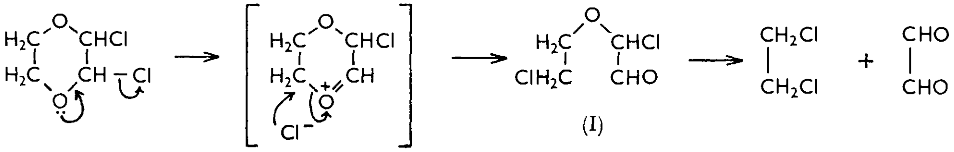
659. *Halogeno-1,4-dioxans and Their Derivatives. Part II.* Thermal Rearrangement, and Reactions of 2,3-Dichloro-1,4-dioxan.*

By L. A. Cort and N. R. Francis.

Thermal rearrangement of 2,3-dichloro-1,4-dioxan to give both 1,2-dichloroethane and glyoxal has been detected, but the extent of this overall rearrangement is very small.

Further cases are reported where the dichlorodioxan fails to yield substitution derivatives. Reaction with acetanilide, with *o*-hydroxyacetanilide, and with acetamide yields in each case some 2-chloroethyl acetate.

In several of its reactions (see, *e.g.*, refs. 1 and 2) 2,3-dichloro-1,4-dioxan appears to act as a source of glyoxal, although anhydrous reaction conditions are specified. Rearrangements of more highly substituted chlorodioxans are known,[3,4] but nothing is known of the tendency of the simple dichlorodioxan to rearrange in the same way. A 1,3-shift of chlorine across the ether link would give chloro-(2-chloroethoxy)acetaldehyde (I); a further rearrangement would give 1,2-dichloroethane and glyoxal.



Both *cis*- and *trans*-2,3-dichloro-1,4-dioxan have been described,[5] a difference between them being that the former absorbs in the infrared region at 875 cm.$^{-1}$ and not at 948 cm.$^{-1}$, whereas the latter absorbs at the higher frequency and not at the lower. On this basis the dichlorodioxan used in the present work was a mixture containing a trace (1%) of the *cis*-isomer. When this material was heated at 160—170° for 4 hr. both chlorine and hydrogen chloride were evolved, and in the infrared region the product showed (new) very weak absorption at 1730 cm.$^{-1}$; this is evidently due to the C=O of glyoxal,[6] but it is apparent that 1,2-dichloroethane could not be detected in the mixture in this way and that the presence of glyoxal alone is insufficient to establish the rearrangement.

Accordingly, the dichlorodioxan was heated at 130—140° for 5 hr. and the material which then adhered to the walls of the reflux condenser was examined by gas–liquid chromatography. Using a column at 117° with Tween 85 as stationary phase gave evidence of the presence of six compounds other than the starting material. Two of these, present to the extent of not more than one hundred parts per million of the sample injected, had the same retention times as authentic glyoxal and 1,2-dichloroethane, respectively. Confirmation was found in another experiment, with a column at 56° with tritolyl phosphate as stationary phase, when the same two components were detected, again with the same retention times as authentic glyoxal and 1,2-dichloroethane, respectively. Volatile material not returned by the condenser was passed through a trap at —40°, and examination of the resulting (small) condensate showed traces only of glyoxal and the dichloroethane; these substances were present in even smaller proportion in the main reaction mixture.

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* " Interaction of *trans*-2,3-dichloro-1,4-dioxan and sulphuric acid " (Cort, *J.*, 1960, 3167) is regarded as Part I.

[1] (*a*) Böeseken, Tellegen, and Henriquez, *J. Amer. Chem. Soc.*, 1933, **55**, 1284; (*b*) *Rev. Trav. chim.*, 1931, **50**, 909; (*c*) Faass and Hilgert, *Chem. Ber.*, 1954, **87**, 1343.

[2] Proštenik and Balenović, *J. Org. Chem.*, 1952, **17**, 379.

[3] Summerbell and Berger, *J. Amer. Chem. Soc.*, 1957, **79**, 6504; 1959, **81**, 633.

[4] Cort and Pearson, *J.*, 1960, 1682.

[5] Summerbell and Lunk, *J. Amer. Chem. Soc.*, 1957, **79**, 4802.

[6] Thompson, *Trans. Faraday Soc.*, 1940, **36**, 988.

Thus it is clear that the overall rearrangement does occur, but, equally, that products of reaction based on glyoxal cannot arise significantly from the actual glyoxal produced in this way. It is possible that the first rearrangement only, to give compound (I), occurs readily and that this monoaldehyde is the reacting species. Unfortunately it has not yet proved possible to synthesise this aldehyde; a necessary intermediate, 2-2′-chloroethoxyethanol, could not be purified.

It is known [7] that at 186° a thermal elimination of hydrogen chloride from the dichlorodioxan leads to 2-chloro-5,6-dihydro-1,4-dioxin (76%), and it would be expected that dihydrodioxin would arise by elimination of chlorine. Of the four remaining peaks on the vapour-phase chromatogram obtained as above, that from the major product had the same retention time as that of authentic 2-chloro-5,6-dihydro-1,4-dioxin. None of the other (unidentified) products (total $<5\%$ of the chlorodihydrodioxin) had a retention time the same as that of ethylene chlorohydrin. If ethylene chlorohydrin was a product of thermal treatment, under the present reaction conditions it is unlikely that it would be detected as such, since it reacts [8] (as an alcohol) with the dichlorodioxan.

There seems to be no recorded case of substitution of the dichlorodioxan leading to a product by the establishment of a C–N linkage (the reference made [9] by Elderfield cannot be traced), and in an endeavour to bring this about the dichlorodioxan was treated with both benzamide and acetanilide, and with the sodio-derivatives of these compounds.

With benzamide itself, the major reaction was one of dehydration, for the product isolated was benzonitrile (as well as a little benzoic acid). This is analogous to reaction with *p*-chlorobenzoic acid, which led [10] to the anhydride of the acid.

With the sodio-derivatives of benzamide and acetanilide, under a variety of experimental conditions, the product was a black tar. This is probably due to an initial elimination giving a dihydrodioxin, which then polymerises; such behaviour has similarly been noted previously.[1a]

Reaction of the dichlorodioxan with acetanilide gave, as well as a black tar, a liquid product identified as 2-chloroethyl acetate; a similar result was obtained with *o*-hydroxyacetanilide. (It is known [1a] that catechol reacts with the dichlorodioxan to give a product which analyses satisfactorily for 2,3-benzo-1,4,5,8-tetraoxadecalin, though no proof of structure has been given.) This unexpected result prompted us to investigate the reaction with acetamide. This was also found to yield 2-chloroethyl acetate; analysis of the liquid product by gas–liquid chromatography also showed the presence of traces ($<5\%$) of acetic acid and acetonitrile.

It is known [11] that dioxan itself gives 2-chloroethyl acetate with acetyl chloride, but that in this case an anhydrous metal chloride must also be present. It has also been found that acetamide and ethylene chlorohydrin react when heated, to give the ester as one product, and that 2-chloro-5,6-dihydro-1,4-dioxin and acetamide react exothermically at 120° but that in this case the ester is not a significant product.

In other experiments, under the anhydrous conditions indicated, the dichlorodioxan gave tars with *NN*′-diphenylurea, urea, *o*-phenylenediamine, *o*-hydroxyaniline, and 1,3-dihydroxyacetone. In the last four cases some 1,4,5,8-tetraoxadecalin was the only recognisable product isolated (in very small yield). There was no reaction with diethyl malonate, and with the sodio-derivative of the ester the only reaction observed was regeneration of the ester.

EXPERIMENTAL

M. p.s are corrected. *trans*-2,3-Dichloro-1,4-dioxan was prepared by chlorination of 1,4-dioxan at 90°, followed by fractionation; it had b. p. 87—88°/18 mm., n_D^{25} 1·4961, m. p. 30—31°.

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[7] (*a*) Astle and Gergel, U.S.P. 2,756,240/1956; (*b*) Astle and Welks, *J. Org. Chem.*, 1961, **26**, 4325.

[8] Böeseken, Tellegen, and Plusjé, *Rec. Trav. chim.*, 1938, **57**, 73.

[9] Elderfield, " Heterocyclic Compounds," Chapman and Hall, Ltd., London, 1957, Vol. VI, p. 17.

[10] Summerbell and Lunk, *J. Amer. Chem. Soc.*, 1958, **80**, 604.

[11] Goldfarb and Smorgonski, *J. Gen. Chem.* (*U.S.S.R.*), 1938, **8**, 1516; *Ber.*, 1936, **69**, 1036.

The infrared absorption spectrum of the supercooled liquid showed no significant absorption at 1730 cm.$^{-1}$; there was definite weak absorption at 948 cm.$^{-1}$ (cf. ref. 5).

The dichloro-ether (5 ml.) was heated for 4 hr. at 160—170°; the gases evolved liberated iodine from aqueous potassium iodide, and bleached litmus paper. The pale brown product showed absorption at a number of new frequencies, one of these being 1730 cm.$^{-1}$ (vw).

[With Mr. W. H. McCambley.] The dichloro-ether (5 ml.) was heated at 130—140° for 5 hr., under a reflux water-condenser, the gases evolved being passed through a trap at $-40°$. The liquid adhering to the walls of the condenser was examined by gas–liquid chromatography on a 4 mm. × 120 cm. column of Tween 85 on " Celite " at 117°, with nitrogen (inlet pressure 80 cm. Hg.) as the carrier gas. With a hydrogen-flame detector, two constituents (other than the starting material) were detected. With a flame-ionisation detector, another four constituents were detected, the two most volatile having the same retention times as authentic glyoxal and 1,2-dichloroethane, respectively. These were present to the extent of not more than one hundred parts per million of the sample injected.

In another experiment, a similar column of tritolyl phosphate at 56° was used; again the two most volatile constituents had the same retention times as authentic glyoxal and 1,2-dichloroethane, respectively. The reaction mixture, and the condensate ($<0{\cdot}1$ ml.) in the trap, both contained glyoxal and the dichloroethane, but in even smaller quantities. On both columns, the untreated starting material showed two peaks only, that arising from the less-volatile constituent (*ca.* 1%) presumably being due to the *cis*-isomer.

We are very grateful to the Technical Services Division of the Distillers Company Limited (at Epsom) for providing facilities for these analyses.

2-2′-*Chloroethoxyethanol.*—Treatment of ethylene chlorohydrin with ethylene oxide (180 g.) in the presence of sulphuric acid as described by Fourneau and Ribas [12] gave, after repeated fractionation, the chloroethoxy-alcohol (52 ml.), b. p. 77—78°/20 mm. Vapour-phase chromatography showed the presence of five minor impurities (total $<2\%$); four of these were more volatile than the alcohol and the purest specimen that could be obtained still contained two of them. An analytically pure α-naphthylurethane could not be prepared.

Reaction with Benzamide.—(*a*) After 1 hr. at 160—170° a mixture of the dichlorodioxan (23·6 g.) and benzamide (36·3 g.) ceased to evolve hydrogen chloride. Distillation furnished fractions (i) b. p. 78—88°/15 mm. (5·1 g.) and (ii) b. p. 124—132°/14 mm. (14·2 g.). The residue did not distil at 180°/14 mm., and extraction with hot chloroform gave ammonium chloride only (1·9 g.) [2,3-dibenzamido-1,4-dioxan [13] has m. p. 247—248° (from chloroform)]. Fraction (ii) crystallised (m. p. and mixed m. p. with benzoic acid 121·5°). Nitration [14] of fraction (i) (0·50 g.) gave *m*-nitrobenzonitrile (0·41 g.), m. p. and mixed m. p. 117—118° (from water).

(*b*) The sodium derivative (prepared as the derivative [15] of acetanilide) of benzamide (12·1 g.) in xylene (100 ml.) was heated to 100° and the dichlorodioxan (7·85 g.) added. The mixture was heated at 180° for 1 hr. and filtered. The filtrate, on cooling, deposited benzamide (2·8 g.) m. p. and mixed m. p. 127—127·5° after recrystallisation. The residue gave a further small quantity (0·4 g.) of benzamide on treatment with methanol, together with intractable material.

Reaction with Acetanilide.—(*a*) The sodium derivative [15] of acetanilide (10·0 g.) in xylene (60 ml.) was heated with the dichlorodioxan (5·82 g.) at 160° for 1 hr. Evaporation of the filtrate from the cold mixture gave acetanilide (1·3 g.), m. p. and mixed m. p. 113—114° after crystallisation. Treatment of the residue with ethanol gave a further small quantity (0·34 g.) of acetanilide, together with intractable material.

(*b*) A mixture of acetanilide (135 g.) and the dichlorodioxan (157 g.) was heated at 150—160° for 9 hr. (until evolution of hydrogen chloride ceased). Distillation gave fractions (i) b. p. 34—62°/29 mm. (25·4 g.) and (ii) b. p. 62—108°/29 mm. (6·9 g.). The residue (196 g.) on extraction with hot water gave neither acetanilide nor an amine (as salt) that could be diazotised and coupled with 2-naphthol.

Fraction (i) was washed with saturated sodium hydrogen carbonate solution and gave on redistillation 2-chloroethyl acetate (10·4 g.), b. p. 144—145°/760 mm., n_D^{25} 1·4232 (Found: C, 39·0; H, 5·9; Cl, 29·1. Calc. for $C_4H_7ClO_2$: C, 39·2; H, 5·9; Cl, 28·9%). This gave, on

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[12] Fourneau and Ribas, *Bull. Soc. chim. France*, 1927, **41**, 1046.
[13] Ruggli, Ratti, and Henzi, *Helv. Chim. Acta*, 1929, **12**, 332.
[14] Baker, Cooper, and Ingold, *J.*, 1928, 430.
[15] Kepp, *Ber.*, 1877, **10**, 328.

a 4 mm. × 180 cm. column of diglycerol on "Celite" at 76°, with nitrogen–hydrogen (25 : 75; inlet pressure 26 cm. Hg.) as the carrier gas, a chromatogram identical with that from authentic 2-chloroethyl acetate (b. p. 144—145°/760 mm., n_D^{25} 1·4212); there was evidence of a trace of high-boiling impurity.

Reaction with o-*Hydroxyacetanilide.*—When a mixture of the dichlorodioxan (5·1 g.) and the phenol (5·0 g.) was heated a vigorous evolution of hydrogen chloride occurred at 160°. From the mixture there was obtained a distillate (1·46 g.), b. p. 63°/29 mm., a sublimate (0·75 g.) at 170°/13 mm., and an intractable black residue (which did not distil at 190°/2·7 mm.).

The sublimate was *o*-hydroxyacetanilide (after recrystallisation, m. p. and mixed m. p. 209—211°). Under the same conditions as above the distillate gave a chromatogram (showing <2% of impurity of higher mol. wt.) identical with that from 2-chloroethyl acetate.

Reaction with Acetamide.—A mixture of the dichlorodioxan (163 g.) and acetamide (129 g.) was heated in an oil-bath. At 140° a clear solution was obtained and a vigorous reaction occurred with evolution of hydrogen chloride; this was allowed to proceed without external heating. Distillation gave fractions (i) b. p. 44—96°/25 mm. (26·0 g.) and (ii) b. p. 116—136°/18 mm. (67·3 g.). The residue (150 g.) did not distil at 140°/18 mm. On storage, fraction (ii) deposited ammonium chloride (21·5 g.).

The major component of fraction (i), under the same conditions as above, gave a gas–liquid chromatogram identical with that from 2-chloroethyl acetate. Minor constituents (total <5%) had the same retention times as acetonitrile and acetic acid, respectively.

Reaction with 1,3-*Dihydroxyacetone.*—Under anhydrous conditions, the dihydroxy-ketone (30·0 g.) and the dichlorodioxan (52·3 g.) were heated in dioxan (100 ml.) at 120—130°, a clear solution being obtained. After 10 hr. evolution of hydrogen chloride had ceased. After distillation of the solvent, the brown residue furnished fractions (i) b. p. 104—114°/18 mm. (pale yellow, 16·4 g.) and (ii) b. p. 88—122°/1·0 mm. (pale yellow, 9·0 g.). The residue (45 g.) did not distil. Fraction (i) deposited crystals (0·88 g.) after 4 weeks. Crystallisation from light petroleum (b. p. 60—80°) gave *trans*-1,4,5,8-tetraoxadecalin, m. p. and mixed m. p. 136—137°. The other distilled products remained as liquids with very wide boiling ranges.

Lack of Reaction with NN′-*Diphenylurea, Urea,* o-*Phenylenediamine, and* o-*Hydroxyaniline.*—With equimolecular quantities (0·1 mole), results were similar to those with 1,3-dihydroxy-acetone. Reaction with the amines was in xylene; the tetraoxadecalin was isolated in both cases (0·24 g., and 1·1 g., respectively). Reaction with the ureas was without solvent; the diphenylurea gave only intractable material, but urea itself again gave the tetraoxadecalin (0·7 g.).

Reaction with Diethyl Monosodiomalonate [with Dr. R. G. PEARSON].—There was apparently no reaction between the dichlorodioxan and a cold solution of diethyl monosodiomalonate in ethanol or diethyl carbonate,[16] on the 0·25 mole scale. In both cases heating on the steam-bath furnished a precipitate of sodium chloride, but the volatile products yielded only solvent and diethyl malonate.

There was no reaction between the dichlorodioxan and diethyl malonate, alone or in pyridine, on the steam-bath.

Reaction of 2-*Chloro*-1,4-*dioxene with Acetamide.*—The chlorodioxene, b. p. 145—147°/760 mm., n_D^{25} 1·466, was prepared according to Astle and Gergel.[7a] Heating the olefin (12·0 g.) with acetamide (5·9 g.) led to a vigorous exothermic reaction at 120°; there appeared to be no product with a b. p. <99°/16 mm.

Reaction of Ethylene Chlorohydrin with Acetamide.—The alcohol (67 ml.) and the amide (59 g.) were heated at 160° during 1½ hr., then cooled. After removal of ammonium chloride (8·4 g.) distillation of the residue furnished a fraction (16·8 g.), b. p. 140—152°/743 mm., n_D^{25} 1·4250, vapour-phase chromatography of which showed it to consist substantially of 2-chloroethyl acetate.

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[16] Wallingford, Thorpe, and Homeyer, *J. Amer. Chem. Soc.*, 1942, **64**, 580.