pentulofuranose.[16] Recrystallized twice from ether–pentane (1:1, v/v), the derivative (300 mg, 23%) had mp 68°; 2,3-*O*-isopropylidene-D-*threo*-pentulofuranose is recorded as having mp 67–68°.[16] Another sample of **17** was converted into the *p*-bromophenylhydrazone which was recrystallized from ethyl acetate: mp 126–128°, $[\alpha]^{20}D$ +20.2 ± 1.0° (15 min) → −30.8 ± 1.0° (7 days, *c* 0.83, pyridine). For the *p*-bromophenylhydrazone of D-*threo*-pentulose, mp 128–129° and $[\alpha]^{20}D$ +24° (15 min) → −31° (pyridine) have been reported.[17]

**1,4-Anhydro-D-arabinitol (19) from 2,3,5-Tri-*O*-benzyl-D-arabinitol (9).**—To a solution of 2,3,5-tri-*O*-benzyl-D-arabinitol (**9**, 4.22 g, 10 mmoles) in dry pyridine (25 ml) was added dropwise a solution of *p*-toluenesulfonyl chloride (2.0 g, 10.5 mmoles) in chloroform (15 ml) which was held at 0°. The solution was stirred at 0° for 2 hr and at room temperature overnight; water was then added and the product was extracted with dichloromethane. The extract was washed with cold 5% sulfuric acid and with water; moisture was removed with sodium sulfate and the solution was concentrated *in vacuo*. The residual syrup was chromatographed on a column of silica gel using benzene–ether (9:1, v/v) to give 1,4-anhydro-2,3,5-tri-*O*-benzyl-D-arabinitol (**18**, 3.0 g, 74%) as a chromatographically homogeneous syrup, $[\alpha]^{20}D$ +0.6° (*c* 3.17, chloroform). The product was sulfur free and its infrared spectrum showed no hydroxyl absorption.

*Anal.* Calcd for $C_{26}H_{28}O_4$ (404.51): C, 77.20; H, 6.98. Found: C, 76.88; H, 6.78.

A sample of **18** (5.0 g) was dissolved in methanol, palladium chloride (0.6 g) was added, and the suspension was shaken with hydrogen at room temperature until absorption of the gas had ceased. After removal of the catalyst, the solution was stirred with Duolite A-4, filtered through a layer of decolorizing carbon, and concentrated *in vacuo* to a colorless syrup, $[\alpha]^{25}D$ +23.7 ± 0.5° (*c* 2.95, methanol). Defaye[18] reported $[\alpha]^{25}D$ +25.3° (*c* 1.583, methanol) for 2,5-anhydro-D-lyxitol (**19** = 1,4-anhydro-D-arabinitol).

*Anal.* Calcd for $C_5H_{10}O_4$ (134.14): C, 44.77; H, 7.51. Found: C, 44.55; H, 7.47.

Acylation of **19** (1.1 g) with *p*-nitrobenzoyl chloride in conventional fashion yielded 3.7 g (78%) of 1,4-anhydro-2,3,5-tri-*O*-*p*-nitrobenzoyl-D-arabinitol (**20**): mp 78–80°; $[\alpha]^{20}D$ −84.3 ± 0.5° (*c* 1.01, chloroform). After recrystallization from benzene, the substance had mp 80–82°; Defaye[18] reported mp 80–81° and $[\alpha]^{25}D$ −85° (chloroform) for this substance while Barker and Fletcher[8] recorded mp 80–82° and $[\alpha]^{20}D$ +85.1° (chloroform) for its enantiomorph.

**2,3,5-Tri-*O*-benzyl-D-arabinono-1,4-lactone (21).**—2,3,5-Tri-*O*-benzyl-D-arabinofuranose (**8**, 2.0 g) was dissolved in a mixture of dimethyl sulfoxide (6 ml) and acetic anhydride (4 ml) and the resulting solution was stored overnight at room temperature. The reaction mixture was poured into ice water (100 ml) and the mixture stirred for 1 hr, the precipitated solid then being removed by filtration, washed thoroughly with water, and dried: yield, 1.9 g (95%); mp 63–65°. The product thus obtained was homogeneous by tlc (benzene–ether, 9:1, v/v). It was recrystallized from cyclohexane (25 ml) to give 1.66 g of fine needles: mp 67°; $[\alpha]^{22}D$ +6.8° (*c* 1.1, chloroform). The infrared spectrum of the substance showed the absorption at 1775 $cm^{-1}$ characteristic of a γ-lactone.

*Anal.* Calcd for $C_{26}H_{26}O_5$ (418.50): C, 74.62; H, 6.26. Found: C, 74.91; H, 6.54.

***N*-Benzyl-2,3,5-tri-*O*-benzyl-D-arabinonamide (22).**—The lactone (**21**, 2 g) was dissolved in benzene (35 ml), benzylamine (5 ml) was added, and the mixture was stirred at room temperature for 2 hr and, finally, boiled gently under reflux for 1 hr. The cooled solution was diluted with benzene and washed successively with 5% hydrochloric acid, aqueous sodium bicarbonate solution, and water. Moisture was removed with magnesium sulfate and the solution was concentrated to give a crystalline residue (2.4 g). Tlc, using benzene–ether (9:1, v/v), showed that the product was contaminated with two faster moving components; no **21** was detected. The crude amide was chromatographed on a column of silica gel using benzene–ether (7:3, v/v), giving, in fractions 35–58, a chromatographically homogeneous material: yield, 2.1 g (84%); mp 91–93°. Recrystallization from ethyl acetate–pentane afforded 1.85 g of the pure amide (**22**): mp 95–96°; $[\alpha]^{20}D$ +37.6 ± 0.5° (*c* 1.78, chloroform).

*Anal.* Calcd for $C_{33}H_{35}NO_5$ (525.65): C, 75.40; H, 6.71; N, 2.66. Found: C, 75.24; H, 6.68; N, 2.70.

**Registry No.**—**2**, 14233-48-8; **3**, 14233-49-9; **4**, 14233-50-2; **5**, 14233-51-3; **6**, 14233-52-4; **7**, 87-79-6; **9**, 14233-53-5; **10**, 14233-54-6; **11**, 14233-55-7; **12**, 14233-56-8; **13**, 14233-57-9; **14**, 14233-58-0; **15**, 14233-59-1; **16**, 14233-60-4; **17**, 14233-61-5; **18**, 14233-62-6; **19**, 14233-63-7; **21**, 14233-64-8; **22**, 14233-65-9.

**Acknowledgment.**—We are indebted to the staff of the Section on Microanalytical Services and Instrumentation of this institute for elemental analyses and optical rotations.

# Photoinduced Reactions. VIII.[1,2] Photosensitized Oxidation of 3,5-Dihalogenophloretic Acids

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*Received February 14, 1967*

In order to elucidate the mechanism by which 3,5-diiodophloretic acid (I) is autoxided to 3,5,3′,5′-tetraiodothyropropionic acid (II), compound I was oxidized with various oxidizing agents, some of which are known to be one-electron transfer oxidizing agents. A small amount of II was detected in the reaction product in one case, while in others only polymers were formed. However, photooxidation of I in the presence of a sensitizer as well as oxidation with hypochlorite or with N-bromosuccinimide did not lead to dimerization or polymerization but to the formation of a spirolactone, 7,9-diiodo-1-oxaspiro[4,5]deca-6,9-diene-2,8-dione. Similar results were obtained with 3,5-dibromo- and 3,5-dichlorophloretic acid. Possible mechanisms for the formation of the spirolactone are discussed.

The last step in the biosynthesis of thyroxine is the conversion of 3,5-diiodotyrosine to thyroxine. Since an elucidation of the mechanism by which this conversion takes place is rendered difficult by the fact that the enzyme systems involved are not sufficiently known, nonenzymic model reactions have been investigated by several workers. These may be classified into two types. One of these, first described by von Mutzenbecher,[3] is the formation of thyroxine by incubation of diiodotyrosine at a slightly alkaline pH. The second kind of model reaction was first proposed by Hillmann[4] and later successfully carried out by Meltzer and Stana-

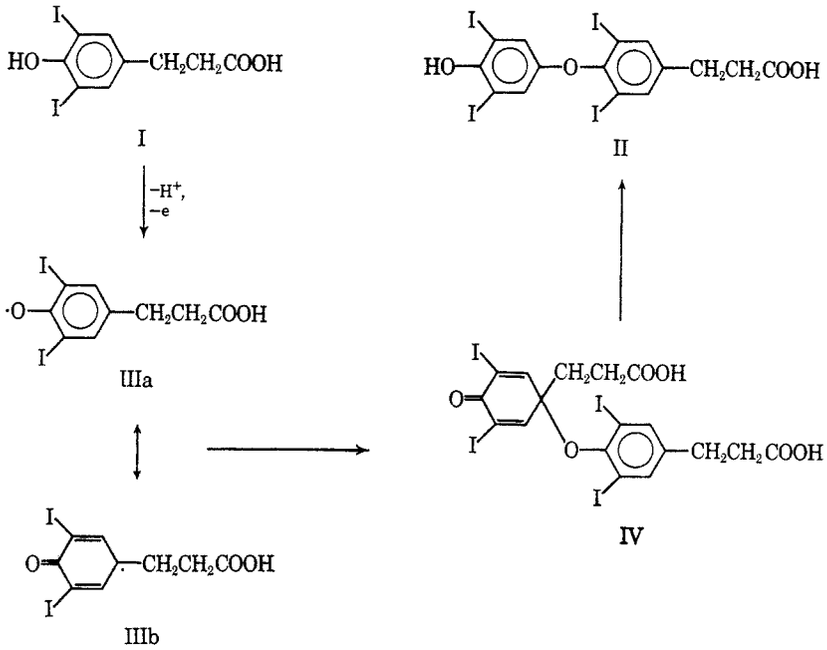
(1) Part VII: T. Matsuura and K. Ogura, *J. Am. Chem. Soc.*, **89**, 3850 (1967).

(2) This work was supported by Public Health Service Research Grant AM 07955 from the National Institute of Arthritis and Metabolic Diseases.

(3) P. von Mutzenbecher, *Z. Physiol. Chem.*, **261**, 253 (1939).

(4) G. Hillmann, *Z. Naturforsch.*, **11B**, 424 (1956).

SCHEME I




back.[5] It is the formation of thyroxine by the reaction of diiodotyrosine with its keto acid analog, 4-hydroxy-3,5-diiodophenylpyruvic acid, in the presence of oxygen and at neutral pH. This second type of model reaction was studied in detail by various workers.[6] Mechanisms which involve a phenoxy radical intermediate have been suggested.[6d,7-9]

The von Mutzenbecher reaction has been extended to the formation of derivatives of thyroxine from the corresponding derivatives of diiodotyrosine, including peptide-linked ones.[10] Matsuura and Cahnmann applied this type of model reaction to deamino side chain analogs of diiodotyrosine and found that the propionic acid analog, 3,5-diiodophloretic acid (I), gave the highest yield of the corresponding thyroxine analog, 3,5,3′,5′-tetraiodothyropropionic acid (II).[11] In the course of this reaction, the aliphatic side chain was eliminated mainly as hydracrylic acid and to a minor extent as dihydracrylic acid.[12] These results are compatible with the mechanism shown in Scheme I which is a modification of the mechanism proposed by Johnson and Tewkesbury[13] for the formation of thyroxine from diiodotyrosine.

According to this mechanism, diiodophloretic acid (I) is first oxidized to the phenoxy radical III, of which two resonating forms (IIIa and IIIb) are shown. Two molecules of the radical then couple to form the quinol ether IV, which is finally converted to 3,5,3′,5′-tetraiodothyropropionic acid (II) by elimination of the side chain attached to the dienone ring of IV. If Scheme I shows the correct mechanism for the formation of II in a Mutzenbecher-type autoxidation of I, then it is logical to assume that any oxidizing agent capable of oxidizing I to its phenoxy radical (III) will also be able to convert I to II. Many examples for the formation of naturally occuring phenol dimers by radical coupling in the presence of one-electron-transfer oxidizing agents have been cited in the literature.[14,15]

In the work described in the present communication, 3,5-diiodophloretic acid was permitted to react with various one-electron-transfer oxidizing agents. In addition, the photooxidation of 3,5-dihalogenophloretic acids with oxygen in the presence of a sensitizer was investigated since this method of oxidation also seems to involve the intermediary formation of a phenoxy radical *via* the transfer of a single electron.[16]

## Results and Discussion

When such one-electron-transfer oxidizing agents as alkaline ferricyanide[17] or tri-*t*-butylphenoxy radical[18] were permitted to react with 3,5-diiodophloretic acid (I), the reaction products consisted only of intractable polymers in addition to some unchanged starting material. No formation of the thyroxine analog (II) was observed. The formation of polymers in the oxidative coupling of a phenol is inevitable if the dimeric coupling product is a phenol which again can undergo oxidative coupling. This may account for the results obtained by

(5) R. I. Meltzer and R. J. Stanaback, *J. Org. Chem.*, **26**, 1977 (1961).

(6) For example, see (a) T. Shiba and H. J. Cahnmann, *ibid.*, **27**, 1773 (1962); (b) A. Nishinaga and T. Matsuura, *ibid.*, **29**, 1812 (1964); (c) T. Shiba, H. J. Cahnmann, T. Matsuura, A. Nishinaga, and H. Sakamoto, *ibid.*, **29**, 3061 (1964); (d) Y. Matsuura, H. Kon, and H. J. Cahnmann, *ibid.*, **29**, 3058 (1964).

(7) T. Matsuura and A. Nishinaga, *J. Chem. Soc. Japan, Pure Chem. Sect.*, **86**, 282 (1965).

(8) H. Blasi, *Biochim. Biophys. Acta*, **121**, 204 (1966).

(9) Recent work by A. Nishinaga, H. Kon, T. Matsuura, and H. J. Cahnmann (unpublished data) indicates that although the phenoxy radical of 4-hydroxy-3,5-diiodophenylpyruvic acid most likely is an intermediate in the reaction; it does not react directly with diiodotyrosine, but is first converted to a peroxide.

(10) (a) R. Pitt-Rivers, *Biochem. J.*, **43**, 223 (1948); (b) R. Pitt-Rivers and A. T. James, *ibid.*, **70**, 173 (1958); (c) M. Sela and S. Sarid, *Nature*, **178**, 540 (1956).

(11) T. Matsuura and H. J. Cahnmann, *J. Am. Chem. Soc.*, **81**, 871 (1959).

(12) H. J. Cahnmann and T. Matsuura, *ibid.*, **82**, 2050 (1960).

(13) T. B. Johnson and L. B. Tewkesbury, Jr., *Proc. Natl. Acad. Sci. U. S.*, **28**, 73 (1942).

(14) For reviews, see (a) D. H. R. Barton and T. Cohen, "Festschrift Arthur Stoll," Birkhäuser, Basel, 1959, p 117; (b) H. Erdtman and C. A. Wachtmeister, *ibid.*, p 144.

(15) D. H. R. Barton, *Proc. Chem. Soc.*, 293 (1963).

(16) T. Matsuura, K. Omura, and R. Nakashima, *Bull. Chem. Soc. Japan*, **38**, 1358 (1965).

(17) Alkaline ferricyanide is known to be an oxidizing agent capable of converting phenols to the corresponding phenoxy radicals. For example, see (a) C. D. Cook and R. C. Woodworth, *J. Am. Chem. Soc.*, **75**, 6242 (1953); (b) E. Müller and K. Ley, *Chem. Ber.*, **87**, 922 (1954).

(18) See ref 17b.

TABLE I

SUMMARY OF DATA FOR THE OXIDATION OF 3,5-DIIODOPHLORETIC ACID (I) WITH VARIOUS OXIDIZING AGENTS IN AQUEOUS MEDIA

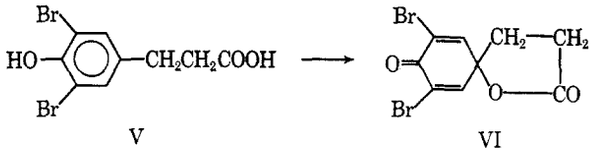
| Oxidizing agent (mole equiv) | pH | Recovered I, % | Reaction products |
|---|---|---|---|
| $K_3Fe(CN)_6$ (1) | 7.4–7.6 | 92 | ... |
| $K_3Fe(CN)_6$ (1) | 8.1–8.3 | 50 | Polymers, II (trace) |
| $K_3Fe(CN)_6$ (1) | 12 | ... | Polymers |
| $MnO_2$ (1) | 9.1–9.4 | 79 | Polymers |
| $MnO_2$ (4) | 7.6–7.8 | 67 | Polymers |
| $KMnO_4$ (1.5) | 7.8–8.1 | 48 | Polymers |
| $Ce(SO_4)_2$ (3) | 7.0–7.5 | 39 | Polymers |
| $H_2O_2$ (10) | 9.0–10.0 | 91 | ... |
| $NaClO_3$ (0.33) | 8.0 | 100 | ... |
| $FeSO_4$–ascorbic acid–$O_2$ | 7.5 | 90 | ... |
| 2,4,6-Tri-*t*-butylphenoxy[a] (1) | ... | ... | Polymers |
| $Na_2S_2O_8$ (2) | 7.7–7.9 | 8 | VII (10%)[b] |

[a] The reaction was carried out in a mixture of benzene and ethyl acetate. The phenoxy radical solution in benzene was slowly added under nitrogen to a solution of I in ethyl acetate. [b] Based on reacted starting material.

us. Since 3,5,3′,5′-tetraiodothyropropionic acid (II) is only sparingly soluble in aqueous media at pH 7.5, it precipitates out of solution in the course of the von Mutzenbecher-type autoxidation of I.[11] The oxidation of I with suitable oxidizing agents other than oxygen in aqueous media at neutral or slighlty alkaline pH was therefore expected to yield II also in the form of a precipitate and it was thought that this might minimize any further oxidation to polymers. However, when I was treated with ferricyanide at pH 7.5, only unchanged starting material was recovered while oxidation at pH 8.1 yielded a minute amount of the thyroxine analog (II) in addition to polymers and starting material. No tetraiodothyropropionic acid (II) could be detected when permanganate, manganese dioxide, or ceric sulfate was used as the oxidizing agent in the range of pH 7–9. Other oxidizing agents such as hydrogen peroxide, sodium chlorate, and ferrous ion–ascorbic acid–oxygen[19] did not react at all with I in aqueous media at pH 7–9. The results are summarized in Table I.

Matsuura and Omura investigated the photosensitized oxidation of hindered phenols which lead to various oxidation products. They suggested that the results can be rationalized by the intermediary formation of phenoxy radicals.[16] This method was applied to the oxidation of I in order to see whether I can be oxidized to II *via* the phenoxy radical III. When a solution of I in phosphate buffer, pH 7.6, was irradiated with a tungsten lamp in the presence of erythrosin while oxygen was bubbled through the reaction mixture, a neutral product $C_9H_6O_3I_2$ was obtained in 18% yield, but no formation of II was observed. The same diiodo compound was also obtained in 24% yield when I was treated with N-bromosuccinimide according to the procedure described by Schmir, Cohen, and Witkop[20] for the preparation of a dibromospirolactone (VI) from 3,5-dibromophloretic acid (V).

The diiodo compound showed infrared bands at 1765 ($\gamma$-lactone) and 1673 $cm^{-1}$ (unsaturated ketone) and an

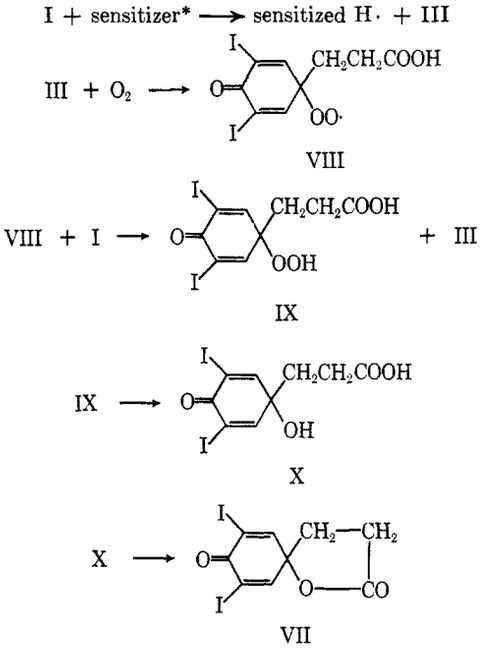


V VI

ultraviolet maximum at 263 m$\mu$ ($\epsilon$ 2800). These data are consistent with a spirolactone structure (VII). A similar photosensitized oxidation of 3,5-dibromophloretic acid (V) yielded the dibromospirolactone (VI) in 23% yield. Both acids I and V were recovered unchanged after photooxidation without sensitizer.

The two pathways given (A and B) may be considered for the formation of the spirolactone VII (as well as of VI) by photooxidation in the presence of a sensitizer. In pathway A, the excited sensitizer abstracts a hydrogen atom from I to yield the radical III in accordance with previous postulates.[16,21,22] This radical combines with triplet oxygen molecule in the ground state to form a hydroperoxy radical (VIII) which is then reduced and lactonized to the spirolactone VII *via* the hydroperoxide IX and the hydroxy acid X.

pathway A



Nickon and Bagli suggested that the photosensitized oxygenation of an allylic system (–C=CCH–) leading to an allylic hydroperoxide (–C(OOH)–C=C–) may proceed *via* the addition of photochemically activated oxygen to this system.[23] Such a mechanism is also applicable to our cases. In pathway B, reactive oxygen, either a sensitizer oxygen complex as proposed by Schenck[24] or singlet excited oxygen, reacts with I by

(19) (a) S. Udenfriend, C. T. Clark, J. Axelrod, and B. B. Brodie, *J. Biol. Chem.*, **208**, 731 (1954); (b) B. B. Brodie, J. Axelrod, P. A. Shore, and S. Udenfriend, *ibid.*, **208**, 741 (1954); (c) R. Breslow and L. N. Lukens, *ibid.*, **235**, 290 (1960).

(20) G. L. Schmir, L. A. Cohen, and B. Witkop, *J. Am. Chem. Soc.*, **81**, 2228 (1959); also see E. J. Corey and L. F. Haffele, *ibid.*, **81**, 2225 (1959).

(21) (a) L. I. Grossweiner and E. F. Zwicker, *J. Phys. Chem.*, **67**, 549 (1963); (b) E. J. Land and G. Porter, *Trans. Faraday Soc.*, **59**, 2061 (1963); (c) J. O. Roebber, *J. Chem. Phys.*, **37**, 1974 (1962).

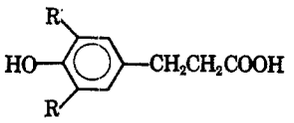
(22) Another one-electron-transfer mechanism must be excluded because it would require the abstraction of an electron not only from the phenoxy ion but also from the carboxylate ion of the diiodophloretic acid which seems most unlikely on account of the high energy necessary for such an electron abstraction.

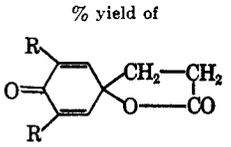
(23) A. Nickon and J. F. Bagli, *J. Am. Chem. Soc.*, **81**, 6330 (1959); **83**, 1498 (1961).

(24) G. O. Schenck, *Angew. Chem.*, **69**, 579 (1957).

TABLE II

REACTION OF 3,5-DIIODO- AND 3,5-DICHLOROPHLORETIC ACIDS WITH HYPOCHLORITE AND HYDROGEN PEROXIDE IN AQUEOUS METHANOL

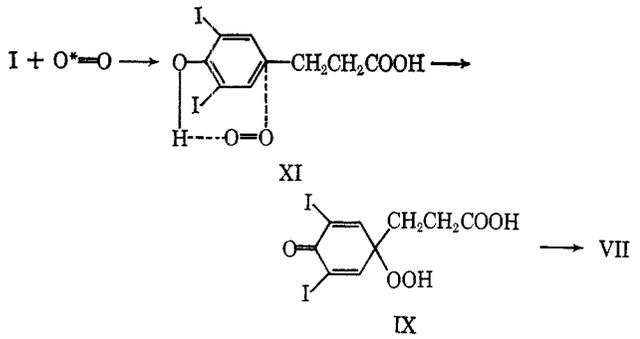




| R | mmoles | NaOCl, mmoles | $H_2O_2$, mmoles | % yield of |
|---|---|---|---|---|
| I | 5 | 17 | 18 | 12 |
| I | 5 | 5.3 | 6.3 | 28[a] |
| I | 2 | 2.1 | 0 | 38[a] |
| I | 2 | 0 | 14[b] | 3 |
| Cl | 5 | 5.3 | 6.3 | 24 |
| Cl | 5 | 5.3 | 0 | 43 |

[a] Based on reacted starting material. [b] The reaction was carried out in the presence of 0.5 ml of concentrated hydrochloric acid in order to see whether diiodophloretic acid reacts with hydrogen peroxide in acidic media.

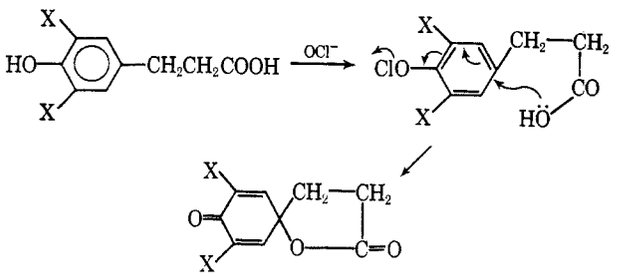
pathway B



a 1,6 addition to form a hydroperoxide (IX)[25] which is then converted to the spirolactone VII as shown for pathway A.[26]

Recently the suggestion that singlet excited oxygen is involved in dye-sensitized photooxygenation of olefins and polycyclic aromatic hydrocarbons was strengthened when several workers demonstrated that singlet oxygen, which can be generated from hydrogen peroxide and hypochlorite, is capable of converting these unsaturated compounds to the same products that are obtained in the photosensitized reaction.[27] Therefore we examined the reaction of dihalogenophloretic acids with hydrogen peroxide and hypochlorite under conditions similar to those described by Foote, *et al.*[27a] When I was oxidized with 3 molar equiv of hydrogen peroxide and hypochlorite, spirolactone VII was obtained in 12% yield and with equimolar amounts of the reagents in 28% yield. However, the spirolactone VII was obtained in even higher yield (38%) with hypochlorite alone (Scheme II), while I hardly reacted with hydrogen peroxide in the absence of hypochlorite. Dichlorophloretic acid also gave a spirolactone, analogous to VII, by the action of hypochlorite with or without hydrogen peroxide. The results are summarized in Table II.

SCHEME II



VI, X = Br
VII, X = I

These results indicate that the formation of the spirolactones VI and VII by hypochlorite oxidation of the corresponding dihalogenophloretic acid does not proceed *via* the addition of singlet excited oxygen but by a two-electron-transfer process similar to the one proposed by Iwasaki and Witkop for the electrolytic oxidation of tyrosine derivatives.[28] Whether the photochemical formation of spirolactones does or does not involve singlet oxygen cannot be decided on the basis of our experiments with hypochlorite and hydrogen peroxide.

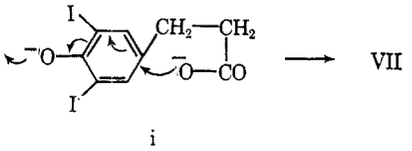
Possible mechanism for the photochemical formation of spirolactones is the initiation of the process by excitation of a charge-transfer complex between the dihalogenophloretic acid and the dye, followed by an attack of the excited complex by ground-state oxygen. Such a mechanism was originally postulated by Fiala.[29] We were unable to detect any charge-transfer absorption in the electronic spectrum of a mixture of I and erythrosin in phosphate buffer, pH 7.6.

## Experimental Section

Melting points were determined in capillary tubes and are uncorrected. Infrared spectra were measured with a JASCO IR-S spectrophotometer and ultraviolet spectra with a Shimazu SV-50 spectrophotometer.

(25) We are indebted to Dr. H. J. Cahnmann, National Institutes of Health, Bethesda, Md., and Dr. C. H. Krauch, Max Planck Institute für Kohlenforschung, Mühlheim, Ruhr, for having suggested this mechanism as a possibility.

(26) As a possible explanation, a pathway involving two electrons abstraction from the dianion i was also taken into consideration. However, this pathway is unlikely since VII was isolated from the acidic and not from the neutral fraction of the reaction mixture.



i

(27) (a) C. S. Foote and S. Wexler, *J. Am. Chem. Soc.*, **86**, 3879, 3880 (1964); (b) C. S. Foote, S. Wexler, and W. Ando, *Tetrahedron Letters*, No. 46, 4111 (1965); (c) E. J. Corey and W. C. Taylor, *J. Am. Chem. Soc.*, **86**, 3881 (1964); (d) K. R. Kopecky and H. J. Reich, *Can. J. Chem.*, **43**, 2265 (1965).

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**Photosensitized Oxidation. A. Of 3,5-Diiodophloretic Acid (I).**—A solution of 2.09 g (5 mmoles) of 3,5-diiodophloretic acid[30] and 0.16 g of erythrosin in 180 ml of 0.05 *M* phosphate buffer, pH 7.60, was irradiated for 6.5 hr with a 500-w tungsten lamp which was placed at a distance of 2 cm from the reaction vessel. During irradiation, oxygen was bubbled through the solution which was cooled with ice water by means of a cold finger so that the reaction temperature was kept between 21 and 23°. The reaction mixture (pH 7.47) was acidified with 6 *N* hydrochloric acid and extracted with 150 ml of ether. The ethereal extracts were washed with aqueous bicarbonate solution to separate acidic products. The ethereal layer was evaporated to give a small amount of a light brown oil, in which the spirolactone VII could not be detected by chromatographic fractionation on silica gel. The bicarbonate extracts were acidified with 6 *N* hydrochloric acid and extracted with 200 ml of ether. After evaporation of the ethereal layer, the residual oil (1.67 g) was chromatographed on 35 g of silica gel. Elution with chloroform–acetone (99:1) yielded 0.37 g (18%) of the crude spirolactone VII. The crude product was digested with ether and the crystals thus obtained were recrystallized from aqueous acetonitrile to yield needles, mp 214–216°, whose infrared spectrum was identical with that of an authentic specimen.

A solution of 2.09 g of I in 200 ml of phosphate buffer, pH 7.6, was irradiated without erythrosin for 8 hr as described above. After working up the reaction mixture, 1.83 g (88%) of I was recovered.

**B. Of 3,5-Dibromophloretic Acid (V).**—A solution of 1.20 g (3.7 mmoles) of 3,5-dibromophloretic acid and 0.16 g of erythrosin in 200 ml of 0.05 M phosphate buffer, pH 7.6, was irradiated for 10 hr under similar conditions to those described under A. The acidic products were chromatographed on 35 g of silica gel. Elution with chloroform–ether (50:1) yielded 0.28 g (24%) of the crude spirolactone VI which, after digestion with ether, gave needles, mp 170–173° (lit.[20] mp 174–176°), whose infrared spectrum was identical with that of an authentic specimen.[20]

**7,9-Diiodo-1-oxaspiro[4.5]deca-6,9-diene-2,8-dione (VII). A. With N-Bromosuccinimide.**—3,5-Diiodophloretic acid (I, 4.18 g) was treated with N-bromosuccinimide according to the procedure described by Schmir, *et al.*[20] The spirolactone VII was obtained as needles (from acetone): mp 225–226° dec; yield, 24%; $\nu_{max}^{Nujol}$ 1790, 1688, and 1608 cm$^{-1}$; $\lambda_{max}^{EtOH}$ 263 mμ (ε 2800) and 295 (2400).

*Anal.* Calcd for $C_9H_6O_3I_2$: C, 25.97; H, 1.45. Found: C, 26.20; H, 1.65.

**B. With Hypochlorite and Hydrogen Peroxide.**—The procedure was essentially the same as that described by Foote and Wexler.[27a] In a typical run, 13 ml (17 mmoles) of 10% aqueous sodium hypochlorite was added below 10° to a solution of 2.1 g (5 mmoles) of 3,5-diiodophloretic acid and 2 ml (18 mmoles) of 30% hydrogen peroxide in 50 ml of methanol in the course of 30 min. Inorganic salts deposited were filtered off and the filtrate was acidified with dilute hydrochloric acid containing a small amount of sodium bisulfite and concentrated under reduced pressure. The mixture was extracted with ether and the ethereal extract was washed with aqueous bicarbonate, then with water, and evaporated. Chromatographic separation of the residue on silica gel yielded 0.25 g (12%) of the spirolactone VII. Several modifications of this reaction were carried out under similar conditions as summarized in Table II.

**C. With Persulfate.**—A solution of 1.37 g (6 mmoles) of ammonium persulfate in 10 ml of water was aded to a solution of 1.28 g (3 mmoles) of 3,5-diiodophloretic acid in 26 ml of 0.25 *N* potassium hydroxide. The mixture was stirred under nitrogen for 50 min, during which period aqueous potassium hydroxide was added from time to time in order to keep the pH of the mixture between 7.7 and 7.9. The reaction mixture was separated into a neutral and an acidic fraction. From the neutral fraction 0.10 g of the spirolactone VII was isolated and from the acidic fraction 0.23 g of the acid I was recovered. The total yield of VII was 10% on the basis of the reacted I.

**7,9-Dichloro-1-oxaspiro[4.5]deca-6,9-diene-2,8-dione.**—This compound was prepared by a procedure similar to that for the preparation of the diiodospirolactone VII (method B). The results are summarized in Table II: mp 155–157°; $\nu_{max}^{Nujol}$ 1790, 1687, and 1610 cm$^{-1}$; $\lambda_{max}^{EtOH}$ 248 mμ (ε 12,800).

*Anal.* Calcd for $C_9H_6O_3Cl_2$: C, 46.38; H, 2.60. Found: C, 46.34; H, 2.82.

**Oxidation of 3,5-Diiodophloretic Acid (I).**—The reaction conditions and the results are summarized in Table I. From 1 to 10 mmoles of 3,5-diiodophloretic acid was dissolved in the minimum amount of 1 *N* potassium hydroxide required for complete dissolution. The solution was adjusted to the desired pH by the addition of alkali or acid and to a molarity of 0.10–0.15 by dilution with water; then the oxidizing agent was added. During the reaction period, the pH of the mixture was kept constant by the addition of alkali or acid. In those cases in which the oxidizing agent was completely consumed in the course of the reaction, the reaction mixture was extracted with 1-butanol after the addition of enough sodium hydroxide to make the mixture about 1 *N* with respect to sodium hydroxide. In other cases, the reaction mixture was acidified with hydrochloric acid, then extracted with 1-butanol, and the butanol extracts washed with 1 *N* sodium hydroxide. After evaporation of the butanol, acidification of the residue yielded 3,5,3′,5′-tetraiodothyropropionic acid (II) whenever it was formed in the reaction. The aqueous layer was acidified with hydrochloric acid and extracted with ether. The ethereal extract was evaporated to give a residue, from which 3,5-diiodophloretic acid (I) was recovered by recrystallization. Intractable material obtained in the course of the oxidation was regarded as polymers and was not further investigated.

**Registry No.**—I, 13811-11-5; V, 13811-12-6; VII, 13811-13-7; 7,9-dichloro-1-oxaspiro[4.5]deca-6,9-diene-2,8-dione, 13811-15-9; 3,5-dichlorophloretic acid, 13811-16-0.

**Acknowledgment.**—The authors wish to express their hearty thanks to Dr. H. J. Cahnmann, National Institutes of Health, Bethesda, Md., for his discussion throughout this work.

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# The Preparation and Properties of Bis(phosphoranylidene)ammonium Chlorides

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*Received March 24, 1967*

Methods have been developed for the preparation of both symmetrical and unsymmetrical bis(phosphoranylidene)ammonium chlorides. The former compounds were synthesized by the pyrolysis of aminophosphonium chlorides, whereas the unsymmetrical compounds were prepared from the reaction of N-lithiophosphinimines with tertiary phosphine dichlorides. Other reactions of the N-lithiophosphinimines are reported. The spectral characterization and the thermal and hydrolytic stabilities of the bis(phosphoranylidene)ammonium chlorides are also discussed.

In recent years considerable attention has been directed toward saltlike compounds containing a [≥P=N=P<]$^+$ moiety in which the positive charge is distributed over all three atoms. Nearly all of the work has centered on compounds (*e.g.*, Ia–d) which appear to be intermediates in the syntheses of phosphoni-

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