CLEAVAGE OF 2-METHYL-5,6-DIHYDRO-2H-PYRANE BY ACID HALIDES

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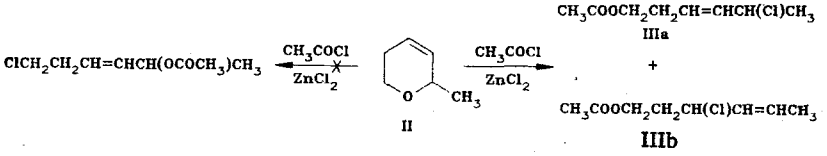
The reaction of 2-methyl-5,6-dihydro-2H-pyrane with a number of acid halides in which the ring is cleaved is accompanied by an allylic rearrangement. The halogen atom in the isomers is replaced in the usual way by nucleophilic reagents, but aqueous alkali causes in addition the formation of 1,3,5-hexatriene and to a lesser extent recyclization to dihydropyrane.

The cleavage of the ether bond in dihydropyranes is of interest as a way of synthesizing various unsaturated compounds that contain functional groups.

It is known that by the action of acetyl bromide in the presence of zinc chloride, 5,6-dihydro-2H-pyrane forms a mixture of isomeric ethers, viz., 1-acetoxy-5-bromo-2- and -3-pentenes [1]. In the case of 4-methyl-5,6-dihydro-2H-pyrane (I) the reaction with acetyl chloride under similar conditions yields mainly a single product, 1-acetoxy-5-chloro-3-methyl-3-pentene [2]. This discrepancy has no satisfactory explanation, and new experimental data are needed to resolve it. The present work is a study of the reaction of 2-methyl-5,6-dihydro-2H-pyrane (II) with a number of aliphatic and aromatic acid halides in the presence of metal halides. We find that when acetyl chloride reacts with II, regardless of reaction conditions and catalyst, two products, IIIa and IIIb, form in 1.5:1 ratio, and cannot be sepearated by the usual methods.

The PMR spectrum of the mixture contains two doublets in the 1.50-1.66 region (CH_3), a singlet at 1.90 (CH_3CO—), and 4 multiplets in the following regions: 2.00-2.50 (CH_2), 3.70-4.10 (—CH_2—O—), 4.10-4.40 (—CHCl—), 5.30-5.70 ppm (—CH=CH—). The addition of a shift reagent shifts the methylene signal at 3.70-4.10 ppm toward the weaker field; this demonstrates a single direction of pyrane cleavage to form 1-acetoxychlorohexenes. The double resonance at the methyne proton (4.10-4.40 ppm) converts one of the methyl doublets (1.50 ppm) to a singlet. This is explainable by the formation, along with the normal reaction product 1-acetoxy-5-chlorohexene-3 (IIIa), of its allyl isomer 1-acetoxy-3-chlorohexene-4 (IIIb);



The IIIa:IIIb ratio is apparently at equilibrium, because it is maintained when the product is heated at 100°C. Under optimum conditions the overall yield is 50% (Table 1).

In all probability, in the case of 5,6-dihydro-2H-pyrane there also occurs allylic rearrangement, but not the twofold ring cleavage. In the reaction of I with acetyl chloride, a similar conversion ought to yield a tertiary halogen derivative with a terminal double bond, but it is known that such products are less stable.

The nature of the halogen (Cl, Br) and the structure of the acid residue (C_3H_7, C_4H_9, C_6H_5) (Table 1) have practically no effect on the reaction with II; consequently it can be presumed that the determining factor is the structure of the ester itself. The isomer ratio (2:1 and 1.2:1) could be determined by PMR only for VII and IX. The thermal stability of the haloesters decreases as the acid residue becomes more complicated. Thus, IX and X decompose when distilled, and are separated by column chromatography.

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TABLE 1. 1-Carbalkoxyhalohexenes, $RCOOCH_2CH_2CH{=}CHCH(X)CH_3$

Isomers a and b	R	X	Bp, °C (p, gPa)	n_D^{20}	R_f*	PMR spectrum, ppm				Found, %			Empirical formula	Calculated, %			Yield, %
						CH_3	CH_3—C(=O)—	—CHX—	—CH=CH—	C	H	Cl(Br)		C	H	Cl(Br)	
III	CH_3	Cl	62 (4)	1,4552	0,46	1,5; 1,9	3,7—4,1	4,1—4,4	5,3—5,7	54,21	7,01	19,63	$C_8H_{13}ClO_2$	54,54	7,38	19,88	51
IV	CH_3	Br	70 (7)	1,4823	0,43	1,6	3,7—4,0	4,0—4,3	5,2—6,3	43,19	5,35	(36,08)	$C_8H_{13}BrO_2$	43,43	5,88	(36,19)	50
V	C_3H_7	Cl	115 (4)	1,4559	0,40	0,6—1,0	3,8—4,1	4,1—4,5	5,2—5,7	58,51	8,03	17,00	$C_{10}H_{17}ClO_2$	58,82	8,33	17,15	35
IV	C_3H_7	Br	112 (4)	1,4310	0,67	0,7—1,0	3,8—4,1	4,1—4,6	5,2—5,7	48,25	6,38	(39,26)	$C_{10}H_{17}BrO_2$	48,19	6,82	(39,12)	46
VII	C_3H_5†	Cl	89 (7)	1,4772	0,46	1,4; 1,5	4,0—4,2	4,2—4,4	5,4—5,7	59,18	7,15	17,03	$C_{10}H_{15}ClO_2$	59,40	7,42	17,32	55
VIII	C_4H_9	Cl	97 (7)	1,4550	0,45	0,7—1,0	3,8—4,1	4,1—4,5	5,1—5,7	60,21	8,25	16,31	$C_{11}H_{19}ClO_2$	60,55	8,71	16,05	38
IX	C_6H_5	Cl	—	1,5235	0,42	1,4; 1,6	4,0—4,2	4,2—4,5	5,4—5,7	65,32	6,19	14,59	$C_{13}H_{15}ClO_2$	65,54	6,30	14,70	50
X	C_6H_5	Br	—	1,5350	0,67	1,6—1,9	4,0—4,2	4,2—4,5	5,0—5,7	55,43	5,51	(28,35)	$C_{13}H_{15}BrO_2$	55,12	5,30	(28,26)	25

*Al_2O_3, 9:1 benzene—alcohol.
†Crotonic acid derivative.

It was shown in [2] that when the chlorester obtained by cleavage of I is heated with aqueous alkali it readily recyclizes back to the dihydropyrane. In our case, isomer IIIa also ought to cyclize, but this reaction is strongly hindered by the presence of the methyl group. Specifically, when a mixture of IIIa and IIIb is heated for 2 h with 40% aqueous KOH the yield of II does not exceed 11%. At the same time 1,3,5-hexatriene is formed in appreciable quantity (21%). In view of the reaction conditions this finding must be considered as unexpected. Moreover, the conversions usual in such cases also take place, viz., saponification of the ester group and replacement of the halogen, because according to GLC data a considerable amount of high-boiling product is formed.

The action of some other nucleophilic reagents (ammonium thiocyanate, piperidine, morpholine) on 1-acetoxychlorohexenes gives products of halogen replacement. The reaction with ammonium thiocyanate is accompanied by partial isomerization to form isothiocyanates, the total amount of which, determined by chemical methods, is 11% [4].

$$CH_3COOCH_2CH_2CH{=}CHCH(SCN)CH_3 \longrightarrow CH_3COOCH_2CH_2CH(NCS)CH{=}CHCH_3$$

In view of the complexity of the mixture it was not possible to estimate the content of the individual isomers by IR or PMR spectroscopy.

EXPERIMENTAL

1. Reaction of 2-Methyl-5,6-dihydro-2H-pyrane with Acid Chlorides. To a suspension of 0.45 g (3 mmole) $ZnCl_2$ in 18 ml anhydrous dichloroethane was added 8.8 g (90 mmole) of 2-methyl-5,6-dihydro-2H-pyrane. To the mixture was added 5.4 g of acetyl chloride (90 mmole) over 2 h at room temperature with stirring; then 10-15 ml water was poured in. The organic layer was separated, washed with $NaHCO_3$ solution and water, and dried with $MgSO_4$. The dichloroethane was removed with a water aspirator and the residue was vacuum-distilled. There was obtained 7.7 g (51%) of 1-acetoxychlorohexenes, bp 62° (4 gPa). Similar experiments were carried out under other conditions and with various acid chlorides (Table 1). After removal of dichloroethane, IX and X were separated from the reaction mixture by column chromatography (Al_2O_3, CCl_4 eluent, d = 10 mm, h = 180 mm).

2. Reaction of 1-Acetoxychlorohexenes with Ammonium Thiocyanate. A mixture of 2.2 g (12 mmole) of 1-acetoxychlorohexenes, 1.5 g (20 mmole) of ammonium thiocyanate, and 7 ml of acetone was stirred at room temperture for 24 h. After the acetone was removed 10 ml of water was added, the mixture was extracted with ether, the extract was dried with $MgSO_4$, and the ether was evaporated. The residue was chromatographed on a column under the conditions described above. There was obtained 1.4 g of a mixture of 1-acetoxythiocyano- and 1-acetoxyisothiocyanohexenes, bp 145° (4 gPa), n_D^{20} 1.0650; R_f 0.58 (Al_2O_3, 9:1 benzene–alcohol). PMR spectrum (CCl_4): 5.3-5.7 (2H, m, CH=CH), 3.8-4.3 (3H, m, CH, CH_2–O), 2.1-2.5 (2H, m, CH_2), 1.95 (3H, s, CH_3CO–), 1.3-1.7 m.d (3H, 2 d, $2CH_3$). Found: C 54.03; H 6.32; N 7.28; S 15.92%. $C_9H_{13}NO_2S$. Calculated: C 54.27; H 6.53; N 7.03; S 16.08%. Isothiocyanate content was determined according to [4].

3. Reaction of 1-Acetoxychlorohexenes with Amines. A mixture of 2.4 g (14 mmole) of 1-acetoxychlorohexenes, 2.5 g (29 mmole) of piperidine, and 5 ml of benzene was stirred at room temperature for 140 h. Then the reaction mixture was treated as in paragraph 2 above. There was obtained 1.3 g (42%) of 1-acetoxy-piperidinohexenes, bp 100° (7.8 gPa), n_D^{20} 1.4715; R_f 0.66 (Al_2O_3, 9:1 benzene–alcohol). PMR spectrum (CCl_4): 5.9-5.5 (2H, m, CH=CH), 3.6-4.1 (3H, M, CH_2–O), 2.5-2.9 (2H, m, CH_2), 2.0-2.5 (4H, m, $2CH_2$), 1.9 (3H, s, CH_3CO–), 1.2-1.7 (6H, m, $3CH_2$), 0.95 ppm (3H, d, CH_3). Found: C 69.02; H 10.12; N 6.03%. $C_{13}H_{23}NO_2$. Calculated: C 69.33; H 10.22; N 6.22%.

1-Acetoxymorpholinohexenes were obtained similarly in 45% yield, bp 105° (7.8 gPa), n_D^{20} 1.4783; R_f 0.75 (Al_2O_3, 9:1 benzene–alcohol). PMR spectrum (CCl_4): 5.0-5.5 (2H, m, CH=CH), 3.6-4.1 (3H, m, CH, CH_2–O–), 3.0-3.5 (4H, m, $2CH_2$), 2.0-2.9 (6H, m, $3CH_2$), 1.9 (3H, s, CH_3CO–), 0.95 ppm (3H, d, CH_3). Found: C 63.15; H 9.31; N 6.51%. $C_{12}H_{21}NO_3$. Calculated: C 63.43; H 9.25; N 6.17%.

4. Reaction of 1-Acetoxychlorohexenes with Aqueous Alkali. A mixture of 7.5 g (40 mmole) of 1-acetoxychlorohexenes and 10 ml of 40% aqueous alkali was heated with stirring for 2 h at 75°. After cooling the mixture was neutralized with 20% hydrochloric acid and extracted with ether. The extract was dried with $MgSO_4$, and the fraction boiling up to 110° was distilled off and analyzed by GLC. There were obtained 11% of 2-methyl-5,6-dihydro-2H-pyrane and 21% of 1,3,5-hexatriene. The analysis was carried out on a LKhM-8MD chromatograph with PID, stain-

less steel column 3000 × 3 mm; stationary phase polyethylene glycol adipate, 20 wt. % on Celite-545 (100-120 mesh); carrier gas helium at 40-45 ml/min, analysis temperature 60°, evaporator temperature 275°.

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SYNTHESIS OF 5-ARYL-2-ALKOXYFURANES FROM 1-AROYL-2,2-DICHLOROCYCLOPROPANES

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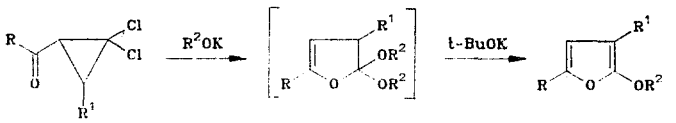
The reaction of 1-aroyl-2,2-dichlorocyclopropanes with a mixture of potassium tert-butylate and potassium methylate (or ethylate) in tert-butyl alcohol gives 5-aryl-2-methoxy(or ethoxy)furanes in good yield.

In studying the chemical properties of gem-dichlorocyclopropyl ketones which have a labile hydrogen in the cyclopropane ring in α-position to the carbonyl, we have found convenient ways to convert them to alicylic derivatives [1-3], 5-aryl-2-dialkylaminofuranes [4], and substituted 2,2-dialkoxy-2,3-dihydrofuranes [1, 2, 5]. In [6] we reported the synthesis of 5-aryl-2-ethoxyfuranes by the reaction of aluminum tert-butylate with the corresponding 2,2-diethoxy-2,3-dihydrofuranes. The present work is devoted to an investigation of a synthesis of alkoxyfuranes from gem-dichlorocyclopropyl ketones in which the separation of the unstable 2,2-dialkoxy-2,3-dihydrofuranes is avoided.

The alkoxyfuranes IIIa-e were obtained in good yield by the reaction of the 1-aroyl-2,2-dichlorocyclopropanes Ia-d with excess potassium tert-butylate and potassium methylate or ethylate in tert-butyl alcohol. According to TLC data, the dihydrofuranes IIa-e [5] form first; their conversion to IIIa-e at a rate sufficient for preparatory application requires an excess of strong base and an increase in temperature. The reaction of the ketones Ia-d with only potassium tert-butylate in tert-butyl alcohol forms a complex mixture of products, whereas in its absence the reaction with the potassium primary alcoholates stops at the stage of the dihydrofuranes IIa-e.



Ia-d IIa-e IIIa-e

I—III a R=C_6H_5, R^1=H, R^2=CH_3; b R=4-$CH_3C_6H_4$, R^1=H, R^2=CH_3; c R=4-$CH_3OC_6H_4$, R^1=H, R^2=CH_3; d R=C_6H_5, R^1=CH_3, R^2=CH_3; e R=C_6H_5, R^1=H, R^2=C_2H_5

We have already [1] considered the scheme by which 2,2-dialkoxy-2,3-dihydrofuranes are probably formed for dichlorocyclopropyl ketones. The splitting out of an alcohol molecule from dihydrofuranes IIa-e which contain aryl substituents is apparently due to the increased acidity of the methylene protons of the dihydrofurane ring, because we were unable to synthesize 5-methyl-2-methoxyfurane from 1-acetyl-2,2-dichlorocyclopropane by this method. In the latter case the reaction stopped at the previously described [2] 2-methyl-2,2-dimethoxy-2,3-dihydrofurane.

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