Some Nucleophilic Substitutions In 2-Cyano-3-Nitroimidazo[1,2-*a*]Pyridine

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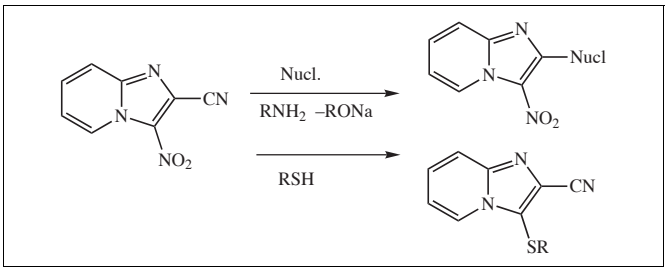

In some nucleophilic substitution reactions of 2-cyano-3-nitroimidazo[1,2-*a*]pyridine, nitrogen (alkylamines, guanidine) and oxygen nucleophiles (alkoxides) underwent substitution of the 2-cyano group, while sulfur nucleophiles (alkylthiols) underwent substitution of the 3-nitro group.

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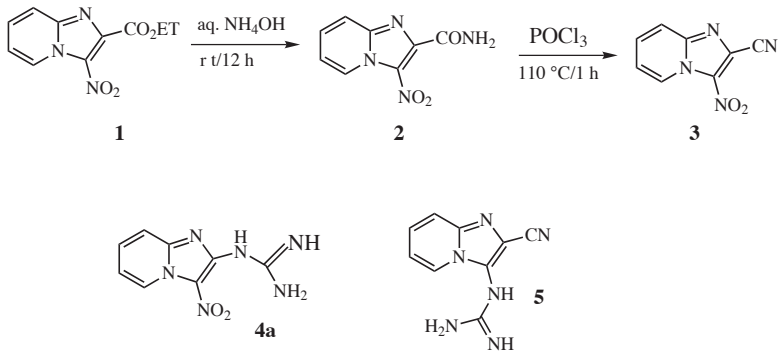
Introduction.

The imidazo[1,2-*a*]pyridine ring is a versatile system which has shown an outstanding array of biological activities [1]. The incorporation of the imidazo[1,2-*a*]pyridine moiety in structures investigated in relation to potential pharmacological activities has continued [2]. Electrophiles predominantly attack on the position 3 of the heterocycle [3]. Furthermore *ipso* electrophilic attack on 3-substituted (Br, NO_2, CHO)-5-methylimidazo[1,2-*a*]pyridines by chlorine (NCS) rendered 3-chloro substituted derivatives albeit in low yields [4]. Nucleophiles attack both positions, 2 and 3, thus the reaction of 2-chloro-3-nitroimidazo[1,2-*a*]-pyridine with diethylamine undergoes substitution of the 2-chloro group [5]. While the nitro functional group has been displaced from the 3-position by thiol nucleophiles if an electron–attracting substituent is present at the 2-position [6].

It is well known that the nitro group is a far better leaving group than the cyano group, particularly in aromatic nucleophilic substitutions [7,8]. Thus, the reaction of methyl 3-nitropyridine-4-carboxylate or 3-nitropyridine-4-carbonitrile undergoes substitution of the 3-nitro group [9]. It is also known that the nitrile group undergoes two types of reaction toward the nucleophile, the nucleophilic substitution as well as the nucleophilic addition. The former example is shown in the conversion of some aldehydes to corresponding esters, where the α-oxonitriles, prepared by hydrocyanation of the aldehydes with hydrogen cyanide followed by oxidation with manganese dioxide, readily gave the corresponding esters by treatment with alcohols [10]. The latter mode, the nucleophilic adition, is shown in the condensation of 2-amino-5-nitrobenzonitrile with 4-nitrobenzonitrile giving 2-(4-nitrophenyl)-4-amino-6-nitroquinazoline [11]. The *cine*-

Scheme I



substitution in the 2-cyano-5-nitrofuran with carbanions and thiols also shows that the nitro group is a better leaving group than the cyano [12].

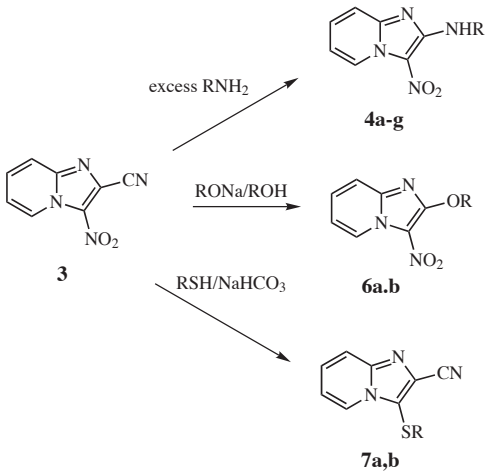
Results and Discussion.

As shown in Scheme 1, 3-nitroimidazo[1,2-*a*]pyridine-2-carbonitrile (**3**) was prepared from ethyl 3-nitroimidazo[1,2-*a*]-pyridine-2-carboxylate (**1**) [13] by ammonolysis with aqueous ammonia to give carboxamide **2** [14], followed by dehydration of the latter with phosphoryl oxychloride. The 3-nitro-2-carbonitrile **3** was then subjected to nucleophilic substitution reactions with guanidine in *n*-butanol. Unexpectedly this process yielded 2-guanidinyl-3-nitroimidazo[1,2-*a*]pyridine (**4a**), not 3-guanidinylimidazo[1,2-*a*]pyridine-2-carbonitrile (**5**), *i.e.* cyanide had been displaced in preference to the better leaving nitro group.

Treatment of **3** with excess amounts of some alkyl amines, as shown in Scheme II, in the absence of solvent gave the corresponding 2-alkylamino-3-nitroimidazo[1,2-*a*]pyridines (**4b-g**) in moderate to high yields. Use of microwave in treatment of **3** with cyclohexylamine reduced the reaction time from 2 h to 14 min and the molar ratio from 8.6 equivalents to 3, and improved the reaction yield from 62% to 97%. Treatment of 3 with aromatic amines caused no substitution. Treatment of 3 with excess amounts of two alkoxides, ethoxide and isopropoxide, in ethyl and isopropyl alcohol respectively, gave corresponding 2-alkoxy-3-nitro-imidazo[1,2-*a*] pyridines (**6a,b**) in moderate yields.

Treatment of **3** with equal anount of two thiols, propane-thiol and ethyl thioglycolate in DMF, gave corresponding 3-alkylthioimidazo[1,2-*a*]pyridine-2-carbonitriles (**7a,b**) in moderate yields. Results for these substitution reactions are summarized in Table 1. It is very interesting that the nitrogen and oxygen nucleophiles showed the substitutions taking place on the 2-cyano (the less favored leaving group), and that sulfur nucleophiles showed the substitution on the 3-nitro (the more favored leaving group).

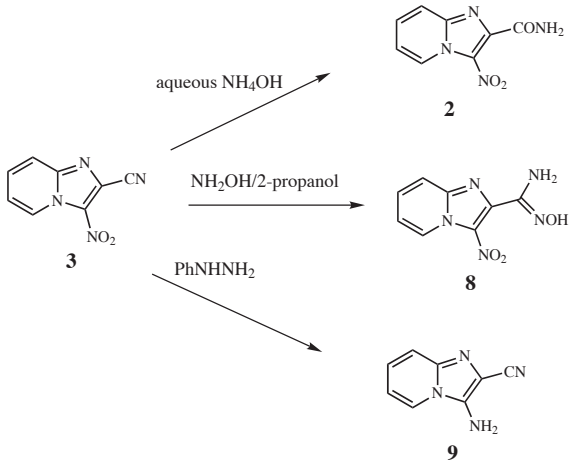
Scheme II



In the ir spectra of products **4a-g** and **6a-b,** the nitrile band disappeared and the nitro absorption bands appeared at ν 1300-1360 and 1500-1528 cm^{-1}. In the ^1H nmr spectra of **4a-g** and **6a,b**, the H-5 signal showed at low field in the interval δ 9.0 - 9.2 as has been established for 3-nitro substituted imidazo-pyridines [5,6] and as a clear indication of the permanence of the 3-nitro group. In the ir spectra of **7a,b**, the cyano bands appeared at 2238-2250 cm^{-1} and the nitro bands disappeared. In the pmr spectra of **7a,b**, the H-5 signals shifted upfield, thus showing the displacement of the 3-nitro by thiol.

As shown in Scheme 3, treatment of **3** with other nitrogen nucleophiles, such as ammonia, hydroxylamine and phenylhydrazine showed no substitution on the 2-cyano or on the 3-nitro. Thus, treatment of **3** with aqueous ammonia at room temperature simply caused the hydrolysis of the nitrile to give 3-nitroimidazo[1,2-*a*] pyridine-2-carboxamide (**2**). Treatment of **3** with hydroxyl amine caused the nucleophilic addition on the nitrile to give 3-nitroimidazo[1,2-*a*]pyridine-2-carbox-amide-oxime (**8**). Treatment of **3** with an excess of phenylhydrazine at 70-75 °C caused the reduction [15] of the 3-nitro to give 3-aminoimidazo[1,2-*a*]pyridine-2-carbonitrile (**9**) in 73% yield.

Scheme III



Although displacement of either group may be mechanistically understandable in terms of an initial Michael type addition to either carbon supporting the leaving group, followed by an elimination process, it is also possible that the site in which the group itself is attached to the imidazopyridine system might be playing a decisive role on the preference for substitution. Therefore further efforts are on the way to determine whether this is the case. It is noteworthy to mention that the nitrile carbon in 3 shows a ^{13}C nmr shift at δ 90, unusually high.

Table 1

Nucleophilic cyanide displacement in 2-cyano-3-nitroimidazoimidazo[1,2-*a*]pyridine **3**.

Compound	R	Reaction conditions	Melting point °C	Yield %
4a	$NH_2C(NH)$	BuONa/BuOH, 80 °C	222-223	65
4b	$PhCH_2$	60-70°C	157-158	77
4c	$(CH_3)_2CH$	60-70°C	153-155	93
4d	Cyclohexyl	60-70°C	157-159	62
4d	Cyclohexyl	Microwave	157-159	97
4e	*n*-Butyl	60-70°C	73.5-74.5	72
4f	Cyclopropyl	60-70°C	186-187	88
4g	(*S*)-(-)-$Ph(CH_3)CH$	60-70°C	102-103.5	48
6a	CH_3CH_2	EtONa, 1.5 mol/EtOH, 10 mL, 60 °C	147-149	75
6b	$(CH_3)_2CH$	*I*PrONa, 1.5 mol /*i*PrOH, 10 mL, 60 °C	142-143	70

Conclusion.

In conclusion, several nitrogen and oxygen nucleophiles have shown a preference for cyanide displacement over the better leaving nitro group in 2-cyano-3-nitroimidazo-[1,2-*a*]pyridine. However alkylthiol nucleophiles did displace the nitro group.

EXPERIMENTAL

Melting points were measured on an Electrothermal melting point apparatus and are uncorrected. The ir spectra were taken on a Perkin Elmer 1600 series FTIR spectrophotometer. ^1H and ^{13}C nmr spectral data were recorded at 300 and 75 MHz respectively using a Bruker DPX 300 MHz NMR spectrometer. Chemical shifts (δ) are given in parts per million downfield from TMS (δ = 0). Mass spectra were obtained with a Jeol JMSAX505HA instrument.

2-Cyano-3-nitroimidazoimidazo[1,2-*a*]pyridine (**3**).

A suspension of 3-nitroimidazo[1,2-*a*]pyridine-2-carboxamide **2** (8.5 g, 41.6 mmol) in $POCl_3$ (85 mL) was stirred at 115 °C for 1 hour. After cooling, the mixture was concentrated under vacuum, and treated with ice (100 g). The yellow solid formed was collected by filtration and washed with cold water (50 mL x 2), and recrystallized from DMSO to afford **3**, 96% yield, mp 166-167 °C (lit. 162 °C [16,17]); Ir (KBr, cm^{-1}) ν 2250 (CN); 1629 (C=C); 1480, 1360 (NO_2); ^1H nmr (deuteriochloroform): δ 9.42 (td, J = 7.0, 1.1 Hz, 1H, H-5); 7.95 (td, J = 9.1, 1.1 Hz, 1H, H-8); 7.81 (ddd, J = 9.1, 7.0, 1.1 Hz, 1H, H-7); 7.5 (td, J = 7.0, 1.1 Hz, 1H, H-6); cmr: 145.3, 131.9, 127.2, 125.8, 120.7, 119.6, 118.9, 111.7; ms: m/z (%) 188 (M^+, 38), 78 (100).

2-Guanidinyl-3-nitroimidazo[1,2-*a*]pyridine (**4a**).

To a sodium *n*-butoxide/butanol solution, prepared from sodium metal (147 mg, 6.38 mmol) and *n*-butanol (20 mL) was added guanidine hydrochloride (508 mg, 5.32 mmol), and 2-cyano-3-nitroimidazo[1,2-*a*]pyridine **3** (1.0 g, 5.32 mmol) was added to the guanidine *n*-butanol solution. The mixture was stirred at 80 °C for 1 hour. After cooling, the solid formed was collected by filtration, washed with cold ethanol, and recrystallized from ethanol to afford **4a**, 65% yield, mp 222-223 °C; Ir (KBr, cm^{-1}) ν 3425, 3335, 3232 (NH); 1627 (C=C); 1482 (NO_2); ^1H nmr (DMSO-d_6): δ 9.37 (td, *J* = 7.0, 1.0 Hz, 1H, H-5); 7.63 (td, *J* = 7.9, 1.0 Hz, 1H, H-7); 7.43 (td, *J* = 8.8, 1.2 Hz, 1H, H-8); 7.14 (bs, 4H, NH_2) 7.12 (td, *J* = 7.0, 1.2 Hz, 1H, H-6); cmr: δ 160.84, 157.2, 144.5 133.2, 129.1, 122.03, 115.1, 114.7; ms; m/z (%) 220 M^+ (6.3), 120 (100).

Anal. Calcd. for $C_8H_8N_6O_2$: C, 43.63; H, 3.66. Found: C, 43.70; H, 3.45.

General Procedure for Preparation of 2-Alkylamino-3-nitroimidazo[1,2-*a*]pyridine **4b-4g**.

A mixture of 2-cyano-3-nitroimidazo[1,2-*a*]pyridine **3** (1.0 g, 5.32 mmol) and alkylamine (16.3 mmol) was stirred at 60-70 °C for 2 hours. After cooling, the solid formed was collected by filtration and washed with cold ethanol, and recrystallized from ethanol to afford the corresponding 2-alkylamino-3-nitroimidazo[1,2-*a*] pyridine **4b-g**.

2-(*N*-Benzyl)amino-3-nitroimidazo[1,2-*a*]pyridine **4b**.

Obtained in 77% yield, mp 157-158 °C; Ir (KBr, cm^{-1}) ν 3339 (NH); 1605 (C=C); 1469, 1317 (NO_2); ^1H nmr (DMSO-d_6): δ 9.25 (d, *J* = 6.8 Hz, 1H, H-5); 8.52 (t, *J* = 4.5 Hz, 1H, N*H*); 7.69 (ddd, *J* = 8.5, 7.2, 1.4 Hz, 1H, H-7); 7.47 (d, *J* = 8.8 Hz, 1H, H-8); 7.39-7.18 (m, 5H, $-C_6H_5$); 7.16 (ddd, *J* = 7.2, 7.0, 1.0 Hz, 1H, H-6); 4.73 (d, *J* = 6.5 Hz, 2H, CH_2); cmr: δ 153.8 (C-2); 146.6 (C-8a); 139.3 (Ar, *ipso*); 134.3 (C-7); 128.7 (C-5); 128.3 (Ar, *m*); 127.3 (Ar, *o*); 126.9 (Ar, *p*); 117.6 (C-3?); 114.7 (C-8);114.1 (C-6); 45.1 (CH_2); ms; m/z (%) 268 M^+ (15.8), 91 (100).

Anal. Calcd. for $C_{14}H_{12}N_4O_2$: C, 62.67; H, 4.50. Found: C, 62.43; H, 4.67.

2-(*N*-Isopropyl)amino-3-nitroimidazo[1,2-*a*]pyridine (**4c**).

Obtained in 93% yield, mp 153-155°C; Ir (KBr cm^{-1}) ν 3369 (NH); l606 (C=C); 1454, 1332 (NO_2); ^1H nmr (DMSO-d_6): δ 9.24 (td, *J* = 6.7, 1.1 Hz, 1H, H-5); 7.73 (td, *J* = 8.0, 1.4 Hz, 1H, H-7); 7.58(d, *J* = 8.4 Hz, 1H, NH); 7.50 (td, *J* = 8.8, 1.1 Hz, 1H, H-8); 7.16 (td, *J* =7.0, 1.2 Hz, 1H, H-6); 4.27 (m, 1H, CH); 1.28 (d, *J* = 6.6 Hz, 6H, CH_3); cmr: δ 153.2, 146.8, 134.4, 128.7, 117.5, 114.7, 114.1, 44.2, 22.3; ms; m/z (%) 220 M^+ (76), 78 (100).

Anal. Calcd. For $C_{10}H_{12}N_4O_2$: C, 54.53; H, 5.49; N, 25.44. Found: C, 54.65; H, 5.74

2-(*N*-Cyclohexyl)amino-3-nitroimidazo[1,2-*a*]pyridine (**4d**).

Obtained in 62% yield, mp 157-159°C. Ir (KBr cm^{-1}) ν 3333 (NH); l606 (C=C); 1461, 1332 (NO_2); ^1H nmr (DMSO-d_6): δ

9.23 (d, *J* = 7.0 Hz, 1H, H-5); 7.73 (td, *J* =8.0, 1.2 Hz, 1H, H-7); 7.57(d, *J* = 8.5 Hz, 1H, NH); 7.51 (d, *J* = 8.8 Hz, 1H, H-8); 7.16 (t, *J* =7.0 Hz, 1H, H-6); 3.93 (m, 1H, $CH_{cyclohexyl}$); 1.18-1.94 (m, 10H, $CH_{2\ (cyclohexyl)}$); cmr: δ 153.1, 146.9, 134.5, 128.7, 117.5, 114.7, 114.1, 51.1, 32.3, 25.1, 24.7; ms; m/z (%) 260 M^+ (97.5), 243 (100).

Anal. Calcd. For $C_{13}H_{16}N_4O_2$: C, 59.98; H, 6.19; N, 21.52. Found: C, 59.68; H, 6.34

2-(*N*-1-Butyl)amino-3-nitroimidazo[1,2-*a*]pyridine (**4e**).

Obtained in 72% yield, mp 73.5-74.5°C. Ir (KBr cm^{-1}) ν 3375 (NH); l606 (C=C); 1461, 1332 (NO_2); ^{1}H nmr (deuteriochloroform): δ 9.37 (ddd, *J* = 6.8, 1.4, 1.0 Hz, 1H, H-5); 7.60 (td, *J* =8.0, 1.5 Hz, 1H, H-7); 7.46(bs, 1H, NH); 7.42 (td, *J* =8.8, 1.1 Hz, 1H, H-8); 7.03 (td, *J* = 7.0, 1.2 Hz, 1H, H-6); 3.65 (m, 2H, $CH_{2\ (n\text{-butyl})}$); 1.72 (m, 2H, $CH_{2\ (n\text{-butyl})}$); 1.47 (m, 2H, $CH_{2\ (n\text{-butyl})}$); 0.98 (t, *J* = 7.3 Hz, 3H, $CH_{3\ (n\text{-butyl})}$); cmr: δ 154.4, 147.2, 133.5, 128.6, 118.0, 114.9, 113.5, 42.1, 31.6, 19.9, 13.6; ms; m/z (%) 234 M^+ (95), 146.2 (100).

Anal. Calcd. For $C_{11}H_{14}N_4O_2$: C, 56.39; H, 6.02; N, 23.91. Found: 56.23; H, 5.81

2-(*N*-Cyclopropyl)amino-3-nitroimidazo[1,2-*a*]pyridine (**4f**).

Obtained in 88% yield, mp 186-187°C. Ir (KBr cm^{-1}) ν 3329 (NH); l611 (C=C); 1468, 1334 (NO_2); ^{1}H nmr (deuteriochloroform): δ 9.38 (td, *J* =6.8, 1.1 Hz, 1H, H-5); 7.62 (td, *J* =7.9, 1.5 Hz, 1H, H-7); 7.53 (td, *J* = 8.8, 1.1 Hz, 1H, H-8) 7.51(bs, 1H, NH); 7.07 (td, *J* =6.9, 1.3 Hz, 1H, H-6); 3.03 (m, 1H, $CH_{cyclopropyl}$); 0.98 (m, 2H, $CH_{2\ (cyclopropyl)}$); 0.76 (m, 2H, $CH_{2\ (cyclopropyl)}$); cmr: δ 155.1, 146.9, 133.4, 128.5, 118.1, 115.3, 113.8, 24.5, 7.3; ms; m/z (%) 218 M^+ (8), 201 (100).

Anal. Calcd. For $C_{10}H_{10}N_4O_2$: C, 55.04; H, 4.61; N, 25.67. Found: C, 55.41; H, 4.85

2-(*N*-(S)-(-)-α-Methylbenzyl)amino-3-nitroimidazo[1,2-*a*]pyridine (**4g**).

Obtained in 48% yield, mp 102-103°C. Ir (KBr cm^{-1}) ν3346 (NH); 1601 (C=C); 1457, 1334 (NO_2); ^{1}H nmr (deuteriochloroform): δ 9.35 (td, *J* = 6.8, 1.2 Hz, 1H, H-5); 7.74 (d, *J* = 8.0 Hz, 1H, NH) 7.56 (td, *J* =8.0, 1.4 Hz, 1H, H-7); 7.45-7.24 (m, 6H, H-8 and Ph) 7.01 (td, *J* =6.8, 1.2 Hz, 1H, H-6); 5.40 (m, 1H, CH); 1.69 (d, *J* = 9.2 Hz, 3H, CH_3); cmr: δ 153.4, 147.0, 142.8, 133.3, 128.66, 128.60, 127.43, 125.96, 115.1, 113.6, 51.8, 22.8; ms; m/z (%) 282 M^+ (27), 265.1 (100).

Anal. Calcd. For $C_{15}H_{14}N_4O_2$: C, 63.81; H, 4.99; N, 19.84. Found: C, 63.64; H, 4.67

General procedure for the synthesis of 2-alkoxy-3 nitroimidazo-[1,2-*a*]pyridine (**6a,b**).

A mixture of 2-cyano-3-nitroimidazo[1,2-*a*]pyridine 3 (1.0 g, 5.32 mmol), sodium alkoxide (8 mmol) and the corresponding alcohol (10 mL) was stirred at ca. 60 °C for 2 hours. After cooling, the solid formed was collected by filtration and washed with cold ethanol, and recrystallized from ethanol to afford the corresponding 2-alkoxy-3-nitroimidazo[1,2-*a*]pyridine 6a,b.

2-Ethoxy-3-nitroimidazo[1,2-*a*]pyridine (**6a**).

Obtained in 75 % yield, mp 147-149°C, Ir (KBr cm^{-1}) ν l540 (C=C); 1486, 1327 (NO_2); 1210, 1022 (C-O-C); ^{1}H nmr ($CDCl_3$): δ 9.47 (td, *J* =6.8, 1.0 Hz, 1H, H-5); 7.69-7.57 (m, 2H, H-8 and H-7); 7.23 (td, *J* =6.8, 1.6 Hz, 1H, H-6); 4.71 (c, *J* = 7.2 Hz, 2H, OCH_2); 1.56 (t, *J* = 7.2 Hz, 3H, CH_3); cmr: δ 158.7, 142.1, 131.7, 128.1, 116.3, 115.5, 66.5, 14.6; ms; m/z (%) 207 M^+ (41), 78.1 (100).

Anal. Calcd. For $C_9H_9N_3O_3$: C, 52.17; H, 4.37; N, 20.28. Found: 52.39, H, 5.74

2-Isopropoxy-3-nitroimidazo[1,2-*a*]pyridine (**6b**).

Obtained in 70 % yield, mp 142-143°C. Ir (KBr cm^{-1}) νl (C=C); (NO_2); (C-O-C); ^{1}H nmr (DMSO-d_6): δ 9.39 (dd, J = 6.6, 1.2 Hz, 1H, H-5); 7.78 (td, *J* =8.0, 1.4 Hz, 1H, H-7); 7.70 (dd, *J* = 7.7, 1.2 Hz, 1H, H-8); 7.36 (td, *J* =6.9, 1.6 Hz, 1H, H-6); 5.44 (m, 1H, CH) ; 1.48 (d, *J* = 6.3 Hz, 6H, CH_3) ; cmr: δ 156.1, 140.2, 131.6, 130.6, 126.3, 114.6, 114.3, 71.8, 20.1; ms; m/z (%) 221 M^+ (51), 222 MH^+ (100).

Anal. Calcd. For $C_{10}H_{11}N_3O_3$: C, 54.29; H, 5.01; N, 18.99.Found: C, 53.91, H, 4.65.

General procedure for the synthesis of compounds **7a,b**.

To a well-stirred, cold solution (ice bath) containing 0.2 g (1.06 mmol) of 2-cyano-3-nitroimidazo[1,2-*a*]pyridine (**3**) and 0.1 mL (1.06 mmol) of methyl thioglycolate in DMF (2.1 mL), 0.09 g of sodium bicarbonate (1.06 mmol) was slowly added. The mixture was stirred for 1 h at low temperature and then at room temperature during 2 h. The solution was poured into ice-water and the precipitated cyanothioester was collected by filtration, washed with water (2x5 mL) and cold ethanol (5 mL) The solid was further purified by re-crystallization from ethanol.

Methyl 2-Cyanoimidazo[1,2-*a*]pyridine-3-thioglycolate (**7a**).

This compound was obtained in 88% yield, mp 96-98°C. Ir (KBr cm^{-1}) ν 2250 (CN); 1742 (C=O); 1436 (C=C); ^{1}H nmr (DMSO-d6): δ 8.67 (td, *J* =8.1, 1.1 Hz, 1H, H-5); 7.76 (td, *J* =9.2, 1.1 Hz, 1H, H-8); 7.60 (s, 2H, SCH_2); 3.57 (m, 2H, OCH_3); cmr: δ 168.89, 146.55, 129.04, 125.82, 124.28, 120.23, 117.87, 115.20, 114.22, 52.28, 36.10; ms; m/z (%) 247 M^+ (31), 174 (100).

Anal. Calcd. For $C_{11}H_9N_3O_2S$: C, 53.43; H, 3.66; N, 16.99.Found: C, 53.38; H, 3.45.

2-Cyano-3-propanethiolimidazo[1,2-*a*]pyridine (**7b**).

This compound was obtained in 74% yield, mp 77-78 °C. Ir (KBr cm^{-1}) ν (CN); (C=C); ^{1}H nmr (deuteriochloroform): δ 8.42 (td, *J* = 7.0, 1.1 Hz, 1H, H-5); 7.68 (td, *J* = 9.2, 1.1 Hz, 1H, H-8); 7.43 (ddd, *J* = 9.2, 6.9, 1.2 Hz, 1H, H-7); 7.09 (td, *J* =6.9, 1.1 Hz, 1H, H-6); 2.78 (t, *J* = 7.4 Hz, 3H, SCH_2); 1.6 (m, 2H, CH_2); 1.03 (t, *J* = 7.4 Hz, 3H, CH_3); cmr: δ 146.76, 133.85, 127.84, 125.08, 124.55, 122.74, 118.76, 114.78, 114.31, 38.03, 23.25, 12.96; ms; m/z (%) 217 M^+ (21), 175 (100).

Anal. Calcd. For $C_{11}H_{11}N_3S$: C, 60.80; H, 5.10; N, 19.33. Found: C, 60.52; H, 4.86.

2-Amidoxime-3-nitroimidazo[1,2-*a*]pyridine (**8**).

2-Cyano-3-nitroimidazo[1,2-*a*]pyridine (0.2g, 1.06 mmol), hydroxylamine hydrochloride (0.36 g, 5.32 mmol) and sodium acetate (0.43 g, 5.32 mmol) were suspended in 2-propanol and heated to a reflux temperature for 2 h. The reaction mixture was allowed to cool to room temperature and the formed solid was collected by filtration and washed with cold water. The title compound was isolated as a yellow solid (0.2 g, 85 % yield), mp 178-180 °C. IR (KBr cm^{-1}) ν 3453, 3353 (NH_2); l643 (C=N); 1485, 1338 (NO_2); ^{1}H nmr (DMSO-d_6): δ 9.86 (s, 1H, OH); 9.35

(d, *J* = 6.4 Hz, 1H, H-5); 7.94 (d, *J* = 8.4 Hz, 1H, H-8); 7.82 (td, *J* = 7.8, 1.3 Hz, 1H, H-7); 7.49 (td, *J* = 7.0, 1.2 Hz, 1H, H-6); 5.92 (s, 2H, NH_2): cmr δ 145.9, 143.9, 141.9, 131.3, 127.6, 118.0, 117.3; ms; m/z (%) 221 M^+ (49), 78.1 (100).

Anal. Calcd. For $C_8H_7N_5O_3$: C, 43.44; H, 3.18; N, 31.66. Found: C, 43.08; H, 2.87

3-Aminoimidazo[1,2-*a*]pyridine-2-carbonitrile (**9**).

A mixture of 2-cyano-3-nitroimidazo[1,2-*a*]pyridine **3** (0.5 g, 2.65 mmol) and phenylhydrazine (25.4 mmol) was stirred at 60-70 °C for 12 hours. After cooling, the solid formed was collected by filtration, washed with ethyl ether (10 mL), and recrystallized from ethanol to afford the corresponding 3-amino-imidazo[1,2-*a*]pyridine-2-carbonitrile (**9**) (0.3 g, 73 % yield), mp 238-239 °C (dec.), lit. mp 209-211 °C [18].

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