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SHORT COMMUNICATIONS

Acid and Alkaline Hydrolysis of Substituted 5-Aryl-1,2-oxazolidine-3,3-dicarbonitriles

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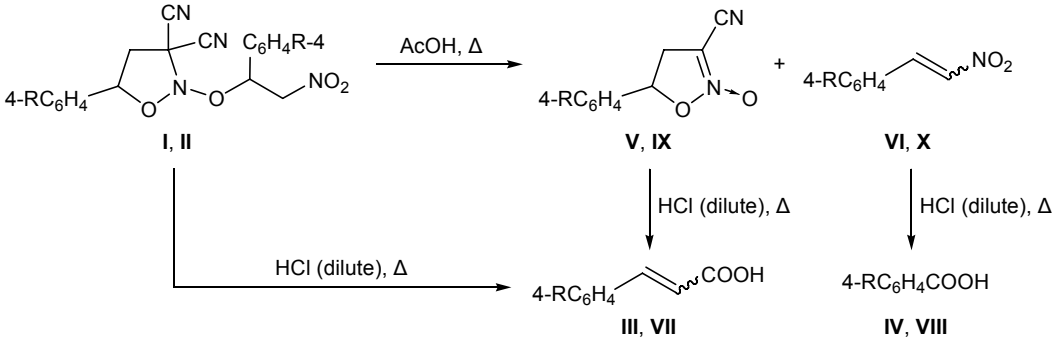
There are no published data on chemical transformations of 2,5-substituted 1,2-oxazolidine-3,3-dicarbonitriles. With a view to elucidate the direction of hydrolysis of substituted 5-aryl-1,2-oxazolidine-3,3-dicarbonitriles we examined the reaction of 2-(2-nitro-1-phenylethoxy)-5-phenyl-1,2-oxazolidine-3,3-dicarbonitrile (**I**) with dilute (1:1) hydrochloric acid. As a result, we obtained cinnamic acid **III** and benzoic acid (**IV**) which were formed, respectively, from the isoxazolidine fragment and side chain of compound **I**.

Presumably, the process involves both cleavage of the isoxazolidine ring at the N^2–C^3 and O^1–C^5 bonds and decomposition of the 2-nitro-1-phenylethoxy substituent. Our attempt to perform hydrolysis of the cyano group in **I** under mild conditions (in acetic acid) resulted in the formation of 5-phenyl-4,5-dihydro-1,2-oxazole-3-carbonitrile 2-oxide (**V**) and 2-nitroethenylbenzene (**VI**). Analogous transformations occurred in acid hydrolysis of 5-(4-methylphenyl)-2-[2-nitro-1-(4-methylphenyl)ethoxy]-1,2-oxazolidine-3,3-dicarbonitrile (**II**) (Scheme 1).

It was reasonable to presume that substituted 4,5-dihydro-1,2-oxazole-3-carbonitriles **V** and **IX** and the corresponding nitroethenes **VI** and **X** are formed as intermediate products in the acid hydrolysis of 1,2-oxazoles **I** and **II** under severe conditions. In fact, by heating compound **V** in dilute hydrochloric acid we obtained cinnamic acid (**III**), while the hydrolysis of nitroethene **VI** under similar conditions gave benzoic acid (**IV**).

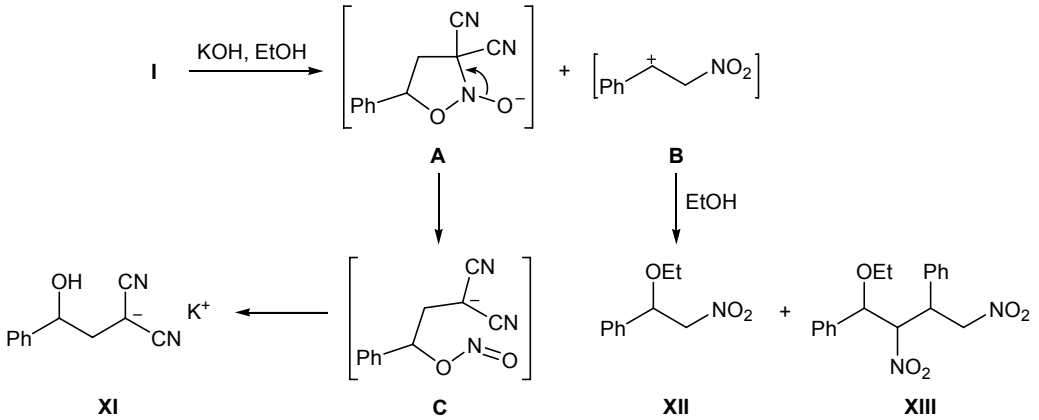
The reaction of compound **I** with an alcoholic solution of alkali under mild conditions afforded 2-(2-hydroxy-2-phenylethyl)propane-1,3-dinitrile potassium salt (**XI**), (1-ethoxy-2-nitroethyl)benzene (**XII**), and (1-ethoxy-2,4-dinitrobutan-1,3-diyl)dibenzene (**XIII**) (Scheme 2). The formation of compounds **XII** and **XIII** suggests initial generation of intermediates **A** and **B**, followed by stabilization of the latter via addition of ethanol molecule with formation of ethoxy derivative **XII**. Intermediate **A** is likely to undergo cleavage of the isoxazole ring at the N^2–C^3 bond to produce compound **XI** through carbanion **C**.

Scheme 1.



I, **III**–**VI**, R = H; **II**, **VII**–**X**, R = Me.

Scheme 2.



Alkaline hydrolysis of isoxazole **I** under severe conditions resulted in the formation of a tarry product which was not identified.

Compounds **III**–**X**, **XII**, and **XIII** showed no depression of the melting point on mixing with authentic samples.

5-Aryl-1,2-oxazolidine-3,3-dicarbonitriles I and II (*general procedure*). A solution of 5 mmol of 2,2-dinitromalononitrile in 10 ml of anhydrous diethyl ether was cooled to 0±5°C, a solution of 10 mmol of ethenylbenzene or 4-ethenyltoluene in diethyl ether was added, and the mixture was kept for 10 days at 25°C. The mixture was evaporated, and the residue was subjected to chromatography in a 10×500-mm column charged with activated silica gel (100–400 μm) using $CHCl_3$ (compound **I**) or benzene (**II**) as eluent.

2-(2-Nitro-1-phenylethoxy)-5-phenyl-1,2-oxazolidine-3,3-dicarbonitrile (I). Yield 0.464 g (25%), mp 115°C. IR spectrum, ν, cm^{-1}: 2245 (C≡N); 1550, 1380 (NO_2); 1070–1030 (ONO). ^1H NMR spectrum, δ, ppm: 3.14 d (2H, CH_2), 4.28 d (2H, CH_2), 5.46 t (1H, CH), 5.82 t (1H, CH), 7.53–7.62 m (10H, C_6H_5). Found, %: C 62.46; H 4.22; N 15.18. $C_{19}H_{16}N_4O_4$. Calculated, %: C 62.64; H 4.40; N 15.38.

5-(4-Methylphenyl)-2-[1-(4-methylphenyl)-2-nitroethoxy]-1,2-oxazolidine-3,3-dicarbonitrile (II). Yield 0.529 g (27%), mp 144°C. IR spectrum, ν, cm^{-1}: 2245 (C≡N); 1550, 1380 (NO_2); 1070–1030 (ONO). ^1H NMR spectrum, δ, ppm: 2.31 s (3H, CH_3), 3.10 d (2H, CH_2), 4.30 d (2H, CH_2), 5.42 t (1H, CH), 5.80 t (1H, CH), 7.15–7.53 m (8H, C_6H_4). Found, %: C 64.11; H 4.91; N 14.08. $C_{21}H_{20}N_4O_4$. Calculated, %: C 64.29; H 5.10; N 14.29.

Hydrolysis of 5-aryl-1,2-oxazolidine-3,3-dicarbonitriles I and II in hydrochloric acid (*general procedure*). A mixture of 5 mmol of compound **I** or **II**, 30 ml of concentrated hydrochloric acid, and 10 ml of water was heated for 2 h under reflux. The mixture was cooled, and the precipitate was filtered off. Yield of cinnamic acid (**III**) 0.414 g (56%), mp 132°C [1]; yield of compound **VII** 0.470 g (58%), mp 198°C [2]. The filtrate was evaporated to isolate 0.122 g (20%) of benzoic acid (**IV**), mp 122°C [3], or 0.150 g (22%) of *p*-toluic acid (**VIII**), mp 178°C [4].

Hydrolysis of 5-aryl-1,2-oxazolidine-3,3-dicarbonitriles I and II in acetic acid (*general procedure*). A mixture of 5 mmol of compound **I** or **II**, 40 ml of acetic acid, and 10 ml of water was heated under reflux until nitrogen dioxide no longer evolved (~1 h). The mixture was evaporated, and the residue was subjected to chromatography using benzene (compounds **V** and **IX**) or hexane (**VI**, **X**) as eluent.

5-Phenyl-4,5-dihydro-1,2-oxazole-3-carbonitrile 2-oxide (V). Yield 0.658 g (70%), mp 90°C (from ethanol) [5].

2-Nitroethenylbenzene (VI). Yield 0.387 g (52%), mp 58°C (from ethanol) [6].

5-(4-Methylphenyl)-4,5-dihydro-1,2-oxazole-3-carbonitrile 2-oxide (IX). Yield 0.737 g (73%), mp 76°C (from ethanol) [5].

1-Methyl-4-(2-nitroethenyl)benzene (X). Yield 0.489 g (60%), mp 97°C (from ethanol) [7].

Hydrolysis of 5-aryl-4,5-dihydro-1,2-oxazole-3-carbonitrile 2-oxides V and IX in hydrochloric acid (*general procedure*). A mixture of 3 mmol of compound **V** or **IX**, 10 ml of concentrated hydrochloric acid, and 5 ml of water was heated for 1.5 h under reflux. The mixture was cooled, and the precipitate was filtered off. Yield of **III** 0.198 g (45%), mp 132°C [1]; yield of **VII** 0.230 g (48%), mp 198°C [2].

Hydrolysis of (2-nitroethenyl)benzenes VI and X in hydrochloric acid (*general procedure*). A mixture

of 3 mmol of compound **VI** or **X**, 10 ml of concentrated hydrochloric acid, and 5 ml of water was heated for 2 h under reflux. After cooling, 0.135 g (41%) of **IV**, mp 122°C [3], or 0.181 g (43%) of **VIII**, mp 178°C [4], was isolated.

Alkaline hydrolysis of 2-(2-nitro-1-phenylethoxy)-5-phenyl-1,2-oxazolidine-3,3-dicarbonitrile (I). A solution of 5 mmol of potassium hydroxide in 20 ml of ethanol was slowly added under stirring to 5 mmol of compound **I**. The mixture was heated for 3 h on a water bath, and the precipitate was filtered off. Yield of compound **XI** 0.717 g (64%), decomposition point 194–196°C (from methanol). IR spectrum, ν, cm^{-1}: 3545 (OH), 2230 (C≡N). ^1H NMR spectrum, δ, ppm: 3.52 d (2H, CH_2), 5.03 d (1H, OH), 5.28 q (1H, CH), 7.51 m (5H, C_6H_5). Found, %: C 58.74; H 3.82; N 12.34. $C_{11}H_9N_2KO$. Calculated, %: C 58.93; H 4.02; N 12.50.

The filtrate was evaporated, the residue was diluted with diethyl ether, and the mixture was acidified with dilute hydrochloric acid to pH 4 (litmus). The organic layer was separated, dried over Na_2SO_4, and evaporated, and the residue was subjected to chromatographic separation. Elution with carbon tetrachloride gave 0.098 g (10%) of compound **XII**, n_D^{20} = 1.5220 [8], and subsequent elution with chloroform afforded 0.086 g (5%) of compound **XIII**, mp 154–155°C [8].

The IR spectra were recorded in KBr on an IKS-29 spectrometer. The ^1H NMR spectra were obtained on a Tesla BS-487C spectrometer (80 MHz) from solutions in D_2O using hexamethyldisiloxane as internal reference. The progress of reactions and the purity of products were monitored by TLC on Silufol UV-254 plates using acetone–hexane (2:3) as eluent; development with iodine vapor.

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