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# The Rates of Hydrolysis and Ethanolysis of Certain Allyl Chloride Derivatives

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The ease of displacement of halide from allylic halides by solvolysis or bimolecular nucleophilic substitution is dependent on the nature of groups attached to the olefin linkage.[1] The results of earlier work on crotyl chloride[2] suggested that the reactivity of allylic halides might to some extent also be dependent on the *cis–trans* configuration of substituents at the double bond. 1,3-Dichloropropene, which is readily separable into geometric isomers which are stable at room temperature,[3] has been chosen for a more critical study of this point.[4]

Data are available on the reaction kinetics of certain other allylic halides for their conversion to ethyl ethers or alcohols at 25° in alcoholic sodium ethoxide solutions or in 50 volume per cent. aqueous ethanol solutions of sodium hydroxide.[2,5] To permit a comparison of the results with these available data the study of the relative reaction rates of the isomeric 1,3-dichloropropenes has been made using these same media. In addition to these results this report includes, also for comparative purposes, similar kinetic data for allyl chloride and for 3,3-dichloropropene.

TABLE I

SUMMARY OF BIMOLECULAR RATE CONSTANTS FOR ETHANOLYSIS AND HYDROLYSIS OF ALLYLIC CHLORIDES AT 25°

| | Runs in ethanol | | | Runs in 50 vol. % aqueous ethanol | | |
|---|---|---|---|---|---|---|
| Chloride | Chloride concn. mole/l. | $NaOC_2H_5$ mole/l. | $k$ hr.$^{-1}$ mole$^{-1}$ l. | Chloride concn. mole/l. | NaOH mole/l. | $k'$ hr.$^{-1}$ mole$^{-1}$ l. |
| α-1,3-Dichloropropene | 0.0968 | 0.2435 | 0.168 | 0.07089 | 0.07670 | 0.364 |
| α-1,3-Dichloropropene | .1935 | .1218 | .202 | .08524 | .04606 | .366 |
| α-1,3-Dichloropropene | .1935 | .2435 | .179 | | | |
| β-1,3-Dichloropropene | .0970 | .2435 | .193 | .07090 | .07704 | .230 |
| β-1,3-Dichloropropene | .1939 | .1218 | .231 | .08601 | .04723 | .261 |
| β-1,3-Dichloropropene | .1939 | .2435 | .202 | | | |
| Allyl chloride[a] | .1533 | .1874 | .062 | .1214 | .0542 | .164 |
| Allyl chloride | .1533 | .0937 | .066 | .1214 | .0525 | .162 |
| 3,3-Dichloropropene | .4118 | .9351 | .000370 | | | Very small[b] |
| 3,3-Dichloropropene | .4141 | .5821 | .000396 | | | |
| Crotyl chloride[c] | | | .20 | | | 1.11 |
| Methylvinylcarbinyl chloride[c] | | | .004 | | | No measurable rate |
| 1,3-Dichloro-1-butene[d] | | | .015 | | | |

[a] Kinetic data for the reaction of allyl chloride with ethoxide ion at 35 and 50° have been reported by Tamele, Ott, Marple and Hearne, *Ind. Eng. Chem.*, **33**, 119 (1941). [b] In attempting to determine $k'$ values for 3,3-dichloropropene it was found that the reaction was probably to a large degree first order with respect to the dichloride concentration. The first order rate constants did however show an appreciable downward drift. The reaction was too slow to permit a convenient determination of the relative contributions of first and second order reactions. [c] Ref. 2. [d] Ref. 5.

**Kinetic Studies.**—The bimolecular rate constants ($k$) for the reactions of the α- and β-1,3-dichloropropenes, allyl chloride and 3,3-dichloropropene with ethoxide ion in ethanol and those ($k'$) for the reactions with hydroxide ion in 50 volume per cent. aqueous ethanol are listed in Table I.[6] Data for other compounds of interest are also listed. The bimolecular rate determinations with the 1,3-dichloropropenes were continued to at least 70% completion, those with allyl chloride to better than 50% and those with the slow reacting 3,3-dichloropropene to about 15%. The solvolytic reactions in ethanol at 25° of the compounds investigated in the present study were too slow to permit kinetic measurements. The first

TABLE II

SUMMARY OF RATE CONSTANTS FOR THE SOLVOLYSIS OF ALLYLIC CHLORIDES IN 50 VOLUME % AQUEOUS ETHANOL AT 25°

| Chloride | Chloride concn., mole/l. | $k_{solv.}$, hr.$^{-1}$ |
|---|---|---|
| α-1,3-Dichloropropene | 0.1097 | $5.73 \times 10^{-4}$ |
| β-1,3-Dichloropropene | .1094 | $5.77 \times 10^{-4}$ |
| Allyl chloride | .1209 | $5.72 \times 10^{-4}$ |
| 3,3-Dichloropropene | .1095 | $5.81 \times 10^{-4}$ |
| Crotyl chloride[2] | | 0.053 |
| Methylvinylcarbinyl chloride[2] | | .044 |
| 1,3-Dichloro-1-butene[5] | | .40 |

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(1) Hughes, *Trans. Faraday Soc.*, **37**, 627 (1941).

(2) Young and Andrews, THIS JOURNAL, **66**, 421 (1944).

(3) (a) Williams, *Trans. Am. Inst. Chem. Engrs.*, **37**, 157 (1941); *Chem. & Met. Eng.*, **47**, 834 (1940); (b) Hatch and Moore, THIS JOURNAL, **66**, 285 (1944).

(4) Hatch and Roberts, *ibid.*, **68**, 1196 (1946), have demonstrated semi-quantitatively a difference in rate for the cuprous chloride catalyzed hydrolysis of these isomers. The results of other studies in which these isomers were heated with dilute sodium hydroxide suggested that their hydrolysis rates were not greatly different.

(5) Andrews, *ibid.*, **68**, 2584 (1946).

(6) There is still doubt as to the correct geometric configurations for the isomers; *cf.* ref. 4 and Andrews and Kepner, *ibid.*, **69**, 2230 (1947). The terms alpha and beta are used respectively to designate the low and high boiling isomers. The authors are inclined to assign the *cis* configuration to the alpha isomer.

order solvolysis constants for the halides in 50 volume per cent. aqueous ethanol at 25° are listed in Table II. No serious drifts in the rate constants were observed in any of the runs except as noted in Table I. This fact is illustrated by Table III which presents detailed kinetic data for certain of the rate runs.

TABLE III

TYPICAL RATE DATA FOR ETHANOLYSIS, HYDROLYSIS AND SOLVOLYSIS OF ALLYLIC CHLORIDES AT 25°

| Chloride | Time, hours | Chloride concn., moles/l. | $OEt^-$ moles/l. | $k$, hr.$^{-1}$ mole$^{-1}$ l. |
|---|---|---|---|---|
| | | A. Ethanolysis | | |
| α-1,3-Dichloropropene | 0 | 0.0968 | 0.2435 | . . . |
| | 1.25 | .0919 | .2386 | 0.173 |
| | 3.00 | .0861 | .2328 | .164 |
| | 11.75 | .0621 | .2088 | .169 |
| | 29.75 | .0341 | .1808 | .172 |
| | 46.75 | .0213 | .1680 | .167 |
| β-1,3-Dichloropropene | 0 | 0.1939 | 0.1218 | . . . |
| | 3.00 | .1781 | .1060 | .249 |
| | 6.75 | .1639 | .0918 | .235 |
| | 11.75 | .1499 | .0778 | .226 |
| | 29.75 | .1181 | .0460 | .223 |
| | 46.75 | .1013 | .0292 | .231 |
| 3,3-Dichloropropene | 0 | 0.4141 | 0.5821 | . . . |
| | 42.0 | .4100 | .5781 | 4.33 × $10^{-3}$ |
| | 88.5 | .4053 | .5734 | 4.34 × $10^{-3}$ |
| | 138.1 | .4011 | .5692 | 4.00 × $10^{-3}$ |
| | 184.5 | .3974 | .5655 | 3.96 × $10^{-3}$ |
| | | B. Hydrolysis in 50 Volume % Aqueous Ethanol | | |
| | | | $OH^-$ moles/l. | $k'$, hr.$^{-1}$ mole$^{-1}$ l. |
| α-1,3-Dichloropropene | 0 | 0.08524 | 0.04606 | . . . |
| | 7 | .07693 | .03775 | 0.352 |
| | 11 | .07293 | .03375 | .361 |
| | 30 | .06029 | .02111 | .370 |
| | 46.5 | .05414 | .01496 | .368 |
| | 70.5 | .04840 | .00922 | .378 |
| β-1,3-Dichloropropene | 0 | 0.07090 | 0.07704 | . . . |
| | 7 | .06230 | .06844 | 0.255 |
| | 11 | .05892 | .06506 | .239 |
| | 22 | .05050 | .05664 | .235 |
| | 46.5 | .03842 | .04456 | .228 |
| | 54 | .03548 | .04162 | .231 |
| | 70.5 | .03106 | .03720 | .226 |
| Allyl chloride | 0 | 0.1214 | 0.0515 | . . . |
| | 6.6 | .1148 | .0449 | 0.176 |
| | 19.0 | .1064 | .0365 | .161 |
| | 26.2 | .1020 | .0321 | .164 |
| | 42.8 | .0945 | .0246 | .163 |
| | 66.9 | .0871 | .0172 | .164 |

C. Solvolysis in 50 Volume % Aqueous Ethanol

| Time, hours | α-1,3-Dichloropropene, moles/l. | $k_{solv.}$ × $10^4$, hr.$^{-1}$ |
|---|---|---|
| 0 | 0.1097 | . . . |
| 47 | 1067 | 5.86 |
| 71 | .1052 | 5.92 |
| 119 | .1024 | 5.76 |
| 215 | .0971 | 5.66 |

The reactions of the 1,3-dichloropropenes in basic media, using an excess of base seemed to reach completion with the consumption of one mole of base per mole of dichloride. The reaction conditions would be expected to result in the formation of 3-chloro-2-propene-1-ol or the corresponding ethyl ether.[7] It would scarcely be anticipated that these conditions were sufficiently vigorous to cause elimination of vinyl halogen.

**Discussion of Results.**—The variations in reactivity of the several different halides may be discussed in terms of the effects of replacing hydrogen by other groups in the 1, 2 or 3 position in allyl chloride.

$$\underset{1}{CH_2}=\underset{2}{CH}—\underset{3}{CH_2Cl}$$

A comparison of the rate constants for the 1,3-dichloropropenes and allyl chloride indicates that the substitution of chlorine at the 1 position enhances to a slight degree, particularly with ethoxide ion, the tendency for the allylic halide to undergo bimolecular nucleophilic replacement reactions. A similar observation may be made in comparing the reactivities of 1,3-dichloro-1-butene and methylvinylcarbinyl chloride with ethoxide ion. These differences may result from the inductive effect of the halogen attached at the 1 position.[8]

The rates of reaction of the isomeric 1,3-dichloropropenes with ethoxide ion are very nearly identical, although the beta isomer appears to be slightly more reactive than the alpha. The situation is reversed in the reactions with hydroxide ion in aqueous media, and the spread in reactivity is more noticeable. The differences in reactivity resulting from differences in geometric configuration of the 1,3-dichloropropanes are too small to be of great theoretical significance at least in the reactions under consideration. It is conceivable that more significant deviations in the kinetic behavior of *cis–trans* allylic isomers would be observed were the influence of the substituent at the 1 position on the rate of replacement of halogen at the 3 position more marked than in this particular case.

It is interesting to note the degree to which the allylic isomer of 1,3-dichloropropene, 3,3-dichloropropene, is inert to bimolecular replacement of halogen. This result is consistent with the observations of Hughes[8] regarding the reactivity of dichloromethane derivatives. The addition of a second halogen substituent at the 3 position in allyl chloride inhibits the reactivity of a system disposed to react by an $S_N^2$ mechanism. The opposite effect was noted in other work. The introduction of an extra α-halogen substituent in a system already disposed to react by an $S_N^1$ process results in a marked increase in activity.

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[7] Kirrmann, Pacaud and Dosque, *Bull. soc. chim.*, [5] **1**, 860 (1934).

[8] Ref. 1, p. 625, presents a similar observation regarding the reactivities of saturated halides.

Thus cinnamal chloride undergoes solvolysis very rapidly.[9]

Of the halides in question only methylvinylcarbinyl chloride, 1,3-dichloro-1-butene and crotyl chloride display reasonably high solvolysis rates. On the other hand only the 1,3-dichloropropenes, allyl chloride and crotyl chloride show marked disposition to undergo bimolecular replacement reactions. These results lend support to the previously reported evidence[2] that the solvolytic reactions of crotyl chloride are very likely to a large degree bimolecular reactions with the solvent.

## Experimental

**The α- and β-1,3-Dichloropropenes.**—A mixture of the two isomers kindly supplied by the Shell Chemical Corporation was separated by fractionation through a four-foot silvered, vacuum-jacketed column packed with glass helices as previously described. Properties of the isomers were as follows: α-, b. p. 103.3-103.5° (762 mm.), $n^{20}_{\mathrm{D}}$ 1.4690; β-, b. p. 112.0-112.3° (762 mm.), $n^{20}_{\mathrm{D}}$ 1.4740.

**3,3-Dichloropropene.**[10]—A mixture of 3,3-dichloropropene and 1,3-dichloropropene was prepared from phosphorus pentachloride and acrolein in a manner similar to that used in preparing 1,3-dichloro-1-butene.[5] The dried crude product was carefully fractionated to isolate the lower-boiling isomer. A sample of b. p. 83.0°, $n^{20}_{\mathrm{D}}$ 1.4510, $d^{20}_{4}$ 1.175 was collected for use in this work.

**Allyl Chloride.**—A sample from Paragon Testing Laboratories was fractionated. A cut of b. p. 44.9-45.0, $n^{19}_{\mathrm{D}}$ 1.4158, was taken for use in this work.

**Kinetic Studies.**—The reaction rates were followed by determining the rate of disappearance of base or of production of acid as previously described.[2,5] Commercial absolute ethanol was further dried by distillation from magnesium ethoxide for use in the rate runs.

## Summary

The reaction kinetics at 25° for the ethanolysis and hydrolysis of the *cis* and *trans* isomers of 1,3-dichloropropene have been studied. The reactivities of the isomers with respect to $S_N2$ replacement or solvolysis are closely similar in these particular reactions. The relative reactivities of certain allylic chlorides as influenced by differences in substituents attached at various positions to the allyl radical are also considered.

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[9] (a) Andrews and Linden, THIS JOURNAL, **69**, 2091 (1947); (b) Andrews, *ibid.*, **69**, 3062 (1947).

[10] Hübner and Geuther, *Ann.*, **114**, 36 (1860).

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# The Absorption Spectra of Certain Carcinogenic Aminoazo Dyes and the Protein-bound Derivatives Formed from These Dyes *in Vivo*[1]

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As a group, the various C-monomethyl derivatives of 4-dimethylaminoazobenzene cover a wide range of carcinogenic activity toward the liver of the rat.[2,3] The potency of one of these compounds, 3′-methyl-4-dimethylaminoazobenzene, exceeds that of the parent dye.[2,4,5] The relative carcinogenicities[3,6] of these dyes and of several closely related compounds are as follows:

| | |
|---|---|
| Azobenzene | 0 |
| 4-Aminoazobenzene | 0 |
| 4-Monomethylaminoazobenzene | 6 |
| 4-Dimethylaminoazobenzene | 6 (reference compound) |
| 4′-Methyl-4-dimethylaminoazobenzene | <1 |
| 3′-Methyl-4-dimethylaminoazobenzene | 10–12 |
| 2′-Methyl-4-dimethyaminoazobenzene | 2–3 |
| 2-Methyl-4-dimethylaminoazobenzene | 0-<1 |
| 3-Methyl-4-dimethylaminoazobenzene | 0 |

Recently the formation of liver tumors in rats fed 4-dimethylaminoazobenzene has been found to be preceeded by and probably casually related to the formation of firmly bound compounds between azo dye metabolites of the parent dye and the liver proteins.[7] Protein-bound dyes have also been found in the livers of rats fed various C-monomethyl derivatives of this dye. Degradation of the proteins by tryptic or alkaline hydrolysis frees the bound dyes and it has been found that the major fraction of the released bound dyes can be extracted from the protein digests only by ethyl ether–ethanol. This polar property distinguishes this fraction from the dye fed and the free dyes found in the liver; hence it has been designated as the "polar bound dye."[7] The occurrence of these dyes in only microgram quantities in the liver has prevented for the time being not only their isolation and characterization but also any exact correlation of the level of bound dye produced by feeding each dye with its carcinogenic potency. Hence as an aid in further analysis the absorption spectra of 4-dimethylaminoazobenzene and its C-monomethyl derivatives in ethanol and aqueous hydrochloric acid–ethanol solution have been determined in the 215–1200 m$\mu$ region; some of these spectra have not been recorded previously. The absorption spectra of the corresponding polar bound dyes in the 400–600 m$\mu$ region are also presented. The principal absorption maxima of the acid forms of the parent and bound dyes occur

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[1] This investigation was aided by grants from the Jane Coffin Childs Memorial Fund for Medical Research, the National Cancer Institute, and the Wisconsin Section of the American Cancer Society.

[2] Miller and Baumann, *Cancer Research*, **5**, 227 (1945).

[3] Miller and Miller, *J. Exp. Med.*, **87**, 139 (1948).

[4] Giese, Miller and Baumann, *Cancer Research*, **5**, 337 (1945).

[5] Giese, Clayton, Miller and Baumann, *ibid.*, **6**, 679 (1946).

[6] Hartwell, "Survey of Compounds which have been Tested for Carcinogenic Activity," Federal Security Agency, United States Public Health Service, 1941.

[7] Miller and Miller, *Cancer Research*, **7**, 468 (1947).