HYDROGENOLYSIS OF ACETALS OF 3-BROMOTETRAHYDROFURAN SERIES BY ETHEREAL SOLUTION OF CHLOROALANE*

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Received May 4th, 1975

2-Alkoxy-3-bromotetrahydrofurans are cleaved by ethereal chloroalane solution exclusively at the endocyclic C—O bond under formation of 4-alkoxy-3-bromo-1-butanols which are further hydrogenolysed at the C—Br bond and afford the corresponding 4-alkoxy-1-butanols. The cleavage of 2-alkoxy-3-bromotetrahydrofurans, as well as the cleavage of 2-alkoxytetrahydrofurans, is controlled by the decomposition of the acetal–chloroalane complexes to the corresponding alkoxycarbonium ions whereas the hydrogenolysis of 4-alkoxy-3-bromo-1-butanols may be characterised as an S_N2 reaction between chloroalane and bromo alcohol. Using LFER approach in the series 2-methoxy-, 2-ethoxy, 2-isopropoxy- and 2-tert-butoxytetrahydrofurans containing hydrogen, bromine or chlorine in the position 3 it was possible to study polar as well as steric effects in the reaction mentioned.

In a previous paper[1] we studied the reaction of acetals of the 3-chlorotetrahydrofuran series with chloroalane and on the basis of LFER treatment, using the found values of k_{rel}, we concluded that the crucial step of the reaction of 2-alkoxy-3-chlorotetrahydrofurans *I* with chloroalane is the monomolecular cleavage of a complex between substrate and reagent leading to the corresponding acyclic alkoxycarbenium ions. In the present study we investigated the reaction of 2-alkoxy-3-bromotetrahydrofurans *II* with chloroalane. We studied this reaction also in the series of 2-methoxy-, 2-ethoxy-, 2-isopropoxy- and 2-tert-butoxytetrahydrofurans, substituted in the position 3 with hydrogen, bromine and chlorine in order to determine not only the effect of various alkoxy groups but also the effect of the substituent in the position 3 on the course of the studied reaction.

EXPERIMENTAL

Temperature data are uncorrected. Gas–liquid chromatographic measurements were performed on a Chrom 3 (Laboratorní přístroje, Prague) instrument, equipped with a catharometer, using columns of internal diameter 0·6 cm, packed with 15% SE 30 W on Chromosorb 30/60 or 4%

* Part XVII in the series Reactions of Chlorinated Furanidines; Part XVI: This Journal *40*, 3670 (1975).

** Part of this work was taken from the Thesis of P. Breinek.

poly(ethylene glycol adipate) on ground porous tile 0·1—0·2 mm; carrier gas hydrogen. The chromatography was carried out either at one temperature or using temperature programming. ^{1}H-NMR spectra were taken on a Tesla BS 487 instrument in tetrachloromethane solutions (unless stated otherwise) with tetramethylsilane as internal standard. The activity of lithium aluminium hydride (Lachema, Brno), used in the reactions, was determined by titration of its ethereal solutions with iodine according to Felkin[2]. Freshly sublimed (*in vacuo*) aluminium chloride (analytical grade, Lachema, Brno) was used. The starting 2-alkoxy-3-chlorotetrahydrofurans *Ia—Id*, 2-alkoxy-3-bromotetrahydrofurans *IIa—IId* and 2-alkoxytetrahydrofurans *IIIa—IIId* were prepared by alcoholysis of 2,3-dichlorotetrahydrofuran, 2,3,-dibromotetrahydrofuran and 2-chlorotetrahydrofuran, resp.; their purity was checked by gas–liquid chromatography and their physical constants were in accord with the literature data[3-5].

4-Alkoxy-3-bromo-1-butanols *IV*

1M ethereal solution of lithium aluminium hydride (130 ml) was added at 0—5°C to 1M ethereal solution of aluminium chloride (130 ml) under nitrogen, the mixture was stirred for 15 minutes and the acetal *II* (0·26 mol), diluted with the same volume of ether, was slowly added. The mixture was refluxed, cooled, decomposed with water, the ethereal layer was separated and the aqueous one was extracted five times with ether (50 ml). The combined ethereal layers were dried, concentrated under normal pressure and distilled *in vacuo*. Physical constants and analyses of the obtained alcohols *IV* are given in Table I; the times listed in this table correspond to the maximum found (GLC) concentration of the alcohols *IV* in the reaction mixture. The purity of the all prepared alcohols *IV* was checked by gas–liquid chromatography. ^{1}H-NMR spectra: *IVa*: δ 1·70 to 2·30 (m, 2 H, CH_2CBr), 3·39 (s, 3 H, OCH_3), 3·58—3·81 (m, 4 H, OCH_2, OCH_2CBr), 3·86 (s, 1 H, OH), 4·02—4·40 (m, 1 H, CHBr); *IVb*: δ 1·23 (t, J = 7·0 Hz, 3 H, CH_3), 1·65—2·41 (m, 2 H, CH_2CBr), 3·54 (q, J = 7·0 Hz, 2 H, OCH_2 in alkoxy group), 3·60—3·88 (m, 4 H, OCH_2, OCH_2CBr), 3·80 (s, 1 H, OH), 4·06—4·41 (m, 1 H, CHBr;) *IVc*: δ 1·19 (d, J = 6·0 Hz, 6 H, 2 CH_3), 1·62—2·38 (m, 2 H, CH_2CBr), 3·42—3·88 (m, 5 H, CH_2O, OCH_2CBr, OCH), 3·98

TABLE I

Reaction of 2-Alkoxy-3-bromotetrahydrofurans *II* with Chloroalane

Acetal *II* time, h	Product *IV* yield, %	B.p., °C/Torr (n_D^{20})	Formula (mol.wt.)	Calculated/Found		
				% C	% H	% Br
IIa	*IVa*	108—109/11	$C_5H_{11}BrO_2$	32·81	6·06	43·65
5	30	(1·4805)	(183·1)	33·02	6·21	42·49
IIb	*IVb*	111/11	$C_6H_{13}BrO_2$	36·57	6·65	40·55
4	46	(1·4750)	(197·1)	36·31	6·85	40·39
IIc	*IVc*	122/24	$C_7H_{15}BrO_2$	39·83	7·16	37·85
3·5	52	(1·4694)	(211·1)	39·86	7·32	37·04
IId	*IVd*	117/11	$C_8H_{17}BrO_2$	42·68	7·61	35·49
3	65	(1·4657)	(225·1)	42·14	7·52	34·86

(s, 1 H, OH), 4·04—4·38 (m, 1 H, CHBr); *IVd*: δ 1·16 (s, 9 H, 3 CH_3), 1·58—2·37 (m, 2 H, CH_2·.CBr), 3·47—3·79 (m, 4 H, OCH_2, OCH_2CBr), 3·93—4·25 (m, 1 H, CHBr), 4·03 (s, 1 H, OH). ^{1}H-NMR spectra were simplified by addition of tris(dipivaloylmethane)europium.

4-Alkoxy-1-butanols *V*

The reactions were carried out analogously as described in the preceding experiment, using 260 ml of 1M ethereal aluminium chloride, 260 ml of 1M ethereal lithium aluminium hydride and 0·26 mol of the acetal *II*. The experimental data are given in Table II. The purity of all products *V* was checked by gas–liquid chromatography. ^{1}H-NMR spectra: *Va*: δ 1·52 (m, 4 H, CH_2—CH_2), 3·26 (s, 3 H, OCH_3), 3·24—3·56 (m, 4 H, OCH_2, OCH_2), 3·79 (broad s, 1 H, OH); *Vb*: δ 1·18 (t, J = 6·5 Hz, 3 H, CH_3), 1·59 (m, 4 H, CH_2CH_2), 3·44 (q, J = 6·5 Hz, 2 H, OCH_2 in alkoxy group), 3·30—3·76 (m, 5 H, OH, OCH_2, OCH_2); *Vc*: δ 1·15 (d, J = 6·5 Hz, 6 H, 2 CH_3), 1·56 (m, 4 H, CH_2CH_2), 3·32—3·66 (m, 5 H, CH_2OCH, OCH_2), 3·96 (s, 1 H, OH); *Vd*: δ 1·16 (s, 9 H, 3 CH_3), 1·56 (m, 4 H, CH_2CH_2), 3·33 (m, 2 H, OCH_2), 3·50 (m, 2 H, OCH_2), 3·92 (s, 1 H, OH).

Determination of Relative Rates of Hydrogenolyses

Relative rates of hydrogenolyses were determined by gas–liquid chromatography from the comparison of molar concentration of the hydrogenolysis products formed from the substrate with the concentration of the products arising from a standard, using the method described in a previous communication[1]. For the determination of relative hydrogenolysis rates of the acetals *I*, *II* and *III* 2·5 . 10^{-3} mol of the acetal, 2·5 . 10^{-3} mol of the standard and 2·5 . 10^{-3} mol of chloroalane were used, reflux time 8 hours. The relative hydrogenolysis rates of the alcohols *IV* were determined using 2·5 . 10^{-3} mol of the alcohol *IV*, 2·5 . 10^{-3} mol of the alcohol *IVc*, used as standard, and 7·5 . 10^{-3} mol of chloroalane; reflux time 5 hours. The obtained results, together with the calculated correlation coefficients and ϱ^* and δ constants, are listed in Tables III and IV.

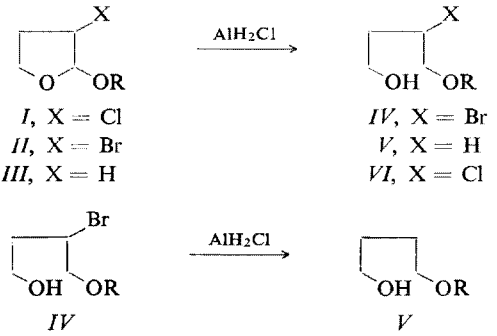
TABLE II

Reaction of 2-Alkoxy-3-bromotetrahydrofurans *II* with Chloroalane

Acetal *II* time, h	Product *V* yield, %	B.p., °C/Torr (n_D^{20})	Ref.[6] b.p., °C/Torr (n_D^t)
IIa	*Va*	60—61/18	60/19
10	66	(1·4187)	(1·4195^{26})
IIb	*Vb*	84—86/15	78/18
11	53	(1·4209)	(1·4201^{26})
IIc	*Vc*	86—88/14	87/15
14	64	(1·4239)	(1·4237^{24})
IId	*Vd*	98—100/18	95—96/17
23	80	(1·4251)	(1·4253^{25})

RESULTS AND DISCUSSION

As seen from Scheme 1, the studied reaction of 2-alkoxy-3-bromotetrahydrofurans *IIa–IId* with chloroalane is analogous to the reaction of 2-alkoxy-3-chlorotetrahydrofurans *Ia–Id* (see ref.[1]) and 2-alkoxytetrahydrofurans[6] *IIIa–IIId*. The endocyclic C—O bond in the compounds *IIa–IId* is cleaved under formation of the corresponding 4-alkoxy-3-bromo-1-butanols *IVa–IVd*. However, contrary to the analogous 4-alkoxy-3-chloro-1-butanols[1] *VIa–VId*, the bromo alcohols *IVa–IVd* are further hydrogenolysed under conditions used in the present study to 4-alkoxy--1-butanols *Va–Vd* which can be prepared directly by the hydrogenolysis of the acetals[6] *IIIa–IIId*.



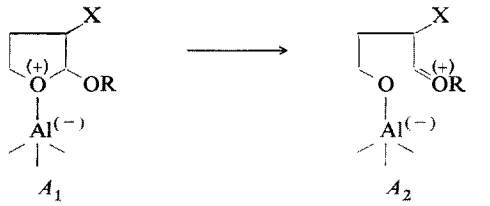
I, X = Cl
II, X = Br
III, X = H

IV, X = Br
V, X = H
VI, X = Cl

IV *V*

In *I–VI*; *a*, R = CH_3; *b*, R = C_2H_5; *c*, R = iso-C_3H_7; *d*, R = tert-C_4H_9.

SCHEME 1



A_1 A_2

As evident from Table III, the more electron-donating alkyls in the alkoxy group accelerate the hydrogenolysis of bromo acetals *IIa–IId* but they have a retarding effect on the same reaction of the bromo alcohols *IVa–IVd*. We assume therefore that in the hydrogenolysis of bromo acetals *II* the decisive reaction step is again the cleavage of the complex A_1 between the acetal and chloroalane leading to the corresponding alicyclic alkoxycarbenium ion A_2. On the other hand, the hydrogenolysis of bromo alcohols *IV* is controlled by the attack at the bromine-substituted carbon of the bromo alcohol; the reaction is thus an S_N2 substitution and chloroalane reacts with bromo alcohols *IV* in the same manner as lithium aluminium hydride does with alkyl halides[7].

TABLE III

Relative Rates of the Reaction of Chloroalane with 2-Alkoxy-3-bromotetrahydrofurans *II* and with 4-Alkoxy-3-bromo-1-butanols *IV*, and the Characteristics of the Correlations $\log k_{rel} = \sigma^* \varrho^*$

Acetal *II*	k_{rel}	R	Alcohol *IV*	k_{rel}
IIa	0·14	CH_3	*IVa*	1·00
IIb	0·30	C_2H_5	*IVb*	0·53
IIc	0·44	iso-C_3H_7	*IVc*	0·27
IId	1·00	tert-C_4H_9	*IVd*	0·11
ϱ^{*a}	−2·75			3·20
r	0·9957			0·9961

[a] Values of σ^* for substituents R were taken from ref.[8].

TABLE IV

Relative Rates of the Reaction of Chloroalane with 2-Methoxy-, 2-Ethoxy-, 2-Isopropoxy- and 2-tert-Butoxytetrahydrofurans, Substituted in Position 3 with Hydrogen, Chlorine or Bromine, and Characteristics of the Correlations

$$\log k_{rel} = \varrho^*(\sigma_i^* - \sigma_0^*) + \delta(E_{s,i} - E_{s,0}) ,$$

(Indexes i and 0 denote the measured compound and the standard, respectively)

Acetal	R = CH_3	R = C_2H_5	R = iso-C_3H_7	R = tert-C_4H_9
III, X = H	*IIIa*	*IIIb*	*IIIc*	*IIId*
k_{rel}	8·65	4·25	4·20	3·55
I, X = Cl	*Ia*	*Ib*	*Ic*	*Id*
k_{rel}	1·00	1·00	1·00	1·00
II, X = Br	*IIa*	*IIb*	*IIc*	*IId*
k_{rel}	0·90	1·54	1·93	2·92
ϱ^{*a}	−0·19	−0·53	−0·75	−1·01
δ	0·37	−0·63	−1·00	−1·80

[a] Values of σ^* and E_s for substituents in position 3 were taken from ref.[8].

Within the series of acetals *Ia–Id*, *IIa–IId* and *IIIa–IIId*, where substituent in the position 2 varies, correlations of the relative reactivities with only σ^* constants of alkyl groups in the alkoxyl are satisfactory and indicate that the steric effect of the substituent in the position 2 is negligible. On the contrary, in the series *Ia*, *IIa*, *IIIa*; *Ib*, *IIb*, *IIIb*; *Ic*, *IIc*, *IIIc*; and *Id*, *IId*, *IIId*, where the varying substituent is in the position 3, the relative reactivities can be correlated neither with only σ^* constants of substituents in the position 3 nor with only their constants E_s. This shows that substituents in the position 3 on tetrahydrofuran ring have polar as well as steric effect on the studied reaction. The correlation of the relative reactivities in the latter series of acetals with varying substituent in position 3 can be achieved using both σ^* and E_s constants for substituents in the position 3 in the extended Taft equation. Table IV lists the calculated constants ϱ^* and δ together with the relative reactivities. These constants are different for each series, however, it is clearly seen that both the constants ϱ^* and δ decrease when going from series *a* to series *d*. We assume that this trend is again in accord with the assumed reaction determining cleavage of the complexes A_1 to alkoxycarbenium ions A_2 because the reaction rate increases with increasing stabilisation of the arising positive charge and it also increases with the increasing bulk of both substituents, which manifests itself in the preference of the acyclic structure of the alkoxycarbenium ion A_2 over the rigid cyclic structure of the complex A_1.

The authors are indebted to Drs M. Kratochvíl and J. Pichler for fruitful discussions.

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Translated by M. Tichý.