Asian Journal of Chemistry; Vol. 24, No. 7 (2012), 2884-2890

ASIAN JOURNAL OF CHEMISTRY

www.asianjournalofchemistry.co.in

Rearrangements of 2-Pyridyl-3-arylaminoisoxazol-5(2*H*)-ones to Imidazo[1,2-a]pyridines under Flash-Vacuum-Pyrolysis

DAVOOD SETAMDIDEH*, SALAH KHANAHMADZADEH and NASRIN KHORSHIDI

Department of Chemistry, Faculty of Sciences, Mahabad Branch, Islamic Azad University, Mahabad 59135-443, Iran

*Corresponding author: Fax: +98 442 2333000; Tel: +98 442 2338608-10; E-mail: davood.setamdideh@gmail.com

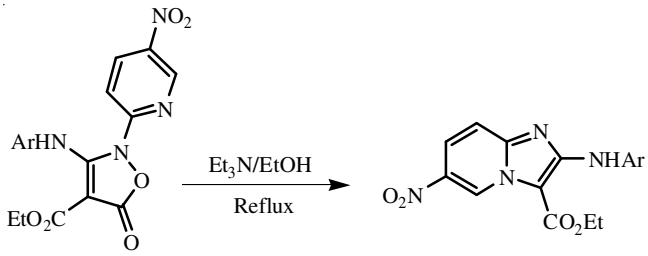
(*Received*: 18 June 2011; *Accepted*: 1 February 2012) AJC-11027

2-Pyridyl-3-arylaminoisoxazol-5(2*H*)-ones, rearranged under flash-vacuum-pyrolysis (FVP) conditions accompanied by elimination of carbon dioxide to give imidazo[1,2-a]pyridines in high to excellent yields (85-95 %).

Key Words: Isoxazolones, Imidazopyridines, Flash-vacuum-pyrolysis.

INTRODUCTION

The thermal or photochemical loss of nitrogen and carbon dioxide from triazoles and isoxazole-5-ones, respectively, have been reported[1]. We have reported that the reactions of 2-pyridyl-3-arylaminoisoxazol-5(2*H*)-ones (**1**, Ar: 4-BrC_6H_4, 4-MeC_6H_4)[2] with triethylamine in ethanol give imidazo annulated compounds (**2**, Ar: 4-BrC_6H_4 (84 %), 4-MeC_6H_4 (75 %) as net products (**Scheme-I**).



1, Ar: 4-BrC_6H_4, 4-MeC_6H_4 2, Ar: 4-BrC_6H_4, 4-MeC_6H_4

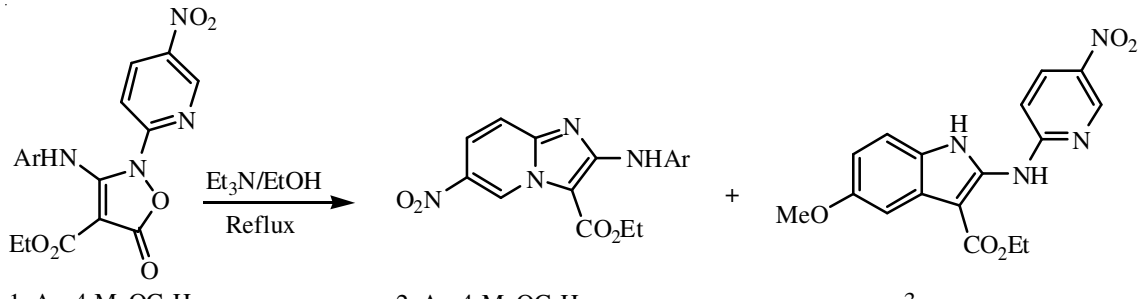
Scheme-I

However, the reaction of ethyl 3-(4-methoxyphenyl)-amino-2-(5-nitropyrid-2-yl)-5-oxo-2,5-dihydroisoxazole-4-carboxylate (**1**, 4-$MeOC_6H_4$) with triethylamine gives imidazo (**2**, 4-$MeOC_6H_4$, 59 %) and indole (**3**, 20 %)[2] annulated compounds respectively (**Scheme-II**).

Herein, we described net rearrangement of ethyl 2-pyridyl-3-arylaminoisoxazol-5(2*H*)-ones (**1**, Ar: 2-MeC_6H_4, 2-$MeOC_6H_4$, 3-MeC_6H_4, 3-BrC_6H_4, 3-$CO_2EtC_6H_4$, 4-$MeOC_6H_4$, 4-MeC_6H_4, 4-BrC_6H_4, 4-$CO_2EtC_6H_4$, 4-$NO_2C_6H_4$) to imidazo[1,2-a]pyridines (**2**, Ar: 2-MeC_6H_4, 2-$MeOC_6H_4$, 3-MeC_6H_4, 3-BrC_6H_4, 3-$CO_2EtC_6H_4$, 4-$MeOC_6H_4$, 4-MeC_6H_4, 4-BrC_6H_4, 4-$CO_2EtC_6H_4$, 4-$NO_2C_6H_4$) under flash-vacuum-pyrolysis (FVP) conditions.

EXPERIMENTAL

General: Freshly distilled solvents were used throughout and anhydrous solvents were dried according to Perrin and Amarego[3]. ^1H NMR and ^{13}C NMR spectra were recorded, in deuterio chloroform, unless otherwise stated, at 500 and



1, Ar: 4-$MeOC_6H_4$ 2, Ar: 4-$MeOC_6H_4$ 3

Scheme-II

125 MHz respectively, with a Bruker DRX-500 Avance spectrometer. Tetramethyl silane (TMS) was used as an internal standard and all signals due to amino protons were exchanged by exchange with D_2O. Infrared spectra were recorded on a Unicam Matsson 1000 Fourier-transform spectrometer. Mass spectra were recorded on a Varian Matt 311 spectrometer and relative abundance of fragments are quoted in parentheses after the m/z values. Melting points were determined on a Philip Harris C4954718 apparatus and are uncorrected. Micronalyses were preformed on a Carlo-Erba Analyzer 1104.

Diethyl (4-bromophenyl)thiocarbamoylmalonate (A typical procedure): Sodium (2.9 g, 0.126 mol) was reacted with absolute ethanol (50 mL) and diethyl malonate (20 g, 18.95 mL, 0.126 mol) was added at room temperature. The reaction mixture was stirred at room temperature for 15 min, 4-bromophenyl isothiocyanate. Yield (26.96 g, 0.126 mol) was added and stirring was continued for further 2 h. The resulting precipitate was filtered off and washed with light petroleum to give the salt as yellow crystals, (39.91 g, 80 %); m.p. 163-164 ºC. The salt was dissolved in water (30-40 mL) and neutralized by dropwise addition of dilute HCl. The mixture was stirred for 15 min and the precipitate was filtered to give the title compound (29.02 g, 77 %) as a pale yellow solid, m.p. 52-53 ºC; ^{1}H NMR ($CDCl_3$) δ (ppm): δ = 1.35 (t, *J* = 7.1 Hz, 6H), 4.321 (q, *J* = 7.1 Hz, 2H), 4.326 (q, *J* = 7.1 Hz, 2H), 5.09 (s, 1H), 7.55 (d, *J* = 8.6 Hz, 2H), 7.73 (d, *J* = 8.6 Hz, 2H), 10.9 (bs, 1H, NH). ^{13}C NMR ($CDCl_3$) δ (ppm): 14.34, 63.63, 67.68, 120.37, 125.13, 132.37, 137.89, 166.08, 188.05. FT-IR (ν_{max}, cm^{-1}): 3285, 1759, 1723, 1548, 1431, 1285, 1146, 1023, 831. The other thiocarbamates (4, Ar: 2-MeC_6H_4, 2-$MeOC_6H_4$, 3-MeC_6H_4, 3-BrC_6H_4, 3-$CO_2EtC_6H_4$, 4-$MeOC_6H_4$, 4-MeC_6H_4, 4-$CO_2EtC_6H_4$, 4-$NO_2C_6H_4$) were made by the same procedure.

Ethyl 3-(2-methylphenyl)amino-5-oxo-2,5-dihydroisoxazole-4-carboxylate (6, 2-MeC_6H_4): To a solution of hydroxylamine hydrochloride (17.37 g, 250 mmol) in water (80 mL), potassium bicarbonate (25.03 g, 250 mmol) was slowly added. Ethanol (300 mL) was added and the resulting potassium chloride was filtered off. Diethyl N-(2-methylphenyl) thiocarbamoylmalonate (15.75 g, 83 mmol) was added to the filtrate and the mixture was stirred at room temperature for 24 h. The reaction mixture was acidified with diluted hydrochloric acid and the white precipitate was collected by vacuum filtration and recrystallized from ethanol to give the desired product as colourless needles. Yield 17.46 g (80 %); m.p. 172-173 ºC. ^{1}H NMR (DMSO-d_6) δ (ppm): 1.35 (t, *J* = 0.2 Hz, 3H); 2.32 (s, 3H), 4.34 (q, *J* = 7.2 Hz, 2H), 6.23 (br. s, exchanged by D_2O addition, 1H); 7.27 (t, *J* = 7.3 Hz, 1H); 7.29 (t, *J* = 7.3 Hz, 1H); 7.43 (d, *J* = 7.3 Hz, 1H); 7.34 (d, *J* = 0.3 Hz, 1H); 9.45 (s, exchanged by D_2O addition, 1H). ^{13}C NMR (DMSO-d_6) δ (ppm): 14.65, 17.77, 60.56, 75.87, 122.91, 127.34, 127.30, 131.45, 133.70, 164.66, 165.56, 167.23. FT-IR (ν_{max}, cm^{-1}): 2976, 1729, 1705, 1654, 1457, 1320, 1218, 1043, 809, 774.

Ethyl 3-(2-methoxyphenyl)amino-5-oxo-2,5-dihydroisoxazole-4-carboxylate (6, 2-$MeOC_6H_4$): The compound was prepared as described above using diethyl N-(2-methoxyphenyl)thiocarbamoylmalonate (5, 2-$MeOC_6H_4$), the mixture was stirred at room temperature for 18 h to give the desired product as white crystals. Yield (90%); m.p. 176-177 ºC. ^{1}H NMR ($CDCl_3$ + DMSO-d_6) δ (ppm): 1.31 (t, *J* = 0.1 Hz, 3H); 3.87 (s, 3H), 4.25 (q, *J* = 7.1 Hz, 2H); 6.77 (td, J_1 = 0.6 Hz, J_2 =1.2 Hz, 1H); 6.79 (td, J_1 =7.6 Hz, J_2 = 1.2 Hz, 1H); 6.89 (td, J_1 = 7.6 Hz, J_2 = 1.2 Hz, 1H); 8.01 (dd, J_1 = 7.6 Hz, J_2 = 1.2 Hz, 1H); 8.76 (br. s, exchanged by D_2O addition, 1H); 10.35 (br. s, exchanged by D_2O addition, 1H). ^{13}C NMR ($CDCl_3$ + DMSO-d_6) δ (ppm): 13.80, 56.17, 61.72, 112.25, 121.51, 121.90, 128.10, 150.56, 159.02, 159.59, 164.01, 170.22. FT-IR (ν_{max}, cm^{-1}): 3213, 3034, 1733, 1717, 1680, 1631, 1585, 1494, 1325, 1227, 1044, 759.

Ethyl 3-(3-methylphenyl)amino-5-oxo-2,5-dihydroisoxazole-4-carboxylate (6, 3-MeC_6H_4): The compound was prepared as described above using diethyl(3-methylphenyl) thiocarbamoylmalonate (5, 3-MeC_6H_4) and refluxing for 16 h to give the desired product as colourless crystals. Yield (75 %), m.p. 108-109 ºC. ^{1}H NMR (DMSO-d_6 + $CDCl_3$) δ (ppm): 1.42 (t, *J* = 7.1 Hz, 3H); 2.40 (s, 3H); 4.35 (q, *J* = 7.1 Hz, 2H); 7.04 (bd, *J* = 7.5 Hz, 1H); 7.06 (bd, *J* = 7.9 Hz, 1H), 7.4 (bs, 1H), 7.35 (t, *J* = 7.7 Hz, 1H); 9.5 (s, 1H, NH). ^{13}C NMR (DMSO-d_6 + $CDCl_3$) δ (ppm): 14.61, 21.37, 60.22, 74.78, 118.21, 121.79, 126.46, 129.50, 135.90, 139.77, 163.33, 165.67, 166.90. FT-IR (ν_{max}, cm^{-1}): 3526, 3317, 1715, 1683, 1584, 1332, 1230, 1173, 1116, 1010, 795.

Ethyl 3-(3-bromophenyl)amino-5-oxo-2,5-dihydroisoxazole-4-carboxylate (6, 3-BrC6H4): This compound was prepared as described above using diethyl (3-bromophenyl) thiocarbamoylmalonate (5, 3-BrC_6H_4) and refluxing for 16 h to give the desired product as colourless crystals. Yield (80 %) as colourless crystals m.p. 100-101 ºC. ^{1}H NMR (DMSO-d_6 + $CDCl_3$): δ 1.40 (t, *J* = 7.1 Hz, 3H), 4.40 (q, *J* = 7.1 Hz, 2H), 6.18 (bs, NH, 1H), 7.26 (dt, J_1 = 8.1 Hz, J_2 = 1.9 Hz, 1H), 7.32 (t, *J* = 7.7 Hz, 1H), 7.38 (dt, J_1 = 7.7 Hz, J_2 = 1.7 Hz, 1H), 7.56 (t, *J* = 1.9 Hz, 1H), 9.38 (bs, NH, 1H), ^{13}C NMR (DMSO-d_6 + $CDCl_3$) δ (ppm): 14.51, 60.32, 75.22, 119.90, 123.05, 123.97, 128.35, 131.09, 137.70, 162.97, 165.50, 166.80. FT-IR (ν_{max}, cm^{-1}): 3523, 3300, 1715, 1706, 1595, 1482, 1417, 1326, 1213, 1122, 1013, 796.

Ethyl 3-(3-ethoxycarbonylphenyl)amino-5-oxo-2,5-dihydroisoxazole-4-carboxylate (6, 3-$CO_2EtC_6H_4$): This compound was prepared as described above using diethyl (3-ethoxycarbonylphenyl)thiocarbamoylmalonate (5, 3-$CO_2EtC_6H_4$) and refluxing for 24 h to give the desired product. Yield (60 %) as white needles, m.p. 187-188 ºC. ^{1}H NMR (DMSO-d_6) δ (ppm) 1.29 (t, *J* = 7.1 Hz, 3H), 1.38 (t, *J* = 7.1 Hz, 3H), 4.20 (q, *J* = 7.1 Hz, 2H), 4.40 (q, *J* = 7.1 Hz, 2H), 4.55 (bs, exchanged by D_2O addition, 1H, NH), 7.50 (t, *J* = 8.0 Hz, 1H), 7.72 (bd, *J* = 7.8 Hz, 1H), 7.70 (dt, J_1 = 8.2 Hz, J_2 = 1.2 Hz, 1H), 8.10 (bs, 1H), 9.15 (s, exchanged by D_2O addition, 1H, NH). ^{13}C NMR (DMSO-d_6) δ (ppm): 14.10, 14.54, 58.291, 60.73, 72.01, 119.66, 122.69, 123.61, 129.34, 130.69, 139.36, 161.40, 164.89, 165.64, 169.19. FT-IR (ν_{max}, cm^{-1}): 3410, 2987, 1700, 1694, 1621, 1565,1482, 1465, 1374, 1300, 1215, 1123, 1074, 1023, 785.

Ethyl 3-(4-methylphenyl)amino-5-oxo-2,5-dihydroisoxazole-4-carboxylate (6, 4-MeC_6H_4): This compound was prepared as described above using diethyl (4-methyl) thiocarbamoylmalonate (5, 4-$MeOC_6H_4$) and Refluxing for 24 h gave colourless crystals. Yield (85 %), m.p. 164-166 ºC (dec.). ^{1}H NMR (DMSO-d_6 + $CDCl_3$) δ (ppm): 0.95 (t, *J* = 7

Hz, 3H), 1.94 (s, 3H), 3.91 (q, *J* = 7 Hz, 2H), 6.78 (d, *J* = 9.2 Hz, 2H), 6.79 (bs, 1H, NH), 6.80 (d, *J* = 9.2 Hz, 2H), 8.85 (bs, 1H, NH). ^{13}C NMR (DMSO-d_6 + $CDCl_3$) δ (ppm): 14.52, 20.85, 60.08, 74.69, 121.53, 130.13, 133.29, 135.64, 163.59, 165.51, 166.74. FT-IR (ν_{max}, cm^{-1}): 3669, 2979, 2746, 1705, 1669, 1615, 1331, 1208, 1115, 1023, 800.

Ethyl 3-(4-methoxyphenyl)amino-5-oxo-2,5-dihydro-isoxazole-4-carboxylate (6, 4-MeOC$_6$H$_4$): This compound was prepared as described above using diethyl (4-methoxy) thiocarbamoylmalonate (5, 4-MeOC$_6$H$_4$) and refluxing for 24 h gave the desired product. Yield (80 %) which was recrystallized from ethanol/acetone (1:1) as a white solid, m.p. 206-207 ºC (dec.); ^{1}H NMR (DMSO-d_6 + $CDCl_3$) δ (ppm): 0.95 (t, *J* = 7.0 Hz, 3H), 3.35 (s, 3H), 3.83 (q, *J* = 7.0 Hz, 2H), 6.38 (d, *J* = 8.5 Hz, 2H), 6.94 (d, *J* = 8.5 Hz, 2H), 6.96 (bs, 1H, NH), 7.70 (bs, 1H, NH); ^{13}C NMR (DMSO-d_6 + $CDCl_3$) δ (ppm): 15.64, 55.55, 58.37, 73.5, 114.6, 118.6, 135.73, 153.7, 165.73, 168.14, 174.81. FT-IR (ν_{max}, cm^{-1}): 3407, 1708, 1615, 1554, 1248, 1077, 792.

Ethyl 3-(4-bromophenyl)amino-5-oxo-2,5-dihydro-isoxazole-4-carboxylate (6, 4-BrC$_6$H$_4$): This compound was prepared as described above using diethyl (4-bromophenyl) thiocarbamoylmalonate (5, 4-BrC$_6$H$_4$) and refluxing for 24 h gave the desired product. Yield (80 %) which was recrystallized from acetone as a white solid, m.p. 200-202 ºC (dec.); ^{1}H NMR (DMSO-d_6) δ (ppm): 1.25 (t, *J* = 7.1 Hz, 3H), 4.21 (q, *J* = 7.1 Hz, 2H), 7.37 (d, *J* = 8.4 Hz, 2H), 7.57 (d, *J* = 8.4 Hz, 2H), 8.30 (bs, 1H, NH), 9.39 (bs, 1H, NH). ^{13}C NMR (DMSO-d_6) δ (ppm): 15.31, 59.96, 74.69, 118.02, 125.08, 132.94, 137.10, 163.53, 164.74, 167.39. FT-IR (ν_{max}, cm^{-1}): 3250, 2950, 2740, 1723, 1696, 1666, 1607, 1563, 1456, 1398, 1316, 1183, 1018, 818.

Ethyl 3-(4-nitrophenyl)amino-5-oxo-2,5-dihydro-isoxazole-4-carboxylate (6, 4-NO$_2$C$_6$H$_4$): This compound was prepared as described above using diethyl (4-nitrophenyl) thiocarbamoylmalonate (5, 2-NO$_2$C$_6$H$_4$) and refluxing for 24 h to give the desired product (65%) as a yellow solid, m.p. 158-160 ºC. ^{1}H NMR (DMSO-d_6 + $CDCl_3$) δ (ppm): 1.30 (t, *J* = 7.1 Hz, 3H), 4.36 (q, *J* = 7.1 Hz, 2H), 6.32 (bs, NH, 1H), 7.51 (d, *J* = 9.1 Hz, 2H), 8.23 (d, *J* = 9.1 Hz, 2H), 9.53 (s, NH, 1H). ^{13}C NMR (DMSO-d_6 + $CDCl_3$) δ (ppm): 14.43, 60.37, 76.45, 118.82, 125.33, 142.68, 143.53, 161.35, 164.74, 168.48. FT-IR (ν_{max}, cm^{-1}): 3470, 1755, 1723, 1681, 1632, 1582, 1518, 1498, 1418, 1345, 1211, 1117, 1021, 857, 790, 745.

Ethyl 3-(4-ethoxycarbonylphenyl)amino-5-oxo-2,5-dihydroisoxazole-4-carboxylate (6, 4-CO$_2$EtC$_6$H$_4$): This compound was prepared as described above using diethyl (4-ethoxycarbonylphenyl)thiocarbamoylmalonate (5, 4-CO$_2$EtC$_6$H$_4$) and refluxing for 24 h to give the desired product yield (70 %) as white needles, m.p. 125-126 ºC. ^{1}H NMR (DMSO-d_6 + $CDCl_3$) δ (ppm): 1.39 (t, *J* = 7.1 Hz, 3H), 1.45 (t, *J* = 7.1 Hz, 3H), 4.38 (q, *J* = 7.1 Hz, 4H), 7.40 (d, *J* = 8.7 Hz, 2H), 7.61 (bs, exchanged by D_2O addition, 1H, NH), 8.09 (d, *J* = 8.7 Hz, 2H), 9.60 (s, exchanged by D_2O addition, 1H, NH). ^{13}C NMR (DMSO-d_6 + $CDCl_3$) δ (ppm): 14.12, 14.24, 60.13, 61.18, 75.79, 119.40, 126.43, 131.10, 140.62, 162.19, 165.22, 165.76, 166.89. FT-IR (ν_{max}, cm^{-1}): 3283, 2980, 2770, 1718, 1690, 1611, 1581, 1478, 1416, 1364, 1319, 1288, 1194, 1120, 1022, 801.

Ethyl 3-(2-methylphenyl)amino-2-(5-nitropyrid-2-yl)-5-oxo-2,5-dihydroisoxazole-4-carboxylate (1, Ar: 2-MeC$_6$H$_4$): Mixture of 2-chloro-5-nitropyridine (634 mg, 4 mmol) and ethyl 3-(2-methylphenyl)amino-5-oxo-2,5-dihydro-isoxazole-4-carboxylate (6, Ar: 2-MeC$_6$H$_4$) (1.048 g, 4 mmol) was heated neat under an atmosphere of nitrogen in an oil bath at 130°C for 3 h. The residue was recrystallized from ethanol to give the desired isoxazolone as yellow crystals. Yield 1.216 g (75 %); m.p. 167-168 ºC. ^{1}H NMR ($CDCl_3$) δ (ppm): 1.29 (t, *J* = 7.1 Hz, 3H); 2.45 (s, 3H); 4.28 (q, *J* = 7.1 Hz, 2H); 7.03 (t, *J* = 7.4 Hz, 1H); 7.16 (d, *J* = 7.4 Hz, 1H); 7.01 (t, *J* = 7.4 Hz, 1H); 7.34 (d, *J* = 7.4 Hz, 1H); 7.53 (d, *J* = 9.1 Hz, 1H); 8.54 (dd, *J* = 9.1 Hz, *J* = 2.5 Hz, 1H); 8.87 (d, *J* = 2.5 Hz, 1H); 10.23 (br.s, exchanged by D_2O addition, 1H, NH). ^{13}C NMR spectrum ($CDCl_3$) δ (ppm): 14.58, 17.87, 61.44, 78.94, 115.24, 123.78, 132.39, 134.66, 137.38, 141.86, 143.45, 141.42, 154.65, 156.12, 161.45, 163.439, 163.69. MS m/z (%): 384 (M^+, 3%), 340 (100), 294 (15), 267 (57), 248 (28), 220 (22), 144 (5), 118 (7), 91 (11), 65 (6). FT-IR (ν_{max}, cm^{-1}): 3050, 1779, 1708, 1615, 1520, 1337, 1200, 1120, 1023, 757.

Ethyl 3-(2-methoxyphenyl)amino-2-(5-nitropyrid-2-yl)-5-oxo-2,5-dihydroisoxazole-4-carboxylate (1, Ar: 2-MeOC$_6$H$_4$): This compound was prepared as described above, using the corresponding (6, Ar: 2-MeOC$_6$H$_4$) and 2-chloro-5-nitropyridine as yellow needles after recrystalization from ethanol. Yield (80 %); m.p. 130-132 °C. ^{1}H NMR ($CDCl_3$) δ (ppm): 1.29 (t, *J* = 7.1 Hz, 3H); 3.97 (s, 3H); 4.30 (q, *J* = 7.1 Hz, 2H,); 6.70 (td, J_1 = 7.8 Hz, J_2 = 1.2 Hz, 1H); 6.98 (dd, J_1 = 7.8 Hz, J_2 = 1.2 Hz, 1H); 7.09 (dd, J_1 = 7.8 Hz, J_2 = 1.2 Hz, 1H); 7.18 (td, J_1 = 7.8 Hz, J_2 = 1.2 Hz, 1H); 7.55 (dd, J_1 = 9.1 Hz, J_2 = 0.5 Hz, 1H); 8.64 (dd, J_1 = 9.1 Hz, J_2 = 2.6 Hz, 1H); 8.97 (d, *J* = 2.6 Hz, 1H); 10.40 (br s, exchanged by D_2O addition, NH, 1H). ^{13}C NMR spectrum ($CDCl_3$) δ (ppm): 14.88, 56.03, 61.95, 79.94, 111.67, 112.82, 121.48, 121.98, 123.51, 124.76, 127.95, 128.12, 134.54, 141.87, 143.55, 151.56; MS m/z (%): 400 (M^+, 4 %), 356 (6), 207 (8), 149 (100), 134 (50), 123 (42), 120 (43), 108 (47), 106 (40), 80 (35), 77 (33), 51 (25), 28 (66). FT-IR (ν_{max}, cm^{-1}): 3450, 1770, 1700, 1600, 1580, 1550, 1525, 1345, 1130, 1020, 760.

Ethyl 3-(3-methylphenyl)amino-2-(5-nitropyrid-2-yl)-5-oxo-2,5-dihydroisoxazole-4-carboxylate (1, Ar: 3-MeC$_6$H$_4$): This compound was prepared as described above using the corresponding isoxazolone (6, Ar: 3-MeC$_6$H$_4$) and 2-chloro-5-nitropyridine to give the desired product as yellow needles. Yield (80 %). m.p. 160-162 ºC. ^{1}HNMR ($CDCl_3$) δ (ppm): 1.29 (t, *J* = 7.1 Hz, 3H), 2.31 (s, 3H), 4.40 (q, *J* = 7.1 Hz, 2H), 6.80 (m, 3H), 7.16 (t, *J* = 7.7 Hz, 1H), 7.59 (d, *J* = 9.1 Hz, 1H), 8.61 (dd, J_1 = 9.1 Hz, J_2 = 2.6 Hz, 1H), 8.96 (d, *J* = 2.6 Hz, 1H), 10.50 (s, NH, 1H). ^{13}C NMR ($CDCl_3$) δ (ppm): 14.45, 22.27, 61.98, 79.86, 115.82, 119.99, 124.64, 128.21, 131.14, 135.34, 138.41, 141.53, 142.45, 144.54, 155.87, 161.13, 164.15, 165.64. FT-IR (ν_{max}, cm^{-1}): 3189, 1790, 1712, 1577, 1521, 1342, 1216, 1183, 1128, 968, 766. MS m/z (%): 384 (M^+, 20 %), 341(26), 340(100), 248(36), 230(31), 158(42), 107(21),91(68), 65(25), 44(86), 40(38).

Ethyl 3-(3-bromophenyl)amino-2-(5-nitropyrid-2-yl)-5-oxo-2,5-dihydroisoxazole-4-carboxylate (1, Ar: 3-BrC$_6$H$_4$): This compound was prepared as described above using the corresponding isoxazolone (6, Ar: 3-BrC$_6$H$_4$) and

2-chloro-5-nitropyridine to give the desired product as yellow needles. Yield (80 %), m.p. 208-209 ºC. ^{1}HNMR (DMSO-d_6 + $CDCl_3$) δ (ppm): 1.20 (t, *J* = 7.2 Hz, 3H), 4.12 (q, *J* = 7.2 Hz, 2H), 7.31 (t, *J* = 2.8 Hz, 1H), 7.4 (dt, J_1 = 8.0 Hz, J_2 = 2.0 Hz, 1H), 7.31 (dt, J_1 = 7.2 Hz, J_2 = 2.0 Hz,1H), 7.45 (t, *J* = 2.0 Hz, 1H), 7.73 (d, *J* = 9.3 Hz, 1H), 8.80 (dd, J_1 = 9.3 Hz, J_2 = 2.8 Hz, 1H), 9.14 (d, *J* = 2.8 Hz, 1H), 10.81 (s, NH, 1H). ^{13}C NMR (DMSO-d_6 + $CDCl_3$) δ 14.50, 60.59, 79.79, 115.43, 120.79, 120.94, 126.15, 129.12, 131.00, 135.23, 139.01, 141.89, 143.70, 154.32, 159.03, 160.82,161.86. FT-IR (ν_{max}, cm^{-1}): 3165, 1777, 1701, 1590, 1550, 1521, 1347, 1208, 1133, 970, 768. MS m/z (%): 450(M^+, 6 %), 448 (M^+, 3 %), 406(55), 405(18), 404(53), 279(55), 224(10), 157(11), 155(12), 78(13), 77(17), 44(100), 40(56).

Ethyl 3-(3-ethoxyphenyl)amino-2-(5-nitropyrid-2-yl)-5-oxo-2,5-dihydroisoxazole-4-carboxylate (1, Ar: 3-$CO_2EtC_6H_4$): This compound was prepared as described above using the corresponding isoxazolone (6, Ar: 3-$EtO_2CC_6H_4$) and 2-chloro-5-nitropyridine to give the desired product (65 %) as cream needles, m.p. 195-196 °C. ^{1}HNMR ($CDCl_3$) δ (ppm): 1.34 (t, *J* = 7.2 Hz, 3H), 1.43 (t, *J* = 7.2 Hz, 3H), 4.35 (q, *J* = 7.2 Hz, 2H), 4.46 (q, *J* = 7.2Hz, 2H), 7.54 (bs, 1H, 7.34 (t, *J* = 7.7 Hz, 1H), 7.61 (d, *J* = 9.3 Hz, 1H), 7.83 (bd, *J* = 7.0 Hz, 2H), 8.59 (dd, J_1 = 9.3 Hz, J_2 = 2.5 Hz, 1H), 8.93 (d, *J* = 2.5 Hz, 1H), 10.64 (s, exchanged by D_2O addition, 1H, NH). ^{13}C NMR ($CDCl_3$) δ (ppm): 14.5, 14.52, 61.21, 61.58, 79.55, 114.70, 123.03, 126.13, 127.36, 129.63, 132.15, 134.80, 138.02, 141.56, 143.66, 153.77, 160.01, 163.13, 163.71, 165.45. FT-IR (ν_{max}, cm^{-1}): 3380, 3111, 2964, 1771, 1731, 1700, 1570, 1538, 1448, 1432, 1341, 1290, 1119, 1031, 974, 866, 761.

Ethyl 3-(4-methylphenyl)amino-2-(5-nitropyrid-2-yl)-5-oxo-2,5-dihydroisoxazole-4-carboxylate (1, Ar: 4-MeC_6H_4): This compound was prepared as described for above using the corresponding isoxazolone (6, Ar: 4-MeC_6H_4) and 2-chloro-5-nitropyridine to give the desired product after recrystalization from ethanol yellow needles. Yield (85 %), m.p. 156-158 ºC. ^{1}H NMR ($CDCl_3$) δ (ppm): 1.29 (t, *J* = 7.05 Hz, 3H), 2.30 (s, 3H), 4.26 (q, *J* = 7.05 Hz, 2H), 7.04 (d, *J* = 8.5 Hz, 2H), 7.07(d, *J* = 8.5 Hz, 2H), 7.07 (d, *J* = 9.0 Hz, 1H), 8.55 (dd, J_1 = 9.0 Hz, J_2 = 2.5 Hz, 1H), 8.91 (d, *J* = 2.5 Hz, 1H), 10.33 (s, 1H, NH). ^{13}C NMR ($CDCl_3$) δ (ppm): 14.66, 21.35, 61.34, 79.05, 115.42, 122.40, 130.29, 134.74, 135.36, 136.83, 141.89, 143.92, 154.28, 160.88, 163.62, 164.19. FT-IR (ν_{max}, cm^{-1}): 3177, 1762, 1700, 1600, 1515, 1338, 1208, 1123, 976, 838. MS m/z (%): 384 (M^+, 13%), 340 (100), 294 (57), 269 (16), 248 (40), 230 (16), 220 (16), 158 (39), 144 (13), 118 (21), 117 (20), 107 (16), 91 (67), 78 (16), 65 (20), 44 (33).

Ethyl 3-(4-methoxyphenyl)amino-2-(5-nitropyrid-2-yl)-5-oxo-2,5-dihydroisoxazole-4-carboxylate (1, Ar: 4-$MeOC_6H_4$): This compound was prepared as described for above using the corresponding isoxazolone (6, Ar: 4-$MeOC_6H_4$) and 2-chloro-5-nitropyridine to give the desired product Yellow needles. Yield (80 %), m.p. 186-188 ºC. ^{1}H NMR ($CDCl_3$) δ (ppm): 1.30 (t, *J* = 7.0 Hz, 3H), 3.77 (s, 3H), 4.26 (q, *J* = 7.0 Hz, 2H), 6.79 (d, *J* = 8.7 Hz, 2H), 7.10 (d, *J* = 8.7 Hz, 2H), 7.52 (d, *J* = 9.0 Hz, 1H), 8.54 (dd, J_1 = 9.0 Hz, J_2 = 2.1 Hz, 1H), 8.93 (bd, *J* = 2.1, 1H), 10.26 (s,1H, NH). ^{13}C NMR ($CDCl_3$) δ (ppm): 14.72, 55.89, 61.36, 78.87, 114.85, 115.59, 124.34, 130.74, 134.68, 141.93, 143.95, 154.33, 158.40, 161.38, 163.69, 164.32. FT-IR (ν_{max}, cm^{-1}): 3823, 1785, 1700, 1592, 1345, 1207, 1115, 1030, 838. MS m/z (%): 400 (M^+, 10 %), 356 (100), 310 (49), 295 (43), 264 (21), 249 (13), 221 (14), 193 (12), 194 (10), 174 (21), 146 (10), 134 (34), 133 (22), 123 (17), 92 (16), 77 (29), 44 (37).

Ethyl 3-(4-bromophenyl)amino-2-(5-nitropyrid-2-yl)-5-oxo-2,5-dihydroisoxazole-4-carboxylate (1, Ar: 4-BrC_6H_4): This compound was prepared as described for above using the corresponding isoxazolone (6, Ar: 4-BrC_6H_4) and 2-chloro-5-nitropyridine to give the desired product yellow needles. Yield (82 %), m.p. 217-218 ºC. ^{1}H NMR (DMSO-d_6 + $CDCl_3$) δ (ppm): 0.99 (t, *J* = 7.0 Hz, 3H), 3.94 (q, *J* = 7.0 Hz, 2H), 6.87 (d, *J* = 8.5 Hz, 2H), 7.18 (d, *J* = 8.5 Hz, 2H), 7.73 (d, *J* = 9.1 Hz, 1H), 8.40 (dd, J_1 = 9.1 Hz, J_2 = 2.3 Hz, 1H), 8.75 (d, *J* = 2.3 Hz, 1H), 10.29 (bs, 1H, NH). ^{13}C NMR (DMSO-d_6 + $CDCl_3$) δ (ppm): 14.41, 60.99, 79.05, 114.63, 119.46, 124.11, 132.46, 135.08, 137.21, 141.66, 143.79, 153.92, 158.31, 161.38, 165.88. FT-IR (ν_{max}, cm^{-1}): 3140, 2965, 1773, 1683, 1591, 1531, 1324, 1188, 1114, 1010, 961, 832. MS m/z (%): 450 (M^+, 27 %), 448 (M^+, 30%), 406(74), 404(77), 279(100), 251(20), 184(35), 182(36), 157(29), 155(29), 102(22), 72(23), 44(59).

Ethyl 3-(4-nitrophenyl)amino-2-(5-nitropyrid-2-yl)-5-oxo-2,5-dihydroisoxazol-4-carboxylate (1, Ar: 4-$NO_2C_6H_4$): This compound was prepared as described for above using the corresponding isoxazolone (6, Ar: 4-$O_2NC_6H_4$) and 2-chloro-5-nitropyridine to give the desired product as cream solid. Yields (65 %) after recrystalization from ethanol, m.p. 223-226 °C. ^{1}H NMR (DMSO-d_6 + $CDCl_3$) δ (ppm): 1.17(t, *J* = 7.1 Hz, 3H), 4.12 (q, *J* = 7.1 Hz, 2H), 7.47 (d, *J* = 9.1 Hz, 2H), 7.69 (d, *J* = 9.1 Hz, 1H), 8.14 (d, *J* = 9.1 Hz, 2H), 8.71 (dd, J_1 = 9.1 Hz, J_2 = 2.7 Hz, 1H), 9.02 (d, *J* = 2.7 Hz, 1H), 10.93 (s, NH,1H). ^{13}C NMR (DMSO-d_6 + $CDCl_3$) δ (ppm): 14.05, 60.21, 80.66, 114.44, 121.61, 124.45, 135.11, 141.52, 143.53, 143.87, 144.43, 153.34, 158.29, 161.61, 162.43. FT-IR (ν_{max}, cm^{-1}): 3114, 1782, 1687, 1602, 1553, 1428, 1337, 1261, 1202, 1122, 1082, 1011, 960, 858, 552. MS m/z (%): 415 (M^+, 12 %), 371(78), 369(11), 325(13), 300(11), 279(29), 189(18), 149(12), 70(11), 44(100), 40(38).

Ethyl 3-(4-ethoxyphenyl)amino-2-(5-nitropyrid-2-yl)-5-oxo-2,5-dihydroisoxazol-4-carboxylate (1, Ar: 4-$CO_2EtC_6H_4$): This compound was prepared as described above using the corresponding isoxazolone (6, Ar: 4-$EtO_2CC_6H_4$) and 2-chloro-5-nitropyridine to give the desired product (70 %) as white needles, m.p. 198-200 ºC. ^{1}H NMR ($CDCl_3$) δ (ppm): 1.20 (t, *J* = 7.1 Hz, 3H), 1.40 (t, *J* = 7.1 Hz, 3H), 4.25 (q, *J* = 7.1 Hz, 2H), 4.39 (q, *J* = 7.1 Hz, 2H), 7.22 (d, *J* = 8.6 Hz, 2H), 7.51 (d, *J* = 9.1 Hz, 1H), 7.96 (d, *J* = 8.4 Hz, 2H), 8.59 (dd, J_1 = 9.1 Hz, J_2 = 2.6 Hz, 1H), 8.90 (d, *J* = 2.6 Hz, 1H), 10.54 (s, exchanged by D_2O addition, 1H, NH). ^{13}C NMR ($CDCl_3$) δ (ppm): 14.52, 29.80, 61.34, 61.33, 79.90, 114.62, 120.91, 128.05, 131.01, 134.73, 141.64, 141.63, 143.32, 153.73, 159.82, 162.88, 163.74, 165.43. FT-IR (ν_{max}, cm^{-1}): 3392, 3148, 2983, 1777, 1713, 1606, 1473, 1428, 1350, 1280, 1200, 1180, 1128, 1023, 864, 756.

Ethyl 2-(2-methylphenyl)amino-6-nitroimidazo[1,2-a] pyridine-3-carboxylate (2, Ar: 2-MeC$_6$H$_4$): Pyrolysis (580 ºC, 0.01 mm Hg, sublimation flask 110 ºC, 1 h) of isoxazolone (1, Ar: 2-MeC$_6$H$_4$) (100 mg, 0.26 mmol) gave the desired imidazole as pale red needles. Yield (79.68 mg, 90 %), m.p. 179-181 ºC. ^{1}H NMR (CDCl$_3$) δ (ppm): 1.55 (t, *J* = 7.1 Hz, 3H), 2.41 (s, 3H), 4.59 (q, *J* = 7.1 Hz, 2H), 7.12 (t, *J* = 7.6 Hz, 1H), 7.33 (d, *J* = 7.6 Hz, 1H), 7.33 (t, *J* = 7.6 Hz, 1H), 7.58 (d, *J* = 9.7 Hz, 1H), 8.21 (dd, J_1 = 9.7 Hz, J_2 = 2.0 Hz, 1H), 8.41 (d, *J* = 7.6 Hz, 1H); 8.97 (br, 1H); 9.27 (br, 1H, exchanged by D$_2$O addition, NH). ^{13}C NMR (CDCl$_3$) δ (ppm): 15.19, 18.22, 61.70, 98.13, 113.16, 124.01, 125.18, 126.90, 127.51, 131.43, 131.92, 135.33, 138.67, 143.99, 153.74, 160.784. FT-IR (ν$_{max}$, cm^{-1}): 3332, 3111, 2978, 1670, 1631, 1609, 1500, 1486, 1343, 1309, 1213, 1087, 756. MS m/z (%): 340 (M$^+$, 1 %), 281 (66), 264 (72), 253 (95), 207 (40), 14 (100), 90 (37), 28 (100).

Ethyl 2-(2-methoxyphenyl)amino-6-nitroimidazo[1,2-a] pyridine-3-carboxylate (2, Ar: 2-MeOC$_6$H$_4$): Pyrolysis (580 °C, 0.01 mm Hg, sublimation flask 110 °C, 1 h) of isoxazolone (1, Ar: 2-MeOC$_6$H$_4$) (100 mg, 0.25 mmol) gave the desired imidazole as yellow needles. Yield (80.36 mg, 90 %), m.p. 219-221 °C. ^{1}H NMR (CDCl$_3$) δ (ppm): 1.61 (t, *J* = 7.0 Hz, 3H), 4.01(s, 3H), 4.57 (q, *J* = 7.0 Hz, 2H), 6.98 (dd, J_1 = 7.5 Hz, J_2 = 1.9 Hz, 1H), 7.05 (td, J_1 = 7.5 Hz, J_2 = 1.9 Hz, 1H), 7.10 (td, J_1 = 7.5 Hz, J_2 = 1.9 Hz 1H); 7.55 (d, *J* = 9.71 Hz, 1H); 8.17 (dd, J_1 = 9.7 Hz, J_2 = 2.31 Hz, 1H), 8.76 (d, *J* = 7.5 Hz, 1H); 8.77 (br.s, 1H); 10.31 (br. s, exchanged by D$_2$O addition, 1H NH). ^{13}C NMR (CDCl$_3$) δ (ppm): 14.51, 55.66, 61.88, 84.50, 96.67, 99.34, 110.13, 114.23, 117.66, 121.21, 122.09, 122.56, 126.77, 129.51, 137.12, 147.12, 154.90. FT-IR (ν$_{max}$, cm^{-1}): 3379, 1674, 1611, 1577, 1467, 1349, 13185, 1301, 1233, 1110, 1035, 752. MS m/z (%): 356 (M$^+$, 3 %), 296 (38), 267 (100), 207 (9), 190 (14), 158 (13), 130 (22), 107 (20), 77 (11), 28 (23).

Ethyl 2-(3-methylphenyl) amino-6-nitroimidazo[1,2-a] pyridine-3-carboxylate (2, Ar: 3-MeC$_6$H$_4$): Pyrolysis (580 °C, 0.01 mm Hg, sublimation flask 110 °C, 1 h) of isoxazolone (1, Ar: 3-MeC$_6$H$_4$) (100 mg, 0.26 mmol) gave the desired imidazole as yellow solid. Yields (74.9 mg, 85 %), m.p. 167-169-221 °C. ^{1}H NMR (CDCl$_3$) δ (ppm): 1.60 (t, *J* = 7.1 Hz, 3H), 2.50 (s,3H), 4.58 (q, *J* = 7.1 Hz, 2H), 6.93 (d, *J* = 7.4 Hz,1H), 7.24 (t, *J* = 7.8 Hz, 1H), 7.51-7.56 (m, 3H), 8.17 (d, *J* = 9.7 Hz,1H), 8.88 (bs,1H), 9.96 (bs,1H). ^{13}C NMR (CDCl$_3$) δ (ppm): 14.79, 21.72, 61.25, 98.78, 114.14, 115.94, 119.50, 122.50, 124.48, 126.97, 129.11, 139.21, 139.34, 145.23, 146.35, 156.23, 167.67. FT-IR (ν$_{max}$, cm^{-1}): 3406, 1657, 1618, 1579, 1556, 1499, 1341, 1310, 1219, 959, 768 MS m/z (%): 340 (M$^+$, 100 %), 296(15), 294(41), 255(24), 248(26), 118(15), 91(27), 86(19), 44(10), 40(36).

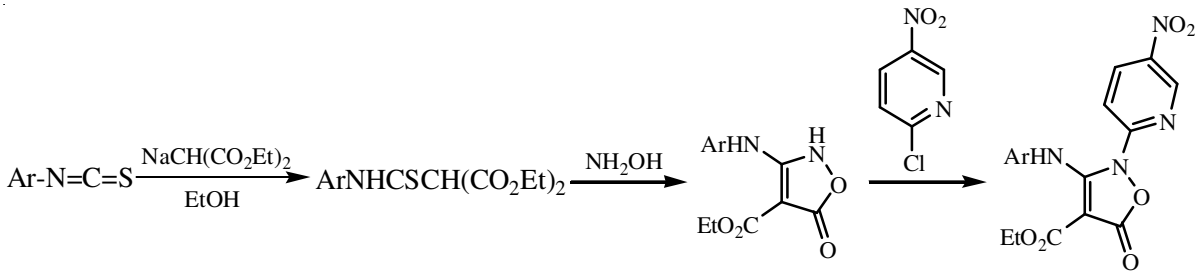
Ethyl 2-(3-Bromophenyl)amino-6-nitroimidazo[1,2-a] pyridine-3-carboxylate (2, Ar: 3-BrC$_6$H$_4$): Pyrolysis (580 °C, 0.01 mm Hg, sublimation flask 110 °C, 1 h) of isoxazolone (1, Ar: 3-BrC$_6$H$_4$) (100 mg, 0.22 mmol) gave the desired imidazole as yellow solid. Yields (80.76 mg, 95 %), m.p. 162-163 °C. ^{1}H NMR ((DMSO-d_6 + CDCl$_3$) δ (ppm): 1.57 (t, *J* = 7.2 Hz,3H), 4.58 (q, *J* = 7.2 Hz, 2H), 7.32 (bdd, J_1 = 8.1 Hz, J_2 = 1.7 Hz, 1H), 7.24 (t, *J* = 7.8 Hz, 1H), 7.59 (dt, J_1 = 7.6 Hz, J_2 = 2.0 Hz, 1H), 7.61 (d, *J* = 9.7 Hz, 1H), 8.12 (bs, 1H), 8.19 (dd, J_1 = 9.7 Hz, J_2 = 2.1 Hz, 1H), 8.94 (bs,1H), 9.88 (bs,1H). ^{13}C NMR (DMSO-d_6 + CDCl$_3$) δ (ppm): 14.74, 61.56, 99.32, 114.71, 116.76, 117.34, 116.23, 121.31, 122.65, 122.63, 125.67, 126.90, 130.54, 137.22, 140.87, 160.31. FT-IR (ν$_{max}$, cm^{-1}): 3309, 1676, 1591, 1568, 1453, 1407, 1341, 1309, 1212, 1139, 1109, 848, 764. MS m/z (%): 406 (M$^+$, 87 %), 404 (M$^+$, 85 %), 279(100), 251(17), 233(13), 206(14), 184(10), 182(11),102(12), 78(12), 77(10), 44(21), 40(55).

Ethyl 2-(3-ethoxyphenyl)amino-6-nitroimidazo[1,2-a] pyridine-3-carboxylate (2, Ar: 3-CO$_2$EtC$_6$H$_4$): Pyrolysis (580 °C, 0.01 mm Hg, sublimation flask 110 °C, 1 h) of isoxazolone (1, Ar: 3-CO$_2$EtC$_6$H$_4$) (100 mg, 0.22 mmol) gave the desired imidazole as yellow solid. Yield (81.94 mg, 92 %), m.p. 172-173 °C. Anal. calc. for C$_{19}$H$_{18}$N$_4$O$_6$: C, 58.28; H,4.52; N,14.07 %; found: C, 58.21; H, 4.41; N,14.32 %. ^{1}H NMR (CDCl$_3$) δ (ppm): 1.47 (t, *J* = 7.1 Hz, 3H), 1.58 (t, *J* = 7.1 Hz, 3H), 4.41 (q, *J* = 7.1 Hz, 2H), 4.58 (q, *J* = 7.1 Hz, 2H), 7.47 (t, *J* = 7.9 Hz, 1H), 7.58 (d, *J* = 9.7 Hz, 1H), 7.78 (bd, *J* = 7.7 Hz, 1H), 8.09 (dd, J_1 = 8.03 Hz, J_2 = 1.3 Hz, 1H), 8.17 (dd, J_1 = 9.7 Hz, J_2 = 1.7 Hz, 1H), 8.26 (bs, 1H), 9.03 (bs, exchanged by D$_2$O addition, 1H, NH), 9.86 (bs, 1H). ^{13}C NMR (CDCl$_3$) δ (ppm): 14.38, 14.65, 61.16, 61.26, 99.14, 114.37, 119.69, 122.57, 122.89, 123.75, 126.96, 129.27, 131.55, 137.12, 139.62, 146.86, 166.40. FT-IR (ν$_{max}$, cm^{-1}): 3406, 3328, 2923, 1716, 1675, 1612, 1576, 1550, 1496, 1346, 1315, 1281, 1230, 1108, 755.

Ethyl 2-(4-methylphenyl)amino-6-nitroimidazo[1,2-a] pyridine-3-carboxylate (2, Ar: 4-MeC$_6$H$_4$): Pyrolysis (580 °C, 0.01 mm Hg, sublimation flask 110 °C, 1 h) of isoxazolone (1, Ar: 4-MeOC$_6$H$_4$) (100 mg, 0.26 mmol) gave the desired imidazole as pale cream needles. Yield (82.34 mg, 93 %), m.p. 187-188 ºC. ^{1}H NMR δ (ppm): 1.27 (t, *J* = 6.9 Hz, 3H, CH$_3$), 2.36 (s, 3H, CH$_3$), 4.57 (q, *J* = 6.9 Hz, 2H, CH$_2$), 7.19 (d, *J* = 8.2 Hz, 2H, Ar), 7.51 (d, *J* = 9.7 Hz, 1H, Ar), 7.59 (bd, *J* = 8.2 Hz, 2H, Ar), 8.15 (bd, *J* = 6.7 Hz, 1H, Ar), 8.85 (bs, 1H, NH), 9.84 (bs, 1H, Ar). ^{13}C NMR δ (ppm): 15.03, 21.22, 61.44, 98.99, 114.30, 119.33, 122.80, 127.26, 130.07, 132.93, 137.11, 147.34, 157.76, 161,15. FT-IR (ν$_{max}$, cm^{-1}): 3455, 1662, 1608, 1555, 1308, 1208, 1015, 822. MS m/z (%): 340 (M$^+$, 100 %), 294(48), 248(27), 220(9), 144(10), 118(13), 91(20), 78(6), 65(6).

Ethyl 2-(4-methoxyphenyl)amino-6-nitroimidazo[1,2-a] pyridine-3-carboxylate (2, Ar: 4-MeOC$_6$H$_4$): Pyrolysis (580 °C, 0.01 mm Hg, sublimation flask 110 °C, 1 h) of isoxazolone (1, Ar: 4-MeOC$_6$H$_4$) (100 mg, 0.25 mmol) gave the title compound as a red solid. Yield (84.55 mg, 95%), m.p. 160-161 ºC; ^{1}H NMR δ (ppm): 1.56 (t, *J* = 7.0 Hz, 3H), 3.85 (s, 3H), 4.58 (q, *J* = 7.0 Hz, 2H), 6.95 (d, *J* = 8.9 Hz, 2H), 7.50 (d, *J* = 9.7 Hz, 1H) 7.62 (bd, *J* = 8.9 Hz, 2H), 8.16 (dd, J_1 = 9.7 Hz, J_2 = 1.9 Hz, 1H), 8.78 (bs, 1H, NH), 9.88 (bs, 1H). ^{13}C NMR δ (ppm): 15.05, 55.97, 61.40, 98.76, 114.19, 114.82, 121.31, 122.86, 127.24, 132.85, 137.15, 147.48, 156.16, 160.86. FT-IR (ν$_{max}$, cm^{-1}): 3130, 1685, 1615, 1515, 1315, 1222, 1199, 1092, 824. MS m/z (%): 356 (M$^+$, 100 %), 310 (34), 295 (43), 264 (12), 249 (12), 221(10), 194 (8), 193 (11), 134 (16), 92 (8), 90 (8), 78 (8).

Ethyl 2-(4-bromophenyl)amino-6-nitroimidazo[1,2-a] pyridine-3-carboxylate (2, Ar: 4-BrC$_6$H$_4$): Pyrolysis (580 ºC, 0.01 mm Hg, sublimation flask 110 ºC, 1 h) of isoxazolone



4 5 6 1

Ar: 2-MeC_6H_4, 2-$MeOC_6H_4$, 3-MeC_6H_4, 3-BrC_6H_4, 3-$CO_2EtC_6H_4$, 4-$MeOC_6H_4$, 4-MeC_6H_4, 4-BrC_6H_4, 4-$CO_2EtC_6H_4$, 4-$NO_2C_6H_4$.

Scheme-III

(1, Ar: 4-BrC_6H_4) (100 mg, 0.23 mmol) gave pale cream needles. Yield (81.17 mg, 90 %), m.p. 195-196 ºC. ^{1}H NMR δ (ppm): 1.57 (t, *J* = 7.1 Hz, 3H), 4.59 (q, *J* = 7.1 Hz, 2H), 7.48 (d, *J* = 8.7 Hz, 2H), 7.56 (d, *J* = 9.7 Hz, 1H), 7.65 (bd, *J* = 8.7 Hz, 2H), 8.19 (dd, J_1 = 9.7 Hz, J_2 = 1.3 Hz, collapsed to doublet, *J* = 8.7 Hz, by irradiation at δ = 9.87, 1H), 8.97 (bs, 1H, NH), 9.87 (bd, *J* = 1.3 Hz, 1H). ^{1}H NMR (DMSO-d_6 δ (ppm): 1.44 (t, *J* = 7.0 Hz, 3H), 4.46 (q, *J* = 7.0 Hz, 2H), 7.49 (d, *J* = 8.5 Hz), 7.68 (d, *J* = 9.7 Hz, 1H), 7.74 (d, *J* = 8.5 Hz, 2H), 8.19 (dd, J_1 = 9.7 Hz, J_2 = 1.6 Hz, 1H), 8.87 (bd, *J* = 1.6, 1H), 9.88 (s,1H, NH). ^{13}C NMR (DMSO-d_6) δ (ppm): 15.25, 61.57, 99.72, 114.62, 114.97, 121.76, 123.93, 127.61, 132.38, 137.66, 140.01, 147.17, 155.28, 160.87. FT-IR (ν_{max}, cm^{-1}): 3285, 2955, 1643, 1611, 1555, 1475, 1331, 1294, 1201, 1102, 1079, 1002, 820. MS m/z (%): 406 (M^+, 62%), 404 (M^+, 64 %), 360 (5), 358 (6), 279 (100), 251 (16), 233 (14), 205 (12), 184 (11), 182 (12), 157 (12), 155 (12), 102 (14), 78 (13), 77 (11).

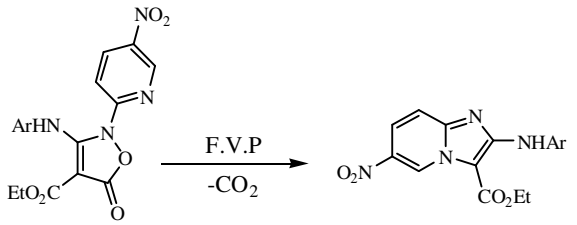
Ethyl 2-(4-nitrophenyl)amino-6-nitroimidazo[1,2-a] pyridine-3-carboxylate (2, Ar: 4-$NO_2C_6H_4$): Pyrolysis (580 ºC, 0.01 mm Hg, sublimation flask 110 ºC, 1 h) of isoxazolone (1, Ar: 4-$NO_2C_6H_4$) (100 mg, 0.24 mmol) gave a green solid. Yield (84.68 mg, 91 %), m.p. 259-261 ºC. ^{1}H NMR (DMSO-d_6 + $CDCl_3$) δ (ppm): 1.44 (t, *J* = 7.1 Hz, 3H), 4.50 (q, *J* = 7.1 Hz, 2H), 7.83 (d, *J* = 9.7 Hz, 1H), 8.08 (d, *J* = 9.2 Hz, 2H), 8.25 (d, *J* = 9.2 Hz, 2H), 8.28 (dd, J_1 = 9.7 Hz, J_2 = 2.4 Hz, 1H), 9.30 (bs, NH, 1H), 10.02 (bd, *J* = 1.9 Hz, 1H). FT-IR (ν_{max}, cm^{-1}): 3381, 1664, 1609, 1575, 1509, 1475, 1317, 1273, 1209, 1102, 860, 749. MS m/z (%) 371 (M^+, 100), 325(12), 280(9), 279(35), 251(11), 205(12), 76(9), 44(16), 40(23).

Ethyl 2-(4-ethoxyphenyl)amino-6-nitroimidazo[1,2-a] pyridine-3-carboxylate (2, Ar: 4-$CO_2EtC_6H_4$): Pyrolysis (580 ºC, 0.01 mm Hg, sublimation flask 110 ºC, 1 h) of isoxazolone (1, Ar: 4-$CO_2EtC_6H_4$). (100 mg, 0.22 mmol) gave the desired imidazole as as bright yellow needles. Yields (81.94 mg, 92 %), m.p. 206-207 ºC. Anal. calc. for $C_{19}H_{18}N_4O_6$: C, 58.28; H,4.52; N,14.07 %; found: C, 58.09; H, 4.36; N,14.17 %. ^{1}H NMR δ (ppm): 1.44 (t, *J* = 7.1 Hz, 3H), 1.57 (t, *J* = 7.1 Hz, 3H), 4.36 (q, *J* = 7.1 Hz, 2H), 4.58 (q, *J* = 7.1 Hz, 2H), 7.58 (d, *J* = 9.6 Hz, 1H), 7.77 (d, *J* = 8.5 Hz, 2H), 8.03 (d, *J* = 8.5 Hz, 2H), 8.18 (dd, J_1 = 9.6 Hz, J_2 = 2.1 Hz, 1H), 9.19 (bs, exchanged by D_2O addition, 1H, NH), 9.86 (bs, 1H). ^{13}C NMR ($CDCl_3$) δ (ppm): 14.45, 14.65, 60.80, 61.46, 99.66, 114.56, 117.47, 122.67, 124.17, 126.99, 131.09, 137.27, 143.47, 146.45, 166.26. FT-IR (ν_{max}, cm^{-1}): 3316, 2985, 1708, 1678, 1607, 1608, 1570, 1547, 1489, 1457, 1435, 1365, 1343, 1314, 1276, 1216, 1175, 1108, 1085, 1015, 857, 767, 755.

RESULTS AND DISCUSSION

The required isoxazolones (**1**) were synthesized by reaction of 2-chloro-5-nitropyridine with 2*H*-isoxazolones (**6**) which in turn were made by modification of the procedure of Worrall[4,5]. Thus, the reaction of the sodium salt of diethylmalonate in ethanol with arylisothiocyanates (**4**) gave the thiocarbamates (**5**) in high yield (60-90 %) and this converted to corresponding isoxazolone (**6**) by reaction with 2 equivalent of hydroxylamine. N-Arylation of isoxazolone (**6**) with 2-chloro-5-nitropyridine in solid phase condition gave the corresponding N-substituted isoxazolones (**1**) in fair yield (65-85%) (**Scheme-III**).

The rearrangement of (**1**) as shown in **Scheme-IV**, proceeded in 85-95 % yield under flash-vacuum-pyrolysis conditions accompanied by elimination of carbon dioxide for 1 h. The reaction pathway leads to net imidazo[1,2-a]pyridines which is consist of electronic requirement of the reaction as shown in **Scheme-V** or with the alternative pathway suggested by Prager *et al.*[6].

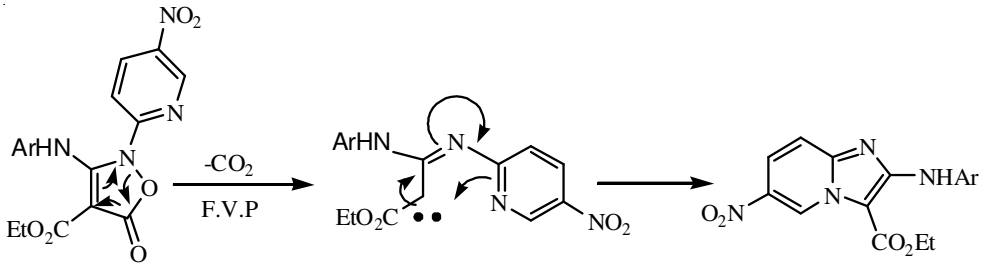


1 2

Ar: 2-MeC_6H_4, 2-$MeOC_6H_4$, 3-MeC_6H_4, 3-BrC_6H_4, 3-$CO_2EtC_6H_4$, 4-$MeOC_6H_4$, 4-MeC_6H_4, 4-BrC_6H_4, 4-$CO_2EtC_6H_4$, 4-$NO_2C_6H_4$.

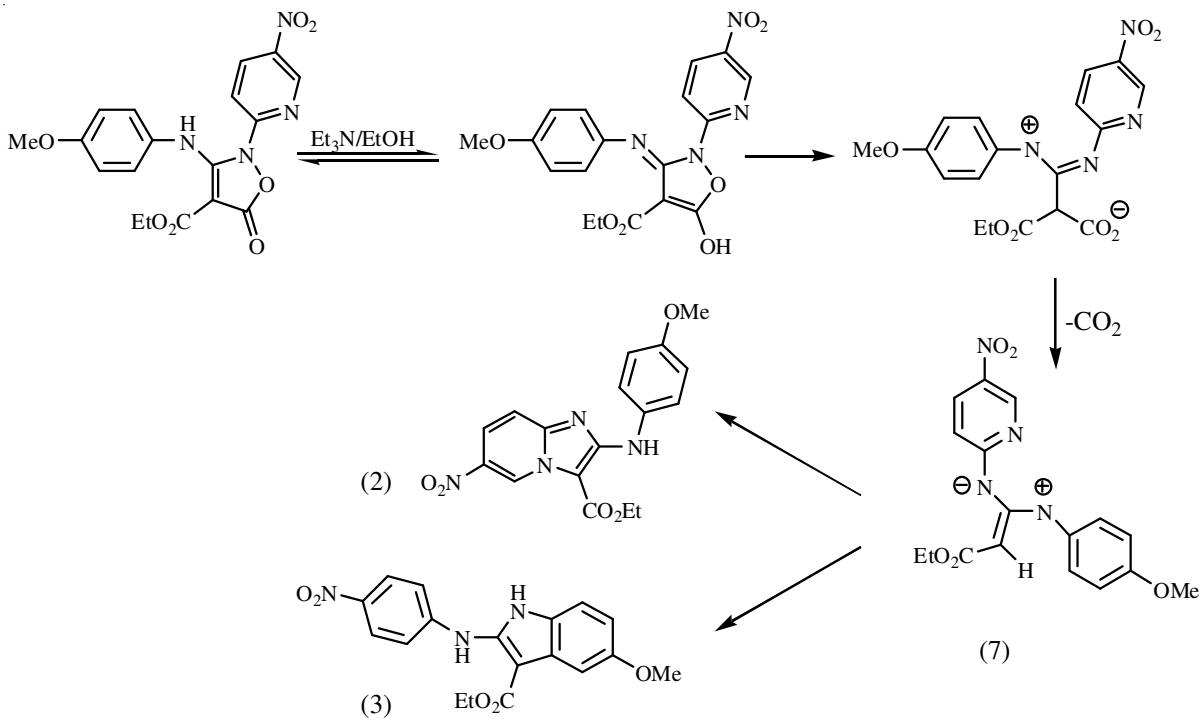
Scheme-IV

With a number of imidazopyridine structures in hand, the structures of all imidazopyridines were confirmed by ^{1}H NMR, ^{13}C NMR, FT-IR, mass spectra or microanalyses. All compounds **2** showed H-7 to have meta coupling with H-5, but the resonance for H-5 could not be clearly observed in compounds **2**. The reason for the extreme broadening of this peak is



Ar: 2-MeC_6H_4, 2-$MeOC_6H_4$, 3-MeC_6H_4, 3-BrC_6H_4, 3-$CO_2EtC_6H_4$, 4-$MeOC_6H_4$, 4-MeC_6H_4, 4-BrC_6H_4, 4-$CO_2EtC_6H_4$, 4-$NO_2C_6H_4$.

Scheme-V



Scheme-VI

unknown, though quadrupole coupling with N-4 is implicated. 4-methoxy derivative (1, Ar: $MeOC_6H_4$) reacts in refluxing ethanol with triethylamine to form a mixture of imidazopyridine (2, Ar: $MeOC_6H_4$) and indole (**3**) in a 2:1 ratio, respectively, but it only rearranges to imidazopyridine under flash-vacuum-pyrolysis conditions. The exact mechanism of this synthetic method has been unclear so far. However, we think that the zwitterionoic (**7**) plays a role under refluxing ethanol with triethylamine (**Scheme-VI**). This is consistent with electronic requirements of the reaction. The zwitterionic (**7**) probably can be stabilized by ethanol as protic solvent, however under flash-vacuum-pyrolysis conditions it can not be produced.

Conclusion

In conclusion we have shown that a variety of 2-pyridyl-3-arylaminoisoxazol-5(2*H*)-ones, rearranged under flash-vacuum-pyrolysis (FVP) conditions to give imidazo [1,2-a] pyridines. These rearrangements, therefore, appear to be generally applicable to the synthesis of imidazoheterocycles which are suitable synthetic intermediates for a series of polycyclic heterocycles with possible pharmaceutical applications[7,8].

ACKNOWLEDGEMENTS

The authors gratefully acknowledged the financial support of this work by the research council of Islamic Azad University branch of Mahabad.

REFERENCES

1. K.A. Ang, J.A. Smith and C. Williams, *Tetrahedron Lett.*, **37**, 675 (1996).
2. J. Khalafy and D. Setamdideh, *Molecules*, **2**, 907 (2002).
3. D.D. Perrin and W.L.F. Amarego, In Purification of Laboratory Chemicals, Pergamon Press, Oxford, U.K. (1988).
4. D.E. Worrall, *J. Am. Chem. Soc.*, **45**, 3092 (1923).
5. D.E. Worrall, *J. Am. Chem. Soc.*, **40**, 415 (1918).
6. N. Nishiwaki, M. Nakanishi, T. Hida, Y. Miya, M. Tamura, K. Hori and M. Ariga, *J. Org. Chem.*, **66**, 7535 (2001).
7. N. Tateja, T. Pham, R. Tuteja, A. Ocham and A. Falaschi, *Biochem. Biophys. Res. Commun.*, **236**, 636 (1997).
8. M. Stiborova, C.A. Bieler, M. Wiessler and E. Frei, *Biochem. Pharmacol.*, **62**, 1675 (2001).