

Reaction of 4,4-Dimethyl-1,3-dioxane with Dinitriles

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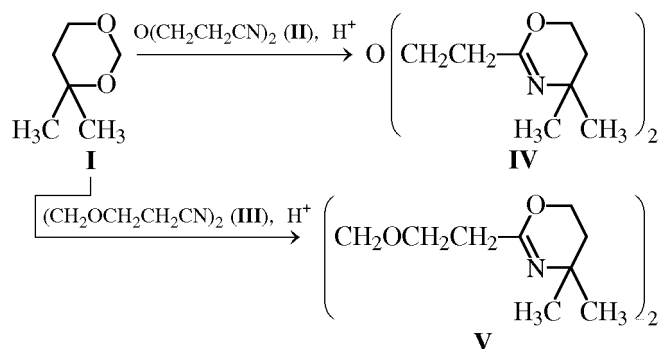
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Abstract—The reaction of 4,4-dimethyl-1,3-dioxane with bis(2-cyano)diethyl ether or 1,2-di(β-cyanoethoxy)ethane yields the corresponding bis[2-(4,4-dimethyl-5,6-dihydro-2-oxazinyl)]diethyl ether and 1,2-di{β-[2-(4,4-dimethyl-5,6-dihydro-2-oxazinyl)]ethoxy}ethane which are readily hydrolyzed under the action of aqueous alkali to give 3-methyl-3-amino-1-butanol.

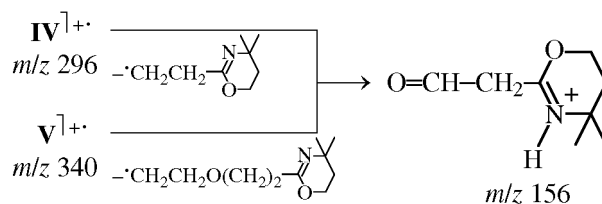
One of the reasonably simple routes to 5,6-dihydro-1,3-oxazines, which are important precursors of 1,3-amino alcohols and aldehyds [1, 2], is based on the reaction of 1,3-dioxanes with acetonitrile [3–5]. As the above transformation is a modification of the Ritter reaction, it follows the principal relationships of formation of a new C–N bond involving the nitrile group [6, 7], on the one hand, and of the majority of heterolytic reactions of 1,3-dioxacycloalkanes [8], on the other hand. In this connection, proceeding with studies of reactions of 1,3-heterocycles with nitriles [9], we examined in this work the reactions of 4,4-dimethyl-1,3-dioxane (**I**), which can be readily prepared by the Prins reaction, with bis(2-cyano)diethyl ether (**II**) and 1,2-di(β-cyanoethoxy)ethane (**III**). These reactions were not reported previously.

The products of these reactions were the corresponding bis[2-(4,4-dimethyl-5,6-dihydro-2-oxazinyl)]diethyl ether (**IV**) and 1,2-di{β-[2-(4,4-dimethyl-5,6-dihydro-2-oxazinyl)]ethoxy}ethane (**V**).



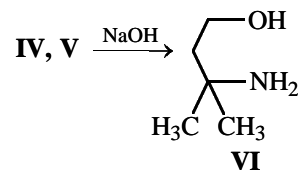
The maximal yield of derivatives **IV** and **V** was 10%. The IR spectra of these compounds contain a strong band $\nu_{\text{C=N}}$ at 1650 cm⁻¹. In addition, the compositions and structures of the obtained compounds

were confirmed by mass spectrometry and ¹H NMR spectroscopy (see table). The molecular ion peaks are lacking in the mass spectra, but the characteristic fragmentation ions are present.



The significantly lower, as compared to the reaction between dioxane **I** and acetonitrile [3–5], yield of compounds **IV** and **V** is probably due to some side polymerization reactions involving dinitriles [6]. Indeed, significant amount of bottoms (up to 60% of the initial weight) remains after vacuum distillation. The other cause is the hydrolytic instability of oxazines **IV** and **V**: noticeable amounts of 3-methyl-3-amino-1-butanol **VI** were detected in the reaction products by GLC.

On hydrolysis with aqueous alkali, compounds **IV** and **V** with the yield of 70–74% give amino alcohol **VI** identified by GLC using a reference sample [3, 10].



The new reactions supplement the known chemical transformations of 1,3-dioxanes [8], though they cannot be recommended as a preparative route to 5,6-dihydro-1,3-oxazine derivatives because of the low yield of the target compounds.

¹H NMR spectra and first fragment ions in the mass spectra of compounds **IV** and **V**

Compound no.	δ , ppm (³ J, Hz)	Assignment ^a	m/z (<i>I</i> _{rel} , %)
IV	1.09 s (6H)	(CH ₃) ₂ -C ⁴	195 (4) [M - C ₅ H ₁₁ NO] ⁺
	1.62 t (2H, <i>J</i> 6.0)	C ⁵ H ₂	156 (100) [M - C ₈ H ₁₄ NO] ⁺
	2.29 t (2H, <i>J</i> 6.5)	CH ₂ -C ²	141 (28) [M - C ₈ H ₁₄ NO - CH ₃] ⁺
	3.59 t (2H, <i>J</i> 6.5)	O-CH ₂ acyclic	
	4.07 t (2H, <i>J</i> 6.0)	C ⁴ H ₂	
V	1.12 s (6H)	(CH ₃) ₂ -C ⁴	156 (40) [M - C ₁₀ H ₁₈ NO ₂] ⁺
	1.55 t (2H, <i>J</i> 6.0)	C ⁵ H ₂	141 (10) [M - C ₁₀ H ₁₈ NO ₂ - CH ₃] ⁺
	2.28 t (2H, <i>J</i> 6.3)	CH ₂ -C ²	
	3.54 t (2H, <i>J</i> 6.3)	O-C-CH ₂ -O	
	3.56 t (2H, <i>J</i> 6.3)	O-CH ₂ -C-C=N	
	4.08 t (2H, <i>J</i> 6.0)	C ⁶ H ₂	

^a The inner atom numbering in the oxazine ring is given.

EXPERIMENTAL

The IR spectra were obtained on a Specord IR-75 spectrophotometer in thin films; the ¹H NMR spectra were recorded on a Tesla BS-497 spectrometer from 20% solutions in CDCl₃, with TMS as internal reference. The mass spectra were measured on an MKh-1321 instrument at the ionizing electron energy of 70 eV. The GLC analysis was carried out on a Tsvet-126 chromatograph (flame-ionization detector, 3000 × 4-mm column, stationary phase 5% OV-17 on Chromaton N-Super, carrier gas argon).

Derivatives of 4,4-dimethyl-5,6-dihydro-1,3-oxazines IV and V. To a mixture of 0.6 mol of dioxane **I** and 0.25 mol of dinitrile **II** or **III** in 150 ml of hexane, 0.3 mol of concentrated H₂SO₄ was slowly added dropwise with stirring and cooling with ice-cold water (attempted addition of 1,3-dioxane to a mixture of dinitrile and sulfuric acid led to tarring). Then the reaction mixture was stirred at room temperature for 24 h and diluted with 100 ml of water; hexane was separated in a separating funnel, and the aqueous layer was extracted with chloroform (2 × 50 ml). After evaporation of the combined organic layers, we recovered 15–20 ml of the initial dioxane **I**. To the remaining aqueous phase, cooled with ice, solid LiOH was added to attain pH 9–10. The separated oily reaction product with a specific odor was extracted with chloroform (4 × 50 ml) and dried over anhydrous MgSO₄; the solvent was removed on a rotary evaporator, and the residue was fractionated in a vacuum. Oxazine **IV**, bp 135–140°C (3 mm Hg), and oxazine **V**, bp 145–150°C (3 mm Hg), were obtained as viscous light yellow liquids with a typical amine odor. In both cases large amount of bottoms remained after vacuum distillation.

Hydrolysis of oxazines **IV** and **V** was carried out by treatment with 20% NaOH by the procedure de-

scribed in [1]. The boiling point of the resulting amino alcohol **VI** was in agreement with the published data [3, 10].

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