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New Purine Derivatives of Potential Plant-Growth Regulating Properties

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2-(CHLOROMETHYL)-purine-6(9*H*)-one (3) was synthesized from reaction of the 5-amino-imidazole-4-carboxamide 1 with 2-chloroacetyl chloride. Also, products 4-7 were obtained from reacting 3 with different reagents. Treatment of 1 with ethyl chloroformate / DMF reagent mixture afforded 9-aryl-1,9-dihydro-6*H*-purin-6-one (9). Product 9 when reacted with some alkyl iodides gave 7-alkylpurinium iodide salts (10) rather than the expected products of type 11 *or* 12. *N*-substituted – purin -6- amines 14a-g, N^1-(purin-6-yl) - benzene-1,2-diamine 14h and hydrazide 14i were synthesized upon treating product 9 with phosphoryl chloride followed by reaction with some selected amines *or* hydrazides . Screening for selected examples from the synthesized products 14 towards wheat plant growth regulation was reported.

Keywords: 6-Substituted-amino purines, Purinium iodide salts and Plant growth regulators.

The important role of the amino group in purine derivatives has been documented not only by its Waston-Crick base-pairing capacity in nucleic acids, but also for its essential presence in purine receptor agonists of A-type and P-type in substrate/inhibitor binding to enzymes of purine metabolism [1-3], as well for its important regulatory pathways [4, 5].

N^6-adenines are especially important substrates owing to their possible cytokinin activity. Natural cytokinins are adenine derivatives with a side chain at the N^6-position, and participate in conjunction with other hormones in most aspects of plant growth and development [6].

Cytokinines are low molecular weight substances (*e.g*. N^6-substituted adenine the main family of the plant hormones cytokinins) found in plants. Cytokinines, together with auxin, play an essential role in plant morphogenesis, having a profound influence on the formation of roots and shoots and their relative growth. The most important role of cytokinines is to promote plant cell division and cell growth and they are involved in retardation of senescence and to stimulate morphogenesis [7- 9].

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Therefore, in continuation to our previous work on 6-aminopurines[10,11] for regulating the growth of several plants *e.g.* cotton, soy-bean, potatoes, the present work was intended to synthesize newer 6-substituted-aminopurines and other related derivatives, structurally related to the well known plant growth regulators "Cytokinines", with the target for evaluating their potential plant-growth regulating properties.

Experimental

All melting points are uncorrected. Microanalyses were carried out by the Micro analytical Laboratory, National Research Center, Cairo, Egypt. Infrared spectra (KBr-disc) were recorded using a Jasco FT/IR-300E spectrophotometer. ^{1}H NMR spectra were recorded in DMSO-d_6 using Varian mercury 300 MHz and Varian Gemini 200 MHz with chemical shift in δ from Me_4Si. Mass spectra were recorded on GC/MS Finnegan SSQ 7000 spectrophotometer.

Plant-growth regulating properties were carried out by the Water Relations and Irrigation Department, Agriculture Division, National Research Centre, Egypt. Wheat seeds are sown in pots containing soil that was not already treated before with any plant-growth regulator(s), and watered as required.

After 21 days from sowing, preliminary screening of some selected examples of the newly synthesized 6-(substituted-amino)-purines was carried out towards the young wheat plant shoots (7 plants/each pot). The young shoots were sprayed weekly with aqueous spray liquor of compounds 14a-h (concentration 100ppm) for 11 week till plants were grown to maturity.

Control experiment was carried out in which the young shoots are sprayed with the same aqueous spraying liquor containing no active ingredient of the tested compounds. Also, another control experiment was carried out for comparison using cultivated wheat plant(s) in a soil which has been not treated before by any plant growth regulator.

5-Amino-1-(4-fluorophenyl)-1H-imidazole-4-carboxamide (1)

A mixture of 2-aminocyanoacetamide (0.01 mol) and triethyl orthoformate (0.02 mol) in acetonitrile (20 ml) was heated under reflux for 1 hr. After cooling, 4-fluoroaniline (0.01 mol) was added to the reaction mixture and reflux was continued for another 15 min. The solid product obtained was filtered off, washed with methanol, dried and crystallized from DMF to give (1): Yield 76 %; m.p. 283-84°C.; Anal. Calc. for $C_{10}H_9FN_4O$ (220.20): C, 54.54; H, 4.12; N, 25. 44. Found: C, 54.50; H, 4.15; N, 25.38; IR (KBr,cm^{-1}):3414, 3329, 3196 (NH), 1666 (C=O).; ^{1}H-NMR (300 MHz, DMSO-d_6,δ/ppm): 5.75(b, 2H, NH_2); 6.90(b, 2H, $CONH_2$); 7.40(m, 3H, 2CH (Ar), H-2); 7.50 (m, 2H, (Ar).; MS (*m/z*) (relative absorbance,%):220 (M^+,100).

2-(Chloromethyl)-9-(4-fluorophenyl)-1H-purine-6(9H)-one (3)

Chloroacetyl chloride (15 mmol) was added dropwise with stirring to a solution of compound 1 (10 mmol) in *N, N*-dimethyl formamide (15 ml), stirring was continued for 4 hr, and then the reaction mixture was poured to ice cooled water. The solid product obtained was filtered off, dried and crystallized from methanol to give (3): Yield 65 %; m.p. 198-200°C.; Anal. Calc. for $C_{12}H_8ClFN_4O$ (278.67): C, 51.72; H, 2.89; N, 20.11. Found: C, 51.75; H, 2.90; N, 20.10; IR (KBr, cm^{-1}): 3441, 3274, 3170 (NH), 1691 (C=O); ^{1}H-NMR (300MHz, DMSO-d_6, δ/ppm): 4.18(s, 2H, CH_2); 7.20-7.60 (m,4H,4CH (Ar)); 8.02 (s, 1H, H-8); 10.28(b, 1H, NH, D_2O-exchangeable).

Ethyl 2-cyano-3-(9-(4-fluorophenyl) -6,9-dihydro-6-oxo-1H-purin-2yl) propanoate (4)

To a mixture of 3 (0.01 mol) and ethyl cyanoacetate (20 mmol) in dimethylsulfoxide (DMSO) (15 ml) a solution of potassium hydroxide (1g in 3 ml water) was added. The reaction mixture was heated for 1hr on a steam-bath. The solvent was evaporated under reduced pressure. The residue was dissolved in water and neutralized by dilute acetic acid; the separated solid product was collected by filtration and crystallized from ethanol to give (4): Yield 74 %, m.p. 283-85°C.; Anal. Calc. for $C_{17}H_{14}FN_5O_3$ (355.32): C, 57.46; H, 3.97; N, 19.71. Found: C, 57.42; H, 3.93; N, 19.67. IR (KBr, cm^{-1}): 3311 (NH), 2207 (C≡N), 1645 (C=O). ^{1}H-NMR (300MHz, DMSO-d_6, δ/ppm): 1.24 (t, 3H, *J*=7.06*Hz*, CH_3); 4.23 (q, 2H, *J*=7.06*Hz*, CH_2-ethyl); 4.66 (d, 2H, CH_2); 6.59 (m, 1H, CH); 7.50 (m, 2H,2CH, (Ar));7.81(m, 2H ,2CH,(Ar)); 8.66 (s, 1H, H-8); 14.10 (s, 1H, NH-D_2O-exchangeable).

9-(4-Fluorophenyl)-2-(hydrazinomethyl)-1H-purin-6(9H)-one (5)

A mixture of 3 (0.01 mol) and hydrazine hydrate (0.015 mol) in absolute ethanol (20 ml) was heated under reflux for 1 hr. The solid product obtained was filtered off and crystallized from methanol to give (5): Yield 79 %, m.p. 272-74°C. Anal. Calc. for $C_{12}H_{11}FN_6O$ (274.25): C, 52.55; H, 4.04; N, 30.64. Found: C, 52.60; H, 4.00; N, 30.60. IR (KBr, cm^{-1}): 3329, 3272, 3197 (NH), 1666 (C=O); MS (*m/z*) (relative absorbance, %): 274 (M^+, 100) 275, 276.

9-(4-Fluorophenyl) -2- ((3-methyl -5-oxo -4,5- dihydro -1H- pyrazol -1-yl) methyl) -1H-purin-6(9H)-one (6)

A mixture of 5 (0.01 mol) and ethyl acetoacetate (10 ml) was heated under reflux for 5 hr. After cooling the solid product obtained was filtered off, washed with cold methanol, dried and crystallized from ethanol to give (6): Yield 73 %, m.p. 260-62°C. Anal. Calc. for $C_{16}H_{13}FN_6O_2$ (340.31): C, 56.47; H, 3.85; N, 24.70. Found: C, 56.35; H, 3.75; N, 24.90. IR (KBr, cm^{-1}): 3330 (NH), 1668 (C=O). ^{1}H-NMR (300MHz, DMSO-d_6,δ/ppm): 2.52(s, 1H, CH_3); 4.96(s, 2H, CH_2); 5.77(s, 2H, CH_2); 7.37-7.61 (m, 5H, 4CH(Ar), H-8), H-8); 12.36(b, 1H, NH,D_2O-exchangeable). MS (*m/z*) (relative absorbance, %): 340 (M^+, 100) 341, 342.

2-((3,5-Dimethyl- 1H-pyrazol-1-yl) methyl) -9-(4-fluorophenyl) -1H- purin-6 (9H)-one (7)

A mixture of 5 (0.01mol) and acetyl acetone (10 ml) was heated under reflux for 5 hr. After cooling the solid product obtained was filtered off, washed with cold methanol, dried and crystallized from ethanol to give (7): Yield 69 %, m.p. 235-37°C. Anal. Calc. for $C_{17}H_{15}FN_6O$ (338.34): C, 60.35; H, 4.47; N, 24.84. Found: C, 60.21; H, 4.50; N, 25.00. IR (KBr, cm^{-1}): 3330 (NH), 1703 (C=O). ^{1}H-NMR (300MHz, DMSO-d_6, δ/ppm): 2.38, 2.50 (2s, 6H, $2CH_3$); 4.75 (s, 2H, CH_2); 7.46 (m, 3H, 2CH (Ar), CH pyrazole), CH-pyrazole); 7.80 (m, 3H, (Ar)); 8.37 (s, 1H, H-8); 12.36 (b, 1H, NH, D_2O-exchangeable). MS (*m/z*) (relative absorbance, %): 338 (M^+, 100) 339, 340.

9-(4-Fluorophenyl)-1H-purin-6(9H)-one (9)

Method A

A mixture of the imidazole 1 (0.01 mol) and formamide (15 ml) was heated at 180-190 ºC (oil-bath temperature) for 2 hr and then left to cool. The separated solid was filtered off, washed several times with cold water, cold ethanol, dried and then crystallized to give product 9.

Method B

To a mixture of ethyl chloroformate (10 ml) and *N*,*N*-dimethyl formamide (5 ml) it was added 1 (0.01 mol). The reaction mixture was then heated under reflux for 15 min and left to cool. The solid product obtained was filtered off, washed with cold ethanol, dried and crystallized from DMF to give (9): Method A: Yield 75%; Method B: Yield 80 %, m.p. 324-6°C. Anal. Calc. for $C_{11}H_7FN_4O$ (230.20): C, 57.39; H, 3.07; N, 24.34. Found: C, 57.35; H, 3.05; N, 24.35. IR (KBr, cm^{-1}): 3113 (NH), 1714 (C=O). ; MS (*m/z*) (relative absorbance, %): 230 (M^+, 100), 231.

9- (4-Fluorophenyl) -7- substituted -6- oxo -6,9 – dihydrophenyl - 1H-purin-7-ium iodide salts (10)

General procedure

A mixture of 9 (0.01 mol) and the desired alkyl iodide (0.012) in *N*, *N*-dimethylformamaide (20 ml) was heated under reflux for 1 hr. The reaction mixture was then concentrated and left to cool. The solid product obtained was filtered off and crystallized from ethanol to give 10.

9- (4-Fluorophenyl) -7- methyl -6- oxo- 6,7,8,9- tetrahydro -1H-purin -9-ium iodide (10a)

Yield 72%, m.p. 313-15°C. Anal. Calc. for $C_{12}H_{12}FIN_4O$ (374.15): C, 38.52; H, 3.23; N, 14.97. Found: C, 38.77; H, 3.18; N, 14.76. IR (KBr, cm^{-1}): 3448 (NH), 1730 (C=O). ^{1}H-NMR (300MHz, DMSO-d_6, δ/ppm): 3.34(s, 3H, CH3); 7.44 (m, 2H, 2CH (Ar); 7.80 (m, 2H, 2CH (Ar)); 8.08 (s, 1H, H-8); 8.44 (s, 1H, H-2); 12.48 (b, 1H, NH, D_2O-exchangeable). Mass (*m/z*) (relative absorbance, %): 242 (M^+-HI).

7-Ethyl-9-(4-fluorophenyl)-6-oxo-6,7,8,9-tetrahydro-1H-purin-9-ium iodide (10b)

Yield 70 %, m.p. 273-75°C. Anal. Calc. for $C_{13}H_{14}FIN_4O$ (388.18): C, 40.22; H, 3.64; N, 14.43. Found: C, 40.40; H, 3.45; N, 14.48. IR (KBr, cm^{-1}): 3445 (NH), 1703 (C=O). ^{1}H-NMR (300MHz, DMSO-d_6, δ/ppm): 1.60(t, 3H, J=7.0 Hz, CH_3); 4.60 (q, 2H, *J*=7.0 Hz,CH_2) ;7.60(m, 2H, 2CH (Ar); 7.90(m, 2H, 2CH (Ar)); 8.50 (s, 1H, H-8);10.10 (s,1H, H-2); 12.40(b,1H, NH,D_2O-exchangeable). Mass (*m/z*) (relative absorbance, %): 260 (M^+-HI).

Preparation of 6-Chloro-9-(4-fluorophenyl)-9H-purine (13)

A mixture of 9 (0.01 mol) and phosphoryl chloride (20 ml) was heated under reflux for 1 hr and left to cool. The reaction mixture was then poured onto crushed ice while stirring. The solid product separated out was filtered off, washed several times with cold water, dried and crystallized from acetonitrile to give (13): Yield 77 %, m.p. 233-5°C.Anal. Calc. for $C_{11}H_6ClFN_4$ (248.64): C, 53.14; H, 2.43; N, 22.53. Found: C, 53.15; H, 2.40; N, 22.50. MS (*m/z*) (relative absorbance, %): 248 (M^+, 100), 250, 249, 251, 249.

6-(Substituted)-9-(4-fluorophenyl)-9H-purines (14a-i)

General procedure

To a solution of 13 (0.01 mol) in absolute ethanol (50 ml), the appropriate amine or hydrazide (0.013 mol) was added in the presence of triethylamine (½ ml). The reaction mixture was heated under reflux for 3 hr. Then, the reaction mixture was concentrated and left to cool. The solid product(s) obtained was filtered off and crystallized from ethanol to give products 14a-i.

9-(4-Fluorophenyl)-N-methyl-9H-purin-6-amine (14a)

Yield 72 %, m.p. 268-70°C. Anal. Calc. for $C_{12}H_{10}FN_5$ (243.24): C, 59.25; H, 4.14; N, 28.79. Found: C, 59.20; H, 4.15; N, 28.75. IR (KBr, cm^{-1}): 3250 (NH). ^{1}H-NMR (300MHz, DMSO-d_6, δ/ppm): 2.75(3H, CH_3); 3.85 (b, 1H, NH; D_2O-exchangeable); 8.16(s, 1H, H-2); 7.2-7.62 (m, Ar-H) Mass (*m/z*) (relative absorbance, %): 243 (M^+, 100), 244

N-Ethyl-9-(4-fluorophenyl)-9H-purin-6-amine (14b)

Yield 88 %, m.p. 273-74°C. Anal. Calc. for $C_{13}H_{12}FN_5$ (257.27): C, 60.69; H, 4.70; N, 27.22. Found: C, 60.64; H, 4.50; N, 27.19. IR (KBr, cm^{-1}): 3228 (NH). ^{1}H-NMR(300MHz, DMSO-d_6, δ/ppm): 1.20(t, 3H, *J*= 7.50 Hz , CH_3); 3.60(q, 2H, *J*= 7.50 Hz , CH_2); 3.90(b, 1H , NH, D_2O-exchangeable);7.45(m, 2H, 2CH (Ar); 7.90 (m, 2H, 2CH (Ar)); 8.25(s, 1H, H-8); 8.55 (s,1H, H-2). Mass (*m/z*) (relative absorbance, %): 257 (M^+, 100), 258, 259.

N,N-Diethyl-9-(4-fluorophenyl)-9H-purin-6-amine (14c)

Yield 80 %, m.p. 101-02°C. Anal. Calc. for $C_{15}H_{16}FN_5$ (285.32): C, 63.14; H, 5.65; N, 24.55. Found: C, 63.12; H, 5.58; N, 24.49. ^{1}H-NMR (300MHz, DMSO-d_6, δ/ppm): 1.20 (t, 6H, *J*= 6.90 Hz, $2CH_3$); 4.00(q, 4H, *J*= 6.90 Hz,

$2CH_2$); 7.40 (m, 2H, 2CH (Ar); 7.95 (m, 2H, 2CH, (Ar)); 8.26(s, 1H, H-8); 8.51 (s, 1H, H-2). MS (*m/z*) (relative absorbance, %): 285 (M^+, 100), 286, 287.

N-(n-Butyl)-9-(4-fluorophenyl)-9H-purin-6-amine (14d)

Yield 76 %, m.p. 103-04°C. Anal. Calc. for $C_{15}H_{16}FN_5$ (285.32): C, 63.14; H, 5.65; N, 24.55. Found: C, 63.15; H, 5.70; N, 24.50. IR (KBr, cm^{-1}): 3241 (NH). ^{1}H-NMR (300MHz, DMSO-d_6, δ/ppm): 0.94 (t, 3H, *J*= 7.20 Hz, CH_3);1.35 (m, 2H, CH_2) ;1.61(m,2H ,$2CH_2$); 3.52(m, 2H, CH_2); 3.90 (b, 1H , NH,D_2O-exchangeable);7.43(m, 2H , 2CH, (Ar) ; 7.93 (m, 2H, 2CH,(Ar)); 8.28 (s,1H, H-8); 8.55(s, 1H, H-2). MS (*m/z*) (relative absorbance, %): 285 (M^+, 100), 286, 287

9-(4-Fluorophenyl)-N-((furan-2-ylmethyl))-9H-purin-6-amine (14e)

Yield 67 %, m.p. 144-45°C. Anal. Calc. for $C_{16}H_{12}FN_5O$ (309.30): C, 62.13; H, 3.91; N, 22.64. Found: C, 62.16; H, 3.87; N, 22.58. IR (KBr, cm^{-1}): 3265(NH). ^{1}H-NMR (300MHz, DMSO-d_6, δ/ppm): 3.60(b, 1H, NH D_2O-exchangeable); 4.80 (s, 2H, CH_2); 6.27(m, 1H, C_3-H-furyl.); 6.38(m, 1H, C_4-H-furyl); 7.42(m, 3H, 2CH,(Ar),C_5-H,furyl); 7.90 (m, 2H, 2CH,(Ar)); 8.32 (s,1H, H-8,); 8.58(s, 1H, H-2). MS (*m/z*) (relative absorbance, %):309 (M^+, 100), 310, 311.

N-Benzyl-9-(4-fluorophenyl)-9H-purin-6-amine (14f)

Yield 85 %, m.p. 163-5°C. Anal. Calc. for $C_{18}H_{14}FN_5$ (319.34): C, 67.70; H, 4.42; N, 21.93. Found: C, 67.50; H, 4.45; N, 21.90. IR (KBr, cm^{-1}): 3213(NH). ^{1}H-NMR (300MHz, DMSO-d_6, δ/ppm): 4.4(s, 2H, CH_2); 6.83 (b, 1H, NH, D_2O-exchangeable); 8.2 (s, 1H, H-2); 7.21-7.65 (m, Ar-H). MS (*m/z*) (relative absorbance, %): 319 (M^+, 100), 320, 321.

N, 9-Bis(4-fluorophenyl)-9H-purin-6-amine (14g)

Yield 64 %, m.p.209-10°C, Anal. Calc. for $C_{17}H_{11}F_2N_5$ (323.30): C, 63.16; H, 3.43; N, 21.66. Found: C, 63.10; H, 3.40; F, N, 22.00. IR (KBr, cm^{-1}): 3406, 3319 (NH). ^{1}H-NMR (300MHz, DMSO-d_6, δ/ppm): 8.2 (s, 1H, H-2); 9.46 (b, 1H, NH, D_2O-exchangeable); 7.20-7.66 (m, Ar-H) MS (*m/z*) (relative absorbance, %): 323(M^+, 100), 324, 325.

N^1-(9-(4-fluorophenyl)-9H-purin-6-yl)benzene-1,2-diamine (14h)

Yield 58 %, m.p. 214-16°C, Anal. Calc. for $C_{17}H_{13}FN_6$ (320.32): C, 63.74; H, 4.09; N, 26.24. Found: C, 63.75; H, 4.05; N, 26.20. IR (KBr, cm^{-1}): 3381, 3275 (NH). ^{1}H-NMR (300MHz, DMSO-d_6, δ/ppm): 4.90 (b, 2H, NH_2 D_2O-exchangeable); 6.60 (m, 1H, CH(Ar); 6.80 (s, 1H, CH, (Ar); 6.95(m, 1H,CH, (Ar); 7.25 (s, 1H, CH, Ar-H); 7.45(m, 2H ,2CH,(Ar); 7.95 (m, 2H, 2CH,(Ar)); 8.25(s, 1H, H-8); 8.70 (s, 1H, H-2); 9.20 (b,1H, NH,D_2O-exchangeable). MS (*m/z*) (relative absorbance, %): 320 (M^+, 100), 321,322.

N'-(9-(4-Fluorophenyl)-9H-purin-6-yl) isonicotinohydrazide (14i)

Yield 65 %, m.p. 297-99°C., Anal. Calc. for $C_{17}H_{12}FN_7O$ (349.32): C, 58.45; H, 3.46; N, 28.07. Found: C, 58.25; H, 3.50; N, 27.95. IR (KBr, cm^{-1}):

3300, 3110 (NH), 1673 (C=O). ^{1}H-NMR(300MHz, DMSO-d_6,δ/ppm): 7.46 (m, 2H,2CH,(Ar); 7.93 (m, 4H, 2CH,Ar-H),8.87(s 2H-pyridine)); 8.38 (s, 1H, H-8); 8.64 (s, 1H, H-2); 8.81 (s, 2H, pyridine); 10.00 (b,1H, NH,D_2O-exchangeable); 11.04 (b, 1H, NH).MS (*m/z*) (relative absorbance, %):349 (M^+, 100), 350, 351.

Preparation of 6-(1H-benzo[d]imidazol-1-yl)-9-(4-fluorophenyl)-9H-purine (15)

Method A

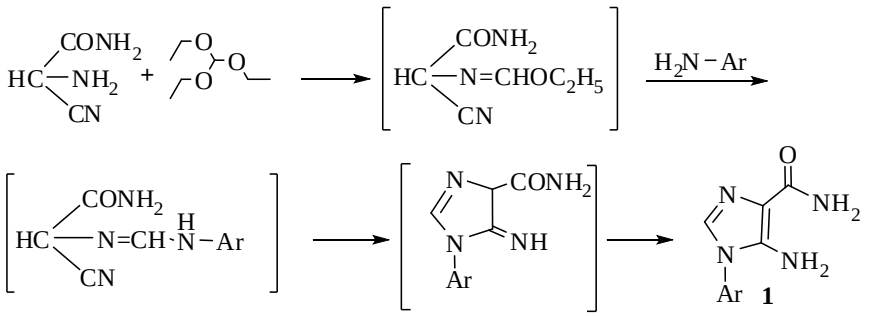
A mixture of 14h (0.01 mol.) and ethyl chloroformate (0.12 mol) in *N, N*-dimethylformamaide (20 ml) was stirred for 3 hr. The solid product obtained was filtered off and crystallized from DMF to give (15).

Method B

A mixture of 14h (0.01mol) and triethyl orthoformate (0.12 mol) in *N, N*-dimethylformamaide (20 ml) was heated under reflux for 3 hr and the reaction mixture was then concentrated under reduced pressure and left to cool. The solid product obtained was filtered off and crystallized from DMF to give (15): Method A: yield 70%; Method B: Yield 87 %, m.p. 316-18°C. Anal. Calc. $C_{18}H_{11}FN_6$ (330.32): C, 65.45; H, 3.36; N, 25.44. Found: C, 65.40; H, 3.35; N, 25.30. ^{1}H-NMR (300MHz, DMSO-d_6, δ/ppm): 7.50(m, 5H, 5CH, (Ar); 7.90 (m, 3H, 3CH, (Ar)); 8.40 (d, 1H, H-8); 8.55 (s, 1H, H-2); 9.90 (s, 1H, H-2(benzimidazole). MS (*m/z*) (relative absorbance, %): 330 (M^+, 100), 331, 332.

Results and Discussion

5-Amino-1-(4-fluorophenyl)-1*H*-imidazole-4-carboxmide (1) was smoothly obtained, in 67% yield, by facile ring closure of ethyl *N*-(carbamoyl-cyanomethyl) formamidate (obtained from triethyl orthoformate and 2-amino-2-cyanoacetamide) upon heating under reflux with *4*-fluoroaniline , in acetonitrile. (Scheme 1)



Ar = 4-fluorophenyl

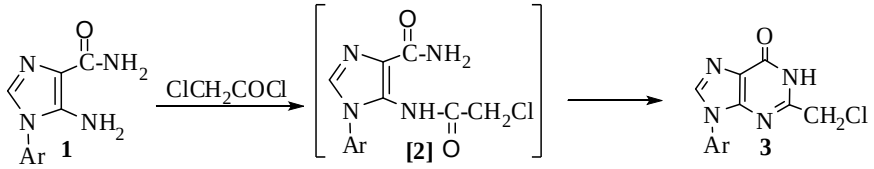
Preparation of 5-Amino-1-(4-fluorophenyl)-1*H*-imidazole-4-carboxmide **1** from ethyl *N*-(carbamoyl-cyanomethyl)formamidate; 67% yield

Scheme1

The infrared absorption spectrum of 1 lacks C≡N absorptions and showed $\upsilon_{C=O}$ (amide) at 1666 cm^{-1}. Also, the spectrum included υ_{NH} due to $-NH_2$ and $CONH_2$ functional groups at 3414 and 3329-3196 cm^{-1} region .

Its ^{1}H-NMR spectrum revealed, generally, the characteristic signals due to NH_2 and $CONH_2$ protons (D_2O-exchangeable) at δ: 5.75 and 6.90 ppm, respectively; beside the H-2 proton signal of the imidazole nucleus. Moreover, its mass spectrum showed a molecular ion peak *m/z* = 220 (M^+, 100%).

When 5-amino-1-(4-fluorophenyl)-1*H*-imidazole-4-carboxamide (1) was left to react with 2-chloroacetyl chloride; 2-(chloromethyl)-9-(4-fluorophenyl)-1*H*-purine-6(9*H*)-one 3 was afforded in 65% yield, presumably, through formation and ring closure of the intermediate [2] (Scheme 2).



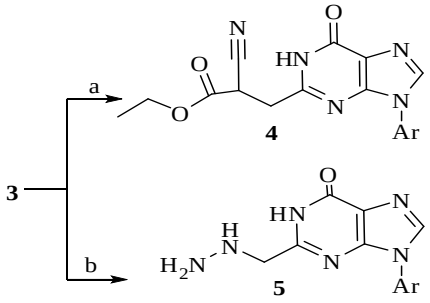
Ar = 4-fluorophenyl

Reaction conditions: chloroacetyl chloride, DMF, strirring at r.t for 4 h, 65% yield

Scheme 2

Structure of product 3 was elucidated from its correct analytical data; besides studying of its IR, ^{1}H-NMR and mass spectral determinations as well by chemical synthesis for some of its related derivatives.

When compound 3 was reacted with ethyl 2-cyanoacetate *or* hydrazine hydrate: ethyl 2-cyano-3-(9-(4-fluorophenyl)-6,9-dihydro-6-oxo-1*H*-purin-2-yl) -propionate (4) and 9-(4-fluorophenyl)-2-(hydrazinomethyl)-1*H*-purin-6(9*H*)-one (5) were afforded in 74 and 79% yield, respectively (Scheme 3).

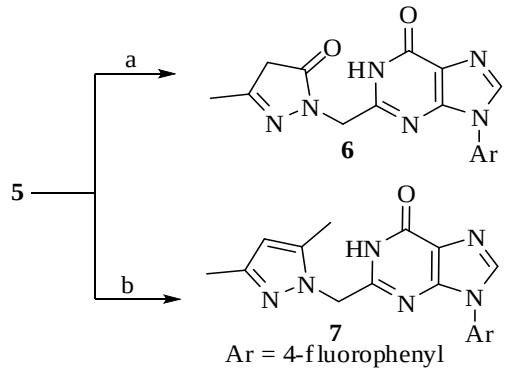


Reaction Conditions:a) Ethyl cyanoacetate, DMSO, KOH, steam-bath heating for 1 hr 74% yield;
b) Hydrazine hydrate, EtOH, heating for 1 hr, 79% yield; Ar = 4-fluorophenyl

Scheme 3

Also, when product 5 was left to react with ethyl 3-oxobutanoate *or* with pentane-2,4-dione the corresponding: 9-(4-fluorophenyl) -2- ((3-methyl- 5- oxo - 4,5- dihydro- 1H- pyrazol-1-yl) methyl)- 1*H*- purin- 6(9*H*)-one (6) and 2-((3,5-dimethyl- 1H-pyrazol- 1-yl)methyl) -9- (4-fluorophenyl)- 1*H*-purin-6(9*H*)-one 7 were obtained in 73 and 69 % yield, respectively (Scheme 4).

IR Spectrum of 6 Showed υ: 3330 (NH), 1668 (C=O), ^{1}H-NMR displayed CH_3, CH_2, NH (D_2O-exchangeable) and H-8 proton signals at 2.52, 4.96&5.77 and 12.36 ppm, respectively. IR Spectrum of 7 Showed υ: 3330 (NH), 1703 (C=O), ^{1}H-NMR revealed CH_3, CH_2, H-8 CH_2 (pyrazole) and NH proton signals at 2.38, 2.50; 4.75; 7.46; 12.36 ppm, respectively**.**



Reaction Conditions:a) Ethyl 3- oxobutan oate, heating for 5 hr 73% yield;
b) Pentane-2,4-dione , heating for 5 hr, 69% yield,

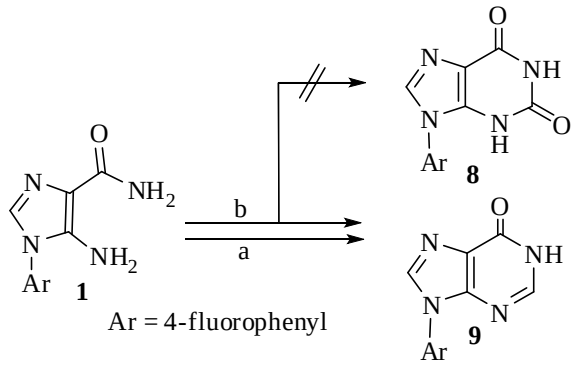
Scheme 4

Moreover, when the imidazole 1 was heated with ethyl chloro-formate/dimethylformamide reagent mixture[12-15] (2:1 ratio by volume), the 9-(4-fluorophenyl)-1*H*-purin-6(9*H*)-one 9 was obtained (80% yield) as a clean cut product. No traces of the expected 9-(4-fluorophenyl)-1*H*-purine-2,6-dione of type 8 was isolated under the present reaction conditions. Product 9; synthesized *via* ethyl chloroformate/DMF method was found to be identical with that obtained from reaction of the imidazole 1 with formamide (formamide is a well known reagent usually employed at relatively high reaction temperatures ~185 ºC for the ring closure of this type of products) [16, 17].

Infrared absorption spectrum of product 9 obtained either from reaction of 1 with ethyl chloroformate / DMF mixture or from reaction of 1 with formamide, was found to be of finger-print similarity.

Thus, its IR spectrum exhibited $\upsilon_{C=O}$ (sharp intense) and υ_{NH} (broad with fine structures) around 1714 and 3300-3500 cm^{-1} , respectively.

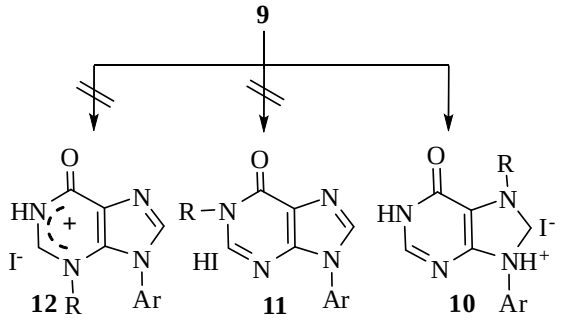
This can be considered as another support for the structure 9 rather than product of type 8 (Scheme 5).



Reaction Conditions:a) Form amid, heating for 2 hr (180-190ºC), 75% yield;
b) $ClCO_2Et$/ DMF , heating for 15 min, 80% yield,

Scheme 5

Furthermore, it was found when product 9 was left to react under reflux with methyl- or ethyl iodide in *N*,*N*-dimethylformamide; the corresponding derivatives: 9- (4-fluorophenyl)-7-methyl-6-oxo-6,7,8,9-tetrahydro-1H-purin-9-ium and 7-ethyl-9-(4-fluorophenyl)-6-oxo-6,7,8,9-tetrahydro-1H-purin-9-ium iodide (10a,b) were obtained in 72 and 70% yield, respectively rather than the expected N^1- *or* N^3-alkyl derivatives of types 11 and 12 (Scheme 6).



10-12 a) R = CH_3, b) R = C_2H_5, Ar = 4-fluorophenyl

Reaction Conditions: Methyl-or ethyl iodide, DMF, heating for 1 hr 72-73% yield

Scheme 6

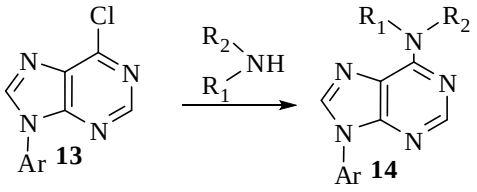
Structural elucidation of products 10 was inferred from:

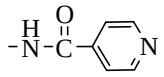
i) Correct analytical data. ii) The IR spectra are nearly similar to the spectrum of their parent 9. iii) ^{1}H-NMR spectra of products 10 showed down

field shifted proton signals (D_2O-exchangeable) around δ: 12.48 ppm due to the presence of NH and thus exclude formation of products of type 11. Also, the spectra revealed the H-8 proton signals slightly down field shifted; accordingly products of type 12 were excluded[18-20]. Therefore, quaternization of product 9 was occurred at position-7 rather than position-1- or position-3 to give products of type 10. iv) When product 9 was heated under reflux with $POCl_3$ the corresponding 6-chloro-9-(*4*-fluorophenyl)-9*H*-purine (13) was readily obtained in an excellent yield.

The present work was planned to employ the 6-chloropurine 13 for synthesizing newer 6-substituted-aminopurine derivatives, structurally related to the well known plant growth regulators "Cytokinines", with the target for evaluating their potential plant-growth regulating properties.

Thus, when the chloropurine 13 was left to react with several alkyl, aralkyl-, and aryl- amines *or* hydrazide in boiling ethanol in the presence of an acid scavenger (*e.g.* triethylamine), the corresponding 6-substitutedamino-purines 14a-g , N^1-[9-(4-fluorophenyl)-9*H*-purin-6-yl]benzene-1,2-diamine (14h) and *N'*-[9-(4-fluorophenyl)-9*H*-purin-6-yl]isonicotinohydrazide (14i), were smoothly afforded (64-85% yield). (Scheme 7)



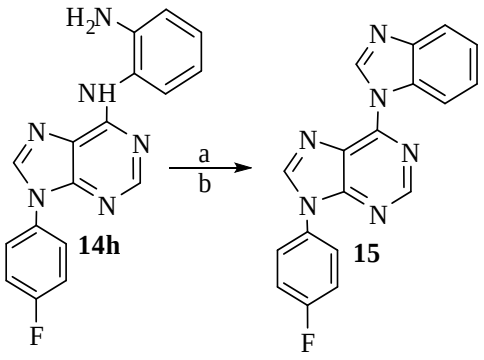
14	R_1	R_2	yield %	**14**	R_1	R_2	yield %
a)	CH_3	H	72	f)	benzyl	H	85
b)	C_2H_5	H	88	g)	C_6H_4-F-*p*	H	64
c)	C_2H_5	C_2H_5	80	h)	$C_6H_4NH_2$-*o*	H	58
d)	CH_2-furyl	H	76	i)		H	65

Ar = 4-fluorophenyl

Scheme 7

IR spectra of products 14a-i showed, generally, υ_{NH} (sharp) absorptions around 3450-3213 cm^{-1} region. The ^{1}H-NMR spectra of products 14 were found in agreement with the proposed structure. Generally, the spectra included H-2 (purine) together with the aromatic proton signals. Also, the NH signals can be easily distinguished in the spectra (broad; D_2O-exchangeable) around δ: 4.00 ppm for products 14b-d and at δ: 10.00 ppm for compound 14g. Also, the spectrum of 14h showed NH_2 and NH proton. signals at δ: 4.90 and 9.20 ppm, respectively. Mass spectra of products 14 were found to agree their proposed structure. For instance the spectra of products 14a-c, h and i molecular ion peaks

m/z: 243(96.50%) 257(15.24%), 286(17.87%), 320(58%) and 349(10%), respectively



Scheme 8

Reaction Conditions:a) Ethyl chloroformate / DMF, heating for 3 hr 70% yield; or
b) Triethyl orthoformate / DMF, , heating for 3 hr, 87% yield,

In between the newly synthesized 6-(substitutedamino) purines 14, product 14h attracted the interest because it has NH_2 and NH groups in *ortho*-position for each others and can be cyclized to build up a new ring at 6-position of the purine moiety. Therefore, when the product: N^1-(9-(4-flurophenyl)-9*H*-purin-6-yl)-benzene-1,2-diamine 14h was left to react with ethyl chloroformate / dimethylformamide reagent mixture for short time; product: 6-(1*H*-benzo[*d*]imidazol-1-yl)-9-(4-fluorophenyl)-9*H*-purine (15) was obtained (87% yield). The latter product was also afforded *via* heating product 14h under reflux with triethyl orthoformate in dimethyl formamide (DMF) for ~ 3 hr (m.p. and mixed m.p. gave no depression).

IR spectrum of product 15 showed absence of NH or NH_2 absorptions. Also, its ^{1}H-NMR spectrum showed H-2 & H-8 of purine proton signals at δ: 9.0 and 8.7 ppm, respectively. Moreover, the spectrum showed H-2 of benzoimidazole moiety attached at 6-position of purine nucleus at δ: 8.08 ppm, beside the aromatic proton signals.

Plant-growth regulating activity of the newly synthesized 6-(substitutedamino)-purines (14a-h)

It was planned in the present work to investigate the potential activity of the newly synthesized *N*-substitutedpurine-6-amines (14a-g) and N^1-purine-benzene-1,2-diamine (14h) towards growth regulation of wheat plant targeting to obtain high plant crop yield.

The average height for plant stems (in cm) as well as for the number of branches are calculated for each of the treated and control experiment. The obtained data are recorded in Table 1 and Fig. 1.

TABLE 1. Screening results for plant-growth regulating activity of the synthesized 6-(substituted amino) purines 14 at 100 ppm concentration.

Compound No.	Stem height(cm) Relative to control (%)	No. of branches / No. of Shoot system (%)
Control	37.00 (100%)	0/7 (0%)
14a	23.43 (63.32)	7/7 (100)
14b	30.40 (82.16)	2/7 (28.57)
14c	33.90 (91.62)	2/7 (28.57)
14d	28.19 (76.19)	9/7 (128.57)
14e	26.93 (72.78)	9/7 (128.50)
14f	24.00 (64.86)	4/7 (57.14)
14g	32.43 (87.65)	0/7 (0%)
14h	29.40 (79.46)	8/7 (114.29)

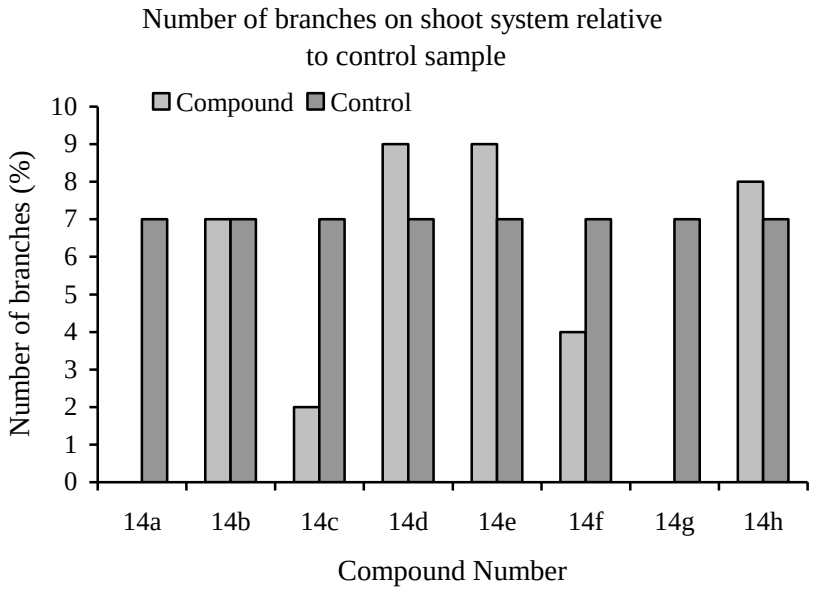


Fig. 1. Number of branches at 100 ppm .

The following comments could be pointed out from the tabulated data:

1- All the tested compounds showed a reduction in stem's height growth ranging from (8.35-36.68%) relative to the control sample.

2- Most of the tested compounds were found to be of moderate/remarkable activity towards increasing the tested wheat plants branching (28.57 – 128.57%) relative to the control.

3- Compounds 14d, e, f, h showed more pronounced remarkable effect for stem reduction as well as for increasing the number of the tested wheat plant branches than the other tested compounds.

4- Compound 14d having alkyl (*n*-butylamino) moiety at 6-position of purine nucleus seemed to be the most active for increasing the number of branches of the tested wheat plant. In comparison, compound 14h having aryl (benzene-1,2-diamine) moiety was of moderate activity than 14d towards stem height shortening.

5- It seemed from ,this preliminary survey, that incorporating selected alkylamino-, arylamino- *or* aralkylamino- moiety at 6-position of purine nucleus, as in cases of products 14d,e,f and h can produce 6-substituted-amino purine derivatives with probable remarkable properties towards wheat plant stem shortening as well as increasing of the plant branching.

The obtained results from the preliminary screening at concentration (100 ppm) for the synthesized 6-substitutedamino-purines 14 encouraged us to repeat screening for the active products 14d, e, f and h using lower concentration (50 ppm) for each product. It was targeted from this screening step to probe and compare the final crop yield of the screened samples compared to control after ripening and harvesting of the tested wheat plants. The results of this screening are shown in Table 2 and Fig. 2.

TABLE 2. Plant-growth regulating activity screening compounds 14d-f at (50ppm) concentration .

Compound No.	Weight of one ear (gm); (%) relative to control
Control	0.56 (100%)
14d	1.36 (243 %)
14e	1.86 (332%)
14f	0.75 (125%)
14h	2.10 (375%)

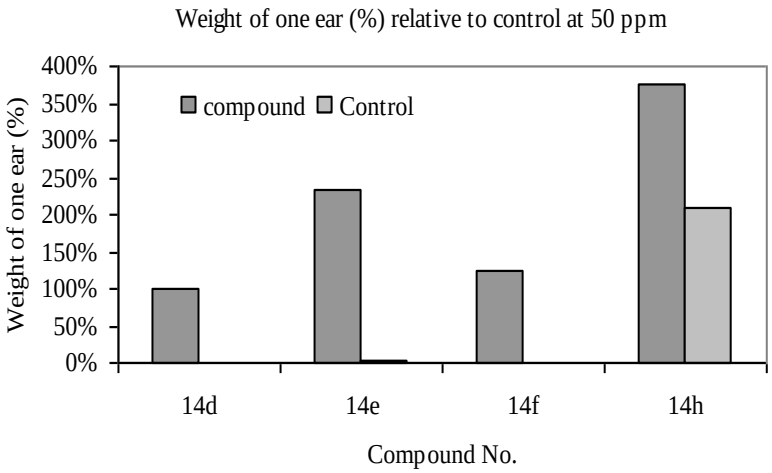


Fig.2. Weight of one ear (%) relative to control at 50 ppm concentration of compounds 14d-f .

The tabulated data (Table 2) cleared that:

After harvesting the wheat plant, it was noticed that all the tested products (14d, e, f and h) were of remarkable effect towards increasing the calculated average weight of one ear. The increase of weight was found to be in the range 125–375% relative to the control.

From the data it can be concluded that:

1- Compounds 14d and 14h were found to increase the branch numbers by 28.57% relative to the control sample and hence the number of the ears on the plant increased causing rising of the final crop of each tested wheat plant by 243% for 14d and 375% for 14h.

2- It was noticed also, that the most active member of the presently tested 6-substitut- ed amino-purine 14 series is: for compound 14h.

Conclusion

Synthesis and characterization of newer 6-substituted-aminopurines and other related derivatives, structurally related to the well known plant growth regulators "Cytokinines", were carried out. Screening of many of the obtained compounds was carried out to probe their potential plant-growth regulation on wheat plant targeting to obtain high plant crop yield. Some derivatives showed promising plant-growth activity. Product N^1-[9-(4-fluorophenyl)-9*H*-purin-6-yl] benzene-1,2-diamine (14a) was found of remarkable activity towards wheat plant-growth regulation as well for gaining high crop yield (weight of each ear) after harvesting the tested wheat plant.

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مشتقات بيورانية جديدة ذات احتمال كمنظمات لنمو النبات

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2-كلورومثيل-9-(4-فلوروفينيل) بيورين-6-اون (3) تم الحصول عليه من تفاعل 5-أمينو-1-(4-فلوروفينيل) -4-اميدازولكربوكساميد (1) مع 2- كلورواستيل كلوريد وايضا تم تحضير 2- سيانو-3- (9-(4-فلوروفينيل)-6-اوكسو-بيورين-2-ايل)بروبيونات (4) ، 9-(4-فلوروفينيل)-2- هيدرازينومثيل-بيورين-6-اون(5)من مركب 3 مع اثيل2- سيانواستات او الهيدريذين المائى وعند مفاعلة المركب 5 مع اثيل-3- اوكسوبيوتنوات بنتان-2،4- ثنائى- اون اعطت المركبات 6 و 7 على الترتيب ، وعند معاملة الاميدازول 1 بمفاعل ايثيل كلوروفورمات/ ثنائى ميثيل فورماميد ، تم الحصول على مشتق الهيبوزانثين 9 بتاتج جيد وكمركب وحيد. عند تفاعل مركب الهيبوزانثين 9 مع يوديد الميثيل أو يوديد الايثيل فى ثنائى ميثيل فورماميد ، نتجت مشتقات ن^{7} – المربعة : 9- (4- فلوروفينيل)-7-ميثيل- بيورينيم-6-أون 10أ ، 9-(4- فلوروفينيل)-7- ايثيل- بيورينيم-6-أون ملح الايوديد 10ب على الترتيب بدلا من ن^{1} - أو ن^{3} - 11، 12.

وعند التسخين لدرجة الغليان لمركب الهيبوزانثين 9 مع كلوريد الفوسفوريل لمدة قصيرة وبدون استخدام أية عوامل مساعدة تم الحصول على مركب 6-كلورو- 9- (4- فلوروفينيل) بيورين (13).، وبمفاعلة بعض الامينات والهيدرازين مع الكلوروبيروين 13 تم تشييد مشتقات جديدة من 6- مشتقات أمينوبيورين 14أ- ومشابهة فى تركيبها لتركيب منظمات نمو النباتات المعروفة تحت اسم " سيتوكينينات" وذلك لقياس مدى فاعليتها كمنظمات لنمو النبات.

تم عمل مسح لبعض مركبات مشيدة مختارة لقياس مدى فعاليتها كمنظمات لنمو نبات القمح ، وجد ان لها تاثيرا مفيدا فى عملية تنظيم نمو النبات ، وايضا وجد لها تاثيرا مفيدا فى زيادة عائد هذا النبات بعد حصاده .