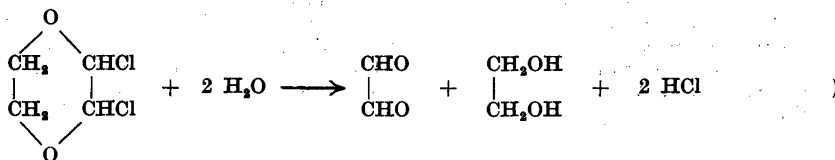


Hydrolysis and Alcoholysis of 2,3-Dichlorodioxan

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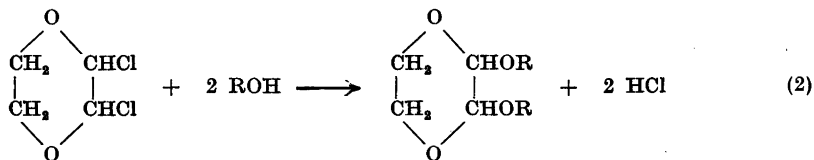
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The chlorine atoms in 2,3-dichlorodioxan are known to be very reactive, and therefore the compound is widely used as a starting material in the preparation of several dioxan derivatives¹⁻³, and in the preparation of glyoxal and its derivatives⁴. The compound hydrolyzes readily according to the equation



Theoretically 2,3-dichlorodioxan is capable in existing in two modifications, the *cis* and *trans* forms, but the two isomers have never been isolated. Butler and Chretcher⁴ have assumed that the compound is a mixture of the two isomers. It is to be noted, however, that in the displacement reactions of the chlorine atoms only one product has been isolated³. The only exception hitherto known is the reaction with ethylene glycol. This reaction yields two different products^{1,2} which were formerly assumed to be the two stereoisomers of 1,4,5,8-naphtodioxan. Furberg and Hassel⁵ have recently shown that the other reaction product is not an isomer of naphtodioxan, but bi-1,3-dioxacyclopentyl(2), and its formation thus involves further complications.

In a previous work⁶ the author investigated the kinetics of the alcoholysis reaction of alkyl halogenomethyl ethers. Since 2,3-dichlorodioxan is also an 1-halogenoether, it seemed of interest to conduct a kinetic investigation of the hydrolysis (1) and alcoholysis (2)



reactions of the compound in order to elucidate the mechanism by which the chlorine atoms are displaced in the solvolytic reactions of the compound and its possible existence as a mixture of two isomers.

EXPERIMENTAL

Materials. 2,3-Dichlorodioxan was prepared by the chlorination of dioxan according to Böesecken, Tellegen and Cohen Henriquez¹ and Baker and Shannon². The product obtained was distilled three times under reduced pressure. The purified product used in the kinetic experiments had a constant boiling point 82° C at 14 mm. (Found: Cl 44.94. Calc. for C₈H₈O₂Cl₂ (157): Cl 45.17.)

95.4 mg of the compound consumed after hydrolysis 23.50 ml of 0.0514 *N* sodium hydroxide, calculated 23.64 ml. The glyoxal formed in the hydrolysis of 56.1 mg of the compound was equivalent to 17.46 ml of 0.0813 *N* iodine, calculated 17.58 ml, determined by the modified bisulphite method described by the author for the determination of certain other aldehydes^{6,7}. The analysis of the products of hydrolysis indicates that 2,3-dichlorodioxan hydrolyzes quantitatively according to eq. (1).

On standing a few weeks the 2,3-dichlorodioxan prepared solidified, *cf.* ref². The melting point of the solid product was 31° C. Some kinetic experiments were also conducted with this form of 2,3-dichlorodioxan. Since the results obtained were identical with those obtained with the liquid 2,3-dichlorodioxan in the same solvents, the latter product was usually employed.

Acetone was a product of E. Merck (*pro analysi*) which was dried over anhydrous potassium carbonate and distilled. 1,4-Dioxan of technical grade (May & Baker Ltd.) was purified according to Hess and Frahm⁸. Ethanol was purified by the method described by Lund and Bjerrum⁹. The water used in the experiments was carbon dioxide-free distilled water. Lithium chloride and lithium perchlorate were purified as described earlier⁶.

Kinetic measurements. In the kinetic measurements, the reactions were carried out in all-glass reaction vessels in an electrically heated water thermostat. A mercury contact regulator maintained the temperature constant within 0.02° C. A well stirred ice-water mixture was used as a thermostat at 0° C. When the reaction solution (water, water-acetone or water-dioxan mixture, or ethanol) had attained the temperature of the thermostat, 2,3-dichlorodioxan was added with vigorous shaking. The progress of the reaction was followed by taking 8–11 samples of the reaction mixture with a semiautomatic pipet during the course of the reaction and analysing both the hydrogen chloride formed and the unreacted 2,3-dichlorodioxan by the method described below. In most cases the initial concentration of 2,3-dichlorodioxan was about 0.05 *M* and the volume of the samples taken was 5 ml. In solvents containing 65 % or more water by weight, lower initial concentrations (0.03–0.01 *M*) were used, since 2,3-dichlorodioxan is less soluble in these solvents. In these experiments the volume of the samples taken from the reaction mixture was 10 or 20 ml. In all experiments the reaction mixture was homogeneous.

For the analysis of the samples taken from the reaction mixture, the following procedure based on preliminary experiments on the kinetics of the reaction was selected. The samples were run into Erlenmeyer flasks which were immersed in an ice-water mixture and which contained an amount of the standard sodium hydroxide solution used in the titrations which approximately neutralized the hydrogen chloride formed (or hydrochloric acid solution in the experiments in which the reaction solution was alkaline), and an amount of acetone or dioxan sufficient to correspond to at least 50 % of the total volume of the solution. By this latter addition, it was possible to stop the reaction efficiently also in such cases in which the reaction was very rapid, since preliminary experiments had indicated that the solvolysis rate is very low when the solvent contains at least 50 % acetone or dioxan, especially at low temperatures (the half-period of the reaction in such a mixture is more than four hours at 5° C). After the sample had been taken, the solution was neutralized with standard sodium hydroxide or hydrochloric acid solution, and the concentration of hydrochloric acid produced at the time of taking of the sample was calculated. An amount of water was then added to the neutralized solution which was sufficient to increase the water content to at least 90 % by volume, after which the

mixture was allowed to stand for half an hour at the room temperature. The hydrochloric acid formed by hydrolysis was then titrated to obtain the concentration of unreacted 2,3-dichlorodioxan at the time of taking of the sample. Preliminary experiments had indicated that the solvolysis rate of 2,3-dichlorodioxan is very high when the solvent contains 90 % or more water, the half-period of the reaction at room temperature being less than one minute. Thus the 2,3-dichlorodioxan present in the sample had time enough to hydrolyze quantitatively according to eq. (1). Approximately 0.05 *N* sodium hydroxide and hydrochloric acid solutions were used in the titrations.

Conducted kinetic measurements indicated that both procedures described above, the analysis of hydrogen chloride formed and the remaining 2,3-dichlorodioxan, gave conforming results and therefore only the results of the determination of the latter were used for the calculation of specific rates. In the hydrolysis reaction in alkaline solution, however, the rate of the decrease of the hydroxyl ion concentration was somewhat higher than the twofold rate of decrease of the 2,3-dichlorodioxan concentration. This is presumably to be attributed to a subsequent reaction, the Cannizzaro reaction of glyoxal: $(\text{CHO})_2 + \text{OH}^- \rightarrow \text{CH}_2(\text{OH})\text{COO}^-$. As will be shown, this complication does not, however, affect the results when the specific rates are calculated from the concentration of unreacted 2,3-dichlorodioxan in the reaction mixture.

RESULTS AND DISCUSSION

The order of the solvolytic reactions. The experiments conducted indicated that the hydrolysis and alcoholysis reactions of 2,3-dichlorodioxan are of the first order, the rate being proportional to the concentration of 2,3-dichlorodioxan in the reaction mixture. The specific rates (*k*) were calculated from the usual equation: $k = 1/t \ln a/(a-x)$, in which *a* denotes the concentration of 2,3-dichlorodioxan at the time of taking of the first sample and *a-x* its concentration after time *t*. In all calculations, the second was used as the unit of time. To save space only two typical experimental runs are given in detail in Tables 1 and 2. The abbreviations "50.8 % dioxan", "25.3 % acetone" etc., used here and in the following, refer to dioxan-water or acetone-water mixtures which contain, respectively, 50.8 % dioxan and 25.3 % acetone by weight, etc.

Table 1. Hydrolysis of 2,3-dichlorodioxan in 50.8 % dioxan at 25° C. *a* = 0.0488

| | | | | | | | | | |
|----------------------------|--------|--------|--------|--------|--------|--------|---------|--------|--------|
| <i>t</i> (min.) | 10 | 20 | 30 | 40 | 50 | 60 | 70 | 80 | 90 |
| <i>a-x</i> | 0.0385 | 0.0306 | 0.0242 | 0.0189 | 0.0148 | 0.0118 | 0.0093 | 0.0072 | 0.0055 |
| 10 ⁴ · <i>k</i> | 3.95 | 3.89 | 3.90 | 3.95 | 3.98 | 3.94 | 3.95 | 3.99 | 4.04 |
| | | | | | | | Average | 3.95 | |

Table 2. Alcoholysis of 2,3-dichlorodioxan in ethanol at 35° C. *a* = 0.0482

| | | | | | | | | | |
|----------------------------|--------|--------|--------|--------|--------|--------|---------|--------|--------|
| <i>t</i> (hrs.) | 6 | 12 | 24 | 30 | 36 | 48 | 56 | 72 | 80 |
| <i>a-x</i> | 0.0420 | 0.0366 | 0.0275 | 0.0240 | 0.0205 | 0.0157 | 0.0130 | 0.0092 | 0.0075 |
| 10 ⁴ · <i>k</i> | 6.38 | 6.37 | 6.50 | 6.46 | 6.60 | 6.49 | 6.51 | 6.39 | 6.46 |
| | | | | | | | Average | 6.47 | |

The solvolytic reactions of 2,3-dichlorodioxan lead to the displacement of both of the chlorine atoms, the displacement of either of which may be the slower and thus rate-determining. The present results indicate that it is the displacement of the first chlorine atom that is the slower reaction, since otherwise the formation of hydrogen chloride would have been rapid at first, which was never observed in the experiments. The first-order equation was satis-

factorily obeyed in all cases independent of whether the decrease of 2,3-dichlorodioxan or the increase in the hydrogen chloride concentration was followed (see above).

Solvolysis in alkaline solution. Table 3 shows an example of experiments in which the hydrolysis of 2,3-dichlorodioxan was investigated in alkaline solution. It is seen that the addition of sodium hydroxide to the reaction solution does not alter the order of the reaction. Table 4 contains the average values of the first-order specific rates obtained with different alkali concentrations. The addition of sodium hydroxide does not influence the reaction rate significantly; at low sodium hydroxide concentrations the rate is practically unaffected, at relatively high concentrations, a slight decrease in the specific rate values is observed.

Table 3. Hydrolysis of 2,3-dichlorodioxan in 50.8 % dioxan at 35° C in the presence of sodium hydroxide. $[\text{NaOH}] = 0.0624$, $a = 0.0381$

| t (min.) | 2 | 4 | 6 | 8 | 13 | 16 | 20 | 25 |
|----------------|--------|--------|--------|--------|--------|--------|---------|--------|
| $a-x$ | 0.0325 | 0.0277 | 0.0239 | 0.0204 | 0.0139 | 0.0116 | 0.0085 | 0.0058 |
| $10^3 \cdot k$ | 1.32 | 1.33 | 1.30 | 1.30 | 1.29 | 1.24 | 1.25 | 1.26 |
| | | | | | | | Average | 1.29 |

Table 4. Influence of sodium hydroxide on the first-order specific rate of the hydrolysis of 2,3-dichlorodioxan in different solvents.

| Solvent | ° C | a | $[\text{NaOH}]$ | $10^3 \cdot k \text{ sec.}^{-1}$ |
|----------------|-----|--------|-----------------|----------------------------------|
| Water | 15 | 0.0105 | — | 11.2 |
| » | 15 | 0.0139 | 0.0504 | 11.2 |
| » | 15 | 0.0123 | 0.0932 | 11.4 |
| 44.1 % acetone | 35 | 0.0340 | — | 1.65 |
| 44.1 » » | 35 | 0.0492 | 0.0972 | 1.68 |
| 44.1 » » | 35 | 0.0510 | 0.1428 | 1.68 |
| 50.8 % dioxan | 35 | 0.0553 | — | 1.26 |
| 50.8 » » | 35 | 0.0381 | 0.0624 | 1.29 |
| 50.8 » » | 35 | 0.0449 | 0.1475 | 1.23 |
| 50.8 » » | 35 | 0.0414 | 0.3030 | 1.05 |
| 50.8 » » | 35 | 0.0436 | 0.3620 | 0.97 |
| 50.8 » » | 35 | 0.0441 | 0.5110 | 0.80 |

The fact that the addition of sodium hydroxide does not alter the order of the reaction and increase its rate indicates that the reaction takes place by the S_N1 mechanism¹⁰, the rate-determining step being the unimolecular reaction involving the ionization of the first of the carbon-chlorine bonds. Similar results were also obtained in the alcoholysis reaction of alkyl halogenomethyl ethers⁶, which reaction was shown to take place by the S_N1 mechanism. It is also interesting to note the recent results of Newth and Phillips¹¹. The authors investigated the solvolytic reactions of *O*-acylglycosyl 1-halides, which contain lactol ring oxygen atom in the 1-position to the halogen atom, and found the reactions to take place by the S_N1 mechanism.

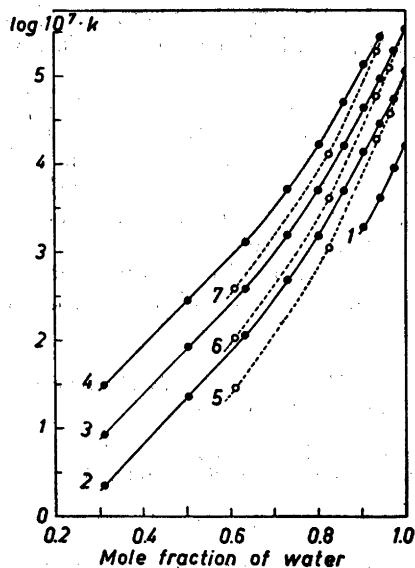


Fig. 1. Influence of solvent on the hydrolysis rate of 2,3-dichlorodioxan. Log k as a function of the mole fraction of water in different acetone-water and dioxan-water mixtures. 1, 2, 3 and 4 acetone-water mixtures at 0°, 15°, 25° and 35° C, 5, 6 and 7 dioxan-water mixtures at 15°, 25° and 35° C, respectively.

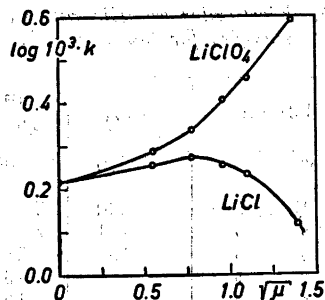
It is interesting that relatively high concentrations of sodium hydroxide lower the rate (Table 4). Similar effects have been also observed by Benfey, Hughes and Ingold¹² in the hydrolysis of diphenyl methyl bromide in aqueous dioxan, which reaction takes place by the S_N1 mechanism.

Small additions of sodium alcoholate do not materially influence the rate of the alcoholysis reaction of 2,3-dichlorodioxan. For instance, the value obtained for the first-order specific rate in ethanol solution at 15° C was $4.17 \cdot 10^{-7} \text{ sec}^{-1}$ in the presence of 0.156 *M* sodium ethylate, whereas the value obtained without the alcoholate addition was $4.04 \cdot 10^{-7} \text{ sec}^{-1}$.

Solvent effects. Fig. 1 shows the dependence of the logarithm of the first-order specific rate of hydrolysis of 2,3-dichlorodioxan on the solvent composition in different acetone-water and dioxan-water mixtures. In both solvent mixtures a very abrupt increase in the specific rate is observed with increasing water content of the solvent; in acetone-water mixtures, for example, the specific rate increases more than $5 \cdot 10^4$ -fold when the mole fraction of water increases from 0.3 to 1.0. The results are in accord with the S_N1 mechanism¹⁰. Since the rate-determining step involves formation of ions, the rate may be expected to increase rapidly with the ionizing power of the solvent. Similar results have been also obtained by Tommila and Jutila¹³ for the hydrolysis of *isopropyl benzenesulphonate* in the same binary mixtures, which reaction was also shown to take place by the S_N1 mechanism. Moreover, it is interesting to note that the inhibiting effect of dioxan is also in the present case somewhat greater than that of acetone for the same mole fractions of the organic components.

Salt effects. The investigation of salt effects furnishes a further criterion for the reaction mechanism. In a S_N1 reaction of an organic halide, two dif-

Fig. 2. Salt effects in the hydrolysis of 2,3-dichlorodioxan in 44.1% acetone at 35°C in the presence of lithium chloride and lithium perchlorate. The dependence of the logarithm of the first-order specific rate on the square root of ionic strength.



ferent salt effects are possible¹⁴. An increase in the rate is to be expected following addition of electrolyte (ionic strength effect), since the rate-determining stage involves formation of ions. If, however, the anion of the added electrolyte is the same as that formed in the reaction, the situation may be reversed. This is because with increasing concentration of the common anion, the rate-determining ionization reaction may be partially reversed whereupon the rate is decreased (mass-law effect). Thus in the presence of non-common-ion salts the rate is always increased, whereas in the presence of common-ion salts the rate is increased or decreased depending on whether the ionic strength effect is strong enough to compensate the influence of the mass-law effect. Examples of both cases are to be found in the literature^{6,11,14}. In an one-stage S_N2 reaction, on the contrary, the mass-law effect is not possible.

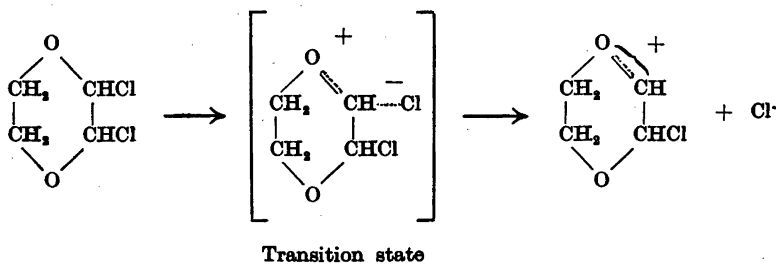
Fig. 2 shows the dependence of the logarithm of the specific rate of the hydrolysis on the square root of the ionic strength in the presence of lithium chloride and lithium perchlorate. As seen from the figure, lithium perchlorate causes the rate to increase continuously with increasing salt concentration, whereas in the case of lithium chloride the rate increases only slightly at lower concentrations. At higher lithium chloride concentrations the rate begins to decrease continuously. This is obviously because the mass-law effect becomes great enough at higher lithium chloride concentrations to overcome the ionic strength effect. The different influence of lithium perchlorate and lithium chloride on the rate is thus in good accord with the S_N1 mechanism.

Parameters of Arrhenius equation. In all solvents investigated the Arrhenius equation was obeyed within the limits of experimental error. Table 5 contains the logarithms of the frequency factors A and the activation energies E for the solvolysis of 2,3-dichlorodioxan in different media with the corresponding values of the first-order specific rates. The values of $\log A$ and E were calculated by the method of least squares. It is seen from the table that in the hydrolysis reaction the activation energy decreases and the frequency factor increases with water concentration. Both effects act in the same direction and thus the rate increases rapidly with increasing water concentration. The variation of $\log A$ and E with the water content of the solvent is similar to that observed by Tommila and Jutila¹³ in the hydrolysis of *iso*-propyl benzenesulphonate in acetone-water mixtures.

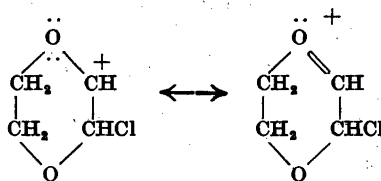
Table 5. First-order specific rates, logarithms of the frequency factors and the activation energies for the solvolysis of 2,3-dichlorodioxan in different solvents.

| Solvent | $10^6 \cdot k \text{ sec.}^{-1}$ | | | | log <i>A</i> | <i>E</i> cal. |
|---------------|----------------------------------|--------|--------|--------|--------------|---------------|
| | 0° C | 15° C | 25° C | 35° C | | |
| Water | 1 580 | 11 200 | 33 200 | | 13.05 | 19 790 |
| 8.1 % acetone | 890 | 5 940 | 18 900 | | 12.79 | 19 800 |
| 16.5 % » | 421 | 2 890 | 9 110 | 27 300 | 12.56 | 19 910 |
| 25.3 % » | 191 | 1 360 | 4 320 | 13 400 | 12.50 | 20 260 |
| 34.5 % » | | 495 | 1 590 | 4 970 | 12.15 | 20 370 |
| 44.1 % » | | 154 | 504 | 1 650 | 12.07 | 20 940 |
| 54.2 % » | | 48.4 | 159 | 519 | 11.57 | 20 950 |
| 64.8 % » | | 11.4 | 39.3 | 131 | 11.41 | 21 560 |
| 75.9 % » | | 2.32 | 8.42 | 28.8 | 11.24 | 22 250 |
| 87.7 % » | | 0.224 | 0.854 | 3.20 | 11.16 | 23 480 |
| 15.4 % dioxan | 581 | 3 780 | 12 400 | | 12.60 | 19 800 |
| 25.6 % » | | 1 930 | 5 910 | 18 600 | 12.45 | 20 000 |
| 50.8 % » | | 113 | 395 | 1 260 | 12.22 | 21 310 |
| 75.6 % » | | 2.88 | 10.6 | 37.7 | 11.68 | 22 710 |
| Ethanol | | 0.404 | 1.65 | 6.47 | 12.20 | 24 520 |

The activation energy for the alcoholysis of 2,3-dichlorodioxan in ethanol, 24 520 cal., is very high compared with the activation energy of methyl chloromethyl ether⁶, 14 510 cal., in the same solvent. The latter reaction is much more rapid; *e. g.*, at 15° C about 160 000 times as rapid as the alcoholysis of 2,3-dichlorodioxan. The effect of structure is in accord with that observed in other S_N1 reactions^{6,10}, since an electron-attracting substituent near the site of the reaction, *e. g.* chlorine atom, may be expected to decrease the ionizability of the bond broken in the rate-determining ionization. The difference between the rate of solvolysis of methyl chloromethyl ether and 2,3-dichlorodioxan seems, however, to be too great to be accounted solely for by the inhibiting effect of the second chlorine atom on the ionization of the first. An additional explanation is suggested below when the reaction mechanism is discussed in more detail. The rate-determining step in the solvolysis of 2,3-dichlorodioxan may be presented as follows (*cf. ref. 6*):



That the reaction takes place by the S_N1 mechanism is to be attributed to the resonance of the nascent cation. The cation formed can be considered as a resonance hybrid of the following two valence bond structures:



In the hybridized structure one of the carbon-oxygen bonds has a partial double-bond character, which demands coplanarity of the adjacent carbon-oxygen and carbon-carbon bonds directly attached to the resonating system¹⁵. Thus the hybridized structure must be able to overcome steric strain, which is due to the cyclic structure of the molecule, and the resonance energy liberated in the formation of the carbonium cation is reduced and the activation energy is relatively high.

The rate-determining ionization in the solvolysis of 2,3-dichlorodioxan is then followed by a rapid reaction with the solvent. The substitution of one of the chlorine atoms is followed by a more rapid displacement of the second, apparently by the S_N1 mechanism. The fact that the displacement of the second chloride atom is more rapid than that of the first is in good accord with the S_N1 mechanism, since hydroxyl and alkoxy groups are less electron-attracting substituents than chlorine (*cf.* ref. 6), and thus their retarding effect on the ionization is smaller.

The present results give no support to the existence of 2,3-dichlorodioxan as a mixture of the two isomerides, the *cis* and *trans* forms; at least the concentration of the other isomer is very low. The different modifications would apparently have different rates of solvolysis and good first-order specific rates could not be obtained for their mixture. The fact that different products have never been isolated in the displacement reactions of the chlorine atoms is in accord with our results. The observations of Summerbell and Bauer³ are interesting in this respect. The authors found that the reaction of chlorine with 2,3-dioxan yields 2,3-dichloro-dioxan, similar to that obtained by the direct chlorination of dioxan. Since normal double-bond addition reactions yield *trans* forms¹⁶, 2,3-dichlorodioxan has presumably *trans* chlorine atoms.

SUMMARY

The kinetics of hydrolysis and alcoholysis of 2,3-dichlorodioxan have been investigated in different solvents and in the presence of electrolytes. The results indicate that the solvolytic reactions of the compound take place by S_N1 mechanism, the rate-determining reaction being the ionization of the first of the carbon-chlorine bonds.

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