STRUCTURES AND CONSTANTS OF THE PRODUCTS OF NITRATION OF 1-ACETYL-1,2,3,4-TETRAHYDROQUINOLIN-4-ONE

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1,2,3,4-Tetrahydroquinolin-4-one and its 1-acetyl derivative were nitrated, and it was established that mixtures of nitroquinolones are formed. 6-Nitro-1,2,3,4-tetrahydroquinolin-4-one, 6,8-dinitro-1,2,3,4-tetrahydroquinolin-4-one, 8-nitro-quinolin-4-one, and 6,8-dinitroquinolin-4-one were isolated by means of preparative chromatography and characterized.

In [1] it was shown that the nitration of 1-acety1-1,2,3,4-tetrahydroquinolin-4-one (Ib) with the usual nitrating mixture at 0°C gives a compound with mp 121°C, which, in the opinion of the authors, is 1-acety1-6-nitro-1,2,3,4-tetrahydroquinolin-4-one (IIb).

In order to confirm the constants of 6-nitro-1,2,3,4-tetrahydroquinolin-4-one (IIa), which we had previously synthesized by decarboxylation of N-(2-carboxy-4-nitrophenyl)- β -alanine [2], we attempted to obtain nitroquinolone IIa by another method, viz. by nitration of quinoline Ib. We carried out the nitration of quinolones Ia, b under various conditions and established that mixtures of nitroquinolones were formed in all cases.

The following compounds were isolated by preparative chromatography from the mixture obtained after acidic hydrolysis when the nitration of quinolone Ib was carried out under the conditions of [1]: 6-nitro-1,2,3,4-tetrahydroquinolin-4-one (IIa), which had mp 232-234°C and, with respect to its constants, properties, and IR spectrum, was identical to the quinolone that we obtained in [2]; and 6,8-dinitroquinolin-4-one (III) with mp 258-260°C.

Workup of the mixture of products of nitration of quinolone Ib with potassium nitrate in sulfuric acid at 0°C gave quinolone III and 8-nitroquinolin-4-one (IV), which corresponds to the quinolone obtained by cyclization of N-(2-nitrophenyl)- β -alanine in polyphosphoric acid (PPA) with subsequent dehydrogenation of the isolated 8-nitro-1,2,3,4-tetrahydroquinolin-4-one [3].



Workup of the mixture of nitro compounds obtained in the nitration of quinolone Ib with nitric acid in acetic anhydride gave 6,8-dinitro-1,2,3,4-tetrahydroquinolin-4-one (V), which corresponds to the quinolone obtained by cyclization of N-(2,4-dinitrophenyl)- β -alanine in PFK [4], and quinolone III. An intense band of a C=O group is observed in the IR spectrum of quinolone III, and there are two bands in the region of the symmetrical stretching vibrations of the NO₂ group that correspond to two nonequivalent nitro groups, but bands of

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Com- pound	mp , ° C	Found, %				Calculated,%			IR spectrum, ν , cm ⁻¹			
		с	н	N	formula	с	н	N	NO2	C=0	CH ₂ CH ₂	NH
IIa	232-234	56,3	4,3	14,4	$C_9H_8N_2O_3$	56,2	4,2	14,6	1327	1668	2863, 2932	3341
ш	258—260	46,5	2,4	17,4	$C_9H_5N_3O_3$	46,0	2,1	17,7	1325, 1346	1648		3107
IV*	200202			14,6	$C_9H_6N_2O_3$	_		14,7	1328	1696	_	3357
V	171—173	45,8	3,1	17,7	$C_9H_7N_3O_5$	45,6	3,0	17,7	1320, 1343	1690	2870, 2930	3366
VI	209—211	39,9	3,3	14,0	$C_{10}H_9N_3O_8$	40,1	3,05	14,0	1340, 1330	1708, 1692	—	3318
					ī					ArCOOH		

TABLE 1. Characteristics of the Nitroquinolones

*In agreement with the literature data [3].

methylene groups are absent. Two doublet signals at 7.0 (J = 8 Hz) and 8.5 ppm (J = 8 Hz), which are due to the α and β protons of the quinoline ring (the signals of the protons attached to the double bond of the other tautomeric form of quinolone III should be observed at considerably stronger field), and a singlet at 10.1 ppm due to the proton of a hydroxy group are observed in the PMR spectrum of quinolone III. These data and the chemical properties of quinolone III make it possible to assume the existence of two tautomeric forms.

In addition, the structure of quinolone III was confirmed by alternative synthesis via the scheme



The formation of quinolone III in the nitration and decarboxycyclization reactions is explained by the tendency of 2,3-dihydroquinolin-4-[1H]ones to undergo aromatization, which is particularly facilitated by the presence of electron-acceptor nitro groups, which decrease the electron density on the carbon atoms in the ring. In addition, the nitro group itself may be an oxidizing agent, thereby undergoing reduction to an amino group in the process. The presence of an aromatic amino group in the filtrates was established by a qualitative test (by diazotization and coupling with β -naphthol).

Quinolone V, which was obtained by decarboxycyclization of N-(2-carboy-4,6-dinitrophenyl)- β -alanine, was completely identical with respect to its constants, properties, and IR and PMR spectra to the dinitroquinolone isolated in the nitration of quinolone I.

EXPERIMENTAL

The IR spectra of KBr pellets of the compounds were recorded with a UR-20 spectrometer. The UV spectra of solutions of the compounds in alcohol were recorded with a Specord UV-vis spectrophotometer. The PMR spectrum was recorded with a Varian T-60 spectrometer with tetramethylsilane as the internal standard.

<u>6-Nitro-1,2,3,4-tetrahydroquinolin-4-one (IIa) and 6,8-Dinitroquinolin-4-one (III).</u> A mixture of 7.6 ml of concentrated H_2SO_4 and 4.5 ml of nitric acid (sp. gr. 1.5) was cooled to 0°C, 7.56 g (0.04 mole) of quinolone Ib was sprinkled in with stirring at this temperature, and the mixture was maintained at 0°C for 30 min, after which it was poured over 500 g of ice. The precipitate was removed by filtration and washed with water to give 4.7 g of a mixture of compounds (mp 100-110°C), from which 2.1 g of a yellow substance with mp 130-135°C was isolated after removal of the acetyl protective group by acid hydrolysis under the conditions in [2]. The mixture was separated preparatively in a layer of Al_2O_3 by elution with alcohol-benzene (2:9). The eluate was distilled, and the residue was crystallized from alcohol to give 0.8 g of quinolone II and 0.2 g of quinolone III. <u>8-Nitroquinolin-4-one (IV) and 6,8-Dinitroquinolin-4-one (III).</u> A 1.47-g (0.01 mole) sample of quinolone Ia was dissolved in 10 ml of concentrated H_2SO_4 , the solution was cooled to -15°C, and a solution of 1.01 g (0.01 mole) of potassium nitrate in 75 ml of concentrated H_2SO_4 was added dropwise with stirring while maintaining the temperature at -5 to 0°C. The mixture was maintained at 0°C for 2 h, after which it was poured over 100 g of ice. The yellow precipitate was removed by filtration and washed with water to give 1.8 g (94%) of a substance with mp 150-160°C, which, according to TLC data, was a mixture of substances. Preparative separation by means of TLC on Al_2O_3 and crystallation from alcohol gave 0.3 g of quinolone IV and 0.2 g of quinolone III.

6,8-Dinitro-1,2,3,4-tetrahydroquinolin-4-one (V) and Quinolone III. A 3.8-g (0.02 mole) sample of quinolone Ib was added with stirring at 0°C to a cooled (to -5°C) mixture of 3.2 ml of nitric acid (sp. gr. 1.4) and 20 ml of acetic anhydride, and the mixture was maintained at 0°C for 2 h, after which it was poured over 300 g of ice. A 10-ml sample of 5% aqueous NaHCO₃ solution was added to the aqueous mixture, and the precipitate was separated and washed with water. After acid hydrolysis, the substance was separated preparatively on silica gel by elution with alcohol to give 0.3 g of quinolone V and 0.2 g of quinolone III.

<u>N-(2-Carboxy-4,6-dinitrophenyl)- β -alanine (VI).</u> A mixture of 24.6 g (0.1 mole) of 2-chloro-3,5-dinitrobenzoic acid, 9.8 g (0.11 mole) of β -alanine, and 94.5 g (1 mole) of phenol was heated with stirring at 120 °C for 5 h, after which it was cooled and treated with petroleum ether. The mixture was filtered, and the substance obtained was crystallized from alcohol. The yield was 18.5 g (62%).

Preparation of 6,8-Dinitro-1,2,3,4-tetrahydroquinolin-4-one (V) and Quinolone III by Decarboxycyclization of Acid VI. A mixture of 4.5 g (0.015 mole) of VI, 2.94 g (0.03 mole) of potassium acetate, and 45 ml of acetic anhydride was heated with stirring at 100-110°C until carbon dioxide evolution ceased (2.5 h) and then at 120-125°C for another 30 min. The acetic anhydride was removed by distillation, and water, ethyl acetate, and 10 ml of 5% aqueous sodium bicarbonate were added to the residue. The organic layer was separated, washed with water, dried with Na₂SO₄, and evaporated to give 1.7 g (31%) of a mixture of quinolones, which was subjected to acid hydrolysis and separated preparatively on silica gel by elution with alcohol to give 0.5 g of quinolone V and 0.2 g of quinolone III.

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