

Article

Coupling of 4-Antipyrinyldiazonium Chloride with Hydrazine, Hydrazones and Hydrazides: Convenient Synthesis of Novel 1,5-Hexaazadienes, 1,4-Pentaazadienes and Tetraazenes Incorporating Antipyrine Moiety

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Abstract: Coupling of 4-antipyrinyldiazonium chloride (**2**) with *N,N'*-dimethylhydrazine and hydrazine hydrate afforded 1,6-di(4-antipyrinyl)hexaaza-1,5-dienes. Whereas, coupling of **2** with the appropriate hydrazone or hydrazide gave tetraazenes or 1,4-pentaazadienes, depending on the molar ratio of the reactants. Diazotization of isonicotinic acid hydrazide followed by coupling with antipyrine and 4-aminoantipyrine was investigated.

Keywords: 1,5-Hexaazadienes, 1,4-pentaazadienes, tetraazenes, polyaza compounds

1. Introduction

Among various pyrazoline derivatives, antipyrine play an important role in the medicinal and biological applications, and its derivatives are the most frequently studied [1-6]. The literature survey reveals that the antipyrine moiety is an important pharmacophore and exhibits outstanding biological activities such as, antibacterial [7-10], analgesic [11-13], anti-inflammatory [12, 13] and anticancer [3, 14] activities. In addition, a number of 4-triazeno-antipyrines are synthesized by *N*-coupling of 4-antipyrinyldiazonium chloride (**2**) with the appropriate amine [15-18], and are used as reagents for spectrophotometric determination of transition metals and mercury. Whereas, there is no report on the coupling of the diazonium salt **2** with hydrazine or hydrazones and hydrazides.

In the present study, the coupling of 4-antipyrinyldiazonium chloride (**2**) with hydrazine, hydrazones and hydrazides was investigated, as a possible route to the synthesis of some new polyaza compounds such as 1,5-hexaazadienes, 1,4-pentaazadienes and tetraazenes incorporating antipyrine moiety. The new compounds might possess considerable synthetic and pharmaceutical interest.

2. Experimental

2.1. General

All melting points (uncorrected) were determined on a Gallenkamp electric melting point apparatus (Sanyo Gallenkamp, Southborough, UK). Elemental microanalyses were carried out on a Carlo Erba 1108 Elemental Analyzer (Heraeus, Hanau, Germany) at the Microanalytical Unit, Al-Azhar University. Infrared spectra were measured on a Mattson 5000 FTIR spectrometer (Mattson Instruments, Inc., Madison, WI, USA). ^1H NMR data were obtained in CDCl_3 or ($\text{DMSO}-d_6$) solution on a Varian XL 400 MHz instrument (Varian, Inc., CA, USA) using TMS as internal standard. Chemical shifts are reported in ppm (δ) downfield from internal TMS. The mass spectra were recorded on a GC-MS QP-1000 EX Shimadzu instrument (Shimadzu, Tokyo, Japan). The course of the reaction and the purity of the synthesized compounds were monitored by TLC using EM science silica gel coated plates, 0.25 mm, 60 GF 254 (Merck, Darmstadt, Germany) with visualization by irradiation with an ultraviolet lamp. Compounds **11**, **13** and **17** are of limited solubility in common ^1H NMR solvents.

2.2. Synthesis

3,4-Dimethyl-1,6-di(4-antipyrinyl)hexaaza-1,5-diene (**3**)

A cold solution of sodium nitrite (0.36 g, 5.2 mmol; in 3 mL water) was added drop wise to a solution of 4-aminoantipyrine (**1**) (1.02 g, 5 mmol) in concentrated HCl (1.5 mL, and water 5 mL) over 10 min with continuous stirring at 0-5 °C to give the diazonium salt **2**. After 10 minutes, a solution of *N,N'* dimethylhydrazinium dihydrochlorid (0.33 g, 2.5 mmol) and Na_2CO_3 (0.2 g) in water (5 mL) was added drop wise over 10 min. with stirring, to the diazonium salt solution at 0-5 °C. Then the pH is adjusted to 8 by addition of saturated sodium carbonate solution. The reaction mixture diluted with water (20 mL), and stirred for 15 min. at room temperature. The product was filtered, washed with water (3×10 mL), dried and crystallized from ethanol to give **3**. Yield 18%, (dark-red powder), mp 190-192 °C; IR (KBr): $\nu = 1676$ (C=O), 1645, 1590, 1536, 1491, 1402, 1301, 1132, 1019, 746, 695 cm^{-1} ; ^1H -NMR (CDCl_3) $\delta = 2.23$ (s, 6H, $2 \times \text{N-CH}_3$), 2.68 (s, 6H, $2 \times \text{C-CH}_3$), 3.48 (s, 6H, $2 \times \text{N-CH}_3$ of antipyrine), 7.24-7.61 ppm (m, 10H, Ar-H); MS (EI, 70 eV): m/z (%) = 488 (30) $[\text{M}]^+$, 473 (28) $[\text{M-Me}]^+$, 458 (56) $[\text{M-(2Me+H)}]^+$, 445 (32) $[\text{M-(3Me)}]^+$, 411 (35) $[\text{M-Ph}]^+$, 302 (31) $[\text{M-(antipyrinyl ion+H)}]^+$, 243 (13), 216 (36) $[\text{antipyrinyl ion+H}]^+$, 171 (32), 157 (41) $[\text{antipyrinyl ion-(2Me+H)}]^+$, 114 (33) $[\text{M-(2} \times \text{antipyrinyl ion)}]^+$, 110 (34). Anal. calcd

for C₂₄H₂₈N₁₀O₂ (488.56): C 59.00, H 5.78, N 28.67%. Found C 58.98, H 5.73, N 28.60%.

1,6-Di(4-antipyrinyl)-hexaaza-1,5-diene (4)

A solution of the diazonium salt **2** (10 mmol), [prepared from 4-aminoantipyrine (**1**) (2.03 g, 10 mmol), in concentrated HCl (4 mL, and water 10 mL), and sodium nitrite (0.83 g, 10.2 mmol; in 5 mL water) at 0-5 °C], was coupled with a cold solution of hydrazine hydrate (0.25 g, 5 mmol, in ethanol 5 mL). The coupling mixture was stirred at 0-5 °C for 15 min., and the pH is then adjusted to 8 with sodium carbonate solution. The reaction mixture diluted with water (20 mL), and stirred for 15 min. at room temperature. The product filtered, dried and crystallized from ethanol to give **4**. Yield 24%, (pale-yellow powder), mp 170-171 °C; IR (KBr): $\nu = 3486$ (NH), 1676 (C=O), 1644, 1590, 1538, 1491, 1400, 1132, 1102, 1019, 727, 695 cm⁻¹; ¹H-NMR (CDCl₃) $\delta = 2.24$ (br. s, 2H, 2 × NH), 2.43 (s, 6H, 2 × C-CH₃), 3.32 (s, 6H, 2 × N-CH₃ of antipyrine), 7.19-7.56 ppm (m, 10H, Ar-H); MS (EI, 70 eV): m/z (%) = 460 (14) [M]⁺, 459 (28) [M-1]⁺, 457 (20), 456 (35), 430 (37) [M-(2Me+H)]⁺, 384 (17), 365 (34), 354 (42) [M-(2Me+Ph)]⁺, 339 (39) [M-(3Me+Ph)]⁺, 306 (17) [M-(2Ph)]⁺, 279 (100), 276 (20) [M-(2Me+2Ph)]⁺, 272 (55) [M-(antipyrinyl ion+H)]⁺, 229 (19) 173 (52) [antipyrinyl ion-(Me)]⁺, 109 (13) [antipyrinyl ion-(Ph+H)]⁺. Anal. calcd for C₂₂H₂₄N₁₀O₂ (460.49): C 57.38, H 5.25, N 30.42%. Found C 57.31, H 5.20, N 30.39%.

3,4-Di(4-antipyrinylazo)-1,6-di(4-antipyrinyl)hexaaza-1,5-diene (5)

This compound was obtained from the diazonium salt **2** (10 mmol) and hydrazine hydrate (0.13 g, 2.5 mmol, in ethanol 5 mL), in the manner described for the synthesis of **4**. The product crystallized from ethanol. Yield 20%, (pale-yellow powder), mp 200-202 °C; IR (KBr): $\nu = 1675$ (C=O), 1644, 1590, 1537, 1491, 1400, 1296, 1132, 1103, 1019, 766, 695 cm⁻¹; ¹H-NMR (CDCl₃) $\delta = 2.51$ (s, 12H, 4 × C-CH₃), 3.41 (s, 12H, 4 × N-CH₃ of antipyrine), 7.28-7.60 ppm (m, 20H, Ar-H); MS (EI, 70 eV): m/z (%) = 888 (56) [M]⁺, 887 (32) [M-1]⁺, 719 (24) [M-(2Ph)]⁺, 705 (22) [M-(2Me+2Ph)]⁺, 701 (42) [M-(antipyrinyl ion)]⁺, 578 (25), 561 (100), 239 (31), 182 (60), 118 (48), 78 (24). Anal. calcd for C₄₄H₄₄N₁₈O₄ (888.94): C 59.45, H 4.99, N 28.36%. Found C 59.41, H 4.93, N 28.30%.

(4-(Diphenylmethylene)tetraaz-1-enyl)-antipyrine (7)

A solution of **1** (0.5 g, 2.5 mmol) in 2 N HCl (1 mL) was cooled in ice bath at 0-5 °C, and diazotized with sodium nitrite solution (0.18 g, 2.7 mmol; in 2 mL water), with stirring for 15 minutes to give **2**. Then a solution of benzophenone-hydrazone (**6**) (0.49 g, 2.5 mmol) dissolved in ethanol-DMF (2:1) (5 mL), was added over 10 minutes with stirring, to the diazonium salt solution at 0-5 °C, and the pH is then adjusted to 8 with sodium carbonate solution. After dilution with water (20 mL), and stirring for 15 min. at room temperature, the product filtered, dried and crystallized from ethanol to give **7**. Yield 30%, (pale-yellow powder), mp 160-162 °C; IR (KBr): $\nu = 3447$ (NH), 1647 (C=O), 1563, 1488, 1443, 1318, 1177, 1075, 1024, 768, 691 cm⁻¹; ¹H-NMR (CDCl₃) $\delta = 2.55$ (s, 3H, C-CH₃), 3.38 (s, 3H, N-CH₃ of antipyrine), 7.19-7.55 (m,

15H, Ar-*H*), 8.75 ppm (s, 1H, *NH*); MS (EI, 70 eV): m/z (%) = 410 (15) $[M]^+$, 381 (11) $[M-2Me]^+$, 333 (3) $[M-Ph]^+$, 305 (13) $[(M-(2Me+Ph))]^+$, 256 (9) $[M-2Ph]^+$, 224 (26) $[M-(antipyrinyl\ ion)]^+$, 229 (33), 215 (35) $[antipyrinylazo\ ion]^+$, 194 (52) $[M-(antipyrinylazo\ ion)]^+$, 179 (19) $[M-3Ph]^+$, 164 (10) $[M-(Me+3Ph)]^+$, 157 (4) $[antipyrinyl\ ion-(2Me)]^+$, 149 (9) $[M-(2Me+3Ph)]^+$, 110 (37) $[antipyrinyl\ ion-(Ph)]^+$, 94 (36), 97 (100), 79 (93). Anal. calcd for $C_{24}H_{22}N_6O$ (410.48): C 70.23, H 5.40, N 20.47%. Found C 70.20, H 5.38, N 20.41%.

4-(5-(4-Antipyrinyl)-3-(diphenylmethyleamino)-pentaaza-1,4-dienyl)-antipyrine (8)

It was obtained from the diazonium salt **2** (2.5 mmol) and benzophenone-hydrazone (**6**) (0.25 g, 1.25 mmol), in the manner described for the synthesis of compound **7**. The product crystallized from ethanol. Yield 22%, (pale-yellow powder), mp 284-285 °C; IR (KBr): ν = 1660 (C=O), 1591, 1536, 1491, 1410, 1347, 1281, 1153, 1018, 770, 712 cm^{-1} ; 1H -NMR (DMSO- d_6) δ = 2.42 (s, 6H, 2 \times C- CH_3), 3.37 (s, 6H, 2 \times N- CH_3 of antipyrine), 7.18-7.56 ppm (m, 20H, Ar-*H*); MS (EI, 70 eV): m/z (%) = 624 (8) $[M]^+$, 532 (11) $[M-(Me+Ph+H)]^+$, 518 (6) $[M-(2Me+Ph)]^+$, 444 (4) $[M-(Ph_2C=N)]^+$, 435 (5) $[M-(antipyrinyl\ ion+2H)]^+$, 250 (14) $[M-(2 \times antipyrinyl\ ion)]^+$, 227 (34), 192 (70), 175 (86), 147 (61), 137 (100), 120 (70). Anal. calcd for $C_{35}H_{32}N_{10}O_2$ (624.69): C 67.29, H 5.16, N 22.42%. Found C 67.22, H 5.10, N 22.39%.

3-(4-(Antipyrinyl)tetraaz-3-enylidene)-indolin-2-one (10)

A solution of the diazonium salt **2** (5 mmol), [prepared from **1** (1.02 g, 5 mmol), in concentrated HCl (3 mL, and water 10 mL), and sodium nitrite (0.36 g, 5.2 mmol; in 5 mL water) at 0-5 °C], was coupled with a cold solution of 3-hydrazoneindolin-2-one (**9**) [19] (0.8 g, 5 mmol) dissolved in ethanol-DMF (1:1) (5 mL). The coupling mixture was stirred at 0-5 °C for 15 min., and the pH adjusted to 8 with sodium carbonate solution. The coupling mixture diluted with water (20 mL), and stirred for 20 min. at room temperature. The product filtered, dried and crystallized from ethanol to give **10**. Yield 45%, (dark brown powder), mp 180-182 °C; IR (KBr): ν = 3450 (NH), 3357 (NH), 1683 (C=O), 1659 (C=O), 1590, 1550, 1463, 1344, 1193, 977, 748, 676 cm^{-1} ; 1H -NMR (DMSO- d_6) δ = 2.65 (s, 3H, C- CH_3), 3.36 (s, 3H, N- CH_3 of antipyrine), 6.68-7.36 (m, 9H, Ar-*H*), 9.55 (s, 1H, *NH*), 10.38 ppm (s, 1H, *NH* of indolin-2-one); MS (EI, 70 eV): m/z (%) = 375 (10) $[M]^+$, 374 (6) $[M-1]^+$, 372 (3) $[M-2]^+$, 215 (10) $[antipyrinylazo\ ion]^+$, 189 (6), 187 (11) $[antipyrinyl\ ion]^+$, 157 (8) $[antipyrinyl\ ion-(2Me)]^+$, 162 (12) $[M-(antipyrinylazo\ ion)]^+$, 145 (7), 116 (15), 104 (46), 95 (9) $[antipyrinyl\ ion-(Me+Ph)]^+$, 77 (48) $[Ph]^+$. Anal. calcd for $C_{19}H_{17}N_7O_2$ (375.38): C 60.79, H 4.56, N 26.12%. Found C 60.73, H 4.52, N 26.07%.

4,4'-(3-(2-Oxoindolin-3-ylideneamino)pentaaza-1,4-diene-1,5-diyl)bis(antipyrine) (11)

This compound was obtained from the diazonium salt **2** (5 mmol) and 3-hydrazoneindolin-2-one (**9**) (0.4 g, 2.5 mmol), in the manner described for the synthesis of compound **10**. The product crystallized from ethanol. Yield 36%, (dark buff powder), mp 295-296 °C; IR (KBr): ν = 3438 (NH), 1730 (C=O), 1614

(C=O), 1462, 1338, 1205, 1157, 1099, 794, 687 cm^{-1} ; MS (EI, 70 eV): m/z (%) = 591 (18) $[\text{M}+2]^+$, 589 (15) $[\text{M}]^+$, 562 (52) $[(\text{M}-2\text{Me})]^+$, 543 (20) $[(\text{M}-3\text{Me})]^+$, 513 (13) $[(\text{M}-\text{Ph})]^+$, 497 (23) $[\text{M}-(\text{Me}+\text{Ph})]^+$, 435 (32) $[\text{M}-2\text{Ph}]^+$, 420 (6) $[\text{M}-(\text{Me}+2\text{Ph})]^+$, 400 (23) $[\text{M}-(\text{antipyrinyl ion}+2\text{H})]^+$, 373 (44) $[\text{M}-(\text{antipyrinylazo ion}+\text{H})]^+$, 186 (32) $[\text{antipyrinyl ion}-(\text{H})]^+$, 189 (38), 145 (18), 172 (37) $[\text{antipyrinyl ion}-(\text{Me})]^+$. Anal. calcd for $\text{C}_{30}\text{H}_{27}\text{N}_{11}\text{O}_3$ (589.61): C 61.11, H 4.62, N 26.13%. Found C 61.03, H 4.60, N 26.11%.

Synthesis of compounds 12 and 13

These compounds were obtained by coupling the diazonium salt **2** (3.4 mmol) with a cold solution of semicarbazide hydrochloride (0.37 g, 3.4 mmol) and Na_2CO_3 (0.4 g) in water (5 mL) or (0.19 g, 1.7 mmol) and Na_2CO_3 (0.2 g) in water (5 mL), with stirring at 0-5 $^\circ\text{C}$, following the same procedure as described for compound **10**. Crystallization of the product from ethanol gave compounds **12** and **13**, respectively.

4-(Antipyrinyl)tetraaz-3-ene-1-carboxamide (12)

Yield 20%, (brown crystals), mp 176-178 $^\circ\text{C}$; IR (KBr): ν = 3485, 3335 (NH, NH_2), 3263, 1730 (C=O), 1655 (C=O), 1591, 1494, 1395, 1315, 1189, 1130, 925, 769 cm^{-1} ; $^1\text{H-NMR}$ (CDCl_3) δ = 2.66 (s, 3H, C- CH_3), 3.11 (s, 1H, N=N-NH), 3.36 (s, 3H, N- CH_3 of antipyrine), 7.18-7.48 (m, 5H, Ar-H), 7.52 (s, 2H, CONH_2), 7.92 ppm (s, 1H, CONH); MS (EI, 70 eV): m/z (%) = 290 (9) $[\text{M}+1]^+$, 289 (11) $[\text{M}]^+$, 288 (2) $[\text{M}-2]^+$, 279 (31), 265 (48), 245 (25) $[\text{M}-(\text{CONH}_2)]^+$, 230 (11) $[\text{M}-(\text{NHCONH}_2)]^+$, 216 (23) $[\text{antipyrinylazo ion}+\text{H}]^+$, 185 (65) $[\text{antipyrinyl ion}-(2\text{H})]^+$, 78 (28), 74 (38) $[\text{NHNHCONH}_2]^+$, 73 (82), 72 (49), 59 (15) $[\text{NHCONH}_2]^+$. Anal. calcd for $\text{C}_{12}\text{H}_{15}\text{N}_7\text{O}_2$ (289.29): C 49.82, H 5.23, N 33.89%. Found C 49.79, H 5.20, N 33.82%.

4-(Antipyrin-4-yl)-2-((antipyrin-4-yl)diazenyl)tetraaz-3-ene-1-carboxamide (13)

Yield 20%, (pale-brown powder), mp 168-169 $^\circ\text{C}$; IR (KBr): ν = 3449, 3336 (NH, NH_2), 1721 (C=O), 1646 (C=O), 1590, 1494, 1398, 1313, 1130, 768, 701 cm^{-1} ; MS (EI, 70 eV): m/z (%) = 503 (22) $[\text{M}]^+$, 487 (9) $[\text{M}-\text{NH}_2]^+$, 458 (11) $[\text{M}-\text{CONH}_2]^+$, 399 (32), 351 (14), 370 (66), 367 (22), 288 (11) $[\text{M}-(\text{antipyrinylazo ion})]^+$, 278 (84), 215 (34) $[\text{antipyrinylazo ion}]^+$, 189 (100) $[\text{antipyrinyl ion}+2\text{H}]^+$. Anal. calcd for $\text{C}_{23}\text{H}_{25}\text{N}_{11}\text{O}_3$ (503.52): C 54.86, H 5.00, N 30.60%. Found C 54.82, H 4.97, N 30.56%.

4,4'-(3-(Isonicotinamido)pentaaza-1,4-diene-1,5-diyl)bis(antipyrine) (15)

This compound was obtained by coupling the diazonium salt **2** (5 mmol) with a cold solution of isonicotinic acid hydrazide (**14**) (0.35 g, 2.5 mmol), dissolved in ethanol (5 mL), with stirring at 0-5 $^\circ\text{C}$, following the procedure described for compound **10**. Crystallization of the product from ethanol gave **15**. Yield 35%, (buff powder), mp 208-210 $^\circ\text{C}$; IR (KBr): ν = 3486 (NH), 1676 (C=O), 1646 (C=O), 1591, 1537, 1492, 1399, 1296, 1131, 1020, 766, 696 cm^{-1} ; $^1\text{H-NMR}$ (CDCl_3) δ = 2.68 (s, 6H, 2 \times C- CH_3), 3.14 (s, 6H,

2 × N-CH₃ of antipyrine), 7.34-7.59 (m, 10H, Ar-H), 7.74 (d, 2H, 3-H, 5-H of pyridine), 7.95 (br. s, 1H, CONH), 8.65 ppm (d, 2H, 2-H, 6-H of pyridine); MS (EI, 70 eV): *m/z* (%) = 565 (7) [M]⁺, 487 (24) [M-pyridinyl ion]⁺, 472 (13) [M-(Me+Ph)]⁺, 350 (1) [M-(antipyrinylazo ion)]⁺, 348 (52), 213 (14) [antipyrinylazo ion-(2H)]⁺, 191 (17) [M-(2 × antipyrinyl ion)]⁺, 95 (14) [antipyrinyl ion-(Me+Ph)]⁺, 77 (34) [Ph]⁺. Anal. calcd for C₂₈H₂₇N₁₁O₃ (565.59): C 59.46, H 4.81, N 27.24%. Found C 59.42, H 4.79, N 27.20%.

Synthesis of compounds 17 and 18

A solution of isonicotinic acid hydrazide (**14**) (0.68 g, 5 mmol), in 2 N HCl (2 mL) was cooled in ice bath at 0-5 °C, and diazotized with sodium nitrite solution (0.36 g, 5.2 mmol; in 2 mL water), with stirring for 15 min. Then a solution of antipyrine (0.94 g, 5 mmol) or 4-aminoantipyrine (1.02 g, 5 mmol) dissolved in ethanol (5 mL), was added over 10 minutes with stirring, to the diazonium salt solution at 0-5 °C, and the pH is then adjusted to 8 with sodium carbonate solution. After dilution with water (20 mL), and stirring for 15 min. at room temperature, the product filtered, dried and crystallized from ethanol to give compounds **17** and **18**.

4-(3-Isonicotinoyltriazene-1-yl)-antipyrine (17)

Yield 30%, (colorless crystals), mp 248-249 °C; IR (KBr): ν = 3429 (NH), 1680 (C=O), 1661 (C=O), 1550, 1494, 1417, 1301, 1226, 1060, 854, 689 cm⁻¹; MS (EI, 70 eV): *m/z* (%) = 338 (28) [M+2]⁺, 336 (11) [M]⁺, 258 (13) [M-(pyridinyl ion)]⁺, 231 (16) [M-(isonicotinoyl ion)]⁺, 120 (100) [isonicotinamido ion-(H)]⁺, 107 (6) [isonicotinoyl ion+H]⁺, 77 (19) [Ph]⁺. Anal. calcd for C₁₇H₁₆N₆O₂ (336.35): C 60.71, H 4.79, N 24.99%. Found C 60.69, H 4.75, N 24.93%.

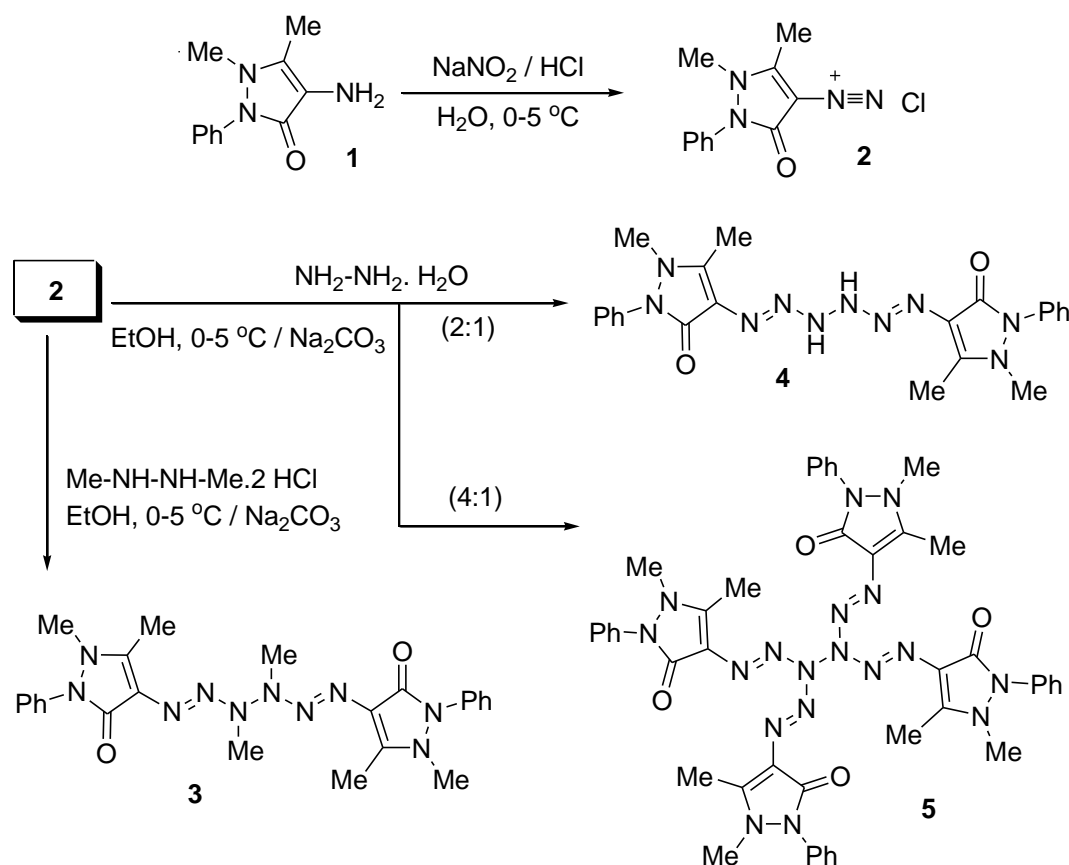
4-(4-Isonicotinoyltetraaz-2-enyl)-antipyrine (18)

Yield 50%, (yellow crystals), mp 270-271 °C; IR (KBr): ν = 3449, 3241 (NH), 1675 (C=O), 1650 (C=O), 1590, 1519, 1486, 1300, 1135, 907, 768, 696 cm⁻¹; ¹H-NMR (CDCl₃) δ = 2.26 (s, 3H, C-CH₃), 2.89 (br. S, 1H, NH), 3.25 (s, 3H, N-CH₃ of antipyrine), 7.28-7.55 ((m, 5H, Ar-H), 7.84 (d, 2H, 3-H, 5-H of pyridine), 8.67 (d, 2H, 2-H, 6-H of pyridine), 9.93 ppm (s, 1H, CONH); MS (EI, 70 eV): *m/z* (%) = 352 (11) [M+1]⁺, 351 (14) [M]⁺, 336 (6) [M-Me]⁺, 275 (23) [M-Ph]⁺, 260 (11) [M-(Me+Ph)]⁺, 258 (12), 197 (44) [M-(Ph+pyridinyl)]⁺, 230 (28) [M-(isonicotinamido ion)]⁺, 202 (29), 187 (15) [antipyrinyl ion]⁺, 189 (56), 120 (10) [isonicotinamido ion-(H)]⁺, 172 (57) [antipyrinyl ion-(Me)]⁺, 170 (100) [antipyrinyl ion-(Me+2H)]⁺, 77 (16) [Ph]⁺. Anal. calcd for C₁₇H₁₇N₇O₂ (351.36): C 58.11, H 4.88, N 27.90%. Found C 58.07, H 4.84, N 27.88%.

3. Results and Discussion

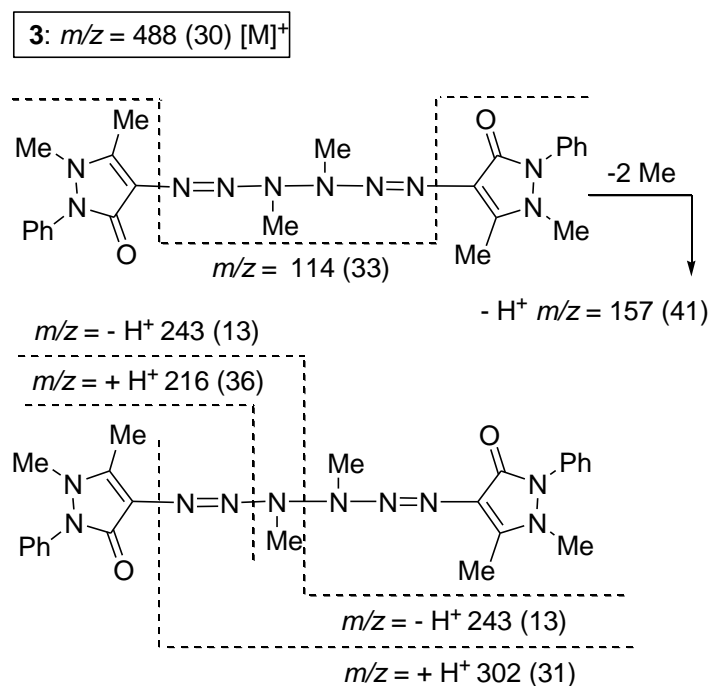
Coupling of 4-antipyrinyldiazonium chloride (**2**) with *N,N'*-dimethylhydrazine gave 3,4-dimethyl-1,6-

di(4-antipyrynyl)hexaaza-1,5-diene (**3**). A similar reaction of **2** with hydrazine hydrate in a molar ratio (2:1) afforded 1,6-di(4-antipyrynyl)-hexaaza-1,5-diene (**4**) (Scheme 1).



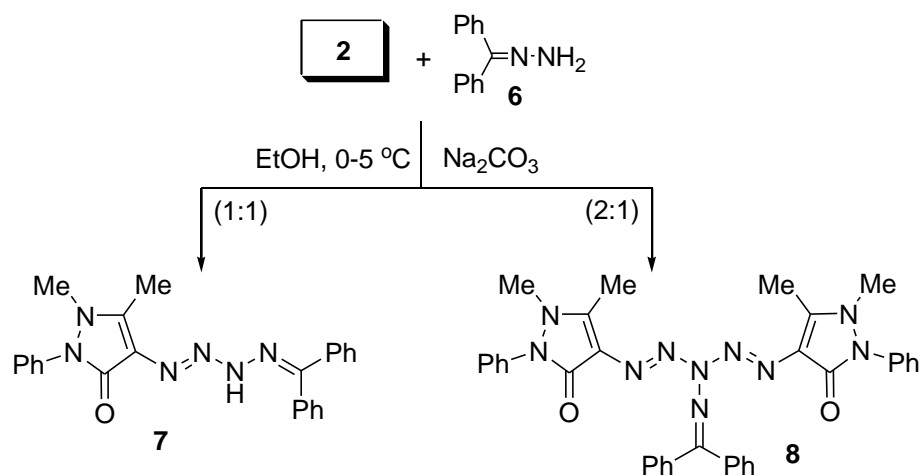
Scheme 1. Coupling of **2** with hydrazine and *N,N'*-dimethylhydrazine

This reaction has also been successfully extended to the synthesis of 3,4-di(4-antipyrynylazo)-1,6-di(4-antipyrynyl)hexaaza-1,5-diene (**5**). The analytical and spectral data provided confirmatory evidence for structures **3-5**. Their mass spectra revealed molecular ion peaks at $m/z = 488$, 460 and 888 , respectively, it underwent fragmentation pattern which supported their structures. The fragmentation pattern of **3** - as an example - is depicted in Scheme 2. The ions at $m/z = 114$ (33%) and 302 (31%) indicated the presence of 3,4-dimethyl-hexaaza-1,5-diene moiety as a structural unit, and the ^1H NMR spectrum supported its structure as it revealed three singlets at $\delta = 2.23$ (6H, $2 \times \text{N-CH}_3$), 2.68 (6H, $2 \times \text{C-CH}_3$), and 3.48 ppm (6H, $2 \times \text{N-CH}_3$ of antipyryne).



Scheme 2. Mass fragmentation pattern of **3**.

In connection with the present study, the coupling reaction between 4-antipyrynyldiazonium chloride (**2**) and hydrazones ($R_2C=N-NH_2$), was investigated as a possible route to tetraazenes and 1,4-pentaazadienes incorporating antipyryne moiety. Thus, coupling of **2** with benzophenone-hydrazone (**6**) afforded (4-(diphenylmethylene)tetraaz-1-enyl)-antipyryne (**7**) (Scheme 3).

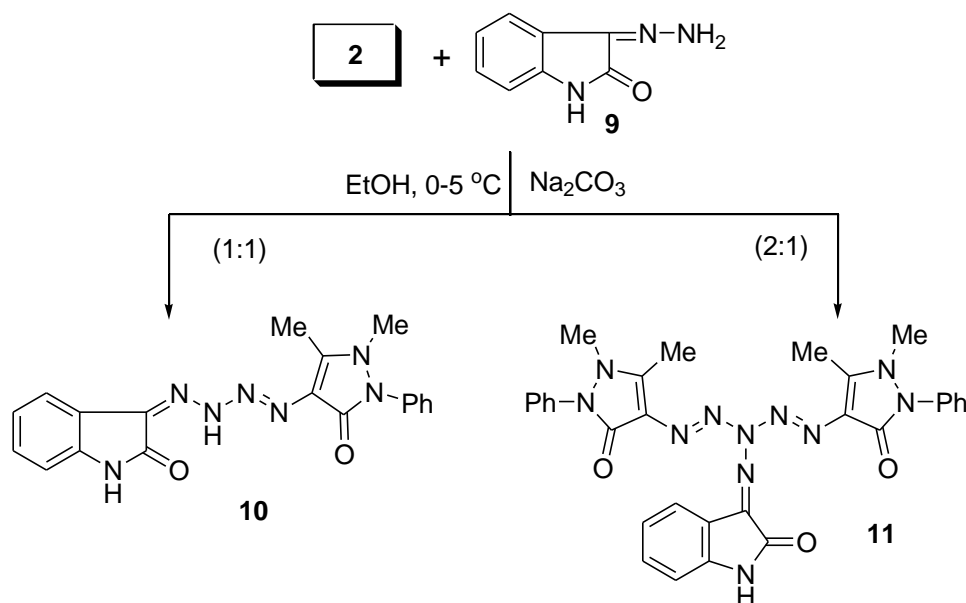


Scheme 3. Coupling of **2** with benzophenone-hydrazone (**6**)

A straightforward access to 4-(5-(4-antipyrynyl)-3-(diphenylmethyleneamino)-pentaaza-1,4-dienyl)-antipyryne (**8**) has been achieved by coupling **2** with the hydrazone **6** in a molar ratio (2:1). This reaction is of particular interest, because no report seems to have appeared in the literature on the coupling

of aryl diazonium salts with hydrazones.

In order to extend the scope of coupling the diazonium salt **2** with hydrazones, and to synthesize tetraazenes and 1,4-pentaazadienes incorporating 2-indolinone and antipyrine moieties, we prepared 3-hydrazoneindolin-2-one (**9**) as previously described [19]. Coupling of **2** with the hydrazone **9**, provides access to 3-(4-(antipyrinyl)tetraaz-3-enylidene)-indolin-2-one (**10**) or 4,4'-(3-(2-oxoindolin-3-ylideneamino)pentaaza-1,4-diene-1,5-diyl)bis(antipyrine) (**11**), depending on the molar ratio of the reactants (Scheme 4). The mass spectra of **10** and **11** contain peaks of the respective molecular ions at $m/z = 375$ (10%) and 589 (15%), and fragmentation patterns which supported their structures.

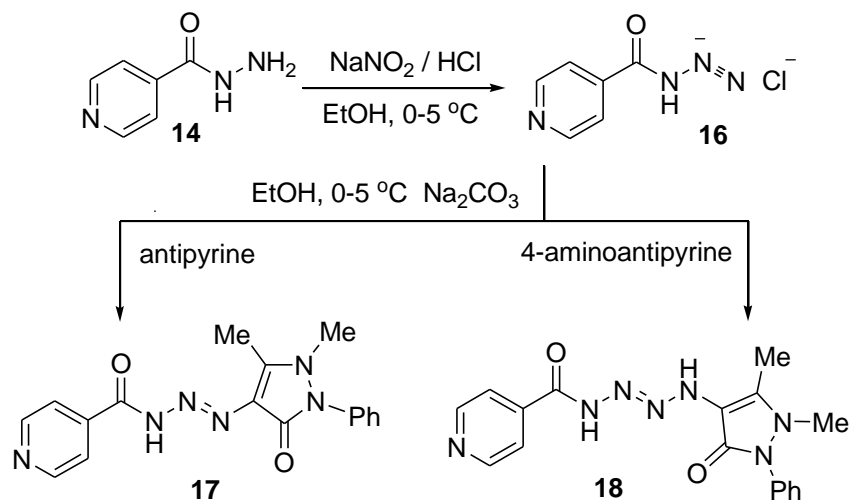


Scheme 4. Synthesis of compounds **10** and **11**.

The formation of **10** and **11** is of interest, because a variety of compounds having 2-indolinone moiety as a structural unit have received significant attention, due to their wide range of biological and pharmaceutical activities [20-23].

In addition, the coupling reaction between 4-antipyrinyldiazonium chloride (**2**) and the appropriate hydrazide, could be valuable in synthesis of functionalized tetraazenes and 1,4-pentaazadienes incorporating antipyrine moiety. In view of that, **2** was treated with semicarbazide hydrochloride in alkaline medium to give 4-(antipyrinyl)tetraaz-3-ene-1-carboxamide (**12**). The same reaction in a molar ratio (2:1) led to the formation of 4-(antipyrin-4-yl)-2-((antipyrin-4-yl)diazenyl)tetraaz-3-ene-1-carboxamide (**13**) (Scheme 5). Confirmatory evidence for structures **12** and **13** was provided by analytical and spectral data.

conceivably function as precursors to 3-acyl-triazenes and 4-acyl-tetrazenes (Scheme 7).



Scheme 7. Synthesis of compounds **17** and **18**

The analytical and spectral data are consistent with the structures proposed for compounds **17** and **18**. Their mass spectra contain peaks of the respective molecular ions at $m/z = 336$ (10%) and 351 (15%), respectively, and fragmentation patterns which supported their structures.

4. Conclusions

A convenient synthetic route to novel polyaza compounds such as 1,5-hexaazadienes, 1,4-pentaazadienes and tetrazenes incorporating antipyrine units has been realized, by coupling of 4-antipyrinyldiazonium chloride with the appropriate hydrazine, hydrazone or hydrazide. In addition, the diazotized hydrazide (**16**) functions as a precursor to the 3-acyl-triazene (**17**) and 4-acyl-tetraazene (**18**). The reactions described in the present study are of particular interest, and of considerable synthetic value in synthesis of polyaza compounds, as numerous diazonium salts could be used in the coupling reaction with hydrazine and its derivatives.

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