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5-Alkyl-5-nitrotetrahydro-1,3-oxazine-2-ones

by

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Summary. The title compounds (I) were obtained by acting with phosgene in the presence of triethylamine on 3-amino-2-alkyl-2-nitropropanol (II). The presence of inter- and intramolecular hydrogen bond mainly between the NH and C=O groups is discussed.

The formation of 5-alkyl-5-nitrotetrahydro-1,3-oxazine-2-ones (**I**, $R=C_2H_5$, n-C_3H_7, n-C_4H_9) from corresponding derivatives of 3-amino- 2-nitropropanol (**II**, $R=C_2H_5$, n-C_3H_7, n-C_4H_9) and phosgene is known, but it has been limited to the instances when R′ was cyclohexyl or benzyl [1, 2].

Now we examined the reaction of phosgene with **II**, when R′ was H, to obtain **I** unsubstituted in position 3.

Aminoalcohols with a primary amino group (**II**, R′=H) were found to react more readily than those with R′ cyclohexyl or benzyl. At room temperature the exothermic reaction was so vigorous that polymers (most likely polyurethanes) were formed. They were insoluble in most organic solvents.

It was necessary to establish the conditions which could moderate the reaction. Low temperature (−10 to −15°C), high dilution of the reagents with solvents, and carefully controlled rate of phosgene introduction were essential to obtain good control over the reaction. Triethylamine was used to neutralize the evolved hydrogen chloride in agreement with the former finding of Testa *et al.* [3] while reacting 2,2-dialkyl-3-aminopropanol with phosgene.

Thus we obtained the yield of ca. 50% theoretical.

Aminoalcohols (**II**) were obtained according to our formerly-described method, i.e. by hydrolysis of the corresponding 5-alkyl-5-nitrotetrahydro-1,3-oxazines [2].

Structure **I** of 5-alkyl-5-nitrotetrahydro-1,3-oxazine-2-ones is in agreement with their chemical properties: they do not form hydrochlorides, are stable in acid and weak alkaline media. They can be classified as cyclic urethanes **I** and they have the character of both δ-lactones and δ-lactams.

It appeared that compounds **I** (R=H) should give relatively readily nucleophilic substitution of hydrogen in position 3 in a way similar to the reactions of imides,

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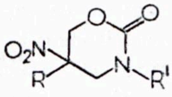
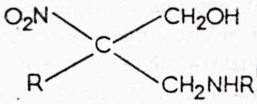
Note: This paper is Part CXIII in the series: Chemistry of Nitroalkanes.

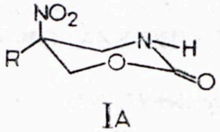
barbiturates, imidazoles, etc. However, no reaction occurred between **I** (R=H) and mercuric chloride. It seems that although the nitro and carbonyl groups reduce the basicity of the molecules the amino group has too weak acid properties.



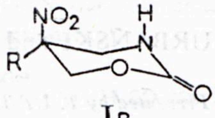
I



II

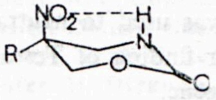


IA

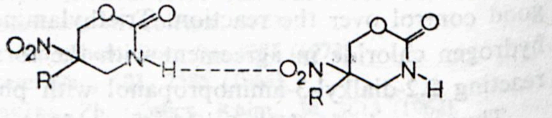


IB

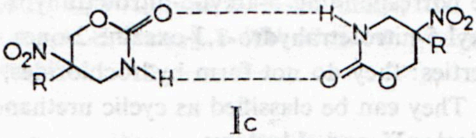
The structure of oxazinones (**I**) (R′=H) was confirmed by IR and NMR spectroscopy. With regard to the conformation, structure **IA** or **IB** should be accepted with the nitro group in the axial position according to previous findings for 5-nitrotetrahydro-1,3-oxazines [4, 5]. It seemed difficult to assess whether hydrogen in position 3 is axial or equatorial. This was originally in agreement with our former results [5] and also of those of Fodor *et al.* [6]. However, Booth and Lemieux [7] on the basis of NMR analysis, as well as Katritzky *et al.* [8] suggested that the proton attached to nitrogen in tetrahydro-1,3-oxazine is in the axial position. Katritzky drew his conclusion from the examination of the IR spectra and dipole moment measurements. While assuming an attracting interaction 1,3 between the NO_2 and NH groups as electron-attracting and electron-donating group, respectively, we suggest hydrogen in position 3 being axial, which would make possible the formation of the hydrogen bond between these two groups, as shown in diagram **Ia**. The hydrogen bond in **Ia** should be weak, as the distance between the oxygen atoms of the nitro group and the nitrogen atom of the NH group is relatively large (ca. 3Å).



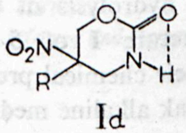
Ia



Ib



Ic



Id

III

We suggest that four structures **Ia—Id** can exist in an equilibrium.

Another feature of compound **I** would be the possibility of existence of the enolic form (**III**). This however should not appreciably affect either IR [8, 9a] or proton NMR [8, 10] spectra.

IR spectra of compounds **I**

a) *N—H stretching vibrations.* The spectra taken in Nujol show two bands 3250—3240 cm^{-1} and 3145—3132 cm^{-1}. The frequencies are considerably lower than in secondary amides and they should be considered as bonded by the hydrogen bonds [7]. They should correspond to intra- (**Ia** and **Id**) and intermolecular (**Ib** and **Ic**) species.

The spectra of dilute solutions in carbon tetrachloride or chloroform (concentrations 1.5×10^{-4} and 10^{-5} mol/l) show three bands: 3428—3425, 3240—3230 and 3155—3140 cm^{-1}. The highesr should correspond to the free NH group and the other to internally bonded ones, such as **Ia** and **Id**. The former possesses the weakest hydrogen bond, as already mentioned.

b) *C=O stretching vibrations.* Strong bands 1740—1703 cm^{-1} in Nujol and 1736—1730 cm^{-1} in solutions could be assigned to both δ-lactones and δ-lactams. According to Bellamy [9b] δ-lactones give bands 1750—1735 cm^{-1} and lactams — 1750—1700 cm^{-1}.

c) *C—O—C vibrations* are manifested by the bands of 1165—1155, 1135—1130, 1095—1975 cm^{-1}, which is in agreement with the findings of Eckstein *et al.* [11] for 5-nitrotetrahydro-1,3-oxazine.

d) *NO_2 asymmetric vibrations* were recorded at a frequency of 1150 cm^{-1}.

NMR spectra

The spectral data for oxazinones (**I**, R′=H) contain one wide signal at $\tau=3$ ppm, two quartets at $\tau=5.48$ and 6.16 ppm, and a group of signals corresponding to alkyls R. The previous findings for 5-nitrotetrahydro-1,3-oxazines [11] indicate the presence of a signal at 7.63—7.77 ppm, which was assigned to N—H, i.e. the proton attached to the ring nitrogen and three quartets at 5.95, 6.5 and 5.6 ppm corresponding to three different methylene groups: at C(2), C(4) and C(6), respectively. In [12] the influence of an intramolecular hydrogen bond between the phenolic OH group and a nitro group was found to be extremely prominent reducing the value of τ of ca. 5.0 ppm for the non-bonded OH group to τ of ca. −0.7 ppm for the bonded group.

On the basis of these findings we suggest that the signal $\tau=3$ ppm should be assigned to the proton at N(3) while bonded by a hydrogen bond according to diagrams **Ia—d**.

Two quartets should be assigned to two methylene groups: at C(4) and C(6) while the moleoule is in the preferred chain conformation with the axial nitro group **IA** or **IB**. The preference should be given to conformation **IB** with the axial proton attached to the ring nitrogen, thus making possible the presence of the hydrogen bond between the NO_2 and NH groups according to **Ia** [13].

Experimental

*5-Alkyl-5-nitrotetrahydro-*1,3*-oxazines* (I). Finely powdered hydrochloride of aminoalcohol (**II**, R = C_2H_5, *n*-C_2H_7, *n*-C_4H_9, R′ = H, 0.035 mol) was suspended in dry ether (250 ml) and a solution of triethylamine (0.105 mol) in chloroform (150 ml) was added. All was stirred at room temperature for 2 h, then cooled to −15° and phosgene (0.035 mol) in the form of a 5-% solution in toluene was added while keeping the temperature below 0°. After all phosgene had beed added, mixing was continued for 1 h and the temperature was allowed to rise to 8—10°. The suspension was kept till the next day. All volatile components were evaporated under reduced pressure, the residual solid was collected and washed with hot benzene. The benzene solution contained the product. Benzene was evaporated to dryness under reduced pressure and the product collected.

The solid substance washed with hot benzene was mainly composed of triethylamine hydrochloride and a small proportion of the product.

The solid was treated with a little amount of water to dissolve triethylamine hydrochloride and the undissolved fraction was added to the main portion of the product.

TABLE

Elemental analysis for compounds I

R	Formulae	Analysis (%): calc. found C	H	N	m. p. (°C)	Yield (%)
C_2H_5	$C_6H_{10}N_2O_4$	41.4 41.6	5.8 5.8	16.1 16.1	118	50
n-C_3H_7	$C_7H_{12}N_2O_4$	44.7 44.8	6.4 6.3	14.9 14.9	123—124	50
n-C_4H_9	$C_8H_{14}N_2O_4$	47.2 47.0	6.9 6.8	13.7 13.3	130—131	40

R′ = H

The product crystallized from benzene. All substances (I) were white crystals, soluble in ethanol, acetone, chloroform, less readily in benzene, and insoluble in water and ether.

The analytical data, m.ps. and yields are given in the Table.

IR spectra were taken with spectrophotometers with sodium chloride optics. Unicam Sp-2 was used to examine the samples in Nujol, and Hilger H-800 — for the samples in solution.

NMR spectra were taken with a Varian HR-60 apparatus of the frequency 60 megacycles.

The authors are much indebted to Dr. M. Witanowski for his helpful discussion of the NMR spectra.

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Т. Урбаньски, А. Шмидт-Шаловска, **5-Алкил-5-митротетрагидро-1,3-оксазин-2-оны**

Содержание. Получено 5-алкил-5-нитротетрагидро-1,3-оксазин-2-оны (I) действием фосгена на 3-амино-2-алкил-2-нитропропанолы (II) в присутствии триэтиламина. Рассмотрено возможность существования межмолекулярной и внутримолекулярной водородной связи между группами NH и $C=O$.