SYNTHESIS AND REACTIONS OF NEW PYRAZOLE DERIVATIVES


Keywords: pyrazoles; pyrazolotriazines; pyrazolotriazoles; pyrazolopyrimidines; pyrazolothiadiazoles

Chemical transformation of 3-amino-5-hydroxy-4-phenylazo-1H-pyrazole (1) provided a series of new pyrazol derivatives such as N-(4-(2-phenyl diazeyanil)-2,5-dihydro-3-hydroxy-1H-pyrazol-5-yl)-2-chloroacetamide (2) obtained in the reaction of 1 with chloroacetyl chloride. Reaction of 2 with malononitrile and ammonium isothiocyanate gave the corresponding 1-(4-(2-phenyldiazenyl)-5-hydroxy-1H-pyrazol-3-yl)-2-amino-4,5-dihydro-5-oxo-1H-pyrral-3-carbonitrile (3) and 3-(2-phenyldiazeyanil)-7-amino-2-hydroxypyrazol[1,5-al]pyrimidin-5(1H)-one (4). Reaction of 1 with P2S5 gave the corresponding 3-amino-5-mercapto-4-phenylazo-1H-pyrazole 5. The reaction of compound 5 with chloroacetic acid, ethyl chloroacetate, tetrahydrofuran, 3-hydroxybenzaldehyde, phenacylbromide and ninyhdrine gave the corresponding N-substituted derivatives (6, 7, 8, 9, 10, 11, 12, 13), respectively. The reaction of compound 7 with hydrazide hydrate and a consecutive cyclization in the presence of glacial acetic acid and sulfuric acid mixture afforded 12. 1-(4-(2-Phenyldiazeyanil)-5-mercapto-1H-pyrazol-3-yl)-3-phenylthioureia 14 was obtained from reaction of 5 with phenyl isothiocyanate, which was transformed into pyrazolothiadiazole 15 and pyrazolotriazole 16 derivatives with bromine in different solvents. 3-Amino-5-hyrdrazino-4-phenylazo-1H-pyrazole 17 was obtained from reaction 5 with hydrazide hydrate. Cyclization of compound 17 by reacting with ethyl acetocetate, acetylacetone, phthalic anhydride and phenacyl bromide gave the corresponding N-phenylypyrazolyl derivatives (18 and 19), pyrazol-2,3-dihydrophthalazine-1,4-dione (20) and pyrazolotriazine (21), respectively. Reaction of 17 with sodium nitrite in the presence acetic acid, ethyl pyruvate and carbon disulfide gave the corresponding pyrazolotetrazole (22), imidazolopyrazole (23) and pyrazolotriazolyl derivatives (26).

Introduction

Pyrazoles and their substituted derivatives are interesting as potential pharmaceuticals, and intermediates in dye industry. Despite the enormous number of substituted pyrazoles reported in the literature only a limited number of bispyrazole derivatives have so for been reported. Our interest in synthesis and reactivity of the parent compounds arises from promise medicinal chemistry1–3 and organometallic complex reactivity. The present investigation is in continuation of our previous work on 3-amino-5-hydroxy-4-phenylazo-1H-pyrazole (1) and all analysis is agreement with the structure.4

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 1H NMR spectra (6 ppm) were recorded on a Varian 300 MHZ spectrometer using CDCl3 as solvent.

N-(4-(2-Phenyldiazeyanil)-2,5-dihydro-3-hydroxy-1H-pyrazol-5-yl)-2-chloroacetamide (2).

To a solution of compound 1 (0.21 g, 1 mmol) in dioxane (30 mL), chloroacetyl chloride (0.09 g, 1 mmol) was added drop wise with stirring at room temperature. The reaction mixture was refluxed for 30 min. at 60 °C, the solution was concentrated to a small volume, poured into ice-cold water and recrystallized from ethonal, yield 60 %. M. p. 210 °C. IR (KBr): 3425 (O=H), 3335 (N-H), 1700 (C=O) cm-1. 1H-NMR(CDCl3): 2.8 (s, 2H, CH2N), 5.0 (s, 1H, NH), 6.8-7.8 (m, 5H, Ar-H), 9.0 (s, 1H, NH), 12.33 (br, 1H, OH). Anal. Calcd. for C18H16N4O2: 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 %.

1-(4-(2-Phenyldiazeyanil)-5-hydroxy-1H-pyrazol-3-yl)-2-amino-4,5-dihydro-5-oxo-1H-pyrral-3-carbonitril (3).

To a solution of compound 2 (0.27 g, 1 mmol) in dioxane (30 mL) a catalytic amount of TEA (triethylamine) (0.5 mL), malononitrile (0.06 mL, 1 mmol) was added. The reaction mixture was refluxed for 4 h, cooled, poured onto cold water and neutralized with dilute HCl, the precipitate was collected, filtered off, dried and recrystallized from dioxane. Yield 54 %. M. p. 300 °C. IR (KBr): 3540 (O-H), 3375 (NH2), 3280 (N-H), 3050 (CH aromatic), 2240 (CN), 1690 (C=O) cm-1. 1H-NMR(CDCl3): 2.3 (s, 2H, CH2), 5.2 (s, 2H, NH2), 7.1-8.9 (m, 5H, Ar-H), 9.2 (s, 2H, NH), 12.3 (br, 1H, OH). Anal. Calcd. for C16H10N4O2: C: 54.36 %; H: 3.58 %; N: 31.70 %; Found: C:54.34 %; H: 3.59 %; N: 31.71 %.

3-(2-Phenyldiazeyanil)-7-amino-2-hydroxy pyrazol[1,5-a]pyrimidin-5(1H)-one (4).

To a solution of compound 2 (0.27 g, 1 mmol) in absolute ethanol (30 mL) containing sodium ethoxide (0.01 g, 1 mmol), ammonium isothiocyanate (0.07 g, 1 mmol) was added. The reaction mixture was refluxed for 5 h. The solid product was collected and recrystallized from ethanol. Yield 69 %. M. p.140 °C. IR (KBr): 3550 (O-H), 3443 (NH2), 3275 (N-H), 3058 (CH aromatic), 1680 (C=O) cm-1. 1H-NMR

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(CDC13): 5.8 (s, 2H, NH2), 6.8-7.8 (m, 6H, Ar-H and pyrimidine-H), 8.9 (s, 1H, NH), 12.0 (br, 1H, OH). Anal. Calcd. for C46H34N8O6: C: 53.13%; H: 4.08%; N: 30.98%. Found: C: 53.11%; H: 4.09%; N: 30.99%.

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

A solution of 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 and the solid precipitate was filtered off, washed several times with water, dried and recrystallized from dimethylformamide. Yield 75%. M. p. 200 °C. IR (KBr): 3432 (NH), 3375 (NH), 2560 (SH) cm⁻¹. 1H-NMR (CDCl3): 6.3 (s, 1H, NH), 6.8-7.6 (m, 5H, Ar-H), 8.5 (s, 2H, NH3), 13.04 (s, 1H, SH). Anal. Calcd. for C18H12N2S: 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%.

2-(4-(2-Phenyldiazeyl)-5-mercapto-1H-pyrazol-3-ylamino)-acetic acid (6)

A solution of compound 5 (0.21 g, 1 mmol), chloro acetic acid (0.08 g, 1 mmol) and sodium acetate (0.07 g, 1 mmol) was heated at reflux temperature for 3 h in absolute ethanol (20 mL), the precipitate was collected and recrystallized from ethanol. Yield 75%. M. p. 256 °C. IR (KBr): 3300 (OH), 3260 (NH), 2641 (SH), 1700 (C=O) cm⁻¹. 1H-NMR (CDCl3): 2.8 (s, 2H, CH3), 5.8 (s, 1H, NH), 7.0-7.8 (m, 5H, Ar-H), 8.9 (s, 1H, NH), 12.0 (s, 1H, OH), 13.2 (s, 1H, SH). Anal. Calcd. for C18H12N2O2S: C: 47.64; H: 3.99; N: 25.25; S: 11.56%. Found: C: 47.26%; H: 3.98; N: 25.28; S: 11.55%.

Ethyl 2-(4-(2-phenyl diazeyl)-5-mercapto-1H-pyrazol-3-ylamino)acetate (7)

A solution of compound 5 (0.21 g, 1 mmol), ethyl chloroacetate (0.11 g, 1 mmol) and sodium acetate (0.07 g, 1 mmol) was dissolved in absolute ethanol (20 mL) and heated at reflux temperature for 3 h. After cooling to room temperature, the precipitate was filtered off, dried and recrystallized from ethanol. Yield 70%. M. p. 246 °C. IR (KBr): 3480 (NH), 2650 (SH), 1710 (C=O) cm⁻¹. 1H-NMR (CDCl3): 1.26 (t, 3H, CH3), 2.8 (s, 2H, CH3), 4.2 (q, 2H, CH3), 5.8 (s, 1H, NH), 7.0-7.8 (m, 5H, Ar-H), 8.9 (s, 1H, NH), 12.9 (s, 1H, SH). Anal. Calcd. for C21H14N2O2S: C: 51.13; H: 4.95; N: 22.93; S: 10.50%. Found: C: 51.14; H: 4.94; N: 22.91; S: 10.52%.

2-(4-(2-Phenyldiazeyl)-5-mercapto-1H-pyrazol-3-ylamino)-acetoxyhydrazide (8)

A solution of compound 7 (0.3 g, 1 mmol) was mixed with a solution containing absolute ethanol (15 mL) and hydrazine hydrate (0.05 g, 1 mmol) and the reaction mixture was heated at reflux temperature for 2 h. After standing overnight at 25 °C, the precipitate formed was filtered off, washed with methanol and light petroleum, dried and recrystallized from dilute acetic acid or water. Yield 70%. M. p. 100 °C. IR (KBr): 3400 (NH), 3381 (NH), (CH3ammonium), 2850 (CH-aliphatic), 2650 (SH), 1686 (C=O) cm⁻¹. 1H-NMR (CDCl3): 4.4 (s, 2H, NH2), 7.1-7.8 (m, 5H, Ar-H), 9.6 (s, 1H, NH), 9.8 (s, 1H, NH), 13.3 (s, 1H, SH).

Synthesis of new pyrazole derivatives

Section A-Research paper

A solution of compound 5 (0.21 g, 1 mmol) and tetrahydrofuran (0.06 g, 1 mmol) in glacial acetic acid (15 mL) were heated at reflux temperature for 8 h. The solvent was reduced to one third of its volume under reduced pressure and after cooling the precipitate formed was collected and recrystallized from ethanol. Yield 52%. M. p. 190 °C. IR (KBr): 3450 (NH), 3055 (CH3ammonium), 2645 (SH) cm⁻¹. 1H-NMR (CDCl3): 1.4 (m, 4H, 2CH2), 2.9 (m, 4H, 2CH2), 5.9 (s, 1H, NH), 7.0-7.8 (m, 5H, Ar-H), 13.2 (s, 1H, SH). Anal. Calcd. for C18H14N2O2S: C: 58.85; H: 2.65; N: 26.39; S: 12.08%. Found: C: 58.84; H: 2.66; N: 26.38; S: 12.09%.

3-(4-(2-Phenyl diazeyl)-5-mercapto-1H-pyrazol-3-yl imino) methylphenol (10).

A solution of compound 5 (0.21 g, 1 mmol) and 3-hydroxybenzaldehyde (0.12 g, 1 mmol) in absolute ethanol (15 mL) was heated at reflux temperature for 7 h, cooling to room temperature, the precipitate formed was filtered off, washed with water several times, dried and recrystallized from ethanol. Yield 80%. M. p. 244 °C. IR (KBr): 3560 (OH), 3450 (NH), 3060 (CH3ammonium), 2590 (SH), 1634 (C=N) cm⁻¹. 1H-NMR (CDCl3): 7.0-7.8 (m, 9H, Ar-H), 8.6 (s, 1H, N=CH), 9.8 (s, 1H, NH), 12.0 (1H,OH), 13.4 (s, 1H, SH). Anal. Calcd. for C18H16N2O2S: C: 60.17; H: 2.84; N: 21.93; S: 9.84%. Found: C: 60.18; H: 2.85; N: 21.94; S: 10.03%.

2-(4-(2-Phenyldiazeyl) 3-amino-1H-pyrazol-5-yl thioc) 1-phenylethanone (11).

A solution of compound 5 (0.21 g, 1 mmol), phenacyl bromide (0.19 g, 1 mmol) and sodium acetate (0.07 g, 1 mmol) were heated at reflux in ethanol (15 mL) for 3 h. The precipitate formed was filtered off, washed with water several times, dried and recrystallized from ethanol. Yield 50%. M. p. 240 °C. IR (KBr): 3450(NH), 3325 (NH), 1700 (C=O) cm⁻¹. 1H-NMR (CDCl3): 2.5 (s, 2H, CH3), 5.8 (s, 1H, NH), 7.0-7.8 (m, 10H, Ar-H), 8.9 (s, 2H, NH2). Anal. Calcd. for C18H16N2O2S: C: 59.05; H: 4.65; N: 21.52; S: 9.82%. Found: C: 59.02; H: 4.68; N: 21.53; S: 9.84%.

N-4,5-Diphenylpyrazolo[3,4-b][1,4]thiazine-3(4H)-diamine (12).

To a solution of compound 11 (0.3 g, 1 mmol) in a glacial acetic acid:sulphuric acid mixture (5 mL:1 mL) were heated on water bath for 5 h. The reaction mixture was allowed to cool, neutralized by sodium carbonate solution (10%). The precipitate formed was collected and recrystallized from acetic acid. Yield 55%. M. p. 300 °C. IR (KBr): 3450 (NH), 3380 (NH), 3050 (CH3ammonium) cm⁻¹. 1H-NMR (CDCl3): 5.8 (s, 1H, NH), 7.0-7.8 (m, 11H, Ar-H and thiazine-H), 8.9 (s, 1H, NH), 9.2 (s, 2H, NH2). Anal. Calcd. for C26H18N2S: C: 63.73; H: 4.40; N: 21.85; S: 10.00%. Found: C: 63.72; H: 4.41; N: 21.84; S: 10.01%.
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2-(4-(2-Phenyldiazenyl)-5-mercapto-1H-pyrazol-3-yl imino)-2H-indene-1,3-dione (13)

A solution of compound 5 (0.12 g, 1 mmol) and ninhydrine (0.17 g, 1 mmol) in absolute ethanol (25 mL) was stirred for 2 h, then the precipitate formed was collected and recrystallized from ethanol. Yield 80 %. M. p. 130 °C. IR (KBr): 3453 (NH), 3058 (CH₃), 2590 (SH), 1688, 1628 (2C=O) cm⁻¹. ¹H-NMR (CDCl₃): 6.8 (s, 1H, NH), 7.0-7.9 (m, 9H, Ar-H), 13.0 (s, 1H, SH), 1.9 (s, 3H, CH₃). Anal. Caled. for C₉H₇N₂O₂S: C: 59.82; H: 3.06; N: 19.38; S: 8.87 %. Found: C: 59.81; H: 3.07; N: 19.39; S: 8.86 %.

1-(4-(2-Phenyldiazenyl)-5-mercapto-1H-pyrazol-3-yl)-3-phenylthiourea (14)

A solution of compound 5 (0.21 g, 1 mmol) and phenylisothiocyanate (0.15 g, 1 mmol) was heated at reflux temperature for 7 h in absolute ethanol (30 mL), the precipitate was collected and recrystallized from chloroform. Yield 57 %. M. p. 100 °C. IR (KBr): 3500 (NH), 3055 (CH₃), 2600 (SH), 1335 (C=S) cm⁻¹. ¹H-NMR (CDCl₃): 6.8 (s, 1H, NH), 7.0-7.8 (m, 10H, Ar-H), 9.2 (s, 1H, NH), 9.8 (s, 1H, NH) and 13.0 (s, 1H, SH). Anal. Caled. for C₁₃H₁₂N₂S: C: 75.21; H: 3.98; N: 23.71; S: 18.09 %. Found: C: 54.23; H: 3.96; N: 23.72; S: 18.08 %.

7-(2-Phenyldiazenyl)-2-(phenylamino)pyrazolo[1,5-b][1,2,4]-thiadiazol-1-yl-6-thiol (15)

To a solution of compound 14 (0.12 g, 1 mmol) in pyridine (20 mL), bromine (0.15 g, 1 mmol) in pyridine (5 mL) was added dropwise at room temperature. The reaction mixture were heated under reflux for 1 h. The mixture was cooled, poured into water with stirring, the solid precipitated was collected, filtered off, washed with water, dried and recrystallized from benzene. Yield 57 %. M. p. 90 °C. IR (KBr): 3450 (NH), 3055 (CH₃), 2680 (SH) cm⁻¹. ¹H-NMR (CDCl₃): 5.8 (s, 1H, NH), 7.0-7.9 (m, 10H, Ar-H), 13.0 (s, 1H, SH). Anal. Caled. for C₁₄H₁₂N₂S: C: 54.52; H: 3.43; N: 23.85; S: 18.19 %. Found: C: 59.53; H: 3.42; N: 23.86; S: 18.18 %.

3-Phenyl-7-(phenyldiazenyl)-3H-pyrazol[1,5-b][1,2,4]triazolo[2,6-d]thiophene (16)

To a solution of compound 14 (0.21 g, 1 mmol) in a glacial acetic acid (20 mL), bromine (0.15 g, 1 mmol) in a glacial acetic acid (5 mL) was added dropwise at room temperature. The reaction mixture were heated under reflux for 1 h, cooled, poured into water with stirring. The solid precipitated was filtered off, washed with water, dried and recrystallized from ethanol. Yield 66 %. M. p. 110 °C. IR (KBr): 3065 (CH₃), 2600, 2590 (SH) cm⁻¹. ¹H-NMR (CDCl₃): 7.0-7.9 (m, 10H, 2Ar-H), 12.9 (s, 1H, SH), 13.2 (s, 1H, SH). Anal. Caled. for C₁₅H₁₁N₃S: C: 62.68; H: 4.65; N: 29.86; S: 22.79 %. Found: C: 42.69; H: 4.64; N: 29.87; S: 22.78 %.

3-Amino-5-hydrazino-4-phenylazo-1H-pyrazole (17)

Hydrazine hydrate (0.05 g, 1 mmol) was added to a solution of compound 5 (0.2 g, 1 mmol) in absolute ethanol (15 mL), the reaction mixture was heated under reflux for 6 h or until the evolution of H₂S ceased, the solid precipitated was filtered off, dried and recrystallized from ethyl acetate. Yield 75 %. M. p. 270 °C. IR (KBr): 3438 (NH₂), 3382 (N-H), 3055 (CH₃) cm⁻¹. ¹H-NMR (CDCl₃): 4.5 (s, 1H, NH), 8.49 (s, 2H, NH₂), 6.56 (s, 2H, NH₂), 66.9-7.3 (m, 5H, Ar-H) and at 8.8 (s, 1H, NH). Anal. Caled. For C₁₅H₁₄N₃O: C: 49.75; H: 5.10; N: 45.14 %. Found: C: 49.76; H: 5.11; N: 45.12 %.

1-(4-(2-Phenyldiazenyl)-3-amino-1H-pyrazol-5-yl)-3-methyl-1H-pyrazol-5(4H)-one (18)

Ethyl acetoacetate (0.1 g, 1 mmol) was added to a solution of compound 17 (0.21 g, 1 mmol) in absolute ethanol (20 mL), the reaction mixture was heated under reflux for 10 h. The solution was concentrated and cooled, the solid precipitated was filtered off, dried and recrystallized from ethanol. Yield 65 %. M. p. 250 °C. IR (KBr): 3450 (NH₂), 3395 (NH), 3045 (CH₃), 1688 (C=O) cm⁻¹. ¹H-NMR (CDCl₃): 2.3 (s, 2H, CH₃), 5.8 (s, 1H, CH₃ of pyrazolone), 7.2-8.0 (m, 5H, Ar-H), 8.9 (s, 2H, NH₂), 12.5 (s, 1H, NH). Anal. Caled. For C₁₅H₁₅N₃O: C: 55.51; H: 3.94; N: 34.85 %. Found: C: 55.50; H: 3.93; N: 34.87 %.

4-(2-Phenyldiazenyl)-5-(3,5-dimethyl-1H-pyrazol-1-yl)-1H-pyrazol-3-amine (19)

Acetyl acetone (0.1 g, 1 mmol) was added to a solution of compound 17 (0.21 g, 1 mmol) in absolute ethanol (20 mL), the reaction mixture was heated under reflux for 10 h. The mixture was concentrated and cooled, the solid precipitated were collected by filtration, dried and recrystallized from benzene. Yield 77 %. M. p. 210 °C. IR (KBr): 3445 (NH₂), 3390 (NH), 3055 (CH₃) cm⁻¹. ¹H-NMR (CDCl₃): 1.5 (s, 6H, 2CH₃), 6.0 (s, 2H, CH₂ of pyrazolone), 7.0-7.8 (m, 5H, Ar-H), 8.4 (s, 2H, NH₂), 13 (s, 1H, NH). Anal. Caled. For C₁₅H₁₆N₄O: C: 60.20; H: 4.69; N: 35.11 %. Found: C: 60.22; H: 4.68; N: 35.10 %.

2-(4-(2-Phenyldiazenyl)-3-amino-1H-pyrazol-5-yl)-2,3-dihydrophthalazine-1,4-dione (20)

Phthalic anhydride (0.14 g, 1 mmol) was dissolved in a solution of compound 17 (0.21 g, 1 mmol) in acetic acid (30 mL), the reaction mixture was heated under reflux for 10 h. The mixture was concentrated, cooled, poured onto crushed ice, the solid precipitated was collected by filtration, dried and recrystallized from chloroform. Yield 80 %. M. p. 256 °C. IR (KBr): 3445 (NH₂), 3368 (NH), 3095 (CH₃), 1670, 1685 (2C=O) cm⁻¹. ¹H-NMR (CDCl₃): 5.8 (s, 1H, NH), 6.2 (s, 1H, NH), 7.0-7.8 (m, 9H, Ar-H), 8.9 (s, 2H, NH₂). Anal. Caled. For C₁₅H₁₄N₄O₂: C: 59.47; H: 2.64; N: 28.56 %. Found: C: 59.45; H: 2.65; N: 28.57 %.
(3-Amino-4-(phenylamino)-4,5-dihydro-1H-pyrazolo[4,3-e]-[1,2,4]triazin-5-yl)(phenyl)methanone (21)

A solution of compound 17 (0.21 g, 1 mmol) and phenacyl bromide (0.1 g, 1 mmol) in absolute ethanol (30 mL) was refluxed for 5 h, the precipitate formed was filtered off, dried and recrystallized from chloroform. Yield 60 %. M. p. 70 °C. IR (KBr): 3468 (NH₂), 3378 (N-H), 3055 (CH aromatic), 1703 (C=O) cm⁻¹. ¹H NMR (CDCl₃): 5.8(s, H, NH), 7.0-7.9 (m, 10H, 2Ar-H), 8.3(s, 1H, NH), 9.2 (s, 1H, NH). Anal. Calcd for C₂₃H₂₃NO₈: C: 58.82; H: 4.34; N: 28.06 %. Found : C; 58.82; H: 4.34; N: 28.05 %.

6-((Acetoxyl)diazenyl)-7-(phenyldiazenyl)-3H-pyrazolo[1,5-d]tetrazole (22)

A solution of sodium nitrite (0.13 g, 1 mmol) in water (10 mL) was added to a cold solution of 17 (0.21 g, 1 mmol) in acetic acid (20 mL). After completion of addition, the ice bath was removed and stirring was continued for 1 h. The precipitate was filtered off, dried and recrystallized from ethanol. Yield 58 %. M. p. 130 °C. IR (KBr): 3440 (N-H), 1703 (C=O) cm⁻¹. ¹H NMR (CDCl₃): 2120 (N₂), 1210 (C=O) cm⁻¹. ¹H-NMR (CDCl₃): 7.0-7.9 (m, 5H, Ar-H), 13.0(s, 1H, NH). Anal. Calcd for C₁₇H₁₇NO₈: C: 39.60; H: 3.33; N: 37.83 %. Found: C; 39.60; H; 3.33; N: 37.83 %.

7-(2-Phenyldiazenyl)-6-hydrazinyl-2-methyl-5H-imidazo[1,2-b]pyrazol-3-ol (23)

A solution of compound 17 (0.21 g, 1 mmol) was refluxed in absolute ethanol (20 mL) containing ethyl pyruvate (0.11 g, 1 mmol) for 5 h. The precipitate formed was filtered off, washed several times with water, dried and recrystallized from dioxane. Yield 55 %. M. p. 180 °C. IR (KBr): 3529 (O-H), 3430 (NH₂), 3358 (N-H), 3030 (CH aromatic) cm⁻¹. ¹H-NMR (CDCl₃): 2.8(s, 3H, CH₃), 4.8(s, 2H, NH₂), 5.8(s, 1H, NH), 7.0-7.8 (m, 5H, Ar-H), 9.6(s, 1H, NH), 12.1 (s, 1H, OH). Anal. Calcd for C₁₇H₁₇NO₈: C: 50.15; H: 4.56; N: 34.12 %. Found: C; 50.16; H: 4.57; N: 34.10 %.

Potassium 5-hydrazinyl-(4-phenyldiazenyl)-1H-pyrazol-3-yl-carbamothioate (24)

To a warmed ethoxide solution prepared by dissolving potassium hydroxide (0.011 g, 1 mmol) in absolute ethanol (30 mL), compound 17 (0.21 g, 1 mmol) and CS₂ (0.07 g, 1 mmol) were added. The reaction mixture was heated under reflux for 2 h in a water bath. After cooling, the mixture was poured onto crushed ice, neutralized by diluted acetic acid and the solid precipitated was collected by filtration, dried and recrystallized from ethanol. Yield 60 %. M. p. 240 °C. IR (KBr): 3355 (NH₂), 3250 (N-H), 3055 (CH aromatic), 1334 (C=S) cm⁻¹. Anal. Calcd for K₂C₇H₇N₂O₂S: C: 40.93; H: 3.77; N: 33.42; S: 21.85 %. Found : C; 40.94; H; 3.76; N: 33.43; S: 21.84 %.

N-[5-hydrazino-(4-phenyldiazenyl)-1H-pyrazol-3-yl]hydrazine-carbothioamide (25):

A mixture of compound 24 (0.29 g, 1 mmol) and hydrazine hydrate (0.05 g, 1 mmol) was heated in absolute ethanol (15 mL) under reflux for 10-12 h. The solids precipitated was collected, filtered off, dried and recrystallized from chloroform. Yield 55 %. M. p. 265 °C. IR (KBr): 3375 (NH₂), 3280 (N-H), 3050 (CH aromatic), 1335(C=S) cm⁻¹. Anal. Calcd for K₂N₇H₇N₄S: C: 41.95; H: 2.81; N: 44.03; S: 11.20 %. Found : C: 41.94; H: 2.82; N: 44.02; S: 11.21 %.

4-(Hydrazinyl-4-phenyldiazenyl-1H-pyrazol-3-yl)-3-phenyl-1H-[1,2,4]triazole-5(4H)-thione (26)

Benzoyl chloride (0.12 g, 1 mmol) was added dropwise to a cold solution of thiosemicarbazide derivative 25 (0.29 g, 1 mmol) in dry pyridine (15 mL), the reaction mixture was heated under reflux for 5 h. The solid precipitated was collected by filtration, washed with water several times, dried and recrystallized from ethanol. Yield 55 %. M. p. 300 °C. IR (KBr): 3540 (O-H), 3375 (NH₂), 3280 (N-H), 3050 (CH aromatic), 2240 (CN), 1690 (C=O) cm⁻¹. ¹H-NMR (CDCl₃): 5.8(s ,1H, NH), 4.4(s, 2H, NH₂), 7.0-7.8 (m, 10H, Ar-H), 8.6(s, 1H, NH), 12.0 (s,1H, NH). Anal. Calcd for K₂C₉H₈N₄S: C: 54.36; H: 3.58; N: 31.70 %; Found : C: 54.34; H: 3.59; N: 31 %.

RESULTS AND DISCUSSION

3-Amino-5-hydroxy-4-phenylazo-1H-pyrazole 1 was prepared and was allowed to react with chloroacetyl chloride in dioxane at room temperature with formation of the acylated product, namely N-(4-(2-phenyldiazenyl)-2,5-dihydro-3-hydroxy-1H-pyrazol-5-yl)-2-chloroacetamide 2. The IR spectra revealed the presence of (C=O) at 1700 cm⁻¹ and the absorption bands characteristic for NH₂ group were disappeared completely. The cyclization of compound 2 with malononitrile or ammonium isothiocyanate in various solvents gave the corresponding pyrazolopyrrol-3-carbonitrile 3 and pyrazolo[1,5-a]pyrimidine 4 derivatives (Scheme 1).

Scheme 1. Synthesis of compounds 1-4.

IR spectrum of compound 3 unambiguously confirmed the presence of NH₂ group vibrations at 3375 and CN group bands at 2240 cm⁻¹. Treatment of compound 1 with P₂S₅ in dry pyridine gave the corresponding 3-amino-5-mercapto-4-phenylazo-1H-pyrazole (5).
Synthesis of new pyrazole derivatives

Treatment of compound 5 with chloroacetic acid, tetrahydrofuran, 3-hydroxybenzaldehyde, phenacyl bromide and ninhydrine gave the corresponding N-alkylation or condensation products (6, 7, 9 and 10, respectively). Reaction of the compound 7 with hydrazine hydrate afforded compound 8. (Scheme 2). Treatment of compound 5 with phenacyl bromide and ninhydrine gave the corresponding N-alkylation or condensation products 11 and 13, respectively.

Reaction of compound 5 with phenyl isothiocyanate gives a pyrazolothiourea derivative (14). The compounds pyrazolothiazide 15 and pyrazolotriazole 16 were obtained by the reaction of 14 with bromine in different solvent. In the IR spectrum of compound 16 the bands appear at 2600 and 2590 cm⁻¹ are characteristic for (SH)groups. (Scheme 3).

3-Amino-5-hydrazino-4-phenylazo-1H-pyrazole 17 was obtained by the reaction of 5 with hydrazine hydrate in the abs. ethanol. Condensation of hydrazinopyrazole 17 with ethyl acetoacetate, acetylacetone, phthalic anhydride and phenacyl bromide in different solvents gave the corresponding N-pyrazolylpyrazole derivatives 18 and 19. N-alkylated pyrazole 20, and pyrazolotriazine 21, respectively (Scheme 4).

In the IR spectrum of compound 13 the bands appear at 1688 and 1682 cm⁻¹, respectively. are characteristic for the C=O groups. The ring closure of compound 11 in the presence of sulphuric acid and acetic acid mixture gave the pyrazolothiazine 12.

Scheme 2. Synthesis of compounds 5-10.

Scheme 3. Synthesis of compounds 11-16.


Diazoitization of compound 17 with sodium nitrite and acetic acid led obtain pyrazolo[1,5-d]tetrazole derivative (22). Cyclization of compound 17 with ethyl pyruvate yielded imidazo[1,2-b]pyrazole (23). The structure of compound 23 has assigned on basis of its spectroscopic data.
The IR revealed the presence of (OH) at 3529 cm\(^{-1}\). Moreover, reaction of 17 with carbon disulfide yielded the corresponding pyrazolocarboxamidithioate. Hydrazonolysis of compound 17 in the presence of hydrazine hydrate afforded pyrazolohydrazinecarbothioamide, which underwent further cyclization with benzoyl chloride in pyridine afforded pyrazolotriazole 26 (Scheme 5). The structures of all these compounds were elucidated from its spectral analysis.

**Conclusion**

3-Amino-5-hydroxy-4-phenylazo-1H-pyrazole 1 was effectively used as a precursor in the preparation of various pyrazole derivatives. N-(4-(2-Phenyldiazenyl)-2,5-dihydro-3-hydroxy-1H-pyrazol-5-yl)-2-chloroacetyl chloride 2 was obtained from reaction of 1 with chloroacetyl chloride, and the further reaction of 2 with malononitrile and ammonium isothiocyanate gave the corresponding 1-(4-(2-phenyldiazenyl)-5-hydroxy-1H-pyrazol-3-yl)-2-amino-4,5-dihydro-5-oxo-1H-pyrrrol-3-carbonitrile 3 and 3-(2-phenyldiazenyl)-7-amino-2-hydroxy pyrazolo[1,5-o]pyrimidin-5(1H)-one 4.

Thiation of 1 with P,Ss gave the corresponding 3-amino-5-mercaptop-4-phenylazo-1H-pyrazole 5. The reaction of compound 5 with chloroacetic acid, ethyl chloroacetate, tetrahydrofuran, 3-hydroxybenzaldehyde, phenacyl bromide and ninhydrine gave the corresponding N-substituted substituted pyrazoles (6, 7, 8, 9, 10, 11, 12, 13), respectively. Hydrazonolysis of 7 in the presence of hydrazine hydrate afforded 8 and cyclization of 11 in the presence of acetic acid and sulfuric acid mixture afforded the compound 12.

The 1-(4-(2-Phenyldiazenyl)-5-mercaptop-1H-pyrazol-3-yl)-3-phenylthiourea 14 was obtained from reaction of 5 with phenyl isothiocyanate. Pyrazolothiadiazole 15 and pyrazolotriazole 16 were obtained by the reaction of 14 with bromine in different solvents.

3-Amino-5-hydrazino-4-phenylazo-1H-pyrazole 17 could be obtained from reaction 5 with hydrazine hydrate.

Cyclization of compound 17 by reacting it with ethyl acetoacetate, acetylacetone, phthalic anhydride and phenacyl bromide gave the corresponding N-pyrazolylpyrazole derivatives 18 and 19, pyrazol-2,3-dihydropthalazine-1,4-dione 20 and pyrazolotriazine 21, respectively.

Reaction of 17 with sodium nitrite in the presence of acetic acid, ethyl pyruvate and carbon disulfide gave the corresponding pyrazolotetrazole 22, imidazolopyrazole 23 and pyrazolotriazine derivatives 26.

**References**


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