ARYLOXYDIHYDROPYRANS

V*. INFLUENCE OF THE NATURE OF THE SUBSTITUENT ON ACETAL FORMATION

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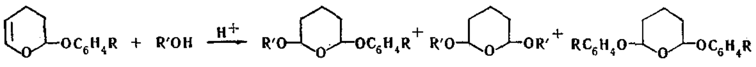
2-Alkoxy-6-aryloxytetrahydropyrans and a number of new 2,6-diaryloxytetrahydropyrans have been synthesized by the reaction of 2-aryloxy-3,4-dihydropyrans with ethanol, propargyl alcohol, phenol, p-cresol, and p-chlorophenol. The nature of the substituents present in the benzene ring of the aryloxydihydropyrans (CH_3, Cl, OCH_3) has a fundamental influence on the yield of these mixed acetals.

Continuing an investigation on the reactivity of the double bond of the dihydropyran ring, in the present work we have studied the condensation of hydroxyl-containing compounds with 2-aryloxy-3,4-dihydropyrans containing various substituents in the benzene ring (I-VI). All the experiments were carried out under the same conditions, which were those previously proposed for the synthesis of acetals from 2-phenoxy-3,4-dihydropyran [1]. It was shown that the reaction of equimolecular amounts of I-VI with alcohols in an acid medium usually forms two symmetrical acetals and one mixed acetal.



I-VI VII-XVIII XIX, XX XXI, XXVI

R=H (I, VII, VIII, XXI); *o*-CH_3 (II, IX, X, XXII); *m*-CH_3 (III, XI, XII, XXIII); *p*-CH_3 (IV, XIII, XIV, XXIV); *p*-Cl (V, XV, XVI, XXV); *p*-OCH_3 (VI, XVII, XVIII, XXVI); R′=C_2H_5 (VII, IX, XI, XIII, XV, XVII, XIX); $HC{\equiv}CCH_2$ (VIII, X, XII, XIV, XVI, XVIII, XX).

The yields of the 2-alkoxy-6-aryloxytetrahydropyrans (VII-XVIII, Tables 1 and 2) depend on the nature of the substituents in the benzene ring of I-VI. Electron-donating groups, particularly when present in the ortho and para positions with respect to the ethereal oxygen, raise, and electron-accepting substituents such as chlorine lower, the percentage formation of the mixed acetals. Thus, for example, the yield of 2-aryloxy-6-ethoxytetrahydropyrans decreases with a rise in the negative induction effect of the substituents (Table 1).

At the same time, the amount of symmetrical reaction products formed rises. Propargyl alcohol is capable of forming more stable mixed acetals with the dihydropyrans I-VI. Apparently for this reason, their yields are higher than in the reaction with ethanol. However, in their influence on the yield of 2-aryloxy-6-propynyloxytetrahydrofurans the substituents of the aryloxy group fall into the same sequence.

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*For Communication V, see [3].

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TABLE 1. Relationship between the Yield of Mixed Acetyl and the Nature of the Substituent in the Phenyl Ring of a 2-Aryloxy-3,4-dihydropyran

	R	*p*-CH_3	*o*-CH_3	*p*-OCH_3	*m*-CH_3	H	*p*-Cl
Yield, %	$R'=C_2H_5$	38	36	32	25	21	14
	$R'=C_3H_3$	45	45	41	37	34	25
	$R'=p\text{-}CH_3C_6H_4$	90	80	79	76	78	77

TABLE 2. 2-Alkoxy-6-aryloxytetrahydropyrans (IX-XVIII)

Compound	R	R′	Bp, °C (pressure, mm)	d_4^{20}	n_D^{20}	MR_D		Empirical fourmula	Found, %		Calculated, %		Yield, %
						found	calculated		C	H	C	H	
IX	*o*-CH_3	C_2H_5	148 (8)	1,0471	1,5005	66,33	65,98	$C_{14}H_{20}O_3$	71,0	8,5	71,2	8,5	36
X	*o*-CH_3	C_3H_3	151 (5)	1,0893	1,5205	68,70	68,60	$C_{15}H_{18}O_3$	73,0	7,3	73,2	7,3	45
XI	*m*-CH_3	C_2H_5	168 (16)	1,0432	1,5000	66,53	65,98	$C_{14}H_{20}O_3$	71,3	8,5	71,2	8,5	25
XII	*m*-CH_3	C_3H_3	142 (2)	1,0875	1,5195	68,71	68,60	$C_{15}H_{18}O_3$	73,4	7,5	73,2	7,3	37
XIII	*p*-CH_3	C_2H_5	141 (3)	1,0512	1,5040	66,36	65,98	$C_{14}H_{20}O_3$	71,1	8,5	71,2	8,4	38
XIV	*p*-CH_3	C_3H_3	146 (3)	1,0870	1,5190	68,68	68,60	$C_{15}H_{18}O_3$	73,4	7,3	73,2	7,3	45
XV	*p*-Cl	C_2H_5	153 (1,5)	1,1694	1,5190	66,45	66,23	$C_{13}H_{17}O_3Cl$	61,1	6,7	60,8	6,6	14
XVI	*p*-Cl	C_3H_3	168 (6)	1,1935	1,5351	69,38	68,85	$C_{14}H_{15}O_3Cl$	63,3	5,7	63,0	5,6	25
XVII	*p*-CH_3O	C_2H_5	201,5 (16)	1,1041	1,5073	67,94	67,62	$C_{14}H_{20}O_4$	66,4	8,0	66,7	7,9	32
XVIII	*p*-CH_3O	C_3H_3	194 (8)	1,1290	1,5237	70,96	70,24	$C_{15}H_{18}O_4$	68,3	6,9	68,7	6,9	41

TABLE 3. 2,6-Diaryloxytetrahydropyrans (XXIV-XXXIII)

Compound	R	R″	mp., °C	Empirical formula	Found, %		Calc., %		Yield, %
					C	H	C	H	
XXIV	*p*-CH$_3$	*p*-CH$_3$	81	$C_{19}H_{22}O_3$	76,9	7,2	76,8	7,4	90
XXV	*p*-Cl	*p*-Cl	92	$C_{17}H_{16}O_3Cl_2$	60,0	4,8	60,2	4,7	97
XXVI	*p*-CH$_3$O	*p*-CH$_3$O	67	$C_{19}H_{22}O_5$	69,0	6,6	69,1	6,7	11 *
XXVII	*o*-CH$_3$	*p*-CH$_3$	78 †	$C_{19}H_{22}O_3$	76,4	7,4	76,8	7,4	80
XXVIII	*o*-CH$_3$	*p*-Cl	92	$C_{18}H_{19}O_3Cl$	67,8	5,9	67,8	6,0	98
XXIX	*m*-CH$_3$	*p*-CH$_3$	81,2‡	$C_{19}H_{22}O_3$	76,9	7,4	76,8	7,4	78
XXX	*m*-CH$_3$	*p*-Cl	91,6	$C_{18}H_{19}O_3Cl$	67,8	6,0	67,8	6,0	93
XXXI	*p*-CH$_3$	*p*-Cl	90,3	$C_{18}H_{19}O_3Cl$	67,7	6,0	67,8	6.0	98
XXXII	*p*-CH$_3$O	*p*-CH$_3$	64,2	$C_{19}H_{22}O_4$	72,5	6,9	72,6	7,0	79
XXXIII	*p*-CH$_3$O	*p*-Cl	74	$C_{18}H_{19}O_4Cl$	64,4	5,7	64,6	5,6	98

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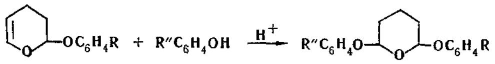
* Compound XXVI was obtained by the reaction of VI with ethanol as a result of disproportionation.

† d_4^{20} 1.1103; n_D^{20} 1.5475; found MR_D 85.17; calculated MR_D 85.47.

‡ bp 186°C (1.5); d_4^{20} 1.1041; n_D^{20} 1.5501; found MR_D 85.76; calculated MR_D 85.47.

Compounds I-VI behave peculiarly with phenols. Regardless of the nature of the substituents in their benzene rings, the starting materials are converted completely into 2,6-diaryloxytetrahydropyrans (XXI, XXIV, XXV, XXVII-XXXIII, Table 3).



XXI, XXIV, XXV, XXVII-XXXIII

XXI R=H; XXVII, XXVIII *o*-CH$_3$; XXIX, XXX *m*-CH$_3$; XXIV, XXXI *p*-CH$_3$; XXV *p*-Cl; XXXII, XXXIII *p*-CH$_3$O;
XXI R″=H; XXIV, XXVII, XXIX, XXXII *p*-CH$_3$; XXV, XXVIII, XXX, XXXI, XXXIII *p*-Cl

No disproportionation of the reaction products is observed, and no symmetrical acetals were isolated in those cases where R and R″ were different. The structure and purity of the 2,6-diaryloxytetrahydropyrans were shown by their infrared spectra and elementary and chromatographic analysis. The influence of substituents on the yields of the tetrahydropyrans XXIV, XXVII, XXIX, and XXXII – the products of the addition of p-cresol to I-VI – was as before (Table 1).

Higher, almost quantitative, yields of acetals (XXV, XXVIII, XXX, XXXI, XXXIII) are given with chlorophenol by all the dihydropyrans I-VI studied. Chlorine, possessing a high electronegativity, ensures a high mobility of the hydrogen atom and this apparently explains the ease with which the addition of chlorophenol to the double bond of the dihydropyan ring takes place. p-Aminophenol differs considerably in its activity in this acetal-forming reaction from the phenols mentioned above. Attempts to add it to the 2-aryloxy-3,4-dihydropyrans I-VI were unsuccessful, and distillation usually gave the initial aryloxydihydropyrans and p-aminophenol. Thus, the activity of the phenols studied in their reaction with the double bond of the dihydropyran ring falls with a decrease in the acidity of the phenol.

Spectral investigations of compounds I-VI show an increase in the C = C stretching vibrations of the pyran ring from 1630 cm^{-1} (for the unsubstituted pyran ring) [2] to 1670-1680 cm^{-1} with the introduction of electron-donating cresoxy substituents into position 2. The shift in the vibrational frequencies under the influence of substituents is in harmony with the σ constants of Hammett's equation [3]. The relationships obtained show that in compounds I-VI the oxygen atom connecting the dihydropyran and aromatic rings transmits the influence of the substituted phenyl radical fairly well. The vinyloxy group in these compounds is more sensitive to the transmission of the of the electronic influences of the substituents of the benzene ring than in simple aryl vinyl ethers. This is confirmed by the investigations in the present work of the electrophilic addition of alcohols and phenols to various 2-aryloxy-3,4-dihydropyrans.

EXPERIMENTAL

The 2-aryloxy-3,4-dihydropyrans (I-VI) were obtained by the condensation of the corresponding aryl vinyl ethers with acrolein in an autoclave with heating [4]. The alcohols were rendered absolute and the phenols were redistilled for the reactions.

2-Ethoxy-6-phenoxytetrahydropyran (VII). With mechanical stirring, three drops of a solution of hydrogen chloride in absolute dioxane was added to a mixture of 17.6 g (0.1 mole) of 2-phenoxy-3,4-dihydropyran (I) and 4.6 g (0.1 mole) of absolute ethanol. The temperature of the reaction mixture rose to 40°C. After 3 h the product was neutralized with potassium carbonate and distilled in vacuum. This gave 4.66 g (21%) of VII, 3.05 g (35%) of 2,6-diethoxytetrahydropyran (XIX) and 1.35 g (10%) of 2,6-diphenoxytetrahydropyran [1].

2-(p-Cresoxy)-6-ethoxytetrahydropyran (XIII) was obtained in a similar manner to VII; in addition to XIII, 19% of XIX and 5% of 2,6-di(p-cresoxy)tetrahydropyran (XIV) were obtained.

The other acetals (Table 2) were obtained under similar conditions.

The 2,6-diaryloxytetrahydropyrans (XXVII-XXXIII, Table 3) were obtained in a similar manner to VII. During the reaction the mixture solidified. The products obtained were crystallized from ethanol.

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