

SYNTHESIS OF ALKYL 1-(SUBSTITUTED PYRIDIN-2-YL)-1*H*-1,2,3-TRIAZOLE-4-CARBOXYLATES BY 'RING SWITCHING' TRANSFORMATION OF 4-OXO-4*H*-PYRIDINO[1,2-*a*]PYRIMIDINE-3-DIAZONIUM TETRAFLUOROBORATES

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Abstract - Substituted 3-amino-4-oxo-4*H*-pyridino[1,2-*a*]pyrimidines (**6**, **7**), available in 2 steps from methyl 2-benzyloxycarbonylamino-3-dimethylamino-propenoate (**3**) and 2-aminopyridines (**1**, **2**), were diazotized into stable diazonium tetrafluoroborates (**8**, **9**). Heating of diazonium salts (**8**, **9**) with primary alcohols furnished alkyl 1-(substituted pyridin-2-yl)-1*H*-1,2,3-triazoles (**11**, **12**) in 30-70% yields.

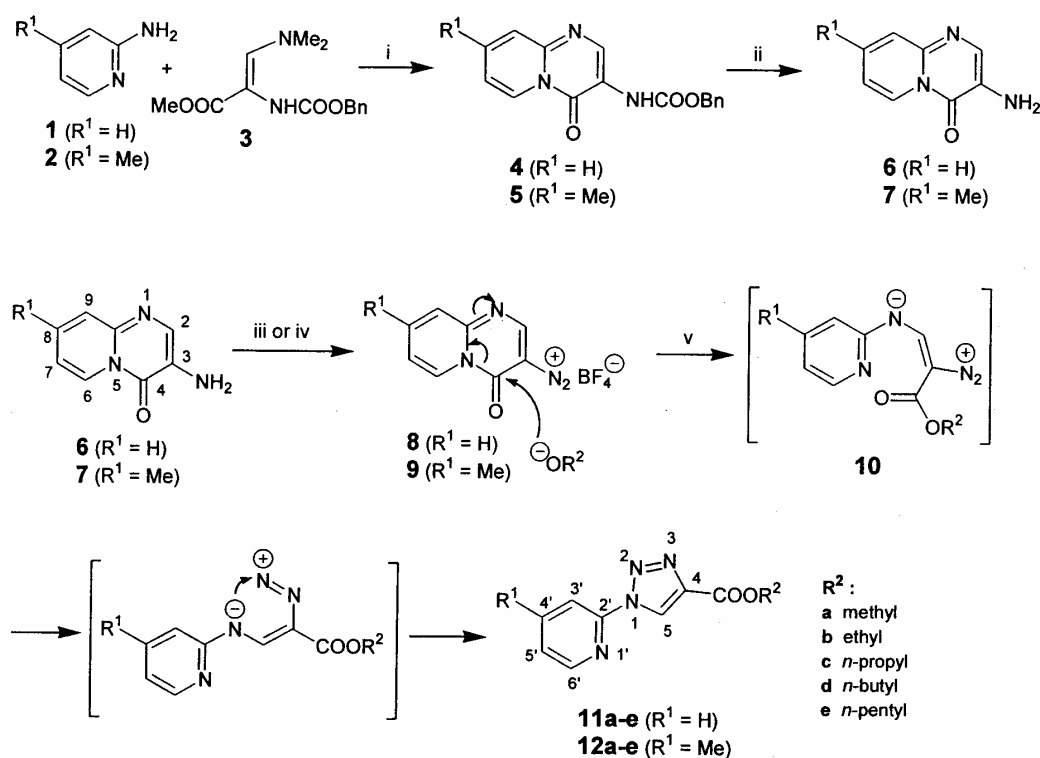
Quinolizines¹ and their 1-aza analogs, pyridino[1,2-*a*]pyrimidines,² are constituents of various naturally occurring alkaloids exhibiting neuroleptic³ analgesic,⁴ antiemetic,⁵ antibacterial,⁶ and antitumor activity.⁷ On the other hand, 1,2,3-triazoles and fused 1,2,3-triazoles also represent an important class of heterocyclic compounds which have found a wide and versatile use in organic synthesis, medicinal chemistry, and industrial applications.⁸ For example, 1*H*-1,2,3-benzotriazole is a highly efficient synthetic auxiliary⁹ and numerous 1,2,3-triazole derivatives exhibit diverse biological activities, such as antiviral,¹⁰ fungicidal,¹¹ muscarinic,¹² antiallergic,¹³ anticoccidial,¹⁴ anti-HIV-1,¹⁵ antiepileptic,¹⁶ antiinflammatory,¹⁷ prostaglandin synthesis inhibition,¹⁸ and others.¹⁹

Recently, 2-substituted 3-(dimethylamino)propenoates proved to be simple and efficient reagents for the preparation of various heterocyclic systems.^{20,21} For example, 3-substituted 4-oxo-4*H*-pyridino[1,2-*a*]pyrimidines can be prepared in one step from 2-aminopyridines and 2-substituted 3-(dimethylamino)propenoates.²⁰⁻²³ Utilization of 2-benzyloxycarbonylamino and 2-vinylamino substituted 3-(dimethylamino)propenoates made 3-amino-4-oxo-4*H*-pyridino[1,2-*a*]pyrimidines available in two steps and good yields from 2-aminopyridine derivatives.^{22,23}

In continuation of our research in this field we studied transformations of 3-amino-4-oxo-4*H*-pyridino[1,2-

a]pyrimidines. The model compounds, 3-amino-4-oxo-4*H*-pyridino[1,2-*a*]pyrimidine (**6**) and 3-amino-8-methyl-4-oxo-4*H*-pyridino[1,2-*a*]pyrimidine (**7**) were prepared in two steps from methyl 2-benzyloxycarbonylamino-3-(dimethylamino)propenoate (**3**) and 2-aminopyridines (**1**) and (**2**), according to the procedure described previously.²² Compounds (**6**) and (**7**) were transformed into the stable diazonium tetrafluoroborates (**8**) and (**9**) in 82-95% yield. Treatment of diazonium salts (**8**, **9**) with primary alcohols at 40-90°C furnished the compounds (**11**, **12**). The explanation for this is the nucleophilic attack of an alcohol to the carbonyl group at 4-position, followed by cleavage of the C(4)-N(5) bond, isomerization around the C(2)-C(3) double bond, and ring closure of the diazonium group to the former N(1) atom to give the corresponding alkyl 1-(substituted pyridin-2-yl)-1*H*-1,2,3-triazole-4-carboxylates (**11a-e**, R¹ = H) and (**12a-e**, R¹ = Me) in 30-70% yields (Scheme 1).

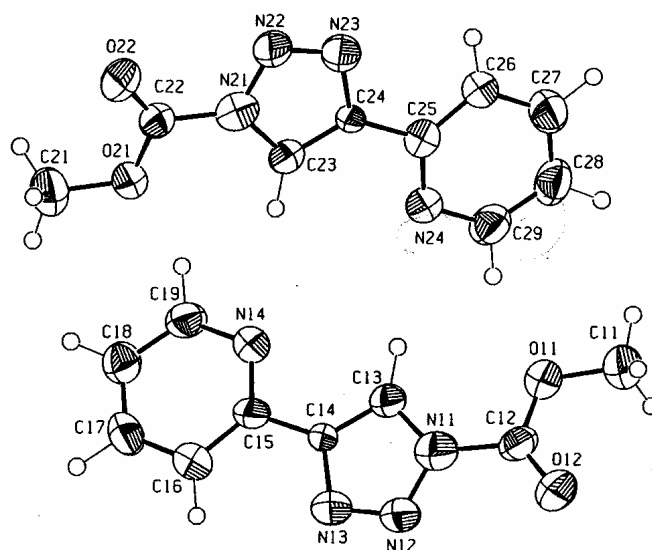
Scheme 1



Reagents and conditions: **i** methyl (Z)-2-[(benzyloxycarbonyl)amino]-3-(dimethylamino)propenoate (**3**), AcOH, reflux, 2.5 h, 82% (R¹ = H), 89% (R¹ = Me); **ii** cyclohexene, 10% Pd-C, ethanol, reflux, 30-90 min, 85% (R¹ = H), 92% (R¹ = Me); **iii** NaNO₂, HCl, H₂O, -5 to 0°, then 50% HBF₄ (**8**, 82%); **iv** BF₃Et₂O, CH₂Cl₂, *t*-BuONO, -15 to 0° (**9**, 95%); **v** R²OH, 40-90°, 30-70%.

This 'ring switching' mechanism is supported by a related example of nucleophile induced ring transformation of 2-azido-4-oxo-4*H*-pyridino[1,2-*a*]pyrimidines into 5-substituted 1-(pyridin-2-yl)-1*H*-tetrazoles.²⁴ The structure of **11 a** was also determined by X-Ray structural analysis (Figure 1)

Figure 1 X-Ray structure of compound (**11a**). The asymmetric unit showing atom labels of the non-hydrogen atoms. Ellipsoids are plotted at 50% probability level.



X-Ray Structure Determination. C₉H₈N₄O₂, M_r=204.2, orthorhombic Pbc2₁, No.: 29, a=3.8560(10), b=21.8770(10), c=22.1170(10) Å, V=1865.7(5) Å³, Z=8, D_x=1.454 Mg/m³, MoK α radiation, λ=0.7106 Å, μ=0.108 mm⁻¹. Diffraction data were collected on the Nonius-Kappa CCD Diffractometer at room temperature using graphite monochromatized MoK α radiation. The crystal dimensions were 0.12 x 0.12 x 0.20 mm. The entire reciprocal sphere was covered by φ and ω scans of 2° per frame. The data collection was performed using the Nonius Collect Software²⁵ while the indexing and scaling of the data were performed using DENZO and SCALEPACK.²⁶ The merging of the reflections up to the minimum d value of 0.80 Å gave R_{int}=0.039 for 1901 unique reflections, 1670 of which were observed (I > 3σ(I)). Absorption correction was not performed due to small absorption coefficient. The structure was solved using SIR92 program²⁷ while the refinement and plotting were done using Xtal3.4 program package.²⁸ The solution program provided all non-hydrogen atoms which were refined with anisotropic displacement factors. The hydrogen atoms could be found among the peaks in the difference Fourier map but were not stable in the refinement, so the final H positions were calculated and kept invariant during the last cycles of the refinement.

Table 1. Fractional Coordinates and Equivalent Temperature Factors (\AA^2). U_{eq} is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x/a	y/b	z/c	U_{eq}
O(11)	0.2855(10)	0.11788(18)	-0.0147(8)	0.058(2)
O(12)	0.5806(14)	0.0435(2)	-0.0611(9)	0.075(3)
O(21)	0.3990(9)	0.13846(16)	0.3588(9)	0.0544(19)
O(22)	0.6986(12)	0.2174(2)	0.3962(9)	0.068(2)
N(11)	0.4135(12)	0.0316(2)	0.0419(9)	0.063(3)
N(12)	0.5264(14)	-0.0264(2)	0.0482(9)	0.060(3)
N(13)	0.4646(13)	-0.0447(2)	0.1028(9)	0.060(3)
N(14)	0.0550(11)	0.04607(19)	0.2169(9)	0.054(2)
N(21)	0.4372(12)	0.2260(2)	0.3000(9)	0.060(3)
N(22)	0.5074(13)	0.2864(2)	0.2929(9)	0.059(3)
N(23)	0.4036(13)	0.3032(2)	0.2403(9)	0.061(3)
N(24)	-0.0071(12)	0.2071(2)	0.1312(9)	0.053(2)
C(11)	0.2870(17)	0.1529(3)	-0.0704(9)	0.069(3)
C(12)	0.4385(14)	0.0638(2)	-0.0173(9)	0.052(3)
C(13)	0.2728(12)	0.0515(2)	0.0951(9)	0.045(2)
C(14)	0.3114(10)	0.00307(18)	0.1322(9)	0.033(2)
C(15)	0.1995(13)	-0.0036(2)	0.1942(9)	0.045(2)
C(16)	0.2383(14)	-0.0586(2)	0.2233(9)	0.057(3)
C(17)	0.1257(16)	-0.0612(3)	0.2822(9)	0.060(3)
C(18)	-0.0262(15)	-0.0111(3)	0.3086(9)	0.058(3)
C(19)	-0.0557(15)	0.0414(2)	0.2742(9)	0.055(3)
C(21)	0.4598(17)	0.1057(3)	0.4146(9)	0.071(4)
C(22)	0.5310(12)	0.1949(2)	0.3570(9)	0.048(3)
C(23)	0.2812(11)	0.2047(2)	0.2491(9)	0.044(2)
C(24)	0.2574(10)	0.25376(17)	0.2128(9)	0.033(2)
C(25)	0.1139(11)	0.2593(2)	0.1533(9)	0.044(3)
C(26)	0.1027(15)	0.3147(2)	0.1253(9)	0.057(3)
C(27)	-0.0391(15)	0.3172(3)	0.0683(9)	0.064(3)
C(28)	-0.1708(16)	0.2629(3)	0.0427(9)	0.067(3)
C(29)	-0.1530(15)	0.2108(3)	0.0762(9)	0.061(3)

Table 2. Bond Distances (Å) and Bond Angles(°) with e,s,d.'s in parentheses.

O11-C11	1.45(2)	O21-C21	1.45(2)
O11-C12	1.323(7)	O21-C22	1.337(6)
O12-C12	1.20(2)	O22-C22	1.19(2)
N11-N12	1.350(7)	N21-N22	1.360(7)
N11-C12	1.49(2)	N21-C22	1.48(2)
N11-C13	1.37(2)	N21-C23	1.36(2)
N12-N13	1.29(3)	N22-N23	1.28(2)
N13-C14	1.366(14)	N23-C24	1.364(13)
N14-C15	1.321(12)	N24-C25	1.325(12)
N14-C19	1.34(3)	N24-C29	1.34(3)
C13-C14	1.349(17)	C23-C24	1.344(17)
C14-C15	1.44(3)	C24-C25	1.43(2)
C15-C16	1.372(14)	C25-C26	1.363(14)
C16-C17	1.37(3)	C26-C27	1.38(3)
C17-C18	1.374(14)	C27-C28	1.412(14)
C18-C19	1.383(16)	C28-C29	1.361(17)
C(11)-O(11)-C(12)	115.7(15)	C(21)-O(21)-C(22)	115.0(13)
N(12)-N(11)-C(12)	121.1(14)	N(22)-N(21)-C(22)	119.7(13)
N(12)-N(11)-C(13)	109.7(14)	N(22)-N(21)-C(23)	109.1(14)
C(12)-N(11)-C(13)	129.1(6)	C(22)-N(21)-C(23)	131.2(6)
N(11)-N(12)-N(13)	109.2(13)	N(21)-N(22)-N(23)	108.7(12)
N(12)-N(13)-C(14)	106.7(9)	N(22)-N(23)-C(24)	107.9(9)
C(15)-N(14)-C(19)	115.6(11)	C(25)-N(24)-C(29)	115.5(11)
O(11)-C(12)-O(12)	124.7(16)	O(21)-C(22)-O(22)	124.5(15)
O(11)-C(12)-N(11)	110.9(14)	O(21)-C(22)-N(21)	111.0(13)
O(12)-C(12)-N(11)	124.3(7)	O(22)-C(22)-N(21)	124.5(8)
N(11)-C(13)-C(14)	103.4(8)	N(21)-C(23)-C(24)	104.7(8)
N(13)-C(14)-C(13)	111.0(16)	N(23)-C(24)-C(23)	109.7(15)
N(13)-C(14)-C(15)	120.2(10)	N(23)-C(24)-C(25)	120.2(10)
C(13)-C(14)-C(15)	128.7(9)	C(23)-C(24)-C(25)	130.0(9)
N(14)-C(15)-C(14)	113.8(11)	N(24)-C(25)-C(24)	113.7(10)
N(14)-C(15)-C(16)	126.1(17)	N(24)-C(25)-C(26)	126.1(16)
C(14)-C(15)-C(16)	120.1(10)	C(24)-C(25)-C(26)	120.2(10)
C(15)-C(16)-C(17)	116.4(10)	C(25)-C(26)-C(27)	117.6(10)
C(16)-C(17)-C(18)	120.4(11)	C(26)-C(27)-C(28)	118.6(10)
C(17)-C(18)-C(19)	117.7(16)	C(27)-C(28)-C(29)	117.9(16)
N(14)-C(19)-C(18)	123.8(9)	N(24)-C(29)-C(28)	124.4(9)

Regina weighting scheme was applied.²⁹ The refinement of 271 variables on F_o magnitudes of 1670 reflections ended with $R=0.069$, $R_w=0.064$. Maximal shift/error was 0.023 and maximal and minimal residual electron densities in the difference Fourier map were 0.48 and $-0.38 \text{ e}/\text{\AA}^3$. Final atomic coordinates and equivalent atomic displacement parameters are given in Table 1, bond distances and angles are presented in Table 2. The asymmetric unit with atom labels is shown in Fig. 1. It consists of two identical molecules with almost identical bond lengths and angles which lie within the expected ranges for the given atoms. The two molecules in the asymmetric unit are related by a pseudo center of inversion which can not be included into the space group symmetry. No short contacts were found in the packing diagram.

In conclusion, 4-oxo-4*H*-pyridino[1,2-*a*]pyrimidine-3-diazonium tetrafluoroborates are transformed in a single step into alkyl 1-(pyridin-2-yl)-1*H*-1,2,3-triazole-4-carboxylates. Since 4-oxo-4*H*-pyridino[1,2-*a*]pyrimidine-3-diazonium salts are easily available in a three step procedure and in good yields from substituted 2-aminopyridines, this method represents the easiest way for the preparation of 1-heteroaryl-1*H*-1,2,3-triazoles.

EXPERIMENTAL

Melting points were taken with a Kofler micro hot stage. The ^1H NMR spectra and ^{13}C NMR spectra were obtained with a Bruker Avance DPX 300 (300 MHz) spectrometer with DMSO-d_6 and CDCl_3 as solvents and Me_4Si as internal standard. IR spectra were recorded with a Perkin-Elmer 1310 spectrophotometer (KBr discs). The microanalyses for C, H, and N were obtained with a Perkin-Elmer CHN Analyser 2400, The MS spectra were recorded with an Autospeck Q (VG-Analytical) spectrometer in Laboratory for Mass Spectroscopy (J. Stefan Institute, Ljubljana). TLC: Merck, Alufolien Kieselgel 60 F 254, 0.2 mm. Column chromatography (CC) was performed on a silica gel (Fluka, Kieselgel 60, 0.04-0.063 mm).

All starting materials were commercially available (in most cases from Fluka) and purified following the standard techniques. 3-Amino-4*H*-pyridino[1,2- α]pyrimidin-4-one (**6**) and 3-amino-8-methyl-4*H*-pyridino[1,2- α]pyrimidin-4-one (**7**) were prepared according to the procedures described in the literature.²² Compounds (**8**, **9**) and (**11**, **12**) were isolated in analytically pure form and therefore no further purification by crystallization was required.

4*H*-Pyridino[1,2- α]pyrimidin-4-one-3-diazonium Tetrafluoroborate (8**).** Aqueous sodium nitrite (20%, 0.6 mL, 1.6 mmol) was added portionwise at $0-5^\circ\text{C}$ to the rapidly stirred solution of 3-amino-4-oxo-4*H*-pyridino[1,2- α]pyrimidine (**6**) (0.242 g, 1.5 mmol) in a mixture of water (2 mL) and concentrated hydrochloric acid (2 mL), and the mixture was stirred at $0-5^\circ$ for 10 min. Completion of the reaction was

checked using the moist potassium iodide-starch paper as an external indicator. A cold solution (0°C) of aqueous fluoroboric acid (50 %, 2 mL, 13.9 mmol) was added and the precipitate was collected by filtration and carefully washed with small portions of cold water, methanol, and ether to give analytically pure **8**.³⁰ Yield: 0.320 g (82%), colorless crystals; mp 209-211°C (decomp). IR (KBr, cm⁻¹): 3060, 2200 (N₂⁺), 1740 (C=O), 1495, 1100 (BF₄⁻). MS (FAB): 261 (MH⁺). ¹H NMR (300 MHz, DMSO-d₆): δ = 8.07 (1H, ddd, *J* = 1.3, 6.8, 7.3 Hz, 7-H), 8.32 (1H, ddd, *J* = 0.7, 1.3, 8.5 Hz, 9-H), 8.78 (1H, ddd, *J* = 1.6, 7.3, 8.5 Hz, 8-H), 9.43 (1H, s, 2-H), 9.44 (1H, ddd, *J* = 0.7, 1.6, 6.8 Hz, 6-H). ¹³C NMR (75.5 MHz, DMSO-d₆): δ = 87.2, 124.4, 128.9, 132.3, 149.7, 153.2, 154.7, 159.3. *Anal.* Calcd for C₈H₅N₄OBF₄: C, 36.96; H 1.94; N 21.55. Found: C, 36.92; H 1.59; N 21.36.

8-Methyl-4-oxo-4H-pyridino[1,2-*α*]pyrimidine-3-diazonium Tetrafluoroborate (9). Boron trifluoride ethyl etherate (0.990 g, 7 mmol) was stirred and cooled in an ice-acetone bath to about -15°C. A solution of 3-amino-8-methyl-4-oxo-4H-pyridino[1,2-*α*]pyrimidine (**7**) (0.613 g, 3.5 mmol) in anhydrous dichloromethane (20 mL) was added and the mixture was stirred at -15°C for 15 min. Then a solution of *tert*-butyl nitrite (0.577 g, 5.6 mmol) in anhydrous dichloromethane (5 mL) was added dropwise into a vigorously stirred suspension. The mixture was then stirred at -15°C for 15 min, warmed to 0-5°C in an ice-water bath and stirred at this temperature for 30 min. The precipitate was collected by filtration and washed with cold chloroform, cold methanol, and ether to give analytically pure **9**. Yield: 0.912 g (95%), colorless crystals; mp 152°-153°C (decomp). IR (cm⁻¹): 2980, 2170 (N₂⁺), 1715 (C=O), 1490, 1050 (BF₄⁻). MS (FAB): 187 (M⁺ - BF₄⁻). ¹H NMR (300 MHz, DMSO-d₆): δ = 2.73 (3H, s, 8-Me), 7.92 (1H, dd, *J* = 1.9, 7.0 Hz, 7-H), 8.17-8.19 (1H, m, 9-H), 9.31 (1H, d, *J* = 7.0 Hz, 6=H), 9.37 (1H, s, 2-H). ¹³C NMR (75.5 MHz, DMSO-d₆): δ = 22.8, 86.2, 125.3, 128.0, 131.3, 151.8, 154.3, 154.8, 159.1. *Anal.* Calcd for C₉H₇N₄OBF₄: C, 39.45; H 2.58; N 20.45. Found: C, 39.63; H 2.56; N 20.31.

General Procedure for the Preparation of Alkyl 1-(Pyridin-2-yl)-1H-1,2,3-triazole-4-carboxylates (11a-e). A mixture of diazonium salt (**8**) (0.100 g, 0.385 mmol) and anhydrous primary alcohol, (20-25 mL) was stirred at 60-90°C for 15 min to 5 h. After completion of the reaction, the volatile components were evaporated *in vacuo* and the residue was purified by column chromatography (silica gel, ethyl acetate). Fractions containing the product were combined and evaporated *in vacuo* to give analytically pure alkyl 1-(pyridin-2-yl)-1H-1,2,3-triazole-4-carboxylates (**11a-e**) in 51-70% yields.

The following compounds were prepared in this manner:

Methyl 1-(Pyridin-2-yl)-1H-1,2,3-triazole-4-carboxylate (11a). This compound was prepared by treatment of diazonium salt (**8**) with methanol (20 mL); reflux for 15 min. Yield: 0.054 g (70%), colorless crystals; mp

133°C. IR (cm⁻¹): 3120, 1730 (C=O), 1460, 1230, 1030, 760. MS (FAB): 205 (MH⁺). ¹H NMR (300 MHz, CDCl₃): δ = 4.01 (3H, s, OMe), 7.41 (1H, ddd, *J* = 1.1, 4.9, 7.5 Hz, 5'-H), 7.96 (1H, ddd, *J* = 1.9, 7.5, 8.3 Hz, 4'-H), 8.24 (1H, ddd, *J* = 1.0, 1.1, 8.3 Hz, 3-H), 8.54 (1H, ddd, *J* = 1.0, 1.9, 4.9 Hz, 6'-H), 9.10 (1H, s, 5-H). ¹³C NMR (75.5 MHz, CDCl₃): δ = 52.7, 114.5, 124.7, 125.2, 139.7, 140.5, 148.9, 149.2, 161.3. *Anal.* Calcd for C₉H₈N₄O₂ (204.2): C, 52.94; H 3.95; N 27.44. Found: C, 52.91 ; H 3.94; N 27.21.

Ethyl 1-(Pyridin-2-yl)-1*H*-1,2,3-triazole-4-carboxylate (11b). This compound was prepared by treatment of diazonium salt (**8**) with ethanol (30 mL); reflux for 30 min. Yield: 0.042 g (51%), white crystals; mp 96°C. IR (cm⁻¹): 3160, 2970, 1740 (C=O), 1455, 1215, 1030. MS (FAB): 219 (MH⁺). ¹H NMR (300 MHz, CDCl₃): δ = 1.44 (3H, t, *J* = 7.1 Hz, OCH₂CH₃), 4.47 (2H, q, *J* = 7.1 Hz, OCH₂CH₃), 7.41 (1H, ddd, *J* = 1.1, 4.9, 7.4 Hz, 5'-H), 7.96 (1H, ddd, *J* = 1.9, 7.4, 8.2 Hz, 4'-H), 8.25 (1H, ddd, *J* = 1.0, 1.1, 8.2 Hz, 3'-H), 8.54 (1H, ddd, *J* = 1.0, 1.9, 4.9 Hz, 6'-H), 9.10 (1H, s, 5-H). ¹³C NMR (75.5 MHz, CDCl₃): δ = 14.7, 61.8, 114.6, 124.7, 125.2, 139.7, 140.9, 149.0, 149.2, 161.0. *Anal.* Calcd for C₁₀H₁₀N₄O₂: C, 55.04; H 4.62; N 25.68. Found: C, 55.24; H 4.79; N 25.48.

***n*-Propyl 1-(Pyridin-2-yl)-1*H*-1,2,3-triazole-4-carboxylate (11c).** This compound was prepared by treatment of diazonium salt (**8**) with *l*-propanol (25 mL) at 60°C for 2 h. Yield: 0.050 g (57%), white crystals; mp 72°C. IR (cm⁻¹): 3135, 2955, 1740 (C=O), 1455, 1210, 1180, 1020. MS (FAB): 233 (MH⁺). ¹H NMR (300 MHz, CDCl₃): δ = 1.04 (3H, t, *J* = 7.4 Hz, OCH₂CH₂CH₃), 1.84 (2H, tq, *J* = 6.8, 7.4 Hz, OCH₂CH₂CH₃), 4.37 (2H, t, *J* = 6.8 Hz, OCH₂CH₂CH₃), 7.41 (1H, ddd, *J* = 1.1, 4.9, 7.5 Hz, 5'-H), 7.96 (1H, ddd, *J* = 1.8, 7.5, 8.3 Hz, 4'-H), 8.25 (1H, ddd, *J* = 0.9, 1.1, 8.3 Hz, 3'-H), 8.54 (1H, ddd, *J* = 0.9, 1.8, 4.9 Hz, 6'-H), 9.07 (1H, s, 5-H). ¹³C NMR (75.5 MHz, CDCl₃): δ = 10.8, 22.4, 67.3, 114.5, 124.7, 125.1, 139.7, 140.8, 149.0, 149.2, 161.0. *Anal.* Calcd for C₁₁H₁₂N₄O₂: C, 56.89; H 5.21; N 24.12. Found: C, 57.13; H 5.11; N 24.31.

***n*-Butyl 1-(Pyridin-2-yl)-1*H*-1,2,3-triazole-4-carboxylate (11d).** This compound was prepared by treatment of diazonium salt (**8**) with *l*-butanol (25 mL) at 90°C for 5 h. Yield: 0.053 g (56%), pale yellow crystals; mp 63-65°C. IR (cm⁻¹): 3160, 2940, 2860, 1720 (C=O), 1465, 1270, 1020. MS (FAB): 247 (MH⁺), (EI): 218 (M⁺-N₂). ¹H NMR (300 MHz, CDCl₃): δ = 1.00 (3H, t, *J* = 7.5 Hz, OCH₂CH₂CH₂CH₃), 1.47-1.55 (2H, m, OCH₂CH₂CH₂CH₃), 1.77-1.86 (2H, m, OCH₂CH₂CH₂CH₃), 4.43 (2H, t, *J* = 6.4 Hz, OCH₂CH₂CH₂CH₃), 7.42 (1H, ddd, *J* = 1.1, 4.9, 7.5 Hz, 5'-H), 7.97 (1H, ddd, *J* = 1.9, 7.5, 8.3 Hz, 4'-H), 8.27 (1H, ddd, *J* = 1.0, 1.1, 8.3 Hz, 3'-H), 8.56 (1H, ddd, *J* = 1.0, 1.9, 4.9 Hz, 6'-H), 9.09 (1H, s, 5-H). ¹³C NMR (75.5 MHz, CDCl₃): δ = 14.1, 19.5, 31.1, 65.7, 114.6, 124.7, 125.1, 139.7, 140.9, 149.0, 149.2, 161.0. *Anal.* Calcd for C₁₂H₁₄N₄O₂: C, 58.53; H 5.73; N 22.75. Found: C, 58.57; H 5.89; N 22.51.

***n*-Pentyl 1-(Pyridin-2-yl)-1*H*-1,2,3-triazole-4-carboxylate (11e).** This compound was prepared by treatment of diazonium salt (**8**) with 1-pentanol (25 mL) at 80°-90 °C for 15 h. Yield: 0.060 g (60%), yellow crystals; mp 57-59 °C. IR (cm⁻¹): 2920, 1720 (C=O), 1450, 1215, 1020. MS (FAB): 261 (MH⁺), ¹H NMR (300 MHz, CDCl₃): δ = 0.93 (3H, t, *J* = 6.8 Hz, OCH₂CH₂CH₂CH₂CH₃), 1.38-1.47 (4H, m, *J* = 6.8 Hz, OCH₂CH₂CH₂CH₂CH₃), 1.77-1.86 (2H, m, OCH₂CH₂CH₂CH₂CH₃), 4.40 (2H, t, *J* = 6.8 Hz, OCH₂CH₂CH₂CH₂CH₃), 7.41 (1H, ddd, *J*= 1.1, 4.9, 7.5 Hz, 5'-H), 7.96 (1H, ddd, *J* = 1.8, 7.5, 8.3 Hz, 4'-H), 8.25 (1H, ddd, *J*= 1.0, 1.1, 8.2 Hz, 3'-H), 8.54 (1H, ddd, *J*= 1.0, 1.8, 4.9 Hz, 6'-H), 9.07 (1H, s, 5-H). ¹³C NMR (75.5 MHz, CDCl₃): δ = 14.3, 22.7, 28.4, 28.8, 65.9, 114.6, 124.7, 125.1, 139.7; 140.9, 149.0, 149.2, 161 .0. *Anal.* Calcd for C₁₃H₁₆N₄O₂: C, 59.99; H 6.20; N 21.52. Found: C, 60.29; H 6.02; N 21.58.

General Procedure for the Preparation of Alkyl 1-(4-Methylpyridin-2-yl)-1*H*-1,2,3-triazole-4-carboxylates 12a-e. Diazonium salt (**9**) (0.100 g, 0.365 mmol) was dissolved in anhydrous acetonitrile (2 mL). Anhydrous primary alcohol (20 mL) was added and the solution was stirred at 40-60°C for 9-16 h. After the completion of reaction, the volatile components were evaporated *in vacuo* and the residue was purified by column chromatography (silica gel, ethyl acetate). Fractions containing the product were combined and evaporated *in vacuo* to give analytically pure alkyl 1 -(4-methylpyridin-2-yl)- 1*H*- 1,2,3-triazole-4-carboxylates (**12a-e**) in 30-42% yields.

The following compounds were prepared in this manner:

Methyl 1-(4-Methylpyridin-2-yl)-1*H*-1,2,3-triazole-4-carboxylate (12a). This compound was prepared by treatment of diazonium salt (**9**) with methanol (25 mL) at 50°C for 9 h. Yield: 0.033 g (42%), white crystals; mp 153-155°C. IR (cm⁻¹): 3180, 1730 (C=O), 1460, 1200, 1025. MS (FAB): 219 (MH⁺), (EI): 190 (M⁺-N₂), ¹H NMR (300 MHz, CDCl₃): δ = 2.50 (3H, s, 4'-Me), 4.00 (3H, s, OMe), 7.21 (1H, dd, *J* = 1.5, 4.8 Hz, 5'-H), 8.08 (1H, dd, *J*= 0.6, 1.5 Hz, 3'-H), 8.37 (1H, dd, *J*= 0.6, 4.8 Hz, 6'-H), 9.08 (1H, s, 5-H). ¹³C NMR (75.5 MHz, CDCl₃): δ = 21.7, 52.7, 115.1, 125.4, 125.7, 140.5, 148.8, 149.0, 151.6, 161.4. *Anal.* Calcd for C₁₀H₁₀N₄O₂: C, 55.04; H 4.62; N 25.68. Found: C, 55.12; H 4.72; N 25.57.

Ethyl 1-(4-Methylpyridin-2-yl)-1*H*-1,2,3-triazole-4-carboxylate (12b). This compound was prepared by treatment of diazonium salt (**9**) with ethanol at 40-50°C for 12 h. Yield: 0.025 g (30%), white crystals; mp 70°-72°C. IR (cm⁻¹): 3160, 2960, 1720 (C=O), 1445, 1180, 1020. MS (FAB): 233 (MH⁺), (EI): 204 (M⁺-N₂). ¹H NMR (300 MHz, CDCl₃): δ = 1.44 (3H, t, *J* = 7.2 Hz, OCH₂CH₃) 2.50 (3H, s, 4'-Me) 4.47 (2H, q, *J*= 7.2 Hz, OCH₂CH₃), 7.21 (1H, dd, *J*= 1.5, 4.9 Hz, 5'-H), 8.08 (1H, dd, *J*= 0.6, 1.5 Hz, 3'-H), 8.37 (1H, dd, *J*= 0.6, 4.9 Hz, 6'-H), 9.06 (1H, s, 5-H). ¹³C NMR (75.5 MHz, CDCl₃): δ = 14.7, 21.7, 61.8, 115.1, 125.3, 125.7, 140.8, 148.8, 149.2, 151.6, 161.0. *Anal.* Calcd for C₁₁H₁₂N₄O₂: C, 56.89; H 5.21; N 24. 12. Found: C, 57.07; H 5.19; N 23.86.

***n*-Propyl 1-(4-Methylpyridin-2-yl)-1*H*-1,2,3-triazole-4-carboxylate (12c).** This compound was prepared by treatment of diazonium salt (**9**) with 1-propanol at 40-50°C for 13 h. Yield: 0.038 g (42%), yellow crystals; mp 68°-69°C. IR (cm⁻¹): 2960, 1710 (C=O), 1460, 1260, 1200, 1020. MS (FAB): 247 (MH⁺), (EI): 218 (M⁺-N₂). ¹H NMR (300 MHz, CDCl₃): δ = 1.04 (3H, t, *J* = 7.2 Hz, OCH₂CH₂CH₃), 1.84 (2H, tq, *J* = 6.8, 7.2 Hz, OCH₂CH₂CH₃), 2.51 (3H, s, 4'-Me), 4.37 (2H, t, *J* = 6.8 Hz, OCH₂CH₂CH₃), 7.21 (1H, dd, *J* = 1.5, 4.9 Hz, 5'-H), 8.08 (1H, dd, *J* = 0.8, 1.5 Hz, 3'-H), 8.37 (1H, dd, *J* = 0.8, 4.9 Hz, 6'-H), 9.05 (1H, s, 5-H). ¹³C NMR (75.5 MHz, CDCl₃): δ = 10.8, 21.7, 22.4, 67.3, 115.1, 125.2, 125.7, 140.7, 148.8, 149.1, 151.7, 161.1. *Anal.* Calcd for C₁₂H₁₄N₄O₂: C, 58.53; H 5.73; N 22.75. Found: C, 58.71; H 5.77; N 22.50.

***n*-Butyl 1-(4-Methylpyridin-2-yl)-1*H*-1,2,3-triazole-4-carboxylate (12d).** This compound was prepared by treatment of diazonium salt (**9**) with 1-propanol at 50-60°C for 15 h. Yield: 0.039 g (41%), yellow crystals; mp 59-61°C. IR (cm⁻¹): 2960, 1730 (C=O), 1460, 1200, 1025. MS (FAB): 261 (MH⁺), (EI): 232 (M⁺-N₂). ¹H NMR (300 MHz, CDCl₃): δ = 0.98 (3H, t, *J* = 7.2 Hz, OCH₂CH₂CH₂CH₃), 1.49 (2H, deg, tt, *J* = 6.8, 7.2 Hz, OCH₂CH₂CH₂CH₃), 1.78 (2H, deg, tt, *J* = 6.8, 6.8 Hz, OCH₂CH₂CH₂CH₃), 2.50 (3H, s, 4'-Me), 4.41 (2H, t, *J* = 6.8 Hz, OCH₂CH₂CH₂CH₃), 7.21 (1H, dd, *J* = 1.4, 5.0 Hz, 5'-H), 8.08 (1H, dd, *J* = 0.7, 1.4 Hz, 3'-H), 8.37 (1H, dd, *J* = 0.7, 4.5 Hz, 6'-H), 9.04 (1H, s, 5-H). ¹³C NMR (75.5 MHz, CDCl₃): δ = 14.1, 21.7, 31.1, 32.4, 65.6, 115.1, 125.2, 125.7, 140.8, 148.8, 149.2, 151.6, 161.1. *Anal.* Calcd for C₁₃H₁₆N₄O₂: C, 59.99; H 6.20; N 21.52. Found: C, 59.64; H 6.08; N 21.40.

***n*-Pentyl 1-(4-Methylpyridin-2-yl)-1*H*-1,2,3-triazole-4-carboxylate (12e).** This compound was prepared by treatment of diazonium salt (**9**) with 1-pentanol at 60°C for 16 h. Yield: 0.030 g (30%), yellow crystals; mp 47-49°C. IR (cm⁻¹): 2960, 1740 (C=O), 1460, 1200, 1025. MS (FAB): 275 (MH⁺), (EI): 275 (MH⁺). ¹H NMR (300 MHz, CDCl₃): δ = 0.93 (3H, t, *J* = 7.1 Hz, OCH₂CH₂CH₂CH₂CH₃), 1.40-1.44 (4H, m, OCH₂CH₂CH₂CH₂CH₃), 1.81 (2H, deg. tt, *J* = 6.8, 6.8 Hz, OCH₂CH₂CH₂CH₂CH₃), 2.50 (3H, s, 4'-Me), 4.40 (2H, t, *J* = 6.8 Hz, OCH₂CH₂CH₂CH₂CH₃), 7.21 (1H, dd, *J* = 1.5, 5.1 Hz, 5'-H), 8.07 (1H, dd, *J* = 0.8, 1.5 Hz, 3'-H), 8.37 (1H, dd, *J* = 0.8, 5.1 Hz, 6'-H), 9.05 (1H, s, 5-H), ¹³C NMR (75.5 MHz, CDCl₃): δ = 14.3, 21.6, 28.8, 30.0, 33.6, 65.8, 115.1, 125.2, 125.7, 140.8, 148.8, 149.2, 151.6, 161.0. *Anal.* Calcd for C₁₄H₁₈N₄O₂: C, 61.30; H 6.61; N 20.42. Found: C, 60.96; H 6.48; N 20.27. HRMS Calcd for C₁₄H₁₉N₄O₂ (MH⁺): 275.150801. Found: 275.151110.

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