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Synthesis of some new dipyrazolyl ketones and pyrazolopyrimidine derivatives

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ABSTRACT

Some new pyrazole heterocycles such as dipyrazolyl ketones **(3-8)**, pyrazolylindazolyl ketone, pyrazolopyrimidines **(11-21)** and bis pyrazolopyrimidines **(18,22 and 23)** have been synthesized starting from 5-amino-1-phenylpyrazole-4-carbohydrazide **(2)**. Molluscicide activity of some new isolated pyrazole heterocycles has been reported.

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KEYWORDS

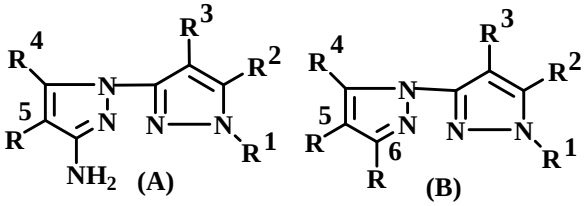
Dipyrazolyl ketones;
Pyrazolopyrimidines;
Molluscicide activity.

INTRODUCTION

Numerous reports have appeared in the literature describing the pharmacological properties of pyrazoles as antitumor[1], antimycotic compound[2], insecticides[3] and herbicides[4]. Motivated by these facts and as extension of our studies on azoles[5,6], the present investigation describes the use of 5-amino-1-phenylpyrazole -4-carbohydrazide **(2)** as a versatile reagent to synthesize some new pyrazole heterocycles. Some of these heterocycles exhibited molluscicide activity against *Biomphalaria alexandrina* snails, the intermediate host of *Schistosoma monsoni*, that cause intestinal bilharzias, the national problem in Egypt.

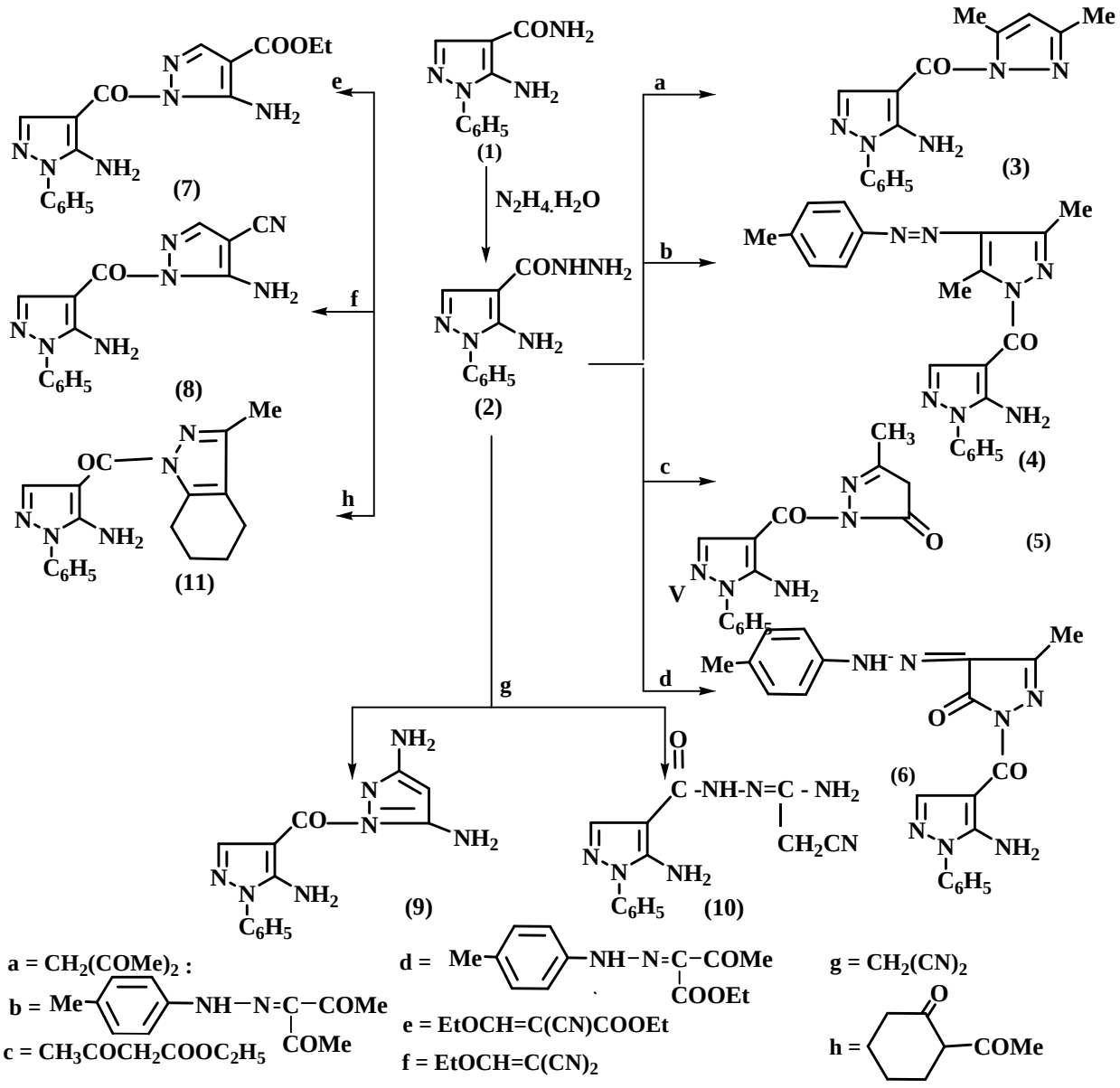
Fusion of 5-amino-1-phenylpyrazole-4-carboxamide (I) with hydrazine hydrate afforded the respective pyrazole-4-carbohyrazide(2) (SCHEME 1)

The structure of **(2)** was fully supported by analytical and spectroscopic data as the mass spectrum of which exhibited molecular ion peak at m/z 217 and a base peak ($M^{+\cdot}$ -$NHNH_2$) at 186. Compound **(2)** was used as a convenient precursor for the synthesis of some new pyrazole heterocycles. The first target was dipyrazolyl ketones as no examples of them were reported in the literature. However some structurally closed pyrazolylpyrazoles were appeared such as aminopyrazolylpyrazoles which are used as broad-leaf weed herbicides (A)[7] and herbicidal 1-(3-pyrazolyl) pyrazoles (B)[8] are known.

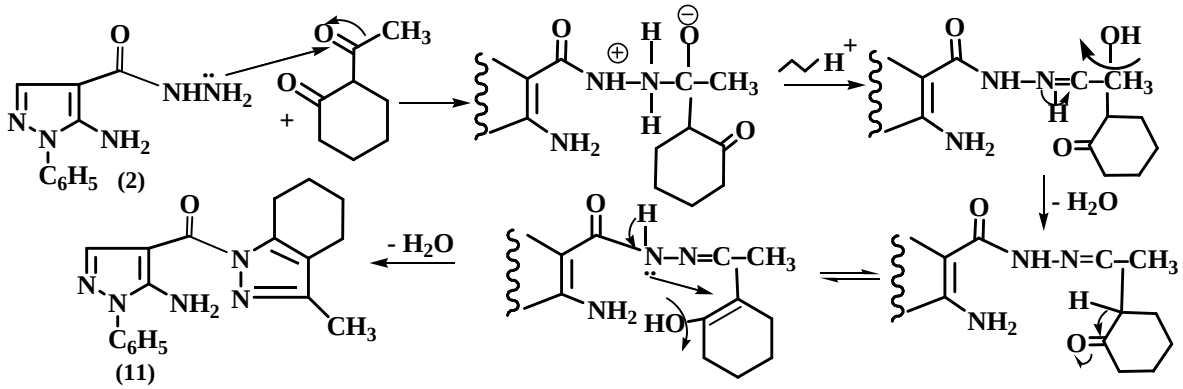


RESULTS AND DISCUSSION

When compound **(2)**was submitted to react with 1,3-dicarbonyl compounds such as pentan-2,4-dione and its diazotized aromatic amine condensed at reactive methylene position of acetylacetone in glacial acetic acid, the dipyrazolyl ketones **(3,4)** were afforded



SCHEME 1



SCHEME 2

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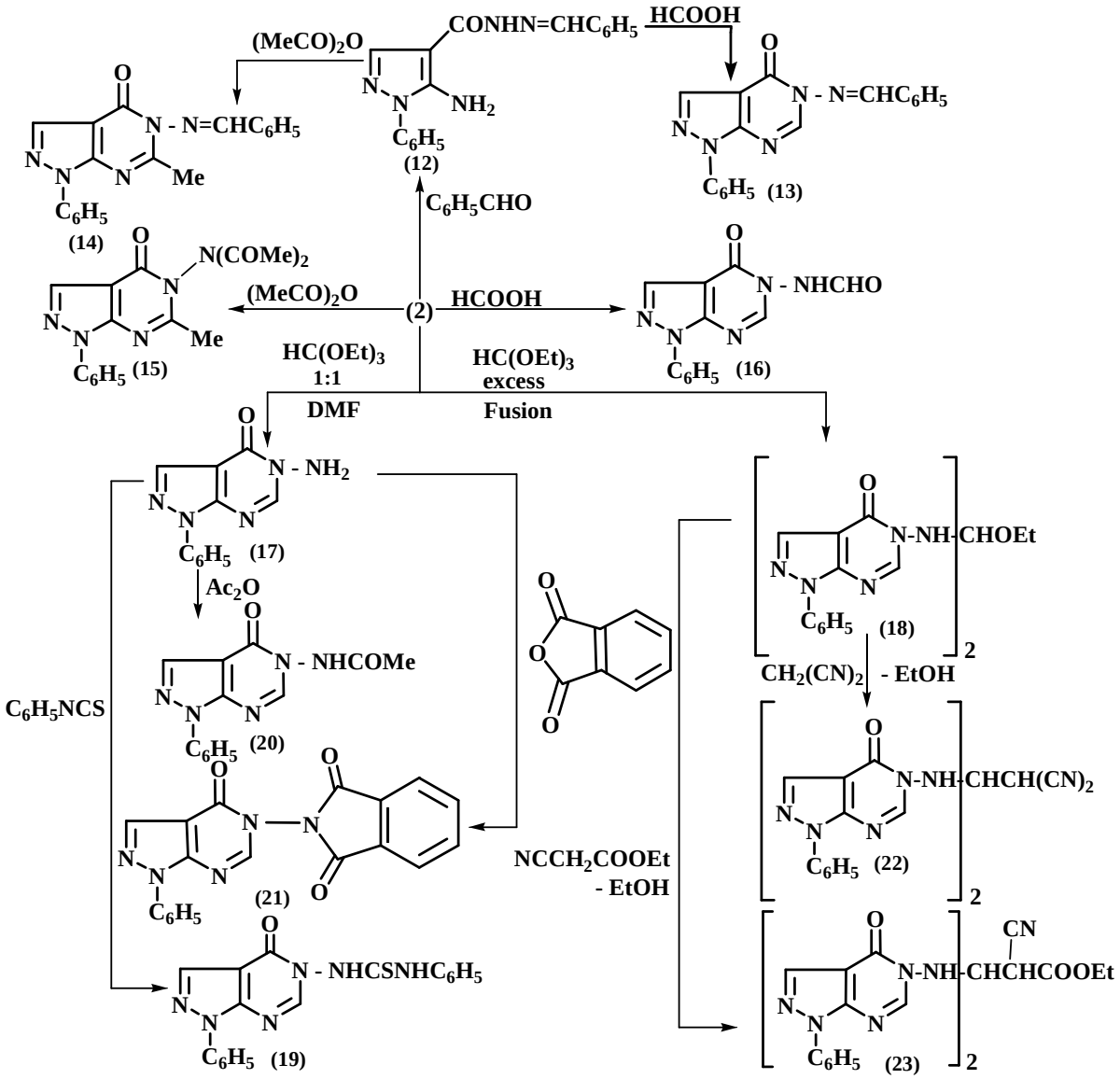


SCHEME 3

respectively (SCHEME 1). The structure of **(3)** was deduced by ^{1}H NMR (DMSO-d_6) which displayed two signals at δ2.54 and 3.36 attributed to the two methyl groups present in the newly built pyrazole moiety. Similarly treatment of **(2)** with ethyl acetoacetate and ethyl 2-(4-tolylhydrazono)-2,3-dioxobutyrate in glacial acetic acid yielded **(5)** and **(6)**, respectively. The MS spectra of **(5)** and **(6)**exhibited molecular ion peaks at m/z 281 and 401, respectively, and a base peak at 186, the stable 5-amino-1-phenylpyrazolyl-4-carbonyl moiety.The synthesis of other dipyrazolyl ketones could also be achieved through the cyclization of the carbohydrazide **(2)** with a Michael-retro-Michael reagent. Accordingly, the reaction of **(2)** with ethyl ethoxymethylenecyanoacetate and ethoxymethyle nemalononitrile in boiling DMF yielded the dipyrazolyl ketones **(7 and 8)**respectively (SCHEME 1). The structure of **(7)** was based on the absence of C≡N band in IR spectrum.

Attempts to synthesize 1-(5-amino-1-phenylpyrazol -4-ylcarbonyl)-3,5-diaminopyrazole **(9)**via treatment of **(2)** with malononitrile in sodium ethoxide were unsuccessful, we have obtained the open chain product -**(10)**, IR of which exhibited the presence of a CN function at

2213cm^{-1}. Also, all trials to cyclize **(10)** was failed. On the other hand, (5-amino-1-phenylpyrazol-4-yl) (3-methylindazolyl) ketone **(11)**was obtained from interaction of **(2)** with 2-acetylcyclohexanone in boiling DMF(SCHEME 1). The structure of **(11)** was elucidated using elemental analysis and MS of which showed molecular ion at m/z 321 with a base peak also at 186. The formation of **(11)**may proceed as shown in SCHEME 2.

We have previously studied the chemistry a bioactive pyrimidines[9]. As pyrazolopyrimidines possess a broad spectrum of biological activities e.g antileukemic[10], hypotensive and anxiolytic[11], it was interesting for us to incorporate a pyrazole into a pyrimidine a molecular frame starting from the carbohydrazide **(2)**. The acid catalysed condensation of **(2)** with benzaldehyde afforded 4-carboxybenzylidenehydrazide **(12)**, which underwent cyclocondensation on treatment with formic acid or with acetic anhydride to afford the pyrazolopyrimidine derivatives **(13 and 14)**, respectively (SCHEME 3). Also, when **(2)** was treated with acetic anhydride, the ring closure took place to form N- acetyl-N-(6-methyl-4-oxo-1-phenyl-pyrazolo[3,4-d]pyrimidin-5-yl) acetamide **(15)**, whereas the formamide derivative **(16)** was obtained on heating **(2)** with formic acid. In addition, carbohydrazide **(2)** underwent cyclization with triethyl orthoformate affording two different products depending on the reaction conditions and the molar ratio of the reactants.

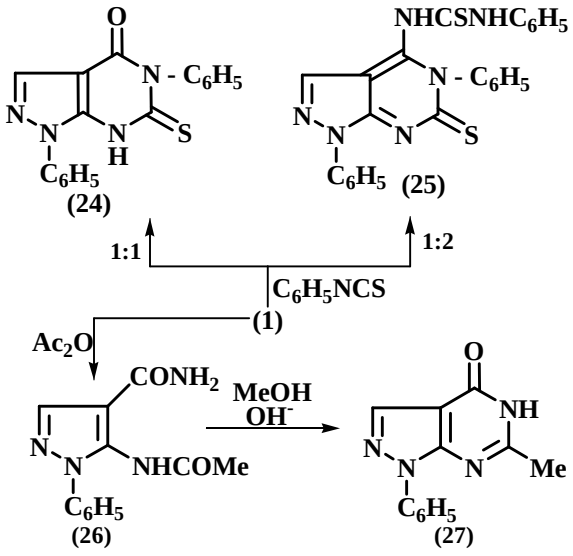
Thus, when **(2)** was allowed to react with triethyl orthoformate in boiling DMF in equimolar ratio, 5-aminopyrazolo[3,4-d]pyrimidine derivative **(17)** was obtained, while fusion of **(2)** with excess triethyl orthoformate yielded bis (pyrazolopyrymidine) derivative **(18)**. Formation of **(18)** is assumed to take place via formation of **(17)** at first followed by condensation of two moles of **(17)** with triethyl orthoformate molecule. The presence of amino group in compound **(17)** was confirmed by its ability to react with phenylisothiocyanate to give N-phenylthiourea derivative **(19)**, while acylation with acetic anhydride and phthalic anhydride afforded the amide **(20)** and the imide **(21)**, respectively. Structure of **(18)** was confirmed by correct elemental analysis and fit spectral data where ^{1}H NMR (DMSO-d_6) displayed a triplet signal at δ 1.3 and a quartet one at 4.36 attributed to ethoxy group in compound **(18)**. Furthermore, the structure of **(18)** was confirmed chemically via its ability to react with active methylene compounds such as malonitrile and ethyl cyanoacetate in basic medium to afford bis(1-phenyl-4-oxo-pyrazolo[3,4–d]pyrimidin-5-ylamino) derivatives **(22,23)** respectively, through nucleophilic substitution reactions.

Moreover, the carboxamide **(1)** underwent cyclization on heating with phenyl isothiocyanate affording two different products, depending on the reaction conditions and the molar ratios of the reactants. Thus, when **(1)** was submitted to react with phenyl isothiocyanate in equimolar ratio it gave a good yield of 1,5-diphenyl-4-oxopyrazolo[3,4-d] pyrimidin-6(7H)-thione **(24)**in boiling acetic acid. Treatment of **(1)** with two moles of phenyl isothiocyanate in acetic acid yielded 1,5-diphenyl-4-phenylthioureido-pyrazolo[3,4-d]pyrimidin-6-thione **(25)**.

Finally, acylation of compound **(1)** with acetic anhydride under fusion condition yielded 5-acetamido-1-phenylpyrazole-4-carboxamide **(26)**, which underwent the ring closure in methanolic sodium hydroxide to give 6-methyl-1-phenylpyrazolo[3,4-d]pyrimidin-4(5H)-one **(27)** (SCHEME 4).

Biological activity

As a part of our research program devoted to the selection of some new pyrazole heterocycles to study their molluscicide activities. *Biomphalaria alexandria* sanils (shell diameter 8-11mm) were collected from



SCHEME 4

canals in Abu-Rawash, Giza, A.R.Egypt and maintained in aquaria filled with dechlorinated water under laboratory conditions (temp. 25 +2^{0}C, pH 7.0-7.7) for three weeks before used in experimental tests. Dried letuce was added daily as food and water was changed weekly. A stock solution of 1000ppm (mass/ volume) of pyrazole heterocycles in dechlorinated tap water (pH 7.5-7.7), as well as, diluted solutions prepared (100ppm, 50ppm, 25ppm, and 10ppm) were prepared. Standara procedures were followed through this study[12]. Statistical analysis of obtained data was carried out according to Litchfield and Wilcoxon method[13].

The molluscicidal activity of some new synthesized pyrazoles against *Biophalaria alexandrina* snails after 24h exposure time are reported in the following TABLE.

EXPERIMENTAL

All melting points reported were uncorrected. The

TABLE : Molluscicide activity

Compound	Composision / ppm			
	100	50	25	10
(1)	100	100	80	40
(2)	0	0	0	0
(3)	100	100	100	10
(4)	0	0	0	0
(10)	0	0	0	0
(11)	0	0	0	0
(18)	0	0	0	0
(20)	0	0	0	0
(21)	0	0	0	0
(22)	0	0	0	0
(23)	0	0	0	0

0 = No mor21tality of snails; 100 = 100% mortality

IR spectra were recorded on a Perkin Elmer 598 spectrophotometer using KBr wafer technique. ^{1}H nmr spectra were measured on a Bruker AC 200 NMR spectro photometer(200MHz) using TMS (δ) as an internal standard. Mass spectra were obtained using GCMS quadrapolar 1000ex Schimadzu instrument (70eV).

5-Amino-1-phenylpyrazole-4-carbohydrazide (2)

A mixture of **(1)** (0.17mol) and hydrazine hydrate (150ml) was stirred and heated on a water bath for 18 h. The solid product that separated out after cooling was acidified with acetic acid. The solid obtained was filtered off and recrystallized from water to give**(2)** as colourless crystals, yield 75 %, m.p. 186^{0}C. M.S (70eV); m/z (/%), 217($M^{\cdot+}$ 15), 186(100): IR ν/cm^{-1}), 3398, 3220 and 3209 (NH_2,NH), 3030 (CH – aromatic),1740 (CO) and 1610 (C=N).

Analysis: (calcd. for $C_{10}H_{11}N_5O$) : C, 55.29; H, 5.06; N, 32.25; (found): C, 55.40; H, 4.90; N, 32.40

1-[5′-Amino-1′-phenylpyrazol-4′-ylcarbonyl]-3,5-dimethypyrazole (3)

A mixture of **(2)** (0.01mol) and acetyl acetone (0.04mol) in DMF(20ml) was heated under reflux for 5h. The reaction mixture was cooled and poured gradually onto crushed ice. The solid obtained was filtered off and recrystallized from methanol-H_2O to give **(3)** as colourless crystals, yield 72%, m.p. 124^{0}C. MS (70eV), m/z(%), 281($M^{\cdot+}$, 61) and 186(100). ^{1}H NMR (DMSO-d_6),δ,2.54 (s, 3H,C3-CH_3),3.36 (s,3H,C5-CH_3),6.19(s,1H,C_4-H pyrazole), 7.44-7.59 (m, 5H, Ar-H), 8.45 (s, 1H, C_3Hpyrazole).IR: ν(cm^{-1}) 3443,3324 (NH_2), 3057 (CH-aromatic), 2924 (CH-aliphatic), 1657 (CO) and 1605 (C=N).

Analysis: (calcd. for $C_{15}H_{15}N_5O$) : C, 64.05; H, 5.33; N, 24.91; (found) : C, 64.70; H, 5.20; N, 24.95

1-[5′-Amino-1′-phenylpyrazol-4′-ylcarbonyl]-3,5-dimethyl-4-(p-tolylazo)pyrazole (4)

A mixture of **(2)** (0.01mol) and 3-(p-tolyl)hydrazono-pentan-2′,4′-dione (0.01mol) in glacial acetic acid (15ml) was heated under reflux for 4h. The solid obtained was filtered off and recrystallized from DMF to give **(4)** as yellow crystals, yield 54 %, m.p. 254^{0}C. IR: ν(cm^{-1}), 3425, 3309 (NH_2), 3050 (CH-aromatic), 2932(CH-aliphatic), 1697(CO) and1604 (C=N).

Analysis: (calcd. for $C_{22}H_{21}N_7O$) : C, 66.16; H, 5.26; H, 24.56; (found) : C, 66.20; H, 5.10; N, 24.50

1-[5′-Amino-1′-phenylpyrazol-4′-ylcarbonyl-]-3-methylpyrazolin-5-one (5)

A mixture of **(2)** (0.01mol) and ethyl acetoacetate (0.012mol) in glacial acetic acid (15ml) was refluxed for 5h. The solid obtained after cooling was filtered off and recrystallised from water to give **(5)** as yellow crystals, yield 68%, m.p. 154-5^{0}C. M.S(70eV) 283, (M^+,26) and base peak at m/z 186. IR:ν(cm^{-1}),3410-3312(NH_2),3010 (CH-aromatic),1705(CO) and 1622 (C=N).

Analysis : (calcd.for $C_{14}H_{13}N_5O_2$) : C, 59.36; H, 4.59;

N, 24.73; (found) : C, 59.30; H, 4.55; N, 24,80

1-[5′-Amino-1′-phenylpyrazol-4′-ylcarbonyl]-3-methyl-4-(p-tolylhydrazono)pyrazolin-5′-one (6)

A mixture of **(2)**(0.01mol) and 2-(p-tolyl) hyrazono butyrate-1′,3′-dione (0.01mole) in glacial acetic acid (15ml) was heated under reflux for 4h. The solid obtained was filtered off and recrystallized from DMF to give **(6)** as orange crystals, yield 50%, m.p.250^{5}C. M.S(70eV) m/z,401(65),186(100). IR: ν(cm^{-1}), 3413,3304(NH_2),3030(CH-aromatic),2921 (CH-aliphatic), 1750, 1702 (CO) and 1619(C=N). ^{1}Hnmr (DMSO-d_6) δ :2.52(s,3H,CH_3),3.36 (s,3H,C_3-CH_3), 6.94 (s,2H, NH_2), 7.25- 7.59(m, 9H,Ar-H) and 8.26(s,1H,C_3-H pyrazole).

Analysis: (calcd. for $C_{21}H_{19}N_7O_2$) : C, 62.84; H, 4.74; N, 24.43; (found) : C, 62.60; H, 4.70; N, 24.45

5-Amino-1-(5′-amino-1′-phenylpyrazol-4′-ylcarbonyl)-4-carboethoxypyrazole (7)

A mixture of **(2)** (0.01mol) and ethyl ethoxymethylenecyanoacetate (0.012 mol) in DMF (20ml) was refluxed for 2h. The solid obtained was filtered off and recrystallized from water to give **(7)** as colourless crystals, yield 78 %, m.p.208^{0}C. IR :ν(cm^{-1}) 3427, 3336, 3280, 3222($2NH_2$), 3034(CH-aromatic), 1729(CO), 1641(C=N). ^{1}HNMR(DMSO-d_6) δ:3.34(s,2H,NH_2), 5.83(s,2H,NH_2), 7.37-8.37(m,5H,Ar-H), 8.05 (d,1H,CH-pyrazole), 8.37 (d,1H, CH-pyrazole) and 8.50 (s,1H,C_3H pyrazole).

Analysis: (calcd. for $C_{16}H_{16}N_6O_3$) : C, 56.47; H, 4.47; N, 24.70; (found) : C, 56.60; H, 4.60; N, 24.77

5-Amino-1-(5′-amino-1′-phenylpyrazol-4′-ylcarbonyl)-4-pyrazolecarbonitrile (8)

A mixture of **(2)**(0.01mol) and ethoxymethylenemalononitrile (0.012mol) was refluxed for 1h. The solid obtained was filtered off and recrystallized from butan-1-ol to give **(8)** as colourless crystals, yield 67%, m.p. 225^{0}C. IR:νcm^{-1}), 3431, 3304, 3219, 3162($2NH_2$), 2228(CN), 1661(CO) and 1619 (C=N)

Analysis: (calcd. for $C_{14}H_{11}N_7O$) : C, 57.34; H, 3.75; N, 33.45; (found) : C, 57.55; H, 3.90; H, 33.37

2-(5′-Amino-1′-phenylpyrazole-4-ylcarbonyl) hydrazonoamino-1-cyanoethane (10)

To a solution of sodium ethoxide (0.02mol) in 50ml absolute ethanol was added malononitrile followed by **(2)** (0.01mol). The reaction mixture was refluxed for 2h left to cool.The solid obtained upon neutralization with dil HCl was filtered off and recrystallized from DMF- water to give **(10)** as brown crystal. Yield 72%, m.p. <280^{0}C. IR: ν(cm^{-1}), 3425, 3339, 3199 (NH,NH_2), 3030(CH-aromatic), 2921(CH-aliphatic), 2213(CN), 1650(CO) and 1618 (C=N).

Analysis : (calcd.for $C_{13}H_{13}N_7O$) : C, 55.12; H, 4.59; N, 34.62; (found) : C, 55.20; H, 4.90; N, 34.50

1-[(5′-Amino-1′-phenylpyrazol-4′-ylcarbonyl)-3-methyl-4,5,6,7-tetrahydroindazole (11)

A mixture of **(2)** (0.01mol) and o-acetyl cyclohexanone (0.01mol) in DMF (20ml) was heated under reflux for 5h. The reaction mixture was cooled and poured gradually onto crushed ice. The solid obtained was filtered off and recrystallized from ethanol to give **(11)**as colourless crystals,yield 70%, m.p. 166^{0}C. MS (70eV)m/z : 321($M.^+$,14.84), 186(100).IR ν(cm^{-1}) 3400, 3291(NH_2), 3068 (CH-aromatic), 2930 (CH-aliphatic),1663 (CO) and 1608 (C=N). ^{1}Hnmr (DMSO-d_6) δ: 1.76(s,3H,CH_3), 2.12-3.36(m,8H,CH_2 at 4,5,6,7 of indazolyl moiety), 2.51(t,2H,CH_3), 2.65 (m,2H,CH_2), 2.99(t,2H,CH_2), 6.97 (s,2H,NH_2), 7.43-7.59(m,5H,Ar-H) and 8.44(s,1H,C_3H pyrazole).

Analysis: (alcd. for $C_{18}H_{19}N_5O$) : C, 67.29; H, 5.92; N, 21.80; (found) : C, 67.50; H, 5.69; N, 21.53

5-Amino-4-(carboybenzylidenehydrazide)-1-phenylpyrazole (12)

A mixture of **(2)**(0.01mol) and benzaldehyde (0.01 mol) and few drops of acetic acid was heated under reflux for 1h. The solid obtained was filtered off and recrystallized from DMF-H_2O to give **(13)**as colourless crystals,yield 77%, m.p. 240^{0}C.IR : ν(cm^{-1}), 3517, 3309, 3224(NH,NH_2), 3055(CH-aromatic), 1650 (CO) and 1642(C=N).

Analysis: (calcd. for $C_{17}H_{15}N_5O$) : C, 66.88; H, 4.91; N, 22.95; (found) : C, 67.00; H, 4.91; N, 22.65

5-Benzylideneamino-1-phenylpyrazolo[3,4-d]pyrimidin-4-one (13)

A solution of **(12)**(0.01mol) in formic acid (20ml) was refluxed for 5h. The reaction mixture was cooled and poured gradually onto crushed ice. The solid obtained was filtered off and recrystallized from ethanol

to give **(12)** as colourless crystals, yield 86%, m.p. 184^{0}C. IR : ν(cm^{-1}), 3057 (CH-aromatic) 2908 (CH-aliphatic), 1711(CO) and 1578 (C=N). ^{1}H NMR (DMSO-d_6)δ5.87(s,1H,N=CH), 7.41-8.47 (m,10H, Ar-H), 8.70(s,1H,C_3-H pyrazole) and 9.17(s,1H,C_6-H pyrimidine).

Analysis: (Calcd. for $C_{18}H_{13}N_5O$) : C, 68.57; H, 4.12; N, 22.22 ; (found) : C, 68.50; H, 4.10; N, 22.29

5-Benzylideneamino-6-methyl-1-phenylpyrazolo [3,4-d]-pyrimidin-4-one (14)

A solution of **(12)** (0.01mol) in acetic anhydride (10ml) was refluxed for 5h. The reaction mixture was cooled and poured gradually onto crushed ice. The solid obtained was filtered off and recrystallized from methanol-H_2O to give **(14)** as pale yellow crystals, yield 64%, m.p. 140^{0}C.IR ν(cm^{-1}): 3050(CH-aromatic), 2950 (CH-aliphatic), 1696(CO) and 1596 (C=N).

Analysis: (calcd. for $C_{19}H_{15}N_5O$) : C, 69.30; H, 4.55; N, 21.27; (Found) : C, 68.90; H, 4.60; N, 21.22

N-Acetyl-N-(6-methyl-4-oxo-1-phenylpyrazolo [3,4-d]-pyramidin-5-yl) acetamide (15)

A solution of **(12)**(0.01mol) in acetic anhydride (20ml) was refluxed for 5h. The reaction mixture was cooled and poured gradually onto crushed ice. The solid obtained was filtered off and recrystallized from ethanol-H_2O to give **(15)** as colourless crystals, yield 66%, m.p.110^{0}C. IR ν(cm^{-1}) : 3171(CH-aromatic), 2927 (CH-aliphatic), 1778,1714,1683 (CO) and 1579 (C=N).^{1}H NMR (DMSO-d_6) δ:2.17(s,3H,C_6-CH_3), 2.27(s,3H,$COCH_3$), 2.45 (s,3H,$COCH_3$), 7.99-8.37(m,5H, Ar-H) and 8.52(s,1H,C_3-H pyrazole).

Analysis: (calcd. for $C_{16}H_{15}N_5O_3$) : C, 59.07; H, 4.61; N, 21.53; (found) : C, 59.00; H, 4.60; N, 21.36

N-(4-Oxo-1-phenylpyrazolo[3,4-d]pyrimidin-5-yl)formamide (16)

A solution of **(2)** (0.01mol) in formic acid (20ml) was refluxed for 5h. The reaction mixture was cooled and poured gradually onto crushed ice. The solid obtained was filtered off and recrystallized from ethanol to give **(16)** as colourless crystals, yield 79%, m.p. 202^{0}C. IR ν(cm^{-1}) : 3237 (NH), 3055(CH-aromatic), 2907 (CH-aliphatic), 1714,1691(CO) and 1581 (C=N). ^{1}N NMR(DMSO-d_6)δ, 5.85(s,1H,NH), 7.41-8.03 (m,5H,Ar-H), 8.43(s,1H,C_3H pyrazole), 8.52 (s,1H,C_6-H pyrimidine) and 11.35(s,1H,aldehydic H).

Analysis: (calcd. for $C_{12}H_9N_5O_2$) : C, 56.47; H, 3.55; N, 27.45; (found) : C, 56.60; H, 3.30; N, 27.66

5-Amino-1-phenylpyrazolo[3,4-d]pyrimidin-4-one (17)

A mixture of **(2)** (0.01mol) and triethyl orthoformate (0.01mol) in DMF(20ml) was heated under reflux for 5h. The reaction mixture was cooled and poured gradually onto crushed ice. The solid obtained was filtered off and recrystallized from DMF to give**(17)** as colourless crystals, yield 70%, m.p. 238^{0}C. MS (70ev) m/z (%), 227(M^+,73,35), 77(100). IR ν(cm^{-1}):3336, 3281(NH_2), 3034(CH- aromatic), 1730 (CO) and 1642(C=N). ^{1}Hnmr (DMSO-d_6) δ : 5.86(s,2H,NH_2), 7.3-8.06 (m,5H,Ar-H), 8040 (s,1H,C_3-H pyrazole), 8.52 (s, H,C6-H pyrimidine).

Analysis: (calcd. for $C_{11}H_9N_5O$) : C, 58.14; H, 3.96; N, 30.83; (found) : C, 57.90; H, 4,00; N, 30.72

N-phenyl-N′-(4-oxo-1-phenylpyrazolo[3,4-d]pyrimidin-5-yl)thiourea (19)

A mixture of **(17)**(0.01mol) and phenyl isothiocyanate (0.01mol) in DMF (20ml) was refluxed for 3h. The reaction mixture was cooled and poured gradually onto crushed ice. The solid obtained was filtered off and recrystallized from DMF-H_2O to give **(19)** as yellow crystals, yield 65%, m.p.>280^{0}C. IR ν(cm^{-1}):3115 (NH),3037 (CH-aromatic), 729(CO), 1597(C=N) and 1223(C=S). ^{1}Hmnr (DMSO-d_6), δ : 3.35(s,1H, SH), 7.36-8.07(m,10H,Ar-H), 8.20 (s,1H,C_3-H pyrazole), 8.33(s,1H,C_6-H pyrimidine) and 12.41 (s,1H,NH).

Analysis: (calcd. for $C_{18}H_{14}N_6OS$) : C, 59.66; H, 3.86; N, 23.20; (found) : C, 59.90; H, 3.80; N, 23.25

N-(4-Oxo-1-phenylpyrazolo[3,4-d]pyrimidin-5-yl)acetamide (20)

A mixture of **(17)** (0.01mol) in acetic anhydride(2ml) was heated at 80^{0}C for 1h. The reaction mixture was cooled and treated with dry ether. The solid obtained was filtered off and recrystallized from methanol to give **(20)** as colourless crystals, yield 68%, m.p. 136^{0}C. IR, ν(cm^{-1}):3445(NH),3038(CH-aromatic), 2940(CH-aliphatic), 1750,1718(CO) and 1676(C=N).

Analysis: (calcd. for $C_{13}H_{11}N_5O_2$) : C, 57.99; H, 4.08; N, 26.02; (found) : C, 57.90; H, 4.00; N, 25.98

N-(4-Oxo-1-phenylpyrazolo[3,4-d]pyrimidin-5-yl)phthalimide (14)

A mixture of **(17)** (0.01mol) and phthalic anhydride (0.01mol) was heated at 190^{0}C for 1h. The reaction mixture was cooled and treated with dry ether. The solid obtained was filtered off and recrystallized from AcOH-H_2O to give **(21)**as pale brown crystals, yield 65%, m.p.>280^{0}C. MS (70eV) m/z : 357($M^{\cdot+}$ 95.99), 77(100). IR, ν(cm^{-1}):3110,3043(CH-aromatic), 1756, 1726(CO) and 1579(C=N). ^{1}Hnmr(DMSO-d_6), δ(ppm): 7.42-8.08 (m,9H,Ar-H), 8.57(s,1H,C_3-H pyrazole) and 9.05(s,1HC_6-H pyrimidine).

Analysis: (calcd. for $C_{19}H_{11}N_5O_3$) : C, 63.86; H, 3.08; N, 19.60; (found) : C, 63.80; H, 3.10; N, 19.57

Bis(4-oxo-1-phenylpyrazolo[3,4-d]pyrimidin-5-ylamino) ethoxymethane (18)

Compound **(2)**(0.01mol) in triethyl orthoformate (20ml) was refluxed for 6 h, and cooled. The solid obtained was filtered off and recrystallized from ethanol to give **(18)**as colourless crystals,yield 80%, m.p.160^{0}C. MS(70eV) m/z,511($M^{\cdot+}$,26.67),77(100).IR, ν(cm^{-1}) :3447(NH), 3042(CH-aromatic, 2946(CH-aliphatic), 1712(CO),1606(C=N).^{1}Hnmr (DMSO-d_6) δ : 1.38 (t,3H,CH_3, ethoxy), 3.41(s,1H,CH,4.36-4.47 (q,2H,CH_2,ethoxy), 5.90 (s,2H, NH), 7.39-8.10 (m,10H,Ar-H), 8.42 (s,2H,2C_3-Hpyrazole), and 8. (s,2H,C_6-H, pyrimidine).

Analysis: (calcd. for $C_{25}H_{22}N_{10}O_3$) : C, 58.82; H, 4.31; N, 27.45; (found) : C, 58.80; H, 4.30; N, 27.44

2-Bis(4-oxo-1-phenylpyrazolo[3,4-d]pyrimidin -5-ylamino) proponitrile (22)

A mixture of **(18)**(0.01mol) and malononitrile (0.01mol) in ethanol (20ml) and few drops of triethyl amine was heated under reflux for 4h. After cooling, the solid product so formed, was collected and recrystallized from butan-1-ol to give **(22)** as brown crystals, yield 68%, m.p. 228^{0}C. IR, ν(cm^{-1}) :3234 (NH), 3066(CH-aromatic), 2972(CH-aliphatic), 2291, 2235(CN), 1680 (CO) and 1594(C=N).

Analysis: (calcd. for $C_{26}H_{18}N_{12}O_2$) : C, 58.87; H, 3.39; N, 31.69; (found) : C, 58.50; H, 3.42; N, 31.62

Ethyl-3,3-bis(4-oxo-1-phenylpyrazolo[3,4-d]pyrimidin-5-ylamino)-2-cyanopropanoate (23)

A mixture of **(18)**(0.01mol) and ethyl cyanoacetate (0.01mol) in ethanol (20ml) and few drops of triethyl amine was refluxed for 4h, and cooled. The solid obtained was filtered off and recrystallized from ethanol-H_2O to give **(23)** as colourless crystals,yield 60%, m.p. 233^{0}C. IR, ν(cm^{-1}) :3250(NH),3024 (CH- aromatic), 2975(CH-aliphatic), 1742(CO, ester), 1682 (CO) and 1595 (C=N).

Analysis : (calcd. for $C_{28}H_{23}N_{11}O_4$) : C, 58.23; H, 3.98; N, 26.68 ; (found) : C, 58.30; H, 4.00; N, 26.75

1,5-Diphenyl-4-oxopyrazolo[3,4-d]pyrimidin-6(7H)-thione (24)

Method A

A mixture of **(1)**(0.01mole) and phenyl isothiocyanate (0.01mol) in acetic acid (30ml) was refluxed for 3h. After cooling, the solid obtained upon dilution with cold water was filtered off and recrystallized from DMF-H_2O to give **(24)** as colourless crystals,yield 70% m.p.> 280^{0}C. IR,ν(cm^{-1}):3449 (NH), 3036 (aromatic-CH), 1682 (C=O), 1636,1594 (C=N an C=C) and 1230(C=S).

Method B

A mixture of **(1)** (0.01mol) and phenyl isothiocyanate (0.01mol) in diphennyl ether (25 ml) was refluxed for 8h. After cooling, the solid obtained was washed with cold ethanol, filtered off and recrystallized from DMF-H_2O to give **(24)** as colourless crystals, yield 60%.m.p.> 280^{0}C ; mixed m.p.> 280^{0}C.

Analysis : (Calcd. for $C_{17}H_{12}N_4OS$) : C, 63.75; H, 3.75; N, 17.50; (Found) : C, 63.80; H, 3.70; N, 17.44

1,5-Diphenyl-4-phenylthioureidopyrazolo[3,4-d]pyrimidin-6-thione (25)

A mixture of **(1)**(0.01mol) and phenyl isothiocyanate (0.02mol) in acetic acid (30ml) was refluxed for 3h. cool, the solid obtained upon dilution with water was filtered off and recrystallized from ethanol-H_2O to give **(25)** as brown crystals,yield 74%. m.p 140^{0}C. IR, ν (cm^{-1}) : 3390, 3250 (2NH), 3037 (aromatic-CH), 1651,1542 (C=N an C=C) and 1226 (C=S). ^{1}Hnmr (DMSO-d_6) δ : 6.40 (s,1H,NH), 6.94-7.69(m, 15 H,Ar-H),7.94 (s,1H, C_3-H of pyrazole) and 8.67 (s,1H,NH).

Analysis : (calcd. for $C_{24}H_{18}N_6S_2$) : C, 63.43; H,

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3.96; N, 18.50; (found) : C, 63.50; H, 3.80; N, 18.43

5-Acetamido-1-phenylpyrazole-4-carboxamide (26)

A mixture of **(1)** (0.01mol) in acetic anhydride (10ml) was heated under reflux for 1h. After cooling, the reaction mixture was poured onto crushed ice and the solid obtained was filtered off and recrystallized from methanol -H_2O to give **(26)** as colourless crystals, yield 81 %, m.p. 140^{0}C. IR, ν(cm^{-1}): 3410, 3286, 3190 (NH_2 and NH), 3080 (aromatic-CH), 2930 (aliphatic–CH) and 1774, 1720 (2C=O).

Analysis : (calcd. for $C_{12}H_{12}N_4O_2$) : 59.01 % C; 4.91 % H; 22.95 % N; (found): 59.00%C; 4.90% H; 22.91% N

6-Methyl-1-phenylpyrazolo[3,4-d]pyrimidin-4(5H)-one (27)

Compound **(26)** (0.01mol) in methanolic sodium hydroxide solution (50cm^3, 2%) was refluxed for 1/2h. and cooled. The reaction mixture was diluted with water and acidified with dilute acetic acid solution. The solid obtained was filtered off and recrystallized from ethanol to give **(27)** as colourless crystals, yield 85, m.p. 250^{0}C. M.S (70eV) m/z,225(12.13), 211(15.78), 184(9.18), 158 (5.62) and 77 (19.58). IR, νcm^{-1}): 3417 (NH), 3024 (aromatic-CH), 2846 (aliphatic-CH), 1681 (C=O) and 1596, 1550 (C=N and C=C). ^{1}Hnmr (DMSO-d_6) δ : 2.42 (s,3H, CH_3), 7.36-8.08 (m, 5H, Ar-H), 8.27 (s, 1H, C_3-H of pyrazole) and 12.32 (s, 1H, NH).

Analysis : (calcd. for $C_{12}H_{10}N_4O$) : C, 63.71; H, 4.42; N, 24.77; (found) : C, 63.50; H, 4.50; N, 24.70

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