REACTION OF 3-NITRO-4,5-DIHYDRO-6H-1,2-OXAZINE N-OXIDE WITH ACETYLENES

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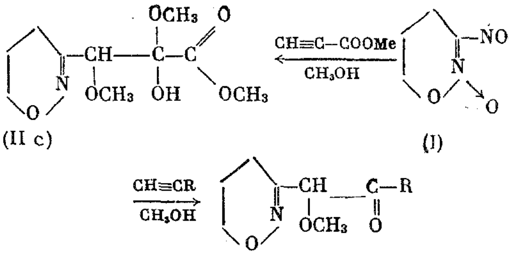
Previously it was shown that the reaction of linear nitronic esters with acetylenes leads to the formation of N-alkoxyaziridine derivatives [1, 2]. The reaction of the cyclic nitronic ester of 3-carbomethoxy-4,5-dihydro-6H-1,2-oxazine N-oxide with acetylenes proceeds in a similar manner to give 2-oxa-1-aza-bicyclo[4,1,0]heptane derivatives [3]. The extension of this reaction to 3-nitro-4,5-dihydro-6H-1,2-oxazine N-oxide (I) unexpectedly led to products that are devoid of the NO_2 group. The reaction of (I) with ethoxyacetylene and phenylacetylene in methanol gave the α-methoxy-3-substituted 4,5-dihydro-6H-1,2-oxazine derivatives. In the case of methyl propiolate the reaction led to the semiketal (IIc).



(II c)

(I)

(II) R=OC_2H_5 (a), C_6H_5 (b)

The frequencies of the vibrations of the NO_2 group are absent in the IR spectra of (IIa-c), while the frequencies, corresponding to the vibrations of the C=O group [1750 cm^{-1} for (IIa), 1695 cm^{-1} for (IIb), and 1735 cm^{-1} for (IIc)], are present; in (IIc) the band at 3490 cm^{-1} corresponds to the vibrations of the OH group. It should be mentioned that in the case of (IIa-c) absorption bands are present in the 1600-1620 cm^{-1} region, but the low intensity of these bands does not permit their reliable assignment to the vibrations of the C=N bond.

In the NMR spectra of (IIa-c) the singlet with δ 4.07 (Ia), 5.18 (IIb), and 3.93 ppm (IIc) corresponds to the methine proton. In (IIa) and (IIb) the CH_3O group appears as a singlet at 3.24 (IIa) and 3.45 ppm (IIb). The NMR spectrum of (IIc) contains two singlets of equal intensity with 3.13 and 3.21 ppm, which correspond to the two nonequivalent CH_3O groups, and a singlet with 3.76 ppm, which is characteristic for the resonance of the protons of the CO_2CH_3 group.

The data of the ^{13}C NMR spectra are given in Table 1. The assignment was made on the basis of the chemical shifts and the results of the experiments using partial double resonance (unadjusted double heteronuclear resonance), which makes it possible to determine the number of protons that are attached directly to the given C atom. In this way we were able to show the presence of a C=N bond in compounds (IIa-c). In all three cases the C^4 signal is observed in the vicinity of 38 ppm. We will point out that the signals of the corresponding carbon atom in aliphatic oximes also lie in the same region [4, 5]. The signals of the C atoms of the C=O group, which, the same as the carbon signals in the C=N groups, do not change during

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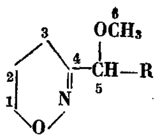
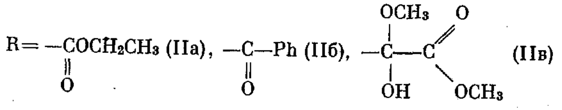
TABLE 1. Data of ^{13}C NMR Spectra of 

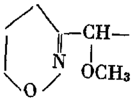
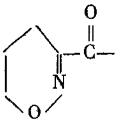
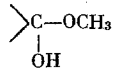


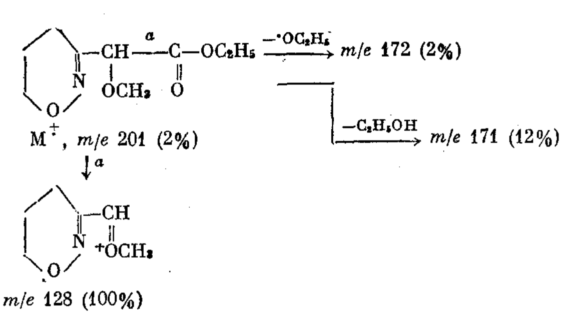
$\mathrm{R}=-\underset{\underset{\textstyle \mathrm{O}}{\|}}{\mathrm{C}}\mathrm{OCH_2CH_3}$ (IIa), $-\underset{\underset{\textstyle \mathrm{O}}{\|}}{\mathrm{C}}-\mathrm{Ph}$ (IIб), $-\overset{\overset{\textstyle \mathrm{OCH_3}}{|}}{\underset{\underset{\textstyle \mathrm{OH}}{|}}{\mathrm{C}}}-\mathrm{C}(=\mathrm{O})\mathrm{OCH_3}$ (IIв)

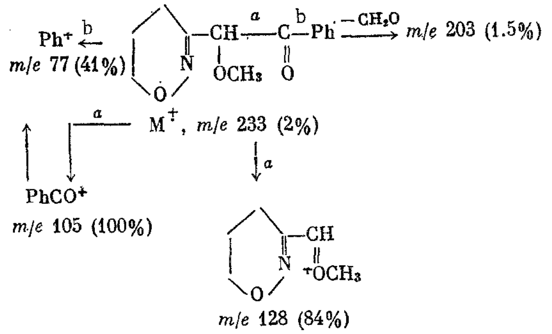
Chemical Shifts, ppm, from CS$_2$ (External standard), with an Accuracy of ±0.1 ppm

Compound	C¹	C²; C³	C⁴	C⁵	C⁶	Others	C atoms
(IIa)	127,3	174,7; 175,0	39,0	111,0	136,0	C=O OCH$_2$ CCH$_3$	24,9 132,3 179,2
(IIб)	127,0	174,7; 175,0	37,8	108,2	136,6	C=O Ph	−1,4 58,5; 64,3; 64,6; 59,4
(IIв)	126,8	174,3; 174,4	37,2	108,9	135,7	$-\underset{|}{\overset{|}{\mathrm{C}}}-$ OCH$_3$ C=O COOCH$_3$	94,8 139,8 22,7 142,5

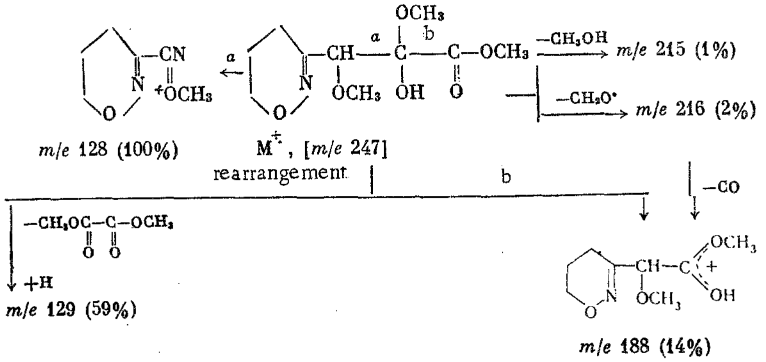
partial double resonance, have chemical shifts that are characteristic for such fragments [6, 7]. The repeating signals in the upfield region (173-175 ppm) should be assigned to the C^2 and C^3 atoms, and the signals at ~127 ppm to the C^1 atom. All of these signals have a triplet structure during partial double resonance. In the spectra of all three compounds the signal in the vicinity of 109 ppm, which gives a doublet during partial double resonance, belongs to the C^5 atoms. The C^6 signal is observed at 136.0 for (IIa) and at 136.6 ppm for (IIb). Of the three signals of the carbon of the methoxyl atoms in the spectrum of compound (IIc) (135.7, 139.8, and 142.5 ppm) this makes it possible to assign the first to the C^6 atom.

As a result, the ^{13}C NMR spectra do not contradict the fact that the common fragment  is present in (IIa-c). We reject the alternate fragment  , since a substantial paramagnetic shift of the carbonyl C atom could be expected in this case [8]. The signals of the carbon atoms of the C$_2$H$_5$O group in (IIa), of the benzene ring in (IIb), and of the carbomethoxyl carbon in (IIc), are all observed in the regions that are usual for such groups [9, 10]. In the spectrum of (IIc) the signals at 139.8 and 94.8 ppm, the first of which forms a quadruplet during partial double resonance, while the second remains a singlet, respectively belong to the methoxyl carbon atom and the quaternary C atom that is attached to the two oxygens [11, 12] of the  $>\underset{\underset{\textstyle \mathrm{OH}}{|}}{\mathrm{C}}-\mathrm{OCH_3}$ grouping. As a result, the data of the ^{13}C NMR spectra do not contradict the postulated (IIa-c) structures. The data of the mass spectra are also in satisfactory agreement with the structure of (IIa-c). The fragmentation of (IIa-c) under electronic impact can be respectively represented by schemes (1)-(3).

 (1)

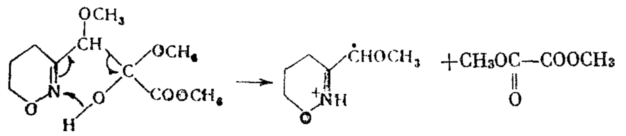


(2)



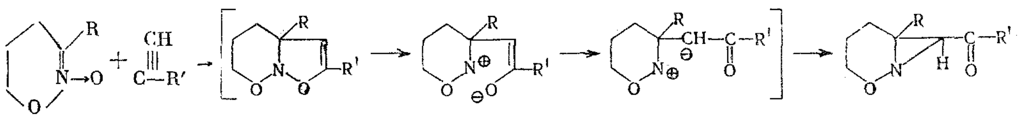
(3)

The ion with m/e 128, which is the most characteristic for all of the studied compounds, is formed as the result of cleavage of the C–C bond that is found β to the ring. The other ions reflect the characteristics of the structure of the side chain. Thus, for (IIb) the above-indicated β-cleavage, with a simultaneous localization of the charge on another portion of the molecule, leads to the stable benzoyl cation (m/e 105; 100%). The formation of the ion with m/e 129 from (IIc) is also associated with the characteristics of its structure: the McLafferty rearrangement is possible in this case, whereas an H atom that is capable of migration is absent in both (IIa) and (IIb)



As a result, on the basis of all of the spectral characteristics the structure of (IIa-c) can be considered proved.

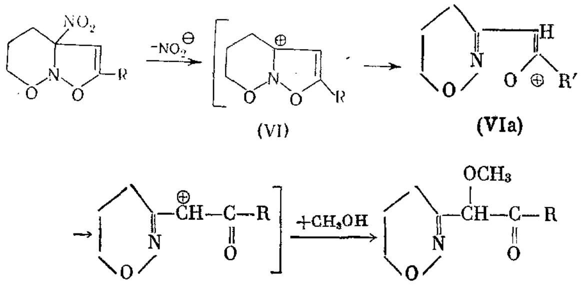
In order to explain the formation of the aziridine ring when nitronic esters are reacted with acetylenes a mechanism was postulated that includes the rearrangement of the intermediate 4-isoxazoline (IV), which is obtained by the 1,3-cycloaddition scheme [1-3]



(III) (IV) (IVа) (IVб) (V)

R=COOCH₃

It is clear that the cleavage of NO_2 in structures of the (IVa, b) (R = NO_2) type would not lead to (IIa-c), since the negatively charged α-C atom cannot be attacked by the CH_3O group. Besides this, (IVa, b) or analogous structures, with opposite charges on the N and O atoms, are apparently not formed as kinetically independent particles, since the reaction of (III) with acetylenes in methanol leads to the same products (V) as in the absence of methanol. The formation of (IIa-c) can be explained by the cleavage of compounds of the (V) (R = NO_2) type by methanol, with the subsequent elimination of the elements of HNO_2. However, this possibility seems improbable if the stability of (V) in methanol is taken into account. It should be mentioned that the reaction of (I) with acetylenes in inert solvents (for example, C_6H_6, THF, or DMF) always led to nonidentifiable tars. As a result, the primary products of the reaction of (I) with acetylenes are thermally unstable compounds, which is apparently associated with the presence of the NO_2 group in them. Consequently, the path that seems to be most probable for the formation of (IIa-c) includes the preliminary cleavage of the $NO_2^{\ominus}$ anion from structures of either the (IV) or (V) type ($R = NO_2$), with the subsequent rearrangement of the intermediately formed C cation, for example:



(VI) (VIa)

(VIb)

It is natural that this scheme is purely formal: (VIa) and (VIb) may not be formed as independent particles, while the rearrangement of (VI) and its attack by methanol can proceed synchronously.

EXPERIMENTAL METHOD

The ^{13}C NMR spectra were taken with the natural amount of ^{13}C on a JNM-PS-100 spectrometer, equipped with a Fourier transformation system, under the conditions of heteronuclear resonance, with a complete suppression of all of the protons. Unadjusted double heteronuclear resonance was used to assign the spectral lines. The mass spectra were taken on a Varian MAT CH-6 instrument, with insertion of the sample into the ion source at an ionizing voltage of 70 eV, an emission current of 100 μA, and an accelerating voltage of 1.75 kV.

Compound (I) was obtained as described in [13].

Preparation of (IIa). With stirring, 1 g of ethoxyacetylene was added to 1 g of (I) in 10 ml of methanol, the mixture was kept at 30-40° for 7 days, and the solvent and ethoxyacetylene were distilled off. Distillation of the residual oil gave 0.96 g (68%) of (IIa), bp 85-86° (0.5 mm); n_D^{20} 1.4670. Found: C 53.47; H 7.54; N 6.62%. $C_9H_{15}NO_4$. Calculated: C 53.73; H 7.46; N 6.96%. NMR spectrum ($CDCl_3$, δ, ppm): singlet 4.07 (CH), singlet 3.24 (OCH_3), multiplet 3.78 (H^6), multiplet 1.97 (H^4, H^5), triplet 1.20 and quadruplet 4.05 (OC_2H_5).

Preparation of (IIb). With stirring, 0.52 g of phenylacetylene was added to 0.5 g of (I) in 10 ml of methanol, the mixture was kept at 45-50° for 18 h, and the methanol and excess phenylacetylene were distilled off. We obtained 0.52 g (64%) of (IIb), mp 77.5-78° (1 : 2 benzene–petroleum ether). Found: C 66.94; H 6.53; N 5.98%. $C_{13}H_{15}NO_3$. Calculated: C 66.95; H 6.44; N 6.01%.

NMR spectrum ($CDCl_3$, δ, ppm): singlet 5.18 (CH), singlet 3.45 (OCH_3), multiplet 3.87 (H^6), and multiplet 1.94 (H^4, H^5).

Preparation of (IIc). With stirring, 0.57 g of methyl propiolate was added to 0.5 g of (I) in 10 ml of methanol, the mixture was heated at 40-45° for 18 h, cooled in dry ice, and the obtained crystals were filtered. We obtained 0.65 g (78%) of (IIc), mp 92-93° (2 : 1 hexane–benzene). Found: C 48.52; H 6.97; N 5.86%. $C_{10}H_{17}NO_6$. Calculated: C 48.58; H 6.88; N 5.67%. NMR spectrum ($CDCl_3$, δ, ppm): singlet 3.93 (CH), two singlets 3.13 and 3.21 (OCH_3), singlet 3.76 ($COOCH_3$), multiplet ~3.8 (H^6), and two multiplets 2.24 and 1.87 (H^4, H^5).

CONCLUSIONS

The reaction of 3-nitro-4,5-dihydro-6H-1,2-oxazine N-oxide with acetylenes in methanol is accompanied by cleavage of the nitro group and leads to the formation of the α-methoxy-3-substituted 4,5-dihydro-6H-1,2-oxazine derivatives.

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