ELECTROPHILIC ADDITION TO 2-FORMYL-2,5-DIALKOXY-2,3-DIHYDRO-γ-PYRANS

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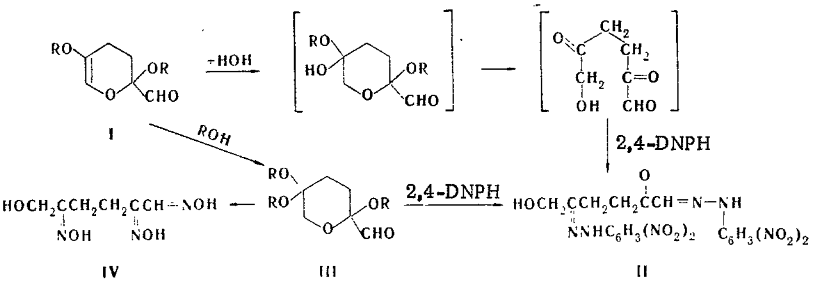
It is shown that polarization of the endocyclic double bond in the electrophilic addition of alcohols and water to 2-formyl-2,5-dialkoxy-2,3-dihydro-γ-pyrans is directed toward the carbon atom in the 6 position.

We have previously obtained 2-formyl-2,5-dialkoxy-2,3-dihydro-γ-pyrans (I) by diene self-condensation of 2-alkoxyacroleins [1]. The establishment of the free-radical character of this reaction in the present research enabled us to considerably accelerate it by the action of UV irradiation and to raise the yields of adducts appreciably. The photochemical reaction proceeds stereoselectively and is not accompanied by the formation of the isomeric addition product that is observed during the thermal process [1].

A peculiar structural feature of pyrans I is the location of the C=C bond between two oxygen atoms. In the present research we set out to determine the direction of polarization of the double bond in dihydropyrans I and its relative activity in electrophilic addition reactions. A linear product of the addition of two molecules of 2,4-dinitrophenylhydrazine (2,4-DNPH) is primarily formed in the hydrolytic cleavage of dihydropyrans I with 2 N hydrochloric acid in the cold in the presence of 2,4-DNPH (I to 2,4-DNPH molar ratio 1 : 2). In a determination of its structure on the basis of the PMR spectra we assigned to it the 6-hydroxy-2,5-dioxohexanal 1,5-bis(2,4-dinitrophenylhydrazone) structure (II), although the isomeric 1,2-bis(hydrazone) structure also seems acceptable. The appearance in the PMR spectrum of a solution of II in dimethyl sulfoxide (DMSO) of a signal in the region peculiar to the alcohol OH group (δ 5.1 ppm) [2] and the character of the splitting (triplet, J = 6.1 Hz) unambiguously attest to the presence of a CH_2OH group in the molecule. This structure is also confirmed by an analysis of the IR spectrum.



The indicated conditions for the hydrolysis of dihydropyran I are most convenient for the isolation of individual bishydrazone II, which is formed in the greatest amount. Possible oxidation and reduction reactions of the adjacent OH group (see [3]) do not occur in this case. A mixture of products of the reaction of 2,4-DNPH with three and four carbonyl groups, which is not amenable to separation by recrystallization, is formed in other cases (on heating, alcohol media, or in the presence of 2,4-DNPH).

Almost quantitative yields of 2-formyl-2,5,5-trialkoxytetrahydro-γ-pyrans (III) are formed by the action of excess alcohol on dihydropyran I at 0° in the presence of a catalytic amount of hydrogen chloride.

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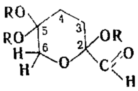
TABLE 1. Parameters of the PMR Spectra of 2-Formyl-2,5,5-Trialkoxytetrahydro-γ-pyrans

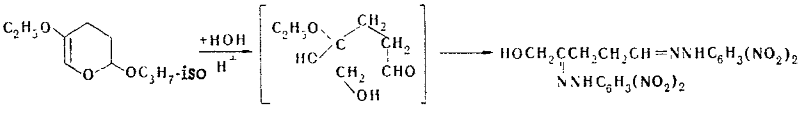


R	Chemical shifts, δ, ppm					J, Hz	
	CHO	3- and 4-H	6-H_e	6-H_a	R	$J_{66'}$	$J_{6'4}$
C_2H_5	9,35	1.67—1.73	3,72	3,36	3,44; 0,92	11,5	2,2
CH_3	9,35	1.67—1.73	3,73	3,37	3,21; 3,19; 3,15	11,5	2.2

Under the indicated conditions, the formation of acetals with the participation of the carbonyl group was not observed even in the presence of a sevenfold excess of the alcohol. An increase in the reaction time and an increase in the reaction temperature (at 70° for 2 h) reduced the yield of II to 40%. When the reaction was carried out at 20° for 3 days (the conditions for the addition of alcohol to 2-formyl-2,3-dihydro-γ-pyran [4]) tetrahydropyran III could not be isolated at all because of pronounced resinification. The structure of III was confirmed by titration with hydroxylamine (which leads to the formation of trioxime IV), by the preparation of a 2,4-DNPH derivative (II) under the conditions of hydrolytic opening of the heteroring, and also by the PMR (see Table 1) and IR spectra.

Both the 6-H chemical shifts (in the case of addition of an OR group to the 6 position the 6-H proton should be observed at weaker field) and the spin–spin coupling constants, which are characteristic for the geminal protons in such systems [5], indicate the presence of two OR groups in the 5 position in the III molecule. The weak-field portion of the quartet at 3.72 ppm, which is due to the equatorial 6'-H proton [6], experiences additional splitting. By double resonance methods (INDOR and total double resonance) we established that it is due to the long-range spin–spin coupling of 6'-H with the protons in the 4 position. A similar interaction through four bonds was previously noted in such systems [7].

In order to confirm the direction of electrophilic attack of the endocyclic double bonds we carried out the reaction of 2-isopropoxy-5-ethoxy-2,3-dihydro-γ-pyran (V) with 2,4-DNPH in an acidic aqueous medium. We obtained 5-hydroxy-4-oxopentanal 1,4-bis(2,4-dinitrophenylhydrazone) (VII). Its formation is possible if ring opening of I occurs through the intermediate formation of VI.



$\mathrm{HOCH_2\underset{\|}{C}CH_2CH_2CH{=}NNHC_6H_3(NO_2)_2}$

$\mathrm{NNHC_6H_3(NO_2)_2}$

V VI VII

Thus the investigated reactions prove the predominant effect of the OR group rather than the endocyclic oxygen atom on polarization of the double bond in 2,5-dialkoxy-2,3-dihydro-γ-pyrans.

EXPERIMENTAL METHOD

The PMR spectra were recorded with a Tesla BF 487B spectrometer (80 MHz) with hexamethyldisiloxane as the standard.

2-Formyl-2,5-diethoxy-2,3-dihydro-γ-pyran (I, R = C_2H_5). A 38-g (0.38 mole) sample of α-ethoxyacrolein was irradiated with the UV light of a PRK-2 lamp (1000 W) for 2.5 h at 120-140°, after which distillation gave 24.5 g (70%) of dihydropyran I (R = C_2H_5) with bp 92-93° (3 mm) and n_D^{20} 1.4585 [1]. The freshly distilled product crystallized on storing in a refrigerator to give a product with mp +6°.

2-Formyl-2,5-dimethoxy-2,3-dihydro-γ-pyran (I, R = CH_3). This compound was obtained in 62% yield by UV irradiation of α-methoxyacrolein at 90-100° for 5 h. Its physical constants were in agreement with the literature values [8].

2-Formyl-2,5-dibutoxy-2,3-dihydro-γ-pyran (I, R = C_4H_9). A 14.0-g (0.11 mole) sample of α-butoxyacrolein was irradiated with UV light at 85-90° for 3 h, after which fractionation gave 8.6 g (62%) of dihydropyran (I) (R = C_4H_9) with bp 136° (3 mm), n_D^{20} 1.4568, and d_4^{20} 1.0111. Found: C 65.9; H 9.7%; MR_D 68.93. $C_{14}H_{24}O_4$. Calculated: C 65.7; H 9.4%; MR_D 69.12.

6-Hydroxy-2,5-dioxohexanal 1,5-Bis(2,4-dinitrophenylhydrazone) (II). A 1.0-g (0.005 mole) sample of dihydropyran I (R = C_2H_5) was added to a solution of 2.0 g (0.01 mole) of 2,4-DNPH in 2 N HCl cooled to +5°, and the resulting precipitate was washed thoroughly with 2 N HCl and water and recrystallized three times from tetrahydrofuran (THF). The yield of the bishydrazone, with mp 203°, was 1.0 g (40%). IR spectrum (KBr pellet): 3490 (OH) and 1725 cm^{-1} (C = O). The PMR spectrum contains signals at δ 12.3 (NH), 7.8-8.8 (C_6H_3), 8.4 (N = CH), 5.1 (OH), 4.0 (doublet, OCH_2), and 2.7 ppm (CH_2). Found: C 42.5; H 3.4; N 22.2%. $C_{17}H_{16}N_8O_8$. Calculated: C 42.9; H 3.2; N 22.2%.

2-Formyl-2,5,5-triethoxytetrahydropyran (III, R = C_2H_5). Five drops of alcohol saturated with HCl were added to a solution of 27.5 g (0.138 mole) of dihydropyran I (R = C_2H_5) in 50 ml (1.05 mole) of absolute alcohol cooled to 0°, and the reaction mixture was held at 0° for 1 h. The solvent was removed, and the residue was distilled to give 26.4 g (92%) of tetrahydropyran III (R = C_2H_5) with bp 107-107.5° (2 mm), n_D^{20} 1.4412, and d_4^{20} 1.0490. Found: C 58.7; H 8.8%; MR_D 61.98. $C_{12}H_{22}O_5$. Calculated: C 58.6; H 8.9%; MR_D 62.04. Absorption at 1733 cm^{-1} (C = O) was noted in the IR spectrum of a thin layer of the product, and absorption in the double-bond region was absent. Titration with hydroxylamine [9] indicated the presence of three carbonyl groups. Hydrolysis of the product in the presence of 2,4-DNPH under the conditions presented for dihydropyran I gave bishydrazone II in 62% yield; no melting-point depression was observed for a mixture of this product with an authentic sample of II. The IR spectrum of the product was identical to the spectrum of II obtained from I.

2-Formyl-2,5,5-trimethoxytetrahydropyran (III, R = CH_3). This compound, with bp 115° (5 mm), n_D^{20} 1.4500 and d_4^{20} 1.1549, was similarly obtained in 60% yield. Found: C 52.6; H 7.7%; MR_D 47.67. $C_9H_{16}O_5$. Calculated: C 53.0; H 7.8%; MR_D 48.14.

2-Isopropyl-5-ethoxy-2,3-dihydro-γ-pyran (V). A mixture of 22.9 g (0.229 mole) of α-ethoxyacrolein and 494 g (4.56 mole) of vinyl isopropyl ether was heated in an autoclave at 160-170° for 12 h, after which rectification gave 6.0 g (20%) of dihydropyran V with bp 61° (2 mm) and n_D^{20} 1.4455 [1].

5-Hydroxy-4-oxopentanal 1,4-Bis(2,4-dinitrophenylhydrazone) (VII). A 1.6-g (0.007 mole) sample of dihydropyran V was added to a solution of 3.0 g (0.015 mole) of 2,4-DNPH in 2 N HCl cooled to +5°. Three recrystallizations of the product from THF gave 2.9 g (70%) of 1,4-bishydrazone VII with mp 231°. Absorption at 3500 cm^{-1} (m, OH) was noted in the IR spectrum of a KBr pellet of the product, and absorption at 1730 cm^{-1} (C = O) was absent. Found: C 42.8; H 3.4; N 23.4%. $C_{17}H_{16}N_8O_9$. Calculated: C 42.9; H 3.4; N 23.5%.

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