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SYNTHESIS OF SOME N-ALKYLATED 1,2,4-TRIAZOLES, 1,3,4-OXADIAZOLES, AND 1,3,4-THIADIAZOLES BASED ON N-(FURAN-2-YL-METHYLIDENE)-4,6-DIMETHYL-1H-PYRAZOLO-[3,4-*b*]PYRIDINE-3-AMINE

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N-(Furan-2-ylmethylidene)-4,6-dimethyl-1H-pyrazolo[3,4-b]pyridine-3-amine was prepared and alkylated with the corresponding halo compounds to afford N-alkylated products. 2-[3-(Furan-2-ylmethylideneamino)-4,6-dimethyl-1H-pyrazolo[3,4-b]pyridin-1-yl]acetohydrazide was converted into the key intermediate thiosemicarbazide, which undergoes cyclization reactions under acidic and basic conditions to give 1,2,4-triazole, 1,3,4-oxadiazole, and 1,3,4-thiadiazole derivatives. Condensation of the hydrazide with monosaccharide aldoses gave the corresponding sugar hydrazones, which on treatment with acetic anhydride readily undergo cyclization reaction to afford oxadiazoline derivatives.

Keywords: aldoses, 1,3,4-oxadiazole, pyrazolopyridine, 1,3,4-thiadiazole, thiosemicarbazide, 1,2,4-triazole, cyclization.

1H-Pyrazolo[3,4-*b*]pyridines comprise a very interesting class of compounds because of their significant and diverse biological and pharmacological activities, such as antimalarial [1], antiproliferative [2], antimicrobial [3–5], cyclin-dependent kinase-inhibiting [6], cardiovascular [7–9], antiviral [10–12], and antileishmanial [13] activities. Pyrazole-fused pyridines and pyrimidines are known to possess a wide range of biological activity. Specifically, pyrazolopyridines exhibit antitubercular and anxiolytic effects [14]. It has been reported that certain compounds bearing a 1,3,4-oxadiazole, 1,3,4-thiadiazole, and 1,2,4-triazole nucleus possess significant anti-inflammatory activity [15, 16]. In this study, we also chose aldose hetarylhydrazones as target molecules since they can provide access to heterocyclic derivatives of carbohydrates which are known as C-nucleoside analogs [17–20]. In view of these reports and in continuation of our recent work on the use of pyrazolo[3,4-*b*]pyridine derivatives to synthesize new heterocyclic compounds [21, 22], we report here the synthesis of a number of new alkylated 4,6-dimethyl-1H-pyrazolo[3,4-*b*]pyridine-3-amines, as well as the formation of 1,2,4-triazole, 1,3,4-oxadiazole, 1,3,4-thiadiazole derivatives, and alditose hydrazones, which cyclized into the corresponding oxadiazolines.

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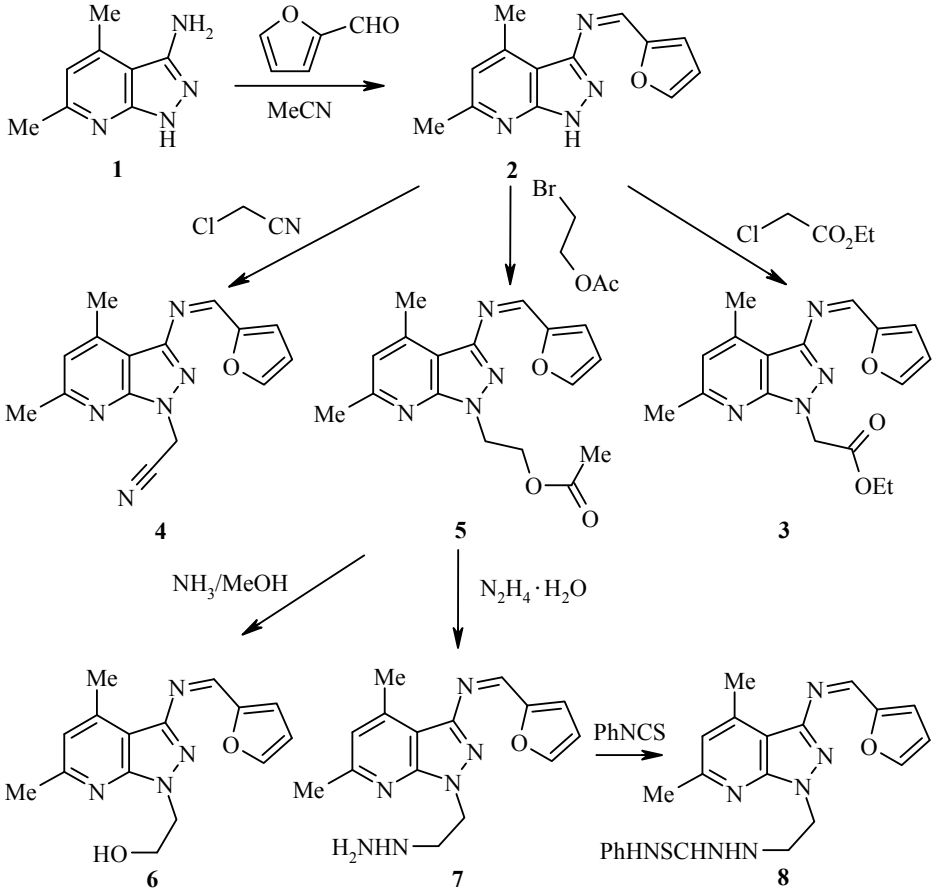
The starting 4,6-dimethyl-1H-pyrazolo[3,4-*b*]pyridine-3-amine (**1**) was prepared according to reported method [23, 24]. It was condensed with furfurol in the presence of a catalytic amount of glacial acetic acid to afford N-(furan-2-ylmethylidene)-4,6-dimethyl-1H-pyrazolo[3,4-*b*]pyridine-3-amine (**2**), which was alkylated, after its treatment with anhydrous potassium carbonate in dry N,N-dimethylformamide, with ethyl chloroacetate, chloroacetonitrile, or bromoethyl acetate to give ethyl [3-(furan-2-ylmethylideneamino)-4,6-dimethyl-1H-pyrazolo[3,4-*b*]pyridin-1-yl]acetate (**3**), [3-(furan-2-ylmethylideneamino)-4,6-dimethyl-1H-pyrazolo[3,4-*b*]pyridin-1-yl]acetonitrile (**4**), and 2-[3-(furan-2-ylmethylideneamino)-4,6-dimethyl-1H-pyrazolo[3,4-*b*]pyridin-1-yl]ethyl acetate (**5**) in good yields (Scheme 1, Table 1). The treatment of compound **5** with ammonia in methanol (1:1) at room temperature resulted in the deprotection of the hydroxyl group, and the corresponding 2-[3-(furan-2-ylmethylideneamino)-4,6-dimethyl-1H-pyrazolo[3,4-*b*]pyridin-1-yl]ethanol (**6**) was obtained and identified by the absence of the acetate methyl group signal and the presence of a broad signal of the hydroxyl group at 4.65 ppm in its ^{1}H NMR spectrum, as well as the characteristic absorption band at 3261 cm^{-1} in its IR spectrum. Compound **5** was condensed with hydrazine hydrate in absolute ethanol to afford N-[furan-2-ylmethylidene]-1-(2-hydrazinylethyl)-4,6-dimethyl-1H-pyrazolo[3,4-*b*]pyridine-3-amine (**7**), which was treated with phenyl isothiocyanate to give the corresponding phenylthiosemicarbazide **8**. IR, NMR, MS, and elemental analysis data support the structures of compounds **7** and **8**.

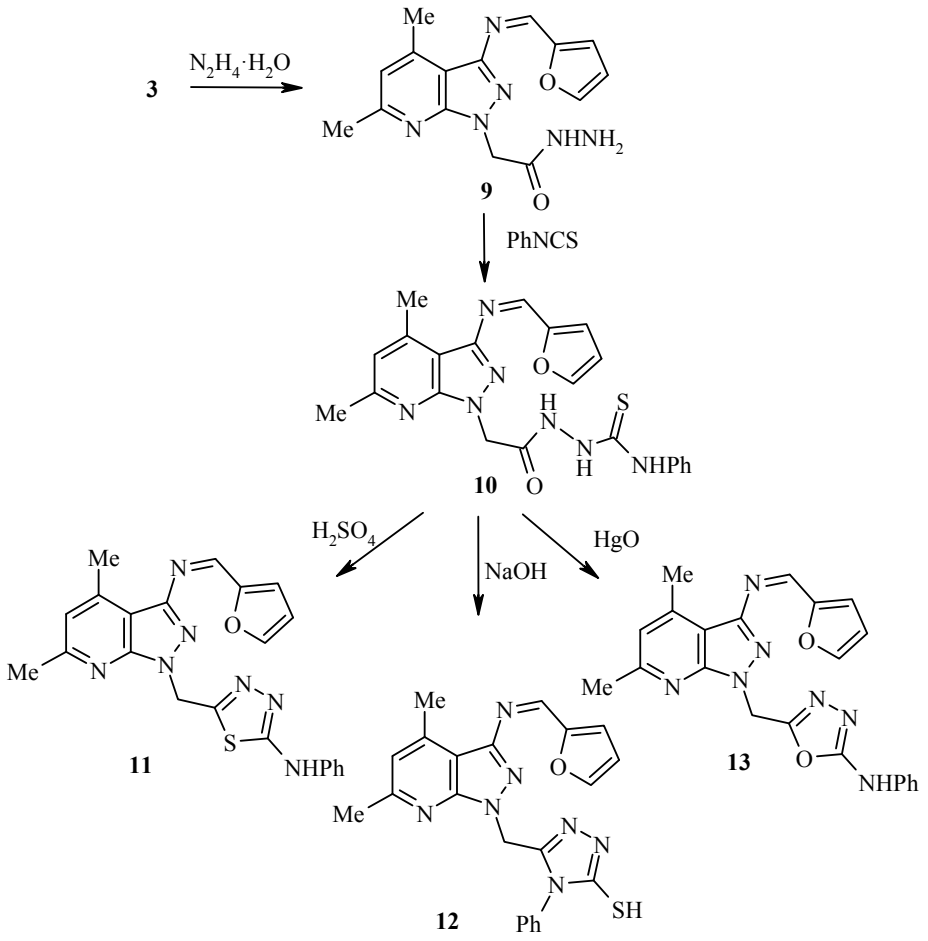
Scheme 1



The ethyl ester derivative **3** was condensed with hydrazine hydrate to afford the corresponding hydrazide **9**. The signals of the ester group were absent in its ^{1}H NMR spectrum, and broad singlets at 5.14 and 10.14 ppm corresponding to NH_2 and NH groups of hydrazide, respectively, were present. Hydrazide **9** reacted with PhNCS to afford the thiosemicarbazide derivative **10** (Scheme 2). Its mass spectrum showed the molecular ion peak at *m/z* 447 and the most intensive peak at *m/z* 312 corresponding to $[M–PhNCS]^+$. From the

thiosemicarbazide **10**, in the presence of concentrated sulfuric acid, 1,3,4-thiadiazole derivative **11** was obtained, which showed in its ^{1}H NMR spectrum the broad band of the NHPh proton at 11.55 ppm. The formation of the thiadiazole ring under such acidic conditions is the result of the loss of nucleophilicity at the N-4 atom of the thiosemicarbazide moiety owing to its protonation and simultaneous increase in the nucleophilicity at the sulfur atom toward the attack of the carbonyl carbon. On the other hand, when the cyclization of compound **10** was carried out under basic conditions, the nucleophilicity at the N-4 atom was enhanced, leading to its attack on the carbonyl carbon atom and cyclization to afford 1,2,4-triazole derivative **12**.

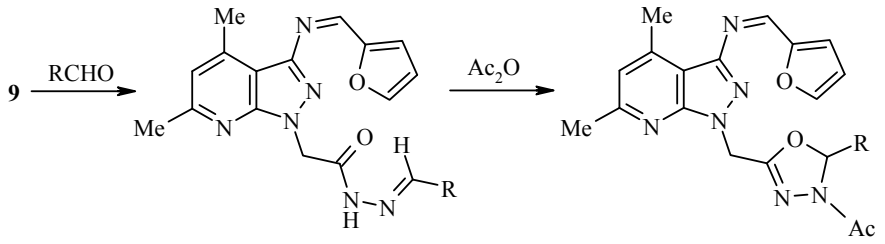
Scheme 2

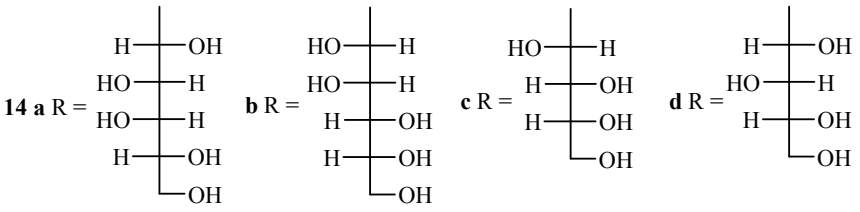


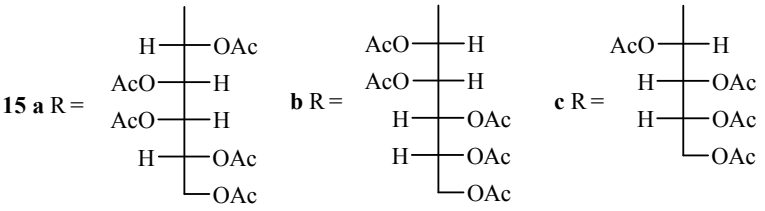
The ^{1}H NMR spectra of triazole **12** showed a broad singlet at 12.05 ppm corresponding to the SH group. Treatment of thiosemicarbazide **10** with mercuric oxide afforded 1,3,4-oxadiazole derivative **13**. The method of cyclization involves desulfurization by HgO. The structures of compounds **10–13** were confirmed using NMR, elemental analysis, and mass spectra (Tables 1–3).

Condensation of hydrazide **9** with aldoses – D-galactose, D-mannose, D-arabinose, and D-xylose – gave the corresponding sugar hydrazones **14a–d** (52–65%). The ^{1}H NMR spectra of the hydrazones **14a–d** confirmed the presence of sugar protons in the range 3.33–4.32 ppm, and the assignment of NH and OH groups was achieved by the addition of D_2O. Formation of the oxadiazoline derivatives **15a–c** was achieved by treatment of hydrazones **14a–c** with acetic anhydride under reflux (Scheme 3). The mechanism of formation of the oxadiazolines could be similar to the one reported in earlier works [25–27]. In the ^{1}H NMR spectra of compounds **15a–c**, the proton of the oxadiazoline ring appears as a singlet at 6.23–6.25 ppm, and the acetamide methyl protons appear as a singlets at 3.59–3.65 ppm. The elemental analysis data (Table 1) and spectra of compounds **14a–d** and **15a–c** (Tables 2 and 3) support the proposed structures.

Scheme 3







EXPERIMENTAL

Melting points were determined on a Buchi melting point apparatus. IR spectra were recorded on a Nicolet 200 FT-IR spectrophotometer (in KBr). ^{1}H and ^{13}C NMR spectra were registered on a Varian Gemini 2000 instrument at 300 and 75.5 MHz, respectively, in DMSO-d_6 ($CDCl_3$ for compound **2**) with TMS as the internal standard. Mass spectra (EI) were registered on a Kratos 50 TC spectrometer. Elemental analysis was performed in the microanalysis lab at Cairo University. Common reagent-grade chemicals were either commercially available and used without further purification or prepared by standard literature procedures. All reactions were monitored by TLC, carried out on 0.2 mm silica gel 60 F-254 (Merck) plates using UV light (254 and 360 nm) for detection.

N-(Furan-2-ylmethylidene)-4,6-dimethyl-1H-pyrazolo[3,4-*b*]pyridine-3-amine (2). To a solution of 3-aminopyrazolopyridine **1** (0.58 g, 3.6 mmol) in MeCN (10 ml), furfurol (5.25 g, 5.47 mmol) was added followed by a few drops of acetic acid, and the reaction mixture was stirred for 5 h at room temperature. The solvent was removed under reduced pressure, and the reaction mixture was diluted with cold water. The separated solid was collected by filtration, washed with water, and dried. The crude product was recrystallized from ethanol to afford compound **2** as a pale-yellow powder.

Ethyl [3-Furan-2-ylmethylideneamino)-4,6-dimethyl-1H-pyrazolo[3,4-*b*]pyridin-1-yl]acetate (3), [3-(Furan-2-ylmethylideneamino)-4,6-dimethyl-1H-pyrazolo-[3,4-*b*]pyridin-1-yl]acetonitrile (4), and **2-[3-(Furan-2-ylmethylideneamino)-4,6-dimethyl-1H-pyrazolo[3,4-*b*]pyridin-1-yl]ethyl Acetate (5) (General method)**. To a stirred suspension of compound **2** (1.20 g, 5 mmol) and K_2CO_3 (1.04 g, 7.5 mmol) in dry DMF (10 ml), the corresponding halo compound (7.5 mmol) – ethyl chloroacetate, chloroacetonitrile, or 2-bromoethyl acetate – was added dropwise. The reaction mixture was stirred at room temperature for 13 h and then poured into ice-cold water with stirring. The obtained solid product was collected by filtration, washed with water, and recrystallized from ethanol to afford pale-yellow crystals.

TABLE 1. Physicochemical Characteristics of Compounds **2–13, 14a–d,** and **15a–c**

Compound	Empirical formula	Found, % / Calculated, %			mp, °C	Yield, %
		C	H	N		
2	$C_{13}H_{12}N_4O$	64.81 / 64.99	4.95 / 5.03	23.18 / 23.32	127–129	87
3	$C_{17}H_{18}N_4O_3$	62.41 / 62.57	5.33 / 5.56	17.10 / 17.17	96–98	92
4	$C_{15}H_{13}N_5O$	64.39 / 64.51	4.42 / 4.69	24.89 / 25.07	110–112	86
5	$C_{17}H_{18}N_4O_3$	62.44 / 62.57	5.40 / 5.56	17.11 / 17.17	120–21	82
6	$C_{15}H_{16}N_4O_2$	63.22 / 63.37	5.42 / 5.67	19.61 / 19.71	170–172	73
7	$C_{15}H_{18}N_6O$	60.23 / 60.39	5.92 / 6.08	28.09 / 28.17	150–152	54
8	$C_{22}H_{23}N_7OS$	60.65 / 60.95	5.17 / 5.35	22.43 / 22.62	160–161	72
9	$C_{15}H_{16}N_6O_2$	57.83 / 57.68	5.29 / 5.16	26.98 / 26.91	236–238	92
10	$C_{22}H_{21}N_7O_2S$	60.11 / 59.05	4.88 / 4.73	22.07 / 21.91	119–121	94
11	$C_{22}H_{19}N_7OS$	61.71 / 61.52	4.33 / 4.46	22.62 / 22.83	190–192	74
12	$C_{22}H_{19}N_7OS$	61.22 / 61.52	4.53 / 4.46	22.71 / 22.83	217–219	67
13	$C_{22}H_{19}N_7O_2$	63.78 / 63.91	4.33 / 4.63	23.51 / 23.27	210–212	85
14a	$C_{21}H_{26}N_6O_7$	53.23 / 53.16	5.33 / 5.52	17.63 / 17.71	259–261	65
14b	$C_{21}H_{26}N_6O_7$	53.12 / 53.16	5.67 / 5.52	17.87 / 17.71	282–284	52
14c	$C_{20}H_{24}N_6O_6$	54.13 / 54.05	5.66 / 5.44	18.82 / 18.91	266–268	59
14d	$C_{20}H_{24}N_6O_6$	53.98 / 54.05	5.34 / 5.44	19.03 / 18.91	273–274	52
15a	$C_{33}H_{38}N_6O_{13}$	54.75 / 54.54	5.42 / 5.27	11.32 / 11.56	144–146	71
15b	$C_{33}H_{38}N_6O_{13}$	54.41 / 54.54	5.18 / 5.27	11.73 / 11.56	161–163	64
15c	$C_{30}H_{34}N_6O_{11}$	54.97 / 55.04	5.11 / 5.24	12.44 / 12.84	155–157	74

2-[3-(Furan-2-ylmethylideneamino)-4,6-dimethyl-1H-pyrazolo[3,4-*b*]pyridin-1-yl]ethanol (6). A mixture of compound **5** (1.30 g, 4 mmol), methanol (30 ml), and 25% aqueous ammonia (30 ml) was stirred at room temperature for 24 h. The solvent was evaporated under reduced pressure, and the residue was triturated with a small volume of ethanol. The yellow precipitate was filtered off, dried, and recrystallized from methanol to give compound **6**.

N-(Furan-2-ylmethylidene)-1-(2-hydrazinylethyl)-4,6-dimethyl-1H-pyrazolo[3,4-*b*]pyridine-3-amine (7). To a suspension of ester **5** (0.65 g, 2 mmol) in ethanol (15 ml), an excess of $N_2H_4 \cdot H_2O$ (4 ml) was added. The reaction mixture was refluxed for 4 h, cooled, and the solid product was collected by filtration, dried, and recrystallized from methanol to give pale-yellow crystals of compound **7** .

TABLE 2. IR and Mass Spectra of Compounds **2–13, 14a–d,** and **15a–c**

Compound	IR spectrum, ν, cm^{-1}	MS, *m/z* (*I*, %)
2	3106 (N–H), 2923, 2853 (C–H aliphatic), 1596 (C=N)	241 $[M + 1]^+$ (35), 240 $[M]^+$ (100), 161 (70), 131 (16)
3	2965, 2929 (C–H aliphatic), 1742 (C=O), 1589 (C=N)	326 $[M]^+$ (35), 281 (100), 240 (31), 131 (10)
4	2957, 2921 (C–H aliphatic), 2219 (C≡N), 1590 (C=N)	280 $[M + 1]^+$ (100), 279 $[M]^+$ (60), 201 (15), 174 (13), 118 (16).
5	2956, 2925 (C–H aliphatic), 1725 (C=O), 1590 (C=N)	327 $[M + 1]^+$ (51), 326 $[M]^+$ (100), 294 (20), 265 (12), 221 (10), 141 (33)
6	3261 (O–H), 2922, 2849 (C–H aliphatic), 1593 (C=N)	285 $[M + 1]^+$ (2), 284 $[M]^+$ (6), 164 (3), 206 (13), 175 (100)
7	3343–3202 ($NHNH_2$), 2938, 2892 (C–H aliphatic), 1589 (C=N)	298 $[M]^+$ (8), 252 (25), 219 (23), 175 (100)
8	3436 and 3244 (N–H), 3047 (C–H aromatic), 2953, 2921 (C–H aliphatic), 1587 (C=N), 1108–1033 (C=S)	434 $[M + 1]^+$ (6), 433 $[M]^+$ (9), 298 (100), 219 (23), 175 (52)
9	3428–3298 ($NHNH_2$), 3184–3046 (C–H aromatic), 2978, 2918 (C–H aliphatic), 1655 (C=O), 1632 (C=N)	313 $[M + 1]^+$ (5), 312 $[M]^+$ (16), 232 (51), 201 (7), 159 (100)
10	3336–3244 (NH), 4035 (C–H aromatic), 2978, 2886 (C–H aliphatic), 1697 (C=O), 1593 (C=N), 1195–1130 (C=S)	448 $[M + 1]^+$ (2), 447 $[M]^+$ (6), 351 (26), 312 $[M – PhNCS]^+$ (100), 276 (24), 175 (100)
11	3316–3285 (NH), 2955–2933 (C–H aliphatic), 1598 (C=N)	430 $[M + 1]^+$ (10), 429 $[M]^+$ (20), 393 (9), 335 (5), 268 (5), 204 (26), 135 (60), 77 (100)
12	3022 (C–H aromatic), 2955–2933 (C–H aliphatic), 2786–2715 (S–H) 1638 (C=N)	429 $[M]^+$ (10), 351 (10), 201 (15), 175 (41), 77 (100)
13	3230 (NH), 3055 (C–H aromatic), 2944–2910 (C–H aliphatic), 1635 (C=N).	413 $[M]^+$ (10), 348 (10), 191 (15), 175 (41), 77 (100)
14a	3460–3350 (O–H), 3210 (N–H), 2944–2921 (C–H aliphatic), 1632, 1567 (C=N)	475 $[M + 1]^+$ (4), 474 $[M]^+$ (10), 225 (2), 155 (3), 175 (41), 110 (100)
14b	3363–3327 (O–H), 3249 (N–H), 2933–2920 (C–H aliphatic), 1643, 1585 (C=N)	475 $[M + 1]^+$ (3), 474 $[M]^+$ (100), 225 (2), 155 (3), 175 (41)
14c	3360–3280 (O–H), 3247 (N–H), 2940–2933 (C–H aliphatic), 1647, 1589 (C=N)	445 $[M + 1]^+$ (3), 444 $[M]^+$ (100), 225 (2), 155 (3), 175 (41)
14d	3459–3360 (O–H), 3242 (N–H), 2933–2922 (C–H aliphatic), 1643, 1577 (C=N)	445 $[M + 1]^+$ (12), 444 $[M]^+$ (60), 225 (10), 155 (26), 175 (100).
15a	2925–2919 (C–H aliphatic), 1755 (C=O ester), 1675–1630 (C=O amide, C=N)	727 $[M + 1]^+$ (3), 726 $[M]^+$ (30), 225 (100)
15b	2930–2922 (C–H aliphatic), 1745 (C=O ester), 1671–1625 (C=O amide, C=N)	727 $[M^+ + 1]$ (10), 726 $[M^+]$ (32), 451 (16), 340 (21), 225 (100)
15c	2940–2898 (CH aliphatic), 1756 (C=O ester), 1665–1621 (C=O amide, C=N)	655 $[M + 1]^+$ (11), 654 $[M]^+$ (6), 451 (15), 340 (10), 225 (100)

1-{2-[3-(Furan-2-ylmethylideneamino)-4,6-dimethyl-1H-pyrazolo[3,4-*b*]pyridin-1-yl]ethyl}-4-phenylthiosemicarbazide (8). To a suspension of compound **7** (0.60 g, 2 mmol) in absolute ethanol (15 ml), PhNCS (0.54 g, 4 mmol) was added. The reaction mixture was heated under reflux for 4 h. The product that separated on cooling was filtered off, washed with ethanol, dried, and recrystallized from methanol to give colorless crystals of compound **8**.

2-[3-(Furan-2-ylmethylideneamino)-4,6-dimethyl-1H-pyrazolo[3,4-*b*]pyridin-1-yl]acetohydrazide (9). A mixture of pyrazolopyridine ester **3** (2.11 g, 6.5 mmol) and $N_2H_4 \cdot H_2O$ (1.25 g, 25 mmol) in ethanol (20 ml) was heated under reflux for 6 h. The excess of solvent was removed under reduced pressure, and the resulting precipitate was filtered off, washed with ethanol, and recrystallized from methanol to give a white powder of compound **9**.

TABLE 3. ^{1}H NMR Spectra of Compounds **2–13, 14a–d,** and **15a–c**

Com-pound	δ, ppm (*J*, Hz)
1	2
2	2.70 (3H, s, CH_3); 2.79 (3H, s, CH_3); 6.57 (1H, s, H-5); 6.77 (1H, dd, *J* = 3.5, *J* = 1.5, H furan); 7.20 (1H, d, *J* = 3.5, H furan); 8.04 (1H, d, *J* = 1.5, H furan); 8.93 (1H, s, N=CH); 12.13 (1H, br. s, NH)
3	1.25 (3H, t, *J* = 7.0, $C\underline{H}_3CH_2$); 2.55 (3H, s, CH_3); 2.65 (3H, s, CH_3); 4.41 (2H, q, *J* = 7.0, $CH_3C\underline{H}_2$); 4.95 (2H, s, NCH_2); 6.60 (1H, s, H-5); 6.79 (1H, dd, *J* = 3.5, *J* = 1.5, H furan); 7.33 (1H, d, *J* = 3.5, H furan); 8.22 (1H, d, *J* = 1.5, H furan); 8.77 (1H, s, N=CH)
4	2.66 (3H, s, CH_3); 2.69 (3H, s, CH_3); 4.65 (2H, s, NCH_2); 6.33 (1H, s, H-5); 6.71 (1H, dd, *J* = 3.5, *J* = 1.5, H furan); 7.53 (1H, d, *J* = 3.5, H furan); 7.77 (1H, d, *J* = 1.5, H furan); 8.81 (1H, s, N=CH)
5	2.61 (3H, s, CH_3); 2.64 (3H, s, CH_3); 2.91 (3H, s, $OCOCH_3$); 3.65 (2H, t, *J* = 7.5, $OCH_2C\underline{H}_2$); 4.33 (2H, t, *J* = 7.5, $OC\underline{H}_2CH_2$); 6.41 (1H, s, H-5); 6.77 (1H, dd, *J* = 3.5, *J* = 1.5, H furan); 7.23 (1H, d, *J* = 3.5, H furan); 7.33 (1H, d, *J* = 1.5, H furan); 8.75 (1H, s, N=CH)
6*	2.43 (3H, s, CH_3); 2.44 (3H, s, CH_3); 3.33 (2H, t, *J* = 7.5, NCH_2); 4.21 (2H, t, *J* = 7.5, OCH_2); 4.65 (1H, br. s, OH); 6.32 (1H, s, H-5); 6.67 (1H, dd, *J* = 3.5, *J* = 1.5, H furan); 6.91 (1H, d, *J* = 3.5, H furan); 7.18 (1H, d, *J* = 1.5, H furan); 8.44 (1H, s, N=CH)
7	2.45 (3H, s, CH_3); 2.51 (3H, s, CH_3); 3.21 (2H, t, *J* = 7.5, $NHCH_2C\underline{H}_2$); 3.86 (2H, m, $NHC\underline{H}_2CH_2$); 4.87 (2H, br. s, NH_2); 6.19 (1H, s, H-5); 6.57 (1H, dd, *J* = 3.5, *J* = 1.5, H furan); 7.08 (1H, d, *J* = 3.5, H furan); 7.32 (1H, d, *J* = 1.5, H furan); 8.51 (1H, s, N=CH); 9.16 (1H, br.s, NH)
8*	2.62 (3H, s, CH_3); 2.68 (3H, s, CH_3); 3.91 (2H, t, *J* = 7.5, $NHCH_2C\underline{H}_2$); 4.48 (2H, m, $NHC\underline{H}_2CH_2$); 6.98 (1H, s, H-5); 7.23 (1H, dd, *J* = 3.5, *J* = 1.5, H furan); 7.45 (1H, d, *J* = 3.5, H furan); 7.88–8.32 (7H, m, H furan, NH, Ph); 8.61 (1H, s, N=CH); 9.16 (1H, br. s, NH); 10.11 (1H, br. s, CSNH)
9	2.43 (3H, s, CH_3); 2.49 (3H, s, CH_3); 4.88 (2H, s, CH_2); 5.14 (2H, br. s, $NHN\underline{H}_2$); 6.71 (1H, s, H-5); 7.33 (1H, dd, *J* = 3.5, *J* = 1.5, H furan); 7.55 (1H, d, *J* = 3.5, H furan); 7.98 (1H, d, *J* = 1.5, H furan); 8.41 (1H, s, N=CH); 10.14 (1H, br. s, CONH)
10	2.55 (3H, s, CH_3); 2.68 (3H, s, CH_3); 4.95 (2H, s, CH_2); 6.98 (1H, s, H-5); 7.34 (1H, dd, *J* = 3.5, *J* = 1.5, H furan); 7.77 (1H, d, *J* = 3.5, H furan); 7.93–8.54 (7H, m, H furan, NH, Ph); 8.77 (1H, s, N=CH); 9.07 (1H, br. s, CSNH); 10.43 (1H, br. s, CONH)
11	2.51 (3H, s, CH_3); 2.64 (3H, s, CH_3); 5.33 (2H, s, NCH_2); 6.33 (1H, s, H-5); 6.68 (1H, dd, *J* = 3.5, *J* = 1.5, H furan); 7.13 (1H, d, *J* = 3.5, H furan); 7.55–7.76 (6H, m, H furan, Ph); 8.19 (1H, s, N=CH); 11.55 (1H, br. s, NHPh)
12	2.50 (3H, s, CH_3); 2.61 (3H, s, CH_3); 5.39 (2H, s, NCH_2); 6.23 (1H, s, H-5); 6.94 (1H, dd, *J* = 3.5, *J* = 1.5, H furan); 7.09 (1H, d, *J* = 3.5, H furan); 7.22–7.75 (6H, m, H furan, Ph); 8.22 (1H, s, N=CH); 12.05 (1H, br. s, SH)
13	2.54 (3H, s, CH_3); 2.59 (3H, s, CH_3); 5.71 (2H, s, NCH_2); 6.13 (1H, s, H-5); 6.88 (1H, dd, *J* = 3.5, *J* = 1.5, H furan); 7.06 (1H, d, *J* = 3.5, H furan); 7.45–7.86 (6H, m, H furan, Ph); 8.33 (1H, s, N=CH); 11.12 (1H, br. s, NHPh)
14a	2.63 (3H, s, CH_3); 2.65 (3H, s, CH_3); 3.41–4.21 (4H, m, 4 C<u>H</u>OH); 3.99–4.11 (5H, br. s, 5OH); 5.06 (2H, s, NCH_2); 5.21 (2H, br. s, $C\underline{H}_2OH$); 6.74 (1H, s, H-5); 7.87 (1H, dd, *J* = 3.5, 1.5, H furan); 7.90 (1H, d, *J* = 3.5, H furan); 8.12 (1H, d, *J* = 1.5, H furan); 8.45 (1H, s, HNN=C<u>H</u>); 8.72 (1H, s, N=CH); 8.93 (1H, br. s, NH)
14b	2.53 (3H, s, CH_3); 2.09 (3H, s, CH_3); 3.20–4.40 (4H, m, 4 C<u>H</u>OH); 4.39–4.65 (5H, br. s, 5 OH); 4.71 (2H, s, NCH_2); 5.51 (2H, br. s, $C\underline{H}_2OH$); 6.33 (1H, s, H-5); 6.63 (1H, dd, *J* = 3.5, *J* = 1.5, H furan); 7.50 (1H, d, *J* = 3.5, H furan); 7.44 (1H, d, *J* = 1.5, H furan); 7.76 (1H, s, HNN=C<u>H</u>); 8.09 (1H, s, N=CH); 8.61 (1H, br. s, NH)
14c	2.59 (3H, s, CH_3); 2.66 (3H, s, CH_3); 3.54–4.32 (3H, m, 3 C<u>H</u>OH); 4.43–4.56 (4H, br. s, 4 OH); 4.86 (2H, s, NCH_2); 5.42 (2H, br. s, $C\underline{H}_2OH$); 6.55 (1H, s, H-5); 6.72 (1H, dd, *J* = 3.5, *J* = 1.5, H furan); 7.55 (1H, d, *J* = 3.5, H furan); 7.66 (1H, d, *J* = 1.5, H furan); 7.81 (1H, s, HNN=C<u>H</u>); 8.16 (1H, s, N=CH); 8.75 (1H, br. s, NH)
14d	2.55 (3H, s, CH_3); 2.61 (3H, s, CH_3); 3.61–4.22 (3H, m, 3 C<u>H</u>OH); 4.42–4.57 (4H, br. s, 4 OH); 4.84 (2H, s, NCH_2); 5.39 (2H, br. s, $C\underline{H}_2OH$); 6.56 (1H, s, H-5); 6.77 (1H, dd, *J* = 3.5, *J* = 1.5 H furan); 6.94 (1H, d, *J* = 3.5, H furan); 7.59 (1H, d, *J* = 1.5, H furan); 7.88 (1H, s, HNN=C<u>H</u>); 8.20 (1H, s, N=CH); 8.77 (1H, br. s, NH)

TABLE 3. (Continued)

1	2
15a	1.91, 1.94, 1.95, 1.98, 2.12 (15H, s, $5OCOCH_3$); 2.39 (3H, s, CH_3); 2.41 (3H, s, CH_3); 3.65 (3H, s, $NCOCH_3$); 4.41–5.08 (4H, m, 4 CHOAc); 5.19 (2H, s, NCH_2); 5.22 (2H, d, *J* = 7.2, CH_2OAc); 6.23 (1H, s, OCHN); 6.65 (1H, s, H-5); 6.85 (1H, dd, *J* = 3.5, *J* = 1.5, H furan); 7.46 (1H, d, *J* = 3.5, H furan); 7.55 (1H, d, *J* = 1.5, H furan); 7.68 (1H, s, N=CH)
15b	1.89, 1.90, 1.93, 1.96, 2.11 (15H, s, $5OCOCH_3$); 2.41 (3H, s, CH_3); 2.51 (3H, s, CH_3); 3.62 (3H, s, $NCOCH_3$); 4.39–5.12 (4H, m, 4 CHOAc); 5.17 (2H, s, NCH_2); 5.09 (2H, d, *J* = 7.2, CH_2OAc); 6.24 (1H, s, OCHN); 6.66 (1H, s, H-5); 7.03 (1H, dd, *J* = 3.5, *J* = 1.5, H furan); 7.43 (1H, d, *J* = 3.5, H furan); 7.68 (1H, d, *J* = 1.5, H furan); 7.75 (1H, s, N=CH)
15c	1.85, 1.88, 1.96, 2.06 (12H, s, $4OCOCH_3$); 2.51 (3H, s, CH_3); 2.56 (3H, s, CH_3); 3.59 (3H, s, $NCOCH_3$); 4.45–5.20 (3H, m, 3 CHOAc); 5.06 (2H, s, NCH_2); 5.17 (2H, d, *J* = 7.2, CH_2OAc); 6.26 (1H, s, OCHN); 6.72 (1H, s, H-5); 7.12 (1H, dd, *J* = 3.5, *J* = 1.5, H furan); 7.43 (1H, d, *J* = 3.5, H furan); 7.62 (1H, d, *J* = 1.5, H furan); 7.81 (1H, s, N=CH)

* ^{13}C NMR spectra, δ, ppm: compound **6** – 18.81, 20.01 (2 CH_3); 45.45, 57.42 (2 CH_2); 102.12, 112.05, 118.54, 122.15, 144.06, 145.14, 149.09, 150.32, 154.17, 158.11; compound **8** – 18.86, 25.54 (2 CH_3); 50.04, 60.71 (2 CH_2); 102.12, 112.05, 118.54, 119.61, 122.15, 125.66, 126.30, 129.63, 129.69, 138.85, 143.49, 144.06, 145.14, 149.09, 150.32, 154.17, 158.11, 179.66 (C=S).

1-[2-(3-Furan-2-ylmethylideneamino)-4,6-dimethyl-1H-pyrazolo[3,4-*b*]pyridin-1-ylacetyl]-4-phenylthiosemicarbazide (10). To a suspension of compound **9** (3.12 g, 10 mmol) in absolute ethanol (20 ml), PhNCS (1.35 g, 10 mmol) was added. The reaction mixture was heated under reflux for 2 h. The product that separated on cooling was filtered off, washed with ethanol, dried, and recrystallized from methanol to give colorless crystals of compound **10**.

N-[3-(Furan-2-ylmethylidene)-4,6-dimethyl-1-[5-(phenylamino)-1,3,4-thiadiazol-2-ylmethyl]-1H-pyrazolo[3,4-*b*]pyridine-3-amine (11). The phenylthiosemicarbazide **10** (0.45 g, 1 mmol) was added within 10 min portionwise with stirring to ice-cooled conc. H_2SO_4 (10 ml). The mixture was stirred for 1 h on an ice bath. Then the mixture was poured onto crushed ice with stirring. The solid that separated was filtered off, washed with water, dried, and recrystallized from methanol to give pale-yellow crystals of compound **11**.

5-[3-(Furan-2-ylmethylideneamino)-4,6-dimethyl-1H-pyrazolo[3,4-*b*]pyridin-1-ylmethyl)-4-phenyl-4H-1,2,4-triazole-3-thiol (12). A solution of compound **10** (0.45 g, 1 mmol) in ethanolic sodium hydroxide (4 N, 50 ml) was refluxed for 4 h on water bath, concentrated, cooled, and filtered. The filtrate was brought to pH 5–6 with HCl and kept for 1–2 h. The separated solid was filtered off, washed with water, dried, and recrystallized from methanol to give a yellow powder of compound **12**.

N-(Furan-2-ylmethylidene)-4,6-dimethyl-1-(5-phenylamino-1,3,4-oxadiazol-2-ylmethyl)-1H-pyrazolo[3,4-*b*]pyridine-3-amine (13). Mercuric oxide (2.37 g, 11 mmol) was added to a solution of compound **10** (4.47 g, 10 mmol) in methanol (20 ml), and the resulting mixture was refluxed for 3 h. The precipitated mercuric sulfide was filtered off and washed with hot methanol. The filtrate on cooling gave a solid product, which was filtered, dried, and recrystallized from methanol to give yellow crystals of compound **13**.

Condensation Reaction of Acetohydrazide 9 with Aldoses (General Method). A solution of the corresponding aldose (10 mmol) in water (3 ml) was treated with a solution of compound **9** (3.12 g, 10 mmol) in ethanol (75 ml) and a few drops of glacial acetic acid. The mixture was refluxed for 5–7 h (monitored by TLC). The excess of ethanol was removed under reduced pressure, and the residue was triturated with a small amount of ethanol. The solid product was filtered off, washed with a small amount of water, dried, and recrystallized from DMF to give colored hydrazones **14a–d**.

1-{5-[3-(Furan-2-ylmethylideneamino)-4,6-dimethyl-1H-pyrazolo[3,4-*b*]pyridin-1-ylmethyl]-2-(1,2,3,4,5-penta-O-acetyl-D-*galacto*-pentitol-1-yl)-1,3,4-oxadiazol-3(2H)-yl}ethanone (15a), 1-{5-[3-(furan-2-ylmethylideneamino)-4,6-dimethyl-1H-pyrazolo[3,4-*b*]pyridin-1-ylmethyl]-2-(1,2,3,4,5-penta-O-acetyl-D-*manno*-pentitol-1-yl)-1,3,4-oxadiazol-3(2H)-yl}ethanone (15b), 1-{5-[3-(furan-2-ylmethylidene amino)-4,6-dimethyl-1H-pyrazolo[3,4-*b*]pyridin-1-ylmethyl]-2-(1,2,3,4,5-penta-O-acetyl-D-*arabino*-tetritol-1-yl)-1,3,4-oxadiazol-3(2H)-yl}ethanone (15c) (General Method). A solution of a hydrazone **14a–c** (1 mmol) in an excess of acetic anhydride (10 ml) was refluxed for 2–5 h. The reaction mixture was cooled and then poured into ice-cold water with stirring. The solid product was collected by filtration. The product was washed with a solution of sodium carbonate followed by water, then dried and recrystallized from methanol to give the corresponding compound **15a–c**.

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