# CHEMICAL TRANSFORMATIONS OF DIOLS
## AND CYCLIC ETHERS. XXXIII*

### Reactions of Diols with Acid Chlorides

By

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A study was made of the reactions of diols with acid chlorides. The effect of the distance between the hydroxy groups on the course of the reaction was examined. The course of the first step of the process, the formation of the diol monoester, was studied. It was found that there is no essential difference between the transformation of diols on the action of acetyl chloride, and that of the monoesters on the action of gaseous HCl. In the formation of the monoesters a complex equilibrium mixture is obtained, containing both diol and diacetate in addition to the monoacetate. With diols of asymmetric structure, both monoacetate isomers are formed. In the case of the chloroacetate formation reaction, the 1,3-diols exhibit the properties of vicinal diols, while in the acyl migration reactions of the monoacetates, both the 1,3- and 1,4-diols do so; the properties characteristic of disjoint diols appear only from the 1,4- and 1,5-diols on, respectively.

## Introduction

Our earlier publications [1, 2] described studies connected with the reactions of acetyl chloride with butan-1,3-diol and several di-primary 1,3-diols. The aim of the present work was to generalize the reaction to 1,n-diols ($n = 2, 3, 4, 5$), and to establish the effect of the distance between the hydroxy groups on the course of the reaction. It was also desired to study the course of the first step of the process, the formation of the diol monoester.

## Experimental results

A study was made of the reactions of various diprimary (Table I) and primary-secondary (Table II) diols with acetyl chloride. Of the primary-tertiary diols, the behaviour of 3-methylbutan-1,3-diol was examined (Table III). The reaction between butan-1,3-diol and benzoyl chloride was studied (Table IV), with the aim of establishing the general regularities. The kinetics of the transformation were investigated in the case of the action of acetyl chloride on butan-1,3-diol (Table V). A study was also made of the first step of the process, the formation of the diol monoester,

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in order to obtain a deeper insight into the reaction (Table VI). With the same purpose, the transformations of various diol monoesters on the action of gaseous HCl were investigated in detail (Table VII). An examination was also made of the reactions between HCl and 1,3-diacetoxybutane in aqueous medium, and HCl and butan-1,3-diol in acetic acid medium, and of the possibilities of using these for preparative purposes (Table VIII).

<div align="center">

*Table I*

*Reaction of 1,n-diols with acetyl chloride*

</div>

| Diol | Temperature, °C | | Chloroacetate yield at 100°C, % [c] |
|------|-----|-----|-----|
| | 25 | 100 | |
| H₂C—CH₂<br>\| \|<br>HO OH | + [a] | + | 34 |
| H₂C—CH₂—CH₂<br>\|     \|<br>OH     OH | + | + | 33 |
| H₂C—CH₂—CH₂—CH₂<br>\|           \|<br>OH         OH | − [b] | + | 43 |
| H₂C—CH₂—CH₂—CH₂—CH₂<br>\|               \|<br>OH             OH | − | + | 52 |

*Remarks:*

    *a*): reaction takes place
    *b*): reaction does not take place
    *c*): side-product mainly chlorohydrin

## Discussion

It can be established from a study of Tables I and II that, under the conditions employed, the 1,2- and 1,3-diols behave similarly, and the fundamental difference is between the 1,3- and 1,4-diols. From every primary-secondary diol, two chloroacetate isomers are formed. The isomer ratio is substantially different only in the case of hexan-1,5-diol. This can be explained by the decomposition of the 1-acetoxy-5-chlorohexane. With 3-methylbutan-1,3-diol, practically only one chloroacetate isomer is formed (Table III); this is to be expected because of the possibility of an $S_N1$ reaction. Benzoyl chloride behaves similarly to acetyl chloride; with butan-1,3-diol it yields two chlorobenzoate isomers (Table IV).

On reaction of the monoesters with gaseous HCl, reactions similar to those with acid chlorides were obsered. It follows from this that there is no essential difference between the two reactions; the main step of the process is the reaction of the ester and HCl. The situation is the same in the case when gaseous HCl is passed into an aqueous diacetate solution, or into a diol—acetic acid mixture. Thus, it is necessary to study the esterification to elucidate the mechanism of the reaction.

In the case of the asymmetric diols there is a possibility for the formation of two monoester isomers. It was earlier generally assumed that, as a result of the

*Table II*

*Reaction of 2,n-diols with acetyl chloride*

| Diol | Temperature, °C | | Chloroacetate yield, % | Isomer ratio, % | |
|---|---|---|---|---|---|
| | 25 | 100 | | $CH_3-CH-(CH_2)_n-CH_2$ <br> OAc ____ Cl | $CH_3-CH-(CH_2)_n-CH_2$ <br> Cl ____ OAc |
| $CH_3-CH-CH_2$ <br> HO ____ OH | + | + | 60* (at 25°C) | 48* | 52* |
| $CH_3-CH-CH_2-CH_2$ <br> HO ____ OH | + | + | 65 (at 25°C) | 64 | 36 |
| $CH_3-CH-CH_2-CH_2-CH_2$ <br> OH ____ OH | — | + | 70 | 50 | 50 |
| $CH_3-CH-CH_2-CH_2-CH_2-CH_2$ <br> OH ____ OH | — | + | 35 | 80 | 20 |

* together with chlorohydrin

higher rate of acylation of the primary hydroxyl group in the case of a primary-secondary diol, only the primary group is acylated [3, 4].

It can be established from our experimental results (Table VI) that on acetyl-ation with acetic anhydride both monoacetate isomers of the diol are formed; in fact, a complex equilibrium mixture arises, which contains not only the mono-acetates, but the diol and the diacetate too. The situation is similar in the case of acetyl chloride, with the difference that here there is also the possibility for the chloroacetate as well. The above features were not observed in the reaction with benzoyl chloride; even when the latter was in considerable excess, hardly any diben-zoate was formed. This corresponds to the observation that the benzoyl group has a much lower tendency to take part in acyl migration reactions than the acetyl group [5].

In the reactions of the monoacetates with gaseous HCl, equilibrium mixtures develop which have the same compositions as in the esterification reactions with

*Table III*

*Reaction of 3-methylbutane-1,3-diol with acetyl chloride*

| Temperature, °C | Chloroacetate yield, % | Isomer ratio, % | |
|---|---|---|---|
| | | $CH_3$ $\quad$ $CH_3-\overset{\mid}{\underset{\mid}{C}}-CH_2-CH_2$ $\quad$ OAc $\quad$ Cl | $CH_3$ $\quad$ $CH_3-\overset{\mid}{\underset{\mid}{C}}-CH_2-CH_2$ $\quad$ Cl $\quad$ OAc |
| 25 | 40 | 5 | 95 |
| 100 | 2 | 0 | 100 |

*Table IV*

*Reaction of butane-1,3-diol with benzoyl chloride*

| Temperature, °C | Chlorobenzoate yield, % | Isomer ratio, % | |
|---|---|---|---|
| | | $CH_3-CH-CH_2-CH_2$ $\quad$ OBz $\qquad$ Cl | $CH_3-CH-CH_2-CH_2$ $\quad$ Cl $\qquad$ OBz |
| 130 | 60 | 50 | 50 |

*Table V*

*Effect of time in the reaction between butane-1,3-diol and acetyl chloride*

| Product | Product distribution (mole %) after | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | 0 hours* | 1 hour | 2 hours | 3 hours | 4 hours | 6 hours | 24 hours | 25 hours |
| mono- and diacetate | 79 | 66 | 57 | 50 | 44 | 41 | 32 | 27 |
| chloroacetates | 20 | 33 | 42 | 49 | 54 | 54 | 55 | 59 |
| chlorohydrins | 1 | 1 | 1 | 1 | 2 | 5 | 13 | 14 |

* the point of time when the total acetyl chloride has been added dropwise to the diol

## Table VI

### Formation of diol monoesters

| Diol (A) | Reagent (B) | Molar ratio (B/A) | Product distribution, mole % | | | | Ratio (C/D) |
|---|---|---|---|---|---|---|---|
| | | | $CH_3-CH-(CH_2)_n-CH_2$ OH OAc (C) | $CH_3-CH-(CH_2)_n-CH_2$ OAc OH (D) | $CH_3-CH-(CH_2)_n-CH_2$ OAc OAc | $CH_3-CH-(CH_2)_n-CH_2$ OH OH | |
| $CH_3-CH-CH_2-CH_2$ OH OH | $Ac_2O$ | 1:1 | 14 | 5 | 40 | 41 | 2.8 |
| $CH_3-CH-CH_2-CH_2-CH_2$ OH OH | $Ac_2O$ | 1:1 | 23 | 12 | 35 | 32 | 1.9 |
| | | | $CH_3-CH-CH_2-CH_2$ OH OBz (OBz)(OH) | | $CH_3-CH-CH_2-CH_2$ OBz OBz | $CH_3-CH-CH_2-CH_2$ OH OH | |
| $CH_3-CH-CH_2-CH_2$ OH OH | BzCl | 2:1 | ~100 | | trace | 0 | |

| Monoester | Temp. °C | Soln. concn. vol. % | Reaction time, min. | Product distribution, mole % | | | | | | Ratio (V/VI) |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | I | II | III | IV | V | VI | |
| CH$_3$—CH—CH$_2$—CH$_2$ <br>     OH        OAc <br>   (OAc)   (OH) | 25 | 50 | 60 | 35 | 6 | 4 | 34.5 | 20,5 | | |
| CH$_3$—CH—CH$_2$—CH$_2$ <br>     OH       OAc | 25 | 50 | 5 | 1 | 0 | 0 | 1 | 67 | 31 | 2.2 |
| CH$_3$—CH—CH$_2$—CH$_2$ <br>     OH       OAc | 25 | 2 | 5 | 1 | 0 | 0 | 1 | 66 | 32 | 2.1 |
| CH$_3$—CH—CH$_2$—CH$_2$ <br>     OH       OAc | 25 | 50 | 60 | 33 | 0 | 0 | 33 | 23 | 11 | 2.1 |
| CH$_3$—CH—CH$_2$—CH$_2$ <br>     OH       OAc | 70 | 50 | 60 | 37 | 3 | 7 | 37 | 11 | 5 | 2.2 |
| CH$_3$—CH—CH$_2$—CH$_2$—CH$_2$—CH$_2$ <br>   OH                   OAc | 25 | 50 | 180 | transformation to only a very small extent | | | | | | |
| CH$_3$—CH—CH$_2$—CH$_2$—CH$_2$—CH$_2$ <br>   OH                   OAc | 70 | 50 | 180 | 18 | 0 | 0 | 18 | 55 | 9 | 6.1 |
| | | | | VII | VIII | IX | X | XI + XII | | |
| CH$_3$—CH—CH$_2$—CH$_2$ <br>     OH       OBz <br>   (OBz)   (OH) | 25 | 50 | 60 | 0 | 33 | 33 | 0 | 33 | | |

I = CH$_3$—CH—(CH$_2$)$_n$—CH$_2$         II = CH$_3$—CH—(CH$_2$)$_n$—CH$_2$
         OH         OH                  OAc        Cl

III = CH$_3$—CH—(CH$_2$)$_n$—CH$_2$       IV = CH$_3$—CH—(CH$_2$)$_n$—CH$_2$
        Cl         OAc               OAc     OAc

V = CH$_3$—CH—(CH$_2$)$_n$—CH$_2$       VI = CH$_3$—CH—(CH$_2$)$_n$—CH$_2$
       OH       OAc             OAc       OH

VII = CH$_3$—CH—CH$_2$—CH$_2$      VIII = CH$_3$—CH—CH$_2$—CH$_2$
       OH       OH             OBz     Cl

IX = CH$_3$—CH—CH$_2$—CH$_2$       X = CH$_3$—CH—CH$_2$—CH$_2$
      Cl       OBz             OBz     OBz

XI = CH$_3$—CH—CH$_2$—CH$_2$       XII = CH$_3$—CH—CH$_2$—CH$_2$
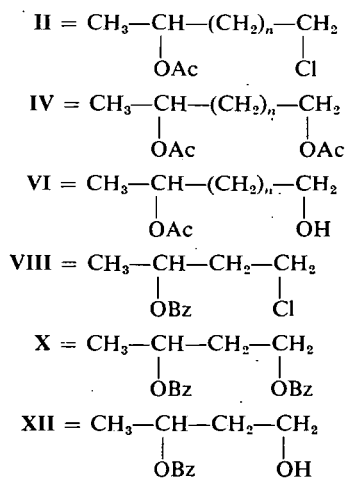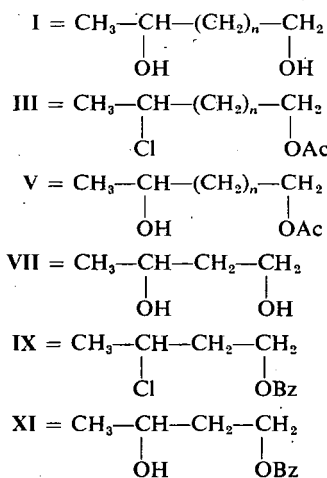      OH      OBz             OBz     OH

### Table VIII

*Formation of chloroacetates from butane-1,3-diol and its acetate on the action of HCl*

| Starting substance | Temp. °C | Initial water content, vol. % | Time, hours | Product distribution, mole % | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | diacetate | monoacetates | chlorohydrins | CH₃-CH-CH₂-CH₂ OAc / Cl | CH₃-CH-CH₂-CH₂ Cl / OAc |
| CH₃—CH—CH₂—CH₂ (OAc, OAc) | 25 | 0 | 1 | hardly any transformation | | | | |
| | 25 | 1 | 1 | 82 | 8 | 0 | 6 | 4 |
| | 25 | 50 | 1 | 15 | 15 | 10 | 36 | 24 |

| Starting substance | Temp. °C | Initial water content, vol. % | Time, hours | starting mixture | chloroacetate yield, % | isomer ratio, % | |
|---|---|---|---|---|---|---|---|
| | | | | | | CH₃-CH-CH₂-CH₂ OAc / Cl | CH₃-CH-CH₂-CH₂ Cl / OAc |
| CH₃—CH—CH₂—CH₂ (OAc, OAc) | 25 | 1 | 14 | aqueous diacetate | 70 | 60 | 40 |
| CH₃—CH—CH₂—CH₂ (OH, OH) | 25 | 0 | 24 | diol-acetic acid in 1:1 molar ratio | 75 | 60 | 40 |

### Table IX

*Reaction of monoacetate mixtures with thionyl chloride*

| Monoacetate mixture | Chromatographic analysis | | Isomer ratio, % | |
|---|---|---|---|---|
| | CH₃-CH-(CH₂)ₙ-CH₂ OAc / OH | CH₃-CH-(CH₂)ₙ-CH₂ OH / OAc | CH₃-CH-(CH₂)ₙ-CH₂ OAc / Cl | CH₃-CH-(CH₂)ₙ-CH₂ Cl / OAc |
| CH₃—CH—CH₂—CH₂ OH(OAc) OAc(OH) | only one peak could be obtained | | 25 | 75 |
| CH₃—CH—CH₂—CH₂—CH₂ OH(OAc) OAc(OH) | 30 | 70 | 30 | 70 |

the acid chlorides. In both cases the following equilibrium is established:

$$\left[\begin{array}{c} CH_3-CH-(CH_2)_n-CH_2 \\ | \\ OH \end{array} \rightleftharpoons \begin{array}{c} CH_3-CH-(CH_2)_n-CH_2 \\ | \\ OAc \end{array} \begin{array}{c} \\ | \\ OAc \end{array} \begin{array}{c} \\ | \\ OH \end{array}\right] \rightleftharpoons$$

$$\rightleftharpoons \left[\begin{array}{c} CH_3-CH-(CH_2)_n-CH_2 \\ | \\ OH \end{array} + \begin{array}{c} CH_3-CH-(CH_2)_n-CH_2 \\ | \\ OH \end{array} \begin{array}{c} \\ | \\ OAc \end{array} \begin{array}{c} \\ | \\ OAc \end{array}\right]$$
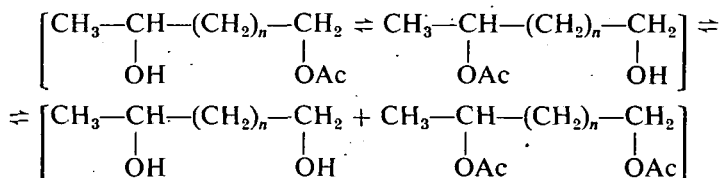
where $n = 0$, 1 or 2.

Because of the considerable differences in the reaction rates, the acyl migration reaction of the monoacetate may be treated as a pre-equilibrium involving its disproportionation to diol and diacetate, as opposed to the formation of chloro-acetates.

The investigations on 1-acetoxypentan-4-ol showed that the rate of the acyl migration is not affected by dilution, and thus it can be regarded as an intramolecular reaction. In the case of 1-acetoxyhexan-5-ol it was found that the rate of the acyl migration is comparable with the rate of the intermolecular trans-esterification leading to disproportionation, and so it is not definitely an intramolecular reaction. In addition, the entire reaction here proceeds substantially more slowly than in the case of the monoacetate of the 1,4-diol.

In this reaction, therefore, a fundamental difference exists between the 1,4- and 1,5-diols. In the case of the chloroacetates, the same is found between the 1,3- and 1,4-diols. Thus, in the formation of the chloroacetates the 1,3-diols behave similarly to vicinal diols, while in the acyl migration both the 1,3- and the 1,4-diols do so; the properties characteristic of disjoint diols are found only from 1,4- and 1,5-diols on, respectively.

### Experimental

*Pentane-1,4-diol* was prepared by the reduction of pentan-1-ol-4-one with 110 atm $H_2$ at 50°C in abs. ethanol in the presence of a Raney nickel catalyst; b.p.$_{40}$: 148—152°C; $n_D^{26}$: 1.4435.

*Hexane-1,5-diol.* Hexan-1-ol-5-one was prepared from acetoacetic ester with 1,3-dibromopropane [6], and this was then reduced as above; b.p.$_5$: 110—116°C; $n_D^{25}$: 1.4476.

*3-Methylbutane-1,3-diol* was prepared from 4,4-dimethylmetadioxane [7]; b.p.$_7$: 90—96°C; $n_D^{22}$: 1.4391.

*1-Acetoxybutan-3-*ol could not be prepared by acetylation of butan-1-ol-3-one and subsequent reduction.

*3-Acetoxybutan-1-*ol could not be prepared. This agrees with other negative results [3].

*1-Acetoxypentan-4-*ol. Pentan-1-ol-4-one was reacted with acetic anhydride, and the product reduced as described above; $n_D^{20}$: 1.4348.

*1-Acetoxyhexan-5-*ol was prepared from hexan-1-ol-5-one by the method described above; $n_D^{25}$: 1.4417.

### Preparation of monoester mixtures

*a)* Butane-1,3-diol was treated with acetic anhydride as in [1], and the mono-acetate separated from the diacetate by preparative gas-chromatography. $n_D^{25}$: 1.4180.

*b)* 1-Acetoxypentan-4-ol was treated with HCl for 5 minutes at 25°C in a 50 vol. % chloroform solution. After the working-up of the product, an almost completely pure mixture of the pentane-1,4-diol monoacetates was obtained.

*c)* Butane-1,3-diol was treated with benzoyl chloride as in [8]. Scarcely any dibenzoate was formed, even when a twofold excess of the acid chloride was used. The vast majority of the product was probably 1-benzoxybutan-3-ol.

## Reaction of diols with acid chlorides

The experiments were carried out by two different methods:

*a)* 5 g powdered anhydrous $CaCl_2$ is added to 0.25 mole diol. With stirring and cooling, 0.25 mole acetyl chloride is added dropwise at such a rate that the internal temperature remains at 9—10°C. The reaction mixture is stirred for 24 hours at 25°C, and then for 1 hour at 50°C. The product is poured onto ice, NaCl added, and extracted with ether. The ethereal phase is neutralized with $NaHCO_3$ solution, dried, the ether is evaporated, and the residue is fractionated. A detailed investigation showed that the reaction is practically completed during stirring for 4 hours at room temperature, and subsequently primarily the amount of chlorohydrin increases.

*b)* 2 g powdered anhydrous $CaCl_2$ is placed into a bomb tube and 0.1 mole diol is added. The bomb tube is cooled below −30°C and 0.1 mole acetyl chloride is added. After sealing-off, the tube is kept at −30°C for 2 hours, and then placed in ice-water. It is allowed to stand at room temperature for 2 hours, and finally kept at 100°C in a furnace for 5 hours. The working-up of the product is the same as in the process used above.

The course of the process was followed by method *a)*, a sample being taken from the reaction mixture at a given point of time. In the case of benzoyl chloride method *b)* was used, with the variation that the temperature was increased to 130°C.

The mixtures of products were studied by identifying the individual components, which were separated by means of preparative gas-chromatography. In order to detect and determine the diols, in certain cases the reaction mixture was not poured into water and the crude product was analyzed.

## Reactions with gaseous HCl

Chloroform solutions of the monoacetates and the monobenzoate were prepared, with the concentrations given in Table VII. 2 g powdered anhydrous $CaCl_2$ was added for each 0.1 mole diol. Dry gaseous HCl was led into the reaction mixture for the given time. The products were neutralized with saturated $NaHCO_3$ solution, and the aqueous phase was saturated with NaCl and extracted with ether. The combined chloroform and ether mixtures were dried and analyzed gas-chromatographically without further purification. In certain cases the neutralization was omitted and the crude product was analyzed; in these cases the detection and determination of the diols was possible.

In the case of 1,3-diacetoxybutane the amounts of water given in Table VIII were added, and then gaseous HCl was led in under the given experimental conditions. Acetic acid was added to butane-1,3-diol in a 1:1 molar ratio, followed by 2 g powdered anhydrous $CaCl_2$ for each 0.1 mole diol. Gaseous HCl was led into the reaction mixture under the conditions given in Table VIII.

## Reaction of monoacetates with thionyl chloride

Gas-chromatographic separation of the two monoacetate isomers was succesful only in the cases of the monoacetates of pentane-1,4-diol and hexane-1,5-diol. In the case of butane-1,3-diol the monoacetate mixture, which presumably also consisted of two components, gave only one peak. For this reason the monoacetate mixtures of butane-1,3-diol and pentane-1,4-diol were reacted with thionyl chloride in pyridine solution [9]. Under such conditions the process should theoretically occur *via* a Walden inversion on both the carbon atoms involved. The results are given in Table IX.

The chromatographic study of the mixture of pentane-1,4-diol monoacetates gave the same result as the thionyl chloride reaction. The two chloroacetate isomers obtained from the butane-1,3-diol monoacetate mixture also indicate that the initial monoacetate mixture contained both isomers, in a ratio corresponding to the chloroacetates formed.

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## ХИМИЧЕСКИЕ ПРЕВРАЩЕНИЯ ДИОЛОВ И ЦИКЛИЧЕСКИХ ЭФИРОВ XXXIII. РЕАКЦИЯ ДИОЛОВ С ХЛОРАНГИДРИДАМИ КАРБОНОВЫХ КИСЛОТ

*Ф. Нотейс, М. Барток и В. Ремпорт*

Нами была исследована реакция взаимодействия диолов хлорангидридами. Было изучено влияние расположения гидроксилов на протекание реакции, а также на протекание первой стадии реакции — образования диол-моноэфира. Нами было найдено, что нет существенной разницы между реакциями превращения, происходящими с диолами под воздействием ацетильхлорида, с одной стороны и моноэфирами под воздействием газообразного хлористого водорода — с другой. С образованием моноэфиров образуется сложная равновесная смесь, в которой наряду с двумя моноацетатами содержатся также диол и диацетат. В случае диолов с ассиметричной структурой образуется оба изомера моноацетата. 1,3-диолы в случае реакции образования хлорацетата, а 1,3- и 1,4-диолы в реакциях переходов ацильных групп ведут себя как 1,2-диолы, реакции характерные для диолов с раздельными гидроксильными группами проявляются только начиная от диолов имеющих гидроксильные группы в положении 1,4-, 1,5,- и выше.