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BASE-INDUCED REARRANGEMENTS OF N-SUBSTITUTED 3-ARYLAMINO-ISOXAZOL-5(2H)-ONES TO 2-ARYL-AMINOIMIDAZO[1,2-*a*]PYRIDINES

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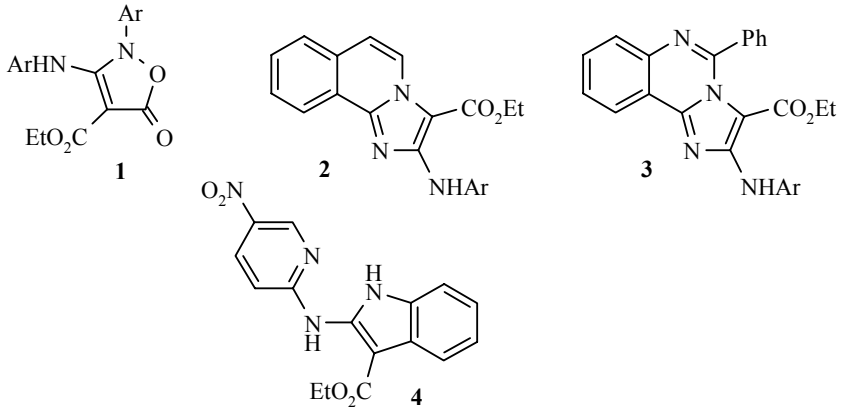
New N-substituted derivatives of 2-substituted 3-phenylamino- and 3-(1-naphthyl)aminoisoxazol-5(2H)-ones were synthesized. The reaction of isoxazolones with 2-chloro-5-nitropyridine gave the corresponding isoxazolones with a nitropyridyl group substituted on N-2. Their rearrangements produced ethyl 2-arylaminoimidazo[1,2-a]pyridine-3-carboxylates in the presence of triethylamine.

Keywords: 2-chloro-5-nitropyridine, imidazopyridines, isoxazolones, triethylamine, base-induced rearrangement.

Isoxazol-5(2H)-ones undergo a photochemically or thermally induced loss of CO_2 to form an iminocarbene [1, 2] or isomerize to a nitronoketene [3], the preferred pathway being greatly influenced by the substituents in positions 2, 3, or 4.

We have previously reported that the reaction of isoxazol-5(2H)-ones **1**, substituted on nitrogen with isoquinoline and quinazoline groups with triethylamine gave imidazoannulated compounds **2** and **3**, respectively. When the N-substituent was 5-nitro-2-pyridyl the 2-aminoindole structure **4** was assigned to the product [4].

The products were formally the same as those obtained in our study of the photochemical and thermal reactions of N-substituted isoxazolones [5]. The reactions of 3-substituted isoxazolones with a base are not so well known, and there are only a few reported reactions [6, 7].



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3-Amino-2-arylisoxazol-5(2H)-ones undergo solvolysis to form 1,3-dipoles that give either imidazopyridines or indoles *via* intramolecular cyclization in the presence of potassium carbonate [8]. It was suggested that the cyclization mode is controlled by the electronegativity of the aryl substituent.

We have recently reported [9] the synthesis and single crystal X-ray structure of ethyl 2-(1,3-benzoxazol-2-yl)-5-oxo-3-(4-toluidino)-2,5-dihydro-4-isoxazolecarboxylate by the reaction of ethyl 5-oxo-3-(4-toluidino)-2,5-dihydro-4-isoxazolecarboxylate with benzoxazole.

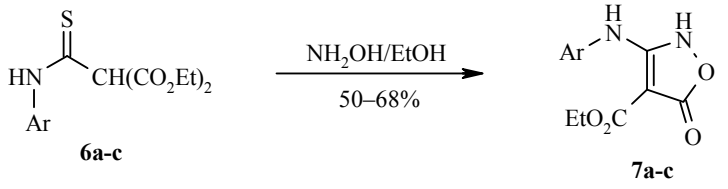
In this paper we report the synthesis of three new 3-arylamino-2-hetarylisoxazol-5(2H)-ones and their base-catalyzed decomposition to the corresponding 2-arylaminoimidazopyridines. The 2-hetaryl group was fixed as the electron deficient 5-nitro-2-pyridyl group, and the 3-aryl groups (2-MeC_6H_4, 2-$MeOC_6H_4$, 1-naphthyl) were all electron rich, but somewhat sterically congested.

The reaction of aryl isothiocyanates ArNCS **5** with sodium diethyl malonate in ethanol gave the corresponding diethyl N-arylthiocarbamoylmalonates **6a–c** in high yield.

The presence of two different ethoxy and carbonyl groups in the carbamates **6a–c** was inferred from their ^{1}H NMR and FT-IR spectra, respectively, due to one ester carbonyl group being H-bonded to the NH, and the other one free.

The reaction of thiocarbamoylmalonates **6a–c** with hydroxylamine by the general method [10] afforded the isoxazolones **7a–c** in good yield (Scheme 1).

Scheme 1

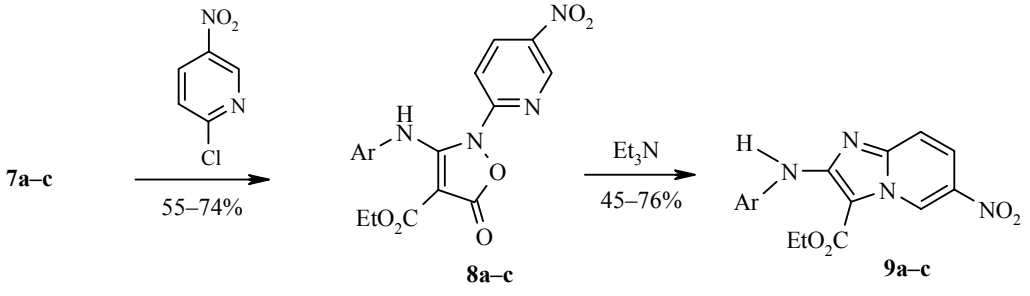


6a-c **7a-c**

a Ar = 2-MeC_6H_4, **b** 2-$MeOC_6H_4$, **c** 1-naphthyl

The reaction of isoxazolones **7a–c** with 2-chloro-5-nitropyridine at 130–140°C for 2 h afforded the corresponding 2-(5-nitropyrid-2-yl) derivatives **8a-c** in 55-74% yield as shown in Scheme 2.

Scheme 2



8a–c **9a–c**

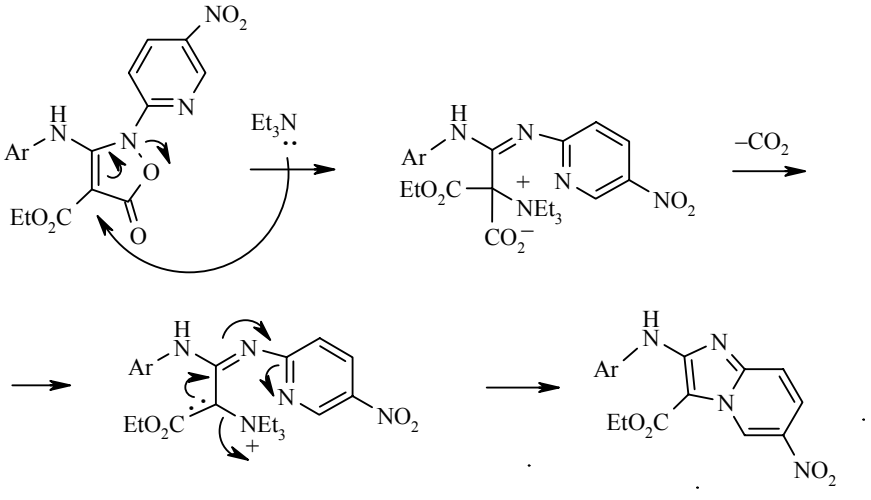
a Ar = 2-MeC_6H_4, **b** 2-$MeOC_6H_4$, **c** 1-naphthyl

The reaction of compounds **8a–c** with triethylamine in ethanol under reflux conditions gave the ethyl 2-arylamino-6-nitroimidazo[1,2-*a*]pyridine-3-carboxylates **9a–c** (Scheme 2).

The mechanisms of rearrangements are consistent with our earlier suggestions [4, 11] for the formation of imidazopyridine (Scheme 3). The present results, when considered with those obtained previously [4, 8],

suggest that the 2-hetaryl group of the 3-arylamino-2-hetarylisoxazol-5(2H)-ones is most likely to intercept the ylide intermediate formed by the reaction with a base, unless the 3-aryl group is both electron rich and sterically unhindered.

Scheme 3



a Ar = 2-MeC_6H_4, **b** 2-$MeOC_6H_4$, **c** 1-naphthyl

The decomposition of 3-arylaminoisoxazolones **8a**–**c** substituted on nitrogen with a nitropyridyl group in the presence of triethylamine provides imidazopyridines **9a**–**c**, which are suitable for the synthesis of intermediates of a series of polycyclic heterocycles that could be expected to have pharmaceutical applications [12, 13].

EXPERIMENTAL

Freshly distilled solvents were used throughout, and anhydrous solvents were dried according to Perrin and Armarego [14]. IR spectra were recorded on a Thermonicolet (Nexus 670) FT-IR spectrometer, using sodium chloride cells and measured as a film or KBr disks. ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR measurements were recorded on a Bruker 400 spectrometer in $CDCl_3$ or DMSO-d_6 using TMS as an internal standard. Melting points were determined on a Philip Harris C4954718 apparatus and are uncorrected. Microanalyses were performed on a Carlo-Erba Analyzer 1104. High resolution mass spectra were recorded on a Varian Matt 311 spectrometer. Mass spectra were determined on a HP 5973 MSD instrument, and relative abundances of fragments are quoted in parentheses after the *m/z* values.

Diethyl N-(2-methylphenyl)thiocarbamoylmalonate (**6a**). Dry ethanol (40 ml) reacted with sodium (2.3 g, 0.10 mol) and after cooling to room temperature diethyl malonate (16.2 g, 15.25 ml, 0.10 mol) was added. The reaction mixture was stirred at room temperature for 30 min and 2-methylphenyl isothiocyanate (14.92 g, 0.10 mol) was added; after 4 h, the yellowish white precipitate of sodium diethyl (2-methyl-phenyl)thiocarbamoylmalonate was formed and collected. The pure salt was dissolved in water (20 ml) and neutralized by dropwise addition of 10% hydrochloric acid to pH 7. The precipitate was collected and washed with light petroleum (5×20 ml) to give diethyl thiocarbamoylmalonate **6a** as yellow oil. Yield 27.8 g (90%). FT-IR spectrum (film), ν, cm^{-1}: 3296, 2983, 1732, 1614, 1588, 1517, 1462, 1369, 1310, 1150, 1027. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.27 (6H, t, *J* = 7.1, $CH_2C\underline{H}_3$); 2.27 (3H, s, CH_3); 4.24 (2H, q, *J* = 7.1, $C\underline{H}_2CH_3$); 4.25 (2H, q, *J* = 7.1, $C\underline{H}_2CH_3$); 5.10 (1H, s, CH); 7.16–7.24 (3H, m, Ar); 7.55–7.57 (1H, m, Ar);

10.48 (1H, br. s, exchanged by D_2O addition, NH). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 14.07, 17.82, 47.10, 61.51, 126.07, 126.48, 127.85, 130.90, 133.39, 137.17, 170.28, 193.72. Found, %: C 58.38; H 6.27; N 4.65. $C_{15}H_{19}NO_4S$. Calculated, %: C 58.23; H 6.19; N 4.53.

Diethyl N-(2-methoxyphenyl)thiocarbamoylmalonate (6b). This compound was prepared as described above, using 2-methoxyphenyl isothiocyanate (13.87 g, 0.08 mmol) and stirring for a further 6 h after addition of isothiocyanate, to give thiocarbamoylmalonate **6b** as a pale yellow solid. Yield 25.69 g (95%); mp 49-51°C. FT-IR spectrum, ν, cm^{-1}: 3241, 1749, 1717, 1607, 1423, 1368, 1310, 1248, 1117, 1019, 746. ^1H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.27 (6H, t, *J* = 7.1, $2CH_2C\underline{H}_3$); 3.88 (3H, s, CH_3); 4.25 (2H, q, *J* = 7.1, $C\underline{H}_2CH_3$); 4.26 (2H, q, *J* = 7.1, $C\underline{H}_2CH_3$); 5.07 (1H, s, CH); 6.92 (1H, dd, *J* = 8.0, *J* = 1.2, Ar); 6.95 (1H, t, *J* = 8.0, Ar); 7.16 (1H, td, *J* = 8.0, *J* = 1.2, Ar); 9.03 (1H, dd, *J* = 8.0, *J* = 1.2, Ar); 11.22 (1H, br. s, exchanged by D_2O addition, NH). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 13.92, 56.20, 62.89, 68.65, 110.66, 120.22, 121.67, 126.94, 128.30, 150.42, 165.58, 185.56. Found, %: C 55.55; H 5.86; N 4.54. $C_{15}H_{19}NO_5S$. Calculated, %: C 55.37; H 5.89; N 4.30.

Diethyl (1-naphthyl)thiocarbamoylmalonate (6c). This compound was prepared as described above, using 1-naphthyl isothiocyanate (9.25 g, 0.05 mmol) and stirring for a further 6 h after addition of isothiocyanate, to give thiocarbamoylmalonate **6c** as a pale yellow solid. Yield 14.84 g (86%); mp 56-57°C. FT-IR spectrum, ν, cm^{-1}: 3224, 1736, 1597, 1503, 1410, 1298, 1172, 1148, 1016, 775. ^1H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.35 (6H, t, *J* = 7.1, $2CH_2C\underline{H}_3$); 4.32 (2H, q, *J* = 7.1, $C\underline{H}_2CH_3$); 4.34 (2H, q, *J* = 7.1, $C\underline{H}_2CH_3$); 5.25 (1H, s, CH), 7.48–7.57 (3H, m, Ar); 7.82 (1H, d, *J* = 8.4, Ar); 7.89 (2H, t, *J* = 8.4, Ar); 8.03 (1H, d, *J* = 8.4, Ar); 10.94 (1H, br. s, exchanged by D_2O addition, NH). Found, %: C 62.35; H 5.34; N 3.92. $C_{18}H_{19}NO_4S$. Calculated, %: C 62.59; H 5.54; N 4.06.

Ethyl 3-(2-methylphenyl)amino-5-oxo-2,5-dihydroisoxazole-4-carboxylate (7a). To a solution of hydroxylamine hydrochloride (17.37 g, 250 mmol) in water (74 ml), potassium bicarbonate (25.03 g, 250 mmol) was slowly added. Ethanol (295 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 refluxed 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 colorless needles. Yield 11.57 g (53%); mp 173-174°C. FT-IR spectrum, ν, cm^{-1}: 2989, 1733, 1707, 1663, 1467, 1325, 1220, 1045, 804, 761. ^1H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 1.25 (3H, t, *J* = 7.1, $CH_2C\underline{H}_3$); 2.26 (3H, s, CH_3), 4.22 (2H, q, *J* = 7.1, $C\underline{H}_2CH_3$); 6.23 (1H, br. s, exchanged by D_2O addition, NH); 7.21 (1H, t, *J* = 7.2, Ar); 7.27 (1H, t, *J* = 7.2, Ar); 7.33 (1H, d, *J* = 7.2, Ar); 7.37 (1H, d, *J* = 7.2, Ar); 9.25 (1H, s, exchanged by D_2O addition, NH). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 14.45, 17.67, 60.48, 75.64, 122.69, 127.14, 127.41, 131.46, 133.71, 164.61, 165.43, 167.31. Found, %: C 55.23; H 5.01; N 9.86. $C_{13}H_{14}N_2O_4.H_2S$. Calculated, %: C 55.90; H 5.41; N 10.03.

Ethyl 3-(2-methoxyphenyl)amino-5-oxo-2,5-dihydroisoxazole-4-carboxylate (7b). The compound was prepared as described above using diethyl N-(2-methoxyphenyl)thiocarbamoylmalonate (9.75 g, 30 mmol) and refluxing for 12 h to give the desired product as white crystals. Yield 5.67 g (68%); mp 178-179°C. FT-IR spectrum, ν, cm^{-1}: 3202, 3044, 1736, 1713, 1676, 1627, 1588, 1492, 1325, 1228, 1041, 752. ^1H NMR spectrum ($CDCl_3$ + DMSO-d_6), δ, ppm (*J*, Hz): 1.27 (3H, t, *J* = 7.1, $CH_2C\underline{H}_3$); 3.85 (3H, s, CH_3), 4.15 (2H, q, *J* = 7.1, $C\underline{H}_2CH_3$); 6.81 (1H, td, *J* = 7.6, *J* = 1.2, Ar); 6.88 (1H, td, *J* = 7.6, *J* = 1.2, Ar); 6.94 (1H, td, *J*= 7.6, *J* = 1.2, Ar); 7.99 (1H, dd, *J* = 7.6, *J* = 1.2, Ar); 8.73 (1H, br. s, exchanged by D_2O addition, NH); 10.35 (1H, br. s, exchanged by D_2O addition, NH). ^{13}C NMR spectrum ($CDCl_3$ + DMSO-d_6), δ, ppm: 13.91, 56.27, 61.80, 112.25, 121.61, 121.94, 128.18, 150.67, 159.11, 159.70, 164.10, 170.31. Found, %: C 52.84; H 5.46; N 9.43. $C_{13}H_{14}N_2O_5 \cdot H_2S$. Calculated, %: C 52.88; H 5.12; N 9.49.

Ethyl 3-(1-naphthyl)amino-5-oxo-2,5-dihydroisoxazole-4-carboxylate (7c). The compound was prepared as described above using diethyl (1-naphthyl)thiocarbamoyl- malonate (10.35 g, 30 mmol) and refluxing for 10 h to give the desired product as a white solid. Yield 4.47 g (50%); mp 127°C (decomposed at 178–180°C). FT-IR spectrum, ν, cm^{-1}: 3438, 3299, 1716, 1676, 1606, 1397, 1313, 1213, 1123, 1027, 782. ^1H NMR spectrum ($CDCl_3$ + DMSO-d_6), δ, ppm (*J*, Hz): 1.29 (3H, t, *J* = 7.1, $CH_2C\underline{H}_3$); 4.26 (2H, q, *J* = 7.1, $\underline{H}_2CH_3$); 7.55 (1H, t, *J* = 7.6, Ar); 7.62 (2H, t, *J* = 8.3, Ar); 7.66 (1H, d, *J* = 7.6, Ar); 7.87 (1H, d, *J* = 8.3, Ar);

7.93 (1H, d, J = 8.3, Ar); 8.01 (1H, d, J = 7.6, Ar); 9.74 (1H, br. s, exchanged by D_2O addition, NH). Found, %: C 64.32; H 4.92; N 9.29. $C_{16}H_{14}N_2O_4$. Calculated, %: C 64.42; H 4.73; N 9.39.

Ethyl 3-(2-methylphenyl)amino-2-(5-nitropyrid-2-yl)-5-oxo-2,5-dihydroisoxazole-4-carboxylate (**8a**). A mixture of 2-chloro-5-nitropyridine (317 mg, 2 mmol) and ethyl 3-(2-methylphenyl)amino-5-oxo-2,5-dihydroisoxazole-4-carboxylate (524 mg, 2 mmol) was heated neat under an atmosphere of nitrogen in an oil bath at 140°C for 2 h. The residue was recrystallized from ethanol to give the desired isoxazolone as yellow crystals. Yield 499 mg (65%); mp 168-170°C. FT-IR spectrum, ν, cm^{-1}: 3060, 1776, 1701, 1610, 1521, 1336, 1200, 1118, 1021, 754. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.28 (3H, t, J = 7.1, $CH_2C\underline{H}_3$); 2.43 (3H, s, CH_3); 4.24 (2H, q, J = 7.1, $C\underline{H}_2CH_3$); 6.98 (1H, t, J = 7.4, Ar); 7.06 (1H, d, J = 7.4, Ar); 7.07 (1H, t, J = 7.4, Ar); 7.24 (1H, d, J = 7.4, Ar); 7.49 (1H, d, J = 9.1, Ar); 8.50 (1H, dd, J = 9.1, J = 2.5, Ar); 8.82 (1H, d, J = 2.5, Ar); 10.16 (1H, br. s, exchanged by D_2O addition, NH). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 14.48, 17.67, 60.44, 78.54, 115.04, 122.78, 131.39, 133.66, 136.38, 141.76, 143.26, 145.42, 153.65, 157.12, 160.95, 163.39, 163.89. Found: *m/z* 384.10698 $[M]^+$. $C_{18}H_{16}N_4O_6$. Calculated : M = 384.10699. Mass spectrum (EI, 70 eV), *m/z* (I_{rel}, %): 384 $[M]^+$ (1), 340 $[(M–CO_2)]^+$ (100), 294 (13), 267 (55), 248 (27), 220 (23), 144 (7), 118 (6), 91 (9), 65 (5). Found, %: C 56.10; H 3.86; N 14.28. $C_{18}H_{16}N_4O_6$. Calculated, %: C 56.25; H 4.16; N 14.58.

Ethyl 3-(2-methoxyphenyl)amino-2-(5-nitropyrid-2-yl)-5-oxo-2,5-dihydroisoxazole-4-carboxylate (**8b**). This compound was prepared as described above, using the corresponding isoxazolone (139 mg, 5 mmol) and 2-chloro-5-nitropyridine (79 mg, 5 mmol), as yellow needles after recrystalization from ethanol. Yield 148 mg (74%); mp 132-136°C. FT-IR spectrum, ν, cm^{-1}: 3448, 1774, 1702, 1600, 1577, 1558, 1523, 1335, 1119, 1021, 752. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.27 (3H, t, J = 7.1, $CH_2C\underline{H}_3$); 3.93 (3H, s, CH_3); 4.25 (2H, q, J = 7.1, $C\underline{H}_2CH_3$); 6.75 (1H, td, J = 7.8, J = 1.2, Ar); 6.92 (1H, dd, J = 7.8, J = 1.2, Ar); 7.06 (1H, dd, J = 7.8, J = 1.2, Ar); 7.11 (1H, td, J = 7.8, J = 1.2, Ar); 7.55 (1H, dd, J = 9.1, J= 0.5, Ar); 8.54 (1H, dd, J = 9.1, J = 2.6, Ar); 8.87 (1H, d, J = 2.6, Ar); 10.40 (1H, br. s, exchanged by D_2O addition, NH). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 14.18, 55.93, 61.35, 79.24, 111.37, 112.32, 120.48, 121.68, 122.11, 124.26, 127.65, 127.87, 134.55, 141.55, 143.53, 151.39. Mass spectrum (EI, 70 eV), *m/z* (I_{rel}, %): 400 $[M]^+$ (3), 356 $[(M–CO_2)]^+$ (1), 207 (9), 149 (100), 134 (54), 123 (32), 120 (45), 108 (45), 106 (50), 80 (30), 77 (28), 51 (20), 28 (71). Found, %: C 54.00; H 4.01; N 14.00. $C_{18}H_{16}N_4O_7$. Calculated, %: C 54.10; H 3.78; N 14.11.

Ethyl 3-(1-naphthyl)amino-2-(5-nitropyrid-2-yl)-5-oxo-2,5-dihydroisoxazole-4-carboxylate (**8c**). This compound was prepared as described above, using the corresponding isoxazolone (596 mg, 2 mmol) and 2-chloro-5-nitropyridine (317 mg, 2 mmol) as yellow needles after recrystalization from ethanol. Yield 462 mg (55%); mp 186–188°C. FT-IR spectrum, ν, cm^{-1}: 3319, 1762, 1669, 1541, 1448, 1310, 1201, 1102, 752. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.60 (3H, t, J = 7.1, $C\underline{H}_2CH_3$); 4.58 (2H, q, J = 7.1, $C\underline{H}_2CH_3$); 7.26 (2H, t, J = 7.6, Ar); 7.28 (1H, d, J = 7.6, Ar); 7.42 (1H, d, J = 9.0, Ar); 7.58 (1H, td, J = 8.3, J = 1.2, Ar); 7.64 (1H, td, J = 8.3, J = 1.2, Ar); 7.70 (1H, d, J = 8.3, Ar); 8.10 (1H, d, J = 8.3, Ar); 8.41 (1H, dd, J = 9.0, J = 2.6, Ar); 9.21 (1H, d, J = 2.6, Ar); 10.65 (1H, br. s, exchanged by D_2O addition, NH). Found, %: C 60.23; H 3.80; N 13.51. $C_{21}H_{16}N_4O_6$. Calculated**,** %: C 60.00; H 3.84; N 13.33.

Ethyl 2-(2-methylphenyl)amino-6-nitroimidazo[1,2-*a*]pyridine-3-carboxylate (**9a**). Isoxazolone **8a** (384 mg, 1 mmol) and triethylamine (0.4 ml) were refluxed in ethanol (10 ml) for 8 h. The reaction mixture was cooled to room temperature and the resulting precipitate was collected to give ethyl 2-(2-methylphenyl)amino-6-nitroimidazo[1,2-*a*]pyridine-3-carboxylate (**9a**) as pale red needles. Yield 284 mg (76%); mp 178-179°C. FT-IR spectrum, ν, cm^{-1}: 3321, 3109, 2980, 1664, 1624, 1602, 1493, 1474, 1342, 1306, 1214, 1081, 757. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.54 (3H, t, J = 7.1, $CH_2C\underline{H}_3$); 2.39 (3H, s, CH_3); 4.57 (2H, q, J = 7.1, $C\underline{H}_2CH_3$); 7.02 (1H, t, J = 7.6, Ar); 7.23 (1H, d, J = 7.6, Ar); 7.30 (1H, t, J = 7.6, Ar); 7.52 (1H, d, J = 9.7, Ar); 8.14 (1H, dd, J = 9.7, J = 2.0, Ar); 8.40 (1H, d, J = 7.6, Ar); 8.94 (1H, br. s, Ar); 9.25 (1H, br. s, exchanged by D_2O addition, NH). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 14.59, 17.72, 61.59, 98.12, 112.86, 123.81, 124.88, 126.85, 127.31, 131.23, 131.81, 135.23, 138.61, 143.89, 153.55, 160.34. Found: 340.11715 $[M]^+$. $C_{17}H_{16}N_4O_4$. Calculated: M = 340.11716. Mass spectrum (EI, 70 eV), *m/z* (I_{rel}, %): 340 $[M]^+$ (1), 281 (65), 264 (73), 253 (90), 207 (45), 146(100), 90 (39), 28 (100). Found, %: C 59.58; H 4.32; N 16.00. $C_{17}H_{16}N_4O_4$. Calculated, %: C 60.00; H 4.70; N 16.47.

Ethyl 2-(2-methoxyphenyl)amino-6-nitroimidazo[1,2-*a*]pyridine-3-carboxylate (**9b**). Isoxazolone **8b** (100 mg, 25 mmol) and triethylamine (0.4 ml) were refluxed in ethanol (10 ml) for 2 h. The reaction mixture was cooled to room temperature and the resulting precipitate was collected to give ethyl 2-(2-methoxyphenyl)amino-6-nitroimidazo[1,2-*a*]pyridine-3-carboxylate (**9b**) as yellow needles. Yield 50 mg (56%); mp 218–220°C. FT-IR spectrum, ν, cm^{-1}: 3378, 1674, 1609, 1575, 1467, 1345, 1315, 1300, 1227, 1097, 1025, 751. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.56 (3H, t, *J* = 7.0, $CH_2C\underline{H}_3$); 3.96 (3H, s, CH_3); 4.54 (2H, q, *J* = 7.0, $C\underline{H}_2CH_3$); 6.93 (1H, dd, *J* = 7.5, *J* = 1.9, Ar); 7.00 (1H, td, *J* = 7.5, *J* = 1.9, Ar); 7.04 (1H, td, *J* = 7.5, *J* = 1.9, Ar); 7.51 (1H, d, *J* = 9.7, Ar); 8.12 (1H, dd, *J* = 9.7, *J* = 2.3, Ar); 8.64 (1H, d, *J* = 7.5, Ar); 8.76 (1H, br. s, Ar); 10.29 (1H, br. s, exchanged by D_2O addition, NH). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 14.49, 55.79, 61.78, 84.69, 96.38, 99.24, 110.03, 114.12, 117.62, 121.21, 122.04, 122.56, 126.67, 129.34, 137.08, 147.12, 154.92. Mass spectrum (EI, 70 eV), *m/z* (I_{rel}, %): 356 $[M]^+$ (1), 296 (38), 267 (100), 207 (9), 190 (14), 158 (13), 130 (22), 107 (20), 77 (11), 28 (23). Found, %: C 57.88; H 4.50; N 16.12. $C_{17}H_{17}N_4O_5$. Calculated, %: C 57.30; H 4.49; N 15.73.

Ethyl 2-(1-naphthyl)amino-6-nitroimidazo[1,2-a]pyridine-3-carboxylate (**9c**). Isoxazolone **8c** (210 mg, 0.5 mmol) and triethylamine (0.4 ml) were refluxed in ethanol (10 ml) for 3 h. The reaction mixture was cooled to room temperature and the resulting precipitate was collected to give ethyl 2-(1-naphthyl)amino-6-nitroimidazo-[1,2-*a*]pyridine-3-carboxylate (**9c**) as brown needles. Yield 85 mg (45%); mp 174-175°C. FT-IR spectrum, ν, cm^{-1}: 3421, 1656, 1605, 1591, 1484, 1342, 1311, 1218, 1107, 771. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.59 (3H, t, *J* = 7.1, $CH_2C\underline{H}_3$); 4.62 (2H, q, *J* = 7.1, $C\underline{H}_2CH_3$); 7.51-7.64 (5H, m, Ar); 7.88 (1H, d, *J* = 9.6, Ar); 8.02-8.12 (1H, m, Ar); 8.13 (1H, dd, *J* = 9.6, *J* = 2.0, Ar); 8.46 (1H, d, *J* = 7.3, Ar); 9.24 (1H, br. s, exchanged by D_2O addition, NH); 9.92 (1H, br. d, *J* = 0.9, Ar). Mass spectrrum (EI, 70 eV), *m/z* (I_{rel}, %): 376 $[M]^+$ (1), 356 (100), 325 (41), 305 (23), 297 (7), 279 (20), 235 (9), 193 (7), 155 (5), 77 (7). Found, %: C 64.20; H 4.62; N 15.01. $C_{20}H_{16}N_4O_4$. Calculated, %: C 63.82; H 4.28; N 14.89.

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