RESEARCH ON PYRAZOLIDINE.

24.* ALKYLATION OF 4-CYCLOALKYLIDENE-1,2-DIPHENYL-3,5-DIOXOPYRAZOLIDINES

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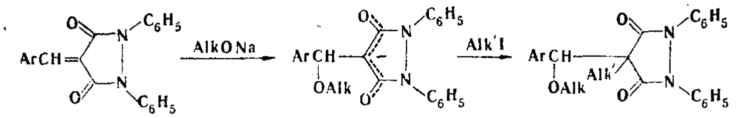
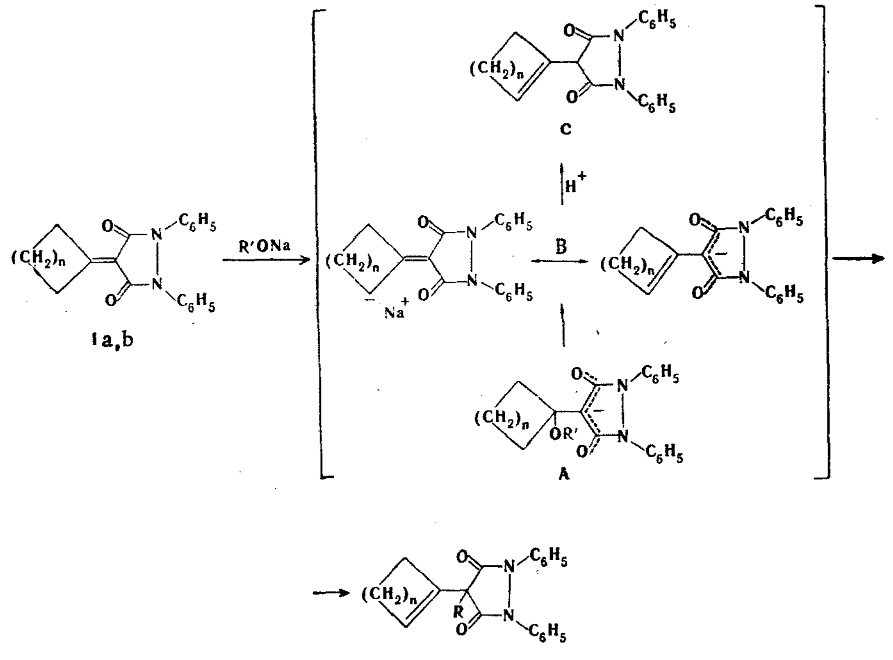
4-Alkyl-4-(1-cycloalkenyl)-1,2-diphenyl-3,5-dioxopyrazolidines were obtained by the reaction of 4-cycloalkylidene-1,2-diphenyl-3,5-dioxopyrazolidines with alkyl halides.

The reaction of 4-benzylidene-substituted 1,2-diphenyl-3,5-dioxopyrazolidine (DDP) with alkyl halides in the presence of sodium ethoxide gives [2] 4-alkyl-4-(1-alkoxybenzyl)-DDP, i.e., an alkoxy group is added to the exocyclic double bond, and this is followed by C-alkylation:



It seemed of interest to study the behavior in the same reaction of 4-cycloalkylidene-DDP (Ia, b), for which one may assume not only the addition of an alkoxy group, which leads to enolate A, but also detachment of a proton from the activated methylene group to give mesomeric enolate B, as well as the A→B transition:



Ia,b

IIa,d

I a n = 3, b n = 2; II a n = 3, R = CH_3; b n = 3, R = C_2H_5; c n = 2, R = CH_3; d n = 2, R = C_2H_5

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*See [1] for communication 23.

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TABLE 1. PMR Spectra of II

Compound	Recording conditions	δ, ppm						
		$CH_2{-}C{=}$	$CH_2{-}C{=}$ and $C{-}CH_2{-}C_4$	ring aliphatic protons	aliphatic and $C{-}CH_2{-}C_4$ protons	H_{vin}, (1 H)	$CH_3{-}C_4$ (3H)	$CH_3{-}C{-}C_4$ (3H)
a	CCl_4, 60 MHz	1,78—2,25 (4H)	—	1,51—1,71 (4H)	—	5,71	1,48	—
b	CCl_4 100 MHz	—	2,16—2,54 (6H)	1,68—2,08 (4H)	—	6,04	—	1,17
c	$CDCl_3$, 60 MHz	2,39 (4H)	—	1,96 (2H)	—	5,84	1,64	—
d	CCl_4 100 MHz	2,5—2,8 (4H)	—	—	2,04—2,5 (4H)	6,0	—	1,21

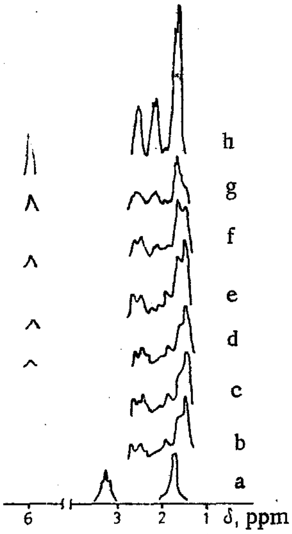

Fig. 1. PMR spectra of Ia in $CDCl_3$ (a), in $CD_3OD + CD_3ONa$ after 5 min (b), after 10 min (c), after 15 min (d), after 25 min (e), after 85 min (f), after 260 min (g), and after 3 days (h).

It was found that 4-alkyl-4-(1-cycloalkenyl)-DDP (IIa-d) are formed as the principal products in the alkylation of 4-cyclohexylidene- and 4-cyclopentylidene-DDP (Ia, b) with metyl and ethyl iodides under the previously described conditions [2].

The absorption maximum in the UV spectra of solutions of II in ethanol and acidic and alkaline ethanol is found at 238-239 nm (the fixed dioxo form of DDP).

Two bands at 1745-1750 and 1713-1718 cm^{-1} (CO of the dioxo form of 3,5-dioxopyrazolidines) are observed in the IR spectra of II.

The PMR spectra of these substances (Table 1) also confirm their structure.

To shed some light on the mechanism of the formation of II we followed the change with time in the character of the PMR spectrum of I in CD_3OD in the presence of an equimolar amount of CD_3ONa.

A triplet of the protons attached to C_2 and C_6 (4H, 3.21 ppm) and a multiplet of aliphatic protons attached to C_3, C_4, and C_5 (6H, 1.68 ppm) are characteristic for the PMR spectrum of 4-cyclohexylidene-DDP I ($CDCl_3$, 60 MHz) (Fig. 1). The addition of a CD_3O group, which is accompanied by the disappearance of the exocyclic double bond and the formation of enolate A ($R = OCD_3$), should give rise to a shift in the four protons attached to C_2 and C_6 to strong field. In fact, when Ia is dissolved in a mixture of CD_3ONa and CD_3OD, the signal at 3.21 ppm vanishes immediately, and signals that are absent in the PMR spectrum of starting I appear at 1.71-2.78 ppm. The signal of the protons attached to C_3-C_5 is simultaneously shifted ∿ 0.2 ppm to strong field. The overall area of the signal at 1.2-2.78 ppm corresponds to 10 protons. However, changes that are in agreement with the $A \to B$ transformation, evidently due to splitting out of a molecule of deuteromethanol, are soon observed in the spectrum. Splitting out of a molecule of CD_3OH ($A \to B$) should lead to the appearance in the PMR spectrum of the signal of a lone vinyl proton attached to C_2. In fact, the previously

TABLE 2. Compounds II

Compound	mp, °C	R_f	UV spectrum		IR spectrum, cm^{-1}	Found, %			Empirical formula	Calculated, %			Yield, %
			λ_{max}, mm	lg ε		C	H	N		C	H	N	
a	166—167	0,67	238	4,3	1750, 1720, 1600, 1490	76,2	6,5	8,5	$C_{22}H_{22}N_2O_2$	76,3	6,4	8,1	57
b	142—143	0,73	239	4,3	1758, 1725, 1595, 1490	76,9	6,5	7,9	$C_{23}H_{24}N_2O_2$	76,6	6,7	7,8	39
c	135—136	0,70	238	4,3	1750, 1718, 1595, 1488	76,1	6,1	8,7	$C_{21}H_{20}N_2O_2$	75,9	6,1	8,4	16
d	132—133	0,71	239	4,3	1760, 1725, 1600, 1500	76,4	6,8	8,2	$C_{22}H_{22}N_2O_2$	76,3	6,4	8,1	21

absent signal at 5.98 ppm, the area of which corresponds to one proton after 3 days, becomes appreciable after 20 min. Intensification of the signal at 1.61 ppm and a decrease in the signal at 1.45 ppm, which subsequently vanishes, are observed simultaneously in the PMR spectrum; this is also in agreement with the A→B transition and the formation of a ring double bond. It should be noted that the signals of the protons of the $-CH_2C=$ groups of enolate B and of the alkylation products II lie at stronger field than the signals of the $-CH_2C=$ groups of starting Ia; this is explained by the electron-acceptor effect of the carbonyl groups in I. When both a freshly prepared solution of I and a solution of I that has stood for 3 days are acidified with trifluoroacetic acid, the resulting PMR spectra are identical to the spectrum of the original I. The formation of possible intermediate B cannot be established.

Similar changes in the PMR spectrum are observed for 4-cyclopentylidene-DDP (Ib) in solution in CD_3ONa + CD_3OD.

Thus the primary process in the reaction of 4-cycloalkylidene-DDP with sodium methoxide is the addition of a methoxy group to the exocyclic double bond, after which the resulting enolate A splits out a molecule of alcohol to give enolate B, which undergoes alkylation. Steric hindrance evidently prevents alkylation of anion A.

EXPERIMENTAL

The electronic absorption spectra of solutions [(1-4) · 10^{-5} M] of the compounds in ethanol and 90% ethanol containing 0.35% HCl or 0.1% KOH were recorded with an SF-16 spectrophotometer. The IR spectra of suspensions of the compounds in mineral oil were obtained with a UR-20 spectrometer. The PMR spectra of the compounds were recorded with Varian T-60 and Varian H-100 spectrometers with hexamethyldisiloxane as the internal standard. Chromatography was carried out on Silufol UV-254 plates in an ethyl acetate—hexane system (2 : 7).

Compounds IIa-d. A 0.1-mole sample of methyl iodide (or ethyl iodide) was added to a solution of 0.01 mole of starting Ia, b in 40 ml of a solution of sodium methoxide (0.022 g-atom of Na), and the mixture was allowed to stand in the dark for 5 days. It was then diluted with 30 ml of water, and the aqueous mixture was extracted with ether. The extract was dried over anhydrous sodium sulfate, and the solvent was removed by distillation. The oily residue began to crystallize when it was triturated with methanol, and was recrystallized from aqueous methanol (Table 2).

A total of 40% of the starting compound was isolated in the synthesis of IIa after acidification of the aqueous solution and extraction with ether.

LITERATURE CITED

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