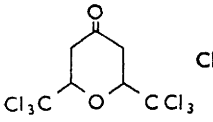
Trihalogenomethyl Compounds of Potential Therapeutic Interest. Part IX.[1] Miscellaneous Reactions

By **R. E. Bowman*** and **W. R. N. Williamson**, Research Department, Parke, Davis & Company, Hounslow, Middx

Novel reaction products of chloral and related compounds are described.

CAUJOLLE and his co-workers described the preparation of tetrahydro-2,5-bis(trichloromethyl)-4*H*-pyran-4-one (I) by reaction of acetone dicarboxylic acid (1 mol.) and chloral hydrate (2 mol.) in buffered solution.[2] In our hands, however, the reaction gave 1,1,1,7,7,7-hexachloro-2,6-dihydroxyheptan-4-one (II; $R^1 = H$, $R^2 = O$). The



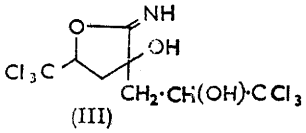
(I)

$Cl_3C{\cdot}CH(OR^1){\cdot}CH_2{\cdot}CR^2{\cdot}CH_2{\cdot}CH(OR^1){\cdot}CCl_3$

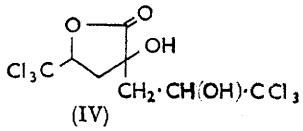
(II)

suggested structure was evident from the i.r. spectrum which showed $\nu_{max.}$ (Nujol) 3448s (OH) and 1710s cm.$^{-1}$ (CO) and the n.m.r. spectrum ($CDCl_3$) which showed signals at τ 6·9 (t, 4H), 6·2 (s, 2H), and 5·25 (q, 2H). The spectrum of the diacetate (II; $R^1 = Ac$, $R^2 = O$) had $\nu_{max.}$ (Nujol) at 1750s (Ac) and 1726m cm.$^{-1}$ (CO) and the triol (II; $R^1 = H$, $R^2 = H,OH$) prepared by lithium borohydride reduction of the hydroxy-ketone, had $\nu_{max.}$ (Nujol) 3400s cm.$^{-1}$ (OH).

An attempted Bucherer–Bergs[3] hydantoin synthesis on the dihydroxy-ketone failed to give the desired hydantoin, but instead a compound formulated as the imino-lactone (III) was precipitated. In the absence of potassium cyanide starting material was recovered from the reaction. Compound (III) showed only end-absorption [$\lambda_{max.}$ (EtOH) 203 (ε 861)] in the u.v. region while the i.r. spectrum showed $\nu_{max.}$ (Nujol) 3410m, 3340s, 3150s,br, and 1585w cm.$^{-1}$. [The compound was not sufficiently soluble in $CDCl_3$ to provide an n.m.r. spectrum and in $(CD_3)_2SO$ the results were indefinite.] Compound (III) yielded ammonium picrate on treatment with picric acid in ether, indicating the



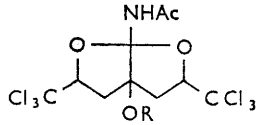
(III)



(IV)

presence of a readily hydrolysable imino-group. The formation of compound (III) is visualised as occurring by cyclisation of the intermediate cyanohydrin and is analogous to the formation of 22-carboximino-17α,20,21-trihydroxy-3,11-diketo-$\Delta^{4,20}$-pregnadiene-17-lactone by the action of potassium cyanide and sodium hydrogen sulphite on cortisone-21-carbaldehyde hydrate.[4] It is likely that 2-hydroxy-2,4-dimethyl-γ-valerolactone[5] is formed in a way when diacetone alcohol is heated with ammonium carbonate and potassium cyanide in ethanol and then treated with concentrated hydrochloric acid. Similarly, hydrolysis of compound (III) with hydrochloric acid gave the lactone (IV), which was isolated as two of its possible diastereoisomers.

Acetylation of compound (III) gave a diacetate (V; R = Ac) having $\lambda_{max.}$ (EtOH) 202 mμ (ε 1540) and $\nu_{max.}$



(V)

(Nujol) 3240 (NH), 1729m (ester CO), 1685s (amide CO), 1509s (amide (II), and 1230s cm.$^{-1}$ (ester C–O). The

[1] Part VIII, R. E. Bowman, K. D. Brunt, C. E. Harrison, and W. R. N. Williamson, preceding paper.

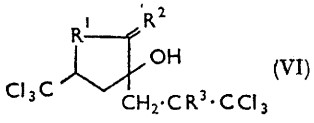
[2] F. Caujolle, P. Couturier, and M. Doumerc, *Bull. Soc. chim. France*, 1950, 22.

[3] *Cf. Chem. Rev.*, 1950, **46**, 432.

[4] W. J. Leanza, J. P. Coubere, E. F. Rogers, and K. Pfister, *J. Amer. Chem. Soc.*, 1954, **76**, 1691.

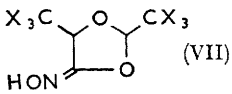
[5] H. R. Henze, T. R. Thompson, and R. J. Speer, *J. Org. Chem.*, 1943, **8**, 17.

n.m.r. spectrum ($CDCl_3$) showed signals at τ 3·25 (s, 1H, NH), 5·1 (quin., 2H, :CH·), 7·1 (m, 4H, CH_2), and 7·9 (d, 6H, CH_3CO). When a deuteriochloroform solution of the compound was shaken with D_2O, the peak at τ 3·25 disappeared very slowly (2—3 days). A possible structure, alternative to (V; R = Ac), which might have been formed by addition of the tertiary hydroxy-group across the imino-double-bond [of (III)] to form an epoxy-acetate can be rejected since the ester carbonyl peak (1729 cm.$^{-1}$ in the i.r. region would be expected to be considerably higher in the acetate of an α-trichloromethyl alcohol.[6] Dreiding models of (V; R = Ac) and the epoxide showed that it is considerably less strained than the epoxide. Acid hydrolysis of the acetate (V; R = Ac) gave the lactone (IV), isolated as its higher-melting isomer, while treatment of the acetate with cold alcoholic ammonia removed the ester acetyl to yield the tertiary alcohol (V; R = H) [$\nu_{max.}$ (Nujol) 3350s, 1660s, and 1520s cm.$^{-1}$]. Similar treatment of the imino-lactone (III) formed the cyclic amidine (VI; $R^1 = R^2 =$ NH, R^3 = H,OH) and chromium trioxide oxidation of the lactone (IV) gave the keto-lactone (VI; $R^1 = R^2 = R^3 = O$).

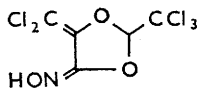


(VI)

Attempts to prepare 1,1,1,5,5,5-hexachloro-3-nitropentane-2,5-diol, required in another synthesis, from nitromethane and chloral hydrate (2 mol.) in aqueous solution with addition of potassium carbonate gave only 1,1,1-trichloro-3-nitropropan-2-ol.[7] On the other hand, a similar reaction between chloral hydrate (2 mol.) and sodium nitroacetate (prepared *in situ* from sodium nitrite and sodium chloroacetate [8]) gave a compound which we formulate as the 2,5-bistrichloromethyl-1,3-dioxolan-4-one oxime (VII; X = Cl) (' chloralide oxime '); the analogous bromo-compound (VII; X = Br) was

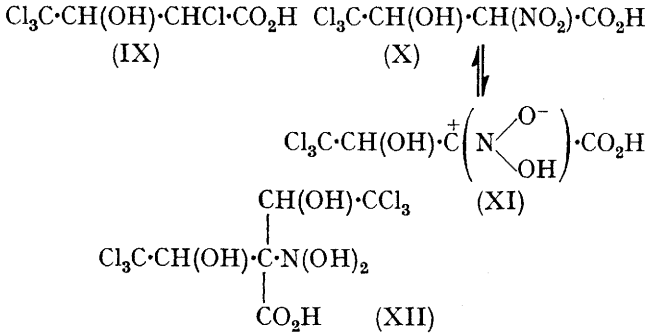


(VII)

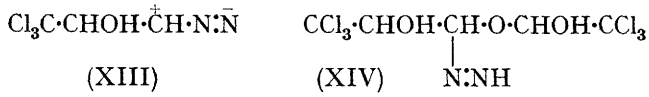


(VIII)

obtained with bromal hydrate. Compound (VII; X = Cl) showed $\nu_{max.}$ (Nujol) 3295, 3195sh (OH), and 1730 cm.$^{-1}$ (C=N) and $\lambda_{min.}$ (EtOH) 205, 257sh, and 268sh mμ (ε 5310, 78·7, 57·8) and with addition of 2N-NaOH $\lambda_{max.}$ 227 and 276sh mμ (ε 4560, 551). The n.m.r. spectrum ($CDCl_3$) showed signals at τ 4·64 (s, 1H), 3·9 (s, 1H), and 2·06 (s, 1H). The bromo-compound (VII; X = Br) showed similar spectral properties. Hydrolysis of compound (VII; X = Cl) for 15 min. in concentrated hydrochloric acid–acetic acid gave the γ-lactone of 3,3,3-trichloro-2-(2,2,2-trichloro-1-hydroxyethoxy)propionic acid (chloralide [9]), and the solution from the hydrolysis gave a colour test for hydroxylamine with sulphanilic acid and α-naphthylamine.[10] Chloralide was also obtained when the compound was oxidised with chromium trioxide in acetic acid. Compound (VII; X = Cl) formed a monoacetate, $\nu_{max.}$ (Nujol) 1788 and 1691 cm.$^{-1}$, n.m.r. ($CDCl_3$) signals at τ 7·79 (s, 3H), 4·48 (s, 1H), and 3·81 (s, 1H). Treatment of the compound with cold 2N-sodium hydroxide removed the elements of hydrogen chloride to yield 5-dichloromethylene-2-trichloromethyl-1,3-dioxolan-4-one oxime (VIII), $\nu_{max.}$ (Nujol) 3240, 3170 (OH), 1687 (C=N), and 1661 cm.$^{-1}$, $\lambda_{max.}$ (EtOH) 250 and 257 mμ (ε 12,900 and 14,400) [*cf.* $\lambda_{max.}$ 230—240 mμ (ε 12,000—23,000) for C=C–C=N system [11]], n.m.r. signals at τ 3·23 (s, 1H) and −1·4 (s, 1H). Compound (VIII) formed a monoacetate, $\nu_{max.}$ (Nujol) 1792, 1696w, and 1664 cm.$^{-1}$, $\lambda_{min.}$ (EtOH) 225 and 262 mμ (ε 10,700 and 11,700). Compound (VII; X = Cl) was not formed when chloral hydrate (2 mol.) was treated with sodium nitroacetate (1 mol.) in buffered solution; instead 1,1,1-trichloro-3-nitropropan-2-ol was obtained; furthermore, 2-chloropropionic acid failed to give an analogous product in the reaction so that it seems likely that the course of the reaction is *via* the intermediates (IX) and (X); the latter could react [as (IX)] with chloral hydrate to give (XII) and thence (VII; X = Cl) by loss of carbon dioxide and two moles of water, with rearrangement of the resulting nitroso-compound.



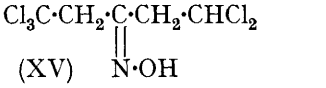
Compound (VII; X = Cl) was also obtained when chloral hydrate and sodium nitrite in aqueous solution were treated at 0—5° with an aqueous acetic acid solution of 3-amino-1,1,1-trichloropropan-2-ol hydrochloride.[7] Presumably the diazo-intermediate (XIII) reacted with chloral hydrate to give the hydrazo-compound (XIV) and from this, by hydrolysis of the



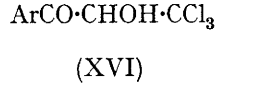
imino-group, loss of water and rearrangement of the resulting nitroso-compound, (VII; X = Cl) could arise.

[6] R. E. Bowman, A. C. White, and W. R. N. Williamson, *J. Chem. Soc.*, 1964, 1086.
[7] M. Compton, H. Higgins, L. MacBeth, J. Osborn, and H. Burkett, *J. Amer. Chem. Soc.*, 1949, **71**, 3229.
[8] J. B. Cohen, ' Practical Organic Chemistry,' Macmillan, London, 1949, p. 109.
[9] R. Otto, *Annalen*, 1887, **239**, 257.
[10] F. Feigl, ' Spot Tests,' Elsevier, New York, 1947, p. 352.
[11] A. E. Gillam and E. S. Stern, ' Introduction to Electronic Absorption Spectroscopy,' Arnold, London, 1954, p. 105.

During hydrogenation of (VII; X = Cl) over platinum the reaction solution took up more than 4 mol. of hydrogen but the product isolated (in poor yield) corresponded to $C_5H_6Cl_5NO_2$. It had $\nu_{max.}$ (Nujol) 3320s, 3170w, and 1710m cm.$^{-1}$; the most likely structure for this product appears to be (XV).

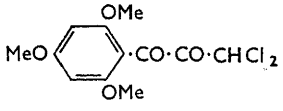


(XV)

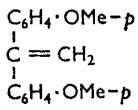


(XVI)

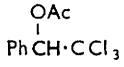
Attempts to prepare the type of α-hydroxy-ketone represented by (XVI) were made. A Hoesch reaction between 1,3,5-trimethoxybenzene and chloral cyanohydrin, however, yielded 3,3-dichloro-1-(2,4,6-trimethoxyphenyl)propane-1,2-dione (XVII) which was identical with authentic material prepared by means of a Hoesch



(XVII)



(XX)



(XIX)

reaction between 1,3,5-trimethoxybenzene and dichloropyruvonitrile. A Friedel–Crafts reaction between benzene and *O*-acetyl-3,3,3-trichlorolactic acid chloride also failed to yield the desired system (XVI) and gave instead the acetate of α-(trichloromethyl)benzyl alcohol (XIX). The reaction had evidently proceeded by loss of carbon monoxide, an effect often observed in highly hindered acid chlorides.[12] This effect may sometimes be overcome by using a more activated compound than benzene, but when the reaction was repeated with anisole the product was 1,1-bis-(*p*-methoxyphenyl)-ethylene (XX) as shown by its i.r. and n.m.r. spectra and by comparison with an authentic sample.[13,14] Gattermann obtained his compound in Friedel–Crafts reaction between anisole and acetyl chloride,[13] and presumably it was formed in our reaction by a similar process involving the acetoxy-group.

EXPERIMENTAL

LP^{40} and LP^{60} refer to light petroleum (b.p. 40—60°) and (b.p. 60—80°) respectively.

1,1,1,7,7,7-Hexachloro-2,6-dihydroxyheptan-4-one (II; R^1 = H, R^2 = O).—Acetone dicarboxylic acid (31·8 g., 0·2 mole) was treated with crushed ice (64 g.) and neutralised with sodium hydrogen carbonate. Acetic acid (2 ml.), sodium acetate (20 g.), and chloral hydrate (87·5 g., 0·5 mole) were added to the solution which was then set aside for 4 days. The precipitate (25·6 g.) was recrystallised from LP^{60}–acetone to give the *dihydroxy-heptanone* as white needles, m.p. 124—126° (Found: C 24·0; H, 2·4; Cl, 60·7. $C_7H_8Cl_6O_3$ requires C, 23·8; H, 2·3; Cl, 60·3%). The *diacetate* formed needles, m.p. 95—96° (sinters 90—95°) from LP^{60} (Found: C, 30·9; H, 2·95. $C_{11}H_{12}Cl_6O_5$ requires C, 30·2; H, 2·7%).

1,1,1,7,7,7-Hexachloroheptane-2,4,6-triol (II; R^1 = H, R^2 = H, OH).—The above dihydroxy-ketone (24 g.) in tetrahydrofuran (100 ml.) was stirred at 10—15° with 1·34M-lithium borohydride in tetrahydrofuran (50 ml.) for 30 min. and was then worked up. The *triol* (6·6 g.) was obtained as microneedles, m.p. 170° (from aqueous methanol) (softens 145°, clears 176°) (Found: C, 24·0; H, 3·0; Cl, 60·6. $C_7H_{10}Cl_6O_3$ requires C, 23·7; H, 2·8; Cl, 60·0%).

Tetrahydro-3-hydroxy-2-imino-α,5-bis(trichloromethyl)-furan-3-ethanol (III).—The above dihydroxy-ketone (240 g.) in 50% ethanol (1·8 l.) was stirred, warmed to 40°, and treated during 5 min. with a powdered mixture of commercial ammonium carbonate (338·4 g.) and potassium cyanide (58·5 g.). External heating was discontinued, but the temperature rose to 44° and the flask was immersed in an ice-bath; stirring was continued until the temperature reached 15°. The washed product (202 g.) had m.p. 178—180° (decomp.) (Found: C, 25·4; H, 2·4; N, 3·7%). A sample recrystallised from ethyl acetate gave the *imino-lactone* (III) as needles, m.p. 198·5° (decomp.) (Found: C, 25·6; H, 2·4; N, 3·85. $C_8H_9Cl_6NO_3$ requires C, 25·3; H, 2·4; N, 3·7%). The i.r. spectrum of this material was virtually identical with that of the crude material above.

Isolation of ammonium picrate from (III). The above imino-lactone (0·315 g.) in ether (500 ml.) was treated with picric acid (0·23 g.) in ether (100 ml.) and kept in an open vessel for 1 week. The crystalline yellow precipitate (0·16 g.) darkened at 225—265° (Found: C, 29·6; H, 2·7; Cl, Nil; N, 22·6. Calc. for $C_6H_6N_4O_7$: C, 29·3; H, 2·4; N, 22·8%); it had an i.r. spectrum (Nujol) identical with that of authentic ammonium picrate (which darkened at 265—270°).

N-(5-Acetyl-3,7-bis(trichloromethyl)-2,8-dioxabicyclo-[3,3,0]octan-1-yl)acetamide (V; R = Ac).—The imino-lactone (III) (30 g.), dissolved in acetic anhydride (500 ml.) and acetyl chloride (500 ml.), was kept at room temperature overnight. The solution was evaporated to dryness and the residue was treated with saturated sodium hydrogen carbonate solution (500 ml.) and then with solid carbonate until the aqueous phase was alkaline. The solid was washed with water and crystallised from methanol to give the *diacetate* (V; R = Ac) (11·42 g.) as shining parallelepipeds, m.p. 179—182° (Found: C, 31·0; H, 2·7; Cl, 45·4; N, 3·5; Ac, 18·1. $C_{12}H_{13}Cl_6NO_5$ requires C, 31·0; H, 2·8; Cl, 45·8; N, 3·0; (2) Ac, 18·5%). Hydrolysis of the diacetate (1 g.) with boiling concentrated hydrochloric acid (10 ml.) and acetic acid (10 ml.) for 40 min. gave a product (0·73 g.), m.p. 195—197° (softens 192—194°), which crystallised from ethyl acetate to give isomer (A) of the lactone (IV) (described below) as microplates (0·105 g.), m.p. 205—208°; an i.r. spectrum of the compound was identical with that of isomer (A) and the m.p. was undepressed on admixture with isomer (A).

N-[5-Hydroxy-3,7-bis(trichloromethyl)-2,8-dioxabicyclo-[3,3,0]octan-1-yl]acetamide (V; R = H).—The diacetate (V; R = Ac) (8·75 g.) in ethanol (440 ml.) was saturated with ammonia at *ca.* 15° and kept in a refrigerator for 2 days. The solution was evaporated to dryness and the residue was crystallised from 50% aqueous methanol to give the *amide* (V; R = H) as white microflakes, m.p. 186—188° (Found: C, 29·0; H, 2·5; N, 2·8. $C_{10}H_{11}Cl_6NO_4$ requires C, 28·5; H, 2·6; N, 3·3%); n.m.r. ($CDCl_3$) signals at τ 3·2 (s, 1H,

[12] G. Baddeley, *Quart. Rev.*, 1954, **8**, 355.
[13] L. Gattermann, *Ber.*, 1889, **22**, 1129.
[14] P. Pfeiffer and R. Wizinger, *Annalen*, 1928, **461**, 132.

NH), 5·1 (m, 3H, OH and :CH·), 7·32 (m, 4H, CH_2), and 7·89(s, 3H, CH_3CO); the signal at τ 3·2 disappeared, and integration for τ 5·1 was reduced to 2H when a deuteriochloroform solution of the compound was shaken with D_2O.

5,5,5-*Trichloro*-2,4-*dihydroxy*-2-(3,3,3-*trichloro*-2-*hydroxypropyl*)-γ-*valerolactone* (IV).—The imino-lactone (III) (15 g.), 2N-hydrochloric acid (600 ml.), and concentrated hydrochloric acid (60 ml.) were warmed for 15 min. on a steam-bath. The compound dissolved and the product was then precipitated. After 2 days at 0° it was washed with water and dried to give the product (15·61 g.), m.p. 185°. Recrystallisation from benzene–acetone (trace) gave a solid which was suspended in boiling LP[60] and treated with acetone until it dissolved. Excess of acetone was boiled off and the solution was set aside to crystallise overnight to give isomer (A) of the *lactone* (IV) (40·5 g.) as white microplates, m.p. 208—211° (decomp.) (Found: C, 25·3; H, 2·1. $C_8H_3Cl_6O_4$ requires C, 25·2; H, 2·1%); $\nu_{max.}$ (Nujol) 3366s (OH), 1764s (CO), 1311s, 1044s, 965s, 893m, and 882m cm.$^{-1}$.

The filtrate from the above crystallisation was diluted with LP[60] and concentrated until precipitation commenced; it was then set aside and allowed to crystallise to give isomer B of the *lactone* (IV) (7·72 g.) as white microneedles, m.p. 177—180° (Found: C, 25·4; H, 2·1%); $\nu_{max.}$ (Nujol) 3366s (OH), 1794, 1764s doublet (CO), 1327m, 1199s, 1115m, 1042m, 1016m, 950s, and 884m, cm.$^{-1}$.

The i.r. spectra of the two isomers showed differences of pattern in the fingerprint region both in Nujol and in chloroform solution.

5,5,5-*Trichloro*-2,4-*dihydroxy*-2-(3,3,3-*trichloroacetonyl*)-γ-*valerolactone* (VI; $R^1 = R^2 = R^3 = O$).—The lactone (IV) (7·62 g.) (as an unseparated mixture of the isomers, of m.p. 182—184°) dissolved in acetic acid (100 ml.) and concentrated sulphuric acid (1 ml.) was stirred and treated portionwise with chromium trioxide (4 g.) (0·25 hr.) (the temperature was held below 30° by using a cold water-bath); the mixture was then stirred for 2 hr. The solution was treated with water (250 ml.) and stirred for 0·5 hr.; the precipitate was twice recrystallised from aqueous methanol to give crystals (1·5 g.), m.p. 165—167°, which left a residue upon combustion. Recrystallisation of this material (A) from methanol–2N-hydrochloric acid (acid solution refluxed 5 min.) gave the *keto-lactone* (VI; $R^1 = R^2 = R^3 = O$) (0·85 g.) as flakes, m.p. 165—167° (Found: C, 25·7; H, 1·5. $C_8H_6Cl_6O_4$ requires C, 25·3; H, 1·6%). Sublimation of a sample of (A) at 160°/0·05 mm. gave the keto-lactone as a white solid, m.p. 165—167° (Found: C, 25·6; H, 1·4%), $\nu_{max.}$ (Nujol) 3450m (OH), 1780s (lactone CO), 1745m (ketone CO), and 1205s cm.$^{-1}$.

3-*Hydroxy*-2-*imino*-α,5-*bis*(*trichloromethyl*)-3-*pyrrolidineethanol* (VI; $R^1 = R^2 = NH$, $R^3 = H,OH$).—The imino-lactone (III) (12 g.) was suspended in ethanol (200 ml.) and the solution was saturated with ammonia at 0—10°; the mixture was then stored in a refrigerator for 4 days. The mixture was evaporated to dryness to give the product (11·2 g.), m.p. 150°; the compound had an i.r. spectrum identical with that of the 2-*imino-pyrrolidine* (2·31 g.) (VI; $R^1 = R^2 = NH$, $R^3 = H,OH$) obtained as white microneedles, m.p. 148—150° (decomp.) from ethyl acetate [Found: C, 25·4; H, 2·7; N, 7·6. Equiv. wt. 380, pK_a (50% EtOH) 5·22. $C_8H_{10}Cl_6N_2O_2$ requires C, 25·3; H, 2·6; N, 7·4; Equiv. wt. 379]; $\nu_{max.}$ (Nujol) 3375m, 3300m, 3200s, and 1600m cm.$^{-1}$.

2,5-*Bistrichloromethyl*-1,3-*dioxolan*-4-*one Oxime* (VII; X = Cl).—(*a*) Chloroacetic acid (200 g.) in water (400 ml.) was treated with sodium carbonate (120 g.) and the solution warmed to complete dissolution. The mixture was cooled and sodium nitrite (146 g.) in water (200 ml.) was added, followed by acetic acid (28 ml.), chloral hydrate (662 g.), and sodium acetate trihydrate (40 g.) in water (400 ml.). The product was precipitated the following day and after 2 days acetic acid was added to readjust the pH from 8—9 to 5—6. A test for nitrite with starch-iodide was then negative. After 5 days the first batch of product (68·3 g.), m.p. 133—136° was recrystallised from LP[60] to give the *oxime* (VII; X = Cl) as needles, m.p. 134—136° (Found: C, 18·1; H, 0·7; Cl, 62·5; N, 4·2. $C_5H_3Cl_6NO_3$ requires C, 17·75; H, 0·9; Cl, 63·0; N, 4·1%). A further batch (81 g.), m.p. 131—134° (i.r. spectrum identical with that of previous crop) was collected after the reaction mixture filtrate had been set aside at room temperature for 2 years.

(*b*) Chloral hydrate (8·25 g.) dissolved in a solution of sodium nitrite (2·07 g.) in water (5 ml.) and acetic acid (0·5 ml.) and cooled to below 10° was treated dropwise (0·75 hr.) with a solution of 3-amino-1,1,1-trichloropropan-2-ol hydrochloride (2·15 g.) in water (5 ml.) and acetic acid (0·5 ml.) so that the temperature remained below 10°; brisk effervescence occurred. At the end of the addition the mixture was stirred at 0° for 0·25 hr. and then at room temperature for 3 hr. The mixture was diluted with water (100 ml.) and then stored for 2 days; the product (0·68 g.), m.p. 125—129° crystallised from LP[60] to give the oxime (VII; X = Cl) (0·5 g.), m.p. 134—135° as needles (Found: C, 17·8; H, 0·7; N, 4·3%); an i.r. spectrum (Nujol) was identical with that of the material obtained in (*a*) above.

Hydrolysis of the Oxime (VII; X = Cl).—The oxime (1 g.) was boiled in concentrated hydrochloric acid (10 ml.) and acetic acid (10 ml.); the mixture was cooled in ice to give a solid (0·29 g.) of m.p. 108—110°, undepressed upon admixture with an authentic chloralide and having an i.r. spectrum identical with the spectrum of chloralide. The filtrate gave further product (0·23 g.) upon addition of water (20 ml.) and this was filtered off; the filtrate was evaporated to small bulk and gave a crimson colour upon addition of sulphanilic acid and α-naphthylamine (test for hydroxyamine).[10]

The acetate of the oxime (VII; X = Cl) (prepared by the acetic anhydride–acetic acid–perchloric acid method) formed *needles*, m.p. 148—150·5° (from benzene) (Found: C, 22·4; H, 1·8; Cl, 56·15; N, 3·6. $C_7H_5Cl_6NO_4$ requires C, 22·1; H, 1·3; Cl, 56·1; N, 3·7%).

2,5-*Bistribromomethyl*-1,3-*dioxolan*-4-*one Oxime* (VII; X = Br).—This compound was prepared (26% yield) by method (*a*) above with bromal hydrate. It formed white crystals from benzene, m.p. 196—197° (Found: C, 10·0; H, 0·1; Br, 79·7; N, 2·6. $C_5H_3Br_6NO_3$ requires C, 9·9; H, 0·5; Br, 79·3; N, 2·3%); $\nu_{max.}$ (Nujol) 3270m (OH) and 1719m cm.$^{-1}$ (C=N); $\lambda_{max.}$ (EtOH) 216sh (ε 7220).

5-*Dichloromethylene*-2-*trichloromethyl*-1,3-*dioxolan*-4-*one Oxime* (VIII).—The oxime (VII; X = Cl) (4·8 g.) was dissolved in 2N-sodium hydroxide (14 ml.) and ice was added to it. The solution was shaken for 10—15 min. and was then poured into 2N-sulphuric acid (25 ml.) containing ice. The product was recrystallised from benzene and then from 50% aqueous ethanol to give the *oxime* (VIII) (4·0 g.) as rods, m.p. 175—176° (Found: C, 19·9; H, 1·0; Cl, 58·5; N, 4·5. $C_5H_2Cl_5NO_3$ requires C, 19·9; H, 0·65; Cl, 58·8; N,

4·6%). The *acetate* formed clusters of microrods, m.p. 121—123°, from LP[60]–benzene (Found: C, 25·0; H, 1·25; N, 4·3. $C_7H_4Cl_5NO_4$ requires C, 24·5; H, 1·2; N, 4·1%).

Catalytic Hydrogenation of the Oxime (VII; R = Cl).—The oxime (VII; X = Cl) (1 g.) in ethanol (30 ml.) containing 2N-hydrochloric acid (10 ml.) absorbed 215 ml. of hydrogen at 21·5°/743 mm. in 130 min. The product was an oil which crystallised from LP[60]–carbon tetrachloride as irregular *rhombs* of the reduction product (XV) (0·14 g.), m.p. 140—142° (softens 135°) (Found: C, 20·6; H, 2·1; N, 4·65. $C_5H_6Cl_5NO_2$ requires C, 20·7; H, 2·1; N, 4·8%).

3,3-*Dichloro*-1-(2,4,6-*triethoxyphenyl*)*propane*-1,2-*dione* (XVII).—(*a*) 1,3,5-Trimethoxybenzene (50·4 g., 0·3 mole) in ether (700 ml.) with choral cyanohydrin (54·15 g., 0·3 mole) was stirred in an ice-bath and dry hydrogen chloride was passed into the mixture for 3 hr. The solution was stored in the refrigerator for 4 days; the precipitate was washed with ether and hydrolysed in water (250 ml.) at 100° for 1 hr. The resulting product was recrystallised from 96% ethanol to give the *diketone* (XVII) (16·83 g.), m.p. 89·5—91° as pale yellow, feathery needles (Found: C, 46·9; H, 4·0; Cl, 22·8. $C_{12}H_{12}Cl_2O_5$ requires C, 46·9; H, 3·9; Cl, 23·1%); $\nu_{max.}$ (Nujol) 1726m (Cl), 1620s, 1597s, and 1564s cm.$^{-1}$ (Ar). After 3 weeks the ethereal filtrate deposited imino-hydrochloride, which yielded further diketone (7·43 g.), m.p. 87—88°; total yield was 29%.

(*b*) 1,3,5-Trimethoxybenzene (19·5 g.) and dichloroacetyl cyanide [15] (16·1 g.) were taken up in ether (100 ml.) and the solution was saturated with hydrogen chloride at 0°; after 3 days further ether (500 ml.) was added. After 3 weeks the product was hydrolysed in water (100 ml.) at 100° for 0·5 hr. and the resulting gum was triturated with 96% ethanol to give a solid which crystallised from aqueous ethanol to give the *diketone* (XVII) (0·1 g.) as pale yellow, feathery needles, m.p. 88—89° (Found: C, 47·0; H, 4·2; Cl, 23·0%); an i.r. spectrum of the product was identical with that of the sample prepared in (*a*) above.

Isolation of α-*Trichloromethylbenzyl Acetate* (XIX).—Dry benzene (150 ml.) and aluminium chloride (13·35 g., 0·1 mole) were stirred and treated with the *O*-acetyl-3,3,3-trichlorolactic acid chloride (25·4 g., 0·1 mole); the mixture was heated under reflux for 1·5 hr. and was then kept at room temperature overnight. The cooled mixture was treated with 2N-hydrochloric acid (100 ml.) and the benzene layer was separated, washed with sodium hydrogen carbonate solution and water; it was then dried ($MgSO_4$) and evaporated. The product was a yellow liquid (6·99 g.), b.p. 116—124°/1·4—1·7 mm., which rapidly crystallised; it was recrystallised from LP[60] to give α-(trichloromethyl)-benzyl acetate (3·15 g.), m.p. 87—88°, as plates (Found: C, 44·4; H, 3·5; Cl, 39·5. Calc. for $C_{10}H_9Cl_3O_2$: C, 44·85; H, 3·4; Cl, 39·8%); $\nu_{max.}$ (Nujol) 1750s, 1736s, and 1220s cm.$^{-1}$. The m.p. of this compound was undepressed on admixture with authentic material, prepared from α-(trichloromethyl)-benzyl alcohol (kindly donated, together with the above acid chloride, by Dr. W. A. Jones).

Isolation of 1,1-*Bis*(p-*methoxyphenyl*)*ethylene* (XX).—Anisole (150 ml.) and the *O*-acetyl-3,3,3-trichlorolactic acid chloride (25·4 g.) were stirred and treated with aluminium chloride (13·35 g.); the temperature was kept at 25—30°. The mixture was stirred at room temperature for 2·5 hr. and was then stored overnight. The mixture was poured into 2N-hydrochloric acid (100 ml.) and crushed ice and was then extracted with ether. The extract was washed with sodium hydrogen carbonate solution and water and then dried ($MgSO_4$). After evaporation of ether and excess of anisole the residue (21·3 g.), m.p. <100°, solidified. It was triturated with LP[60] and recrystallised twice from 96% ethanol to give the ethylene (XX) (2·01 g.), m.p. 141—141·5°, as plates (Found: C, 79·6; H, 6·45; OMe, 22·2%; *M*(Rast), 224. $C_{16}H_{16}O_2$ requires C, 80·0; H, 6·7; (2) OMe, 25·8%, *M*, 240); $\nu_{max.}$ (Nujol), 1600s, 1565w, 1025s, 900s, 845s, and 830 cm.$^{-1}$: n.m.r. ($CDCl_3$) signals at τ 2·9 (m, 8H), 4·7 (s, 2H), and 6·2 (s, 6H).

Prepared from *p*-methoxyphenylmagnesium bromide and ethyl acetate,[14] the ethylene (XX) formed white flakes, m.p. 140—141° from 96% ethanol (Found: C, 80·1; H, 6·8%); its m.p. was undepressed on admixture with the previous sample and the i.r. spectra of the two samples were identical.

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[15] A. Kotz and K. Otto, *J. prakt. Chem.*, 1913 [2], **88**, 548.