RESEARCH ON THE CHEMISTRY OF PYRAZOLIDINE

XXI.* PRODUCTS OF THE REACTION OF 4-ARYLIDENE-1,2-DIPHENYL-3,5-DIOXYPYRAZOLIDINES WITH ALKOXIDES AND ALKYLATION OF THEM

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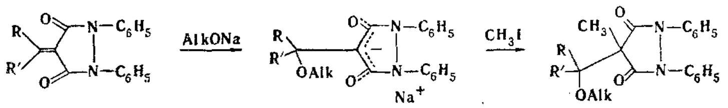
Sodium alkoxides readily add to the exocyclic double bond of variously substituted 4-benzylidene derivatives of 1,2-diphenyl-3,5-dioxopyrazolidine to give the sodium salts of 4-(1-alkoxybenzyl)-1,2-diphenyl-3,5-dioxopyrazolidines, the methylation of which leads to 4-methyl-4-(1-alkoxy-benzyl)-1,2-diphenyl-3,5-dioxopyrazolidines. This confirms the previously expressed assumption that the reason for the stability of the N—N bond and the exocyclic double bond of 4-benzylidene-1,2-diphenyl-3,5-dioxopyrazolidine in alkaline media with respect to catalytic hydrogenolysis is the formation under these conditions of a stable enolate.

We have previously expressed the assumption [2] that the reason for the resistance of the N—N bond and the exocyclic double bond of 4-arylidene-1,2-diphenyl-3,5-dioxopyrazolidines in ethanol containing KOH to catalytic hydrogenolysis is the addition of a hydroxyl group to the exocyclic double bond to give stable enolate anions [3]. This sort of direction of the reaction might have been expected considering the ability of these compounds [4] to add various nucleophilic reagents to the exocyclic double bond. The character of the UV spectra of 4-benzylidene derivatives in alkaline ethanol [2, 5] was also in agreement with the indicated assumption. However, the products of the addition of alkali or alkoxide to 4-benzylidenedioxopyrazolidines were not isolated. The preparation and some properties of compounds of this sort are described in the present paper.

Enol salts (V-X, Table 1), which can be isolated in quantitative yield by the addition of excess absolute ether, are formed in the reaction of 4-benzylidene derivative I and its substituted derivatives (II-IV) with an equimolecular amount of sodium alkoxide in the corresponding absolute alcohol (methanol, ethanol, and butanol).



I–IV V–X XI–XIV

I R=C_6H_5, R′=H; II R=p-$O_2NC_6H_4$, R′=H; III R=p-$CH_3OC_6H_4$, R′=H; IV R=R′=C_6H_5

The IR spectra of V-X are in good agreement with the structure assigned to them. An absorption band with a maximum at 1665-1675 cm^{-1} of medium or weak intensity and an intense broad band with maxima at 1610 and 1580 cm^{-1} are observed in the spectra of the addition products in place of the characteristic [for the starting dioxopyrazolidines (I-IV)] dicarbonyl doublet with maxima at 1680-1720 cm^{-1}. The position of the absorption maxima is almost the same as in the IR spectrum of the potassium salt of 4-butyl-1,2-diphenyl-3,5-dioxopyrazolidine (1664, 1596, and 1570 cm^{-1}); this is additional proof in favor of the enolate anion structure of V-X. The signal of a single benzyl proton (α-H) is observed in the PMR spectra of V-VII at δ 5.26-5.40 ppm, along with the signals of the protons of the corresponding alkoxy groups (Table 2).

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*See [1] for communication XX.

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TABLE 1. Characteristics of the Products of the Addition of Sodium Alkoxides to 4-Arylidene-1,2-diphenyl-3,5-dioxopyrazolidines

Compound	R	R′	Alk	Empirical formula	N, % found	N, % calc.	IR spectrum, cm^{-1}
V	C_6H_5	H	CH_3	$C_{23}H_{19}N_2O_3Na$	7,4	7,1	1580, 1610, 1675
VI	C_6H_5	H	C_2H_5	$C_{24}H_{21}N_2O_3Na$	7,0	6,9	1580, 1610, 1670
VII	C_6H_5	H	C_4H_9	$C_{26}H_{25}N_2O_3Na$	6,4	6,4	1585, 1610, 1665
VIII	$C_6H_4NO_2$-*p*	H	CH_3	$C_{23}H_{18}N_3O_5Na$	9,8	9,5	1346, 1528, 1585, 1605, 1667
IX	3,4-$(CH_3O)_2C_6H_3$	H	CH_3	$C_{25}H_{23}N_2O_5Na$	5,9	6,2	1585, 1605, 1665
X	C_6H_5	C_6H_5	CH_3	$C_{29}H_{23}N_2O_3Na$	6,0	6,0	1580, 1608, 1670

TABLE 2. PMR Spectra (in δ units) of the Protons of the Products of the Addition of Alkoxides to 4-Arylidene-1,2-diphenyl-3,5-dioxopyrazolidines and of the Alkylation Products (XI-XIV)

Compound	Recording conditions*	δ, ppm α-H	δ, ppm 4-CH_3	δ, ppm OAlk
V	CD_3OD, HMDS 100 MHz	5,26		3,37
VI	CD_3OD, HMDS 100 MHz	5,37		3,57; 1,21
VII	CD_3OD, HMDS 100 MHz	5,40		3,50; 1,6; 0,91
XI	CCl_4, HMDS 50 MHz	4,37	1,17	3,04
XII	CCl_4, TMS 60 MHz	4,56	1,26	3,17
XIII	CCl_4, TMS 40 MHz	4,45	1,31	3,27†
XIV	$CDCl_3$, HMDS 60 MHz	4,72	1,31	3,31; 1,02

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*Abbreviations: HMDS is hexamethyldisiloxane, and TMS is tetramethylsilane.

† The signals of the methoxy groups in $(CH_3O)_2C_6H_3$ are observed at 3.91 and 3.79 ppm.

In order to obtain neutral compounds containing an alkoxy group fixed in the α-position, we studied the alkylation of pyrazolidines I-IV in ethanol in the presence of sodium methoxide. 4-Methyl-4-(1-methoxybenzyl)-1,2-diphenyl-3,5-dioxopyrazolidine (XI) was isolated in 47% yield from the reaction of methyl iodide with I. Alkylation products of the same structure (XII, XIII) are also formed with II and III, but the yields are low (8-13%), and a large part of the starting materials are recovered. In the case of IV, no alkylation product at all could be isolated. Steric factors apparently play a substantial role in the alkylation of I-IV, as indicated by the negative results of alkylation with other bulkier (than methyl iodide) alkyl halides, particularly ethyl iodide, propyl iodide, and butyl bromide. Alkylation product XIV containing an ethoxy group in the α-position was also obtained when sodium methoxide was replaced by sodium ethoxide in the case of II.

A doublet with maxima at 1750-1765 and 1710-1730 cm^{-1}, which is characteristic for the β-dicarbonyl form of 3,5-dioxopyrazolidines, is observed in the IR spectra of XI-XIV.

The absorption maximum in the UV spectra of all of the compounds is at 238 nm and does not change its position on passing from neutral to acidic or alkaline media. The PMR spectra of XI-XIV (Table 2) also confirm their structures.

Thus the data obtained confirm the previously expressed assumption that the reason for the resistance of 4-arylidene-1,2-diphenyl-3,5-dioxopyrazolidines in alkaline media to catalytic hydrogenation is the formation of a stable enolate under these conditions.

EXPERIMENTAL

The UV spectra were recorded as previously indicated in [2]. The IR spectra of suspensions in mineral oil were recorded with a UR-10 spectrometer.

Sodium Salts of 4-(1-Alkoxybenzyl)-1,2-diphenyl-3,5-dioxopyrazolidines (V-X, Tables 1 and 2). An equimolecular amount of I-IV was added to a freshly prepared solution of sodium alkoxide in the minimum amount of the corresponding alcohol, and the mixture was stirred in the cold until a colorless solution had formed. An excess of absolute ether was then added, and the finely crystalline precipitate was removed by filtration and dried. The yield was close to quantitative.

4-Methyl-4-(1-methoxybenzyl)-1,2-diphenyl-3,5-dioxopyrazolidine (XI). A 1.7 g (0.005 mole) sample of I was added to 20 ml of freshly prepared 1% solution of sodium methoxide in absolute methanol, and 7.1 g (0.05 mole) of methyl iodide was added. The mixture was stored in a dark place for 4 days, after which it was diluted with water and extracted with ether. Acidification of the aqueous solution yielded 0.74 g (42%) of starting I with mp 163-164°. The ether extract was washed successively with a weak alkali solution and water until it was neutral, and it was then dried with anhydrous sodium sulfate and evaporated to dryness. Recrystallization of the residue from aqueous methanol gave 0.9 g (47%) of a colorless crystalline substance with mp 127-128° and R_f 0.59 [activity II aluminum oxide, chloroform–benzene (3 : 1)]; development in UV light. UV spectrum (neutral, acid, and alkaline solutions in ethanol): λ_{max} 238 nm (log ε 4.30). IR spectrum: 1750, 1711, 1600 cm^{-1}. Found, %: C 74.7; H 5.9; N 7.4. $C_{24}H_{21}N_2O_3$. Calculated, %: C 74.8; H 5.5; N 7.3.

4-Methyl-4-(1-methoxy-4-nitrobenzyl)-1,2-diphenyl-3,5-dioxopyrazolidine (XII). This compound was obtained as in the preceding experiment in 8% yield (87% of the starting II was recovered). The colorless product had mp 159-160° (from aqueous methanol) and R_f 0.59 [Silufol, petroleum ether–chloroform–methanol (9 : 4 : 1)]. UV spectrum (neutral, acid, and alkaline solutions in ethanol): λ_{max} 238 nm (log ε 4.25). IR spectrum: 1755, 1722, 1600, 1530 cm^{-1}. Found, %: N 9.6. $C_{24}H_{21}N_3O_5$. Calculated, %: N 9.8.

4-Methyl-4-(1-methoxyveratryl)-1,2-diphenyl-3,5-dioxopyrazolidine (XIII). This compound was obtained in 13% yield (85% of the starting III was recovered) by the method used to prepare XI. The light-yellow crystalline product had mp 156-157° (from methanol) and R_f 0.12 [alkaline aluminum oxide, benzene–chloroform (13 : 2)]. UV spectrum (neutral, acid, and alkaline solutions in ethanol): λ_{max} 238 nm (log ε 4.3). IR spectrum: 1758, 1732, 1600 cm^{-1}. Found, %: C 69.9; H 6.4; N 6.4. $C_{26}H_{26}N_2O_5$. Calculated, %: C 69.9; H 5.9; N 6.3.

4-Methyl-4-(1-ethoxy-4-nitrobenzyl)-1,2-diphenyl-3,5-dioxopyrazolidine (XIV). This compound was obtained in 30% yield by the method used to prepare XII, except that sodium ethoxide in ethanol was used. The colorless crystalline product had mp 133-134° and R_f 0.76 [Silufol, petroleum ether–chloroform–methanol (9 : 4 : 1)]. Found, %: N 9.8. $C_{25}H_{23}N_3O_5$. Calculated, %: N 9.5. UV spectrum (neutral, acid, and alkaline solutions in ethanol): λ_{max} 238 nm (log ε 4.26). IR spectrum: 1764, 1730, 1600, 1530 cm^{-1}.

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