The Reactions of Alcohols with Highly Chlorinated Cyclopentenones

EDWARD D. WEIL AND JEROME LINDER

Research Department, Hooker Chemical Corporation, Niagara Falls, New York

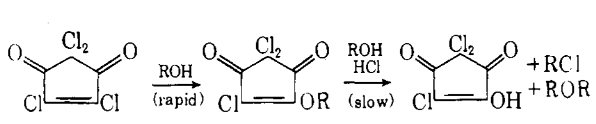
Received December 28, 1962

Alcoholysis of tetrachlorocyclopentene-3,5-dione and hexachloro-2-cyclopentenone yielded 1-hydroxy-2,4,4-trichlorocyclopentene-3,5-dione and 3-hydroxy-2,4,4,5,5-pentachloro-2-cyclopentenone, respectively. In the presence of base, the same ketones underwent ring opening with alcohol to yield esters. 2,3,4,4,5-Pentachloro-2-cyclopentenone was found to react with methanol to yield a product hitherto known as the methanol adduct of hexachloroindone and which now has been shown to be 4-carbomethoxy-2,3,3a,4,5,6,7-heptachloro-3a,4-dihydroindone, the chemistry and stereochemistry of which were further elucidated. The reactions of phenolates with tetrachlorocyclopentene-3,5-dione and hexachloro-2-cyclopentenone were shown to yield 1-aryloxy-2,4,4-trichlorocyclopentene-3,5-diones and 3-aryloxy-2,4,4,5,5-pentachloro-2-cyclopentenones, respectively.

In connection with research directed toward pesticidal derivatives of hexachlorocyclopentadiene, we have studied the reactions of certain ketone derivatives thereof with alcohols and phenols.

The reaction of ethanol with tetrachlorocyclopentene-3,5-dione (I) at reflux recently has been reported[1] to yield 1-ethoxy-2,4,4-trichlorocyclopentene-3,5-dione (IIa). In work conducted in our laboratory prior to this report, we had observed that a more prolonged period of refluxing of tetrachlorocyclopentene-3,5-dione with methanol or ethanol yielded, instead of an ether, a water-soluble crystalline compound $C_5HCl_3O_3$ having the properties of a strong monobasic acid. This product is assigned the enolic structure, 1-hydroxy-2,4,4-trichlorocyclopentene-3,5-dione (III), on the basis of the infrared spectrum which shows a carbonyl band (close doublet) at 5.77 μ, a single C=C stretching band at 6.06 μ, and an OH stretching band at 3.10 μ. The position of the C=O absorption is close to that of the stronger of the two carbonyl absorption bands in tetrachlorocyclopentene-3,5-dione.[1] The enol III is identical to the compound $C_5HCl_3O_3$ identified in the older literature[2] as trichlorocyclopentane-1,2,4-trione, a chlorination product of chloranilic acid.

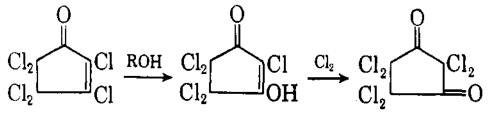
Further investigation showed that the ether IIa or its methyl homolog IIb are the initial products in the reaction of tetrachlorocyclopentene-3,5-dione with excess ethanol or methanol and that the ethers are then cleaved to the enol in a relatively slow step by the alcoholic hydrogen chloride solution.



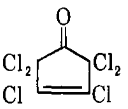
I IIa, R=C_2H_5 b, R=CH_3 III

The conversions of I to IIa and thence to III are analogous to reported reactions of tetrabromocyclopentene-3,5-dione with alcohol.[3]

The α,β-unsaturated monoketone, hexachloro-2-cyclopentenone (IV), similarly was found to react with lower primary alcohols to yield a stable water-soluble crystalline enol, $C_5HCl_5O_2$, to which the structure 3-hydroxy-2,4,4,5,5-pentachloro-2-cyclopentenone (V) is assigned.



IV V VI



VIII

The enol V is strongly acidic in aqueous solution (pH 2.3 at 0.15% concentration) and is titratable with aqueous base to a sharp phenolphthalein or congo red end point without concurrent evolution of chloride ion. The neutralization equivalent has the correct value for $C_5Cl_5O(OH)$. The infrared spectrum of V shows a single carbonyl band at 5.8 μ and a broad absorption at 6.1–6.4 μ which may be attributed to the carbon-to-carbon double bond and possibly also to intermolecularly hydrogen-bonded carbonyl. Evidence for the -OH group is the presence of an infrared absorption band at 2.80–2.85 μ.

The 1,3-relationship of the hydroxy and carbonyl groups was proved by the chlorination of the enol V in aqueous solution to form the known hexachlorocyclopentane-1,3-dione (VI),[4] which was further characterized by ammonolysis to the known amide $CHCl_2COCCl_2CCl_2CONH_2$ (VII).[4]

It is interesting to note that Zincke and Rohde[4] postulated the enol structure V as a hypothetical intermediate in the chlorination of 4,4,5,5-tetrachlorocyclopentane-1,3-dione to hexachlorocyclopentane-1,3-dione; they did not, however, isolate the enol or prove its presence.

The unconjugated ketone, hexachloro-3-cyclopentenone (VIII), did not react with methanol on prolonged refluxing. This is not unexpected since the vinylic chlorine atoms cannot be mesomerically activated by the carbonyl group.

2,3,4,4,5-Pentachloro-2-cyclopentenone (IX) on refluxing with methanol yielded a crystalline compound $C_{11}H_3O_3Cl_7$ (X) which was found to be identical with the known reaction product[5] of octachloro-3a,4,7,7a-tetrahydro-4,7-methanoindene-1,8-dione (XI) with methanol. This product was considered by Zincke and Pfaffendorf to be a hemiketal ($C_{10}H_4Cl_6O_2$)

---

[1] A. Roedig and G. Märkl, *Ann.*, **636**, 1 (1960).

[2] A. Hantzsch, *Chem. Ber.*, **21**, 2421 (1888); **25**, 833 (1892); see also J. U. Nef, *Am. Chem. J.*, **12**, 482 (1890), and H. Landolt, *Chem. Ber.*, **25**, 842 (1892). These authors considered an enolic structure to be a possible tautomer of the triketone structure but seem to have assumed the enol would be 1-hydroxy-2,5,5-trichlorocyclopentene-3,4-dione. This latter structure, having an α-diketone structure, appears unlikely in view of the absence of absorption in the visible spectrum. The position of the OH stretching band of III suggests intramolecular hydrogen bonding when compared to the OH stretching band of V (*vide infra*), further supporting the assigned enolic structure of III.

[3] T. Zincke and E. Weishaupt, *Ann.*, **437**, 86 (1923).

[4] T. Zincke and A. Rohde, *ibid.*, **299**, 378 (1898). The amide VII may actually exist as a cyclic hydroxylactam, since it exhibits only a single carbonyl band at 5.72 μ.

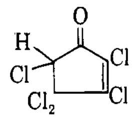
[5] T. Zincke and W. Pfaffendorf, *ibid.*, **394**, 3 (1912)

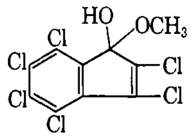
TABLE I

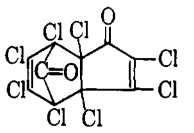
ULTRAVIOLET AND VISIBLE SPECTRA (IN ACETONITRILE SOLUTIONS)[a]

Compound	Absorption maxima (mμ) (molar extinction coefficients in parentheses)
$C_{11}H_3O_3Cl_7$ isomer, m.p. 136° (Xc)	236 (15,500), 286 (7190), 346 (7750)
$C_{11}H_3O_3Cl_7$ isomer, m.p. 171–172° (XV)	244 (12,500), 295 (6210), 346 (7680)
$C_{12}H_5O_3Cl_7$ (XVI)	264 (7750), 285 (sh), 340 (9600)
Octachloro-3a,4,7,7a-tetrahydro-4,7-methanoindene-1,8-dione (XI)	266 (17,800)
Hexachloro-2-cyclopentenone (IV)	260 (8870), 294 (sh, approx. 3100)
Perchloroindone	266 (28,500), 353 (1730), 415 (1080)
4-Carbomethoxypentachloroindone (XII)	250 (2400), 266 (33,500), 352 (970), 410 (580)
4-Carbethoxypentachloroindone (XVII)	265 (43,150), 358 (570), 408 (800)
4-Carbomethoxyheptachloroindan-1-one (XIII)	232 (11,200), 277 (10,500), 315 (1640), 324 (1690)
Octachloro-3a,7a-dihydroindone	250 (18,400), 266 (2100)
Methyl *cis*-pentachloropentadienoate (XX)	231 (13,100)
Hexachlorobutadiene	249 (3550)

[a] Acetonitrile was chosen because of its good solvent properties for all compounds of interest and good ultraviolet transmittance.

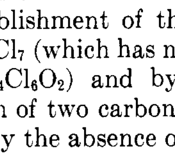

IX

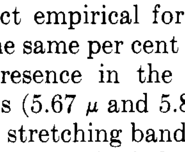

Xa

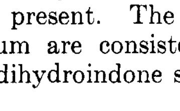

XI

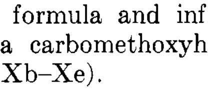
(Xa) of perchloroindone, on the basis of the elemental analysis for chlorine and the thermal conversion to perchloroindone.

The incorrectness of Zincke's structure is proved by the establishment of the correct empirical formula as $C_{11}H_3O_3Cl_7$ (which has nearly the same per cent chlorine as $C_{10}H_4Cl_6O_2$) and by the presence in the infrared spectrum of two carbonyl bands (5.67 μ and 5.83 μ), as well as by the absence of O—H stretching bands. The absence of a band in the 5.4–5.5-μ region[6] shows that the carbonyl bridge originally present in XI is no longer present. The empirical formula and infrared spectrum are consistent with a carbomethoxyheptachlorodihydroindone structure (Xb–Xe).


Xb


Xc


Xd


Xe

Support for structures Xb or Xc as opposed to structures Xd or Xe is given by comparison of the ultraviolet spectrum of X to the spectra of various model compounds (Table I). A strong absorption maximum occurs at a wave length (346 mμ) considerably longer than the strong maxima shown by hexachloro-2-cyclopentenone (IV) (260 mμ, shoulder 294 mμ) or octachloro-3a,4,7,7a-tetrahydro-4,7-methanoindene-1,8-dione (XI) (266 mμ),[7] suggesting that X has a much longer conjugated system than either of these 2-cyclopentenones. That the "cisoid" diene–ester system of structure Xd or Xe would not produce such an absorption maximum may be argued on several grounds. First, the absorption maximum of methyl pentachloropentadienoate falls at 231 mμ. The hypothetical "cisoid" form of this ester would, therefore, be predicted to absorb in the vicinity of 231 + 39 or 270 mμ.[8] Secondly, octachloro-3a,7a-dihydroindone,[5] a model compound having the perchlorinated *cis*-diene structure in a six-membered carbocyclic ring, has its longest wave length maximum at 266 mμ. That the placing of a carbalkoxy group in conjugation with this type of diene system would not be expected to lengthen greatly the absorption maximum may be judged from a comparison of the spectrum of methyl pentachloropentadienoate to hexachlorobutadiene. In this case, the result of replacing a chlorine atom by a carbomethoxy group is actually to reduce slightly the wave length of the absorption maximum.

The reported ultraviolet spectrum of 2,3,5,6-tetraphenyl-3a,4-dihydroindone,[9] a compound having the same chromophore as structure Xc, exhibited three strong bands, at 400 mμ (ε 8000), 305.5 mμ (ε 14,800), and 235 mμ (ε 16,300), thus resembling the observed spectrum of X reasonably closely in view of the differences in ring substitution.

Finally, structure Xc was substantiated and structure Xb eliminated by the following sequence of reactions: X (Xc) was treated with sodium iodide in acetone, rapidly liberating one mole of iodine and yielding an intensely yellow ester $C_{11}H_3O_3Cl_5$ (XII) which had an infrared, visible, and ultraviolet spectrum closely resembling that of perchloroindone. Compound XII when treated with excess ammonia, aniline, or morpholine underwent replacement of a single chlorine atom by an amino, anilino, or morpholino group to yield, in each case, an intensely red-colored crystalline product resembling those obtained by analogous reactions of perchloroindone. Therefore, XII was formulated as a carbomethoxypentachloroindone.

---

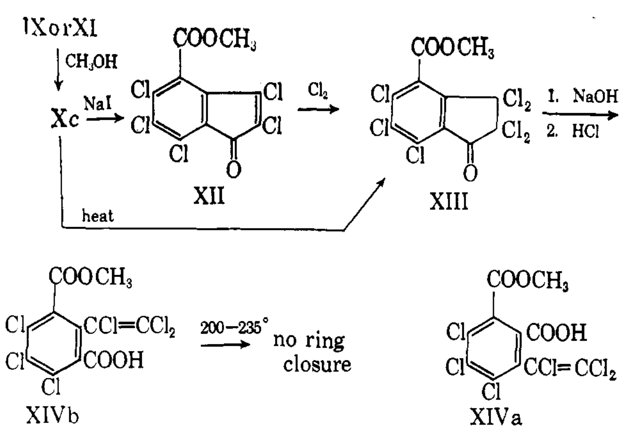
(6) E. T. McBee, D. K. Smith, and H. E. Ungnade, *J. Am. Chem. Soc.*, **77**, 559 (1955); P. Yates and P. Eaton, *Tetrahedron*, **12**, 13 (1961).

(7) This maximum as determined in the present investigation. E. T. McBee, D. K. Smith, and H. E. Ungnade, ref. 6, present a spectrum which they considered to be that of octachloro-3a,4,7,7a-tetrahydro-4,7-methanoindene-1,8-dione in ethanol plus hydrochloric acid, or a "halochromic salt" of this ketone. The absorption maxima at 235 and 340 mμ in the McBee, *et al.*, spectrum appear to be mainly attributable not to XI but to the ester ketone XVI. Rapidly fading bands at 213–214 and 254 mμ are observed when freshly prepared solutions of XI in ethanol are examined (see Experimental).

(8) That is assuming the cisoid–transoid diene absorption difference of 39 mμ is as found in studies of the ultraviolet spectra of steroids; see for discussion, L. Fieser and Mary Fieser, "Natural Products Related to Phenanthrene," 3rd Ed., Reinhold Publishing Co., New York, N. Y., 1949, pp. 185–188.

(9) Helen S. French, *J. Am. Chem. Soc.*, **74**, 514 (1952).

Chlorination of XII yielded a carbomethoxyheptachloroindan-1-one (XIII), $C_{11}H_3O_3Cl_7$, which, upon treatment with sodium hydroxide, underwent ring opening to yield (after acidification) a trichlorovinyltrichlorobenzenedicarboxylic acid monomethyl ester. If X had possessed structure Xb, then the previous reaction sequence would have led to an *o*-phthalic acid monomethyl ester (XIVa) having the carboxyl group adjacent to the carbomethoxy group, whereas if X has the structure Xc, this reaction sequence would have led to an isophthalic acid monoethyl ester (XIVb). That the product was actually 2-(trichlorovinyl)-4,5,6-trichloroisophthalic acid monomethyl ester (XIVb) was established by determining that ring closure to an anhydride could not be made to occur even under conditions substantially more rigorous than required to convert tetrachloro-*o*-phthalic acid monomethyl ester to tetrachlorophthalic anhydride. This reaction sequence is formulated as shown.



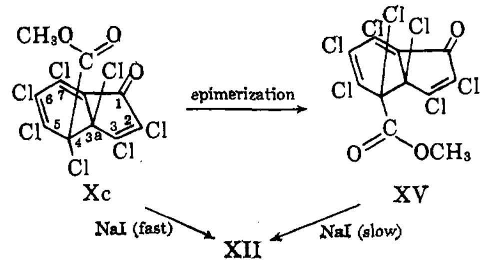
It was found that XIII also could be produced in one step from Xc by prolonged heating slightly above the melting point of Xc, or by heating a solution of Xc in glacial acetic acid at 100°. The conversion of Xc to XIII in acetic acid solution was accelerated by passage of chlorine into the solution. The reaction in the absence of added chlorine may occur by splitting out of the 3a- and 4-chlorine atoms and readdition of this chlorine to the 2,3-double bond; if so, the latter reaction must be relatively faster since none of the less-chlorinated intermediate XII could be detected by infrared examination of the partially converted thermal reaction product. The catalysis of the reaction by chlorine is explicable on the basis of chlorine addition to the 2,3-double bond of Xc to give a relatively unstable nonachlorinated intermediate which then loses the 3a- and 4-chlorine atoms to form XIII. At higher temperatures, XIII apparently decomposes to perchloroindone, since heating Xc at 150° for a prolonged period gave principally perchloroindone. Zincke and Pfaffendorf[5] had observed the conversion of their "perchloroindone methylate" (Xc) to perchloroindone on heating under unspecified conditions.

The stereochemistry of Xc was elucidated on the basis of the following transformations.

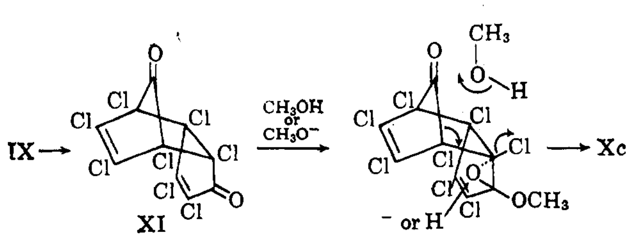
Compound X (Xc) when allowed to stand in aqueous acetone solution slowly underwent a transformation to an isomeric $C_{11}H_3O_3Cl_7$ (XV) of lower solubility and higher melting point (171–172°). The infrared spectra in the carbonyl and carbon-to-carbon double bond stretching regions and the ultraviolet spectra of X (Xc), and XV were found to be nearly identical, indicating no change in the conjugated system. Like Xc, XV when treated with sodium iodide in acetone liberated iodine and yielded XII.

The rearranged $C_{11}H_3O_3Cl_7$ isomer XV would appear to have the 3a- and 4-chlorine atoms *cis* to one another since it was found that this isomer liberated iodine from sodium iodide at a much slower rate than does the original $C_{11}H_3O_3Cl_7$ isomer (Xc). It seems well established that the elimination of vicinal halogens by iodide ion proceeds more readily where the vicinal halogens are *trans* to each other (as in Xc) rather than *cis* (XV).[10,11]

The rearrangement of Xc to XV can be explained as an epimerization involving the labile allylic chlorines. In order for the α,β-unsaturated ketone system of the five-membered ring to approach coplanarity with the diene system of the six-membered ring in Xc, the chlorine atom α to the carbomethoxy and the chlorine atom of the ring junction β to the carbomethoxy are forced into close proximity. In the epimerized compound XV, less crowding occurs as can be seen from inspection of a molecular model.



The conversion of 2,3,4,4,5-pentachloro-2-cyclopentenone (IX) to Xc upon treatment with methanol may be explained on the basis of the initial dehydrochlorination of IX to tetrachlorocyclopentadienone which has long been known to dimerize to XI, the *endo* Diels–Alder dimer.[4,12] In the subsequent reaction of XI with methanol, it would seem possible *a priori* for either the 3a- or the 7a-chlorine atom to be removed, and it is necessary to seek an explanation for the observed preferential removal of the 7a-chlorine. It is possible that the release of the 7a-chlorine is favored by anchimeric attack on the 7a-carbon atom by the oxygen attached to the 1-carbon, this oxygen being rendered nucleophilic and sterically capable of such attack as a result of methoxide attachment at the 1-carbon atom.



On the basis of analogous infrared, ultraviolet, and analytical evidence, Zincke's product from the reaction of octachloro-3a,4,7,7a-tetrahydro-4,7-methanoindene-

---

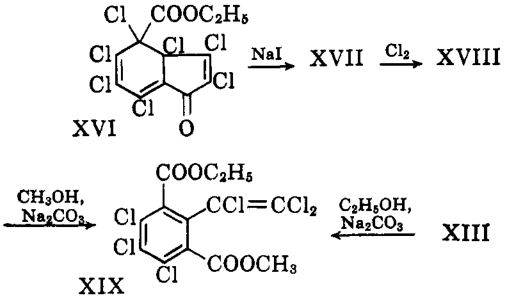
(10) W. G. Young, D. Pressman, and C. D. Coryell, *J. Am. Chem. Soc.*, **61**, 1640 (1939).

(11) J. Weinstock, S. N. Lewis, and F. G. Bordwell, *ibid.*, **78**, 6072 (1956).

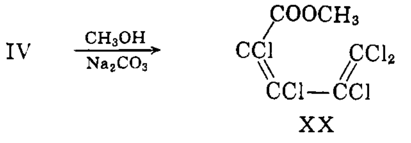
(12) The *endo* configuration appears to be firmly established by the photochemical conversion of XI to a cage structure. Thesis of P. Eaton, Harvard University, 1960, Chap. III.

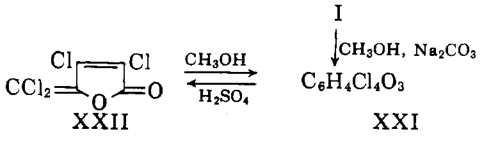
1,8-dione (XI) and ethanol (to which he ascribed the perchloroindone hemiketal structure),[5] appears to be actually an ethyl analog (XVI) of Xc. Its infrared spectrum is nearly superimposable on that of Xc. Its ultraviolet spectrum exhibits the strong peak at 340 mμ indicating the same extended conjugated system as is present in the methyl homolog.

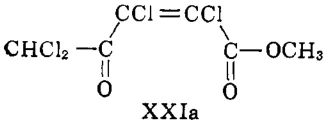
That the carbethoxy group of XVI is in the 4-position rather than the 7-position was proved by a sequence of reactions which at the same time rigorously confirmed the same structural relationship in the methyl homolog (Xc). XVI was treated with sodium iodide to obtain the carbethoxypentachloroindone (XVII). This was then treated with chlorine to chlorinate additively the nonaromatic double bond, yielding the carbethoxyheptachloroindan-1-one (XVIII). The latter, upon reaction with methanol and sodium carbonate, yielded a methyl ethyl trichlorovinyltrichloroisophthalate (XIX), which was found to be identical with the methyl ethyl ester obtained by treatment of the carbomethoxyheptachloroindan-1-one (XIII) with ethanol and sodium carbonate. If the carbalkoxy group had been in the 7-position in either XVI or Xc (or both), isomeric esters rather than identical methyl ethyl esters would have been obtained. Therefore, XVI is proved to be 4-carbethoxy-2,3,3a,4,5,6,7-heptachloro-3a,4-dihydroindone, XVII is 4-carbethoxy-2,3,5,6,7-pentachloroindone, and XVIII is 4-carbethoxy-2,2,3,3,5,6,7-heptachloroindan-1-one.



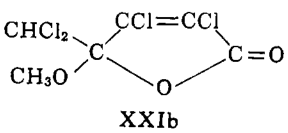
The reactions of tetrachlorocyclopentene-3,4-dione (I) and hexachloro-2-cyclopentenone (IV) with alcohols in the presence of bases are markedly different from the reactions of these ketones with alcohols in the absence of bases. With excess methanol in the presence of one molar equivalent of sodium carbonate, hexachloro-2-cyclopentenone (IV) is found to undergo rapid conversion at room temperature to the known methyl ester of pentachloropentadienoic acid (XX) (probably *cis*).







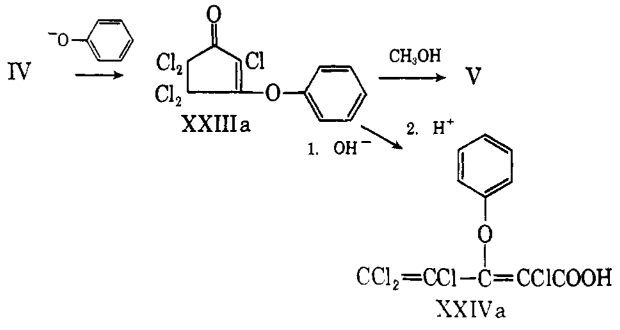
XXIa



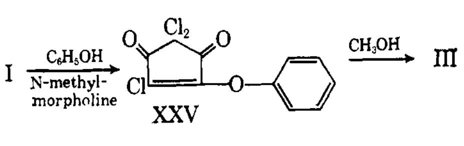
XXIb

Under similar conditions, tetrachlorocyclopentene-3,5-dione (I) is found to react with methanol, yielding a crystalline ester $C_6H_4Cl_4O_3$, m.p. 91–92° (XXI). This product proved to be the same as the product reported by Roedig and Märkl[1] from the reaction of perchloroprotoanemonin (XXII) with methanol. Roedig and Märkl considered this compound to be the methyl ester of 2,3,5,5-tetrachloro-2-penten-4-on-1-oic acid (XXIa); however, the infrared spectrum indicates that no ketone carbonyl is present and that the carbonyl band (5.52 μ) is more characteristic of a lactone than a normal ester. Consequently, the lactonic (pseudoester) structure XXIb appears more probable. It was found possible to convert XXI back to perchloroprotoanemonin by treatment with sulfuric acid.

Still different in character were the reactions of I and IV with phenol. In the absence of a base, hexachloro-2-cyclopentenone (IV) failed to react with phenol up to 150°, at about which temperature charring occurred. The reaction of IV with salts of phenols, instead of yielding the phenyl ester of pentachloropentadienoic acid, yielded phenoxypentachloro-2-cyclopentenones (XXIII). By analogy with other nucleophilic displacements of a chlorine atom of hexachloro-2-cyclopentenone known to occur without ring opening (*e.g.*, reaction with methyl alcohol, ammonia, or aniline), it would be expected that the vinyl chlorine located β with respect to the carbonyl group would be the site of the displacement. That the product of the reaction with phenoxide actually is the expected 3-phenoxy-2,4,4,5,5-pentachloro-2-cyclopentenone (XXIIIa) was confirmed by methanolysis to obtain 3-hydroxy-2,4,4,5,5-pentachloro-2-cyclopentenone (V). Treatment of XXIIIa and its substituted phenyl analogs with aqueous base brought about ring opening with release of one molar equivalent of chloride ion and formation of 3-phenoxy-2,4,5,5-tetrachloropentadienoic acid (XXIVa) and its analogs.



The reaction of tetrachlorocyclopentene-3,5-dione (I) with phenol in the presence of an equimolar amount of N-methylmorpholine yielded a compound having the correct analysis for 1-phenoxy-2,4,4-trichlorocyclopentene-3,5-dione (XXV). This structure was confirmed by the reaction of XXV with methanol at reflux to produce phenol plus the enol III.



Experimental[13]

1-Ethoxy-2,4,4-trichlorocyclopentene-3,5-dione (IIa).—The literature conditions[1] were followed, but a more satisfactory method of isolation was found. Tetrachlorocyclopentene-3,5-dione (I) (50 g.) and anhydrous ethanol (200 ml.) were refluxed for 10 min., rapidly cooled, and poured into water. Volhard titration of the supernatant aqueous layer showed 0.65 equiv. HCl/equiv. I. The precipitated oil was extracted with methylene chloride and dried over magnesium sulfate, the solvent evaporated, and a small liquid foreshot distilled under aspirator vacuum through a small Vigreux column until crystals began to sublime into the column. The residue was recrystallized from aqueous ethanol to obtain 34 g. (65%) of 1-ethoxy-2,4,4-trichlorocyclopentene-3,5-dione, m.p. 65–66° (lit.[1] m.p. 64.5–65.5°); $\lambda_{\max}^{\text{Nujol}}$ 5.74 (C═O), 5.61 (sh) (C═O), and 6.20 μ (C═C).

1-Methoxy-2,4,4-trichlorocyclopentene-3,5-dione (IIb).—A mixture of 46.5 g. of tetrachlorocyclopentene-3,5-dione (I) and 200 ml. of anhydrous methanol was heated at reflux for 1 hr. The resulting solution was cooled and poured into water. The heavy organic layer was separated and crystallized from hexane to obtain 12 g. (26%) of colorless crystals, m.p. 51°.

Anal. Calcd. for $C_6H_3O_3Cl_3$: C, 31.40; H, 1.32; Cl, 46.36. Found: C, 31.25; H, 1.34; Cl, 46.1.

1-Hydroxy-2,4,4-trichlorocyclopentene-3,5-dione (III).—A solution of tetrachlorocyclopentene-3,5-dione (I) (70 g.) in anhydrous methanol (100 ml.) was refluxed for 20 hr. Nineteen grams of condensate was collected in a Dry Ice-cooled trap connected to the outlet of the reflux condenser. This condensate was shown by boiling range and infrared spectrum to be a mixture of methyl chloride and dimethyl ether, with a small amount of methanol.

The reaction mixture was stripped free of methanol and dissolved hydrogen chloride under aspirator vacuum, leaving 66 g. of waxy crystalline residue, m.p. 86–113°. Infrared comparison of this crude product to the purified product showed it to be principally III; thus the yield was nearly quantitative. Recrystallization, after decolorization with charcoal, from benzene–heptane mixture gave colorless highly hygroscopic needles, m.p. 125° (lit.[2] m.p. 125°), having a neut. equiv. of 215 (theory for $C_5HO_3Cl_3$, 215.4) by titration with 0.1 *N* sodium hydroxide to a congo red end point; $\lambda_{\max}^{\text{Nujol}}$ 3.10 (s), 5.77 (s, close doublet), 6.06 (s), 7.30 (s, partly Nujol), 7.4 (w), 7.93 (m), 8.82 (w), 10.51 (s), 11.60 (m), 12.82 (m), 13.28 (m), 14.88 μ (w). The spectrum of "trichlorocyclopentane-1,2,4-trione," made from chloranilic acid by sodium hypochlorite–chlorine oxidation,[2] was found to be identical.

By substituting anhydrous ethanol for methanol in the above procedure, the same product was obtained, also in high yield. Ethyl chloride was the principal compound found in the Dry Ice trap, with minor amounts of diethyl ether, as determined by boiling range and density.

A solution of the diketone I in 35% aqueous dioxane held at the reflux temperature for 20 hr. was found by Volhard titration (of an aliquot) to contain 1 molar equiv. of hydrochloric acid. This solution on evaporation under oil-pump vacuum yielded a dark semicrystalline residue which, by infrared spectrum, was found to be primarily the enol III. Tenacious dark-colored impurities in the product made this method of synthesis of III less satisfactory than the reaction of I with methanol or ethanol.

Determination of Reaction Sequence.—To clarify the course of the reaction yielding the enol (III) a solution of 50 g. (213 meq.) of tetrachlorocyclopentene-1,3-dione in 200 ml. of anhydrous ethanol was refluxed and aliquots were removed at intervals for titration. The total acid content was determined by titration with aqueous 0.1 *N* sodium hydroxide to a congo red end point and the hydrogen chloride content was determined by Volhard chloride determination. No gaseous hydrogen chloride was emitted from the condenser. The enol content was calculated as the difference between the two titration values. The following results were obtained: 10 min., 150 meq. HCl, 12 meq. enol; 60 min., 123 meq. HCl, 95 meq. enol; 240 min., 40 meq. HCl, 183 meq. enol; 1320 min., 11 meq. HCl, 209 meq. enol.

3-Hydroxy-2,4,4,5,5-pentachloro-2-cyclopentenone (V).—One hundred grams of hexachloro-2-cyclopentenone (IV) was refluxed for 20 hr. with 100 ml. of dry methanol in a flask fitted with a water-cooled condenser, the outlet of which was attached to a Dry Ice-cooled trap. In this trap was collected 18 g. of colorless liquid which was found by determination of boiling range and infrared spectrum to be a mixture of methyl chloride and dimethyl ether.

The methanol was then stripped under aspirator vacuum and the residue freed of most of the unchanged hexachloro-2-cyclopentenone by heating at 100° and 0.2 mm. in a short-path still until no further liquid distilled. The residual solid was then recrystallized from about 1 l. of benzene to obtain 63 g. (67%) of water-soluble light gray prisms, m.p. 136–137°; $\lambda_{\max}^{\text{Nujol}}$ 2.83–2.88 (s), 5.80 (s), 6.15–6.40 (s, broad), 8.0–8.1 (s, broad), 9.36 (s), 9.58 (sh), 10.33 (m), 11.35 (m), 12.18 (m), 12.63 (m), 13.52 (m), 13.77 (m), 14.67 (m), 15.10 μ (w).

Anal. Calcd. for $C_5HO_2Cl_5$: C, 22.21; H, 0.37; Cl, 65.58; neut. equiv., 270.3. Found: C, 22.39; H, 0.42; Cl, 65.3; neut. equiv., 269.5.

Chlorination of 3-Hydroxy-2,4,4,5,5-pentachloro-2-cyclopentenone (V) to Hexachlorocyclopentane-1,3-dione (VI).—A solution of 80 g. of V in 500 ml. of water at room temperature was treated with a rapid stream of chlorine gas for 15 min. An immediate white crystalline precipitate formed and a mild exotherm was noted. The precipitate was removed by filtration. Volhard titration of the filtrate after purging of the dissolved chlorine showed 87% of the theoretical chloride ion assuming replacement of a single hydrogen atom. After drying in vacuum at 60°, the colorless crystalline product weighed 76 g. (84%) and melted sharply at 73°. The compound was identified as hexachlorocyclopentane-1,3-dione, reported[4] to melt at 70°. The infrared spectrum (Fluorolube mull) showed $\lambda_{\max}$ at 5.60 μ (shoulder at 5.55) (C═O), but no bands in the carbon-to-carbon double bond region, nor in the carbon-to-hydrogen stretching region. An authentic sample, produced by chlorinating tetrachlorocyclopentene-3,5-dione in liquid chlorine solution in a sealed Pyrex tube at 40–50° for 4 days under illumination by a 250-w. mercury vapor lamp, was found to have the same infrared spectrum as the product made by chlorination of V.

Following the literature directions,[4] the product was treated in benzene solution with gaseous ammonia to obtain colorless prisms, observed m.p. 155.5–156°, corresponding to the amide $CHCl_2COCCl_2CCl_2CONH_2$ obtained by these authors from hexachlorocyclopentane-1,3-dione; $\lambda_{\max}^{\text{Nujol}}$ 2.89 (s), 3.09 (s), 3.18 (w), 5.72 (s), 7.04 (m), 7.51 (s), 8.03 (m), 8.56 (m), 9.45 (s), 9.84 (s), 11.09 (w), 12.04 (m), 12.40 (m), 12.70 (w), 13.44 (m), 14.22 μ (m).

Attempted Reaction of Hexachloro-3-cyclopentenone (VIII) with Methanol.—A solution of 28.9 g. of hexachloro-3-cyclopentenone in 100 ml. of methanol was refluxed for 20 hr. No methyl chloride, methyl ether, nor hydrogen chloride was evolved, and the ketone was recovered unchanged.

Reaction of 2,3,4,4,5-Pentachloro-2-cyclopentenone (IX) with Methanol. 4-Carbomethoxy-2,3,3a,4,5,6,7-heptachloro-3a,4-dihydroindone (Xc).—A 25.4-g. sample of 2,3,4,4,5-pentachloro-2-cyclopentenone (IX) was refluxed with 100 ml. of methanol. After 1.5 hr., the reaction mixture was chilled and the resultant crystalline precipitate removed by filtration to obtain 13 g. of pale yellow crystals, m.p. 124–130° (Xc). This product after recrystallization from benzene–methanol mixture had m.p. 136° and did not depress the melting point of the compound (observed m.p. 136°) obtained by reaction of octachloro-3a,4,7,7a-tetrahydro-4,7-methanoindene-1,8-dione (XI) with methanol.[5]

The infrared spectrum showed $\lambda_{\max}^{\text{Nujol}}$ 5.67 (s), 5.83 (s), 6.15 (s), 6.31 (m), 6.52 (s), 6.94 (m), 8.0 (s), 8.17 (s), 8.28 (m), 8.85 (w), 9.16 (s), 10.01 (m), 10.11 (m), 10.45 (s), 10.73 (w), 11.28 (w), 11.47 (m), 12.08 (m), 12.52 (w), 12.78 (m), 12.92 (s), 13.24 (m), 13.96 (s), 14.82 μ (m).

Anal. Calcd. for $C_{11}H_3O_3Cl_7$: C, 30.63; H, 0.70; Cl, 57.54. Found: C, 30.83; H, 0.81; Cl, 57.6.

Isomerization of 4-Carbomethoxy-2,3,3a,4,5,6,7-heptachloro-3a,4-dihydroindone (Xc to XV).—A solution of 4.26 g. of $C_{11}H_3O_3Cl_7$ (Xc) in 50 ml. of acetone and 5 ml. of water was allowed to stand at room temperature for 10 days. Volhard titration of an aliquot showed substantially no chloride (after dilution of the aliquot with water and extraction with benzene to remove organic chlorine compounds). A crystalline precipitate was removed by filtration to obtain 2.8 g. (66%) of pale yellowish crystals, m.p. 171–172°; $\lambda_{\max}^{\text{Nujol}}$ 5.71 (C═O), 5.81 (C═C), 6.15 (C═C), and 6.34 μ (C═C).

Anal. Calcd. for $C_{11}H_3Cl_7O_3$: C, 30.63; H, 0.70; Cl, 57.54. Found: C, 30.87; H, 0.83; Cl, 57.5.

---

[13] Melting points given are uncorrected. The infrared spectra were determined by means of a Beckman Model IR-4 recording infrared spectrophotometer. The ultraviolet and visible spectra were run on a Cary Model 14 recording spectrophotometer.

4-Carbomethoxy-2,3,5,6,7-pentachloroindone-1 (XII).—To a solution of 30 g. of Xc in 500 ml. of acetone at 25° was added a solution of 100 g. of sodium iodide in 500 ml. of acetone. Iodine was evolved immediately. An aliquot was taken 15 sec. after admixture, rapidly added to excess water to quench the reaction by causing precipitation of the organic reactant, and the iodine quickly titrated with 0.1 *N* sodium thiosulfate. It was found that the theoretical 1 mole of iodine per mole of organic reactant had been evolved. A further aliquot held for 1 hr. before quenching and titration showed 1.02 moles of iodine per mole of organic reactant. The bulk of the reaction mixture was worked up after 15 min. by addition to water, the precipitated solids being removed by filtration and washed with water until the washings were colorless, and the solid dried in air to obtain 23 g. (92%) of brilliant yellow crystalline solid, m.p. 154.5–155°. The product is soluble in hot benzene, and moderately soluble in hot heptane. Recrystallization from the latter yielded 21 g. of yellow crystals, m.p. 157–158°.

Anal. Calcd. for $C_{11}H_3O_3Cl_5$: C, 36.65; H, 0.84; Cl, 49.19. Found: C, 36.62; H, 0.92; Cl, 49.1.

A similar reaction was conducted using the isomeric $C_{11}H_3O_3Cl_7$, m.p. 171–172° (XV). Aliquots taken at various times after admixture showed the following number of moles of iodine per mole of $C_{11}H_3O_3Cl_7$: 40 sec., 0.203 mole; 480 sec., 0.90 mole; 1670 sec., 0.95 mole. These data indicate a first-order or pseudo-first-order reaction with $t_{1/2}$ of 140 sec. (25°). The product, isolated as described previously, was found by infrared, melting point, and mixture melting point to be identical with the product from iodide reduction of $C_{11}H_3O_3Cl_7$, m.p. 136° (Xc).

3-Amino-4-carbomethoxy-2,5,6,7-tetrachloroindone.—Five grams of 4-carbomethoxy-2,3,5,6,7-pentachloroindone (XII) dissolved in 200 ml. of benzene was treated with gaseous ammonia for 1.25 hr. The precipitate was filtered out and washed with water, benzene, and warm acetic acid, leaving undissolved 4.3 g. of red needles, m.p. 241° dec.

Anal. Calcd. for $C_{11}H_5O_3NCl_4$: C, 38.74; H, 1.48; Cl, 41.60; N, 4.11. Found: C, 38.50; H, 1.54; Cl, 41.6; N, 3.88.

3-Anilino-4-carbomethoxy-2,5,6,7-tetrachloroindone.—A 0.5-g. sample of 4-carbomethoxypentachloroindone (XII), and 1 ml. of aniline were heated in benzene–methanol solution on the steam bath for 1 hr., the mixture evaporated to dryness, and the residue leached with water. The insoluble product was recrystallized from aqueous acetic acid to obtain 0.5 g. of red crystalline product, m.p. 171–173°.

Anal. Calcd. for $C_{17}H_9O_3NCl_4$: C, 48.95; H, 2.17; N, 3.36. Found: C, 48.81; H, 2.21; N, 3.27.

3-Morpholino-4-carbomethoxy-2,5,6,7-tetrachloroindone.—A 0.5-g. sample of 4-carbomethoxypentachloroindone (XII) and 0.5 g. of morpholine were heated in benzene–methanol solution on the steam bath for 1 hr., the mixture then evaporated to dryness, and the residue leached with water. The insoluble product was recrystallized from benzene–heptane to obtain 0.4 g. of red needles, m.p. 168–169°.

Anal. Calcd. for $C_{15}H_{11}O_4NCl_4$: C, 43.82; H, 2.70; N, 3.41. Found: C, 43.79; H, 2.88; N, 3.2.

4-Carbomethoxy-2,2,3,3,5,6,7-heptachloroindan-1-one (XIII).—Chlorine gas was passed into a solution of 30 g. of the indone (XII) in 300 ml. of glacial acetic acid at 95–100° (steam bath) for 63 hr. The solution was then poured into 2 l. of water, the gummy precipitate extracted with methylene chloride, the extract washed, dried over calcium chloride, and evaporated. The residue was recrystallized from heptane (charcoal treatment) to obtain 19 g. (53%) of colorless prisms, m.p. 102–103°; λ_{max}^{Nujol} 5.63 (s) (C=O), 5.70 (vs) (C=O), and 6.32 μ (C=C).

Anal. Calcd. for $C_{11}H_3O_3Cl_7$: C, 30.63; H, 0.70; Cl, 57.54. Found: C, 30.83; H, 0.78; Cl, 57.4.

To 0.317 g. of XIII in 50 cc. of acetone was added 25.00 cc. of 0.1003 *N* sodium hydroxide. After 1 hr., the solution was back-titrated with 0.1 *N* hydrochloric acid, indicating the consumption of 1 meq. of sodium hydroxide per 214 mg. of XIII (theory, 215.7 mg./meq.). A similar experiment in which the alkaline solution was subjected to Volhard titration indicated the release of 1 meq. of chloride per 428 mg. of XIII (theory, 431.5 mg./meq.).

Conversion of 4-Carbomethoxy-2,3,3a,4,5,6,7-heptachloro-3a,4-dihydroindone (Xc) to 4-Carbomethoxy-2,2,3,3,5,6,7-heptachloroindan-1-one (XIII) and/or Perchloroindone.—(A) Chlorine was passed for 2.5 days into a solution of 20 g. of Xc in 200 ml. of glacial acetic acid on the steam bath. The reaction mixture was then evaporated under reduced pressure, the residue dissolved in methylene chloride, washed with water, and, after removal of the methylene chloride, recrystallized from heptane. There was obtained 16 g. of nearly colorless crystals, m.p. 101–102°, found by ultraviolet and infrared examination to be identical to XIII. (B) This experiment was repeated without the introduction of chlorine. The crude product was analyzed by infrared, using pure Xc and XIII as standards, and found to contain Xc and XIII in the ratio of 1.4:1, accompanied by a minor amount of unidentified impurities. (C) In a sealed tube, 3 g. of Xc was heated at 140° for 2.5 days. Upon cooling and opening the tube, considerable pressure was released and a phosgene-like odor was noted. The tube contents were analyzed by infrared and found to contain no Xc, about 20% perchloroindone, the remainder being XIII. (D) At 150° for 3 days, Xc was converted to a product which, by infrared analysis, was found to be predominantly perchloroindone. The latter also was isolated by recrystallization from hot heptane and characterized by melting point.

2-(Trichlorovinyl)-4,5,6-trichloroisophthalic Acid Monomethyl Ester (XIVb).—To a solution of 2.07 g. of the indanone (XIII) in 100 ml. of acetone was added 100 ml. of 0.1 *N* aqueous sodium hydroxide. After about 15 min. the solution was titrated with 0.1 *N* aqueous hydrochloric acid to a phenolphthalein end point. The reaction mixture was then concentrated to a small volume to remove the acetone, filtered with a small amount of charcoal, and the clear filtrate acidified strongly with hydrochloric acid. The precipitate was removed by filtration and recrystallized from benzene–heptane mixture to obtain 0.7 g. of colorless crystals, m.p. 149–150°; λ_{max}^{Nujol} 5.71 (m), 5.79 (s), 6.04 (w), 6.25 (w), 6.46 (m), 7.73 (s), 8.07 (vs), 8.37 (w), 8.69 (m), 9.71 (w), 10.20 (w), 10.66 (m), 10.96 (m), 11.15 (w), 11.64 (m), 12.26 (m), 14.02 μ (w).

Anal. Calcd. for $C_{11}H_4O_4Cl_6$: C, 32.00; H, 0.98; Cl, 51.53. neut. equiv., 412.5. Found: C, 32.10; H, 0.86; Cl, 51.2; neut. equiv., 410.5.

Thermal Behavior of XIVb.—When XIVb was heated under nitrogen at 200° for 8 hr., the infrared spectrum was unchanged. When heated under nitrogen at 235° for 1 hr., the spectrum was largely unchanged except for small impurity bands, but no new carbonyl bands appeared, in particular no trace of carbonyl bands was observed in the vicinity of 5.40 and 5.62 μ, the location of the carbonyl bands of tetrachlorophthalic anhydride.

Comparison experiments with the monomethyl ester of tetrachlorophthalic acid indicated 100% conversion (measured by titration) to tetrachlorophthalic anhydride at 200° in 2 min., and 70% conversion at 150° in 15 min.[14]

Product of Octachloro-3a,4,7,7a-tetrahydro-4,7-methanoindene-1,8-dione (XI) and Ethanol. 4-Carbethoxy-2,3,3a,4,5,6,7-heptachloro-3a,4-dihydroindone (XVI).—The product was prepared by allowing an ethanolic solution of XI[5] to stand at room temperature for several days. After four recrystallizations from heptane, the compound melted at 95–95.5° (Zincke and Pfaffendorf[5] report the product to melt at 99° but give no analytical data); λ_{max}^{Nujol} 5.66 (s), 5.79 (s), 6.15 (s), 6.29 (m), 6.51 (s), 7.96 (s), 8.19 (s), 8.34 (m), 8.88 (w), 9.20 (s), 9.82 (s), 10.29 (s), 10.74 (m), 11.35 (w), 11.60 (m), 12.23 (w), 12.49 (m), 12.73 (m), 12.94 (s), 13.26 (m), 13.97 (s), 14.80 μ (m), thus resembling quite closely the spectrum of Xc.

Anal. Calcd. for $C_{12}H_5O_3Cl_7$: C, 32.36; H, 1.13; Cl, 55.73. Found: C, 32.32; H, 1.33; Cl, 55.9.

4-Carbethoxy-2,3,5,6,7-pentachloroindone (XVII).—The reduction of the ester described previously was conducted with sodium iodide in the manner employed for the methyl homolog, to obtain yellow crystals, m.p. 101–102° (recrystallized from benzene–heptane); λ_{max}^{Nujol} 5.73 (vs) (C=O), 5.78 (s) (C=O), 6.27 (mw) (C=C) and 6.40 μ (m) (C=C).

Anal. Calcd. for $C_{12}H_5O_3Cl_5$: C, 38.49; H, 1.35. Found: C, 38.65; H, 1.42.

4-Carbethoxy-2,2,3,3,5,6,7-heptachloroindan-1-one (XVIII).—The chlorination of 7 g. of XVII was conducted as in the case of the methyl ester, to obtain 4 g. (47%) of nearly colorless crystals, m.p. 97–99° (from heptane); λ_{max}^{Nujol} 5.60 (C=O), 5.70 (sh) (C=O), 6.39 (C=C), and 6.43 μ (sh) (C=C?).

Anal. Calcd. for $C_{12}H_5O_3Cl_7$: C, 32.36; H, 1.13; Cl, 55.73. Found: C, 32.11; H, 1.16; Cl, 56.3.

2-Trichlorovinyl-4,5,6-trichloroisophthalic Acid Methyl Ethyl Ester (XIX).—(A) From 4-carbomethoxy-2,2,3,3,5,6,7-hepta-

---

[14] V. Meyer and J. Sudborough, *Ber.*, **27**, 3149 (1894), reported this ester to melt with decomposition to the anhydride at 142°; the rate of heating was not indicated.

chloroindan-1-one.—A solution of 1 g. of XIII was refluxed with 0.5 g. of soda ash in anhydrous ethanol for 80 min., then cooled, diluted with water, and the organic product extracted with benzene to obtain, on evaporation of the benzene and four recrystallizations from aqueous methanol, 0.5 g. of colorless needles, m.p. 65–66°. (B) From 4-carbethoxy-2,2,3,3,5,6,7-heptachloroindan-1-one.—In an analogous manner, the carbethoxy ketone (XVIII) was treated with methanol and sodium carbonate to obtain colorless needles, m.p. 64.5–65.5°. The two products did not give a depressed mixture melting point and had identical infrared spectra.

Anal. Calcd. for $C_{13}H_8O_4Cl_6$: C, 35.42; H, 1.83. Found: C, 35.37; H, 1.83.

Ultraviolet Spectra of Solutions of Octachloro-3a,4,7,7a-tetrahydro-4,7-methanoindene-1,8-dione (XI) and Ethanolysis Product (XVI) in Ethanol.—Solutions of 0.001 g. of XI in 25 ml. of absolute ethanol plus 0.5 ml. of concentrated hydrochloric acid were made up and examined spectroscopically after standing for various lengths of time at room temperature (24–26°). For comparison, pure XVI also was examined at the same concentration in the alcohol–hydrochloric acid solvent. The results are recorded in Table II.

TABLE II

EXTINCTION COEFFICIENTS OF OBSERVED BANDS[a]

Time	213–214 mμ	235–236 mμ	254 mμ	338–342 mμ
7 min.	13,400	Masked	9100	300
3 hr.	13,100	Masked	Shoulder	2800
24 hr.	Masked	12,200	Masked	5700
2 weeks	Masked	16,400	Masked	5700
Pure compound XVI		15,400		7400

[a] Values of bands at 213–214 and 254 mμ calculated using molecular weight of $C_{10}Cl_8O_2$; values of bands at 235–236 and 338–342 mμ calculated using molecular weight of $C_{12}H_6O_3Cl_7$.

Compound XVI in absolute ethanol without hydrochloric acid had bands at 236 mμ (ε 19,800), 282 (8700), and 340 (9960).

Reaction of Methanol with Tetrachlorocyclopentene-3,5-dione (I) in the Presence of Sodium Carbonate.—To a solution of 23.4 g. (0.1 mole) of tetrachlorocyclopentene-3,5-dione (I) in 100 ml. of methanol was added 10.6 g. (0.1 mole) of anhydrous sodium carbonate over about 5 min. with stirring and cooling to prevent the exothermic reaction from exceeding 40°. A red color developed. After agitating 10 min. longer, the reaction mixture was chilled in the refrigerator overnight, filtered, and the solids washed with water to remove inorganic salts. The undissolved solids were dried in air and recrystallized from heptane to obtain 13 g. (49%) of large colorless prisms, m.p. 91–92° (XXI); $\lambda_{\max}^{\text{Nujol}}$ 5.52 (C=O) and 6.08 μ (C=C). The infrared spectrum was identical with that of an authentic specimen prepared from perchloroprotoanemonin.[1]

TABLE III

3-ARYLOXY-2,4,4,5,5-PENTACHLORO-2-CYCLOPENTENONES (XXIII)

Aryloxy group	Base employed	Yield, %	M.p., °C.	Empirical formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Chlorine, % Calcd.	Chlorine, % Found
Phenoxy (XXIIIa)	NaOH	35	66.5–67.5	$C_{11}H_5O_2Cl_5$	38.13	37.92	1.45	1.52	51.17	51.2
p-Cresoxy	$(C_2H_5)_3N$	45	91.5–92.5	$C_{12}H_7O_2Cl_5$	39.98	39.86	1.96	1.95	49.18	48.9
p-Chlorophenoxy	$(C_2H_5)_3N$	40	92–93	$C_{11}H_4O_2Cl_6$	34.69	34.82	1.06	1.02	55.86	55.8
2,4-Dichlorophenoxy	NaOH	21	72.5–73	$C_{11}H_3O_2Cl_7$	31.81	32.04	0.73	0.74	59.76	59.8
2,4,5-Trichlorophenoxy	$(C_2H_5)_3N$	50	108–108.5	$C_{11}H_2O_2Cl_8$	29.37	29.48	0.45	0.60	63.07	62.6

TABLE IV

3-ARYLOXY-2,4,5,5-TETRACHLORO-2,4-PENTADIENOIC ACIDS (XXIV)

Aryloxy group	M.p., C°	Yield, %	Empirical formula	Neut. equiv. Calcd.	Neut. equiv. Found	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Chlorine, % Calcd.	Chlorine, % Found
Phenoxy (XXIVa)	146–148[a]	[c]	$C_{11}H_6Cl_4O_3$	328.0	330	40.28	40.16	1.84	1.90	43.24	42.7
p-Cresoxy	136–138[b]	20	$C_{12}H_8Cl_4O_3$	342.0	340	42.14	42.04	2.36	2.36	41.47	41.2
p-Chlorophenoxy	140–142[b]	44	$C_{11}H_5Cl_5O_3$	362.4	359	36.45	36.40	1.39	1.34	48.91	48.6
2,4-Dichlorophenoxy	138–139[a]	85	$C_{11}H_4Cl_6O_3$	396.9	392	33.29	33.40	1.02	1.11	53.60	53.2
2,4,5-Trichlorophenoxy	149–150[a]	[c]	$C_{11}H_3Cl_7O_3$	431.3	432	30.63	30.36	0.70	0.91	57.54	56.9

[a] From hexane–benzene. [b] From hexane. [c] Not measured.

This product was converted to perchloroprotoanemonin (identified by melting point and infrared spectrum) by heating with four parts by weight of concentrated sulfuric acid at 140° for 20 min., pouring the mixture onto crushed ice, extracting the resultant mixture with chloroform, and recrystallizing the extracted product from chilled hexane.

Reaction of Hexachloro-2-cyclopentenone (IV) with Methanol in the Presence of Sodium Carbonate.[15]—To a solution of 289 g. (1 mole) of hexachloro-2-cyclopentenone in 1000 ml. of methanol was added 106 g. (1 mole) of anhydrous sodium carbonate with agitation. Water-bath cooling was employed to prevent the temperature from exceeding 50°. After 2 hr., at which time the temperature had declined to 25°, the mixture was filtered, the filtrate evaporated under reduced pressure to remove methanol, and the remaining oil distilled to obtain 206 g. (72.4%) of methyl pentachloropentadienoate (XX), a light yellow liquid, b.p. 68° (0.3 mm.); $\lambda_{\max}$ 5.75 (C=O), 6.18 μ (C=C). The spectrum was identical to that of a sample prepared by methanolysis of pentachloropentadienoyl chloride.[1]

Anal. Calcd. for $C_6H_3Cl_5O_2$: C, 25.34; H, 1.06; Cl, 62.34. Found: C, 25.09; H, 1.02; Cl, 62.1.

3-(Aryloxy)-2,4,4,5,5-pentachloro-2-cyclopentenones (XXIII).—A mixture of 2 moles of the phenol, 1 mole of sodium hydroxide or triethylamine, and 1 mole of hexachloro-2-cyclopentenone was heated on the steam bath until Volhard titration of the chloride ion in an aliquot indicated substantial completion of the reaction (generally 3–12 hr.). The reaction mixture was then stripped free of excess phenol at 0.1–0.5 mm. (maximum pot temperature, 160°), and the residual reaction product then dissolved in hexane. After filtration of insoluble salts, the hexane was chilled and concentrated when necessary to bring about crystallization. The crude products were recrystallized from hexane. The products obtained using various phenols are indicated in Table III.

Methanolysis of 3-Phenoxy-2,4,4,5,5-pentachloro-2-cyclopentenone (XXIIIa).—A solution of 3.46 g. (10 meq.) of XXIIIa in 100 ml. of methanol was refluxed for 60 hr., at which time titration of a small aliquot indicated 85% conversion to a substance acidic to congo red; Volhard titration showed substantially no hydrogen chloride. The methanol was distilled and the residue taken up in water and heptane. The water layer was evaporated and the residue, after drying at 100° under aspirator vacuum, was recrystallized from benzene (filtered hot to remove insolubles) to obtain, on cooling and dilution with heptane, 1 g. of gray crystals, m.p. 129–132°, found by infrared to be 3-hydroxypentachloro-2-cyclopentenone (V).

3-Aryloxy-2,4,5,5-tetrachloro-2,4-pentadienoic Acids (XXIV).—A 0.05-mole sample of aryloxypentachlorocyclopentenone (XXIII) was stirred with 0.2 mole of sodium hydroxide in 4000 ml. of water at 60° until most of the solid dissolved. The solution was filtered and the filtrate acidified with hydrochloric acid. The

---

(15) This reaction was found by Dr. Edward Leon of this laboratory, to whom we are indebted for permission to include it in the present article.

precipitated solid was filtered out and recrystallized from benzene or hexane–benzene mixture. The products obtained are indicated in Table IV.

1-Phenoxy-2,4,4-trichlorocyclopentene-3,5-dione (XXV).—A mixture of 117 g. of tetrachlorocyclopentene-3,5-dione, 51 g. of methylmorpholine, and 250 g. of phenol was heated on the steam bath for 48 hr. The excess phenol was then stripped under vacuum and the remaining material dissolved in benzene. Insoluble salts were filtered out, the mother liquor evaporated, and the remaining liquid distilled to obtain a yellowish liquid, b.p. 129–132° (0.25 mm.). After recrystallization from hexane and aqueous acetic acid, there was obtained 45 g. (31%) of a yellowish solid, m.p. 62–63°.

Anal. Calcd. for $C_{11}H_5Cl_3O_3$: C, 45.32; H, 1.73. Found: C, 45.23; H, 1.69.

Reaction of 1-Phenoxy-2,4,4-trichlorocyclopentene-3,5-dione (XXV) with Methanol.—A solution of 4 g. of XXV in 25 ml. of methanol was refluxed for 36 hr. Titration of an aliquot of the solution to a congo red end point followed by a Volhard titration showed that one molar equivalent of strong acid had been formed, but negligible hydrogen chloride. The reaction mixture was evaporated free of methanol, the residual oil taken up in water, insolubles removed by hexane extraction, and the water solution evaporated under aspirator vacuum on the steam bath. The residual 2 g. of crystalline solid was found by infrared to be identical to the enol III.

Acknowledgment.—The authors wish to acknowledge the assistance of Mr. Abram Davis and Mr. John Michalovic in obtaining and interpreting the spectral data presented herein.

Epimerization of Axial Steroid Alcohols Accompanying Lead Tetraacetate Oxidative Coupling

GEORGE B. SPERO, JOHN L. THOMPSON, WILLIAM P. SCHNEIDER, AND FRED KAGAN

Research Laboratories of The Upjohn Company, Kalamazoo, Michigan

Received January 18, 1963

Reaction of lead tetraacetate with 11β (axial) steroid alcohols results in formation of the same $1\alpha,11\alpha$-epoxides as are obtained from the corresponding 11α (equatorial) epimers. Deuterium labeling experiments show that this unusual epimerization occurs with quantitative retention of the C-11 hydrogen.

A recent communication[1a] reporting the striking epimerization of a secondary alcohol through photolysis of its nitrite ester prompts us to report our experience in epimerization of steroid alcohols with lead tetraacetate.[1b] The reaction of steroid secondary alcohols with lead tetraacetate to effect substitution of an unactivated δ carbon atom which is favorably situated in respect to the hydroxyl, was first reported by Jeger and co-workers.[2] Subsequently additional reports from that group and from others[3a,b,4] followed. With C-11 hydroxylated steroids the $1,11\alpha$-epoxides have been obtained from the 11α-epimers.[5] The 11β-epimers have been reported by various investigators to give only oxidation to the 11-ketone,[6] and $11\beta,18$-epoxide,[7] or, in the presence of iodine, the $11\beta,19$-epoxide.[3]

Our experience with the lead tetraacetate reaction on steroid C-11 alcohols differs from the above reports with respect to the 11β-epimers, in that epimerization accompanies oxidative coupling.

Reaction of either 11β-hydroxyprogesterone bisethylene ketal (Ia) or 11α-hydroxyprogesterone bisethylene ketal (IIa) with lead tetraacetate in boiling cyclohexane gave the same $1\alpha,11\alpha$-epoxide IIIa. The structure of the epoxide was determined by its n.m.r. spectrum and by its conversion to the known 11α-hydroxy-1,4-pregnadiene-3,20-dione (Va)[8a,b] through ketal removal followed by base-catalyzed β-elimination of epoxide bond at C-1.[9] The previous series of conversions was done separately on $1\alpha,11\alpha$-epoxide material derived from both the 11α- and 11β-hydroxy epimers. At all stages, the products (III, IV, and V) were demonstrated to be identical by mixture melting point, rotation, and infrared spectra comparisons. These conversions, in addition to locating the position of the epoxy oxygen, served to establish the α-configuration of the oxygen bond at C-11. A study of models suggested the preferred attachment at C-1 to be on the α side. This is substantiated by the Swiss work.[5] The $1\alpha,11\alpha$-oxygen bridge constrains the A-ring to the boat form providing a rigid A,B,C ring system. This rigidity may explain the failure of the double bond to isomerize from the C-5 to the C-4 position on acid-catalyzed removal of the ketal group as in III → IV.

The yield of epoxide III from the 11α-epimer was about double (50–60%) that obtained from the 11β-epimer (25–30%). A major side reaction of the 11β-epimer was oxidation to 11-ketoprogesterone bisethylene ketal. With both epimers some loss of ketal at C-20 occurred.

In addition to Ia and IIa, a second pair of epimeric steroid C-11 alcohols, 11α- and 11β-hydroxypregnenolone 3-acetate,[10] was similarly treated with lead tetraacetate. Only one epoxide was obtained from both and was designated as $1\alpha,11\alpha$-epoxypregnenolone acetate by analogy with the results obtained from I and II and

[1] (a) A. Nickon, J. R. Mahajan, and F. J. McGuire, *J. Org. Chem.*, **26**, 3617 (1961); (b) After submission of our manuscript, a paper by K. Heusler, J. Kalvoda, G. Anner, and A. Wettstein, *Helv. Chim. Acta*, **46**, 352 (1963), appeared, which also describes the epimerization of steroid hydroxyl groups with lead tetraacetate.

[2] G. Cainelli, M. Lj. Mihailović, D. Arigoni, and O. Jeger, *ibid.*, **42**, 1124 (1959).

[3] (a) Ch. Meystre, K. Heusler, J. Kalvoda, P. Wieland, G. Anner, and A. Wettstein, *Experientia*, **17**, 475 (1961); (b) Ch. Meystre, K. Heusler, J. Kalvoda, P. Wieland, G. Anner, and A. Wettstein, *Helv. Chim. Acta*, **45**, 1317 (1962), and references cited therein.

[4] A. Bowers, E. Denot, L. Cuéllar Ibáñex, Ma. Elena Cabezas, and H. J. Ringold, *J. Org. Chem.*, **27**, 1862 (1962).

[5] J. Kalvoda, G. Anner, D. Arigoni, K. Heusler, H. Immer, O. Jeger, M. Lj. Mihailović, K. Schaffner, and A. Wettstein, *Helv. Chim. Acta*, **44**, 186 (1961).

[6] A. Bowers and E. Denot, *J. Am. Chem. Soc.*, **82**, 4956 (1960).

[7] P. F. Beal and J. E. Pike, *Chem. Ind.*, 1505 (1960).

[8] (a) H. A. Kroll, J. F. Pagano, and R. W. Thoma, U. S. Patent 2,822,-318 (February 4, 1958); (b) S. E. Eppstein, P. D. Meister, and A. Weintraub, U. S. Patent 2,883,400 (April 21, 1959).

[9] The publication by Jeger and co-workers[5] on the preparation and structure proof of IIIa appeared subsequent to completion of our work and followed essentially the same path. Our physical constants for IIIa and IVa are in agreement with those reported by them. The melting point given by Jeger, *et al.*, for Va seems to be in error and does not correspond with ours which is in agreement with that given in ref. 8a,b.

[10] W. J. Wechter and H. C. Murray, *J. Org. Chem.*, **28**, 755 (1963).