The Reactivity of Aminodiazaphenanthrenes

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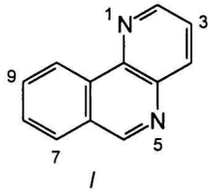
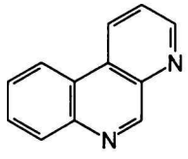
Isomeric 10-amino-1,5-diazaphenanthrene and 7-amino-4,6-diazaphenanthrene were diazotized and the reactivity of diazonium salts was investigated by coupling with aniline and 2-naphthol as well as by reactions with potassium iodide.

Structures of synthesized compounds have been confirmed by ^{1}H NMR and mass spectrometry data.

Azaaromatics are intensively studied due to their chemical reactivity, biological properties, and applications [1—3]. Isomeric 1,5- and 4,6-diazaphenanthrenes (daps) *I* and *II* and related compounds, a topic of our research, deserve attention for their reactivity [4, 5] as well as their antibacterial and antineoplastic properties [6—8].



I



II

The presence of nitrogen atoms in molecule of daps allows formation of complexes with metal ions [9], *N*-oxides [10, 11], and quaternary salts [12, 13]; some quaternary salts are precursors of ylides useful in 1,3-dipolar cycloaddition reactions [14].

RESULTS AND DISCUSSION

In a continuation of our studies of aminodaps *III* and *IV*, concerning their use in the synthesis of four-ring systems [15, 16], in the present work we describe their diazotization and the reactivity of diazonium salts formed.

The diazonium salts *V* and *VI* have been submitted *in situ* to coupling reactions leading to azodiazaphenanthrenes and to the replacement of the diazonium group. Also two acylation reactions of *III* have been made.

We used aniline and 2-naphthol as coupling reagents; the reaction with aniline was carried out in acetic acid and that with 2-naphthol in the sodium hydroxide solution. In these processes azo dyes 1,5-dap-10-azo-4′-aniline *VII*, 1′-(1,5-dap-10-azo)-2′-naphthol *VIII*, 4,6-dap-7-azo-4′-aniline *IX*, and 1′-(4,6-dap-7-azo)-2′-naphthol *X* have been obtained.

As an example of the replacement of diazonium group the reaction of *V* and *VI* with potassium iodide, leading to 10-iodo-1,5-dap *XI* and 7-iodo-4,6-dap *XII*, has been chosen.

Acetylation and benzoylation of *III* afforded 10-acetamido-1,5-dap *XIII* and 10-benzoylamido-4,6-dap *XIV*, respectively; analogous acylations of *IV* have been published earlier [5].

The performed reactions are shown in Scheme 1.

Structures of obtained compounds *VII*—*XIV* have been confirmed by their ^{1}H NMR and MS data as well as by elemental analysis results. Compounds *IX* and *X* have been submitted to biological tests against gram-positive and gram-negative bacteria; results are reported in [8], together with those of related dap derivatives.

The ^{1}H NMR spectra of synthesized compounds were compared with those of the parent daps [6, 17, 18]. The signals of H-9 in *VII* and *VIII* and that of H-8 in *IX* are shifted downfield due to the presence of the azo group; in iododaps the signals of H-9 of *XI* and H-8 of *XII* are shifted upfield. In both acylamino derivatives *XIII* and *XIV*, the result of the electron-donating character of the acetamido and benzamido groups is the upfield shift of signals of H-7 protons.

EXPERIMENTAL

Melting points have been determined on an Electrothermal I A 910 apparatus. Thin-layer chromatography was performed on 60 F 254 (Merck) precoated DC aluminium sheets.

^{1}H NMR spectra have been recorded on a Unity

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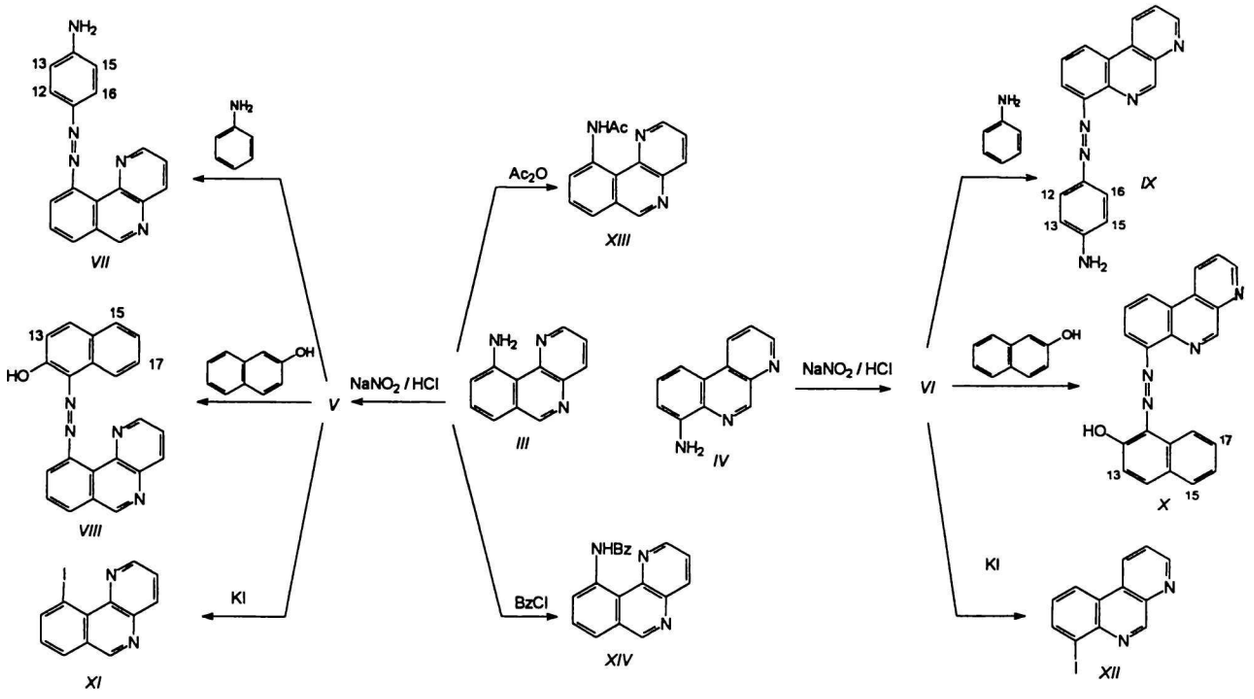

Scheme 1

plus 500 MHz spectrometer in DMSO-d_6, with $SiMe_4$ as internal standard. MS spectra have been registered on an AMD-601 (70 eV) mass spectrometer.

The synthesis of starting aminodaps *III* and *IV* involved the reduction of appropriate nitro derivatives obtained by nitration of daps *I* and *II* [5].

Synthesis of *VII* and *IX*

To *III* or *IV* (1.95 g; 10 mmol) in HCl (1 : 1) (3 cm^3; 5 mmol) at 5—7 °C the solution of $NaNO_2$ (0.69 g; 10 mmol) in water (2 cm^3) was added dropwise. After 10 min stirring the reaction mixture was left for 5 min and the formed *V* or *VI* was treated *in situ* with aniline (0.93 g; 10 mmol) in glacial acetic acid (6 cm^3) at 0 °C, with stirring.

The reaction mixture was left for 10 min and the formed yellow solid was recrystallized from isoamyl alcohol.

VII: Small yellow crystals, m.p. = 76—77 °C, yield 30 %. For $C_{18}H_{13}N_5$ (M_r = 299.34) w_i(found)/% (i): 72.1 (C), 4.3 (H), 23.7 (N); w_i(calc.)/% (i): 72.2 (C), 4.4 (H), 23.4 (N). ^{1}H NMR spectrum, δ: 9.51 (s, 1H, H-6), 9.14 (dd, 1H, $J_{2,3}$ = 4.2 Hz, $J_{2,4}$ = 1.7 Hz, H-2), 9.08 (dd, 1H, $J_{9,8}$ = 7.9 Hz, $J_{9,7}$ = 1.1 Hz, H-9), 8.50 (dd, 1H, $J_{4,3}$ = 8.4 Hz, H-4), 8.34 (dd, 1H, $J_{7,8}$ = 8.4 Hz, H-7), 8.06 (dd, 1H, H-8), 7.97 (dd, 1H, H-3), 7.88 (dd, 2H, $J_{12,13}$ = 8.7 Hz, $J_{12,16}$ = 2.9 Hz, H-12, H-16), 6.62 (dd, 2H, $J_{15,16}$ = 8.7 Hz, $J_{15,13}$ = 2.6 Hz, H-13, H-15), 5.31 (s, 2H, NH_2). Mass spectrum: m/z (I_r/%): 299 (M^+; 30).

IX: Small brown crystals, m.p. = 71—72 °C, yield 15 %. For $C_{18}H_{13}N_5$ (M_r = 299.34) w_i(found)/% (i): 72.0 (C), 4.4 (H), 23.3 (N); w_i(calc.)/% (i): 72.2 (C), 4.4 (H), 23.4 (N). ^{1}H NMR spectrum, δ: 9.38 (s, 1H, H-5), 9.10 (dd, 1H, $J_{3,2}$ = 4.7 Hz, $J_{3,1}$ = 1.8 Hz, H-3), 9.05 (dd, 1H, $J_{1,2}$ = 8.5 Hz, H-1), 8.56 (dd, 1H, $J_{10,9}$ = 7.5 Hz, $J_{10,8}$ = 1.1 Hz, H-10), 7.93 (dd, 1H, $J_{8,9}$ = 7.9 Hz, H-8), 7.90 (dd, 1H, H-9), 7.86 (dd, 1H, H-2), 7.20 (dd, 2H, $J_{12,13}$ = 8.7 Hz, $J_{12,16}$ = 2.8 Hz, H-12, H-16), 7.01 (dd, 2H, $J_{13,15}$ = 2.6 Hz, H-13, H-15), 5.72 (s, 2H, NH_2). Mass spectrum: m/z (I_r/%): 299 (M^+; 52).

Synthesis of *VIII* and *X*

V or *VI* formed from *III* or *IV* (1.95 g; 10 mmol) was treated with the solution of 2-naphthol (1.44 g; 10 mmol) in 20 % NaOH (10 cm^3) at 0 °C. The reaction mixture was left for 12 h, the solid filtered off and recrystallized from ethanol.

VIII: Small red crystals, m.p. = 209—210 °C, yield 60 %. For $C_{22}H_{15}ON_4$ (M_r = 351.39) w_i(found)/% (i): 74.8 (C), 4.3 (H), 15.9 (N); w_i(calc.)/% (i): 75.2 (C), 4.3 (H), 16.0 (N). ^{1}H NMR spectrum, δ: 9.51 (s, 1H, H-6), 9.11 (dd, 1H, $J_{2,3}$ = 4.2 Hz, $J_{2,4}$ = 1.7 Hz, H-2), 9.08 (dd, 1H, $J_{9,8}$ = 7.9 Hz, $J_{9,7}$ = 1.1 Hz, H-9), 8.53 (dd, 1H, $J_{4,3}$ = 8.4 Hz, H-4), 8.33 (dd, 1H, $J_{7,8}$ = 8.4 Hz, H-7), 7.96 (dd, 1H, H-8), 7.88 (dd, 1H, H-3), 7.75 (dd, 1H, $J_{18,17}$ = 7.4 Hz, $J_{18,16}$ = 1.4 Hz, H-18), 7.65 (dd, 1H, $J_{15,16}$ = 8.3 Hz, $J_{15,17}$ = 1.4 Hz, H-15), 7.36 (d, 1H, $J_{14,13}$ = 9.1 Hz, H-14), 7.23 (ddd, 1H, $J_{17,18}$ = 7.4 Hz, $J_{17,16}$ = 7.0 Hz, H-17), 7.12 (ddd, 1H, H-16), 7.10 (d, 1H, H-13), 3.43 (s, 1H, OH). Mass spectrum:

m/z (I_r/%): 351 (M^+; 52).

X: Small red crystals, m.p. = 205—206 °C, yield 51.5 %. For $C_{22}H_{15}ON_4$ (M_r = 351.39) w_i(found)/% (i): 75.2 (C), 4.3 (H), 16.0 (N); w_i(calc.)/% (i): 75.2 (C), 4.3 (H), 16.0 (N). ^{1}H NMR spectrum, δ: 9.33 (s, 1H, H-5), 9.11 (dd, 1H, $J_{3,2}$ = 4.7 Hz, $J_{3,1}$ = 1.8 Hz, H-3), 8.82 (dd, 1H, $J_{1,2}$ = 8.5 Hz, H-1), 8.78 (dd, 1H, $J_{10,9}$ = 7.5 Hz, $J_{10,8}$ = 1.1 Hz, H-10), 8.72 (dd,1H, $J_{8,9}$ = 7.9 Hz, H-8), 8.25 (dd, 1H, H-9), 7.78 (dd, 1H, $J_{2,1}$ = 8.5 Hz, H-2), 7.60 (dd, 1H, $J_{18,17}$ = 7.4 Hz, $J_{18,16}$ = 1.4 Hz, H-18), 7.53 (dd, 1H, $J_{15,16}$ = 8.3 Hz, $J_{15,17}$ = 1.4 Hz, H-15), 7.46 (d, 1H, $J_{14,13}$ = 9.1 Hz, H-14), 7.42 (ddd, 1H, $J_{17,16}$ = 7.0 Hz, H-17), 7.31 (ddd, 1H, H-16), 7.13 (d, 1H, H-13), 3.15 (s, 1H, OH). Mass spectrum: m/z (I_r/%): 351 (M^+; 44).

Synthesis of *XI* and *XII*

V or *VI* formed from *III* or *IV* (1.95 g; 10 mmol) was treated *in situ* with potassium iodide (1.66 g; 10 mmol) at room temperature. The resulting solid was recrystallized from heptane.

XI: Brown crystals, m.p. = 281—282 °C, yield 50.5 %. For $C_{12}H_7N_2I$ w_i(found)/% (i): 47.0 (C), 3.51 (H), 9.2 (N); w_i(calc.)/% (i): 47.1 (C), 2.8 (H), 9.2 (N). ^{1}H NMR spectrum, δ: 9.31 (s, 1H, H-6), 8.96 (dd, 1H, $J_{2,3}$ = 4.2 Hz, $J_{2,4}$ = 1.7 Hz, H-2), 8.54 (dd, 1H, $J_{9,8}$ = 7.9 Hz, $J_{9,7}$ = 1.1 Hz, H-9), 8.35 (dd, 1H, $J_{4,3}$ = 8.4 Hz, H-4), 8.15 (dd, 1H, $J_{7,8}$ = 8.4 Hz, H-7), 8.05 (dd, 1H, H-8), 7.85 (dd, 1H, H-3). Mass spectrum: m/z (I_r/%): 306 (M^+; 70.2).

XII: Brown crystals, m.p. = 295—296 °C, yield 60 %. For $C_{12}H_7N_2I$ (M_r = 306.10) w_i(found)/% (i): 46.9 (C), 3.5 (H), 9.2 (N); w_i(calc.)/% (i): 47.1 (C), 2.8 (H), 9.2 (N). ^{1}H NMR spectrum, δ: 9.80 (s, 1H, H-5), 9.20 (dd, 1H, $J_{3,2}$ = 4.7 Hz, $J_{3,1}$ = 1.8 Hz, H-3), 8.60 (dd, 1H, $J_{1,2}$ = 8.5 Hz, H-1), 8.35 (dd, 1H, $J_{10,9}$ = 7.5 Hz, $J_{10,8}$ = 1.1 Hz, H-10), 8.20 (dd, 1H, $J_{8,9}$ = 7.9 Hz, H-8), 8.00 (dd, 1H, H-9), 7.90 (dd, 1H, H-2). Mass spectrum: m/z (I_r/%): 306 (M^+; 50).

Synthesis of *XIII*

Compound *III* (1.95 g; 10 mmol) was refluxed for 15 min with acetic anhydride (1.10 g; 10 mmol) and pyridine (7 cm^3). To the cold reaction mixture water (50 cm^3) and 10 % hydrochloric acid (10 cm^3) were added.

The formed solid was filtered off, washed with water and recrystallized from ethanol as *XIII*, small colourless crystals, m.p. = 230—231 °C, yield 70.5 %. For $C_{14}H_{11}ON_3$ (M_r = 237.26) w_i(found)/% (i): 71.0 (C), 4.6 (H), 17.8 (N); w_i(calc.)/% (i): 70.9 (C), 4.7 (H), 17.7 (N). ^{1}H NMR spectrum, δ: 9.38 (s, 1H, H-6), 9.10 (dd, 1H, $J_{2,3}$ = 4.2 Hz, $J_{2,4}$ = 1.7 Hz, H-2), 9.05 (dd, 1H, $J_{9,8}$ = 7.9 Hz, $J_{9,7}$ = 1.1 Hz, H-9), 8.57 (dd, 1H, $J_{4,3}$ = 8.4 Hz, H-4), 7.93 (dd, 1H, $J_{7,8}$ = 8.4 Hz, H-7), 7.84—7.90 (m, 2H, H-3, H-8), 3.39 (s, 1H, NH), 2.50 (s, 3H, CH_3). Mass spectrum: m/z (I_r/%): 237 (M^+; 75.8).

Synthesis of *XIV*

To a solution of *III* (1.95 g; 10 mmol) in anhydrous pyridine (20 cm^3), benzoyl chloride (1.40 g; 10 mmol) was added dropwise and the mixture was heated on a water bath at 60—70 °C for 10 min.

To the cooled mixture water (*ca.* 10 cm^3) was added, the precipitate was filtered off, washed with 10 % hydrochloric acid, followed by water, and recrystallized from heptane as *XIV*, small colourless crystals, m.p. = 270—271 °C, yield 50 %. For $C_{19}H_{13}ON_3$ (M_r = 299.33) w_i(found)/% (i): 75.9 (C), 4.4 (H), 41.8 (N); w_i(calc.)/% (i): 76.2 (C), 4.4 (H), 42.0 (N). ^{1}H NMR spectrum, δ: 9.42 (s, 1H, H-6), 9.34 (dd,1H, $J_{2,3}$ = 4.2 Hz, $J_{2,4}$ = 1.7 Hz, H-2), 9.15 (dd, 1H, $J_{9,8}$ = 7.9 Hz, $J_{9,7}$ = 1.1 Hz, H-9), 8.60 (dd, 1H, $J_{4,3}$ = 8.4 Hz, H-4), 8.18 (dd, 1H, $J_{7,8}$ = 8.4 Hz, H-7), 8.16 (dd, 1H, H-8), 8.00 (dd, 1H, H-3), 7.92 (dd, 2H, $J_{12,13}$ = 7.4 Hz, $J_{12,14}$ = 1.7 Hz, H-12, H-16), 7.60—7.75 (m, 3H, H-13, H-14, H-15), 3.36 (s, 1H, NH). Mass spectrum: m/z (I_r/%): 299 (M^+; 68).

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