ISOXAZOLIDINE DERIVATIVES WITH A CYCLOPROPYL RESIDUE

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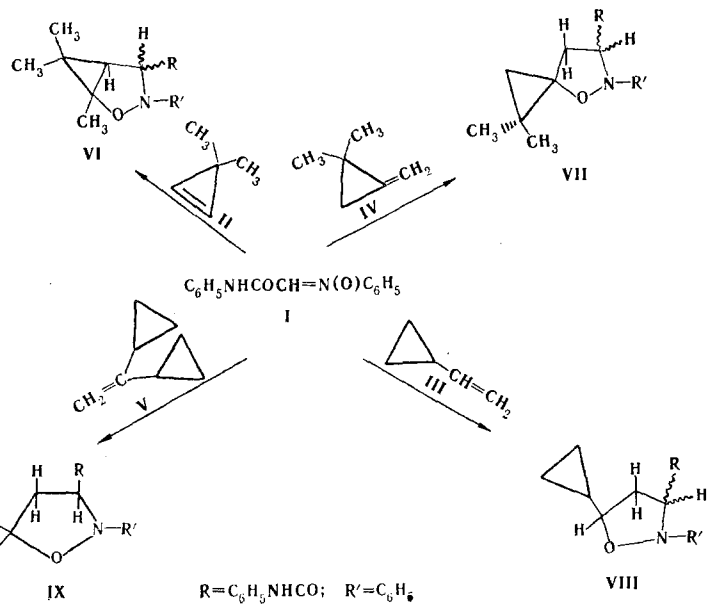
Olefins of the cyclopropane series add to N-(phenylaminooxoethylidene)aniline N-oxide to give the corresponding isoxazolidines with retention of the three-membered ring. The rate constants of the reaction were determined.

The isoxazolidines that are formed in the 1,3 cycloaddition of alkenes to nitrones display different stabilities, depending on the nature of the reacting substances, and their secondary transformations may lead to unexpected reaction products [1, 2]. It seemed of interest to use olefins of the cyclopropane series to synthesize the corresponding isoxazolidines, since this problem has not yet been examined in the literature up until now.

In the present research we studied the reaction of N-(phenylaminooxoethylidene)aniline N-oxide (I) with 1,3,3-trimethylcyclopropene (II), vinyl cyclopropane (III), 2,2-dimethylmethylenecyclopropane (IV), and 1,1-dicyclopropylethylene (V). The course of the reactions with the olefins was monitored by means of thin-layer chromatography (TLC) on aluminum oxide. On the basis of the PMR spectra and the results of elementary analysis it was concluded that all of the alkenes form 1:1 adducts. An analysis of the spectra shows that the adducts contain a three-membered ring; the addition of the nitrone proceeds structurally specifically to give 5-substituted isoxazolidines. Thus the 4-H proton shows up in the spectrum of VI at 3.47 ppm in the form of a doublet with a splitting constant of 4 Hz and at 3.61 ppm in the form of a broad singlet; this corresponds to the formation of diastereomeric forms of the adduct with cis and trans orientations of the 4- and 5-H protons in a ratio of 3:1 (with respect to the integral intensity of the proton signals).



The presence of a triplet of the 3-H proton (1H) at 4.20 ppm in the spectrum of VII constitutes evidence for the direction of addition of the nitrone to olefin III. The form of the 3-H signal in the spectra of adducts VIII and IX also confirms their structure: the 3-H proton for adduct

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TABLE 1. Synthesized Isoxazolidines VI-IX

Compound	mp, °C	R_f	PMR spectrum, ppm	Found, %			Empirical formula	Calc., %			Yield, %
				C	H	N		C	H	N	
1,6,6-Trimethyl-3-phenyl-4-phenylcarbamoyl-2-oxa-3-azabicyclo[3.1.0]hexane (VI)	116—118	0,64	1,00—1,75 (10H, m, 1-CH_3, 6-CH_3, 6-CH_3, 5-H); 3,47 (d, J=4 Hz); 3,61 (br. s, 1H, 4-H); 6,50—8,00 (10H, m, $2C_6H_5$); 9,0 (1H, s, NH)	74,3	6,5	8,4	$C_{20}H_{22}N_2O_2$	74,5	6,8	8,6	96
6,6-Dimethyl-2-phenyl-3-phenylcarbamoyl-1-oxa-2-aza-spiro-[2,3]heptane (VII)	180—182	0,62	0,93 (3H, s, 6-CH_3); 1,08 (3H, s, 6-CH_3); 2,40 (2H, d, 7-H); 2,76 (2H, d, 4-H); 4,20 (1H, t, 3-H); 6,50—8,00 (10H, m, $2C_6H_5$); 9,0 (1H, s, NH)	74,6	6,6	8,3	$C_{20}H_{22}N_2O_2$	74,5	6,8	8,6	92
2-Phenyl-3-phenylcarbamoyl-5-cyclopropyl-isoxazolidine (VIII)	112—113	0,57	0,08—1,05 (5H, m, cyclopropyl); 2,50—3,00 (2H, m, 4-H); 3,30—3,48 (1H, m, 5-H); 4,05—4,48 (1H, m, 3-H); 6,50—8,00 (10H, m, $2C_6H_5$); 9,0 (1H, s, NH)	73,7	6,5	8,8	$C_{19}H_{20}N_2O_2$	74,0	6,5	9,0	90
2-Phenyl-3-phenylcarbamoyl-5,5-dicylopropyl-isoxazolidine (IX)	150—152	0,76	0,45—1,33 (10H, m, cyclopropyl); 2,28—2,38 (2H, m, 4-H); 4,08 (1H, t, 3-H); 6,50—8,00 (10H, m, $2C_6H_5$); 9,0 (1H, s, NH)	75,7	6,9	7,8	$C_{22}H_{24}N_2O_2$	75,3	6,9	8,0	81

VIII shows up at 4.05-4.48 ppm in the form of a multiplet, which is associated with splitting of the signal by the nonequivalent protons of the adjacent methylene group; the 3-H proton in the spectrum of IX shows up in the form of a triplet at 4.08 ppm.

In order to quantitatively characterize the dipolarophile activities of the investigated olefins we determined the rates of reaction of olefins II, III, and V with nitrone I under monomolecular reaction conditions. The rate constants that we found, viz., 0.70, 0.37, and 0.20 min^{-1}, respectively, constitute evidence for the significant activity of strained olefin II.

EXPERIMENTAL

The PMR spectra of solutions of the compounds in $CDCl_3$ were obtained with a Tesla JNM-BS487A spectrometer (80 MHz) at 30°C with hexamethyldisiloxane as the internal standard. Thin-layer chromatography (TLC) was carried out on activity II Al_2O_3 [benzene—ethanol (10:1)].

1,3,3-Trimethylcyclopropene (II) was obtained by pyrolysis of mesityl oxide tosylhydrazone [3]. 2,2-Dimethylmethylenecyclopropane (III) was prepared by isomerizatin of olefin II in the presence of potassium tert-butoxide [3]. Vinylcyclopropane (IV) was synthesized by dehydration of 1-cyclopropylethanol [4] and was distilled with a column. 1,1-Dicyclopropylethylene (V) was obtained by dehydration of 1,1-dicyclopropylethanol in the presence of concentrated H_2SO_4 [5]. The constants of the olefins obtained were in agreement with the literature data.

Reaction of Olefins II-V with Nitrone I. A solution of 0.5 g (0.002 mole) of nitrone I and 1 ml (0.01 mole) of the corresponding olefin in 2 ml of o-xylene was allowed to stand at 20°C for 1-2 days. The solvent was then removed, ethanol was added, and the precipitated crystals were removed by filtration and washed with ethanol to give VI-IX (see Table 1).

The rates of the reaction of the nitrone with olefins II, III, and V were monitored from the change in the signal of the NH group in the PMR spectrum at 12.37 ppm for the starting nitrone. The nitrone concentration at a given moment was determined from a calibration

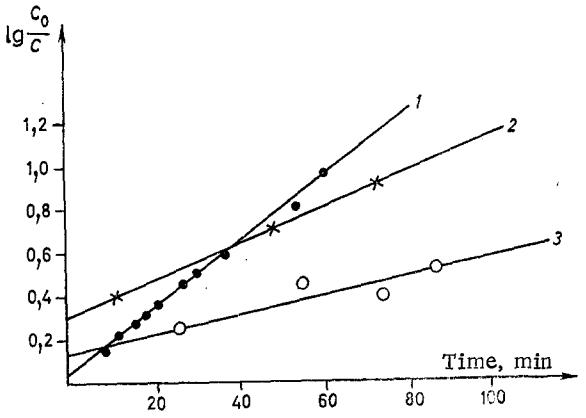

Fig. 1. Dependence of log C_0/C on the reaction time: 1) adduct VI, 2) adduct VIII, 3) adduct IX.

graph, for the construction of which we recorded the dependence of the intensity of the signal of the NH group on the nitrone concentration. The log $C_0/C = f(t)$ dependence is presented in Fig. 1 (C_0 is the initial concentration, and C is the nitrone concentration at time t).

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EFFECT OF THE SUBSTITUENT IN THE THIOPHENE RING ON THE [3,3]-SIGMATROPIC REARRANGEMENT OF ALLYL THIENYL SULFIDES

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The thio Claisen rearrangement of a number of 5-substituted allyl 2-thienyl sulfides was studied. On the basis of kinetic data it is shown that substituents that decrease the aromatic character of the transition state decrease the reactivity of the sulfide.

The thio Claisen rearrangement of allyl thienyl sulfides proceeds under relatively mild conditions and to a lesser extent than in the case of allyl phenyl sulfides and is complicated by side processes [1, 2]. 5-Substituted allyl 2-thienyl sulfides are therefore convenient subjects for the study of the effect of substituents in the aromatic ring on the thio Claisen rearrangement.

Sulfides Ia-f undergo rearrangement to isomeric 5-X-3-allylthiophene-2-thiols (IIIa-f), which were isolated in individual form. A study of the kinetics of the rearrangement of all

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