338. *Chlorination, and Bromination, of Cyclic Acetals.*

By L. A. CORT and RONALD G. PEARSON.

Chlorination of *trans*-1,4,5,8-tetraoxadecalin yielded 2,3-dioxo-1,4-dioxan, in addition to di-2-chloroethyl oxalate. Bromination yielded only di-2-bromoethyl oxalate. Chlorination of 1,3-dioxolan yielded 2-chloroethyl formate [not the compound hitherto described (2-chloro-1,3-dioxolan)], and bromination yielded 2-bromoethyl formate. This is taken as evidence of rearrangement of α-chloro-acetals comparable with that for α-bromo-acetals, and further evidence is adduced which shows that the rearrangement is thermal.

Interaction of the halogeno-esters with *p*-anisidine and with thiourea is described.

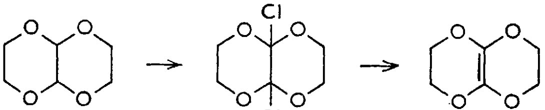
trans-1,4,5,8-TETRAOXADECALIN (I), first obtained by Donciu,[1] from glyoxal and ethylene glycol, was obtained from 2,3-dichloro-1,4-dioxan and ethylene glycol by Böeseken, Tellegen, and Henriquez;[2] they assigned to it this *trans*-structure, without rigorously establishing the constitution. Analysis[3] of the *X*-ray diffraction pattern of an addition compound showed this designation to be, in fact, correct. An isomer obtained in the

---

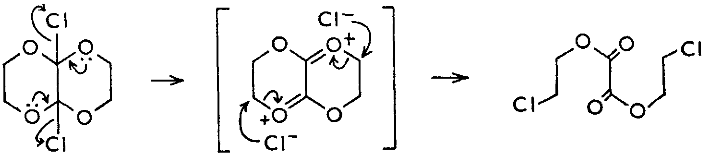
[1] Donciu, *Monatsh.*, 1895, **16**, 8.
[2] Böeseken, Tellegen, and Henriquez, *Rec. Trav. chim.*, 1931, **50**, 909.
[3] Hassel and Rømming, *Acta Chem. Scand.*, 1956, **10**, 138.

same reaction by Böeseken and his co-workers and long thought to be the *cis*-isomer has now been identified as bi-1,3-dioxolan-2-yl.[4]

We have investigated the possibility of reactions (I) ⟶ (II) ⟶ (III), for ozonolysis of the final product should lead to 2,7-dioxo-1,3,5,8-tetraoxacyclodecane, which would provide an independent chemical proof of the structure of the starting material.


(I) (II) (III)

Chlorination of compound (I) in carbon tetrachloride with ultraviolet irradiation is said [5] to give a very high yield of a dichloro-derivative, though no chemistry of this derivative is described apart from its reaction with phosphorus pentasulphide–alcohol mixtures; the starting material there used was not pure (cf. Baker and Shannon [6]). After early failures (unless iodine was present), we repeated this reaction although the pure compound is much less soluble in carbon tetrachloride than is that used by Buntin.[5] Chlorination to the point where a dichloro-derivative was expected, sometimes gave di-2-chloroethyl oxalate [7] as the only product, suggesting that the expected product (II) had rearranged



as shown. Rearrangement of (unstable intermediate) α-bromo-acetals has been postulated previously.[8] It probably proceeds *via* an oxonium salt, for the hydrolysis of α-chloro-ethers is believed to proceed in this manner,[9] and an oxonium salt has been reported [10] from hydrogen bromide and 1,4-dioxan at 101°, which breaks down to regenerate the starting materials or give 2,2′-dibromodiethyl ether. In the present instance, rearrangement of the dichloro-compound (II) might involve two oxygen atoms from the same ring, leading to 2,3-dioxo-1,4-dioxan and 1,2-dichloroethane, and in some experiments we did obtain the former. 1,2-Dichloroethane has not been identified as a product; when mixtures were examined for it only a very small yield (*e.g.* 0·35 g. from 60 g.) of a liquid of the expected b. p. was isolated, and this gave no characteristic derivatives (Marvell and Joncich [7] were similarly unable to isolate ethyl bromide).

trans-1,4,5,8-Tetraoxadecalin (I) was unaffected by bromine, by *N*-bromosuccinimide in boiling carbon tetrachloride with irradiation, and by bromine–potassium chlorate in dioxan; with *N*-bromosuccinimide at 120° (sealed tube; 15 hours) it gave only di-2-bromoethyl oxalate, in very low yield.

1,3-Dioxolan, however, reacts very readily with bromine or, in carbon tetrachloride, with *N*-bromosuccinimide, probably giving initially 2- and 4-bromo-1,3-dioxolan. The former rearranges rapidly to 2-bromoethyl formate; the latter probably eliminates hydrogen

---

[4] Faass and Hilgert, *Chem. Ber.*, 1954, **87**, 1343; Furberg and Hassel, *Acta Chem. Scand.*, 1950, **4**, 1584.

[5] Buntin, U.S.P. 2,749,271/1956.

[6] Baker and Shannon, *J.*, 1933, 1598.

[7] Cort and Pearson, *Chem. and Ind.*, 1959, 515.

[8] McElvain and Davie, *J. Amer. Chem. Soc.*, 1952, **74**, 1816; McElvain and Kundiger, *ibid.*, 1942, **64**, 254; Marvell and Joncich, *ibid.*, 1951, **73**, 973.

[9] Ingold, "Structure and Mechanism in Organic Chemistry," G. Bell and Sons, Ltd., London, 1953, p. 333.

[10] Van Cleave and Blake, *Canad. J. Chem.*, 1951, **29**, 785.

bromide and the resulting 1,3-dioxole polymerises, there being analogous reactions for chloro-1,4-dioxan[11] (the distillate fore-run always blackened on storage, with evolution of hydrogen bromide). The yield of ester was far greater when *N*-bromosuccinimide was used, though there is no doubt that the yield with bromine could be considerably improved if the hydrogen bromide produced were removed from the sphere of reaction.

We therefore re-examined the chlorination of 1,3-dioxolan, which is reported to give an inseparable mixture of 2- and 4-chloro-1,3-dioxolan;[6] the evidence for this is that repeated distillation at diminished pressure gave a product which, after hydrolysis, yielded glyoxal bis-2,4-dinitrophenylhydrazone that could arise only from the 4-chloro-isomer. The 2-chlorodioxolan would not yield a carbonyl compound, but neither would 2-chloroethyl formate, and these two isomeric compounds could not be distinguished by their hydrolysis products alone. It seemed likely that the major product obtained by Baker and Shannon[6] was the ester; and by distillation at atmospheric pressure we obtained the ester in an overall yield of 45%, the 4-chloro-1,3-dioxolan breaking down to products at the higher distillation temperature which do not co-distil with the ester.

It is possible, of course, that if the rearrangement of α-halogeno-acetals is caused by heat (as has been demonstrated for α-halogeno-ethers[12]), then halogenation at low temperatures should lead to the α-halogeno-acetal. Our results show that it is very unlikely that such derivatives of cyclic acetals will be capable of isolation.

Between 1500 and 2500 cm.$^{-1}$ 1,3-dioxolan shows no selective absorption in the infrared region,[13] and 2-chloroethyl and 2-bromoethyl formate show strong absorption at 1723 cm.$^{-1}$ (Thompson and Torkington record absorption at 1722—1724 cm.$^{-1}$ for C:O in alkyl formates[14]). When 1,3-dioxolan at 0° is treated with a slow stream of chlorine for five minutes the mixture shows medium-intensity absorption at 1723 cm.$^{-1}$. This band may also be detected when 10 ml. of 1,3-dioxolan are treated at 20° with three drops of bromine. Compound (I) also shows no selective absorption between 1500 and 2500 cm.$^{-1}$, but the di-2-halogenoethyl oxalates show strong absorption in this region, the chloro-ester at 1771 and 1747, and the bromo-ester at 1774 and 1745 cm.$^{-1}$ (Hampton and Newell[15] record 1746 cm.$^{-1}$ for C:O in dibutyl oxalate). After chlorine has been passed for one hour through a solution of compound (I) in carbon tetrachloride at 30—40°, irradiated with ultraviolet light, and the solvent evaporated isothermally, the residue shows medium-intensity absorption at about 1760 cm.$^{-1}$. If the residue is heated in boiling carbon tetrachloride for one hour the absorption intensity increases somewhat; if this residue is heated at 150—160° for 15 minutes the band becomes as strong as for the pure ester, and the absorption curve begins to separate into the two peaks. [That the initial absorption is not due to the breakdown to glyoxal is shown by the fact that two minutes are required before the residue (or the pure starting acetal) gives a precipitate with Brady's reagent whereas traces of authentic glyoxal give a precipitate immediately.]

This indicates that, when halogenation occurs readily, the α-halogeno-acetal begins to rearrange at once under mild conditions, and that under the reaction conditions used in the present experiments, and in those used by Baker and Shannon,[6] the rearrangement is complete.

During the chlorination of compound (I) attempts were made to isolate monochloro-derivatives (or rearrangement products thereof), but without success: mixtures were obtained in low yields, much starting material was recovered, and there were large losses due to the formation of very volatile products.

In an endeavour to characterise these halogeno-esters without affecting the ester linkage, the halogeno-esters have been treated with *p*-anisidine and with thiourea. *p*-Anisidine with 2-chloroethyl formate and di-2-chloroethyl oxalate gave *p*-anisidides, but with

---

[11] Summerbell and Bauer, *J. Amer. Chem. Soc.*, 1935, **57**, 2364.
[12] Summerbell and Berger, *J. Amer. Chem. Soc.*, 1959, **81**, 635; 1957, **79**, 6504.
[13] Barker, Bourne, Pinkard, and Whiffen, *J.*, 1959, 802.
[14] Thompson and Torkington, *J.*, 1945, 640.
[15] Hampton and Newell, *Analyt. Chem.*, 1949, **21**, 914.

2-bromoethyl formate gave only an unidentified product, $C_{17}H_{21}O_2N_2Br$. Di-2-bromoethyl oxalate reacted with thiourea in 95% ethanol but gave neither a pure product nor a picrate; 2-bromoethyl formate gave *S*-2-hydroxyethylthiuronium picrate, indicating hydrolysis.

In the presence of sodium iodide, 2-chloroethyl formate with thiourea in acetone gave an unidentified product (as picrate), which was neither *S*-2-hydroxyethylthiourea nor the 2-formyloxyethyl compound; if water was added with the picric acid, *S*-2-hydroxyethylthiuronium picrate was obtained.

EXPERIMENTAL

M. p.s are corrected. Light petroleum refers to the fraction of b. p. 60—80°. Ethanol refers to the 95% alcohol.

trans-1,4,5,8-Dioxadecalin (I) was prepared as described previously.[16] There was quantitative recovery after chlorine had been passed for 18½ hr. into a solution of it in carbon tetrachloride at 65—70° shielded from ultraviolet light.

Chlorination of Compound (I).—(*a*) Chlorine was led into the molten compound (55 g.) containing a crystal of iodine, at 140°, until 1 mol. was absorbed. Distillation then furnished a fraction, b. p. 134—152°/0·6 mm. (4·2 g.), from which crystals, m. p. 116—136° (0·2 g.), were deposited. Recrystallisation from benzene furnished 2,3-dioxo-1,4-dioxan as needles, m. p. and mixed m. p. 144—145·5° (Found: C, 41·0; H, 3·8. Calc. for $C_4H_4O_4$: C, 41·4; H, 3·5%). The infrared absorption (in Nujol) was identical with that of the ester (m. p. 144—144·5°) prepared as described by Carothers *et al.*[17] with a broad band at 1770 cm.$^{-1}$.

(*b*) During chlorination of 60 g., as above, material volatile at 140° was passed through a water-condenser and then through a trap at 0°. The liquid condensate (1·4 g.) furnished a fraction, b. p. 80—98°/764 mm. (0·35 g.), from which no solid derivative could be obtained when it was treated with potassium hydroxide and α-naphthol in ethanol.

(*c*) Chlorination of 67 g., as above, was continued until 0·5 mol. had been absorbed. Keeping the mixture at 80—95°/17 mm. for 5 hr. furnished a sublimate (22·6 g.), m. p. 127—135°; one recrystallisation from carbon tetrachloride raised the m. p. to 133—138°, undepressed on admixture with the starting material. The liquid residue from the sublimation was distilled and the following fractions were collected, the chlorine content (%) being as shown: (i) b. p. 98—108°/0·2 mm. (6·4 g.; Cl, 20·6); (ii) b. p. 108—125°/0·2 mm. (3·3 g.; Cl, 26·0); (iii) b. p. 125—150°/0·2 mm. (1·6 g.; Cl, 25·4); the residue (14·5 g.; Cl, 14·8) did not distil at 245°/0·2 mm. (Calc. for $C_6H_9O_4Cl$: Cl, 19·7%.)

Di-2-bromoethyl Oxalate.—By the method of Contardi and Ercoli[17] the ester was prepared from oxalic acid (64% yield); it crystallised from benzene–light petroleum in plates, m. p. 55·0—55·5° (Found: C, 23·4; H, 2·8; Br, 53·0. Calc. for $C_6H_8O_4Br_2$: C, 23·7; H, 2·7; Br, 52·7%).

Bromination.—Compound (I) (19·5 g.) and *N*-bromosuccinimide (25·2 g.) were heated in a sealed tube for 22 hr. at 120°. The product was extracted (Soxhlet) with carbon tetrachloride. After distillation of the solvent the residue (4·2 g.) was held at 85°/14 mm. for 4 hr., unchanged compound (I) (0·22 g.) subliming. Recrystallisation of the unsublimed material from benzene–light petroleum gave di-2-bromoethyl oxalate (0·5 g.), m. p. and mixed m. p. 55·0—55·5°. The two samples had identical infrared spectra in CS_2 in the range 4000—650 cm.$^{-1}$, with strong absorption at 1774 and 1745 cm.$^{-1}$.

Chlorination of 1,3-*Dioxolan.*—1,3-Dioxolan (266 g.) containing iodine (0·5 g.) was chlorinated at the b. p. (exothermic reaction) until there was no further increase in weight (3 days). The product was distilled at atmospheric pressure; the main fraction, after three more distillations, yielded 2-chloroethyl formate (185 g.), b. p. 131—132°/763 mm., n_D^{25} 1·4251 (Found: C, 33·2; H, 4·6; Cl, 32·6. Calc. for $C_3H_5O_2Cl$: C, 33·2; H, 4·6; Cl, 32·7%).

2-Chloroethyl formate, prepared according to the method of Contardi and Ercoli[17] from formic acid and ethylene chlorohydrin (60% yield), had b. p. 131—132°/764 mm., n_D^{25} 1·4251 (Found: Cl, 33·1%), and an identical infrared spectrum with strong absorption at 1723 cm.$^{-1}$.

Bromination of 1,3-*Dioxolan.*—(a) *With bromine.* Bromine (294 g.) was added dropwise

---

[16] Contardi and Ercoli, *Internat. Congr. Chem.* (*Madrid*), 1934, **5**, 163.

[17] Carothers, Arvin, and Dorough, *J. Amer. Chem. Soc.*, 1930, **52**, 3292.

to 1,3-dioxolan (136 g.) at 0°. The total product (425·5 g.) was distilled repeatedly under diminished pressure, to give 2-*bromoethyl formate* (37 g.), b. p. 147—149°/765 mm., 44·0—44·5°/13 mm., n_D^{25} 1·4611 (Found: C, 23·4; H, 3·0; Br, 52·4. $C_3H_5O_2Br$ requires C, 23·6; H, 3·3; Br, 52·2%).

In another experiment, where all distillations after the first were conducted at atmospheric pressure, the yield of ester was almost exactly the same.

(b) *With* N-*bromosuccinimide*. Bromination of 1,3-dioxolan (23·5 g.) in carbon tetrachloride (25 ml.) with *N*-bromosuccinimide (50 g.) as given by Marvell and Joncich [7] for acetals, followed by distillation at reduced pressure, gave 2-bromoethyl formate (13·4 g.), b. p. 44·0—44·5°/13 mm., n_D^{25} 1·4611 (Found: C, 24·0; H, 3·2%).

A higher-boiling fraction (124—125°/13 mm.; Br, 52·8%), after hydrolysis with water at 80° and treatment with Brady's reagent, gave a mixture of derivatives. These, separated with ethanol, were identified as glyoxal bis-2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 333—336° (decomp.), and formaldehyde 2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 164—166°; they were present in approximately equal quantities.

Reaction of the Halogeno-esters with p-*Anisidine*.—(a) *Di-2-chloroethyl oxalate*. A mixture of the ester (2·2 g.; from oxalic acid) and *p*-anisidine (2·5 g.), when heated at 100°, resolidified after 15 min. Crystallisation from tetrachloroethane and then dioxan–water furnished the di-*p*-anisidide of oxalic acid, m. p. 263·5—264·5°, as a colourless microcrystalline solid (lit.,[18] m. p. 260—261°) (Found: C, 64·4; H, 5·4; N, 9·2. Calc. for $C_{16}H_{16}O_4N_2$: C, 64·0; H, 5·3; N, 9·3%).

The ester prepared from compound (I) gave the same derivative; the mixed m. p. showed no depression and the two samples had identical infrared spectra in the range 4000—650 cm.$^{-1}$.

(b) 2-*Chloroethyl formate*. The ester (10 g.; from 1,3-dioxolan) was boiled in benzene (30 ml.) with *p*-anisidine (11·3 g.) for 1 hr. After removal of the solvent, the solid product, the *p*-anisidide (5·2 g.) of formic acid, separated as prisms from ethanol or (better) as needles from benzene–light petroleum; it had m. p. 78° (lit.,[19] m. p. 81°) (Found: C, 63·6; H, 5·9; N, 9·0. Calc. for $C_8H_9O_2N$: C, 63·6; H, 6·0; N, 9·3%). The ester from authentic formic acid when treated similarly also furnished this derivative, m. p. and mixed m. p. 78°.

(c) 2-*Bromoethyl formate*. The ester (30 g.; from 1,3-dioxolan) and *p*-anisidine (24 ·1 g.) were heated together on a steam-bath for 1½ hr. The cold mixture was triturated with methanol (10 ml.), and after 3 days the crystals were collected (11·2 g.). These were insoluble in ether, dioxan, acetone, benzene, and cold water, and soluble in methanol, and hot water. Crystallisation from methanol–dioxan (poor recovery) gave pale yellow needles of a *substance*, $C_{17}H_{21}O_2N_2Br$, m. p. 287—289° (decomp.) (Found: C, 55·9, 56·2; H, 5·55, 5·45; N, 7·5, 7·5; Br, 21·8, 21·5. $C_{17}H_{21}O_2N_2Br$ requires C, 55·9; H, 5·8; N, 7·7; Br, 21·9%).

When this material (3·5 g.) was treated with dilute aqueous sodium hydroxide and acetic anhydride there separated from the mixture colourless crystals (1·7 g.), m. p. 116—124°, giving acet-*p*-anisidide as plates (from water), m. p. and mixed m. p. 127°.

S-2-*Hydroxyethylthiuronium Picrate*.—Prepared in the usual manner (in ethanol) from ethylene bromohydrin, the picrate was obtained in yellow prisms (from water), m. p. 234—242° (decomp.) with previous melting at 162—164° and resolidification at 168° (lit.,[20] m. p. 155—156°) (Found: C, 31·5; H, 3·0; N, 19·8; S, 9·3. Calc. for $C_9H_{11}O_8N_5S$: C, 31·0; H, 3·2; N, 20·1; S, 9·2%). The picrate was recovered quantitatively after being boiled for 8 hr. in acetone.

Interaction of the Halogeno-esters with Thiourea.—(a) 2-*Chloroethyl formate*. The ester (3·6 g.; from 1,3-dioxolan), sodium iodide (5·0 g.), and thiourea (3·5 g.) were boiled together in acetone (15 ml.) for 8 hr. Picric acid (10 g.) was added to the cold mixture, then water (15 ml.), and the mixture boiled to give a clear solution; negligible solid separated on cooling. The solution was evaporated to half bulk, and an equal volume of water added. On cooling, there separated yellow prisms of *S*-2-hydroxyethylthiuronium picrate (3·2 g.), which after crystallisation from water had m. p. and mixed m. p. 236—246° (decomp.) with previous melting and resolidification at 162—163° (Found: C, 31·3; H, 2·9; N, 20·0; S, 9·0%).

Repetition of the experiment (with 14·5 g. of ester) in acetone alone as solvent at all stages gave yellow needles (21·1 g.) of a picrate, m. p. 240—244° (decomp.) (from acetone–benzene) (Found: C, 36·0, 36·0; H, 3·0, 2·8; N, 19·4, 19·5; S, 8·8, 8·9%). The m. p. was unchanged

---

[18] Bischoff and Fröhlich, *Ber.*, 1906, **39**, 3975.

[19] Fröhlich and Wedekind, *Ber.*, 1907, **40**, 1009.

[20] Jureček and Večeřa, *Coll. Czech. Chem. Comm.*, 1951, **16**, 95.

after the compound had been boiled for 12 hr. in water. Mixed with the picrate obtained previously, it had m. p. 159°, resolidifying at 167°, and remelting at 220—232° (decomp.).

(b) 2-*Bromoethyl formate*. This ester (3·6 g.) on treatment with thiourea in ethanol led to yellow prisms (3·5 g.) of *S*-2-hydroxyethylthiuronium picrate, m. p. 242—252° (decomp.) with previous melting and resolidification at 163—166° (Found: C, 31·4; H, 3·1; N, 19·8; S, 9·0%).

The authors thank The Chemical Society and Imperial Chemical Industries Limited for grants, and Brotherton Ltd. for a gift of chemicals, also Dr. V. S. Griffiths of the Spectroscopy Department for making available facilities for the measurement of spectra.

BATTERSEA COLLEGE OF TECHNOLOGY,
LONDON, S.W.11.

[*Received, October 5th,* 1959.]