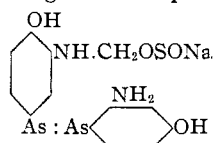


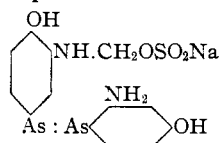
formation of bisulfite derivatives often being of a secondary nature.

The following are examples of true neoarsphenamines.



No. 5

Dihydroxy-diamino-arsenobenzene-
N-monomethylene-sulfoxylate



No. 6

Corresponding bisulfite
derivative

The toxicological and therapeutic actions of the French drugs are compared with those of other arsphenamine preparations in the appended table. The figures show the results obtained in this laboratory with representative commercial samples, using mice infected with *trypanosoma equiperdum*.

TABLE III
RELATIVE DOSES

Preparations	RELATIVE DOSES		
	As %	Curative dose G. per k.	Tolerated dose G. per k.
Arsphenamines.....	30	0.0075-0.0125	0.15-0.19
Sodium arsphenamines.....	20	0.015 -0.025	0.25-0.3
Neoarsphenamines.....	20	0.0225-0.04	0.3 -0.4
French neo mixtures.....	20	0.04 -0.06	0.4 -0.5

TORONTO, CANADA

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF YALE UNIVERSITY]

A SYNTHESIS OF BETA-CHLORO-ALLYL CHLORIDE

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The interesting properties possessed by compounds containing the allyl group ($\text{CH}_2\text{:CH.CH}_2$) have invited chemical investigation, even during the earlier periods in the development of organic chemistry. In addition to synthetic applications, it has been shown, particularly during the last decade, that the allyl residue possesses interesting properties from a pharmacological standpoint. In consideration of the importance of allyl compounds it is therefore surprising that so little attention has been paid β -chloro-allyl chloride, $\text{CHCl:CH.CH}_2\text{Cl}$. This may be attributed in part to the fact that the literature contains no procedure for its successful preparation. Its non-availability, as well as the necessity for utilizing it in some investigations in progress in this laboratory, led the writers to develop a synthesis which afford its preparation on a practical scale.

¹ This paper is constructed from a dissertation presented by Edwin J. Fischer to the Faculty of the Graduate School of Yale University in candidacy for the degree of Doctor of Philosophy.

Information bearing on the preparation and properties of chloro-allyl chloride is found in literature of a comparatively early date; it has been shown to be one of the products resulting from the following reactions: (1) dichlorohydrin and phosphorus pentachloride;² (2) trichlorohydrin and potassium hydroxide;³ (3) acrolein and phosphorus pentachloride;⁴ (4) dichlorohydrin and phosphorus pentoxide;⁵ (5) dichlorohydrin and phosphorus oxychloride.⁶ Methods 4 and 5 offer the most practical means of synthesis and both require the use of α,γ -dichlorohydrin. It therefore became necessary for the writers to develop a method for preparing the latter pure and in quantity. A mixture, consisting of α,γ -dichlorohydrin with a small amount of α,β -dichlorohydrin, is formed by the action of hydrogen chloride upon glycerol. The boiling points of these two compounds are very close together and consequently the symmetrical halide cannot be obtained absolutely pure by this method. It has been shown by Reboul,⁷ and later by Hubner⁸ and Markownikow,⁹ that epichlorohydrin will combine with conc. hydrochloric acid in such a manner that only α,γ -dichlorohydrin is obtained and none of its unsymmetrical isomer. Since either dichlorohydrin may be converted into epichlorohydrin by treatment with alkali, a method is thereby available for the conversion of the mixture of crude dichlorohydrins into pure α,γ -dichlorohydrin. Each of these reactions has been carefully studied with the object of securing maximum yields, and many improvements in the original directions have, therefore, been made. The conversion of glycerol into dichlorohydrin was accomplished in yields averaging 80 to 90% by the use of glacial acetic acid as a catalyst. The poorest yield in the synthesis was the preparation of epichlorohydrin which was seldom better than 60%. This was due to the partial conversion of the dichlorohydrin into glycerol instead of epichlorohydrin. The final step was readily accomplished in yields averaging 80%.

The synthesis of chloro-allyl chloride from dichlorohydrin involves a process of dehydration. An extensive investigation has been made of the action of many of the common dehydrating agents upon this compound, in order to obtain one which would produce chloro-allyl chloride in quantity.

² Berthelot and Luca, *Ann. chim. phys.*, [3] **52**, 438 (1858).

³ (a) Reboul, *ibid.*, [3] **60**, 37 (1860). (b) Friedel and Silva, *Compt. rend.*, **75**, 81 (1872).

⁴ Geuther, *Z. Chem.*, **8**, 26 (1865). Van Romburgh, *Compt. rend.*, **92**, 1110 (1881); *Bull. soc. chim.*, [2] **36**, 550 (1881); *ibid.*, **37**, 98 (1882).

⁵ Friedel and Silva, *Compt. rend.*, **75**, 81 (1872). Harteuistein, *J. prakt. chem.*, **7**, 308 (1873). Martinoff, *Ber.*, **8**, 1318 (1875).

⁶ Friedel and Silva, *Compt. rend.*, **75**, 81 (1872); *Ber.*, **5**, 649 (1872).

⁷ Reboul, *Ann. Spl.*, **1**, 225 (1861).

⁸ Hubner and Muller, *Ann.*, **159**, 176 (1871).

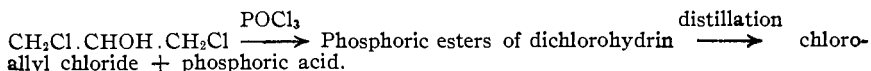
⁹ Markownikow, *ibid.*, **208**, 352 (1881).

Only two of these reagents, namely phosphorus pentoxide and phosphorus oxychloride, were successfully applied.

Preliminary experiments demonstrated in a surprising manner that none of the methods utilizing phosphorus pentoxide, as described in the literature, would give more than exceedingly small amounts of chloro-allyl chloride. After investigating the action of phosphorus pentoxide under many conditions it was found that the best procedure gave yields averaging 35-40%, calculated from dichlorohydrin. The writers obtained conclusive evidence to the effect that this reaction is not one of simple dehydration, but on the contrary one involving the intermediate formation of a phosphoric ester, which subsequently decomposes upon distillation.

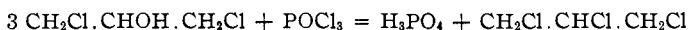
The most practical synthesis of chloro-allyl chloride from dichlorohydrin involves the use of phosphorus oxychloride. Although this reagent has been mentioned before⁶ in this connection, it was primarily employed for the preparation of trichlorohydrin, and the formation of chloro-allyl chloride, as a by-product, was incidental in connection with the preparation of the former. So far as the writers are aware this is the first practical application of this compound for the preparation of an olefin from an alcohol. An average yield of 75% may be regularly obtained by the procedure finally adopted, and it has been applied to 500 g. quantities of dichlorohydrin quite as successfully as with small runs. The actual yield is no doubt at least 5% better than that stated, but a loss of chloro-allyl chloride is occasioned in the purification process in which a small amount of water is utilized for the removal of any unchanged phosphorus oxychloride, and partial hydrolysis is thereby incurred. The remaining 20% is accounted for in unchanged dichlorohydrin and a small amount of trichlorohydrin.

The mechanism of the action of phosphorus oxychloride on α,γ -dichlorohydrin is extremely interesting. Reaction between the two is evidenced by the evolution of hydrogen chloride. This would suggest the following reaction, analogous to the decomposition of phosphorous oxychloride with water: $2\text{POCl}_3 + 3\text{H}_2\text{O} = \text{P}_2\text{O}_5 + 6\text{HCl}$. However, chloro-allyl chloride (b. p. 109°) cannot be obtained until the temperature of the mixture reaches 225°, when it distills into the receiver. Obviously an intermediate phosphoric acid ester must be formed in the reaction, and the high temperature is, therefore, necessary in order to effect its decomposition into phosphoric acid and chloro-allyl chloride. The reaction may therefore be expressed as follows:



The small amount of trichlorohydrin may be accounted for by the follow-

ing reaction in which phosphorus oxychloride functions as a halogenating agent.



In fact, this reaction can be so controlled as to yield considerable quantities of trichlorohydrin.

Although the writers were unable to obtain chloro-allyl chloride by the use of other dehydrating agents, the results in connection with these reagents are of theoretical interest.

When iodine or potassium hydrogen sulfate was employed there was no appreciable reaction and the dichlorohydrin was largely recovered. On the other hand, zinc chloride, sirupy phosphoric acid and boric anhydride were too drastic in their action upon dichlorohydrin. The reactions were accompanied by profound decomposition and chloro-allyl chloride could not be obtained. In the case of boric anhydride there was evident ester formation but the decomposition of the boric ester upon distillation was accompanied with considerable charring.

It has been stated by Jaroschenko¹⁰ that phosphorus trichloride will function as a dehydrating agent with secondary alcohols,¹¹ and will replace the hydroxyl by chlorine in the case of the tertiary. The latter reaction seemed to predominate when it was applied to dichlorohydrin, and although in some experiments material having a boiling point near that of chloro-allyl chloride could be obtained, the latter could not definitely be identified or isolated from the mixture of phosphorous ester decomposition products. This low-boiling material was always formed by a characteristic decomposition which occurred when the contents of the distilling flask had reached approximately 250°. This gave definite evidence to the effect that ester formation also occurs in this reaction, as with phosphorus oxychloride.

When thionyl chloride, SOCl_2 , was employed there was evidence of reaction and a small amount of material was obtained which appeared to be a stable ester of sulfurous acid. However no chloro-allyl chloride could be obtained by the use of this reagent.

In a future publication the writers hope to present further data concerning the nature of the esters formed in the interaction of dichlorohydrin with phosphorus oxychloride, phosphorus trichloride and thionyl chloride.

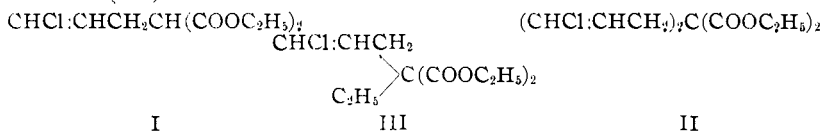
Some interesting results were observed in the interaction of anhydrous oxalic acid and dichlorohydrin. It was hoped that conditions could be evolved whereby the dichlorohydrin could be converted into chloro-allyl chloride in a manner similar to the characteristic decomposition of glycerol into allyl alcohol, rather than undergo the formic acid decomposition.

¹⁰ Jaroschenko, *Chem. Zentr.*, 1897, II, 334.

¹¹ Cf. Milobendski, *ibid.*, 1899, I, 249.

Under all conditions however, formic acid was produced in amounts proportional to the quantity of oxalic acid employed. We obtained no evidence to show that the reaction would proceed in the sense of the allyl alcohol decomposition.

As stated above, very little application has been made of chloro-allyl chloride for synthetic purposes. The work which has been done indicates that its chemical properties are normal with respect to the olefinic group, and also its ability to function as an alkyl halide, so far as the primary (CH_2Cl) halide group is concerned. With regard to the latter property, the writers have carried out some preliminary experiments designed to show that it may be utilized for the alkylation of malonic esters. The homologs which have been prepared are diethyl chloro-allyl malonate (I), diethyl dichloro-allyl malonate (II), and diethyl ethyl-chloro-allyl malonate (III).



The condensation of these malonic ester derivatives with urea is now being investigated.

Experimental Part

The Action of Hydrogen Chloride upon Glycerol

Crude α,γ -Dichlorohydrin.¹²—Although this compound may be prepared by the action of dry hydrogen chloride upon glycerol alone¹³ the reaction is very slow. Reboul¹⁴ early observed that it could be facilitated by the addition of an equal volume of glacial acetic acid, while more economical modifications have been suggested in recent patent literature.¹⁵ The latter stipulates the use of comparatively small amounts of organic acids as catalysts. A minimum of 2% and a maximum of 30% of the weight of the glycerol is suggested. Glacial acetic acid, propionic, succinic azelaic and cinnamic acids are among the organic acids which may be used for this purpose. Preliminary experiments demonstrated conclusively the slowness of reaction when acetic acid was omitted from the reaction mixture. The reaction was carefully studied, therefore, with particular regard to the effect of various amounts of acetic acid and the time factors on the yield of dichlorohydrin. These experiments clearly

¹² For ordinary purposes the dichlorohydrin used for the preparation of chloro-allyl chloride may be that resulting from the action of hydrogen chloride on glycerol. When especial purity is required it is necessary to remove the α,β -dichlorohydrin which contaminates the α,γ -derivative, when prepared as above.

¹³ Fauconnier and Sanson, *Bull. soc. chim.*, **50**, 213 (1888).

¹⁴ Ref. 3a, p. 18.

¹⁵ Ger. pat. 197,308.

demonstrated that within limits there is apparently no relation between the amounts of acetic acid used and the total yield of dichlorohydrin. However, our experience has shown that an average of 6% of acetic acid will give uniformly satisfactory results. The absorption of hydrogen chloride is very rapid in the presence of the acetic acid, and the time factor is apparently dependent, to a large degree, upon the rate at which the gas is passed through the mixture.

Apparatus.—A 2-liter distilling flask fitted with a 1-hole stopper, containing a glass delivery tube extending to the bottom of the flask. The delivery tube is connected with a hydrogen chloride generator.

Procedure.—The glycerol is first dehydrated by heating at 160° for 2 hours. Nine hundred g. of dry glycerol is weighed into the tared distilling flask; 6% by weight (54 g.) of glacial acetic acid is added and dry hydrogen chloride passed into the mixture, which is heated at 100°, until the absorption of the gas is complete. This is indicated when hydrogen chloride fumes are plainly visible at the open side-arm of the distilling bulb. A very close and satisfactory check on the progress of the reaction can be made by noting the increase in weight of the reaction mixture, the theoretical increase necessary for the formation of dichlorohydrin having been previously calculated.

After the reaction is complete, the product is distilled at 15 mm. pressure. Three fractions are thereby obtained. The first consists of an aqueous hydrochloric acid distillate, boiling between 35° and 70°. This distillate contains some dichlorohydrin which distills with the hydrochloric acid. The second fraction is a mixture of the isomeric dichlorohydrins and boils between 70° and 110°. A small amount of monochlorohydrin distills above 120°, and there is a residue of polyglycerides in the flask. It is necessary to neutralize the hydrochloric acid fraction with sodium carbonate in order to precipitate the dichlorohydrin which is soluble in the acid. The material thus recovered, is added to the main portion, and the combined dichlorohydrin mixture distilled at atmospheric pressure, the fraction boiling between 176–179° being collected. A yield of 1087 g. (87%) may be obtained by this procedure.

Epichlorohydrin.—Although this compound has been described by several investigators,¹⁶ the directions for its preparation are wholly inadequate.

Apparatus.—A 1-liter round-bottomed flask is equipped with a mechanical stirrer and a dropping funnel.

Procedure.—Two hundred g. of crude dichlorohydrin is added, with constant stirring, to 75 g. of sodium hydroxide, dissolved in 150 cc. of water, while the flask containing the reaction mixture is immersed in water at 12–15°. The sodium chloride which has separated from the solution is removed by suction filtration, and the epichlorohydrin extracted with ether and dried over anhydrous sodium sulfate. After removal of the ether, the pure epichlorohydrin may be obtained by distillation of the crude material at atmospheric pressure. The boiling point of the pure compound is 117°. The yield averages 86 g., or 60%. The yield is not higher on account of the transformation of some of the dichlorohydrin into glycerol.¹⁷

The most important factor in this preparation is that of temperature. Even at 25° the yields are materially diminished (31%), and when no temperature control is effected, the yield drops to 11%. It is important to note in this connection that Pre-

¹⁶ Berthelot, *Ann. chim. phys.*, [3] 41, 299 (1854). (b) Ref. 3a, p. 22. (c) Ref. 7. Tollens and Munder, *Z. Chem.*, 14, 252 (1871). (d) Prevost, *J. prakt. Chem.*, 12, 160 (1875). (e) Ref. 13. Tornoe, *Ber.*, 21, 1290 (1888). (f) Bigot, *Ann. chim. phys.*, [6] 22, 436, 479 (1891).

¹⁷ Claus, *Ber.*, 10, 557 (1877).

vost^{16d} heated a mixture of alkali and dichlorohydrin and reported the formation of epichlorohydrin. This is obviously contrary to all the evidence which was obtained in the present investigation. Furthermore, it was found that no essential difference in yield is produced by adding the alkali to the dichlorohydrin instead of in the reverse order.

Pure α,γ -Dichlorohydrin, $\text{CH}_2\text{Cl}.\text{CHOH}.\text{CH}_2\text{Cl}$.—Apparatus. A 1-liter round-bottomed flask equipped with a dropping funnel and a mechanical stirrer was used.

Procedure.—Three hundred and twenty g. of conc. hydrochloric acid is slowly added to 300 g. of pure epichlorohydrin. Considerable heat is evolved by each addition of the acid and the reaction mixture must, therefore, be thoroughly cooled and constantly stirred. When all of the acid has been added, the excess is neutralized with solid sodium carbonate. The dichlorohydrin is then extracted with ether and dried over anhydrous sodium sulfate. After removal of the ether the pure dichlorohydrin is obtained by distillation at atmospheric pressure (b. p. 177°). A yield of 335 g. (80%) may be consistently obtained.

Chloro-allyl Chloride

A. By the Action of Phosphorus Oxychloride upon Dichlorohydrin.—

A convenient apparatus for this reaction is a 1.5-liter round-bottomed Pyrex flask, which is connected with a water-cooled return condenser.

Two hundred and forty g. (2 moles), of phosphorus oxychloride is added to 300 g. (3 moles) of α,γ -dichlorohydrin. There is no appreciable reaction at room temperature and hence no precautions need be taken with respect to the addition of the phosphorus oxychloride, such as the use of a dropping funnel. The contents of the flask are now digested for 3 hours on a steam-bath, followed by a digestion for approximately 5 hours at a temperature of 180° in an oil-bath. During the heating periods there is a continuous evolution of hydrogen chloride. Completion of reaction is indicated when phosphorus oxychloride ceases to distil into the condenser. The flask is now disconnected from the reflux condenser and equipped with a rubber stopper and delivery tube for the purpose of distilling under diminished pressure. When there is no unaltered phosphorus oxychloride there is an entire absence of distillate until the temperature of the reaction mixture has reached 225°. Between 225° and 230° decomposition of the phosphoric esters takes place and β -chloro-allyl chloride distils into the receiver. About 242–245 g. of crude chloro-allyl chloride is thus obtained. This material is first distilled at atmospheric pressure in order to separate trichlorohydrin (b. p. 155°) and unchanged dichlorohydrin (b. p. 177°), which together total usually about 30 g. The chloro-allyl chloride (205 g.) is collected between 105° and 112°. For most purposes this product is of sufficient purity. It contains frequently a small amount of phosphorus oxychloride which cannot be removed by distillation. This impurity may be completely removed by washing the chloro-allyl chloride with a small amount of cold water, followed by drying over anhydrous sodium sulfate. The washing process is disadvantageous in one respect, in that it causes a slight loss of chloro-allyl chloride.

The yield of pure chloro-allyl chloride, resulting from distillation of the water-washed material is 195 g. or 75%. This product is a colorless oil, possessing an odor suggesting that of chloroform. It boils at 107–109° at atmospheric pressure, without decomposition.

The quantities of reagents and the manipulative procedure which have been given above for the preparation of chloro-allyl chloride were the result of a series of experiments which are recorded in Tables I and II. In Table I the destructive distillation of the phosphoric esters was carried

out at atmospheric pressures only. In both tables the water purification of the crude chloro-allyl chloride was omitted, with the exception of Expts. 6 and 7, Table II.

Considering Table I, the best proportions for a maximum yield of the compound are shown in Expts. 1 to 3. When the amount of phosphorus oxychloride was increased the excess was recovered, but the yield of chloro-allyl chloride was decreased. Moreover an excess of the phosphorus halide made for the production of slightly increased quantities of trichlorohydrin. On the other hand, when more than 3 moles of dichlorohydrin was used the yield of chloro-allyl chloride was greatly diminished.

TABLE I
THE PREPARATION OF β -CHLORO-ALLYL CHLORIDE FROM DICHLOROHYDRIN AND PHOSPHORUS OXYCHLORIDE

Expt.	POCl ₃	Dichloro-	POCl ₃	Dichloro-	Crude	Pure	Yield
	G.	hydrin			Moles	hydrin	
		G.		Moles	allyl	allyl	%
					chloride	chloride	
1	40	50	2	3	40	30	71
2	40	50	2	3	41	31	72
3	20	25	2	3	22	17	78
4	45	50	2 ¹ / ₄	3	29	24	56
5	50	50	2 ¹ / ₂	3	34	27	62
6	55	50	2 ³ / ₄	3	38	26	60
7	60	50	3	3	41	24	55
8	30	25	3	3	17	12	55
9	65	50	3 ¹ / ₂	3	41	28	65
10	35	50	2	3 ¹ / ₂	36	29	69
11	30	50	2	4	32	22	51
12	24	50	2	5	32	8	18
13	20	50	2	6	35	2	4

In Table II are shown the results of experiments which were carried out for the purpose of improving the yields of the best experiments recorded in Table I, through changes in manipulative procedure. For the purpose of minimizing decomposition, the usual digestion at 180° was omitted in Expts. 1 to 3. However considerable unchanged oxychloride was obtained and the yield of chloro-allyl chloride was considerably decreased. In order to avoid decomposition, the reaction mixture in Expt. 4 was dropped into the hot distilling flask. However, the yield was thus slightly decreased. In Expts. 5 to 7 the distillation was carried out under diminished pressure. The temperature of decomposition remained at 225–230° as in distillation at ordinary pressure. However, the distillation of the chloro-allyl chloride from the reaction mixture was facilitated, with the result that there was less decomposition and the yields were somewhat better. Exclusive of Expts. 6 and 7, the crude chloro-allyl chloride from all the

experiments was purified by distillation only. Chloro-allyl chloride thus prepared frequently contained a very small amount of phosphorus oxychloride. In Expts. 6 and 7 this impurity was removed by washing with water as described above. A 5 to 10% loss of chloro-allyl chloride is occasioned by this treatment but the product thus obtained is very pure. This is shown by the following typical analytical results.

Analyses. Calc. for $C_3H_4Cl_2$: Cl, 63.96. Found: 63.80, 63.74.

Expt. 7 is typical of the results when larger quantities are employed, and the manipulation in this case includes diminished pressure distillation and the water purification process. A representative experiment of this type is that described above in detail.

TABLE II
THE PREPARATION OF β -CHLORO-ALLYL CHLORIDE FROM DICHLOROHYDRIN AND PHOSPHORUS OXYCHLORIDE

Expt.	POCl ₃	Dichloro- hydrin	POCl ₃	Dichloro- hydrin	Crude chloro- allyl chloride	Pure chloro- allyl chloride	Yield %
	G.		Moles	Moles	G.	G.	
1	35	50	2	3 $\frac{1}{2}$	35	28	65
2	35	50	2	3 $\frac{1}{2}$	33	24	55
3	35	50	2	3 $\frac{1}{2}$	24	10	23
4	40	50	2	3	37	29	69
5	40	50	2	3	42	35	81
6	80	100	2	3	82	64	74
7	240	300	2	3	242	193	74

B. By the Action of Phosphorus Pentoxide on Dichlorohydrin.—

A few preliminary experiments were carried out in order to duplicate, so far as possible, the literature directions covering this method for the preparation of chloro-allyl chloride. Although various proportions of phosphorus pentoxide were employed, the reaction was attended with so much decomposition that little or no chloro-allyl chloride could be obtained by these methods. In order to minimize this decomposition the reaction was carried out in the presence of benzene and the results were very significant.

Seventy-five g. of pure α,γ -dichlorohydrin was dissolved in 125 g. of benzene, and 85 g. of phosphorus pentoxide was then added in small portions. The reaction mixture became very hot. After all the oxide had been added the mixture was heated upon an oil-bath at 120° for 1 hour. The benzene solution was decanted from the sirupy residue and distilled. The distillate proved to be *pure benzene*. The residue was subjected to destructive distillation at 200° while carbon dioxide was passed through the system. There was some charring, and decomposition was indicated by the evolution of hydrogen chloride fumes. The crude oil in the distillate was redistilled and 8 g. of chloro-allyl chloride was thereby obtained, together with 12 g. of unchanged dichlorohydrin. The former had apparently resulted from the destructive distillation of a phosphoric acid ester.

The fact that the diluent greatly tempered the violence of the reaction led to a modification of the original procedure in which the dichlorohydrin was added directly to the

phosphorus pentoxide, which was thoroughly mixed with a quantity of dry sand for the purpose of furnishing as large a surface of the oxide as possible. The general procedure was as follows. The required amount of oxide was thoroughly mixed with 2 parts of dry sand. The dichlorohydrin was then added drop by drop, following which the mixture was heated on the steam-bath for an hour in order to insure complete reaction. It was finally distilled from an oil-bath at 175–210° and chloro-allyl chloride thereby obtained. There was considerable charring and decomposition. The crude product was purified by redistillation; b. p., 107–109°.

Several experiments were carried out in accordance with this method and the results are given in Table III. In Expts. 4 to 7 carbon dioxide was passed through the train of apparatus and this modification of the procedure facilitated the distillation and obviated the decomposition to some extent.

TABLE III

THE PREPARATION OF β -CHLORO-ALLYL CHLORIDE FROM DICHLOROHYDRIN AND PHOSPHORUS PENTOXIDE

Expt.	P ₂ O ₅ G.	Dichloro- hydrin G.	P ₂ O ₅ Moles	Dichloro- hydrin Moles	Crude	Pure	Yield %
					chloro- allyl chloride G.	chloro- allyl chloride G.	
1	25	25	1	1	7
2	55	50	1	1	6
3	55	50	1	1	12
4	250	175	1 ¹ / ₄	1	50	44	30
5	85	50	1 ¹ / ₂	1	17	16	38
6	110	50	2	1	17	16	38
7	110	50	2	1	18	17	40

Action of Sirupy Phosphoric Acid upon Dichlorohydrin.—One hundred cc. of sirupy phosphoric acid was placed in a 1-liter distilling flask, which was attached to a condenser in the usual manner for distillation. The contents were then heated in an oil-bath to 230–240°. Fifty g. of pure dichlorohydrin was then slowly added through the dropping funnel which extended to the bottom of the flask. Decomposition was shown by the evolution of hydrogen chloride fumes and blackening of the reaction mixture. The distillate, which was dark colored, weighed 42 g. It was neutralized with a little sodium carbonate solution, extracted with ether, dried over anhydrous sodium sulfate and distilled. The product thus obtained boiled at 160–175° and was apparently composed largely of unchanged dichlorohydrin with some decomposition products. The results were even less favorable when the reagents were mixed prior to distillation. In neither case was there evidence of the formation of chloro-allyl chloride.

Action of Oxalic Acid upon Dichlorohydrin.—The general procedure consisted in digesting a calculated quantity of dichlorohydrin with anhydrous oxalic acid for 3 to 5 hours. One-half g. of ammonium chloride was also added to the mixture in order to facilitate the allyl alcohol type of decomposition. In each experiment reaction took place at 130–150°. The acid dissolved, and carbon dioxide and some hydrogen chloride were evolved. Upon distillation 2 fractions were always obtained, the lower boiling at 100–125°, and the higher one at 177° (dichlorohydrin). The lower fraction was largely formic acid, and no chloro-allyl chloride could be obtained. A series of these experiments is recorded in Table IV. In Expt. 1 the proportions are the same as those which are commonly employed for the preparation of formic acid from glycerol and oxalic acid.

The highest yield of formic acid was obtained in this experiment with only a small amount of recovered dichlorohydrin. Theoretically, the latter should have been recovered in this type of decomposition. In Expt. 4 the proportions were reversed and 4 moles of dichlorohydrin were used to 1 of oxalic acid. These conditions, including temperature, are analogous to those which promote formation of allyl alcohol in the interaction of oxalic acid and glycerol, yet no chloro-allyl chloride could be obtained. In this experiment a large proportion of the dichlorohydrin was recovered unchanged.

TABLE IV
THE ACTION OF OXALIC ACID ON DICHLOROHYDRIN

Expt.	Oxalic acid	Dichloro- hydrin	Oxalic acid	Dichloro- hydrin	Temp. ° C.	Formic acid	Unchanged dichloro- hydrin
	G.	G.	Moles	Moles		G.	G.
1	56	20	4	1	160	23	6
2	35	50	1	1	250	13	31
3	18	50	1	2	250	5	47
4	9	50	1	4	250	2	48

The Action of Potassium Hydrogen Sulfate upon Dichlorohydrin.—Fifty g. of potassium hydrogen sulfate and 25 g. of dichlorohydrin were heated in an oil-bath at a temperature of 200–210° for 2 hours. There was no evidence of reaction and only a slight charring occurred. The mixture was then distilled while carbon dioxide was passed through the apparatus. Twenty g. of unchanged dichlorohydrin was thus obtained.

The Action of Sulfuric Acid upon Dichlorohydrin.—The action of both dil. (60%) and conc. sulfuric acid was investigated. Neither reagent gave chloro-allyl chloride. When dil. acid was used, but little reaction occurred. On the other hand, with conc. acid excessive decomposition took place and the alcohol was largely destroyed.

The Action of Boric Anhydride upon Dichlorohydrin.—Fifteen g. of boric anhydride and 25 g. of dichlorohydrin were heated under a reflux condenser upon an oil-bath at a temperature of 275–300° for 5 hours. When the mixture was distilled there was considerable charring and decomposition, and hydrogen chloride was evolved. Only 2 g. of distillate was obtained. A similar result was obtained when the digestion was carried out at 160°, and the distillation performed under diminished pressure. In both cases there was evidence of reaction between the anhydride and dichlorohydrin. The boric anhydride dissolved in the dichlorohydrin and a solid mass formed as it cooled. It is quite possible that an ester was formed only to suffer complete decomposition upon distillation.

The Action of Zinc Chloride upon Dichlorohydrin.—Twenty-five g. of dichlorohydrin and 31 g. of anhydrous zinc chloride were heated in an oil-bath. When the temperature of the bath reached 145°, reaction took place and the mixture was distilled at once. About 5 g. of a pungent smelling liquid was obtained, and the residue in the flask was considerably charred. In an attempt to avoid this decomposition, the dichlorohydrin was slowly added to the zinc chloride (heated to 175° in an oil-bath) by means of a dropping funnel. It was hoped that the chloro-allyl chloride, if formed, would distil immediately and decomposition might therefore be avoided. Profound decomposition again took place and there was no evidence of the formation of chloro-allyl chloride.

Action of Iodine upon Dichlorohydrin.—Iodine has been utilized¹⁸ as a catalytic agent in the dehydration of tertiary alcohols, and secondary alcohols have also been shown to behave in an analogous manner, but the reaction is much slower. When 50 g. of dichlorohydrin was heated with 0.5 g. of iodine in an oil-bath at 200–250° for 10 hours

¹⁸ Hibbert, THIS JOURNAL, 37, 1748 (1915).

and then distilled, the compound was recovered unchanged.

Action of Thionyl Chloride upon Dichlorohydrin.—The action of thionyl chloride should theoretically lead to the formation of an unstable ester of sulfurous acid, which on distillation should give chloro-allyl chloride in a manner similar to the phosphate. Twelve g. of thionyl chloride and 25 g. of dichlorohydrin were digested on a steam-bath for 1 hour. A reaction occurred and hydrogen chloride fumes were evolved. Upon distillation from an oil bath at a temperature of 230–250°, 18 g. of a colorless oil was obtained and there was only a small residue in the flask. A small amount of oil, boiling at 163–169° was obtained after repeated distillation of this product. Although sulfur analyses were inconclusive it seemed very evident that the writers were dealing with a mixture of dichlorohydrin and a stable sulfurous acid ester of dichlorohydrin. This reaction will be more thoroughly investigated.

Action of Phosphorus Trichloride upon Dichlorohydrin.—The following procedure was used in all the experiments. The calculated quantities of dichlorohydrin and phosphorus trichloride were heated for 2 hours on a steam-bath. Reaction was indicated by the evolution of hydrogen chloride. The mixture was distilled from an oil-bath at 250–260° and the resulting product was redistilled. Two fractions were always obtained. The lower one had no definite boiling point (95–140°), while the higher fraction boiled at 155–160° and consisted of trichlorohydrin with small amounts of dichlorohydrin. The results of a series of experiments are given in Table V. The proportions of phosphorus trichloride to dichlorohydrin necessary to effect ester formation are represented in the conditions of Expt. 1, yet the principal product of this experiment was trichlorohydrin. When the amounts of phosphorus trichloride were *increased*, a *decrease* in the amount of trichlorohydrin was observed, while the low-boiling material, consisting of some trichlorohydrin and possibly esters of phosphorous acid, or their decomposition products, was increased. This low-boiling material, which could not be separated into definite components, may possibly have contained some chloro-allyl chloride. Since it was not formed until the reaction mixture was heated above 250°, it is evident that it was produced in part by the decomposition of ester combinations. This material gave qualitative tests for phosphorus, but it was impossible to obtain definite fractions by distillation.

TABLE V
ACTION OF PHOSPHORUS TRICHLORIDE ON DICHLOROHYDRIN

Expt.	Dichloro-	PCl ₃	Dichloro-	PCl ₃	Trichloro-	Low-
	hydrin		hydrin			hydrin
	G.	G.	Moles	Moles	G.	fraction
						G.
1	25	9	3	1	15	..
2	25	13.5	2	1	6	10
3	25	18	3	2	6	13
4	25	27	1	1	8	13

The Utilization of β -Chloro-allyl Chloride for the Preparation of Derivatives of Diethyl Malonate

Diethyl Chloro-allyl-malonate, CHCl:CH.CH₂.CH.(COOC₂H₅)₂.—Four and two-tenths g. of sodium was dissolved in 75 g. of absolute alcohol and 29 g. of diethyl malonate was then slowly added to this solution during constant agitation. The mixture was then cooled and 22 g. of chloro-allyl chloride was added in small portions. The solution became neutral to turmeric paper after standing for 12 hours. To insure complete reaction it was finally heated upon the steam-bath for an hour. The precipitate of sodium chloride was filtered and the alcohol removed from the filtrate under diminished pressure. A small amount of water was added to the residue, and the oil which separated was ex-

tracted with ether and dried over sodium sulfate. After removal of the ether the residual oil was distilled under atmospheric pressure. The distillation was accompanied with some decomposition and the product boiled between 255–275°. When the distillation was carried out under diminished pressure (12 mm.) the ester boiled at 161–163° without decomposition. The yield of pure ester was 11 g., or 26%. This new ester is a pale yellow-colored oil, possessing the characteristic pleasant odor of malonic esters.

Analysis. Calc. for $C_{10}H_{16}O_4Cl$: Cl, 15.14. Found: 15.36.

Diethyl Di-chloro-allyl-malonate, $(ClCH:CH.CH_2)_2C(COOC_2H_5)_2$.—Fourteen and five-tenths g. of diethyl malonate was added to a solution of 4.2 g. of sodium in 50 g. of absolute alcohol; 22 g. of chloro-allyl chloride was then slowly added, with shaking. A precipitation of sodium chloride occurred, and the mixture became yellow in color. It was allowed to stand for 12 hours and at the end of this time was neutral to turmeric. The ester was isolated in manner similar to that described under the preparation of the monochloro-allyl compound. The crude oil was purified for analysis by distillation under diminished pressure; b. p., 190° at 12 mm. The yield of pure ester was 9 g., or 32%. The compound is a pale yellow-colored oil possessing a pleasant ester-like odor. It boils at 300° under atmospheric pressure, but is partially decomposed by this treatment.

Analyses. Calc. for $C_{13}H_{18}O_4Cl_2$: Cl, 22.98. Found: 23.15, 23.30.

Diethyl Ethyl-chloro-allyl-malonate, $(CHCl:CH.CH_2)(C_2H_5)C(COOC_2H_5)_2$.—The diethyl ethyl-malonate used in this experiment was prepared according to the directions given by Conrad and Bischoff.¹⁹ Three and one-tenth g. of sodium was dissolved in 50 g. of absolute alcohol; 25 g. of diethyl ethyl-malonate was added, followed by 15 g. of chloro-allyl chloride. The mixture became neutral upon standing and the ester was isolated in the usual manner. The crude oil distilled at 157–160° at 12 mm. The yield was 7 g. or 20%. The ester is a colorless oil of fruity odor.

Analysis. Calc. for $C_{12}H_{19}O_4Cl$: Cl, 13.53. Found: 13.85.

Summary

1. The object of the investigation has been to develop a practical method for the preparation of β -chloro-allyl chloride.

2. Complete directions are given for the transformation of glycerol into the necessary intermediate, *pure* α,γ -dichlorohydrin, as indicated by the expression,

Glycerol \longrightarrow crude dichlorohydrin \longrightarrow epichlorohydrin \longrightarrow pure dichlorohydrin

3. The alcohol, α,γ -dichlorohydrin, may be converted into chloro-allyl chloride by phosphorus oxychloride or phosphorus pentoxide. Of these, the former is the more practical reagent, giving yields of the olefin averaging 75%.

4. The dehydration of dichlorohydrin in the case of both phosphorus oxychloride and phosphorus pentoxide is preceded by ester formation and chloro-allyl chloride is produced by the decomposition of these intermediate products.

5. The action of other dehydrating agents has also been investigated, namely, potassium hydrogen sulfate, sulfuric acid, oxalic acid, boric anhydride, thionyl chloride and phosphorus trichloride. Chloro-allyl chloride could not be obtained by the use of these compounds.

¹⁹ Conrad and Bischoff, *Ann.*, **204**, 129 (1880).

(i. Chloro-allyl chloride has been utilized as an alkylating agent in the preparation of some new derivatives of diethyl malonate.

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[CONTRIBUTION FROM THE MASSACHUSETTS INSTITUTE OF TECHNOLOGY, LABORATORY OF ORGANIC CHEMISTRY]

THE UREA DEARRANGEMENT

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Ammonia and cyanic (or isocyanic) acid combine in two ways, to form ammonium cyanate or to form urea. Each of these products is readily converted into the other, or better, each in solution is in equilibrium with a certain amount of the other. An aqueous solution of ammonium cyanate yields urea¹ on evaporation, and an aqueous solution of urea after boiling gives a precipitate of silver cyanate² if silver nitrate is added. When a solution of urea is treated with nitrous acid in the cold, ammonium nitrite is formed and cyanic acid³ is liberated, and the recent work of Werner⁴ has brought to light still other facts in support of the opinion that urea is an addition compound of ammonia and *isocyanic* acid. When urea is heated, it yields, in addition to biuret, precisely the compounds⁵ which would be formed by the dry heating of ammonium cyanate. As ammonia and isocyanic acid combine with each other to form ammonium cyanate and urea, or better, a mixture of the two, so these two substances under suitable conditions break down into ammonia and isocyanic acid. There are reversible changes as follows:⁶ $\text{NH}_4\text{NCO} \rightleftharpoons \text{NH}_3 + \text{HNCO} \rightleftharpoons \text{NH}_2\text{---CO---NH}_2$. As the conversion of ammonium cyanate into urea is generally known as an instance of the "urea rearrangement," so for the purpose of the present paper it will be convenient to denominate the reverse of this change as the "urea dearrangement." The urea dearrangement provides a simple means for interpreting and correlating a considerable number of reactions in the urea and guanidine series. It provides a ready means for the synthesis of certain substituted ureas and thio-ureas. The present paper brings forward evidence to show

¹ Wöhler, *Pogg. Ann. Physik*, **12**, 253 (1828).

² Wöhler and Liebig, *Ann.*, **26**, 301 (1838). Walker and Hambley, *J. Chem. Soc.*, **67**, 747, 751 (1895).

³ Wöhler and Liebig, *Ann.*, **26**, 261 (1838).

⁴ Werner, many papers on carbamides. *J. Chem. Soc.*, **117**, 1356 (1920), etc.

⁵ Wöhler, *Pogg. Ann. Physik*, **15**, 622 (1829). *Ann. chim. phys.*, [2] **43**, 67 (1830). Weidemann, *J. prakt. Chem.*, [1] **43**, 277 (1848). *Pogg. Ann. Physik*, **74**, 78 (1849). *Ann.*, **68**, 325 (1848). Hofmann, *Ber.*, **4**, 262 (1871). Schiff, *Ann.*, **299**, 236 (1898).

⁶ We use the familiar formula for urea. Werner's formula, whatever may be said for it in the case of urea, is not well adapted to the interpretation of our reactions in the case of the substituted ureas.