NITRATION OF 1-METHYL-2-PYRIDONE

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Nitration of 1-methyl-2-pyridone with 70% nitric acid or fuming nitric acid at 0-20°C proceeds in the 3 and 5 positions to give a mixture of mononitro isomers, the structures of which were proved by PMR spectroscopy. Mainly 3,5-dinitro-1-methyl-2-pyridone is formed by the action of fuming nitric acid or a nitrating mixture at 90°.

Selective entry of substituents into the 3 or 5 position of the heteroring is observed in some electrophilic substitution reactions of 2-pyridones. While chlorination of 2-pyridone [1], for example, proceeds (under the monosubstitution conditions) only in the 5 position, the substituent enters the 3 position in the nitration of 6-phenyl-2-pyridone [2]. The possible stabilization of the transition state, because of the formation of a "chelate" bond between the hydroxy and nitro groups, was assumed to be the explanation for the indicated selectivity during nitration [2, 3].

If the formation of such bonds is excluded, one may expect nonselective reaction, for example, in the nitration of N-substituted 2-pyridones, for which the formation of such chelates is impossible. In the present research we have investigated the action of nitric acid and a nitrating mixture (under various conditions) on 1-methyl-2-pyridone (I) (see Table 1), regarding the nitration of which contradictory data are presented in [4-6].

According to our data, the nitration of I under mild conditions (70% nitric acid at 20°C) leads to a mixture of 3- and 5-nitro-1-methyl-2-pyridones in a ratio of 2:1 [according to the results of gas-liquid chromatography (GLC)].



Both isomers (II and III) were isolated by chromatography. Their structure was confirmed by comparison of their PMR spectra with the spectra described for 3- and 5-nitro-1-methyl-2-pyridones obtained by methylation of 3-nitro-2-pyridone and diazotization of 5-nitro-2-aminopyridine, respectively [7].

Nitrating agent	t, °C, time, h'	Yield of nitration products, %		
		3-NO ₂ (II)	5-NO ₂ (111)	3,5-di-NO ₂ (IV)
HNO ₃ (<i>d</i> 1,41; 70%) Same	20, 48 20, 240	35,0 46,4	17,0* 17,6	27,0
$HNO_3^{"}$ (d 1,50; 98%) Same	90, 1 0, 3 90, 3	26,0 24,0 Traces	16,0 Traces	Traces 30,0
H_2SO_4 (d 1,84) + HNO ₃ (d 1,50) Same	0, 3 90, 3	28,5 Traces	14,3 Traces	11,0 41,0

TABLE 1. Conditions for the Nitration of 1-Methyl-2-pyridone (I) and Composition and Yields of the Reaction Products

*A total of 40% of the starting 1-methyl-2-pyridone was isolated.

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Raising the temperature in nitration with 70% nitric acid to 90° does not promote selectivity of the reaction; increasing the reaction time leads to 3,5-dinitro-1-methyl-2-pyridone (IV) and mononitro isomers II and III.

Nitration of pyridone I with fuming nitric acid (sp. gr. 1.5) at 0° gives a mixture of II and III in a ratio of 3:2, while the action of this reagent at 90° leads to dinitro compound IV.



We obtained 3-nitro isomer II, 5-nitro isomer III, and dinitro compound IV in the nitration of I with a mixture of concentrated sulfuric acid and fuming nitric acid at 0°; the chief product at 90° was dinitropyridone IV along with small amounts of the 3- and 5-nitro isomers.

The structure of 3,5-dinitro-1-methyl-2-pyridone (IV) is confirmed by its PMR spectrum, in which there are two doublets at 8.81 and 9.40 ppm (signals from the protons in the 4 and 6 positions, respectively) with a coupling constant (J) of 3 Hz.

Thus the nitration of 1-methyl-2-pyridone proceeds nonselectively under monosubsubstitution conditions. An increase in the acidity of the nitrating agent is not reflected substantially in the ratio of mononitro products. An increase in temperature leads to the production of primarily dinitro compound IV.

EXPERIMENTAL

The PMR spectra of dimethyl sulfoxide solutions were recorded with a Varian T-60 spectrometer with hexamethyldisiloxane (HMDS) as the internal standard. Gas-liquid chromatography (GLC) was carried out with a Pai analytical argon chromatograph with a 1-m-long column with a diameter of 4 mm (QF 11%). The carrier gas was argon, the flow rate was 100 cm³/min, and the temperature was 200°.

<u>Nitration with 70% Nitric Acid at 20°</u>. A 4.5-g (0.041 mole) sample of pyridone I was added dropwise with stirring at 20° to 45 ml (0.72 mole) of HNO_3 (sp. gr. 1.41) in the course of 80 min, after which the mixture was allowed to stand for 2 days. It was then poured into ice water, and the aqueous mixture was neutralized with 40% sodium hydroxide solution and extracted with chloroform. The starting pyridone (I), 5-nitro-1-methyl-2-pyridone (III), and 3-nitro-1-methyl-2-pyridone (II) in a ratio of 2:1:2 (retention times of 1 min 30 sec, 2 min 10 sec, and 7 min 31 sec, respectively) were detected in the dried (with magnesium sulfate) chloroform solution by GLC. The solvent was evaporated, and the residue was recrystallized from benzene to give 3.3 g of a mixture of II and III with mp 130-140° and R_f 0.60 and 0.78 (in chloroform) in 52% yield.

<u>Nitration with 70% Nitric Acid at 90°.</u> A 3.5-g (0.032 mole) sample of I was added in the course of an hour to 35 ml (0.54 mole) of 70% HNO₃ (sp. gr. 1.41) at 40°, after which the mixture was heated on a boiling-water bath for 1 h. It was then cooled and poured into ice water, and the aqueous mixture was neutralized with 40% sodium hydroxide solution and extracted with chloroform in an extractor. Thin-layer chromatography (TLC) of the dried chloroform solution on Al_2O_3 showed the presence of three substances with R_f 0.07, 0.60, and 0.78. Chromatography of this solution with a column filled with 400 g of Al_2O_3 yielded the following materials successively: 1) 5-nitro-1-methyl-2-pyridone (III) with mp 174-175° [from benzene, 1.26 g (26%), R_f 0.78. PMR spectrum (δ , ppm): 6.49 (H, d, * 3-H), 8.10 (1H, q, 4-H), 9.11 (1H, q, 6-H). According to [7], this substance has mp 173-175°]; 2) 3-nitro-1-methyl-2-pyridone (II) with mp 175-176° [from benzene, 1.26 g (26%), R_f 0.60. PMR spectrum (δ , ppm): 6.36 (1H, t, 5-H), 8.20 (1H, t, 6-H), 8.32 (1H, t, 4-H). According to [7], this compound has mp 175-177°]; 3) 3,5-dinitro-1-methyl-2-pyridone with mp 177° [from ethanol, 0.25 g (4.4%), R_f 0.07. According to [8], this compound has mp 175-177°].

<u>Nitration with Fuming Nitric Acid at 0°</u>. A 1.5 ml (0.014 mole) sample of I was added dropwise with stirring at 0° to 15 ml (0.35 mole) of fuming HNO_3 (sp. gr. 1.5), and the mixture was stirred at 0° for another 3 h, after which it was poured into ice water. The aqueous mixture was neutralized with 40% sodium hydroxide solution and extracted with chloroform in an extractor. The chloroform solution was dried over magnesium sulfate and worked up to give 0.8 g (40%) of a mixture of 3- and 5-mononitro isomers III and III in a ratio of 2:1 according to GLC (the retention times were 7 min 31 sec and 2 min 11 sec, respectively).

^{*}The following abbreviations were adopted: d is doublet, q is quartet, and t is triplet.

<u>Nitration with Fuming Nitric Acid at 90°</u>. <u>3,5-Dinitro-1-methyl-2-pyridone (IV)</u>. A 2.5-g (0.023 mole) sample of the pyridone was added dropwise with stirring to 25 ml (0.58 mole) of fuming HNO₃ (sp. gr. 1.5), after which stirring was continued and the mixture was heated at 90° for 3 h. It was then cooled and poured into ice water. The aqueous mixture was neutralized with 40% sodium hydroxide solution, and the precipitated pale-yellow crystals were removed by filtration and washed with ice water to give 0.8 g of 3,5-dinitro-1-methyl-2-pyridone [IV, mp 177° (from ethanol), R_f 0.07]. PMR spectrum (δ , ppm): 8.81 (1H, d, 4-H), 9.40 (1H, d, 6-H). According to [8], this compound has mp 175-177°. The mother liquor was extracted with chloroform to give yellow crystals (0.55 g) of the dinitro compound (IV, R_f 0.07) containing a small amount of mononitro isomers (R_f 0.60 and 0.78 in chloroform according to TLC).

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