283. *The Preparation of 2 : 3-Dimercaptopropanol from 2 : 3-Dichloropropanol.*

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A study of the addition of chlorine to allyl alcohol has revealed that the best solvent is hydrochloric acid. The preparation of 2 : 3-dimercaptopropanol from 2 : 3-dichloropropanol is described.

The preparation of 2 : 3-dimercaptopropanol (British Anti-Lewisite or " BAL ") from 2 : 3-dibromopropanol and cold alcoholic sodium hydrogen sulphide has been described by Stocken (*J.*, 1947, 952). During 1941 its preparation from 2 : 3-dichloropropanol was investigated. Dichloropropanol does not react sufficiently well with cold alcoholic sodium hydrogen sulphide, but, if the reaction is performed in a pressure vessel at 70—80°, dimercaptopropanol can be obtained in 50—60% yield. It is unnecessary to use alcoholic sodium ethoxide for the preparation of the sodium hydrogen sulphide; sodium hydroxide in methanol can be used equally well. Ammonium hydrogen sulphide gave less satisfactory yields.

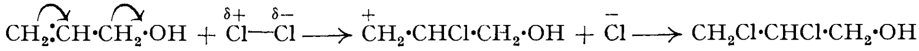
Although dibromopropanol can be prepared in excellent yield by addition of bromine to allyl alcohol, addition of chlorine proceeds less satisfactorily. King and Pyman (*J.*, 1914, **105**, 1257) obtained a 40% yield, using carbon disulphide as solvent, and this appears to be the best yield recorded in the literature. The addition proceeds with copious evolution of hydrogen chloride and production of much high boiling point material. The use of other non-aqueous solvents, *e.g.*, chloroform or carbon tetrachloride, led to no improvement in yield, and consequently it was decided to investigate the addition of chlorine to allyl benzoate and to allyl acetate.

The addition of chlorine to allyl benzoate in non-aqueous solvents was found to be favoured by low temperature, absence of light, and addition of dry charcoal; the reaction is probably heterogeneous—hence the improvement in presence of charcoal. Carbon tetrachloride was the most satisfactory solvent, and an 84% yield of pure dichloropropyl benzoate could be regularly obtained. The addition of chlorine to allyl alcohol was not improved by these conditions.

Unfortunately, no really satisfactory method of hydrolysing dichloropropyl benzoate was found, and direct conversion of the ester into dimercaptopropanol was vitiated by the contamination of the product with trimercaptopropane. The replacement of the benzoate by the thiol group is not without analogies; Auger and Billy (*Compt. rend.*, 1903, **136**, 555) obtained ethylthiol by heating ethyl benzoate with alcoholic sodium hydrogen sulphide at 180°. The more facile replacement with dichloropropyl benzoate may be due to the loss of sodium benzoate from an intermediate of the type $\cdot CH(SNa)\cdot CH_2\cdot OBz$ to form a propylene sulphide which reacts further with sodium hydrogen sulphide.

Dichloropropyl acetate is readily hydrolysed by hot dilute hydrochloric acid, but the addition of chlorine to allyl acetate did not proceed satisfactorily under the conditions of King and Pyman for allyl alcohol, those found satisfactory for allyl benzoate, or those later found favourable for allyl alcohol.

On the assumption that the addition of chlorine to allyl alcohol proceeds by a mechanism of the following type :



$$CH_2{:}CH\cdot CH_2\cdot OH + \overset{\delta+}{Cl}—\overset{\delta-}{Cl} \longrightarrow \overset{+}{C}H_2\cdot CHCl\cdot CH_2\cdot OH + \overset{-}{Cl} \longrightarrow CH_2Cl\cdot CHCl\cdot CH_2\cdot OH$$

it was decided to investigate the addition in presence of substances capable of releasing chlorine anions. Concentrated hydrochloric acid and hydrochloric acid–ether mixtures gave promising results, and yields of about 60% could be obtained with hydrochloric acid–ether mixtures when the solvent was saturated with hydrogen chloride. Even better yields were obtained by using hydrochloric acid as the only solvent and maintaining the saturation with hydrogen chloride by a slow stream of the gas during the addition of chlorine. The yields of addition product were sensitive to the proportion of solvent, and the best yield (71%) was obtained with equal volumes of allyl alcohol and concentrated hydrochloric acid.

Experimental.

2 : 3-*Dimercaptopropanol.*—(1) A solution of sodium (34 g.) in methanol (400 ml.) was saturated at 0° with dry hydrogen sulphide; dichloropropanol (34 g.) was added and the mixture heated in pressure bottles at 70—80° for 6 hours. The cooled mixture was acidified to Congo-red paper with concentrated

hydrochloric acid, filtered, and evaporated in a vacuum below 50° until oil separated; water was added to dissolve precipitated salt and the oil extracted with chloroform. The product was fractionated at 0·2—0·25 mm., and the fraction, b. p. 70—96°, refractionated; yield, 16·2 g. of dimercaptopropanol, b. p. 85—92°/0·2 mm., or 50% (Found by iodine titration : SH, 49·5. Calc. for $C_3H_8OS_2$: SH, 53·2%). No attempt was made to obtain purer material than this, which is 93% pure.

By a similar process *s*-dichloro*iso*propanol gave 65—70% yields of 90% pure dimercapto*iso*propanol, and the mixed dichlorohydrin, b. p. 175—183°, obtained by addition of hypochlorous acid to allyl chloride gave 60—66% yields of a mixed dimercaptopropanol containing 90—92% of dithiol. With ammonium hydrogen sulphide (6 mols. per mol. of dichloropropanol) poorer yields were obtained; *e.g.*, after 12 hours at 70—75° a yield of only 33% was obtained, and 20% of unchanged dichloropropanol was recovered.

(2) Flake sodium hydroxide (50 g.) was covered with methanol (400 ml.) and the mixture saturated with dry hydrogen sulphide at 0°; the sodium hydroxide dissolved slowly, leaving a little fine sediment. Dichloropropanol (30 g.), heated with this solution at 75—80° for 6 hours, gave a 63% yield of 92% pure dimercaptopropanol.

By a similar process dichloropropyl benzoate gave a product, b. p. 75—80°/0·15 mm. or about 10° below that of dimercaptopropanol, which contained some trimercaptopropane (Found : SH, 62·3. Calc. for $C_3H_8OS_2$: SH, 53·2; and for $C_3H_8S_3$: SH, 70·7%).

2 : 3-*Dichloropropyl Benzoate*.—The addition of chlorine to allyl benzoate was studied under various conditions; the results are summarised in Table I.

TABLE I.

Addition of chlorine to allyl benzoate.

Solvent and conditions.	Yield of dichloropropyl benzoate (%). Crude.	Pure.
1. Carbon disulphide	57·4	—
2. Carbon disulphide in the dark	66·6	62
3. Carbon disulphide + dry $CaCO_3$ in the dark	67·6	—
4. Carbon tetrachloride in the dark	67·0	63·5
5. Carbon tetrachloride + norite in the dark	88·6	84
6. As 5, but on 3 times the scale	—	84
7. Chloroform + norite in the dark	77·6	—
8. Tetrachloroethane + norite in the dark	74·0	—

The proportion of allyl benzoate to solvent in each experiment was 40 g. of ester to 150 ml. of solvent; for these amounts 5 g. of dry norite was used in expts. 5—8. The norite was thoroughly dried by being heated and shaken, and was covered with solvent while still warm. Solutions were cooled to − 10°, stirred, and treated with dry chlorine (10% excess, prepared from permanganate and hydrochloric acid). The reaction is strongly exothermic and the chlorine stream was regulated so as to keep the temperature at as near − 5° as possible.

Excess of chlorine was removed by bisulphite, the solvent distilled off, and the product fractionated; the crude ester was collected over 10° (150—160°/12 mm.), the pure ester at 158—160°/12 mm. [Found (expt. 5) : C, 51·3; H, 4·4. Calc. for $C_{10}H_{10}O_2Cl_2$: C, 51·5; H, 4·3%].

Dichloropropyl benzoate is hydrolysed with difficulty by acid unless alcohol is present : the ester (50 g.) was boiled with concentrated hydrochloric acid (100 ml.) and alcohol (200 ml.) for 3 hours; alcohol was distilled off between 80—90° (100 ml.) and boiling continued for another 3 hours; the mixture was diluted, neutralised, and extracted with chloroform; fractionation of the product gave 15·5 g. of dichloropropanol (b. p. 180—188°; 56% yield) and higher fractions which still contained chlorine.

2 : 3-*Dichloropropyl Acetate*.—Since this ester is readily hydrolysed by boiling dilute hydrochloric acid, the addition of chlorine to allyl acetate was studied. The results are summarised in Table II.

TABLE II.

Addition of chlorine to allyl acetate.

Solvent and conditions.	Yield of crude dichloropropyl acetate, b. p. 195—200° (%).
1. Carbon disulphide	36·0
2. Carbon tetrachloride + norite in the dark	60·0
3. Conc. hydrochloric acid + ether (2 : 1 by vol.)	59·7
4. Conc. hydrochloric acid + ether (1 : 1 by vol.) saturated with hydrogen chloride	62·0

Expt. 1 repeats the conditions of King and Pyman (*loc. cit.*) for allyl alcohol, expt. 2 those found satisfactory for allyl benzoate, and expts. 3 and 4 those found favourable for allyl alcohol (see below).

The Addition of Chlorine to Allyl Alcohol.—The main results are summarised in Table III. Expt. 1 repeats King and Pyman's conditions, but their recorded yield (40%) was only attained once. Expt. 2 repeats the conditions found satisfactory for allyl benzoate.

TABLE III.

Addition of chlorine to allyl alcohol.

	Solvent and conditions for 29 g. (34 ml.) of allyl alcohol (0·5 mol.).	Yield of dichloropropanol, b. p. 180—185° (%).
1.	Carbon disulphide (100 ml.) at —5°	35—40
2.	Carbon tetrachloride (120 ml.) + norite (5 g.) at —5° in the dark	30·4
3.	Dry ether (100 ml.) containing HCl (10 g.) at —5°	48·0
4.	Conc. hydrochloric acid (100 ml.) at 0°	42·0
5.	20% (w/v) $CaCl_2$ in conc. hydrochloric acid (100 ml.) at 0°	45·6
6.	Acetic acid (70 ml.) + conc. hydrochloric acid (30 ml.) at 0°	35·4
7.	Conc. hydrochloric acid + ether (100 ml., 2 : 1 by vol. mixture) at —5°	48·7
8.	Conc. hydrochloric acid + dioxan (100 ml., 1 : 1 by vol. mixture) at —5°	39·0
9.	Conc. hydrochloric acid (40 ml.) + ether (80 ml.) at 0°	62·0
10.	,, ,, (50 ml.) ,, (50 ml.) ,,	63·4
11.	,, ,, (80 ml.) ,, (40 ml.) ,,	63·3
12.	,, ,, (50 ml.) ,, (25 ml.) ,,	62·4
13.	,, ,, (80 ml.) ,, (40 ml.) at 5—10°	60·5
14.	,, ,, (80 ml.) + *iso*propyl ether (40 ml.) at 5—10°	55·5
15.	,, ,, (50 ml.) ,, ,, (50 ml.) ,,	63·2
16.	,, ,, (40 ml.) ,, ,, (80 ml.) ,,	67·0
17.	,, ,, (25 ml.) ,, ,, (75 ml.) ,,	50·0
18.	*iso*Propyl ether (100 ml.) at 5—10°	57·7
19.	Conc. hydrochloric acid (120 ml.) at 0°	57·2
20.	,, ,, (80 ml.) ,,	65·7
21.	,, ,, (34 ml.) ,,	71·3
22.	,, ,, (17 ml.) ,,	69·7
23.	No solvent, allyl alcohol saturated with HCl gas at 0°	45·0

In expts 9—18 the solvents were saturated with hydrogen chloride at 0° before the addition of allyl alcohol. It will be noticed that the yields were scarcely affected by working at a slightly higher temperature, and *iso*propyl ether could be used in place of ether. In expts. 19—22 the allyl alcohol–acid mixtures were saturated at 0° with hydrogen chloride, and a steady stream of the gas maintained during the addition of chlorine. The influence of the proportions of acid to allyl alcohol is interesting; equal volumes appeared to give the best results, but the yields may have been influenced by the method of isolation, which was by diluting the reaction mixture and extracting the product at least 4 times with chloroform or methylene chloride. Dichloropropanol is appreciably soluble in dilute hydrochloric acid, and the presence of a large excess of acid makes the extraction more laborious. For large-scale work a process of continuous extraction would be advisable.

Dichloropropanol was isolated by two distillations; a fraction, b. p. 170—190°, was collected and redistilled, the fraction, b. p. 180—185°, being collected; pure dichloropropanol has b. p. 182—183°.

The work described in this paper, which is published with the permission of the Ministry of Supply, was done while the author was a member of Sir Robert Robinson's team in the Dyson Perrins Laboratory, Oxford.

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