RECYCLIZATION AND PHOTOREARRANGEMENTS OF 2-ACETYL-4,4-DIALKYL-2-BUTEN-4-OLIDE OXIMES

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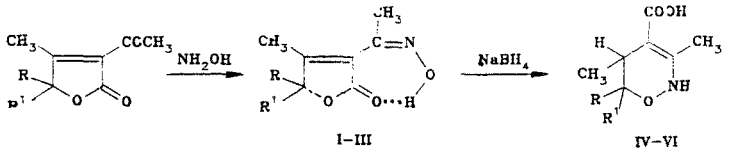
Recyclization to derivatives of dihydro-1,2-oxazines was realized by the reaction of 2-acetyl-3-methyl-4,4-dialkyl-2-buten-4-olide oximes with sodium borohydride. The UV-irradiation-initiated Beckmann rearrangement of the oximes cited above leads to 4,4-dialkyl-2-buten-4-olide-2-carboxylic acid N-methylamides.

As we have previously shown, in contrast to saturated 2-acetyl-substituted γ-lactones, the reaction of which with hydroxylamine proceeds with recyclization to oxazoline derivatives [1], unsaturated 2-acetyl-γ-lactones [2] react with hydroxylamine with retention of the lactone ring and the formation of the corresponding oximes I-III, the structures of which were proved by IR and PMR spectral data and the results of elementary analysis.

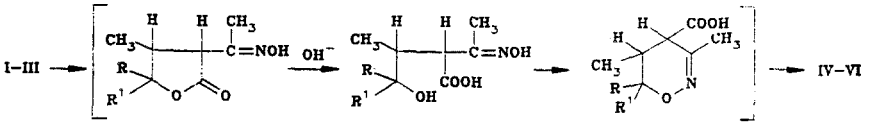


I-III IV-VI

I, IV $R=R^1=CH_3$; II, V $R,R^1=(CH_2)_4$; III, VI $R,R^1=(CH_2)_5$

In the present research we studied the reduction of oximes I-III with sodium borohydride. Recyclization of the unsaturated lactone to 5,6-dihydro-1,2-oxazine derivatives IV-VI was observed when the reaction was carried out in 70% aqueous ethanol.

In all likelihood , the indicated reaction proceeds with cleavage of the intermediately formed saturated lactone ring in the basic medium and subsequent cyclization of the γ-oximino alcohol formed to dihydro-1,2-oxazine derivatives, which, in contrast to the literature data (100°C [3]), proceeds at room temperature.



The structures of IV–VI are confirmed by their IR, PMR, and mass-spectral characteristics, which are presented in Table 1. It is apparent from the scheme (presented below) of the principal pathways of the mass spectrometric fragmentation of the IV–VI molecules that this fragmentation proceeds via a single pathway with the formation in the first steps of $[M - CH_3]^+$, $[M - OH]^+$, $[M - CO_2]^+$, and $[M - CO_2H]^+$ ions and then $[M - CO_2 - CH_3]^+$ $[M - CO_2H - CH_3]^+$, $[M - CH_3 - OH]^+$, and $[M - CH_3 - H_2O]^+$ ions. A peak of a fragment with m/z 82, which is the result of the elimination of a molecule of ketone RR^1CO from the $[M - CO_2H]^+$ ions, is present in the mass spectra of all three compounds.

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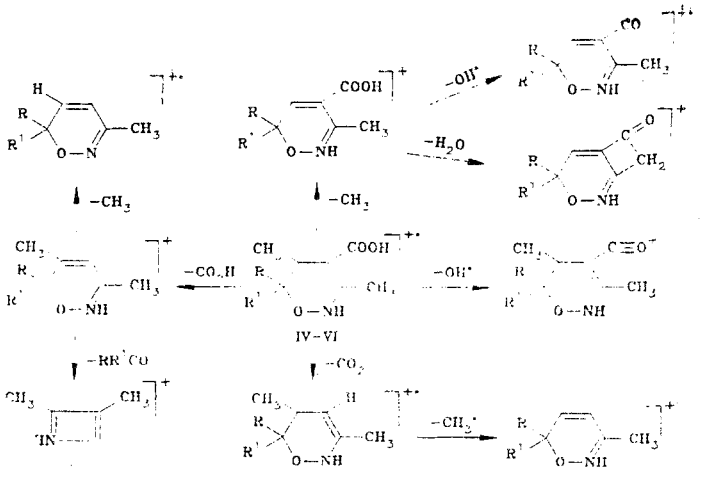
TABLE 1. Properties of the Synthesized Compounds

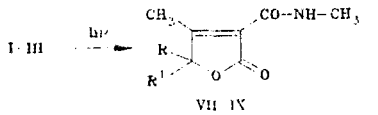
Compound	Empirical formula	T_{mp}, °C	R_f*	IR spectrum, cm^{-1}	PMR spectrum, ppm	Yield, %
I	$C_9H_{13}NO_3$	114...116	0,50	1620 (C=C), 1655 (C=N), 1735 (C=O), 3360 (OH)	1,10 (6H, s Me_2); 1,95 s 4-Me); 2,30 s, 3-Me), 13,1 s, OH)	60,7
II	$C_{11}H_{15}NO_3$	150...151	0,54	1620 (C=C), 1640 (C=N), 1730 (C=O), 3330 (OH)	1,60...1,90 (8H, m $(CH_2)_4$); 1,95 (s 4-Me); 2,05 s 3-Me), 11,3 (s, OH)	66,0
III	$C_{12}H_{17}NO_3$	127...129	0,59	1620 (C=C), 1645 (C=N), 1730 (C=O), 3320 (OH)	1,50...1,90 (10H, m $(CH_2)_5$); 1,95 (s, 4-Me); 2,10(s 3-Me); 11,5 (s, OH)	57,0
IV	$C_9H_{15}NO_3$	124...126	0,54	1600 (C=C), 1695 (C=O), 2800...2600, 3230 (NH)	1,25 (6H, s Me_2); 1,4 (3H, d, J = =7 Hz 5-Me), 2,10 (s, 3-Me), 2,60 (H, q, J=7 Hz 5-H)	75,6
V	$C_{11}H_{17}NO_3$	130...132	0,56	1610 (C=C), 1690 (C=O), 2800...2600, 3200 (NH)	1,10 (3H, d, J = =6,5 Hz 5-Me); 1,25...1,70 (8H, m $(CH_2)_4$); 2,05 (s, 3-Me), 2,40 (H, q, J=6,5 Hz 5-H)	89,0
VI	$C_{12}H_{19}NO_3$	152...154	0,61	1610 (C=C), 1690 (C=O), 2800...2600, 3240 (NH)	1,05 (3H, d J = =7 Hz 5-Me); 1,20...1,65 (10H, m $(CH_2)_5$); 2,00 (s, 3-Me); 2,40 (H, q J=7 Hz 5-H)	88,8
VII	$C_9H_{13}NO_3$	—	0,60	1630 (C=C), 1685 (C=O), 1755 (C=O), 3370 (NH)	1,44 (6H, s, Me_2); 2,28 (s, 4-Me); 2,40 (s, MeNH); 7,50 (s, NH)	83,5
VIII	$C_{11}H_{15}NO_3$	—	0,57	1630 (C=C), 1685 (C=O), 1760 (C=O), 3370 (NH)	1,25...2,25 (8H, m $(CH_2)_4$); 2,48 (s, 4-Me); 2,60 (s, MeNH); 7,80 (s, NH)	85,0
IX	$C_{12}H_{17}NO_3$	104...105	0,69	1625 (C=C), 1690 (C=O), 1755 (C=O), 3365 (NH)	1,00...2,00 (10H, m $(CH_2)_5$); 2,27 (s, 4-Me); 2,45 (s, MeNH); 6,60 (s, NH)	81,0

*The eluent for I–III and VII–IX was acetone–benzene (1:3), and the eluent for IV–VI was acetone–benzene (1:1).



The acid-base titration that we carried out also provides evidence for the presence of COOH and NH groups in the IV–VI molecules.

The photoarrangement of oximes I–III was studied. Irradiation of them in acetonitrile led to the formation of acid N-methylamides VII–IX as the products in high yields.

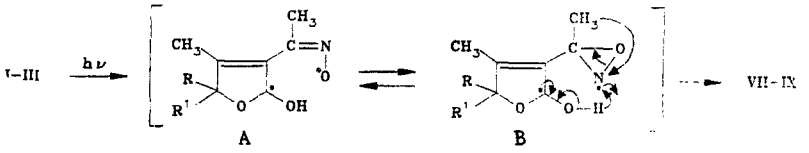


VII IX

VII $R=R^1=CH_3$; VIII R, $R^1=(CH_2)_4$; IX R, $R^1=(CH_2)_5$

The structures of the amides obtained were determined on the basis of IR and PMR spectral data (Table 1), as well as on the basis of their chemical transformations: the acidic hydrolysis of amides VII–IX with 20% sulfuric acid by the method in [4] led to the formation of the corresponding acids, which were identified by GLC.

It is known that oximes of α, β-unsaturated ketones undergo a Beckman photorearrangement in protic solvents or in solutions of organic acids [5, 6]; from this it was assumed that protonation is one of the steps in the rearrangement mechanism or that this transformation proceeds through polar transition states. However, the rearrangement of betenolide oximes I–III that we investigated is unique in its own way in that it proceeds in an aprotic solvent, evidently via a mechanism involving intramolecular transfer of a hydrogen atom from the oximino group to the lactone carbonyl group with the formation of lactyl biradical A. According to the IR spectral data, this is favored by the formation of an intramolecular hydrogen bond between the lactone carbonyl group and the hydroxy group in the starting oxime. It is assumed that intermediate biradical A, like heteroaromatic N-oxides, may form oxaziridine intermediate B, which leads to the rearrangement products.



A B

The rearrangement of oxime I under the influence of phosphorus pentachloride in ether, which we carried out by the method in [7], led to a complex mixture of products, despite the fact that phosphorus pentachloride is considered to be the most stereospecific and regioselective catalyst for the Beckmann rearrangement [8].

Thus the UV-irradiation-initiated rearrangement of 2-acetyl-2-buten-4-olide oximes has a number of advantages over the usual Beckmann rearrangement (high regioselectivity, the mildness of the conditions, and the simplicity involved in carrying out the experiments) and is an interesting and valuable synthetic alternative acid-catalyzed rearrangement.

EXPERIMENTAL

The IR spectra of suspensions of the synthesized compounds in mineral oil were recorded with a UR-20 spectrometer. The PMR spectra were recorded with Varian T-60 and Perkin–Elmer R-12B spectrometers (60 MHz) with d_6-DMSO and d_5-pyridine as the solvents. The internal standards were HMDS and TMS. The mass spectra were recorded with an MKh-1303 spectrometer with direct introduction of the samples into the ion source at an ionization energy of 30 eV.

The irradiation of solutions of oximes I–III was carried out in a flat-bottomed reactor made of Pyrex glass or quartz and equipped with a jacket for water cooling, a bubbler, and a condenser; the process was carried out at 18-20°C in a nitrogen atmosphere. Two PRK-2M lamps (375 W) situated horizontally on the bottom of a mirror illuminating boat at a distance of 15 cm from the bottom of the reactor served as the sources of UV irradiation. Products VII–IX were isolated by preparative TLC on 20 by 20 cm plates (L 40/100 silica gel). The purity of the products was monitored by TLC on Silufol UV-254 plates (development in UV light or with iodine vapors) and GLC with an LKhM-8-MD chromatography; the detector was a catharometer (2 m by 3 mm), the support was Chromaton N-AW HMDS (0.16-0.20 mm), the liquid phase was 5% QF-1, the carrier gas was helium, and the flow rate was 40 ml/h.

The characteristics of I–IX are presented in Table 1.

2-Acetyl-3-methyl-4,4-dialkyl-2-buten-4-olide Oximes I–III. A concentrated alcohol solution of 1.4 g (0.02 mole) of hydroxylamine hydrochloride was added with stirring to a solution of 0.02 mole of 2-acetyl-3-methyl-4,4-dialkyl-2-buten-4-olide in a mixture of 15-20 ml of ethanol and 3-5 ml of water, after which an aqueous solution of 1.4 g (0.01 mole) of

potassium carbonate was added in small portions. The reaction mixture was then stirred at room temperature for 1 h and allowed to stand overnight. The crystals of the precipitated salt were separated by filtration, the filtrate was evaporated in vacuo, and the residue was recrystallized from alcohol–water (1:5).

3,5-Dimethyl-4-carboxy-6,6-dialkyl-5,6-dihydro-2H-1,2-oxazines IV–VI. A 1.8-g (0.05 mole) sample of sodium borohydride was added to a solution of 0.01 mole of oxime I–III in 25 ml of 70% ethanol, and the reaction mixture was stirred at room temperature for 3-4 h. It was then acidified to pH 4-5 with 5-7% hydrochloric acid and stirred for another 0.5 h. The reaction mixture was filtered, the filtrate was evaporated in vacuo, and the residue was recrystallized from 40% ethanol.

3-Methyl-4,4-dialkyl-2-buten-4-olide-2-carboxylic Acid N-Methylamides VII–IX. A solution was 0.85 g (0.005 mole) of oxime I in 22 ml of acetonitrile was placed in a Pyrex glass photolysis reactor. After irradiation for 5 h, the solvent was removed by distillation with a rotary evaporator at 55-60°C (25 mm), and the residue – a viscous oil – was chromatographed on 20 by 20 cm silica gel L 40/100 plates in an acetone–benzene (1:3) system. Workup of the zone with R_f 0.6 gave amide VII in the form of an orange oil. Analysis by GLC (column temperature 190°C): R_t 2.8 min.

Similarly, from 0.38 g (0.002 mole) of oxime II in 20 ml of acetonitrile after 4.5 h of irradiation, removal of the solvent by distillation, and chromatography, the zone with R_f 0.57 yielded amide VIII (orange oil). Analysis by GLC (column temperature 240°C): R_t 20 min.

Similarly, from 1.0 g (0.0045 mole) of oxime III in 12 ml of acetonitrile after 5 h of irradiation, removal of the solvent by distillation, and chromatography, the zone with R_f 0.57 yielded amide IX (an orange oil that crystallized on standing). Analysis by GLC (column temperature 240°C): R_t 2.3 min.

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