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OXIDATION OF THE SIDE CHAIN IN NITRATION OF 1,6-SUBSTITUTED PYRROLO[1,2-*a*]PYRAZINES

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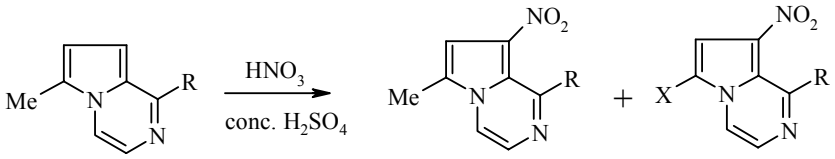
In nitration of 1,6-dimethylpyrrolo[1,2-*a*]pyrazine (**1a**) and 1-ethyl-6-methylpyrrolo[1,2-*a*]pyrazine (**1b**) [1], along with the expected corresponding 8-nitro derivatives **2a,b** we isolated 1-methyl-8-nitropyrrolo[1,2-*a*]-pyrazine-6-carbaldehyde (**3a**) when using nitric acid (d = 1.35 g/ml or d = 1.42 g/ml), or (1-ethyl-8-nitro-pyrrolo[1,2-*a*]pyrazin-6-yl)methanol (**3b**) for nitration by a nitrating mixture with nitric acid (d = 1.42 g/ml).



1a,**b** **2a**,**b** **3a**,**b**

1-3 a R = Me, **b** R = Et; **3 a** X = CHO, **b** X = CH_2OH

For compound **3a**, a singlet from the proton of the formyl group at 9.92 ppm in the ^{1}H NMR spectrum and a signal from the carbonyl C atom at 179.89 ppm in the ^{13}C NMR spectrum are characteristic. In the ^{1}H NMR spectrum of compound **3b**, there is a signal at 4.95 ppm corresponding to the two protons of the hydroxymethyl group.

In the mass spectra of pyrrolo[1,2-*a*]pyrazines **3a** and **3b**, we detect the molecular ions $[M]^+$ 205 and 221 respectively. Products of nitration of the methyl group at the 6 position of the heterocycles are probably formed as intermediates, which then when treated with sulfuric acid are converted to the aldehyde or alcohol according to the Nef reaction [2].

The ^{1}H and ^{13}C NMR spectra were recorded on a Varian VXR-400 (400 MHz), solvent $CDCl_3$, internal standard TMS. The mass spectra were recorded on a Kratos-MS with ionization energy 70 eV.

Nitric acid of the appropriate concentration (6 mmol) was added dropwise with stirring to a solution (cooled down to 0°C) of pyrrolo[1,2-*a*]pyrazines **1a** or **1b** (2 mmol) in conc. H_2SO_4 (3 ml). The mixture was stirred for 72 h at 20°C and then poured over crushed ice. The aqueous solution was neutralized with sodium carbonate, and then the precipitate formed was filtered out and washed with hot water. The mother liquor was extracted with benzene and dried through 3Å sieves. The precipitate and the evaporated extract were combined and chromatographed on a column with Silpearl silica gel in the system benzene–ethyl acetate, 3:1.

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1,6-Dimethyl-8-nitropyrrolo[1,2-*a*]pyrazine (2a). Yield 13% (HNO_3 *d* = 1.35 g/ml) and 17% (HNO_3 *d* = 1.42 g/ml); mp 164-166°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.94 (3H, s, 6-CH_3); 3.04 (3H, s, 1-CH_3); 7.32 (1H, s, H-7); 7.62 (1H, d, J_{34} = 4.27, H-3); 7.86 (1H, d, J_{43} = 4.27, H-4). Found, %: C 56.36; H 4.57; N 21.52. $C_9H_9N_3O_2$. Calculated, %: C 56.54; H 4.71; N 21.99.

1-Ethyl-6-methyl-8-nitropyrrolo[1,2-*a*]pyrazine (2b). Yield 70% (HNO_3 *d* = 1.35 g/ml) and 15% (HNO_3 *d* = 1.42 g/ml); mp 128-130°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.35 (3H, t, *J* = 7.39, $CH_2\underline{CH_3}$); 2.49 (3H, s, 6-CH_3); 3.43 (2H, q, *J* = 7.39, $\underline{CH_2}CH_3$); 7.34 (1H, s, H-7); 7.63 (1H, d, J_{34} = 4.78, H-3); 7.92 (1H, d, J_{43} = 4.78, H-4). Found, %: C 58.34; H 5.55; N 20.21. $C_9H_{11}N_3O_2$. Calculated, %: C 58.54; H 5.37; N 20.49.

1-Methyl-8-nitropyrrolo[1,2-*a*]pyrazine-6-carbaldehyde (3a). Yield 10% (HNO_3 *d* = 1.35 g/ml) and 3% (HNO_3 *d* = 1.42 g/ml); mp 204°C (decomposition). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.09 (3H, s, 1-CH_3); 8.14 (1H, s, H-7); 8.18 (1H, d, J_{34} = 4.37, H-3); 9.51 (1H, d, J_{43} = 4.37, H-4); 9.92 (1H, s, CHO). ^{13}C NMR spectrum, δ, ppm: 26.64 (CH_3); 117.97 ($C_{(7)}$); 122.09 ($C_{(6)}$); 123.82 ($C_{(4)}$); 125.26 ($C_{(8)}$); 128.49 ($C_{(9)}$); 133.79 ($C_{(3)}$); 154.09 ($C_{(1)}$); 179.89 (CHO). Found, %: C 52.36; H 3.02; N 20.37. $C_9H_7N_3O_3$. Calculated, %: C 52.68; H 3.41; N 20.49.

(1-Ethyl-8-nitropyrrolo[1,2-*a*]pyrazin-6-yl)methanol (3b). Yield 9% (HNO_3 *d* = 1.42 g/ml); mp 144-146°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.34 (3H, t, *J* = 7.28, $CH_2\underline{CH_3}$); 3.42 (2H, q, *J* = 7.28, $\underline{CH_2}CH_3$), 4.95 (2H, s, $\underline{CH_2}OH$); 7.47 (1H, s, H-7); 7.94 (1H, d, J_{34} = 4.25, H-3), 8.08 (1H, d, J_{43} = 4.25, H-4). ^{13}C NMR spectrum, δ, ppm: 13.26 ($CH_2\underline{CH_3}$); 31.66 ($\underline{CH_2}CH_3$); 56.18 (CH_2OH); 114.07 ($C_{(7)}$); 115.45 ($C_{(4)}$); 115.55 ($C_{(6)}$); 123.11 ($C_{(8)}$); 124.86 ($C_{(9)}$); 126.78 ($C_{(1)}$); 130.53 ($C_{(3)}$). Found, %: C 54.10; H 4.77; N 18.88. $C_{10}H_{11}N_3O_3$. Calculated, %: C 54.29; H 4.98; N 19.00.

REFERENCES

1. V. I. Terenin, E. V. Kabanova, and Yu. G. Bundel, *Khim. Geterotsikl. Soedin.*, 763 (1991).
2. W. E. Noland, *Chem. Rev.*, **55**, 137 (1955).