CONVENIENT SYNTHESIS OF SOME NEW PURINE ANALOGUES INCORPORATING FURAN NUCLEUS

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Sodium 3-(furan-2-yl)-3-oxoprop-1-en-1-olate was used as precursor for synthesis of some novel derivatives of various fused heterocyclic ring systems namely pyrazolo[1,5-*a*]pyrimidines, triazolo[1,5-*a*]pyrimidines, benzo[4,5]imidazo-[l,2-*a*]pyrimidines, pyrazolo[5,l-*c*]triazines, l,2,4-triazolo[4,3-*c*]triazines, benzo[4,5]imidazo[2,1-*c*]triazines. The structures of the newly synthesized compounds were established on the basis of their spectral data, elemental analyses and alternate synthetic routes wherever possible.

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Introduction

Pyrazolo[l,5-*a*]pyrimidines which are purine analogues proved to have wide varieties of useful pharmaceutical activities such as antitrypanisommal activity,[1] antischistosomal activity,[2] activity as HMG-CoA reductase inhibitors,[3] COX-2 selective inhibitors,[4] AMP phosphodiesterase inhibitors,[5] KDR kinase inhibitors,[6] selective peripheral benzodiazepine receptor ligands[7] and as antianxiety agents.[8] Other pharmaceutical activities, such as agents for the treatment of sleep disorders[9] and as oncological agents[4,10] have been reported. Also, several pyrazolotriazines and triazolotriazines, as adenine analogues, were used as antagonists, antischistosomal and antitumor agents.[15-17] Such utilities have stimulated recent interest in the synthesis of these ring systems. Also, A large number of heterocyclic compounds containing pyridine rings are associated with diverse pharmacological properties such as antimicrobial,[18,19] anticancer,[20] anticonvulsant,[21] antiviral,[22] anti-HlV,[23] antifungal and antimycobacterial activities.[24] In continuation of our interest in the synthesis of heterocycles,[25,26] we report herein a convenient general method for synthesis of various zoloazines namely pyrazolo[1,5-a]pyrimidines, triazolo[1,5-*a*]pyrimidines, benzo[4,5]imidazo-[l,2-*a*]pyrimidines, pyrazolo[5,l-c]1,2,4-triazines, l,2,4-triazolo[3,4-c]1,2,4-triazines, benzo[4,5]imidazo[2,1-*c*]1,2,4-triazines containing furan moiety.

EXPERIMENTALS

All melting points were determined on an electrothermal apparatus and are uncorrected. IR spectra were recorded (KBr discs) on a Nicolet Avatar 370 CSL FT-IR 8201 PC spectrophotometer. ^{1}H & ^{13}C NMR spectra were recorded in $CDCl_3$ and $(CD_3)_2SO$ solutions on a Varian Gemini 300 MHz and 400 MHz spectrometer and chemical shifts are expressed in δ units using TMS as an internal reference. Mass spectra were recorded on a GC-MS QP1000 EX Shimadzu. Elemental analyses were carried out at the Micro analytical Center of Cairo University. The calculation of heat of formation, ΔH, for compounds **19a** and **22a** was carried out by Hyper Chem. program.

Sodium 3-(furan-2-yl)-3-oxoprop-1-en-1-olate (3)

A solution of 2-acetylfurane (**1**) (5.25 g, 25 mmol) in ether (25 mL) was added dropwise to a mixture of sodium methoxide and ethyl formate (**2**) (25 mmol for each) in dry ether (50 mL) with stirring in ice-bath at 0-5 ^{o}C, for 2 h. The resulting solid collected to give **3** without crystallization.

Pyrazolo[1,5-*a*]pyrimidines (8a, 8b), triazolo[1,5-a]pyrimidine (14) and imidazo[1,2-a]pyrimidine (15)

General procedure

A mixture of the sodium salt of **3** (1.6 g, 10 mmol) and the appropriate heterocyclic amines **5a-d** (10 mmol for each), in a solution consisting of piperidene (2.5 mL), water (5 mL) and acetic acid (2 mL), were heated under reflux for about 10 min, acetic acid (1.5 mL) was added to the reaction mixture while boiling, then the mixture was cooled and the resulting solid was collected and recrystallized from the proper solvent to give **8a , 8b**, **14** and **15**, respectively.

Alternate synthetic route for 8a

Method A: A mixture of 2-acetylfurane (**1**) (9.5 mmole) and *N*,*N*-dimethyl-N'-(3-phenyl-1*H*-pyrazol-5-yl)formamidine (**13**) (1.06 g, 5 mmol) in ethanol (10 mL) was heated under reflux for 3 h. The resulting solid was collected and recrystallized from ethanol gave product identical in all aspects (m.p., mixed m.p. and spectra) with **8a**

Method B: Equimolecular amounts of 3-(dimethylamino)-1-(furan-2-yl)prop-2-en-1-one (**12**) (0.82 g, 5 mmole), the appropriate heterocyclic amines **5a-d** (5 mmol) in acetic acid (10 mL) containing ammonium acetate (0.32 g, 5

mmole) were boiled under reflux for 4 h. The resulting solid was collected and recrystallized from the proper solvent to give **8a, 8b**, **14** and **15**, respectively.

7-(Furan-2-yl)-2-phenylpyrazolo[1,5-*a*]pyrimidine (8a)

This compound was obtained as pale yellow crystals from AcOH, Yield: 79 %, m.p.: 127-30 °C. FT-IR (KBr, cm^{-1}): 3059 ν(CH), 1611 ν(C=N), 1565 ν(C=C). ^{1}H NMR (300 MHz, DMSO-d_6): δ = 5.99 (s, 1H, pyrazole H-5), 6.84 (d, 1H, *J* = 4 Hz, furan H-4), 7.00 (d, 1H, *J* = 4Hz, furan H-3), 7.42-7.99 (m, 7H, ArH's and furan H-5), 8.75 (s, 1H, pyrimidine H-4). ^{13}C NMR: δ = 100.89, 102.23, 120.12, 125.90, 127.30, 128.85, 130.57, 132.68, 134.42, 144.49, 146.21, 146.98, 149.18, 154.23. MS (EI, m/z (%)): 262 (M+1, 34.2 %), 261 (M^+, 100.0 %), 244 (21.9 %), 232 (21.9 %), 207 (5.3 %), 142 (14.0 %), 130 (14.9 %), 103 (22.8 %), 92 (20.2 %), 77 (76.3 %), 76 (42.1 %), 75 (26.3 %), 64 (21.9 %). Calcd. for $C_{16}H_{11}N_3O$ (261.28) C, 73.55; H, 4.24; N, 16.08 Found: C, 73.68; H, 4.35; N, 16.16 %.

7-(Furan-2-yl)pyrazolo[1,5-*a*]pyrimidine-3-carbonitrile (8b)

This compound was obtained as white crystals from EtOH, Yield: 70 %, m.p. 196-200 °C. FT-IR (KBr, cm^{-1}): 3059 ν(CH), 2228 ν(CN), 1632 ν(C=N), 1572 ν(C=C). ^{1}H NMR (300 MHz, DMSO-d_6): δ = 6.75 (d, 1H, *J* = 4 Hz, furan H-4), 7.10 (d, 1H, *J* = 4Hz, furan H-3), 7.60 (d, 1H, ArH) 7.74 (d, 1H, *J* = 4 Hz, furan H-5), 8.27 (s, 1H, pyrazole H-4), 9.12 (d, 1H, *J* = 4 Hz, pyrimidine H-4). ^{13}C NMR: δ = 82, 101, 113, 119, 125, 133, 135, 145, 146, 149, 153. MS (EI, m/z (%)): 210 (M^+, 100.0 %), 181 (29.9 %), 104 (11.5 %), 94 (13.8 %), 76 (23.0 %), 65 (33.3 %). Calcd. for $C_{11}H_6N_4O$ (210.19) C, 62.86. H, 2.88; N, 26.66 Found: C, 63.00; H, 2.71; N, 26.75 %.

5-(Furan-2-yl)-[1,2,4]triazolo[4,3-*a*]pyrimidine (14)

Brown crystals from EtOH, yield: 70 %, m.p.: 181-84 °C. FT-IR (KBr**,** cm^{-1}**):** 3059 ν(CH), 1616 ν(C=N), 1570 ν(C=C). ^{1}H NMR (300 MHz, DMSO-d_6): δ = 6.73 (d, 1H, *J* = 4 Hz, furan H-4), 7.51 (d, 1H, *J* = 4Hz, furan H-3), 7.75(d, 1H, ArH), 8.18 (d, 1H, *J* = 4 Hz, furan H-5), 8.57 (s, 1H, pyrazole H-4), 8.82 (d, 1H, *J* = 4 Hz, pyrimidine H-4). ^{13}C NMR: δ = 111, 112, 131, 135, 142, 144, 146, 152, 159. MS **(**EI, m/z (%)): 186 (M^+, 33.3 %), 130 (60.0 %), 75 (53.0%), 64 (40.0%), 62 (35.3%). Calcd. for $C_9H_6N_4O$ (186.17) C, 58.06; H, 3.25; N, 30.09 Found: C, 58.18; H, 3.34; N, 29.85 %.

4-Furan-2-yl-benzo[4,5]imidazo[1,2-*a*]pyrimidine (15)

Dark brown crystals from AcOH, yield: 75 %, m.p.: >300 °C. FT-IR (KBr, cm-1): 3059 ν(CH), 1635 ν(C=N), 1579 ν(C=C). ^{1}H NMR (300 MHz, DMSO-d_6): δ = 6.75 (d, 1H, J = 4 Hz, furan H-4), 7.10 (d, 1H, J = 4Hz, furan H-3), 7.60 (d, 1H, ArH) 7.74 (d, 1H, J = 4 Hz, furan H-5), 8.27 (m, 4H, ArH's), 9.12 (d, 1H, J = 4 Hz, pyrimidine H-4);.^{13}C NMR: δ = 109, 111, 113, 115, 121, 123, 126, 129, 131, 140, 144, 146, 157, 159; MS (EI, m/z (%)): 235 (M+, 13.2 %), 234 (M-1, 21.1 %), 148 (26.3%), 133 (26.3 %), 112 (34.2 %), 100 (23. 7%), 95 (73.7 %), 84 (36.8 %), 78 (34.2 %), 64 (100.0%). Calcd. for C14H9N3O (235.24) C, 71.48; H, 3.86; N, 17.86 Found: C, 71.36; H, 4.00; N, 17.77 %.

Pyrazolo[5,1-*c*]1,2,4-triazines (22a and 22b)

General procedure

A solution of the appropriate diazonium salt of heterocyclic 5-amino-3-phenylpyrazole (**16a**) and 5-amino-4-cyanopyrazole (**16b**) was added to a cold mixture of the appropriate **3** or **12** (5 mmol for each) and sodium acetate (0.41 gm, 5mmole) in ethanol (40 mL) at 0-5 °C, while stirring for 30 min. The reaction mixture was stirred for 3 h. The resulting solid was collected and recrystallized from the proper solvent to give **22a** and **22b**, respectively.

4-(Furan-2-yl)-7-phenylpyrazolo[5,1-*c*]1,2,4-triazine (22a)

This compound was obtained as yellowish brown crystals from AcOH, Yield: 80%, m.p.: 248-51 °C. FT-IR (KBr, cm^{-1}): 3059 ν(CH), 1638 ν(C=N), 1569 ν(C=C). ^{1}H NMR (300 MHz, DMSO-d_6): δ = 6.75 (d, 1H, *J* = 4 Hz, furan H-4), 7.45-7.62 (m, 4H, ArH's and pyrazole H-4), 7.74 (d, 1H, *J* = 4 Hz, furan H-3), 7.90-7.93 (m, 2H, ArH's), 8.10 (d, 1H, *J* = 4 Hz, furan H-5), 9.20 (s, 1H, ArH). ^{13}C NMR: δ = 102.23, 114.89, 121.19, 124.21, 125.96, 127.40, 128.53, 129.88, 134.34, 144.98, 146.67, 154.58, 154.67; MS (EI, m/z (%)): 262 (M^+, 68.4 %), 131 (36.8 %), 129 (52.6 %), 115 (26.3 %), 104 (31.6 %), (77 (68.4 %), 72 (94.7 %), 69 (63.2 %), 55 (100 %). Calcd. for $C_{15}H_{10}N_4O$ (262.27) C, 68.69; H, 3.84; N, 21.36 Found: C, 68.74; H, 4.00; N, 21.52 %.

4-(Furan-2-yl)pyrazolo[5,1-*c*]1,2,4-triazine-8-carbonitrile (22b)

This compound was obtained as pale brown crystals from EtOH, Yield: 77 %, m.p.: > 300 °C. FT-IR (KBr, cm^{-1}): 3059 ν(CH), 2235 ν(CN), 1635 ν(C=N), 1569 ν(C=C). ^{1}H NMR (300 MHz, DMSO-d_6): δ = 6.75 (d, 1H, *J* = 4 Hz, furan H-4), 7.10 (d, 1H, *J* = 4Hz, furan H-3), 7.96 (d, 1H, *J* = 4 Hz, furan H-5), 8.27 (s, 1H, pyrazole H-4), 9.12 (d, 1H, *J* = 4 Hz, pyrimidine H-4). ^{13}C NMR: δ = 82, 114, 115, 123, 125, 126, 143, 145, 146, 148. MS (EI, m/z (%)): 211 (M^+, 3.6 %), 210 (M-1, 14.5 %), 150 (7.3 %), 149 (32.7 %), 141 (14.5 %), 122 (14.5 %), 112 (10.9 %), 110 (40.0 %), 108 (47.3 %),94 (54.5 %), 85 (36.4 %), 77 (38.2 %), 73 (30.9 %), 64 (38.2 %), 53 (100.0 %). Calcd. for $C_{10}H_5N_5O$ (211.18) C, 56.87; H, 2.39; N, 33.16 Found: C, 56.94; H, 2.45; N, 33.38 %.

4-(Furan-2-yl)-1,2,4-triazolo[5,1-*c*]1,2,4-triazine (24)

A solution of 1,2,4-triazol-3-diazonium nitrate (16c) (5 mmol) (which is prepared from 3-amino-1,2,4-triazol and sodium nitrite in nitric acid at 0-5 °C), was added to a mixture of the appropriate 3 or 12 (5 mmol) and sodium acetate (0.41 gm, 5 mmol) in ethanol (40 mL) at 0-5 °C, during a period 30 min while stirring. The reaction mixture was stirred for further 3 h and was kept in a refrigerator overnight. The resulting solid was collected and recrystallized from ethanol as pale yellow crystals, Yield 70 %, m.p.: > 300 °C; FT-IR (KBr, cm^{-1}): 3055 ν(CH), 1631

ν(C=N), 1549 ν(C=C). ^{1}H NMR (300 MHz, DMSO-d_6): δ = 6.75 (d, 1H, *J* = 4 Hz, furan H-4), 7.10 (d, 1H, *J* = 4Hz, furan H-3), 7.96 (d, 1H, *J* = 4 Hz, furan H-5), 9.12 (s, 2H, ArH's, tetrazole H-5 and triazine H-6). MS (EI, m/z (%)): 187 (M^+, 4.9%), 145 (6.7 %), 114 (75.7 %), 95 (11.6 %), 88 (6.5%), 86 (98.9 %), 74 (5.6 %), 56 (100.0 %). Calcd. for $C_8H_5N_5O$ (187.16) C, 51.34; H, 2.69; N, 37.42 Found: C, 51.41; H, 2.45; N, 37.38 %.

4-Furan-2-yl-benzo[4,5]imidazo[2,1-*c*][1,2,4]triazine (25).

A solution of benzimidazol-2-diazonium sulphate (16d) (5 mmol) (which is prepared from 2-aminobenzimidazole and sodium nitrite in sulphuric acid at 0-5 °C), was added dropwise to a mixture of the appropriate 3 or 12 (5 mmol) and sodium acetate (0.41 gm, 5 mmol) in ethanol (40 mL) while stirring at 0-5 °C, over a period 30 min. The reaction mixture was stirred for another 3 h and was kept in a refrigerator overnight. The resulting solid was collected and recrystallized from ethanol as dark brown crystals, Yield 74 %, m.p.: 151-54 °C. FT-IR (KBr, cm^{-1}): 3055 ν(CH), 1649 ν(C=N), 1562 ν(C=C). ^{1}H NMR (300 MHz, DMSO-d_6): δ = 6.84 (d, 1H, *J* = 4 Hz, furan H-4), 7.32 (m, 2H, AreH's), 7.58 (m, 1H, ArH), 7.80 (d, 1H, *J* = 4 Hz, furan H-5), 8.01 (d, 1H, *J* = 8Hz, ArH), 8.70 (d, 1H, J = 8 Hz, ArH), 9.62 (s, 1H, triazine H-6). MS (EI, m/z (%)): 236 (M^+, 1.54 %), 181 (4.26 %), 95 (100.0 %), 66 (10.66 %); Calcd. for $C_{13}H_8N_4O$ (236.23) C, 66.10; H, 3.41; N, 23.72 Found: C, 66.22; H, 3.53; N, 23.48 %.

2-(2-Arylhydrazono)-3-(furan-2-yl)-3-oxopropanal 26a-d

The appropriate of benzenediazonium chloride (**25a**), 4-methylbenzenediazonium chloride (**25b**), 4-nitro-benzenediazonium chloride (**25c**) or 2,4-dinitro-benzenedizonium chloride (**25d**) (5 mmole) was added drop wise with continuous cooling and stirring to a solution of the sodium salt of 1-(furan-2-yl)-3-hydroxyprop-2-en-1-one (**3**) or 3-(dimethylamino)-1-(furan-2-yl)prop-2-en-1-one (**11**) (5 mmole), in ethanol (15 mL) at 0-5 °C. Sodium acetate was used as a buffer. The reaction mixture was stirred for another 3 h. Then, it was kept in a refrigerator overnight; the resulting solid was collected, washed with water and recrystallized from the proper solvent to give the corresponding **26a-d**, respectively.

2-(2-Phenylhydrazono)-3-(furan-2-yl)-3-oxopropanal (26a)

This compound was obtained as yellow crystals from EtOH, Yield: 93 %, m.p.: 128-30 °C. FT-IR (KBr, cm^{-1}): 3127 ν(NH), 3059 ν(CH), 1642 ν(CO), 1500 ν(C=C). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.61 (d, 1H, *J* = 4 Hz, furan H-4), 7.25-7.73 (m, 6H, ArH's and furans protons), 7.74 (d, 1H, *J* = 4 Hz, furan H-3), 10.14 (s, 1H, CHO), 14.80 (s, br., 1H, NH). MS (EI, m/z (%)): 242 (M^+, 28.1 %), 241 (9.8 %), 214 (10.1 %), 213 (13.3 %), 185 (7.3 %), 158 (10.5 %), 130 (10.1 %), 122 (47.0 %), 95 (100 %), 77 (60.7 %), 65 (61.6 %). Calcd. for $C_{13}H_{10}N_2O_3$ (242.23) C, 64.46; H, 4.16; N, 11.56 Found: C, 64.62; H, 4.27; N, 11.68 %.

2-(2-p-Tolylhydrazono)-3-(furan-2-yl)-3-oxopropanal (26b)

This compound was obtained as yellowish brown crystals from EtOH, Yield: 93 %, m.p.: 140-42 °C. FT-IR (KBr, cm^{-1}): 3125 ν(NH), 3058 ν(CH), 1667 ν(CO), 1615 ν(C=N) 1589 (C=C). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.27 (s, 3H, CH_3), 6.61 (d, 1H, *J* = 4 Hz, furan H-4), 7.25-7.73 (m, 5H, ArH's and furans protons), 7.74 (d, 1H, *J* = 4 Hz, furan H-3), 9.925 (s, 1H, CHO), 14.36 (s, br., 1H, NH). ^{13}C NMR: δ = 19.85, 112.20, 117.19, 128.48, 131.12, 137.35, 140.99, 146.18, 149.28, 151.55, 179.85, 192.87. MS (EI, m/z (%)): 256 (M^+, 40.9 %), 149 (59.1 %), 148 (90.9 %), 94 (86.4 %), 79 (54.6 %), 77 (27.3 %), 71 (40.9 %), 68 (27.3 %), 66 (27.3 %), 65 (63.6 %), 55 (27.3 %). Calcd. for $C_{14}H_{12}N_2O_3$ (256.26) C, 65.62; H, 4.72; N, 10.93 Found: C, 65.81; H, 4.54; N, 11.12 %.

2-(2-p-Nitrophenylhydrazono)-3-(furan-2-yl)-3-oxopropanal (26c)

This compound was obtained as redish brown crystals from AcOH, Yield: 93 %, m.p.: 207-209 °C. FT-IR (KBr, cm^{-1}): 3111 ν(NH), 3058 ν(CH), 1651 ν(CO), 1625 ν(C=N) 1599 (C=C). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.85 (d, 1H, *J* = 4 Hz, furan H-4), 7.25-7.73 (m, 5H, ArH's and furans protons), 7.74 (d, 1H, *J* = 4 Hz, furan H-3), 9.93 (s, 1H, CHO), 14.08 (s, br., 1H, NH). ^{13}C NMR: δ = 112.50, 117.24, 123.82, 128.39, 145.24, 146.38, 147.58, 149.21, 152.22, 179.88, 192.54. MS (EI, m/z (%)): 286 (M-1, 30.0 %), 258 (M-2, 100.0 %), 260 (50.0 %), 177 (25.0 %), 176 (45.0 %), 163 (65.0 %), 137 (70.0 %), 122 (45.0 %), 108 (65 %), 91 (80.0 %), 77 (55 %), 76 (60.0 %), 75 (65.0 %), 64 (40 %), 62 (80 %). Calcd. for $C_{13}H_9N_3O_5$ (287.23) C, 54.36; H, 3.16; N, 14.63 Found: C, 54.57; H, 3.30; N, 14.48 %.

2-(2-(2,4-Dinitrophenyl)hydrazono)-3-(furan-2-yl)-3-oxopropanal (26d)

This compound was obtained as yellowish brown crystals from AcOH, Yield: 96 %, m p.: 156-58 °C. FT-IR (KBr, cm^{-1}): 3111 ν(NH), 3058 ν(CH), 1651 ν(CO), 1625 ν(C=N) 1599 (C=C). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.83 (d, 1H, *J* = 4 Hz, furan H-4), 7.09-8.94 (m, 5H, ArH's and furans protons), 9.95 (s, 1H, CHO), 15.14 (s, br., 1H, NH). MS (EI, m/z (%)): 332 (M^+, 0.2 %), 122 (27 %), 95 (100.0 %), 94 (37.6 %), 83 (9.8 %), 77 (3.2 %), 76 (2.9 %). Calcd. for $C_{13}H_8N_4O_7$ (332.23) C, 47.00; H, 2.43; N, 16.86 Found: C, 47.12; H, 2.28; N, 16.00 %.

(4H-Pyrazol-4-ylidene)-2-phenylhydrazine (27a-d)

Method A: Equimolecular amounts of the appropriate **30a-d** and the appropriate hydrazine hydrate, 4-nitrophenylhydrazine (5 mmol of each) in ethanol (10 mL) were refluxed for 4 h. The resulting solid, so formed, after cooling was recrystallized from the proper solvent to give **27a-g**, respectively.

Method B: Arenediazonium chloride was prepared by reacting 5 mmol of an aromatic amine (aniline, p-toluidine, 4-nitroaniline, or 2,4-dinitroaniline) with HCl (6 M, 3 mL) and sodium nitrite (0.37 g, 5 mmol) at 0-5 °C. A solution of the appropriate arenediazonium chloride (5 mmole), was

added to a mixture of 3-(furan-2-yl)-1*H*-pyrazole (**32**) (0.67 g, 5 mmol) and sodium acetate (0.41 gm, 5 mmole) in ethanol (30 mL) at 0-5 °C, while stirring. The reaction mixture is stirred for 3 h and was kept in a refrigerator overnight. The resulting solid, was collected, washed with water and recrystallized to give identical products in all aspects (m.p., mixed m.p., and spectra) with those obtained by method A.

1-(3-(Furan-2-yl)-4H-pyrazol-4-ylidene)-2-phenylhydrazine (27a)

This compound was obtained as dark brown crystals from AcOH, Yield: 70 %, m.p.: 202-205 °C. FT-IR (KBr, cm^{-1}): 3132 ν(NH), 3055 ν(CH), 1511 ν(C=C). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.62 (d, 1H, *J* = 4 Hz, furan H-4), 7.27-8.14 (m, 7H, ArH's and furans protons), 9.14 (s, 1H, ArH), 15.14 (s, br., 1H, NH). ^{13}C NMR: 104.52, 106.38, 114.28, 120.45, 130.12, 131.47, 135.82, 144.35, 145.47, 147.56, 151.37. MS (EI, m/z (%)): 238 (M^+, 5.9 %), 211 (5.1 %), 161 (18.7 %),105 (12.1 %), 77 (100.0 %), 76 (41.0 %), 65 (11.0 %). Calcd. for $C_{13}H_{10}N_4O$ (238.24) C, 65.54; H, 4.23; N, 23.52 Found: C, 65.35; H, 4.34; N, 23.68 %.

1-(3-(Furan-2-yl)-4H-pyrazol-4-ylidene)-2-p-tolylhydrazine (27b)

This compound was obtained as yellow crystals from AcOH, Yield: 71 %, m.p.: 200-203 °C. FT-IR (KBr, cm^{-1}): 3139 ν(NH), 3055 ν(CH), 1601 ν(C=C). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.34 (s, 3H, CH_3), 6.62 (d, 1H, *J* = 4 Hz, furan H-4), 7.27-8.14 (m, 6H, ArH's and furans protons), 9.14 (s, 1H, ArH), 15.14 (s, br., 1H, NH). ^{13}C NMR: δ = 20.22, 103.88, 106.19, 118.43, 130.72, 131.88, 135.58, 137.25, 139.66, 144.14, 145.28, 151.33. MS (EI, m/z (%)): 252 (M^+, 89.4 %), 251(M-1, 37.6 %), 161 (100.0 %),149 (12.9 %), 133 (42.4 %), 106 (63.5 %), 91 (78.8 %), 77 (35.3 %), 76 (40.1 %), 54 (74.5 %), 50 (61.2 %). Calcd. for $C_{14}H_{12}N_4O$ (252.27) C, 66.65; H, 4.79; N, 22.21 Found: C, 66.52; H, 4.93; N, 22.36 %.

1-(3-(Furan-2-yl)-4H-pyrazol-4-ylidene)-2-(4-nitrophenyl)hydrazine (27c)

This compound was obtained as pale brown crystals from AcOH, Yield: 73 %, m.p.: 208-210 °C. FT-IR (KBr, cm^{-1}): 3297 ν(NH), 3055 ν(CH), 1627 ν(C=N), 1589 ν(C=C). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.62 (d, 1H, *J* = 4 Hz, furan H-4), 7.27-8.14 (m, 6H, ArH's and furans protons), 9.14 (s, 1H, ArH), 15.14 (s, br., 1H, NH). MS (EI, m/z (%)): 283 (M^+, 50 %), 282 (M-1, 11.2 %), 273 (7.7 %), 203 (8.8 %), 175 (16.8 %), 161 (100.0 %),149 (5.11 %), 133 (33.7 %), 106 (59.2 %), 91 (17.9 %), 77 (34.2 %), 75 (38.8 %), 64 (28.6 %), 54 (20.9 %), 50 (61.2 %). Calcd. for $C_{13}H_9N_5O_3$ (283.24) C, 55.13; H, 3.20; N, 24.73 Found: C, 55.33; H, 3.15; N, 24.86 %.

1-(3-(Furan-2-yl)-4H-pyrazol-4-ylidene)-2-(2,4-dinitrophenyl)hydrazine (27d)

This compound was obtained as redish brown crystals from AcOH, Yield: 80 %, m.p.: 260-64 °C. FT-IR (KBr, cm^{-1}): 3297 ν(NH), 3055 ν(CH), 1627 ν(C=N), 1589 ν(C=C). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.62 (d, 1H, *J* = 4 Hz, furan H-4), 7.27-8.14 (m, 5H, ArH's and furans protons), 9.14 (s, 1H, ArH), 15.14 (s, br., 1H, NH). MS (EI, m/z (%)): 328 (M^+, 14.9 %), 311 (24.1 %), 310 (26.7 %), 295 (18.2 %), 161 (100.0 %), 133 (29.7 %), 119 (11.9 %), 106 (46.9 %), 92 (10.6 %), 78 (24.1 %), 77 (31.7 %), 76 (43.2 %), 63 (14.9 %), 51 (69.3 %). Calcd. for $C_{13}H_8N_6O_5$ (328.24) C, 47.57; H, 2.46; N, 25.60 Found: C, 47.79; H, 2.35; N, 25.82 %.

1-(3-(Furan-2-yl)-1-(4-nitrophenyl)-1H-pyrazol-4-yl)-2-phenyldiazene (27e)

This compound was obtained as redish brown crystals from AcOH, Yield: 85 %, m.p.: 284-86 °C. FT-IR (KBr, cm^{-1}): 3055 ν(CH), 1608 ν(C=N), 1562, 1372 ν(NO_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.62 (d, 1H, *J* = 4 Hz, furan H-4), 7.02 (d, 1H, J = 4Hz, furan H-3), 7.42-8.25 (m, 11H, ArH's and furans protons). MS (EI, m/z (%)): 360 (M+1, 11.4 %), 241 (20.0 %), 211 (26.7 %), 163 (34.3 %), 158 (28.6 %), 126 (20.0 %), 114 (28.6 %), 94 (100 %), 88 (28.6 %), 75 (37.1 %), 77 (82.9 %), 65 (31.4 %), 51 (28.6 %). Calcd. for $C_{19}H_{13}N_5O_3$ (359.34) C, 63.51; H, 3.65; N, 19.49 Found: C, 63.63; H, 3.58; N, 19.65 %.

1-(3-(Furan-2-yl)-1-(4-nitrophenyl)-1H-pyrazol-4-yl)-2-p-tolyldiazene (27f)

This compound was obtained as dark brown crystals from AcOH, Yield: 83 %, m.p.: 264-67 °C. FT-IR (KBr, cm^{-1}): 3058 ν(CH), 1615 ν(C=N), 1562, 1372 ν(NO_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.38 (s, 3H, CH_3), 6.62 (d, 1H, *J* = 4 Hz, furan H-4), 7.02 (d, 1H, J = 4Hz, furan H-3), 7.42-8.25 (m, 10H, ArH's and furans protons). Calcd. for $C_{20}H_{15}N_5O_3$ (373.36) C, C, 64.34; H, 4.05; N, 18.76 Found: C, 64.48; H, 4.21; N, 18.55 %.

1-(3-(Furan-2-yl)-1-(4-nitrophenyl)-1H-pyrazol-4-yl)-2-(4-nitrophenyl)diazene (27g)

This compound was obtained as yellowish brown crystals from DMf, Yield: 78 %, m.p.: 285-89° C. **FT-IR (KBr, cm^{-1}):** 3055 ν(CH), 1608 ν(C=N), 1562, 1372 ν(NO_2). **^{1}H NMR (300 MHz, $CDCl_3$):** δ = 6.62 (d, 1H, *J* = 4 Hz, furan H-4), 7.02 (d, 1H, J = 4Hz, furan H-3), 7.42-8.25 (m, 10H, ArH's and furans protons). **MS (EI, m/z (%)):** 405 (M+1, 2.5 %), 284 (15.7 %), 217 (7.6 %), 203 (8.6 %), 157 (7.6 %), 164 (5.1 %), 122 (15.7 %), 106 (10.7 %), 95 (100.0 %), 76 (14.7 %), 63 (34.0 %), 51 (21.3 %). Calcd. for $C_{19}H_{12}N_6O_5$ (404.34) C, 56.44; H, 2.99; N, 20.78 Found: C, 56.57; H, 3.12; N, 20.98 %.

Pyrazoles 28a and 28b

A mixture of 3-(dimethylamino)-1-(furan-2-yl)prop-2-en-1-one (11) (0.82 gm, 5 mmol) and hydrazine hydrate or 4-nitrophenylhydrazine (5 mmol) in ethanol (15 mL) was boiled under reflux for 4 h. The resulting solid was collected and recrystallized from the proper solvent to give **28a** and **28b**, respectively.

3-(Furan-2-yl)-1H-pyrazole (28a)

This compound was obtained as white crystals from water, Yield: 51 %, m.p.: 101-103 °C. FT-IR (KBr, cm^{-1}): 3149 ν(NH), 3033 ν(CH), 1634 ν(C=N), 1165 ν(C=C). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.49 (d, 1H, *J* = 4 Hz), 6.51 (d, 1H, *J* = 4Hz), 6.69 (d, 1H, J = 4 Hz), 7.48 (d, 1H, *J* = 4 Hz, CH), 7.66 (s, 1H), 11.66 (s, br., 1H, NH). ^{13}C NMR: δ = 103.25, 108.54, 111.48, 132.45, 132.78, 138.25, 151.72. MS (EI, m/z (%)): 134 (M^+, 57.1 %), 133 (M-1, 100.0 %), 51 (7.1 %). Calcd. for $C_7H_6N_2O$ (134.14) C, 62.68; H, 4.51; N, 20.88 Found: C, 62.87; H, 4.62; N, 21.10 %.

3-(Furan-2-yl)-1-(4-nitrophenyl)-1H-pyrazole (28b)

This compound was obtained as red crystals from AcOH, Yield: 83 %, m.p.: 140-43 °C. FT-IR (KBr, cm^{-1}): 3058 ν(CH), 1615 ν(C=N), 1562, 1372 ν(NO_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.49 (d, 1H, *J* = 4 Hz), 6.51 (d, 1H, *J* = 4Hz), 6.69 (d, 1H, J = 4 Hz), 7.48 (d, 1H, *J* = 4 Hz, CH), 7.96 (m, 3H, ArH's), 8.3 (m, 2H), ArH's). MS (EI, m/z (%)): 256 (M+1, 100 %) , 255 (M^+, 61 %), 254 (M-1, 98.9 %), 253 (49.4 %), 175 (17.9 %), 146 (14.6 %), 102 (14 %), 74 (9.8 %). Calcd. for $C_{13}H_9N_3O_3$ (255.23) C, 61.18; H, 3.55; N, 16.46 Found: C, 61.25; H, 3.64; N, 16.38 %.

Ethyl 6-(furan-2-yl)-2-methylpyridine-3-carboxylate (29) and 1-(6-(furan-2-yl)-2-methylpyridin-3-yl)ethanone (30)

***General procedure*:** Equimolecular amounts of 3-(dimethylamino)-1-(furan-2-yl)prop-2-en-1-one (**11**) and ethyl acetoacetate or acetylacetone (5 mmol, each) in acetic acid (10 mL) and ammonium acetate (5 mmol) were boiled under reflux for 4 h. The resulting solid, was collected and recrystallized from the proper solvent to give **32** and **33,** respectively.

Ethyl 6-(furan-2-yl)-2-methylpyridine-3-carboxylate (29)

This compound was obtained as dark brown crystals from benzene, Yield: 77 %, m.p.: 78-81 °C. FT-IR (KBr, cm^{-1}): 3058, 2929 ν(CH), 1715 ν(CO, ester),1646 ν(C=N), 1582 ν(C=C). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.33 (t, 3H, J = 7.5 Hz, CH_2CH_3), 2.72 (s, 3H, CH_3), 4.22 (q, 2H, J = 7.5 Hz, CH_2CH_3), 6.49 (d, 1H, *J* = 4 Hz, furan H-4), 6.51 (d, 1H, *J* = 4Hz, furan H-3), 6.69 (d, 1H, J = 4 Hz), furan H-5), 7.96 (d, 2H, J = 4 Hz, ArH's) ^{13}C NMR: δ = 14.84, 26.00, 61.66, 107.29, 109.97, 116.78, 125.12, 141.64, 143.88, 155.48, 166.27, 158.87, 165.12. MS (EI, m/z (%)): 231 (M^+, 2.6 %), 149 (4.1 %), 80 (5.5 %), 78 (100.0 %), 75 (5.9 %), 65 (3.3 %). Calcd. for $C_{13}H_{13}NO_3$ (231.25) C, 67.52; H, 5.67; N, 6.06 Found: C, 67.68; H, 5.79; N, 6.12 %.

1-(6-(Furan-2-yl)-2-methylpyridin-3-yl)ethanone (30)

This compound was obtained as dark brown crystals from AcOH, Yield: 76 %, m.p.: > 300 °C. FT-IR (KBr, cm^{-1}): 3058, 2923 ν(CH), 1701 ν(CO), 1634 ν(C=N), 1563 ν(C=C). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.34 (s, 3H, CH_3), 2.42 (s, 3H, CH_3), 6.49 (d, 1H, *J* = 4 Hz, furan H-4), 6.51 (d, 1H, *J* = 4Hz, furan H-3), 6.69 (d, 1H, J = 4 Hz, furan H-5), 7.63-8.00 (m, 2H), ArH's). ^{13}C NMR: δ = 25.85, 27.64, 113.87, 114.25, 119.15, 131.57, 132.58, 143.82, 148.67, 152.75, 158.17, 199.47. MS (EI, m/z (%)): 202 (M+1, 36.4 %), 201 (M^+, 45.5 %), 174 (54.5 %), 149 (54.5 %), 82 (63.6 %), 72 (54.4 %), 60 (100.0 %), 57 (91 %), 55 (18.2 %). Calcd. for $C_{12}H_{11}NO_2$ (201.22) C, 71.63; H, 5.51; N, 6.96 Found: C, 71.78; H, 5.38; N, 7.14 %.

6-(Furan-2-yl)-2-methylpyridine-3-carbohydrazide (31)

A mixture of ethyl 6-(furan-2-yl)-2-methylpyridine-3-carboxylate (**29**) (1.15 g, 5 mmol) and hydrazine hydrate (1 mL) in ethanol (10 mL) were boiled under reflux for 4 h. The resulting solid, was cooled and recrystallized to give **31** as dark brown crystals from AcOH, Yield: 97 %, m.p.: > 300 °C. FT-IR (KBr, cm^{-1}): 3429, 3317 ν(NH, NH_2), 3064, 2982 ν(CH), 1715 ν(CO), 1635 ν(C=N), 1583 ν(C=C). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.52 (s, 3H, CH_3), 6.49 (d, 1H, *J* = 4 Hz, furan H-4), 6.51 (d, 1H, *J* = 4Hz, furan H-3), 6.69 (d, 1H, J = 4 Hz, furan H-5), 7.63-8.00 (m, 2H, ArH's), 9.75 (s, br., 3H, NH, NH_2). Calcd. for $C_{11}H_{11}N_3O_2$ (217.22) C, 60.82; H, 5.10; N, 19.34 Found: C, 60.95; H, 5.32; N, 19.57 %

Azido(6-(furan-2-yl)-2-methylpyridin-3-yl)methanone (32)

Saturated solution of sodium nitrite was added portionwise to a stirred solution of 6-(furan-2-yl)-2-methylpyridine-3-carbohydrazide (**31**) (1.08 g, 5 mmol) in hydrochloric acid (15 mL, 6 M) at 0-5°C till effervescence ceased. The reaction mixture stirred for 1 h. The resulting solid, was filtered, washed with water and recrystallized from acetic acid to give the **32**, as dark brown crystals, Yield: 80 %, m.p.: > 300 °C. FT-IR (KBr, cm^{-1}): 3058 ν(CH), 2116 ν(azide group), 1712 ν(CO), 1633 ν(C=N), 1592 ν(C=C). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.52 (s, 3H, CH_3), 6.49 (d, 1H, *J* = 4 Hz, furan H-4), 6.51 (d, 1H, *J* = 4Hz, furan H-3), 6.69 (d, 1H, J = 4 Hz, furan H-5), 7.54 (d, 1H, J = 8 Hz, ArH), 7.89 (d, 1H, J = 8 Hz, ArH). MS (EI, m/z (%)): 230 (M+2, 50 %), 186 (50 %), 65 (25 %), 61 (45 %), 60 (65 %), 58 (25 %), 57 (100.0 %), 55 (45 %), 50 (25 %). Calcd. for $C_{11}H_8N_4O_2$ (228.21) C, 57.89; H, 3.53; N, 24.55 Found: C, 58.00; H, 3.35; N, 24.68 %

Synthesis of urea 33a-d

A mixture of the azido **32** and appropriate aniline, *p*-toluidine, *p*-nitoaniline or 2,4-dinitroaniline (5 mmol) in dioxane (20 mL) was refluxed for 4 h. The resulting solid, so formed, was collected and recrystallized to yield **33a-d**, respectively.

1-(6-(Furan-2-yl)-2-methylpyridin-3-yl)-3-phenylurea (33a)

This compound was obtained as dark brown crystals from DMF, Yield: 79 %, m.p.: > 300 °C. FT-IR (KBr, cm^{-1}): 3369 ν(NH), 3058 ν(CH), 1712 ν(CO). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.12 (s, 3H, CH_3), 6.49 (d, 1H, *J* = 4 Hz, furan H-4), 6.51 (d, 1H, *J* = 4Hz, furan H-5), 6.13-7.17 (m, 3H, ArH's), 7.26 (d, 1H, J = 4 Hz), 7.29-7.85 (m, 4H, *ArH's)*, 8.49 (s, br., 2H, NH_2). MS (EI, m/z (%)): 293 (M^+, 0.45 %),

203 (22.41 %), 186 (100.0 %);), 158(23.33 %), 130 (16.81 %), 107 (37.07 %), 103 (40.36 %), 94 (11.84 %), 91 (19.42 %), 77 (29.39 %), 60 (26.39 %). Calcd. for $C_{17}H_{15}N_3O_2$ (293.32) C, 69.61; H, 5.15; N, 14.33 Found: C, 69.72; H, 5.30; N, 14.45 %.

1-(6-(Furan-2-yl)-2-methylpyridin-3-yl)-3-p-tolylurea (33b)

This compound was obtained as dark brown crystals from DMF, Yield: 91 %, m.p.: > 300 °C. FT-IR (KBr, cm^{-1}): 3396 ν(NH), 3058 ν(CH), 1704 ν(CO, 1600 ν(C=C)). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.12 (s, 3H, CH_3), 2.35 (s, 3H, CH_3), 6.49 (d, 1H, *J* = 4 Hz, furan H-4), 6.51 (d, 1H, *J* = 4Hz, furan H-5), 6.13-7.17 (m, 3H, ArH's), 7.26 (d, 1H, J = 4 Hz), 7.29-7.85 (m, 3H, ArH's), 8.49 (s, br., 2H, NH_2). ^{13}C NMR: δ = 19.37, 20.88, 108.27, 106.44, 114.11, 121.22, 129.98, 132.44, 137.18, 140.24, 143.51, 145.27, 147.67, 154.18, 154.89. MS (EI, m/z (%)): 307 (M^+, 0.33 %), 305 (15.09 %), 231 (11.14 %);), 210 (5.40 %), 192 (11.01 %), 186 (19.69 %), 181 (13.32 %), 167 (18.16 %), 154 (17.29 %), 145 (16.95 %), 134 (12.90 %), 119 (27.03 %), 109 (14.00 %), 92 (100.0 %), 82 (13.35 %), 64 (39.84 %). Calcd. for $C_{18}H_{17}N_3O_2$ (307.35) C, 70.34; H, 5.58; N, 13.67 Found: C, C, 70.45; H, 5.71; N, 13.85 %.

1-(6-(Furan-2-yl)-2-methylpyridin-3-yl)-3-(4-nitrophenyl)urea (33c)

This compound was obtained as deep red crystals from AcOH, Yield: 82 %, m.p.: > 300 °C. FT-IR (KBr, cm^{-1}): 3365 ν(NH), 3058 ν(CH), 1708 ν(CO), 1615 ν(C=N), 1562, 1370 ν(NO_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.12 (s, 3H, CH_3), 6.49 (d, 1H, *J* = 4 Hz, furan H-4), 6.51 (d, 1H, *J* = 4Hz, furan H-3), 7.21-7.28 (m, 5H, ArH's and furan H-5), 7.92 (d, 1H, *J* = 8 Hz, ArH), 8. (d, 1H, *J* = 8 Hz, ArH), 9.13 (s, br., 2H, NH). Calcd. for $C_{17}H_{14}N_4O_4$ (338.32) C, 60.35; H, 4.17; N, 16.56 Found: C, 60.52; H, 4.25; N, 16.68 %.

1-(6-(Furan-2-yl)-2-methylpyridin-3-yl)-3-(2,4-dinitrophenyl)-urea (33d)

This compound was obtained as yellowish brown crystals from AcOH, Yield: 83 %, m.p.: > 300 °C. FT-IR (KBr, cm^{-1}): 3442 ν(NH), 3058 ν(CH), 1705 ν(CO), 1615 ν(C=N), 1521, 1384 ν(NO_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.12 (s, 3H, CH_3),), 6.49 (d, 1H, *J* = 4 Hz, furan H-4), 6.51 (d, 1H, *J* = 4Hz, furan H-3), 7.21-7.29 (m, 2H, ArH and furan H-5), 7.88 (d, 1H, J = 8 Hz, ArH), 8.42-8.65 (m, 2H, ArH's), 8.92 (s, 1H, ArH), 10.35 (s, br. 2H, NH). Calcd. for $C_{17}H_{13}N_5O_6$ (383.32) C C, 53.27; H, 3.42; N, 18.27 Found: C, 53.27; H, 3.42; N, 18.27 %.

Synthesis of aryl carbamates 34a-c

A mixture of **32** (5 mmol) and phenol (0.5 g, 5 mmol) in dry benzene (20 mL) was refluxed for 4 h. The resulting solid, so formed, was collected and recrystallized to give **34a-c**.

Phenyl 6-(furan-2-yl)-2-methylpyridin-3-ylcarbamate (34a)

This compound was obtained as dark brown crystals from AcOH, Yield: 82 %, m.p.: > 300 °C. FT-IR (KBr, cm^{-1}): 3361 ν(NH), 3058 ν(CH), 1708 ν(CO), 1615 ν(C=N). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.12 (s, 3H, CH_3), 6.49 (d, 1H, *J* = 4 Hz, furan H-4), 6.51 (d, 1H, *J* = 4Hz, furan H-3), 6.392-7.35 (m, 7H, ArH's and furan H-5), 7.92 (d, 1H, *J* = 8 Hz, ArH), 9.56 (s, br., 1H, NH). ^{13}C NMR: δ = 19.32, 105.77, 110.27, 114.51, 121.87, 124.83, 130.24, 130.87, 136.74, 143.57, 146.59, 147.99, 153.34, 153.87, 154.28. Calcd. for $C_{17}H_{14}N_2O_3$ (294.3) C, 69.38; H, 4.79; N, 9.52 Found: C, 69.52; H, 4.95; N, 9.68 %.

4-Nitrophenyl 6-(furan-2-yl)-2-methylpyridin-3-ylcarbamate (34b)

This compound was obtained as dark brown crystals from DMF, Yield: 77 %, m.p.: 184-87 °C. FT-IR (KBr, cm^{-1}): 3442 ν(NH), 3058 ν(CH), 1708 ν(CO), 1615 ν(C=N), 1562, 1370 ν(NO_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.12 (s, 3H, CH_3), 6.49 (d, 1H, *J* = 4 Hz, furan H-4), 6.51 (d, 1H, *J* = 4Hz, furan H-3), 6.39-7.35 (m, 6H, ArH's and furan H-5), 7.92 (d, 1H, *J* = 8 Hz, ArH), 9.56 (s, br., 1H, NH). MS (EI, m/z (%)): 339 (M^+, 62.2 %), 247 (100.0 %), 158 (19.6 %);), 152 (24.5 %), 131 (14.0 %), 130 (23.2 %), 118 (18.1 %), 109 (6.7 %), 93 (14.2 %), 77 (30.3 %), 67 (21.3 %), 51 (8.3 %). Calcd. for $C_{17}H_{13}N_3O_5$ (339.3) C, 60.18; H, 3.86; N, 12.38 Found: C, 60.25; H, 4.00; N, 12.45 %.

2,4,6-trinitrophenyl 6-(furan-2-yl)-2-methylpyridin-3-ylcarba-mate (34c)

This compound was obtained as yellowish brown crystals from AcOH, Yield: 83 %, m.p.: > 300 °C. FT-IR (KBr, cm^{-1}): 3438 ν(NH), 3090 ν(CH), 1716 ν(CO), 1612 ν(C=N), 1561, 1384 ν(NO_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.12 (s, 3H, CH_3), 6.49 (d, 1H, *J* = 4 Hz, furan H-4), 6.51 (d, 1H, *J* = 4Hz, furan H-3), 7.20 (d, 1H, *J* = 4Hz, furan H-5), (6.39 (d, 1H, *J* = 8Hz, ArH), 7.92 (d, 1H, *J* = 8 Hz, ArH), 9.15 (s, 2H, ArH's), 9.56 (s, br., 1H, NH). MS (EI, m/z (%)): 429 (M^+, 12.5 %), 389 (86.7 %), 134 (13.4 %);), 127 (10.1 %), 121 (100.0 %). Calcd. for $C_{17}H_{11}N_5O_9$ (429.3) C, 47.56; H, 2.58; N, 16.31 Found: C, 47.67; H, 2.62; N, 16.55 %.

Ethyl 2-amino-6-(furan-2-yl)pyridine-3-carboxylate (35)

A mixture of 3-(dimethylamino)-1-(furan-2-yl)prop-2-en-1-one (11) (0.83, 5 mmol), ethyl cyanoacetate (0.56 g, 5 mmol) and ammonium acetate (0.35 g 5 mmol) in acetic acid (10 mL) was refluxed for 4 h. The solid resulting after cooling was collected and recrystallized from diluted acetic acid to give **35** as white crystals from AcOH, Yield: 69 %, m.p.: 333-36 °C. FT-IR (KBr, cm^{-1}): 3378 ν(NH), 3058 ν(CH), 1694 ν(CO), 1644 ν(C=N), 1562 ν(C=C). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.27 (t, 3H, J = 7.5 Hz, $CH_2\underline{CH_3}$), 2.12 (q, 2H, J = 7.5 Hz, $\underline{CH_2}CH_3$), 6.49 (d, 1H, *J* = 4 Hz, furan H-4), 6.51 (d, 1H, *J* = 4Hz, furan H-3), 7.20 (d, 1H, *J* = 4Hz, furan H-5), 7.25 (d, 1H, *J* = 8Hz, ArH), 7.92 (d, 1H, *J* = 8 Hz, ArH), 12.58 (s, br., 1H, NH_2). MS (EI, m/z (%)): 232 (M^+, 5.9 %), 203 (64.4.7 %), 189 (13.9 %);), 187 (28.9 %), 160 (13.9 %), 132 (12.8 %), 105 (25 %), 77 (23.3 %), 65 (12.8 %). Calcd. for $C_{12}H_{12}N_2O_3$ (232.24) C, 62.06; H, 5.21; N, 12.06 Found: C, 61.92; H, 4.83; N, 5.89 %.

(2-Amino-6-(furan-2-yl)pyridin-3-yl)(phenyl)methanone (36)

A mixture of 3-(dimethylamino)-1-(furan-2-yl)prop-2-en-1-one (**11**) (0.83, 5 mmol), benzoylacetonitrile (0.74 g, 5 mmol) and ammonium acetate (0.35 g 5 mmol) in acetic acid (10 mL) was refluxed for 4 h. The solid resulting on cooling was collected and recrystallized from diluted acetic acid to give **36** as pale brown crystals from AcOH, Yield: 80 %, m.p.: 210-14 °C. FT-IR (KBr, cm^{-1}): 3370, 3167 ν(NH_2), 3058 ν(CH), 1648 ν(CO, conjugated), 1615 ν(C=N), 1571 ν(C=C). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.49 (d, 1H, *J* = 4 Hz, furan H-4), 6.51 (d, 1H, *J* = 4Hz, furan H-3), 7.20 (d, 1H, *J* = 4Hz, furan H-5), 7.61-7.85 (m, 7H, ArH's), 9.85 (s, br., 2H, NH_2) MS (EI, m/z (%)): 264 (M^+, 73.1 %), 256 (100.0 %), 248 (42.3 %);), 218 (26.9 %), 185 (42.3 %), 161 (26.9 %), 105 (19.2 %), 77 (88.2 %), 66 (42.3 %) Calcd. for $C_{16}H_{12}N_2O_2$ (264.28) C, 72.72; H, 4.58; N, 10.60 Found: C, 72.95; H, 4.67; N, 10.84 %.

Results and Discussion

Treatment of sodium 3-(furan-2-yl)-3-oxoprop-1-en-1-olate (**3**), which was prepared by reacting 2-acetylfuran **(1)** and ethyl formate **(2)** in methanolic sodium methoxide, followed by 5-amino-3-phenylpyrazole (**5a**) in acetic acid, in the presence of piperidenium acetate yielded 7-(furan-2-yl)-2-phenylpyrazolo[1,5-*a*]pyrimidine (**8a**) (Scheme 1).

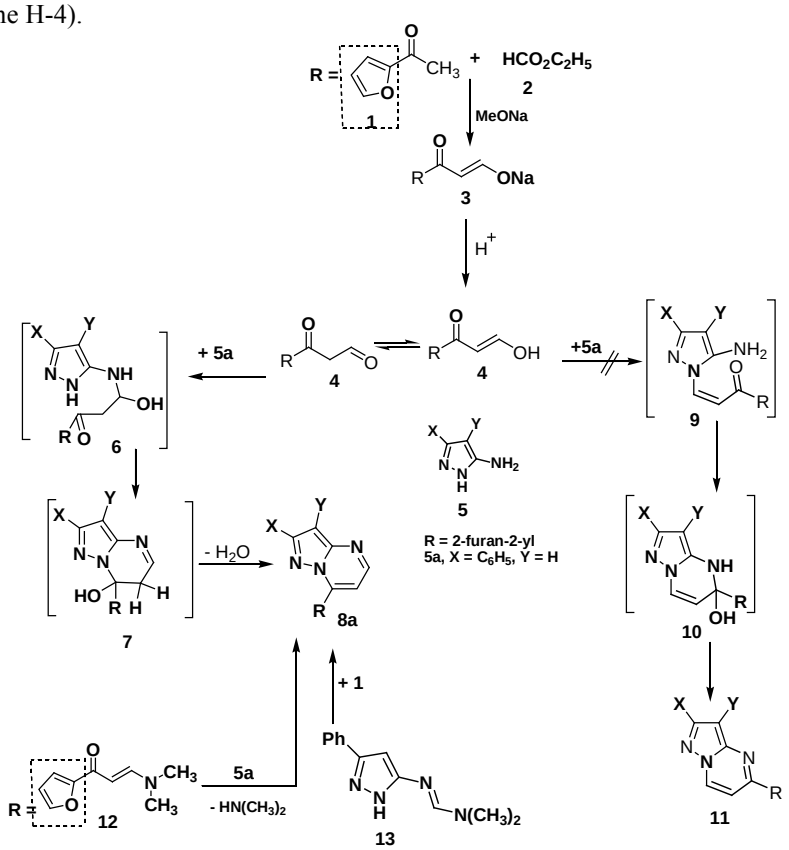
The structure of **8a** was established by elemental analysis, spectral data and alternative synthesis. For example, its ^{1}H-NMR spectrum revealed multiplet signal at δ 5.99 (s, 1H, pyrazole H-5), 6.84 (d, 1H, *J* = 4 Hz, furan H-4), 7.00 (d, 1H, *J* = 4Hz, furan H-3), 7.42-7.99 (m, 7H, ArH's and furan H-5), 8.75 (s, 1H, pyrimidine H-4).

The formation of compounds **8a** is assumed to take place via an initial Michael addition of the exocyclic amino group in compound **5a** to the formyl group of **4** to give the acyclic non-isolable intermediate **6** which undergoes cyclization and aromatization *via* loss one molecule of water to give **8a** as end product. Structure of **8a** was further confirmed by its independent synthesis by reacting equimolecular amounts of *N,N*-dimethyl-*N′*-(3-phenyl-1*H*-pyrazol-5-yl)formamidine (**13**) with 2-acetylfuran (**1**) in refluxing ethanol or treatment of 3-(dimethylamino)-1-(furan-2-yl)prop-2-en-1-one [27] (**12)** with **5a** in boiling acetic acid. The product isolated, in each case, proved identical in all aspects (m.p., mixed m.p. and spectra) with those of the assigned structure **8a** (Scheme 1)**.**

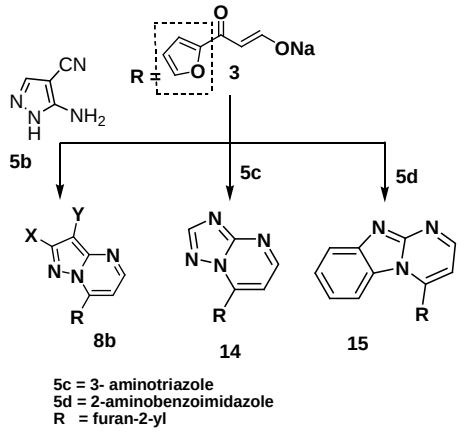
Analogously, reaction of compound **3** or **11** reacted with each of 5-amino-4-cyanopyrazole (**5b**), 3-aminotriazole (**5c**) or 2-aminbenzoimidazole (**5d**) in acetic acid in the presence of piperidenium acetate or ammonium acetate afforded 7-(furan-2-yl)pyrazolo[1,5-*a*]pyrimidine-3-carbonitrile (**8b),** 7-(furan-2-yl)-1,2,4-triazolo-[1,5-*a*]pyrimidine (**14**) and 4-furan-2-yl-benzo[4,5]imidazo[1,2-*a*]pyrimidine (**15**), respectively (Scheme 2).

Treatment of diazotized 5-amino-3-phenylpyrazole (**16a**) with the sodium 3-(furan-2-yl)-3-oxoprop-1-en-1-olate (**3**) in ethanol containing sodium acetate gave 4-(furan-2-yl)-7-phenylpyrazolo[5,1-*c*]1,2,4-triazine (**22a**) in a good yield (Scheme 3).

Structure of **22a** was elucidated by elemental analysis, spectral data and alternative synthetic route.



Scheme 1. Synthesis of 7-(furan-2-yl)-2-phenylpyrazolo[1,5-*a*]pyriminidine (**8a**)



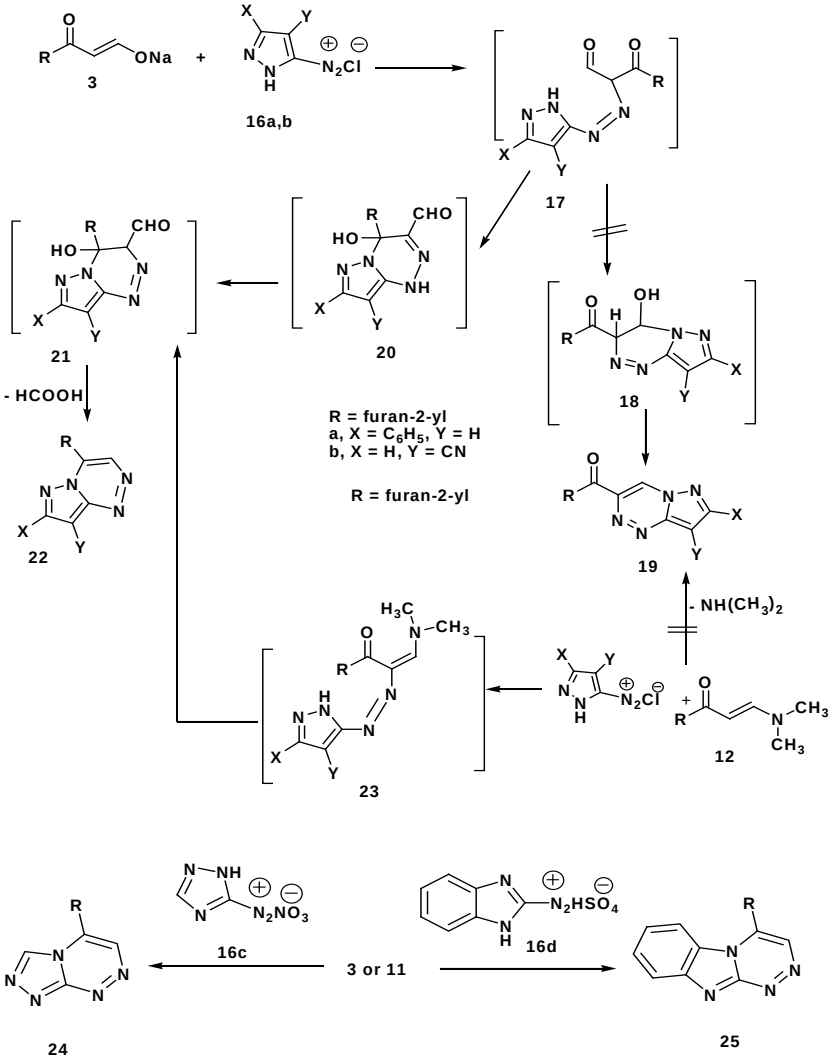
Scheme 2. Synthesis of pyrazolo[1,5-*a*]pyrimidine (**8b**), 1,2,4-triazolo-[1,5-*a*]pyrimidine (**14**) and benzo[4,5]imidazo[1,2-*a*]pyrimidine (**15**).

For example, its infrared spectrum revealed no bands between in the region 1650-2000 cm^{-1} due to the absence of any carbonyl group. Its mass spectrum showed m/z = 262. On the basis of these results, the structure **19** was ruled out.

The formation of **22a** seems to occur via coupling of diazonium chloride **16a** with **3** to form the intermediate **20** which then cyclized to give intermediate **21,** which in turn undergoes elimination of formic acid to give **22a** as the end product. Also, the formation of **22a** rather than **19a** is also evidenced by our finding that the calculated heat of formation of **22a** (ΔH = 170.581 kcal mol^{-1}) is higher than of **19a** (ΔH = 145.961 kcal mol^{-1}).

Reaction of 3-(dimethylamino)-1-(furan-2-yl)prop-2-en-1-one (**12**) with **16a** in ethanolic sodium acetate solution gave a product identical in all aspects (m.p., mixed m.p. and spectra) with **22a** isolated above from the reaction of **16a** with **3** (Scheme 3).

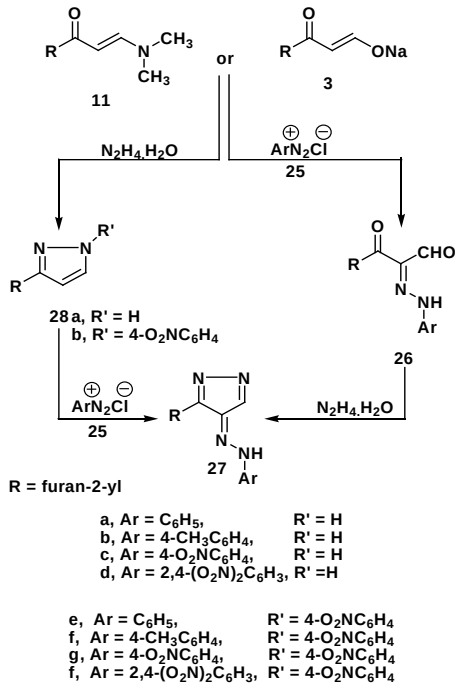
Analogously, coupling of the diazotized 5-amino-4-cyanopyrazole (**16b**), 3-amino-1,2,4-triazole (**16c**) and 2-aminobenzimidazole (**16d**) with the appropriate **3** or **12** in ethanolic sodium acetate afforded 4-(furan-2-yl)pyrazolo[5,1-*c*]1,2,4-triazine-8-carbonitrile (**22b**), 4-(furan-2-yl)-1,2,4-triazolo[5,1-*c*]1,2,4-triazine (**24**) and 4-furan-2-yl-benzo[4,5]imidazo[2,1-c]1,2,4-triazine (**25**), respectively (*cf.* Scheme 3).



Scheme 3. Synthesis of 4-(furan-2-yl)pyrazolo[5,1-*c*]1,2,3-triazine-8-carbonitrile (**21b**), 4-(furan-2-yl)-1,2,4-triazolo[5,1-*c*]1,2,4-triazine (**24**) and 4-furan-2-yl-benzo[4,5]imidazo[2,1-*c*]1,2,4-triazine (**25**).

Reactions of **3** or **11** with benzenediazonium chloride (**25a**) in ethanol containing sodium acetate as a buffer solution yielded 2-(2-phenylhydrazono)-3-(furan-2-yl)-3-oxopropanal (**26a**) (Scheme 4). Structure of **26a** was confirmed by elemental analysis, spectral data and chemical transformations. ^{1}H-NMR spectrum of **26a** showed signal at δ = 6.61 (d, 1H, *J* = 4 Hz, furan H-4), 7.25-7.73 (m, 6H, ArH's and furans protons), 7.74 (d, 1H, *J* = 4 Hz, furan H-3), 10.14 (s, 1H, CHO), 14.80 (s, br., 1H, NH). Compound **26a** was refluxed with hydrazine hydrate in ethanol to give 1-(3-(furan-2-yl)-4*H*-pyrazol-4-ylidene)-2-phenylhydrazine (**27a**). Further, compound **11** reactes with hydrazine hydrate to give 3-(furan-2-yl)-1*H*-pyrazole (**28**). The compound **28** reacted with benzenediazonium chloride in ethanolic sodium acetate solution to afford a product identical in all aspect (m.p., mixed m.p. and spectra) with **27a** which was prepared as described in Scheme 4. Similarly, treatment of the appropriate aryenediazonium chlorides (**25b-d**) with **3** or **11** in cold ethanolic sodium acetate solution gave the corresponding (**26b-f**) respectively.

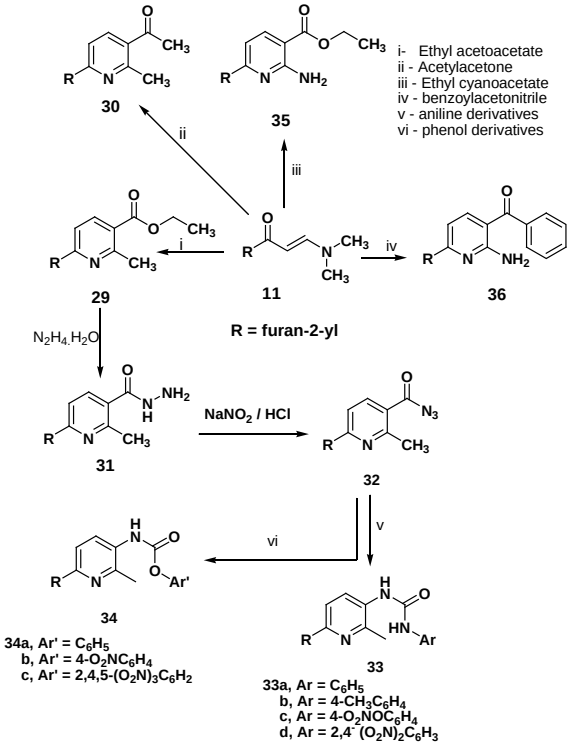
Reaction of 3-(dimethylamino)-1-(furan-2-yl)prop-2-en-1-one (**11**) with ethyl acetoaetate or acetylacetone in boiling acetic acid containing ammonium acetate under reflux gave ethyl 6-(furan-2-yl)-2-methylpyridine-3-carboxylate (**29**) and 1-(6-(furan-2-yl)-2-methylpyridin-3-yl)ethanone (**30**), respectively (Scheme 5). Structures of (**29**) and (**30**) were confirmed by elemental analysis, spectral data and chemical transformation. ^{1}HNMR spectrum of **29** showed signals at δ = 1.33 (t, 3H, J = 7.5 Hz, CH_2CH_3), 2.72 (s, 3H, CH_3), 4.22 (q, 2H, J = 7.5 Hz, CH_2CH_3), 6.49 (d, 1H, furan H-4), 6.51 (d, 1H, furan H-3), 6.69 (d, 1H, Furan H-5), 7.96 (s, 2H, ArH's). Thus, treatment of compound (**29**) with hydrazine hydrate gave 6-(furan-2-yl)-2-methylpyridine-3-carbohydrazide (**31**), which is converted to azido(6-(furan-2-yl)-2-methylpyridin-3-yl)methanone **(32)** by aqueous sodium nitrite in hydrochloric acid (6 M) in an ice-bath.



Scheme 4. Synthesis of hydrazones (**26**) and pyrazoles (**27**) and (**28)**

Structure of **32** was confirmed by elemental analysis, spectral data and chemical transformation. Frther, compound **32** reacted separately with the appropriate aromatic amines (aniline, p-toluidine, 4-nitroaniline, 2,4-dinitroaniline) in dry dioxan or with phenols (phenol, 4-nitrophenol, 2,4,6-trinitrophenol) in dry benzene to afford substituted urea (**33a-d**) and aryl carbamates (**34a-c**) respectively.

Finally, treatment of the enaminone **11** separately with ethyl cyanoacetate and benzoylacetonitrile gave ethyl 2-amino-6-(furan-2-yl)pyridine-3-carboxylate (**35**) and (2-amino-6-(furan-2-yl)pyridin-3-yl)(phenyl)methanone (**36**), respectively (Scheme 5).



Scheme 5. Synthesis of hydrazides (**31**), azides (**32**), urea derivatives (**33 a-d**), aryl carbamates (**34**) and pyridines (**35 and 36**).

Conclusion

In conclusion, compounds of type **3** and **12** proved to be useful precursors for synthesis of various fused heterocycles via their reactions with 5-aminopyrazoles, 3-aminotriazole, 2-aminobenzoimidazole and diazotized heterocyclic amines. The structures of the newly synthesized compounds were confirmed by spectral data, alternate synthesis and elemental analyses.

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