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RESEARCH ON THE CHEMISTRY OF PYRAZOLIDINE.

25.* ALKYLATION OF 4-CYCLOHEXYLIDENE-1-PHENYL-3,5-DIOXOPYRAZOLIDINE

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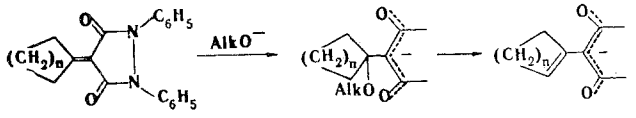
Products of alkylation in the 2 and 4 positions, as well as at the C_3=O group, were obtained by the reaction of 1-phenyl-4-cyclohexylidene-3,5-dioxopyrazolidine with alkyl halides in the presence of sodium methoxide. The reaction of sodium deuteromethoxide with 1-phenyl-4-cyclohexylidene-3,5-dioxopyrazolidine was studied.

It is known that 4-arylidene- and 4-cycloalkylidene-substituted 1,2-diphenyl-3,5-dioxopyrazolidines (I, II) react with sodium alkoxides as organic Lewis acids by adding an alkoxy group to the exocyclic polarized double bond [1, 2]. In the case of II one observed successive splitting out of a molecule of alcohol to give enolate III. The structure of enolates III is confirmed by spectroscopy and the production of the corresponding alkylation products.



II III

n = 2, 3

It seemed of interest to study the behavior in this reaction of a 4-cycloalkylidene-1-phenyl-3,5-dioxopyrazolidine in which, in addition to C—H acidity and the properties of an organic Lewis acid, N—H and O—H acidities are also possible, which permits the formation of a large number of products of reaction with alkoxides.

With this in mind we investigated the PMR spectra of a solution of 1-phenyl-4-cyclohexylidene-3,5-dioxopyrazolidine (IV) in deuteromethanol in the presence of sodium deuteromethoxide. The PMR spectrum of starting IV in $CDCl_3$ is similar to the PMR spectrum of II (n = 3) and contains signals of six aliphatic (1.68 ppm) and four allyl (3.17 ppm) protons, as well as the signal of the proton of an NH group, the position of which (8.5-9.08 ppm) depends on the concentration. These results constitute evidence that IV exists in the dioxo form in $CDCl_3$. Disappearance of the signal of allyl protons and the appearance of the previously absent signals at 2.08, 2.42, and 5.91 ppm are observed in the spectrum of a solution of starting IV in CD_3OD after the addition of one equivalent of CD_3ONa in deuteromethanol. These changes are similar to those observed when a solution of CD_3ONa in deutero-

*See [1] for Communication 24.

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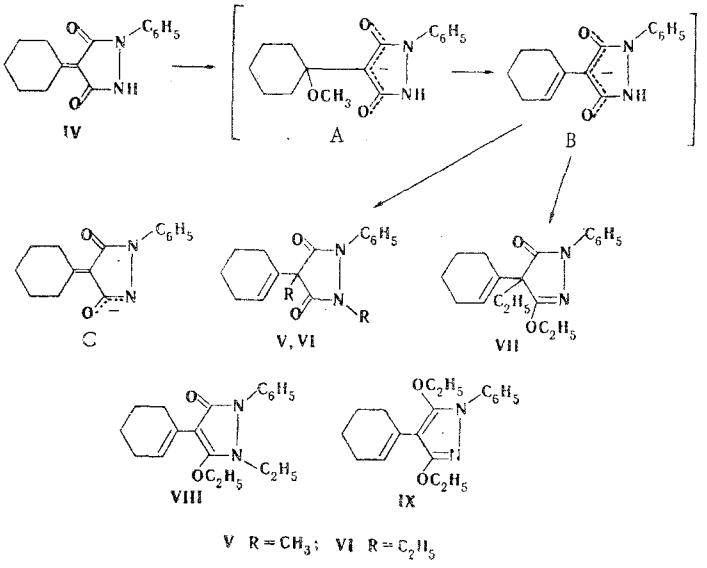
TABLE 1. Constants and Yields of the Compounds Obtained

Compound	mp, °C (crystallization solvent)	R_f	IR spectrum, cm^{-1}	UV spectrum, λ_{max}, nm (log ε)			Found, %			Empirical formula	Calculated, %			Yield, %
				water	NaOH	HCl	C	H	N		C	H	N	
IV	169—170 (ethanol)	0,08	1720, 1685	260 (4,3), 365—380 (3,1)	266 (4,3), 385—400 (2,7)	257 (4,4), 365—375 (3,0)	69,9	6,3	10,8	$C_{15}H_{16}N_2O_2$	70,3	6,3	10,9	65
V	73—74 (heptane)	0,22	1748, 1710	238 (4,0)	238 (4,0)	238 (4,0)	72,1	7,1	10,1	$C_{17}H_{20}N_2O_2$	71,8	7,1	9,9	55
VI	60—61 (petroleum ether)	0,31	1748, 1718	236 (4,1)	236 (4,0)	236 (4,0)	73,4	7,9	9,3	$C_{19}H_{24}N_2O_2$	73,1	7,7	9,0	12
VII	128—129 (aqueous methanol)	0,78	1720, 1620	242 (4,2), 276 (3,9)	242 (4,2), 276 (3,8)	242 (4,2), 276 (4,0)	72,7	7,5	9,1	$C_{19}H_{24}N_2O_2$	73,1	7,7	9,0	3,7

methanol is added to a solution of II (n = 3) in CD_3OD [1]. As in the case of II, one observed a gradual increase in the areas of the new signals; however, this increase takes place considerably more rapidly, and after 7 h, the area of the signal at 5.91 ppm (the vinyl proton of the 1-cyclohexenyl substituent) corresponds to one proton. When two equivalents of CD_3ONa in deuteromethanol are added to a solution of IV in CD_3OD, the indicated changes in the spectrum occur immediately. The area of the signals at 2.45, 2.05, and 1.59 ppm corresponds to eight protons, while the area of the signal at 5.85 ppm corresponds to one proton.



V $R = CH_3$; VI $R = C_2H_5$

The results obtained in this research make it possible to exclude iminol salt C from consideration as a species that does not contain a vinyl proton and constitute evidence for the initial addition of an alkoxy group to the exocyclic double bond of IV to give enolate A with subsequent rapid splitting out of a molecule of alcohol, resulting in mesomeric anion B.

Thus IV behaves in the same was as its diphenyl analog II; however, replacement of the phenyl group by a hydrogen atom on passing from II to IV increases the rate of the indicated transformations significantly.

1,4-Dialkyl-2-phenyl-4-(1-cyclohexenyl)-3,5-dioxopyrazolidines V and VI, which have similar mobilities in thin-layer chromatography (TLC), were obtained in the alkylation of IV in the presence of sodium methoxide under the previously described conditions [1]; their structures are confirmed by the character of the UV and IR spectra (see Table 1) and the PMR spectroscopic data.

In the ethylation of IV the reaction proceeds primarily via a different pathway, and, in addition to VI, we isolated a second compound, which is also a diethyl-substituted species. The UV spectrum of this compound contains not just one intense absorption band, as in the case of V and VI, but rather two such bands at 242 and 276 nm, which do not undergo any change in their position and intensity when the solution is acidified and made alkaline. The presence in the IR spectrum of this compound of frequencies that are characteristic for carbonyl absorption (1720 cm^{-1}) makes it possible to exclude isomer IX, which does not contain a carbonyl group. Signals of protons of two weak-field methylene groups should have been observed in the PMR spectrum of VIII. In fact, however, only the signal of one O-methylene group (4.44 ppm) is observed in the spectrum of the second ethylation product, and this makes it possible to exclude from consideration both alternative structures and to adopt the VII structure, which is in unambiguous agreement with the spectral data.

Thus in the case of compounds that have an unsubstituted NH group alkylation of the pyrazolidine ring may take place in two directions, viz., at the nitrogen and oxygen atoms, as is characteristic for all amide systems.

EXPERIMENTAL

The electronic absorption spectra of solutions of the compounds in ethanol and in 90% ethanol containing 0.35% HCl and 0.1% KOH for $(1\text{-}4)\cdot10^{-5}$ M solutions were recorded with an SF-16 spectrophotometer. The IR spectra of mineral oil suspensions of the compounds were obtained with a UR-20 spectrometer. The PMR spectra were obtained with a Varian T-60 spectrometer with hexamethyldisiloxane as the internal standard. Thin-layer chromatography (TLC) was carried out on Silufol UV-254 plates in a benzene–chloroform system (1:5).

1-Phenyl-4-cyclohexylidene-3,5-dioxopyrazolidine (IV). A solution of 10 g (0.07 mole) of 1-phenyl-3,5-dioxopyrazolidine in 25 ml of cyclohexanone was refluxed on a water bath for 8 h, after which it was cooled, and 9.5 g of a yellow crystalline substance was separated (see Table 1).

1-Phenyl-2,4-dimethyl-4-(1-cyclohexenyl)-3,5-dioxopyrazolidin (V). A 4.56-g (0.02 mole) sample of IV was dissolved in sodium methoxide (0.04 mole of sodium in 30 ml of absolute methanol), 17 g (0.12 mole) of methyl iodide was added, and the mixture was allowed to stand in a dark place for 96 h. It was then evaporated to half its original volume, diluted with 20 ml of water, and extracted three times with 20 ml of ether. The ether extract was dried over anhydrous sodium sulfate and evaporated to dryness. The residual colorless oil (100%) was triturated with methanol to give a white substance (see Table 1).

1-Phenyl-3-ethoxy-4-ethyl-4-(1-cyclohexenyl)pyrazol-5-one (VII). Alkylation was carried out as described above with ethyl iodide in this case. Evaporation of the ether extract gave 80% of a light-yellow oil, from which a white crystalline substance was isolated by recrystallization (see Table 1).

1-Phenyl-2,4-diethyl-4-(1-cyclohexenyl)-3,5-dioxopyrazolidine (VI). The aqueous methanol mother liquor remaining after the separation of VII was evaporated to dryness to give an oil, from which by chromatography in a layer of aluminum oxide (activity II) with a thickness of 4 mm on 20 by 20 cm plates (elution with chloroform) we isolated a colorless chromatographically homogeneous oil, which began to crystallize on standing (see Table 1).

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