Tetrahedron. Vol. 26, pp. 4771 to 4775. Pergamon Press 1970. Printed in Great Britain

A NOVEL SYNTHESIS OF A β-CHLOROETHER

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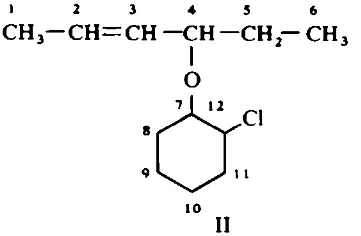
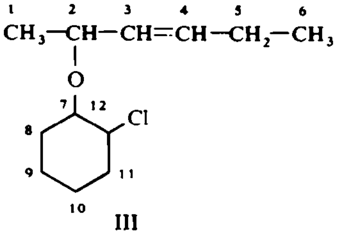
(*Received in USA 22 June 1970; Received in the UK for publication 2 July 1970*)

Abstract—Cyclohexene oxide and a mixture of allylic chlorides, 4-chlorohexene-2 and 2-chlorohexene-3 (I), react at 150° to form the isomeric β-chloroethers, 4-(2-chlorocyclohexyloxy)hexene-2 (II) and 2-(2-chlorocyclohexyloxy)hexene-3 (III). An identical reaction occurs at 50° catalyzed by cadmium and zinc chlorides.

DURING the course of an investigation of the thermal degradation of polyvinyl chloride and the mechanism of its stabilization, a novel reaction was detected. A model of the degrading polymer (an equimolar mixture of 4-chlorohexene-2 and 2-chlorohexene-3, I)[1] heated to 150° in the presence of oxirane compounds resulted in the formation of an unexpected product.* The anticipated degradation products, based on previously recognized theories of oxirane stabilizer action,[2] were 2,4-hexadiene and hydrogen chloride. The latter would react with the oxirane function to form the corresponding chlorohydrin In our studies, the major product from the reaction of an equimolar ratio of I and cyclohexene oxide was a mixture of β-chloroethers, 4-(2-chlorocyclohexyloxy)hexene-2, (II) and 2-(2-chlorocyclohexyloxy)hexene-3(III) b.p. 78–80° (0·75 mm).† The only known evidence which bears similarity to this type of reaction

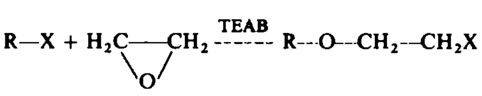


II



III

was disclosed in a recent paper in which the collaborators report the formation of β-haloethers from epoxides and active halides catalyzed by tetraethyl ammonium bromide (1).[3]



$$R{-}X + H_2C\underset{O}{-}CH_2 \xrightarrow{\text{TEAB}} R{-}O{-}CH_2{-}CH_2X \qquad (1)$$

The structure of the chloroether mixture of II and III was assigned on the basis of the following data: mass spectra: *m/e* 216 (m.w.), 201 (—CH_3), 187 (—C_2H_5), 181 (—Cl), 83 (—$C_6H_{10}ClO$); ν_{max} (CCl_4) 3070 (m), 3100 (s), 1675 (w-unsymmetric C=C),

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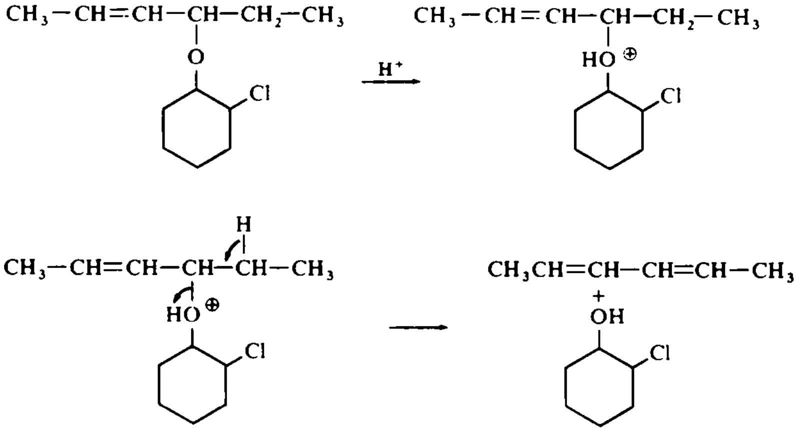
* The 50/50 mixture of the allylic chlorides was obtained by the method of Shonle and Watson[1] and was used without separation.

† Boiling points are uncorrected.

1110 (s-ether), 970 (s-*trans* double bond) cm^{-1}; NMR (CCl_4) (ppm): 1·00 (doublet of triplets, positions II_6 and III_6), 1·75 (doublet, position III_1), 1·50 (multiplet, positions II_5 and III_5), 2·10 (doublet of doublets, position II_1), 3·60 (multiplet, positions $II_{4,7,12}$ and $III_{2,7,12}$), 5·45 (multiplet, vinylic hydrogens).*

Chemical evidence for the structure was provided by a rapid degradation of the ether at 150° with trace quantities of hydrogen chloride; a quantitative conversion to cyclohexene chlorohydrin and 2,4-hexadiene was observed. Scheme 1 suggests the initial protonation of an ether oxygen (1a) with subsequent collapse of the charged species to the observed products (1b).

SCHEME 1



(1a)

(1b)

The etherification was carried out at 150° in solvents of varying dielectric constants.† In n-hexane (ε −1·89) there was no reaction, whereas, under identical reaction conditions, complete consumption of the reactants was observed after 15 min in acetonitrile (ε −26·30). The primary component of the reaction mixture in the latter solvent was the ether mixture (II and III, 60%) accompanied by cyclohexene chlorohydrin (20%) and several unidentified products. After 1 hr in methyl ethyl ketone (ε −18·50), exclusive formation of the isomeric chloroethers was observed. Reaction rate data were determined in MEK using 1:1 and 2:1 molar ratios of cyclohexene oxide: allylic hexenyl chloride mixture and the rates obtained were $-2·99 \times 10^{-3}$ min^{-1} and $-3·92 \times 10^{-3}$ min^{-1}, respectively.‡ The reaction rates clearly parallel the solvent dielectric constants and immediately suggests an ionic mechanism.[4] We propose an ionic mechanism in which the rate controlling step is the initial formation of an allylic carbonium ion (Scheme 2). Subsequent nucleophilic attack

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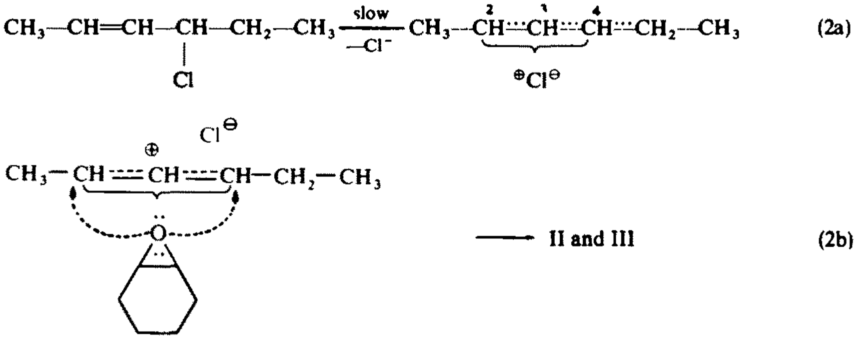
* The compounds were isolated by preparative vapor phase chromatography and were not separated. An unequivocal interpretation of the NMR spectrum was complicated by the possible presence of several diastereomers.

† These reactions were carried out in Pyrex ampoules sealed at reduced pressure (5 mm) under a nitrogen atmosphere.

‡ The inconsistency observed in the rate measurements could be ascribed to some competition from bimolecular substitution.[5,6]

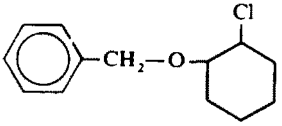
by an oxirane function then occurs with concommitant ring opening of the epoxide assisted by the chloride ion. The nucleophile may attack with equal facility at either C-2 or C-4.

SCHEME II



$$CH_3{-}CH{=}CH{-}\underset{\displaystyle Cl}{\underset{|}{CH}}{-}CH_2{-}CH_3 \xrightarrow[-Cl^-]{slow} CH_3{-}\underbrace{\overset{2}{C}H{\cdots}\overset{3}{C}H{\cdots}\overset{4}{C}H}_{\oplus Cl^{\ominus}}{\cdots}CH_2{-}CH_3 \qquad (2a)$$

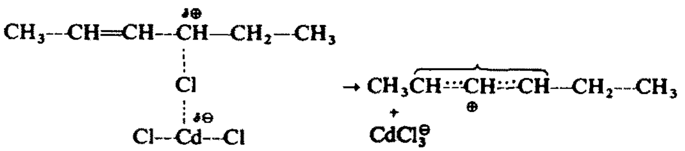
Analogous reactions in which the oxirane moiety was propylene oxide also gave isomeric mixtures of β-chloroethers. The product isolated from the reaction of benzyl chloride with cyclohexene oxide was identified as IV by NMR and infrared analyses. Only dehydrohalogenation was evident with tertiary butyl chloride and cyclohexene oxide as the reactants; cyclohexene chlorohydrin and isobutene were the only observed products.



IV

Attempts to gather rate data utilizing molar ratios of oxirane: allylic chloride less than one were futile. The sole products isolated from this study were cyclohexene chlorohydrin and 2,4-hexadiene. VPC analyses revealed initial formation of II and III followed by a rapid degradation. This observation may be interpreted by the degradation described in Scheme 1; apparently some thermal degradation of the allylic chloride generates a sufficient quantity of hydrogen chloride to catalyze the degradation of the β-chloroether.

The addition of trace quantities of cadmium or zinc chloride to a tetrahydrofuran solution of cyclohexene oxide and the allylic hexenyl chloride mixture markedly catalyzed ether formation at 50°. The sparingly soluble salts tend to assist the removal of a chloride ion in the slow ionization step with subsequent formation of the allylic carbonium ion described below in equation 3. Nucleophilic oxirane may finally attack as described in Scheme 2.



$$\begin{array}{c} CH_3{-}CH{=}CH{-}\overset{\delta\oplus}{C}H{-}CH_2{-}CH_3 \\ \vdots \\ Cl \\ \vdots\ {\scriptstyle\delta\ominus} \\ Cl{-}Cd{-}Cl \end{array} \rightarrow \begin{array}{c} CH_3\overbrace{CH{\cdots}CH{\cdots}CH}{-}CH_2{-}CH_3 \\ + \qquad \oplus \\ CdCl_3^{\ominus} \end{array} \qquad (3)$$

This involvement of the covalent cadmium and zinc salts should not be unexpected since cadmium and zinc may readily undergo sp^3 complex formation with the chloride ion.[7] The $CdCl_3^-$ formed in Eq 3 could react even more rapidly with a second allylic chloride to form the allylic carbonium ion. This reactive species may undergo either etherification or collapse to form 2,4-hexadiene and cyclohexene chlorohydrin. Kinetic studies indicate a first order rate in ether formation when utilizing 1:1 ($3{\cdot}32 \times 10^{-3}$ min^{-1}), 1:2 ($2{\cdot}91 \times 10^{-3}$ min^{-1}) and 1:4 ($2{\cdot}97 \times 10^{-3}$ min^{-1}) molar ratios of allylic chloride: oxide.

These reactions suggest facile methods for converting epoxides into β-chloroethers when using active halogen substrates.

EXPERIMENTAL

The NMR data reported here were obtained with a Varian-A-60-A Nuclear Magnetic Resonance Spectrometer (solvent—CCl_4). All analyses were performed on an F and M Model 5750 VPC equipped with a 6 foot, stainless steel column packed with 15% Apiezon-L on Chromosorb-W. A temperature program from 40° to 200° (10°/min) gave the following order of elution: solvent, 2,4-hexadiene, allylic hexenyl chlorides (2 peaks), cyclohexene oxide, chlorohydrin, and finally, the isomeric β-chloroethers (a single peak).

A. *Preparation of* β-*chloroethers* (II *and* III). Equimolar ratios of cyclohexene oxide and the allylic hexenyl chloride mixture were prepared and transferred to 11 mm, thick-walled Pyrex tubes. The tubes were then evacuated (5 mm Hg) and sealed under N_2. The sealed ampoules were finally immersed in a constant temp oil bath at 150° ± 2°. After 3 hr, VPC analysis revealed a 60% conversion to the ether mixture (II and III); the only other product identified was cyclohexene chlorohydrin (25%). (Found: C, 66·79; H, 10·12; Cl, 16·25. Calc. for $C_{12}H_{21}ClO$: C, 66·80; H, 9·33; Cl, 16·43%).

B. *Reaction of benzyl chloride with cyclohexene oxide.* To a soln of 6·5 g (0·050 mole) benzyl chloride in 25 ml THF, a soln of 10·0 g (0·0102 mole) cyclohexene oxide (1 mole excess) in 10 ml THF was added. The mixture was magnetically stirred for 3 hr at 125°. The soln was cooled; VPC analysis indicated a 50% consumption of reactants and the presence of a new product. The solvent was removed at reduced press followed by vacuum distillation to obtain 3·0 g (0·015 mole) of IV as a colorless viscous liquid (b.p. −106–110°, 2 mm Hg). The NMR spectrum (in CCl_4) exhibits singlets at 7·4 ppm (phenyl protons) and 4·6 ppm (benzylic methylene protons); multiplets appear at 3·9 and 3·4 (—O—CH and —CHCl, respectively). The cyclohexyl protons absorption occurred as an unresolved multiplet centered at 1·6 ppm. IR analysis showed absorption characteristic of an aromatic ring (3030 and 1660–2000 cm^{-1}) and an ether linkage at 1100 cm^{-1}.

C. *Reaction of t-butyl chloride and cyclohexene oxide.* A soln of t-BuCl (4·6 g, 0·05 mole), cyclohexene oxide (10·0 g, 0·10 mole) and 25 ml THF was prepared. Aliquots (2 ml) of the reaction mixture were transferred to heavy-walled Pyrex reaction tubes sealed at atm press and finally placed in an oil bath heated to 175°. After 4 hr, VPC analysis revealed the presence of cyclohexene chlorohydrin and isobutene resulting from the dehydrohalogenation of t-BuCl. No ether was observed.

D. *Reaction of propylene oxide with* I. Equimolar ratios of reactants were prepared and the reaction was performed as described in A. Mass spectral analysis indicated the formation of several isomeric β-chloroethers.* IR spectrum possessed absorption at 1675, 1110 and 970 cm^{-1} and was void of absorption in the OH region. No further analysis was attempted due to the complexity of the mixture.

E. *Kinetics.* Uncatalyzed-stock solns were prepared 0·1 M in allylic hexenyl chloride and 0·1 and 0·2 M in cyclohexene oxide with methyl ethyl ketone as solvent. Aliquots (2 ml) were introduced into heavy-walled Pyrex reaction tubes and sealed at 5 mm Hg under N_2 The tubes were then placed in an oil bath at 150° and periodically removed for analysis The concentration of unreacted allylic chloride was determined by VPC and used to obtain the kinetic data

Catalyzed etherification. Stock solutions were prepared as described previously using THF as the solvent. Anhyd cadmium chloride (0·05 g) was placed in 50 ml aliquots of stock soln contained in a 100 ml 2-necked flask equipped with a condenser and serum cap. Portions were removed periodically for VPC analysis in which the concentration of ether formed was calculated to provide kinetic data.

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* Mass spectral and infrared analyses were run on samples collected via preparative VPC.

Acknowledgement—The author wishes to thank Dr. J. E. McKeon for many helpful suggestions during the course of this investigation and in the preparation of the manuscript. Acknowledgement is also extended to Dr. J. H. Fager for NMR interpretations.

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