CHEMICAL TRANSFORMATIONS OF 3-AMINO-5-HYDROXY-4-PHENYLAZO-1*H*-PYRAZOLE

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Reaction of 3-amino-5-hydroxy-4-phenylazo-1H-pyrazole (**1**) with phenacyl bromide, acetic acid anhydride, benzoyl chloride and aromatic aldehydes gave 3-N-alkylated/acylated derivatives (**2**, **4** and **5**) and the corresponding Schiff bases (**6**), respectively. Ring closure for compound **2** in acetic anhydride afforded pyrazolopyrimidine **3**. Reaction of **1** with acetylacetone, ethyl acetoacetate, ethyl cyanoacetate, diethyl malonate and ninhydrine resulted in pyrazolo[1,5-*a*]pyrimidine-5(*H*)-one (**7**, **8**, **9**), pyrazolo[1,5-*a*]pyrimidine-5,7(1*H*,6*H*))-dione **(10)** and pyrazol-3-ylimino-1H-indene-1,3-(2*H*)-dione (**12**) derivatives. Reaction of active methylene group of (phenyldiazenyl)pyrazolo[1,5-*a*]pyrimidin-5,7(1H,6H)-dione (**10)** with phenyldiazonium chloride gave 2-phenylhydrazono derivative (**11**). Moreover, reaction of **1** with $POCl_3$ and P_2S_5 resulted in 5-chloro (**13**) and 5-mercapto (**15**) derivatives, while phthalic anhydride, chloroacetyl chloride, aroyl thiocyanates and ammonium thiocyanate gave the corresponding 3-N-substituted derivatives. Hydrazenolysis of **13** in presence of hydrazine hydrate afforded the 5-hydrazino derivative. The 2-mercapto -7-(phenyladiazenyl)-2,5-dihydropyrazolo[1,5-b]triazole-6-ol (20) and 2-amino -7-(phenyladiazenyl)-2,5-dihydropyrazolo[1,5-*b*][1,2,4]-thiadiazol-6-ol (**21**) were obtained by the reaction of 1-(5-hydroxy)-4-(phenyldiazenyl)-1*H*-pyrtazol-3-yl)thiourea with bromine in different solvents. The structures of newly synthesized compounds have been established by IR, ^{1}H NMR and elemental analysis.

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Introduction

Pyrazole ring is a prominent structural motif found in numerous pharmaceutically active compounds, therefore, the synthesis and selective functionalization of pyrazoles are in the focus of organic synthesis. Pyrazoles have been reported to possess antibacterial activity, inhibitor activity against DNA gyrase and topoisomerase IV at their respective ATP-binding sites. Moreover, pyrazole ring containing compounds have received considerable attention owing to their diverse chemotherapeutic potentials including versalite antineoplastic activities, antileukemic, antitumor, antiproliferative agents, GABA receptor antagonists etc. Some pyrazoles act as insecticides, anti-inflamatory and antimicrobial agents.[1-4]

In continuation of our recent work aiming of the synthesis of heterocyclic systems with remarkable biological importance, some new pyrazole derivatives have been prepared and characterized.

Experimental

Melting points were recorded using SMP30 Melting Point Apparatus (Stuart) and are uncorrected. The IR spectra were record on KBr discs using a FTIR 600 Series spectrophotometer (JASCO) and ^{1}H NMR spectra (δ ppm) were recorded on a Varian 300 MHZ spectrometer using $CDCl_3$ as solvent. Elemental analyses were carried out at Micro Analytical Center of Cairo University.

3-Amino-5-hydroxy-4-phenylazo-1*H*-pyrazole (1)

Compound **1** was prepared according to literature procedure and all analysis is agreement with the structure.[2]

2-((4-Phenyldiazenyl)-5-hydroxy-1*H*-pyrazol-3-ylamino)-1-phenylethanone (2)

To a solution of **1** (0.2 g, 1 mmol) in acetic acid (20 mL), phenacyl bromide (0.19 g, 1 mmol) was added and refluxed for 7 h. The soltuon was concentrated and left to cool. The precipitate was filtered off and recrystallized from acetic acid. Yield 75 %, m.p. 200 ^{0}C. Anal. Calcd for $C_{17}H_{15}N_5O_2$ (321.323): C; 63.54; H, 4.70; N, 21.79. Found: C, 63.53; H, 4.72; N, 21.78. IR (KBr) : 3500, 3138, 1680, 1615 cm^{-1} corresponding to OH, NH, C=O, C=N. ^{1}H NMR ($CDCl_3$) δ = 4.2 (s, 2H, CH_2), 7.0-7.5 (m, 10H, Ar-H), 8.2 (s, 1H, NH), 11.0 (s, 1H, NH), 12.0 (s, 1H, OH) .

3-Phenyl-7-(phenyldiazenyl)-5*H*-imidazol[1,2-*b*]pyrazol-6-ol (3)

A solution of compound **2** (0.15 g, 1 mmol) in acetic anhydride (20 mL) was refluxed for 6 h. The solution was cooled and poured into ice. A precipitate was formed, which was crystallized from ethanol. Yield: 66 %, m.p. 300 ^{0}C. Anal. Calcd for $C_{17}H_{13}N_5O$ (303.3): C, 67.32; H, 4.32; N, 23.09. Found: C, 67.34; H, 4.31; N, 23.08. IR (KBr): 3450, 3310, 3010, 1618 cm^{-1} corresponding to OH, NH, $CH_{aromatic}$, C=N. ^{1}H NMR ($CDCl_3$) δ = 7.5-8.0 (m, 11H, Ar-H and H-pyrazole), 8.0 (s, 1H, NH), 8.4 (s, 1H, NH), 12.0 (s, 1H, OH).

***N*-(4-(Phenyldiazenyl)-5-hydroxy-1*H*-pyrazol-3yl)acetamide (4)**

To a solution of compound **1** (0.2 g, 1 mmol) in acetic anhydride (20 mL), pyridine (0.05 mL) was added and the mixture was refluxed for 5 h. The mixture was cooled and poured into ice-cold dilute HCl (5 mL) and stirred till the

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crude product begins to precipitate. The precipitate was filtered off and crystallized from ethanol. Yield: 65 %, m.p. 160 ^{0}C . Anal. Calcd for $C_{11}H_{11}N_5O_2$ (245.23): C, 53.87; H, 4.53; N, 28.55.Found: C, 53.89; H, 4.52; N, 28.54. IR (KBr) : 3460, 3300, 3190, 3046, 1710, 1610, 1560 cm^{-1} corresponding to OH, NH, C-$H_{aromatic}$, C=O, C=N, C=C . The ^{1}H NMR ($CDCl_3$) δ = 1.29 (t, 3H, CH_3), 7.4-7.8 (m, 5H, Ar-H), 8.4 (s, 1H, NH), 11.8 (s, 1H, NH), 12.9 (s, 1H, OH).

4-(Phenyldiazenyl)-3-(arylmethyleneamino)-1*H*-pyrazol-5-ol derivatives (5a-d)

An aromatic aldehyde (benzaldehyde, p-chlorobenzaldehyde, p-nitrobenzaldehyde, anisaldehyde) (1 mmol) was added to the solution of compound **1** (0.2 g, 1 mmol) in n-butanol (20 mL), The mixture was refluxed for 5-7 h and then the solvent was removed under reduced pressure. The solid residue was triatureted with n-butanol, residue was filtered off and recrystallized from n-butanol. Compound **5a:** Yield 65%, m.p. 285 °C. Anal. Calcd. for $C_{16}H_{13}N_5O$ (291.298): C, 65.96; H, 4.49; N, 24.05. Found: C,65.95; H, 4.48; N, 24.07. IR (KBr): 3500, 3215, 3190, 3046, 1652, 1610, 1560 cm^{-1} corresponding to OH, NH, C-$H_{aromatic}$, C=N and C=C linkages. ^{1}H NMR ($CDCl_3$) δ = 7.0-7.5 (m, 10H, Ar-H), 8.6 (s, 1H, NH), 8.9 (s, 1H, N=CH), 12.0 (s, 1H, OH).

Compound **5b**: Yield 70 %, m.p. 280 °C. Anal. Calcd. for $C_{16}H_{12}N_5OCl$ (325.743): C, 58.99; H, 3.71; N, 21.50. Found : C,58.98; H,3.73; N,21.49.

Compound **5c**: Yield 63 %, m.p. 287 °C. Anal. Calcd. for $C_{16}H_{12}N_6O_3$ (336.295): C, 57.14; H, 3.59; N, 24.99. Found: C, 57.16; H, 3.58; N, 24.98.

Compound **5d**: Yield 61 %, m.p. 283 °C. Anal Calcd. for $C_{17}H_{15}N_5O_2$ (321.323): C, 63.54; H, 4.70; N, 21.79.Found : C, 63.55; H, 4.71; N, 21.77.

***N*-(4-(phenyldiazenyl)-5-hydroxy-1*H*-pyrazol-3yl)phenyl-carboxamide (6)**

Benzoyl chloride (0.12 g , 1 mmol) and pyridine (0.5 ml) were added to a solution of compound **1** (0.2 g, 1 mmol) without solvent. The mixture was heated for 5 h. After cooling the mixture was poured into ice-cold dilute HCl (5 mL). The precipitate formed was filtered off and recrystallized from ethanol. Yield 50 %, m.p. 190 °C. Anal. Calcd. for $C_{16}H_{13}N_5O_2$ (307.297): C, 62.53; H, 4.26; N, 22.79. Found: C, 62.55; H, 4.25; N, 22.78. IR (KBr) : 3500, 3284, 3168, 3062, 1710, 1596, 1545 cm^{-1} corresponding to OH, NH, C-$H_{aromatic}$, C=O, C=N and C=C linkages. ^{1}H NMR ($CDCl_3$) δ = 7.4-7.8 (m, 10H, Ar-H), 8.4 (s, 1H, NH), 11.8 (s, 1H, NH) and 12.9(s, 1H, OH).

3-(Phenyldiazenyl)-5,7-dimethyl-1,5-dihydropyrazolo[1,5-*a*]pyrimidin-2-one (7)

Acetylacetone (0.1 g, 1 mmol) was added to the solution of compound **1** (0.2 g, 1 mmol) in absolute ethanol (20 mL), the reaction mixture was heated under reflux for 7 h, the solvent was removed under reduced pressure and the solid residue of **7** was collected. Yield 65 %, m.p. 220 °C. Anal. Calcd. for $C_{14}H_{15}N_5O$ (269.294): C, 62.44; H, 5.62; N, 26.00.Found: C, 62.41; H, 5.64; N, 26.01. IR (KBr): 3500, 3284, 3168, 3062, 1710, 1669, 1596, 1545, 1375 cm^{-1} corresponding to OH, NH, C-$H_{aromatic}$, C=O, C=N, C=C, CH_3. ^{1}H NMR ($CDCl_3$) δ 1.8 (s, 3H, CH_3), 2.1 (s, 3H, CH_3), 7.0-7.5 (m, 6H, Ar-H, H-pyrimidine), 8.4 (s, 1H, NH), 11.9 (s, 1H, OH).

3-(Phenyldiazenyl)-2-hydroxy-5-methylpyrazolo[1,5-*a*]pyrimidin-7(1*H*)-one (8)

To a solution of compound **1** (0.2 g, 1 mmol) in acetic acid (20 mL), ethyl acetoacetate (0.11 g, 1 mmol) was added and the reaction mixture was refluxed for 5 h. The solvent was removed under reduced pressure, the precipitate was filtered off and recrystallized from acetic acid. Yield 60 %, m.p. 240 °C . Anal. Calcd. for $C_{13}H_{13}N_5O_2$ (271.267): C, 53.65; H, 4.09; N, 22.75. Found: C, 53.63; H, 4.07; N, 22.70. IR (KBr): 3500, 3460, 3053, 3062, 1720, 1670, 1590 cm^{-1} correspond to OH, NH, C-$H_{aromatic}$, C=O, C=N and C=C linkages. ^{1}H NMR ($CDCl_3$) δ = 1.7 (s, 3H, CH_3), 7.5-8.0 (m, 6H, Ar-H, H-pyrimidine), 8.4 (s, 1H, NH), 11.0 (s, 1H, NH), 12.0 (s, 1H, OH).

7-Amino-3-(phenyldiazenyl)-2-hydroxypyrazolo[1,5-*a*]pyrimidin-5(1*H*)-one (9)

A solution of compound **1** (0.2 g, 1 mmol) and ethyl cyanoacetate was heated at 180 °C in oil bath for 3 h. The mixture was cooled and then washed with ethanol several times. The residue was filtered off and recrystallized from butanol. Yield 75 %, m.p. 180 °C. Anal. Calcd. for $C_{12}H_{12}N_6O_2$(272.256): C, 52.94; H, 4.45; N, 30.86. Found: C, 52.92; H, 4.46; N, 30.87. IR (KBr): 3508, 3406, 3300, 3173, 3010, 1668 cm^{-1} corresponding to OH, NH, NH_2, C-$H_{aromatic}$. ^{1}H NMR ($CDCl_3$) δ = 6.5 (s, 2H, NH_2), 7.0-8.0 (m, 6H, Ar-H, H-pyrimidine), 8.4 (s, 1H, NH), 11.0 (s, 1H, OH), 12.6 (s, 1H, OH).

(Phenyldiazenyl)pyrazolo[1,5-*a*]pyrimidin-5,7(1*H*,6*H*)-dione (10)

Equimolar amounts of compound **1** (0.21 g , 1 mmol) and diethylmalonate (0.16 g, 1 mmol) were dissolved in a solution of sodium ethoxide (0.01 g, 1 mmol) in abs. ethanol (20 mL) and left under reflux for 10 h. The precipitate was formed during cooling was recrystallized from ether. Yield 65 %. M.p. 300 °C . Anal.: Calcd for $C_{12}H_9N_5O_3$ (271.224): C, 53.14; H, 3.35; N, 25.83. Found : C, 53.15; H, 3.33; N, 25.84. IR (KBr): 3300, 3210, 3080, 1710, 1625, 1566 cm^{-1} corresponding to OH, NH, C-$H_{aromatic}$, 2C=O, C=N. ^{1}H NMR ($CDCl_3$) δ = 7.0-7.5 (m, 6H, Ar-H, H-pyrimidine), 8.0 (s, 1H, NH), 8.4 (s, 1H, NH), 12.0 (s, 1H, OH).

2-Hydroxyl-3-(phenyldiazenyl)-6-(2-phenylhydrazono)-6,7–dihydropyrazolo[1,5-*a*]pyrimidin-5,7-(1*H*,6*H*)–dione (11)

An ice–cold mixture of compound **1** (0.26 g, 1 mmol) and sodium acetate (0.07g, 1 mmol) in ethanol (25 mL) was added dropwise with stirring to the solution of the diazonium salt over 10 min, the stirring continued for furthet 30 min. The reaction mixture was left to stand for 2 h at

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room temperature, the precipitate formed was collected and recrystallized from ethanol. Yield 84 %, m.p.60 °C. Anal. Calcd. for $C_{18}H_{13}N_7O_3$ (375.33): C, 57.59; H, 3.49; N, 26.12. Found: C, 57.60; H, 3.50; N, 26.00. IR (KBr): 3300, 3200, 3100, 3020, 1710, 1625, 1590 cm^{-1} corresponding to OH, NH, C-$H_{aromatic}$, 2C=O, C=N. ^{1}H NMR ($CDCl_3$) δ = 7.0-7.5 (m, 11H, Ar-H, NH), 8.0 (s, 1H, NH), 8.4 (s, 1H, NH) and 12.0 (s, 1H, OH).

2-(5-Hydroxy-4-(2-phenylhydrazinyl)-1*H*-pyrazol-3ylimino)-1*H*-indene-1,3-(2*H*)-dione (12)

Mixture of compound **1** (0.21 g, 1 mmol) and ninhydrine (0.17g, 1 mmol) in abolute ethanol (25 mL) was stirred for 2 h. The solid product was collected and recrystallized from ethanol. Yield 81 %, m.p. 190 °C. Anal. Calcd. for $C_{18}H_{15}N_5O_4$ (365.331): C, 59.17; H, 4.14; N, 19.17. Found: C, 59.15; H, 4.15; N, 19.18. IR (KBr): 3500, 3400, 3061, 1722, 1591 cm^{-1} corresponding to OH, NH, C-$H_{aromatic}$, C=O, C=N. ^{1}HNMR ($CDCl_3$) δ = 7.0-7.5 (m, 9H, Ar-H), 8.4 (s,1H, NH), 12.0 (s, 1H, OH).

3-Amino-5-chloro-4-phenylazo-1*H*-pyrazole (13)

A solution of compound **1** (0.2 g, 1 mmol) in phosphorus oxychloride (20 mL) was refluxed on a hot plate for 2 h. The reaction mixture was cooled and diluted with ice-cold water. The resulting precipitate was filtered off and recrystallized from chloroform. Yield 66 %, m.p. 170 °C. Anal. Calcd. for $C_9H_8N_5Cl$ (221.642): C, 48.76; H, 3.64; N, 31.59; Cl 1.59. Found: C, 48.75; H, 3.67; N, 31.58; Cl, 1.58. IR (KBr): 3443, 3389, 2857, 1612, 1525 cm^{-1} corresponding to NH_2, NH, C-$H_{aromatic}$, C=N, C=C. ^{1}H NMR ($CDCl_3$) δ = 6.0 (s, 2H, NH_2), 7.0-7.5 (m, 5H, Ar-H), 8.5 (s, 1H, NH).

3-Amino-5-hydrazino-4-phenylazo-1*H*-pyrazole (14)

To a solution of compound **13** (0.21 g, 1 mmol) in ethanol (30 mL), hydrazine hydrate (0.05 g, 1 mmol) was added and the mixture was heated at 90 °C for 6 h. On cooling a precipitate was formed. This precipitate was filtered off and recrystallized from dioxane. Yield 75 %, m.p. 270 °C. Anal. Calcd. for $C_9H_{11}N_7$ (217.227): C, 49.75; H, 5.11; N, 45.14. Found : C, 49.74; H, 5.13; N, 45.13. IR (KBr): 3381, 3197, 3010, 2960, 1634, 1562cm^{-1} corresponding to NH, NH_2, C-$H_{aromatic}$, C=N, C=C. ^{1}H NMR ($CDCl_3$) δ = 4.9 (s, 2H, NH_2), 6.5 (s, 2H, NH_2), 7.0-7.5 (m, 5H, Ar-H), 8.4 (s, 1H, NH), 11.0(s, 1H, NH).

3-Amino-5-mercapto-4-phenylazo-1*H*-pyrazole (15)

The compound **1** (0.2 g, 1 mmol) was heated at reflux temperature in dry pyridine (20 mL) containing phosphorus pentasulfide (0.2 g, 1 mmol) for 5 h. The solution was acidified with dil. HCl, the precipitate formed was filtered off and washed several times with water then recrystallized from DMF. Yield 75 %, m.p. 200 °C. Anal. Calcd. for $C_9H_9N_5S$ (219.262): C, 49.29; H, 4.14; N, 31.49; S, 14.62. Found: C, 49.28; H, 4.15; N, 31.48; S, 14.63. IR (KBr): 3606, 3303, 3177, 1399 cm^{-1} corresponding to NH, NH_2, C-$H_{aromatic}$, C=S. ^{1}H NMR ($CDCl_3$) δ = 6.5 (s, 2H, NH_2), 7.0-7.7 (m, 5H, Ar-H), 8.4 (s, 1H, NH), 13.0 (s, 1H, SH).

2-(5-Hydroxy-4-(phenyldiazenyl)-1*H*-pyrazolo-3yl)isoindoline-1,3-dione (16)

Equimolar amounts of compound **1** (0.21 g , 1 mmol), phthalic anhydride (0.14 g, 1 mmol) and sodium ethoxide (0.01 g, 1 mmol) were dissolved in absolute ethanol (20 mL) and the mixture was refluxed for 10 h. After cooling, the formed precipitate was recrystallized from chloroform. Yield 85 %, m.p. 300 °C. Anal. Calcd for $C_{17}H_{11}N_5O_3$ (333.290): C, 61.25; H, 3.33; N, 21.01. Found: C, 61.24; H, 3.34; N, 21.00. IR (KBr): 3400, 3310, 3080, 1700, 1650, 1560 cm^{-1} corresponding to OH, NH, C-$H_{aromatic}$, 2C=O, C=N. ^{1}H NMR ($CDCl_3$) δ = 7.0-7.5 (m, 9H, Ar-H), 8.3 (s, 1H, NH) , 12.0 (s, 1H, OH).

2-Chloro-*N*-(5-hydroxy-4-(phenyldiazenyl)-1*H*-pyrazol-3yl)-acetamide (17)

To a solution of compound **1** (0.21 g, 1 mmol) in dioxane (30 mL), chloroacetyl chloride (0.09 g, 1 mmol) was added dropwise with stirring at room temperature. The reaction mixture was heated for 30 min at 60 °C, the solution was concentrated to a small volume, poured into ice-cold water and the precipitate formed was recrystallized from ethanol. Yield 60 %, m.p. 210 °C. Anal. Calcd for $C_{11}H_{10}N_5O_2Cl$ (279.676): C, 47.24; H, 3.60; N, 25.04; Cl, 12.67. Found: C, 47.21; H, 3.61; N, 25.05; Cl, 12.68. IR (KBr): 3505, 3410, 1700 cm^{-1} corresponding to OH, NH, C=O. ^{1}H NMR ($CDCl_3$) δ = 2.8 (s, 2H, CH_2), 7.0-7.5 (m, 5H, Ar-H), 8.4 (s, 1H, NH), 11.0 (s, 1H, NH), 12.0 (s, 1H, OH).

***N*-Benzoyl-[5-hydroxy-4-phenylazo-1*H*-pyrazol-3-yl]thiourea (18)**

A mixture of benzoyl chloride (0.12 g, 1 mmol) and ammonium isothiocyanate (0.07 g, 1 mmol) was refluxed in dry acetone (20 mL) for 15 min. Then the compound **1** was added, the mixture was refluxed for 2 h, poured into ice water, the precipitate formed was filtered off, washed with water and recrystallized from ethanol**.** Yield 69 %, m.p. 140 ^{0}C. Anal. Calcd for $C_{17}H_{14}N_6O_2S$ (366.387): C, 55.73; H, 3.85; N, 22.94; S, 8.75. Found: C, 55.74; H, 3.84; N, 22.95; S, 8.74. IR (KBr): 3560, 3440, 3130, 1720, 1383 cm^{-1} corresponding to OH, NH, C-$H_{aromatic}$, C=O, C=S. ^{1}H NMR ($CDCl_3$) δ = 7.0-7.6 (m, 10H, Ar-H), 8.7 (s, 1H, NH), 10.5 (s, 1H, NH), 11.0 (s, 1H, NH), 12.0 (s, 1H, OH).

1-(5-Hydroxy-4-(phenyldiazenyl)-1*H*-pyrazol-3-yl)thiourea (19)

A solution of compound **1** (0.21 g, 1 mmol) in absolute ethanol (30 mL) containing conc. HCl (0.05 mL) and ammonium thiocyanate (0.07 g, 1 mmol) was refluxed for 2 h. The precipitate formed was recrystallized from ethanol. Yield 55 %, m.p. 240 ^{0}C. Anal. Calcd for $C_{10}H_9N_6OS$ (261.278): C, 45.96; H, 3.47; N, 32.16; S, 12.27. Found: C, 45.97; H, 3.48; N, 32.17; S, 12.24. IR (KBr): 3500, 3210, 3100, 3030, 1333 cm^{-1} corresponding to OH, NH, NH_2, C-$H_{aromatic}$, C=S. ^{1}H NMR ($CDCl_3$) δ = 6.8 (s, 2H, NH_2), 7.0-7.7 (m, 5H, Ar-H), 7.9 (s, 1H, NH), 11.0 (s, 1H, NH), 12.0 (s, 1H, OH).

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2-Mercapto-7-(phenyldiazenyl)-2,5-dihydropyrazolo[1,5-*b*][1,2,4]triazol-6-ol (20)

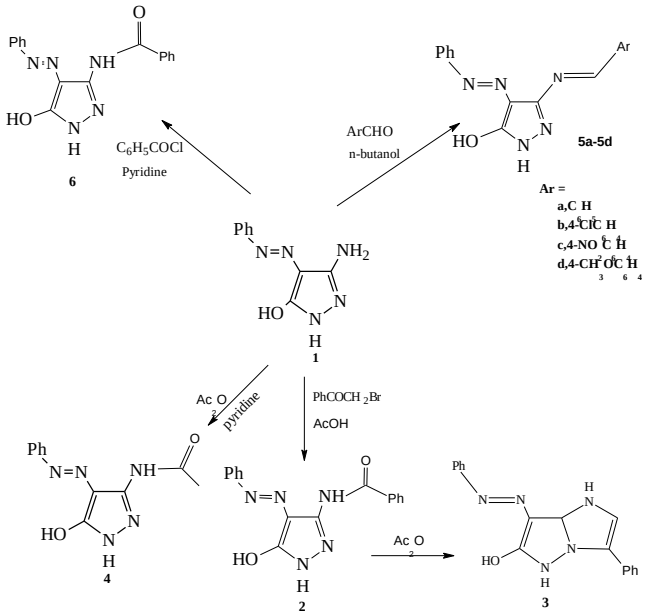
To a solution of compound **19** (0.26 g, 1 mmol) in pyridine (20 mL), bromine (0.15g, 1 mmol) in pyridine (5 mL) was added dropwise at room temperature. The mixture was refluxed for 1 h, cooled, poured into water with stirring, the precipitate formed was filtered off, washed with water and recrystallized from ethanol. Yield 65 %, m.p. 140 °C. Anal. Calcd for $C_{10}H_7N_6OS$ (259.262): C, 46.33; H, 2.73; N, 32.42; S, 12.36. Found: C, 46.35; H, 2.71; N, 32.43; S, 12.35. IR (KBr): 3500, 3400, 3180, 3019 cm^{-1} corresponding to OH, NH, NH_2, C-$H_{aromatic}$. ^1H NMR ($CDCl_3$) δ = 7.0-7.5 (m, 5H, Ar-H), 8.4 (s, 1H, NH), 12.0 (s, 1H, OH), 13.9 (s, 1H, SH).

2-Amino-7-(phenyldiazenyl)-2,5-dihydropyrazolo[1,5-*b*][1,2,4]-thiadiazol-6-ol (21)

To a solution of compound **19** (0.26 g, 1 mmol) in glacial acetic acid (20 mL) bromine (0.15 g, 1 mmol) in glacial acetic acid (5 mL) was added dropwise at room temperature. The mixture was refluxed for 1 h, cooled, poured into water with stirring, the precipitate formed was filtered off and recrystallized from ethanol. Yield 66 %, m.p. 120 °C. Anal. Calcd for $C_{10}H_8N_6OS$ (260.27): C, 46.15; H, 3.09; N, 32.29; S, 12.32. Found: C, 46.12; H, 3.08; N, 32.28; S, 12.37. IR (KBr): 3530, 3300, 3160, 3030 cm^{-1} corresponding to OH, NH, NH_2, C-$H_{aromatic}$. ^1H NMR ($CDCl_3$) δ = 6.5 (s, 2H, NH_2), 7.0-7.6 (m, 5H, Ar-H), 8.4 (s, 1H, NH), 12.0 (s, 1H, OH).

RESULTS AND DISCUSSION

Treatment of the compound **1** with phenacyl bromide, acetic anhydride, substituted benzaldehyde and benzoyl chloride in different solvents afforded the corresponding N-alkylated/acylated or condensation products **2**, **4**, **5** and **6**, respectively (Scheme 1).

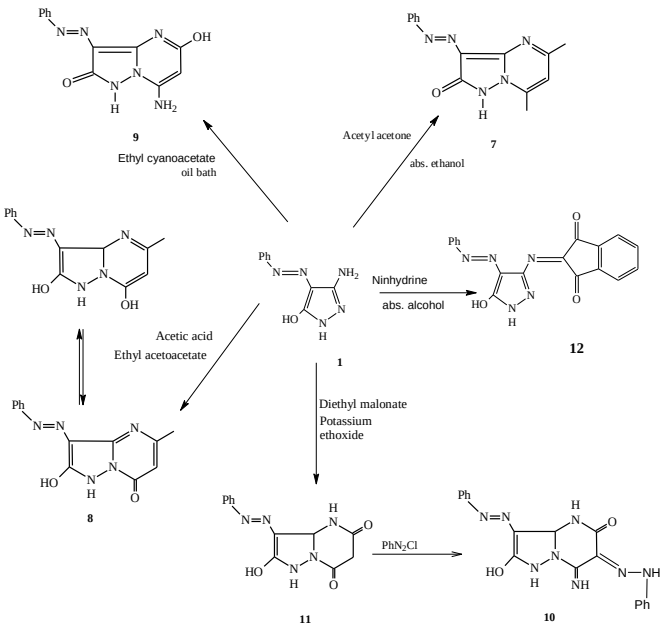


Scheme 1. Synthesis of compounds (**2**) – (**6**).

The ring clousure of compound **2** in acetic anhydride gave the corresponding imidazolopyrazole compound **3.** The IR and NMR spectra of the products confirm that the expected structural blocks were indeed incorporated into the starting molecule. IR spectrum of compound **2** revealed the absorption band at 1680 cm^{-1} for C=O group. Its ^1H NMR showed the presence of signals at δ 8.2 and 4.2 ppm characteristic for NH_2 and CH_2, respectively. IR spectrum of **5** revealed the presence of band at 3215 cm^{-1} for NH, and 1620 cm^{-1}. ^1H NMR showed signals at δ 8.6 ppm for NH. The IR, ^1H NMR and elemental analysis data of compounds **4** and **6** are also in agreement with the structures. IR spectra showed bands at 1710 cm^{-1} for amidic carbonyl groups, while, ^1H NMR of **4** and **6** revealed the presence signals at δ 11.8 ppm for NH_2, in addition to the aromatic proton at δ 7.4-7.8 ppm.

Condensation reaction of **1** with acetylacetone, ethyl cyanoacetate, ethyl acetoacetate or diethylmalonate in different solvent followed by cyclization gave the corresponding pyrazolo[1,5-*a*]pyrimidine derivatives **7**-**10**, respectively (Scheme 2).

However, the reaction of **1** with ninhydrine afforded Schiff' base **11**. The active methylene group in compound **11** reacts with phenyldiazonium chloride affording the hydrazone of pyrazolopyrimidine (**10) (**Scheme 2**).**



Scheme 2. Synthesis of compounds (**7**) – (**12**).

The structures of compounds **7-12** were assigned by their IR, ^1H NMR and elemental analysis data. IR spectrum of 7 showed absorption band at 1669 cm^{-1} corresponding to CN group and the absorption band for NH_2 is absent. The IR spectrum of **8** revealed the presence of bands at 3460 and 1720 cm^{-1} for NH and C=O groups, respectively, and the bands of NH_2 group are missing. In the IR spectrum of **9,** the bands belong to NH_2 group and C=O amidic group (3300, 3173 and 1668 have appeared. ^1H NMR spectrum of **10** showed the methinyl proton and aromatic protons at δ 7.0-7.5 ppm.

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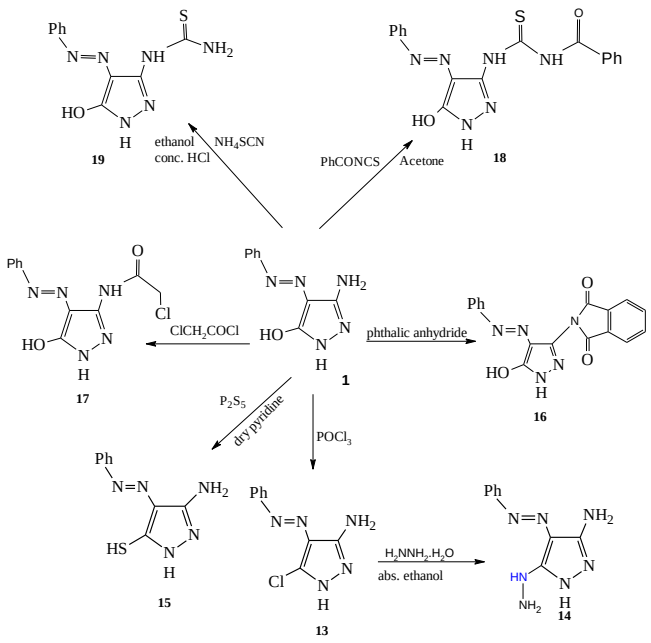
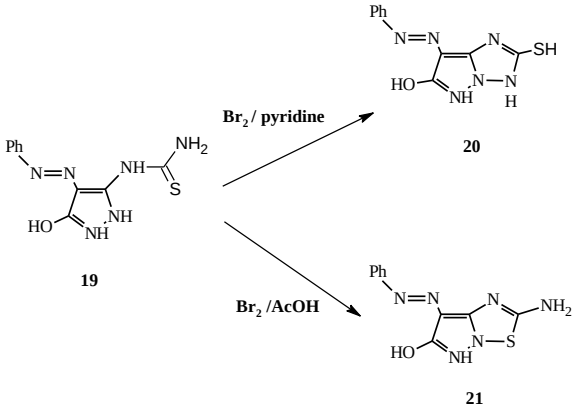


Scheme 3. Synthesis of compounds (**11**) – (**16**).

The reaction of **1** with $POCl_3$ and P_2S_5 resulted the formation of 5-chloro and 5-mercapto, substituted pyrazole compounds, respectively (**13** and **15).** Reaction with Phthalic anhydride resulted in 3-phthalimidoyl derivative (**16**) while that with chloroacetyl chloride resulted in an N-acylated derivative (**17**). Phenyl isothiocyanate and ammonium thiocyanate gave the corresponding thiourea derivatives (**18** and **19)**, respectively (Scheme 3).

Hydrazinolysis of compound **13** with hydrazine hydrate afforded the hydrazinopyrazole derivative **14**. The structure of the products formed in the reactions, given in (Scheme 3), were assigned by IR, ^{1}H NMR and elemental analysis. The IR of compounds **13-19** showed the absence of absorption bands for NH_2 indicating the involving of NH_2 groups in the reactions. In case of compound **16**, the bands appear at 1700 and 1650 cm^{-1}, which are characteristic of the C=O groups.

The ^{1}H NMR and elemental analysis of compounds **13-19** are in agreement with the expected structures.



Scheme 4. Synthesis of compounds **20** and **21**.

A pyrazolotriazole **20** and a pyrazolothiadiazole **21** derivative could be obtained in the reaction of **19** with bromine in different solvent. In these reactions the solvent polarity controls the involvement of NH_2 or C=S groups in the cyclization reactions (Scheme 4). The spectral data of **20** an32d **21** confirm the proposed structures.

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