2233 cm^{-1}) and appear at 2118 (N_3) and 2194 cm^{-1} (C≡C) for **4d**.

The electron-donating effect of the substituent at the triple bond increases the electron density of the alkyne fragment, thus favoring the cyclization (Fig. 1).

This scenario is true for the formation of compound **6**. However, if the substituent in position 4 of the anthraquinone framework has a stronger +*M* effect (toluidine group), it seems to be sufficient for the stabilization of the diazonium salt, which allows the diazo group to be replaced by an azido group.

Cyclization of azides **4d,e** in boiling toluene for 5—10 min gave compounds **5d,e** in 67 and 80% yields, respectively.

To sum up, the present investigation confirmed our previous results and conclusions that the outcome of the diazotization of 1-amino-2-ethynyl-9,10-anthraquinones depends on the substituents in both the ethynyl and anthraquinone parts of the substrate molecule. The electron-donating substituents (NHAr, OH) in position 4 stabilize the diazonium salt, preventing its electrophilic cyclization by means of the triple bond. This allows replacement of the diazo group by an azido group followed by closure of the isoxazole ring, with the triple bond being intact. This reaction opens up a new route to not easily accessible 3-ethynyl-6*H*-anthra[1,9-*cd*]isoxazol-6-ones. In contrast, a combination of an acyl substituent in position 4 of the anthraquinone framework and an electron-donating substituent at the triple bond leads to 5-acetoxy-3-R-1*H*-naphtho[2,3-*g*]indazole-6,11-diones, products of 5-*exo-dig* cyclization.

Experimental

IR spectra were recorded on a Bruker Vector 22 spectrometer (KBr pellets). NMR spectra were recorded on a Bruker AV 400 spectrometer (400.13 MHz) in $CDCl_3$ and DMSO-d_6. Mass spectra were measured on a Thermo Scientific DFS double-focusing mass spectrometer (Thermo Electron Corporation) (direct inlet probe, ionization chamber temperature 220—270 °C, ionizing voltage 70 eV). For column chromatography, Merck 60 silica gel (0.063—0.2 mm) and Al_2O_3 (Brockmann activity II, 0.05—0.15 mm, Russian specification 6-09-3916-75). The course of the reactions was monitored by TLC on Silufol 60 F254 plates. Trimethylsilylacetylene, 3-phenoxypropyne, Et_3N, $Pd(PPh_3)_2Cl_2$, and CuI (Aldrich) were used as purchased. 4-Ethynylisoquinoline was prepared as described earlier.[15]

1-Amino-4-hydroxy-2-[(trimethylsilyl)ethynyl]-9,10-anthraquinone (1). Trimethylsilylacetylene (4.1 mL, 24 mmol) was added to a solution of 1-amino-2-bromo-4-hydroxy-9,10-anthraquinone[16] (6.36 g, 20 mmol), $Pd(PPh_3)_2Cl_2$ (60 mg), PPh_3 (60 mg), CuI (30 mg), and Et_3N (5 mL) in toluene (150 mL). The reaction mixture was stirred under argon at 43 °C for 10 h. After completion of the reaction, the mixture was cooled and evaporated to dryness. The product was isolated by column chromatography on Al_2O_3 (d = 2.5 cm, h = 1 cm) with toluene as an eluent. The solvent was removed *in vacuo*. Yield 5.91 g (88%), m.p. 144—146 °C (from benzene). ^{1}H NMR ($CDCl_3$), δ: 0.34 (s, 9 H, H(13), H(14), H(15)); 7.33 (s, 1 H, H(3)); 7.73—7.84 (m, 2 H, H(6), H(7)); 8.30—8.36 (m, 2 H, H(5), H(8)); 13.34 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$), δ: 0.33 (C(13), C(14), C(15)); 98.42, 107.00 (C(11), C(12)); 108.84; 113.86; 121.18; 126.27; 126.75; 129.92; 132.67; 132.81; 134.10; 134.64; 146.29 (C(4)); 155.61 (C(1)); 182.79, 187.09 (C(9), C(10)). HRMS, found: m/z 335.0970 $[M]^+$. $C_{19}H_{17}NO_3Si$. Calculated: M = 335.0972. IR, ν/cm^{-1}: 1629 (C=O); 2149 (C≡C); 3433 (NH_2).

1-Amino-4-hydroxy-2-[(isoquinolin-4-yl)ethynyl]-9,10-anthraquinone (2a) was obtained as described for compound **1**. The reaction was carried out at 65 °C for 12 h. Yield 0.67 g (85%), m.p. 281—282 °C (from DMSO). ^{1}H NMR ($CDCl_3$), δ: 7.55 (s, 1 H, H(3)); 7.72—7.90 (m, 4 H, H(17), H(18), H(19), H(20)); 8.07, 8.29 (both d, 1 H each, H(5), H(8), J = 8.3 Hz); 8.34—8.40 (m, 2 H, H(6), H(7)); 8.85, 9.29 (both s, 1 H each, H(14), H(16)); 13.36 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$), δ: 90.29, 95.23 (C(11), C(12)); 114.29; 114.35; 120.85; 124.51; 126.42; 126.91; 127.66; 128.17; 128.23; 129.96; 131.71; 132.76; 133.03; 133.11; 134.30; 134.70; 135.10; 146.09; 147.03; 153.17; 155.69; 183.16, 187.32 (C(9), C(10)). HRMS, found: m/z 390.1000 $[M]^+$. $C_{25}H_{14}N_2O_3$. Calculated: M = 390.0999. IR, ν/cm^{-1}: 1625 (C=O); 2198 (C≡C); 3456 (NH_2).

1-Amino-4-hydroxy-2-[(2,3,5,6-tetramethylphenyl)ethynyl]-9,10-anthraquinone (2c) was obtained as described for compound **1**. The reaction was carried out at 75 °C for 1 h. Yield 0.72 g (94%), m.p. 278—280 °C (from dioxane). ^{1}H NMR ($CDCl_3$),

δ: 2.22 (s, 6 H, C(15)—Me, C(17)—Me); 2.42 (s, 6 H, C(14)—Me, C(18)—Me); 6.94 (br.s, 1 H, H(16)); 7.39 (s, 1 H, H(3)); 7.71—7.81 (m, 2 H, H(6), H(7)); 8.29—8.36 (m, 2 H, H(5), H(8)); 13.43 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$), δ: 17.74 (C(15)—$\underline{C}H_3$, C(17)—$\underline{C}H_3$); 19.74 (C(14)—$\underline{C}H_3$, C(18)—$\underline{C}H_3$); 90.92, 99.90 (C(11), C(12)); 113.55; 121.70; 122.60; 126.31; 126.84; 129.10; 132.73; 132.83; 132.91; 133.70; 134.03; 134.10; 134.81; 136.19; 146.11 (C(4)); 156.12 (C(1)); 183.04, 187.01 (C(9), C(10)). HRMS, found: *m/z* 395.1510 $[M]^+$. $C_{26}H_{21}NO_3$. Calculated: M = 395.1516. IR, ν/cm^{-1}: 1620, 1633 (C=O); 2187 (C≡C); 3460 (NH_2).

1-Amino-2-ethynyl-4-hydroxy-9,10-anthraquinone (2b). Potassium carbonate (0.28 g, 2 mmol) was added to a solution of 1-amino-4-hydroxy-2-[(trimethylsilyl)ethynyl]-9,10-anthraquinone (**1**) (6.7 g, 20 mmol) in MeOH (55 mL). The reaction mixture was stirred at ~20 °C for 3 h and diluted with water (60 mL). The precipitate that formed was filtered off. Yield 4.93 g (93%), m.p. 212—214 °C. ^{1}H NMR (DMSO-d_6), δ: 5.03 (s, 1 H, H(12)); 7.48 (s, 1 H, H(3)); 7.8 (br.s, 2 H, NH_2); 7.85—7.94 (m, 2 H, H(6), H(7)); 8.18—8.24 (m, 2 H, H(5), H(8)); 13.22 (s, 1 H, OH). ^{13}C NMR (DMSO-d_6), δ: 92.80, 108.40 (C(11), C(12)); 114.13; 121.02; 126.59; 127.04; 130.88; 131.99; 132.56; 133.97; 134.76; 135.45; 147.38; 155.08; 182.47, 187.40 (C(9), C(10)). HRMS, found: *m/z* 263.0578 $[M]^+$. $C_{16}H_9NO_3$. Calculated: M = 263.0577. IR, ν/cm^{-1}: 1626 (C=O); 2104 (C≡C); 3278 (≡$\underline{C}$—$\underline{H}$); 3406 (NH_2).

4-Acetoxy-1-amino-2-[(isoquinolin-4-yl)ethynyl]-9,10-anthraquinone (3a). Acetic anhydride (2 mL) was added to a solution of 1-amino-4-hydroxy-2-[(isoquinolin-4-yl)ethynyl]-9,10-anthraquinone (**2a**) (0.67 g, 1.71 mmol) in pyridine (15 mL). The reaction mixture was stirred at 85 °C for 17 h. After completion of the reaction, the mixture was cooled and poured onto ice. The precipitate that formed was filtered off and washed with water and ethanol. The product was isolated by column chromatography on SiO_2 (*d* = 2 cm, *h* = 5 cm) with ethyl acetate as an eluent. The solvent was removed *in vacuo*. Yield 0.63 g (86%), m.p. 288—291 °C (from DMF). ^{1}H NMR ($CDCl_3$), δ: 2.47 (s, 3 H, C(21)Me); 7.50 (s, 1 H, H(3)); 7.68—7.78 (m, 3 H, H(17), H(18), H(19)); 7.75 (t, 1 H, H(6) (or H(7)), *J* = 8.0 Hz); 8.04 (d, 1 H, H(20), *J* = 8.0 Hz); 8.18 (dd, 1 H, H(5) (or H(8)), *J* = 7.1 Hz, *J* = 1.8 Hz); 8.24—8.29 (m, 2 H, H(8) (or H(5)), H(7) (or H(6)); 8.81, 9.26 (both s, 1 H each, H(14), H(16)). ^{13}C NMR ($CDCl_3$), δ: 21.06 (C(21)—$\underline{C}H_3$); 90.12, 95.14 (C(11), C(12)); 113.10; 114.50; 116.51; 124.55; 124.69; 126.58; 126.67; 127.67; 128.15; 128.20; 131.65; 133.44; 133.48; 133.64; 133.83; 133.91; 135.07; 140.22; 146.90 (C(16)); 149.74 (C(1)); 153.04 (C(14)); 170.12 (C(21)); 181.98, 184.93 (C(9), C(10)). HRMS, found: *m/z* 432.1103 $[M]^+$. $C_{27}H_{16}N_2O_4$. Calculated: M = 432.1105. IR, ν/cm^{-1}: 1633, 1660, 1757 (C=O); 2200 (C≡C); 3429 (NH_2).

4-Acetoxy-1-amino-2-ethynyl-9,10-anthraquinone (3b) was obtained from compound **2b** as described for compound **3a**. The reaction was carried out at 55 °C for 3.5 h. Yield 0.49 g (69%), m.p. 295—296 °C (from dioxane). ^{1}H NMR ($CDCl_3$), δ: 2.46 (s, 3 H, C(21)Me); 3.71 (s, 1 H, H(12)); 7.35 (s, 1 H, H(3)); 7.72, 7.77 (both td, 1 H each, H(6), H(7), *J* = 7.5 Hz, *J* = 1.6 Hz); 8.17, 8.27 (both dd, 1 H each, H(5), H(8), *J* = 7.5 Hz, *J* = 1.6 Hz). ^{13}C NMR ($CDCl_3$), δ: 21.02 (C(21)—$\underline{C}H_3$); 87.86, 112.89 (C(11), C(12)); 115.61; 122.18; 124.83; 126.04; 126.54; 126.65; 133.99; 133.63; 133.82; 134.43; 139.85; 150.27 (C(1)); 170.03 (C(21)); 182.02, 184.82 (C(9), C(10)). HRMS, found: *m/z* 305.0686 $[M]^+$. $C_{18}H_{11}NO_4$. Calculated: M = 305.0683. IR, ν/cm^{-1}: 1637, 1664, 1749 (C=O); 2096 (C≡C); 3246 (≡$\underline{C}$—$\underline{H}$); 3473 (NH_2).

4-Acetoxy-1-amino-2-[(2,3,5,6-tetramethylphenyl)ethynyl]-9,10-anthraquinone (3c) was obtained from compound **2c** as described for compound **3a**. The reaction was carried out at 75 °C for 22 h. Yield 0.71 g (89%), m.p. 268—270 °C (from toluene). ^{1}H NMR ($CDCl_3$), δ: 2.22 (s, 6 H, C(15)Me, C(17)Me); 2.45 (s, 6 H, C(14)Me, C(18)Me); 2.45 (s, 3 H, C(21)Me); 6.94 (br.s, 1 H, H(16)); 7.36 (s, 1 H, H(3)); 7.67—7.75 (m, 2 H, H(6), H(7)); 8.15 (d, 1 H, H(5) (or H(8)), *J* = 7.0 Hz); 8.15 (d, 1 H, H(8) (or H(5)), *J* = 7.2 Hz). ^{13}C NMR ($CDCl_3$), δ: 17.92 (C(15)$\underline{C}H_3$, C(17)$\underline{C}H_3$); 19.94 (C(14)$\underline{C}H_3$, C(18)$\underline{C}H_3$); 21.23 (C(21)$\underline{C}H_3$); 90.83, 99.84 (C(11), C(12)); 112.81; 118.38; 121.94; 123.81; 126.63; 126.71; 132.68; 133.20; 133.38; 133.66; 133.77; 133.79; 133.83; 136.17; 140.51; 149.71; 170.27 (C(21)); 182.04, 184.97 (C(9), C(10)). HRMS, found: *m/z* 437.1616 $[M]^+$. $C_{28}H_{23}NO_4$. Calculated: M = 437.1622. IR, ν/cm^{-1}: 1633, 1656, 1764 (C=O); 2189 (C≡C); 3465 (NH_2).

1-Amino-2-[(2,3,5,6-tetramethylphenyl)ethynyl]-4-(*p*-toluidino)-9,10-anthraquinone (3d). 1-Ethynyl-2,3,5,6-tetramethylbenzene (**9**) (0.52 g, 3.3 mmol) was added to a mixture of 1-amino-2-bromo-4-(*p*-toluidino)-9,10-anthraquinone[17] (1.22 g, 3 mmol), $Pd(PPh_3)_2Cl_2$ (10 mg), CuI (10 mg), and Et_3N (2 mL) in toluene (10 mL). The reaction mixture was stirred under argon at 75 °C for 9 h. After completion of the reaction, the mixture was cooled and the precipitate that formed was filtered off and washed with methanol, water, and again methanol. Yield 1.17 g (79%), m.p. 232—234 °C (from toluene). ^{1}H NMR ($CDCl_3$), δ: 2.21 (s, 6 H, C(22)Me, C(24)Me); 2.37 (s, 3 H, C(16)Me); 2.38 (s, 6 H, C(21)Me, C(25)Me); 6.93 (br.s, 1 H, H(23)); 7.16—7.22 (m, 4 H, H(14), H(15), H(17), H(18)); 7.69 (s, 1 H, H(3)); 7.70—7.73 (m, 2 H, H(5), H(8)); 8.31—8.35 (m, 2 H, H(6), H(7)); 12.01 (br.s, 1 H, NH). ^{13}C NMR ($CDCl_3$), δ: 17.79 (C(22)$\underline{C}H_3$, C(24)$\underline{C}H_3$); 19.77 (C(21)$\underline{C}H_3$, C(25)$\underline{C}H_3$); 20.85 (C(16)$\underline{C}H_3$); 91.06, 98.59 (C(11), C(12)); 110.18; 111.32; 121.43; 121.73; 123.66; 126.15; 126.22; 126.28; 130.02; 132.46; 132.49; 132.53; 133.61; 134.05; 134.22; 134.42; 136.10; 136.90; 142.52; 145.48; 183.01, 183.54 (C(9), C(10)). HRMS, found: *m/z* 484.2139 $[M]^+$. $C_{33}H_{28}N_2O_2$. Calculated: M = 484.2145. IR, ν/cm^{-1}: 1614 (C=O); 2187 (C≡C); 3066 (NH); 3456 (NH_2).

1-Amino-2-(3-phenoxyprop-1-ynyl)-4-(*p*-toluidino)-9,10-anthraquinone (3e) was obtained from 1-amino-2-bromo-4-(*p*-toluidino)-9,10-anthraquinone and 3-phenoxypropyne as described for compound **3d**. The reaction was carried out at 55 °C for 3.5 h. Yield 0.62 g (45%), m.p. 215—216 °C (from benzene). ^{1}H NMR ($CDCl_3$), δ: 2.39 (s, 3 H, C(16)Me); 4.98 (s, 2 H, H(20)); 7.01—7.06 (m, 3 H, H(22), H(24), H(26)); 7.14 (d, 2 H, H(14), H(18), *J* = 8.3 Hz); 7.22 (d, 2 H, H(15), H(17), *J* = 8.3 Hz); 7.32—7.36 (m, 2 H, H(23), H(25)); 7.58 (s, 1 H, H(3)); 7.72—7.74 (m, 2 H, H(6), H(7)); 8.32—8.34 (m, 2 H, H(5), H(8)); 11.86 (br.s, 1 H, NH). ^{13}C NMR ($CDCl_3$), δ: 20.86 (C(16)—$\underline{C}H_3$); 56.30 (C(20)); 81.79, 93.76 (C(11), C(12)); 110.17; 111.69; 115.03; 119.28; 121.91; 124.17; 126.19; 126.27; 127.27; 129.55; 130.08; 132.64; 132.67; 133.99; 134.27; 134.57; 136.64; 142.34; 145.49; 157.12; 183.30, 183.54 (C(9), C(10)). HRMS, found: *m/z* 458.16058 $[M]^+$. $C_{30}H_{22}N_2O_3$. Calculated: M = 458.16303. IR, ν/cm^{-1}: 1628 (C=O); 2232 (C≡C); 3058 (NH); 3443 (NH_2).

1-Azido-4-hydroxy-2-[(isoquinolin-4-yl)ethynyl]-9,10-anthraquinone (4a). A solution of $NaNO_2$ (0.1 g, 1.44 mmol) in H_2SO_4 (ρ = 1.84 g cm^{-3}, 1 mL) was added dropwise at ~20 °C to a suspension of 4-acetoxy-1-amino-2-[(isoquinolin-4-yl)ethyn-

yl]-9,10-anthraquinone (**3a**) (0.38 g, 0.9 mmol) in glacial AcOH (5 mL). The reaction mixture was stirred for 15 min. After completion of the reaction, the mixture was diluted with an equal volume of water and then a solution of NaN_3 (0.12 g) in water (2 mL) was added with stirring. The resulting mixture was kept for 5 h. After the reaction was completed, the precipitate that formed was filtered off and washed with water and ethanol. Yield 0.33 g (88%). IR, ν/cm^{-1}: 1631, 1664 (C=O); 2119 (N_3); 2206 (C≡C).

1-Azido-2-ethynyl-4-hydroxy-9,10-anthraquinone (4b) was obtained from compound **3b** as described for compound **4a**. The diazotization time was 15 min; the reaction with NaN_3 was carried out for 5 h. Yield 0.097 g (91%). IR, ν/cm^{-1}: 1633, 1658 (C=O); 2047—2170 (N_3 and C≡C, unresolved lines); 3263 (≡C—H).

1-Azido-2-[(2,3,5,6-tetramethylphenyl)ethynyl]-4-(*p*-toluidino)-9,10-anthraquinone (4d). Isopropyl nitrite (0.1 g, 1.5 mmol) was added dropwise at ~20 °C to a suspension of 1-amino-2-[(2,3,5,6-tetramethylphenyl)ethynyl]-4-(*p*-toluidino)-9,10-anthraquinone (**3d**) (0.38 g, 0.79 mmol) in glacial AcOH (10 mL). Then the reaction mixture was heated to 50 °C and stirred for 2 h. After completion of the reaction, the mixture was diluted with an equal volume of water and filtered. A solution of NaN_3 (0.15 g) in water (2 mL) was added with stirring to the mother liquor and the resulting mixture was kept for 2 h. The precipitate that formed was filtered off and washed with water and ethanol. Yield 0.38 g (94%). IR, ν/cm^{-1}: 1624, 1660 (C=O); 2118 (N_3); 2194 (C≡C).

1-Azido-2-(3-phenoxyprop-1-ynyl)-4-(*p*-toluidino)-9,10-anthraquinone (4e) was obtained from compound **3e** as described for compound **4d**, with the exception that the temperature of the reaction mixture was always maintained at 25 °C. The diazotization time was 55 min; the reaction with NaN_3 was carried out for 2 h. Yield 0.14 g (60%). IR, ν/cm^{-1}: 1628, 1662 (C=O); 2128 (N_3, C≡C).

5-Hydroxy-3-[(isoquinolin-4-yl)ethynyl]-6*H*-anthra[1,9-*cd*]-isoxazol-6-one (5a). A solution of 1-azido-4-hydroxy-2-[(isoquinolin-4-yl)ethynyl]-9,10-anthraquinone (**4a**) (0.33 g, 0.79 mmol) in toluene (3 mL) was refluxed for 3 h. After completion of the reaction, the mixture was cooled. The precipitate that formed was filtered off and washed with ethanol. Yield 0.25 g (81%), m.p. 249—251 °C (from DMSO). ^{1}H NMR ($CDCl_3$), δ: 7.70—7.72 (m, 3 H, H(4), H(19), H(20)); 7.85—7.92 (m, 2 H, H(8), H(9)); 8.08 (d, 1 H, H(18) (or H(21)), *J* = 8.0 Hz); 8.23 (d, 1 H, H(21) (or H(18)), *J* = 8.3 Hz); 8.40 (d, 1 H, H(7) (or H(10)), *J* = 8.3 Hz); 8.49 (d, 1 H, H(10) (or H(7)), *J* = 7.5 Hz); 8.80, 9.26 (both s, 1 H each, H(15), H(17)). HRMS, found: *m/z* 388.0844 [M]$^+$. $C_{25}H_{12}N_2O_3$. Calculated: M = 388.0842. IR, ν/cm^{-1}: 1641, 1683 (C=O); 2202 (C≡C). The ^{13}C NMR spectrum of compound **5a** was not recorded because of its low solubility. Found (%): C, 76.49; H, 3.18; N, 6.38. $C_{25}H_{12}N_2O_3$. Calculated (%): C, 77.31; H, 3.11; N, 7.21.

3-Ethynyl-5-hydroxy-6*H*-anthra[1,9-*cd*]isoxazol-6-one (5b) was obtained from compound **4b** as described for compound **5a**. The reflux time was 25 min. Yield 0.25 g (83%), m.p. 180 °C (decomp.). ^{1}H NMR ($CDCl_3$), δ: 3.84 (s, 1 H, H(13)); 7.18 (s, 1 H, H(4)); 7.77, 7.91 (both td, 1 H each, H(8), H(9), *J* = 8.3 Hz, *J* = 1.3 Hz); 8.32, 8.57 (both d, 1 H each, H(7), H(10), *J* = 8.0 Hz). ^{13}C NMR ($CDCl_3$), δ: 77.23, 89.68 (C(12), C(13)); 104.78; 116.00; 122.83; 123.64; 124.71; 127.25; 128.01; 128.92; 132.72; 137.30; 151.43; 155.96; 167.17; 178.29 (C(6)). HRMS, found: *m/z* 261.0418 [M]$^+$. $C_{16}H_7NO_3$. Calculated: M = 261.0421. IR, ν/cm^{-1}: 1635, 1683 (C=O); 2108 (C≡C); 3265 (≡C—H).

3-[(2,3,5,6-Tetramethylphenyl)ethynyl]-5-(*p*-toluidino)-6*H*-anthra[1,9-*cd*]isoxazol-6-one (5d) was obtained from compound **4d** as described for compound **5a**. The reflux time was 10 min. Yield 0.04 g (67%), m.p. 261—263 °C. ^{1}H NMR ($CDCl_3$), δ: 2.21 (s, 6 H, C(22)Me, C(24)Me); 2.41 (s, 3 H, C(17)Me); 2.46 (s, 6 H, C(21)Me, C(25)Me); 6.95 (br.s, 1 H, H(23)); 7.23—7.25 (m, 2 H, H(16), H(18)); 7.28—7.30 (m, 2 H, H(15), H(19)); 7.56 (s, 1 H, H(4)); 7.63, 7.76 (both t, 1 H each, H(8), H(9), *J* = 7.0 Hz); 8.12, 8.55 (both d, 1 H each, H(7), H(10), *J* = 8.0 Hz); 11.47 (br.s, 1 H, NH). ^{13}C NMR ($CDCl_3$), δ: 17.75 (C(22)CH_3, C(24)CH_3); 19.73 (C(21)CH_3, C(25)CH_3); 21.00 (C(17)CH_3); 91.62, 100.25 (C(12), C(13)); 101.53; 117.15; 121.66; 121.69; 122.16; 124.25; 125.36; 125.65; 128.26; 128.48; 130.31; 132.01; 132.58; 132.85; 133.52; 134.73; 136.61; 137.04; 149.45; 151.63; 156.28; 180.11 (C(6)). HRMS, found: *m/z* 482.1987 [M]$^+$. $C_{33}H_{26}N_2O_2$. Calculated: M = 482.1989. IR, ν/cm^{-1}: 1620, 1672 (C=O); 2194 (C≡C).

3-(3-Phenoxyprop-1-ynyl)-5-(*p*-toluidino)-6*H*-anthra[1,9-*cd*]-isoxazol-6-one (5e) was obtained from compound **4e** as described for compound **5a**. The reflux time was 5 min. Yield 0.1 g (80%), m.p. 196—198 °C (from benzene). ^{1}H NMR ($CDCl_3$), δ: 2.43 (s, 3 H, C(17)Me); 5.01 (s, 2 H, H(20)); 6.99—7.04 (m, 3 H, H(15), H(19), H(24)); 7.22—7.34 (m, 6 H, H(16), H(18), H(22), H(23), H(25), H(26)); 7.53 (s, 1 H, H(4)); 7.66, 7.79 (both t, 1 H each, H(8), H(9), *J* = 8.0 Hz); 8.15, 8.55 (both d, 1 H each, H(7), H(10), *J* = 7.8 Hz); 11.36 (s, 1 H, NH). ^{13}C NMR ($CDCl_3$), δ: 21.12 (C(17)CH_3); 56.64 (C(20)); 81.55, 94.57 (C(12), C(13)); 101.91; 114.97; 117.14; 119.60; 121.79; 122.40; 124.69; 125.47; 128.36; 128.47; 128.83; 129.60; 130.54; 132.35; 132.61; 134.52; 137.08; 149.10; 151.22; 156.67; 157.59; 180.55 (C(6)). HRMS, found: *m/z* 456.1465 [M]$^+$. $C_{30}H_{20}N_2O_3$. Calculated: M = 456.1468. IR, ν/cm^{-1}: 1621, 1675 (C=O); 2211 (C≡C); 3057 (NH).

5-Acetoxy-3-(2,3,5,6-tetramethylbenzoyl)-1*H*-naphtho[2,3-*g*]-indazole-6,11-dione (6). A solution of $NaNO_2$ (0.1 g, 1.5 mmol) in H_2SO_4 (1 mL) was added dropwise at ~20 °C to a suspension of 4-acetoxy-1-amino-2-[(2,3,5,6-tetramethylphenyl)ethynyl]-9,10-anthraquinone (**3c**) (0.44 g, 1 mmol) in glacial AcOH (20 mL). The reaction mixture was stirred for 20 min. After completion of the reaction, the mixture was poured onto ice. The precipitate that formed was filtered off, washed with water and methanol, and dried at 130 °C for 20 min. Yield 0.34 g (80%), m.p. 296—298 °C. ^{1}H NMR (600.30 MHz, DMSO-d_6, 50 °C), δ: 1.96 (s, 6 H, C(14)Me, C(18)Me); 2.23 (s, 6 H, C(15)Me, C(17)Me); 2.47 (s, 3 H, C(19)Me); 7.09 (s, 1 H, H(16)); 7.94—7.97 (m, 2 H, H(9), H(8)); 8.17—8.19 (m, 1 H, H(10) (or H(7))); 8.21—8.23 (m, 1 H, H(7) (or H(10))); 8.44 (s, 1 H, H(4)). ^{13}C NMR (150.96 MHz, DMSO-d_6, 50 °C), δ: 15.88 (C(14)CH_3, C(18)CH_3); 18.84 (C(15)CH_3, C(17)CH_3); 20.77 (C(19)CH_3); 119.49; 122.60 (C(4)); 123.78 (C(5a)); 125.27; 125.87 (C(7), C(10)); 126.74 (C(10), C(7)); 128.99 (C(14), C(18)); 131.44 (C(16)); 131.84 (C(6a) (or C(10a))); 133.18 (C(10a) (or C(6a))); 133.38 (C(15), C(17)); 134.32 (C(8) (or C(9))); 134.71 (C(9) (or C(8))); 135.29 (C(3b)); 140.19 (C(13)); 143.18 (C(3)); 145.01 (C(5)); 169.48 (C(19)); 181.57 (C(11) (or C(6))); 182.79 (C(6) (or C(11))); 195.83 (C(12)). The HMBC experiment was tuned to *J* = 7 Hz. HRMS, found: *m/z* 466.1519 [M]$^+$. $C_{28}H_{22}N_2O_5$. Calculated: M = 466.1523. IR, ν/cm^{-1}: 1616, 1672, 1778 (C=O).

5-Hydroxy-3-(2,3,5,6-tetramethylbenzoyl)-1*H*-naphtho-[2,3-*g*]indazole-6,11-dione (7). 5-Acetoxy-3-(2,3,5,6-tetramethylbenzoyl)-1*H*-naphtho[2,3-*g*]indazole-6,11-dione (**6**) (0.23 g, 0.5 mmol) was added to a stirred solution of KOH (0.4 g, 7 mmol) in ethanol (4 mL). The reaction mixture was kept at ~20 °C for 1 h. After completion of the reaction, the mixture was diluted with water (20 mL) and acidified with HCl. The precipitate that formed was filtered off, washed with water and methanol, dried at 130 °C for 1 h, and purified by column chromatography on SiO_2 (d = 1 cm, h = 3 cm) with CH_2Cl_2 as an eluent. Yield 0.16 g (76%), m.p. 317—318 °C. ^{1}H NMR (DMSO-d_6), δ: 1.91 (s, 6 H, C(14)Me, C(18)Me); 2.19 (s, 6 H, C(15)Me, C(17)Me); 7.06 (s, 1 H, H(16)); 7.97—7.99 (m, 2 H, H(8), H(9)); 8.06 (br.s, 1 H, H(4)); 8.20—8.22, 8.26—8.29 (both m, 1 H each, H(7), H(10)); 12.04 (s, 1 H, NH); 14.48 (s, 1 H, OH). The ^{13}C NMR spectrum of compound **7** was not recorded because of its low solubility. HRMS, found: m/z 424.1414 $[M]^+$. $C_{26}H_{20}N_2O_4$. Calculated: M = 424.1418. IR, ν/cm^{-1}: 1614, 1639 (C=O).

1-Ethynyl-2,3,5,6-tetramethylbenzene (9). A mixture of 2-methyl-4-(2,3,5,6-tetramethylphenyl)but-3-yn-2-ol[18] (4.32 g, 20 mmol) and KOH (1.46 g) was refluxed in anhydrous toluene (50 mL) for 2 h. The final mixture was purified by column chromatography on Al_2O_3 (d = 38 mm, h = 120 mm) and SiO_2 (d = 38 mm, h = 40 mm) with toluene as an eluent (V = 4 L). The solvent was removed *in vacuo*. Yield 1.75 g (55%), m.p. 50—51 °C (from hexane). ^{1}H NMR ($CDCl_3$), δ: 2.28 (s, 6 H, C(3)Me, C(5)Me); 2.45 (s, 6 H, C(2)Me, C(6)Me); 3.53 (s, 1 H, (C≡C)H); 6.99 (s, 1 H, H(4)). ^{13}C NMR ($CDCl_3$), δ: 17.39 (C(3)$\underline{C}H_3$, C(5)$\underline{C}H_3$); 19.76 (C(2)$\underline{C}H_3$, C(6)$\underline{C}H_3$); 82.27 (C≡$\underline{C}$H); 84.35; 122.03; 131.51; 133.20; 136.48. HRMS, found: m/z 158.1091 $[M]^+$. $C_{12}H_{14}$. Calculated: M = 158.1090. IR, ν/cm^{-1}: 2090 (C≡C); 3284 (≡$\underline{C}$—$\underline{H}$).

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