

## PROTOTROPIC REARRANGEMENT IN REACTIONS OF 4-ALKOXY-3-CHLORO-1-BUTANOLS WITH BASES

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Reaction of 4-alkoxy-2-chloro-1-butanols (*I*) and their acetates *II* with bases depends on the base and reaction conditions employed and affords complex mixtures of fragmentation products or mixtures of 4-alkoxy-2-buten-1-ols (*III*) and 4-alkoxy-3-buten-1-ols (*IV*) or almost pure *trans-IV*. Hydrogenolysis of 2,5-dihydro-2,5-dimethoxyfuran (*V*) by chloroalane leads to *trans-4-methoxy-2-buten-1-ol (trans-IIIa)*. Vinyl ethers *IV* undergo an acid-catalyzed cyclisation to the corresponding 2-alkoxytetrahydrofurans *VI*.

We have described<sup>1</sup> a simple method which affords high yields of 4-alkoxy-3-chloro-1-butanols (*I*) and their acetates<sup>2</sup> *II*. The present communication describes our studies of the behaviour of compounds *I* and *II* in their reactions with bases.

Reactions of  $\gamma$ -halohydrins (or 1,3-diols) or their esters with aqueous potassium hydroxide<sup>3,4</sup> or potassium tert-butoxide<sup>5</sup> are often used in the synthesis of oxetanes. Compounds *I* can be looked upon as  $\gamma$ -chlorohydrins, as well as  $\beta$ -chloro ethers, the latter suggesting that the chlorine atom will resist considerably a nucleophilic substitution<sup>6</sup>. In actual fact, reaction of both alcohols *I* and esters *II* with aqueous potassium hydroxide at 373 K afforded products of hydrolysis and/or elimination in about 80% yields and it was not possible to prove the formation of the corresponding oxetanes. The mixtures of elimination products were separated only on the analytical scale using an efficient capillary column. We found that these mixtures consist invariably of four components, two of which represent about 85–90% of the mixture and their ratio is 1 : 1 to 1 : 2 depending on the starting compound. The elemental analyses of the mixtures corresponded exactly to the values calculated for alkoxy-butenols. Also their <sup>1</sup>H-NMR, spectra, simplified by working with hexadeuterio-dimethyl sulfoxide solutions<sup>7</sup> and by using shift reagents, indicated that the main portions of the mixtures are always the corresponding *trans-4-alkoxy-2-buten-1-ols (trans-III)* together with *trans-4-alkoxy-3-buten-1-ols (trans-IV)*. As shown in Table I, the <sup>1</sup>H-NMR studies involved the determination of the coupling constants between olefinic protons<sup>8</sup> and comparison of calculated<sup>9</sup> and found chemical shifts of these protons.

Reaction of the compounds *I* and *II* with aqueous potassium hydroxide at 449 K resulted in a substantial decrease in the yields of the elimination products (about 40%), and the main part of the product consisted of volatile unsaturated compounds and polyformaldehyde. However, the elimination product proved to be almost chromatographically pure *trans*-4-alkoxy-3-buten-1-ol (*trans-IV*), the structure of which was unequivocally determined by <sup>1</sup>H-NMR spectroscopy. We assume that the volatile unsaturated compounds and polyformaldehyde are formed by fragmentation of the starting compounds *I* and *II*; for which process we know many analogies<sup>5,10</sup>.

The formation of only one elimination product in the reaction with aqueous potassium hydroxide at 449 K is difficult to explain exclusively in terms of higher regio-specificity. We therefore considered the possibility of a prototropic rearrangement of the primarily formed *trans*-4-alkoxy-2-buten-1-ols (*trans-III*) to the vinyl ethers *trans-IV*. Similar rearrangements have been already observed<sup>11-13</sup> and even the use of allyl group as a protecting group in sugar chemistry<sup>14,15-17</sup> is based on them; however, usually stronger bases are employed. Therefore, the mixture of elimination products, obtained by the reaction of compounds *I* and *II* with potassium hydroxide at 373 K, was treated with the same reagent at 448 K and indeed almost pure *trans*-4-alkoxy-3-buten-1-ols (*trans-IV*) were isolated. Using potassium tert-butoxide

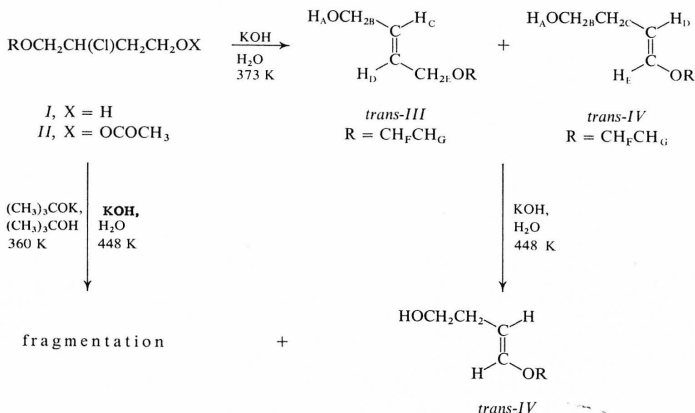
TABLE I

Chemical Shifts ( $\delta$ ) and Coupling Constants ( $J$ , Hz) in the <sup>1</sup>H-NMR Spectra of *trans*-4-Alkoxy-2-buten-1-ols (*trans-III*) and *trans*-4-Alkoxy-3-buten-1-ols (*trans-IV*)

| Compound                | $\delta H_A$ | $\delta H_B$ | $J_{BC}$ | $J_{BD}$ | $\delta H_C^a$ | $J_{CD}$          | $J_{CE}$ | $\delta H_D^{a,b}$ | $J_{DE}$          | $\delta H_E^{a,b}$ | $\delta H_F$ | $J_{FG}$ | $\delta H_G$ |
|-------------------------|--------------|--------------|----------|----------|----------------|-------------------|----------|--------------------|-------------------|--------------------|--------------|----------|--------------|
| <i>IIIa</i>             | 2.74         | 4.17         | 6.0      | 1.2      | 5.75           | 11.5 <sup>d</sup> | 1.5      | 5.75               | 6.5               | 4.0                | 3.34         | —        | —            |
| <i>IIIb<sup>c</sup></i> | 3.32         | 4.00         | 6.0      | 1.0      | 5.70           | 11.5 <sup>d</sup> | 1.5      | 5.70               | 6.5               | 3.86               | 3.42         | 6.5      | 1.16         |
| <i>IIIc</i>             | 4.15         | 3.80         | 6.0      | 1.0      | 5.81           | 11.5 <sup>d</sup> | 1.5      | 5.81               | 6.5               | 3.63               | 3.55         | 7.0      | 1.15         |
| <i>IIId</i>             | 2.73         | 4.18         | 6.0      | 1.0      | 5.82           | 11.5 <sup>d</sup> | 1.5      | 5.82               | 6.5               | 4.05               | —            | —        | 1.20         |
| <i>IVa</i>              | 1.80         | 3.55         | —        | —        | 2.18           | 7.0               | 1.0      | 4.67               | 12.5 <sup>d</sup> | 6.39               | 3.53         | —        | —            |
| <i>IVb</i>              | 2.74         | 3.55         | 7.0      | —        | 2.20           | 7.5               | 1.0      | 4.70               | 12.5 <sup>d</sup> | 6.32               | 3.72         | 7.3      | 1.26         |
| <i>IVc</i>              | 2.75         | 3.50         | —        | —        | 2.15           | 8.0               | 1.0      | 4.76               | 12.5 <sup>d</sup> | 6.15               | 3.95         | 7.5      | 1.20         |
| <i>IVd</i>              | 2.73         | 3.55         | —        | —        | 2.17           | 7.5               | 1.5      | 4.90               | 12.5 <sup>d</sup> | 6.32               | —            | —        | 1.26         |

<sup>a</sup> For compounds *III* calculated according to ref.<sup>9</sup>  $\delta H_D = \delta H_D$ , *cis*: 5.88, *trans*: 5.93. <sup>b</sup> For compounds *IV* calculated according to ref.<sup>9</sup>  $\delta H_D$  *cis*: 4.44, *trans*: 4.66;  $\delta H_E$  *cis*: 6.13, *trans*: 6.16. <sup>c</sup> In CCl<sub>4</sub>. <sup>d</sup> For analogous systems the literature<sup>13,20-23</sup> gives the following coupling constants of the olefinic protons: *trans*- $J$  in the range 11.1–13.5 Hz, *cis*- $J$  in the range 4.2–7.2 Hz.

in tert-butanol instead of aqueous potassium hydroxide resulted in no substantial change. Due to a lower temperature used in this reaction (360 K) the fragmentation was more pronounced and thus the reaction is less suitable for practical application. The discussed facts are summarized in Scheme 1.

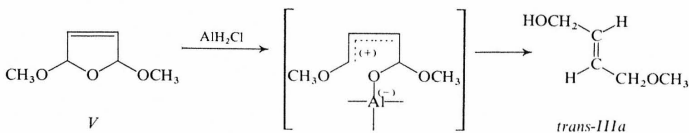


SCHEME 1

By all I-IV; a, R = CH<sub>3</sub>; b, R = C<sub>2</sub>H<sub>5</sub>; c, R = iso-C<sub>3</sub>H<sub>7</sub>; d, R = tert-C<sub>4</sub>H<sub>9</sub>.

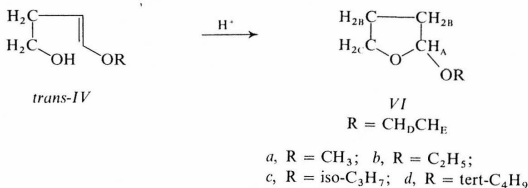
Since we obtained no *trans*-4-alkoxy-2-buten-1-ol (*trans*-III) in the pure state, we intended to identify at least one compound of this class by its spectral and chromatographic comparison with a standard. Since the preparation of defined isomers of any of compounds IIIa-III d is not known we tried to prepare *cis*-4-methoxy-2-buten-1-ol (*cis*-IIIa) by hydrogenolysis of 2,5-dihydro-2,5-dimethoxyfuran (V) with chloroalane according to Scheme 2. However, the sole product, isolated from the reaction mixture, was a compound which is, according to <sup>1</sup>H-NMR spectrum, *trans*-4-methoxy-2-buten-1-ol (*trans*-IIIa) and which is chromatographically identical with the second main elimination product of the reaction of the alcohol Ia with potassium hydroxide at 373 K. We regard this fact as a further confirmation of the *trans*-configuration of our compounds III and, moreover, as an indication that the hydrogenolysis of compound V with chloroalane proceeds *via* an alkoxy-carbenium

ion of an allylic type which is stable enough to enable total isomerisation of the double bond.



SCHEME 2

Acid-catalyzed intramolecular addition of the prepared *trans*-4-alkoxy-3-buten-1-ols (*trans-IV*) led to the corresponding 2-alkoxytetrahydrofurans (*VI*) (Scheme 3), constituting thus chemical proof of their structure.



SCHEME 3

## EXPERIMENTAL

Boiling points are uncorrected. Gas-liquid chromatographic measurements were performed on a Chrom II chromatograph (Laboratorní přístroje, Prague) equipped with a flame-ionisation detector; 22 m glass capillary column, coated with Emulphor (BASF, West Germany), carrier gas nitrogen. <sup>1</sup>H-NMR spectra were taken on a Tesla BS 487 instrument in deuteriochloroform (unless stated otherwise) with tetramethylsilane as internal standard. The <sup>1</sup>H-NMR spectra were simplified by use of tris(dipivaloylmethanato)europium and tris[2-(trifluoromethylhydroxymethylene)-(+)-camphorato]europium (Aldrich). The starting 4-alkoxy-3-chloro-1-butanols (*I*) and their acetates *II* were prepared according to ref.<sup>1</sup> and ref.<sup>2</sup>, respectively. The purity of compounds *I* and *II* was checked by gas-liquid chromatography; their physical constants agreed with those given in the literature.

Reaction of 4-Alkoxy-3-chloro-1-butanols (*I*) and 1-Acetoxy-4-alkoxy-3-chlorobutanes (*II*) with Potassium Hydroxide

*At 373 K:* A mixture of 0.25 mol of 4-alkoxy-3-chloro-1-butanol (*I*) or 1-acetoxy-4-alkoxy-3-chlorobutane (*II*), 1 mol of solid potassium hydroxide and 0.1 mol of water was heated under reflux to 373 K for 2 h, cooled to room temperature and diluted with 200 ml of water. The organic layer was separated and the aqueous layer extracted with ether (5 . 25 ml). The combined organic layers were dried over sodium or magnesium sulphate, taken down under normal pressure and distilled *in vacuo*. The yields, composition of the obtained mixtures, their physical constants, chromatographic characteristics and analyses are given in Table II. The <sup>1</sup>H-NMR spectra of the principal components of the mixtures are given in Table I.

*At 448 K:* The same mixture of the reactants as in the above experiment was heated to 448 K for 2 h. The work-up procedure was the same as above up to the point of drying of the ethereal extracts. The aqueous layer contained an insoluble white precipitate which was characterized as polyformaldehyde by elemental analysis and acid-catalyzed cleavage. The organic layer was taken down and the residue distilled under normal pressure till the temperature of the distillate reached 366 K. These fractions (about 50% of the products) contained, according to gas-liquid chromatography, several compounds and showed unsaturation. They were not studied further. The residue was distilled under diminished pressure affording *trans*-4-alkoxy-3-buten-1-ols (*trans-IV*). Yields, physical constants and elemental analyses of these compounds are shown in Table III, their <sup>1</sup>H-NMR spectra are given in Table I.

TABLE II

Mixtures of Stereoisomeric Elimination Products *III* and *IV* Obtained by the Reaction of 4-Alkoxy-3-chloro-1-butanols (*I*) and 1-Acetoxy-4-alkoxy-3-chlorobutanes (*II*) with Potassium Hydroxide at 373 K

| Mixture<br>(yield, %)    | B.p., K/kPa<br>$n_D^{20}$ | Formula<br>mol.w.                             | Calculated/Found |       | Composition <sup>a</sup>                        |   |
|--------------------------|---------------------------|---|------------------|-------|---|---|
|                          |                           |   | % C              | % H   | <i>cis-III</i> <sup>b</sup><br><i>trans-III</i> | <i>cis-IV</i> <sup>b</sup><br><i>trans-IV</i> |
| <i>IIIa, IVa</i><br>75   | 344—45/2.5                | C <sub>5</sub> H <sub>10</sub> O <sub>2</sub> | 58.80            | 9.87  | 1 375 (9)                                       | 1 355 (6)                                     |
|                          | 1.4475                    | 102.1   | 58.63            | 9.58  | 1 450 (27)                                      | 1 420 (58)                                    |
| <i>IIIb, IVb</i><br>85   | 350—54/2.0                | C <sub>6</sub> H <sub>12</sub> O <sub>2</sub> | 62.04            | 10.41 | 1 385 (2)                                       | 1 370 (3)                                     |
|                          | 1.4471                    | 116.2   | 61.97            | 10.04 | 1 465 (41)                                      | 1 495 (54)                                    |
| <i>IIIc, IVc</i><br>88   | 361—64/1.6                | C <sub>7</sub> H <sub>14</sub> O <sub>2</sub> | 64.58            | 10.84 | 1 465 (2)                                       | 1 420 (4)                                     |
|                          | 1.4445                    | 130.2   | 64.32            | 10.76 | 1 550 (45)                                      | 1 500 (49)                                    |
| <i>III d, IV d</i><br>84 | 383—88/1.6                | C <sub>8</sub> H <sub>16</sub> O <sub>2</sub> | 66.63            | 11.18 | 1 490 (3)                                       | 1 450 (10)                                    |
|                          | 1.4478                    | 144.2   | 66.39            | 11.14 | 1 555 (34)                                      | 1 530 (53)                                    |

<sup>a</sup> The first number is the Kovats index ( $I_{\text{Emulphor}}^{380}$ ), the second one is relative percentage. <sup>b</sup> Structures of the components denoted as *cis-III* and *cis-IV* are only tentative.

Isomerisation of *trans*-4-Alkoxy-2-buten-1-ols (*trans*-III) with Aqueous Potassium Hydroxide at 448 K

A mixture of alkoxybutenols III and IV, obtained by the reaction of alcohols I or acetates II with potassium hydroxide at 373 K, was heated with an excess of potassium hydroxide and water

TABLE III

*trans*-4-Alkoxy-3-buten-1-ols (*trans*-IV), Prepared by the Reaction of 4-Alkoxy-3-chloro-1-butanols (I) or Their Acetates II with Potassium Hydroxide at 448 K

| Compound | Yield % | B.p., K/kPa<br>$n_D^{20}$ | Formula<br>mol.w.                                      | Calculated/Found |       |
|----------|---------|---------------------------|--|------------------|-------|
|          |         |                           |  | % C              | % H   |
| IVa      | 42      | 337/1.6                   | C <sub>5</sub> H <sub>10</sub> O <sub>2</sub><br>102.1 | 58.80            | 9.87  |
|          |         | 1.4465                    |  | 58.56            | 9.72  |
| IVb      | 40      | 345/2.0                   | C <sub>6</sub> H <sub>12</sub> O <sub>2</sub><br>116.2 | 62.04            | 10.41 |
|          |         | 1.4458                    |  | 61.93            | 10.28 |
| IVc      | 57      | 357/1.6                   | C <sub>7</sub> H <sub>14</sub> O <sub>2</sub><br>130.2 | 64.58            | 10.84 |
|          |         | 1.4440                    |  | 64.47            | 10.74 |
| IVd      | 50      | 352/1.6                   | C <sub>8</sub> H <sub>16</sub> O <sub>2</sub><br>144.2 | 66.63            | 11.18 |
|          |         | 1.4470                    |  | 66.48            | 11.03 |

TABLE IV

Cyclisation of *trans*-4-Alkoxy-3-buten-1-ols (*trans*-IV) to 2-Alkoxytetrahydrofurans (VI) (see Scheme 3)

| Starting compound | Product yield, % | B.p., K/kPa<br>$n_D^{20}$ | Reported b.p., K/kPa<br>$n_D^{20}$ | Chemical shifts ( $\delta$ ) |                |                |                |                |
|-------------------|------------------|---------------------------|------------------------------------|------------------------------|----------------|----------------|----------------|----------------|
|                   |                  |                           |                                    | H <sub>A</sub>               | H <sub>B</sub> | H <sub>C</sub> | H <sub>D</sub> | H <sub>E</sub> |
| IVa               | VIa              | 378/101.3                 | 373—377/100.3 <sup>16</sup>        | 5.10                         | 1.85           | 3.65           | 3.90           | —              |
|                   | 56               | 1.4121                    | 1.4126                             |                              |                |                |                |                |
| IVb               | VIb              | 398/101.3                 | 395—397/100.3 <sup>17</sup>        | 5.12                         | 1.88           | 3.59           | 3.80           | 1.19           |
|                   | 62               | 1.4045                    | 1.3951                             |                              |                |                |                |                |
| IVc               | VIc              | 338/3.3                   | 313—314/1.6 <sup>18</sup>          | 5.27                         | 1.86           | 3.88           | 3.88           | 1.16           |
|                   | 54               | 1.4190                    | 1.4198                             |                              |                |                |                |                |
| IVd               | VI d             | 320/2.0                   | 307—314/1.3 <sup>19</sup>          | 5.48                         | 1.89           | 3.86           | —              | 1.21           |
|                   | 58               | 1.4176                    | 1.4186                             |                              |                |                |                |                |

(KOH : H<sub>2</sub>O 20 : 1) to 448 K for 2 h. The work-up procedure, described in the preceding experiment, afforded pure *trans*-4-alkoxy-3-buten-1-ols (*trans-IV*); its physical constants were identical with those given in Table II and III. The yields, based on the starting alcohol *I* or acetate *II*: *trans-IVa* 58%, *trans-IVb* 69%, *trans-IVc* 72% and *trans-IVd* 70%.

Reactions of 4-Alkoxy-3-chloro-1-butanols (*I*) and 1-Acetoxy-4-alkoxy-3-chlorobutanes (*II*) with Potassium Tert-butoxide in Tert-butyl Alcohol

A mixture of the alcohol *I* or the acetate *II* (0.05 mol) and potassium tert-butoxide (0.0055 mol) in tert-butyl alcohol (4.5 ml) was refluxed for 2 h. The reaction mixtures were worked up as usual and analysed by gas-liquid chromatography which revealed that the product consisted mainly of volatile unsaturated compounds with only minor amounts of alkoxybutenols *III* and *IV*. The reaction was not performed on the preparative scale.

Hydrogenolysis of 2,5-Dihydro-2,5-dimethoxyfuran (*V*) with Chloroalane

A solution of 2,5-dihydro-2,5-dimethoxyfuran (*V*) (0.34 mol) in ether (50 ml) was added dropwise\* during 40 min to a boiling mixture of 1M ethereal solution (250 ml) of lithium aluminium hydride and 1M ethereal solution (250 ml) of aluminium chloride. The mixture was refluxed for 90 min, decomposed by addition of saturated aqueous ammonium chloride solution (150 ml), and the ethereal layer was separated. The aqueous layer was extracted with ether (4 × 50 ml) and the combined ethereal layers were dried over sodium sulphate and taken down under normal pressure. The residue was distilled under diminished pressure on a column, yielding 9.9 g (34%) of *trans*-4-methoxy-2-buten-1-ol (*trans-IIIa*), b.p. 344–345 K/2.5 kPa,  $n_D^{20}$  1.4475. For C<sub>5</sub>H<sub>10</sub>O<sub>2</sub> (102.1) calculated: 58.80% C, 9.87% H; found: 58.67% C, 9.74% H. <sup>1</sup>H-NMR spectrum of this product was identical with that listed in Table I.

Cyclisation of 4-Alkoxy-3-buten-1-ols (*trans-IV*) to 2-Alkoxytetrahydrofuran (*VI*)

A mixture of 0.1 mol of *trans*-4-alkoxy-3-buten-1-ol (*trans-IV*), 30 ml of tetrachloromethane and a few crystals of *p*-toluenesulphonic acid was refluxed for 2 h. After cooling the mixture was shaken with 5 ml of a saturated aqueous solution of sodium carbonate, the organic layer was separated, dried over sodium sulphate and distilled. The yields, physical constants and <sup>1</sup>H-NMR spectra of the obtained 2-alkoxytetrahydrofurans (*VI*) are listed in Table IV.

\* The reaction is very exothermic but it is advisable to follow exactly the described procedure since addition of compound *V* to the solution of chloroalane at lower temperatures results in the formation of a solid complex which undergoes violent or even explosive decomposition at higher temperatures.

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