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154. **Fumio Kai and Shigeo Seki**: Studies on Acetylenic Compounds Ⅳ.[*1] Synthesis and Oxygenolytic Solvolysis of Tri- and Tetra-iodoallene.

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In the preliminary communication[1] the authors described the new reactions concerning the formation of tri- and tetra-iodoallene (Ⅲ and Ⅳ) from 1,3-diiodopropropyne (Ⅱ) and the oxygenolytic alcoholysis of Ⅳ to yield alkyl triiodoacrylate (XIII). Further investigation on the initial reactions has now disclosed a part of the interesting nature of this new class of compounds.

In this report, the authors describe synthesis and oxygenolytic solvolysis of Ⅲ and Ⅳ in detail as well as the discussion on the reaction mechanism in the formation and the oxygenolysis of them.

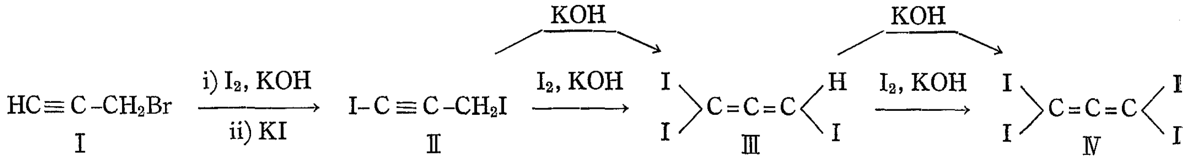

Chart 1.

Synthesis of Tri- and Tetraiodoallene

3-Bromo-1-propyne (I) was iodinated with one mole of iodine and potassium hydroxide in aqueous methanol at 10~25° and the resulting reaction mixture was saturated with potassium iodide to make the bromine-iodine exchange complete. Distillation of the ether extract of the filtrate diluted with water gave 1,3-diiodopropyne (Ⅱ) in a fairly good yield (58 %).

Reaction of Ⅱ with about one mole of potassium hydroxide in methanol or aqueous methanol at 60° gave Ⅲ, pale yellow plates, m.p. 80~82° (decomp.), in 80% yield. Ⅲ could be recrystallized from carbon tetrachloride or methanol. Sodium methoxide in absolute methanol also could be used instead of potassium hydroxide to give the same result. As a more convenient procedures for preparation of Ⅲ, reaction processes, I→Ⅱ and Ⅱ→Ⅲ are recommended to be carried out without isolation of Ⅱ, from where Ⅲ was obtained in 50~67% yield based on I.

Convertion of Ⅱ to Ⅲ by the action of alkali hydroxide or alkali alkoxide as catalyst involves an intermolecular transfer reaction of iodine. However, one iodine atom in Ⅲ need not necessarily be introduced intermolecularly. Thus, when one mole of the iodinating reagent (iodine and potassium hydroxide) was reacted on Ⅱ in aqueous methanol at 60°, Ⅲ was also obtained in 70% yield. Analogously, Ⅲ was converted to Ⅳ by the action of potassium hydroxide as well as by the action of iodine and potassium hydroxide. Dilution of the reaction mixture with water gave large yellow crystals (Ⅳ) which could be recrystallized from proper solvent, *e.g.*, methanol, carbon tetrachloride or acetic acid. Pure Ⅳ thus obtained, yellow prisms or plates, melted at 93~94° with decomposition. The reaction Ⅲ→Ⅳ by the action of potassium hydroxide gave a remarkably lower yield and required more drastic

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[*1] The earlier published works on this subject should be entitled according to the following partition : Part I. Arg. Biol. Chem. (Tokyo), **27**, 150 (1963). Part Ⅱ. This Bulletin, **11**, 1205 (1963). Part Ⅲ. RADIOISOTOPES (Tokyo), **14**, 480 (1965).

[*2] Morooka, Kohoku-ku, Yokohama (甲斐文夫, 関 誠夫).

conditions than the convertion, Ⅱ→Ⅲ, with potassium hydroxide. By the use of iodine and potassium hydroxide, however, Ⅲ could be converted to Ⅳ in 70% yield. The best yield of Ⅳ based on I could be achieved when the reaction processes (I→Ⅳ) were performed according to the procedures described above without isolating any intermediate compound. The reactions are summarized in Chart 1. They show the close resemblance in chemical reactivites between acetylenic and allenic compound, particulary in the reactivities of ethynyl and 1,2-propadienyl hydrogen or iodine, both having positive character and ease of removal by the attack of alkali reagent.

The infrared absorption spectra of Ⅱ, Ⅲ and Ⅳ are shown in Fig. 1. Ⅲ and Ⅳ show a strong allenic absorption band each at 1928 and 1915 cm^{-1} in carbon tetrachloride due to the C=C=C bond streching.2) The C–H streching vibration of Ⅲ appears at 3050 cm.$^{-1}$ Ⅱ shows a strong band at 2200 cm^{-1} due to the C≡C bond streching and a band in the region of C=C=C streching vibration frequency. The nuclear magnetic resonance spectrum of Ⅲ in carbon tetrachloride shows one singal at 4.55τ due to the allenic hydrogen of Ⅲ.[*3] Ⅳ showed no proton magnetic resonance in carbon tetrachloride. Molecular weight determinations of Ⅲ and Ⅳ by the method of freezing point depression of benzene solution gave the good agreement with the calculated values.1) Reduction of Ⅱ, Ⅲ and Ⅳ with sodium borohydride in ethanol at 50° released the quantitative amount of iodide ions (two, three and four moles, respectively) which were titrated with a standard solution of potassium iodate.

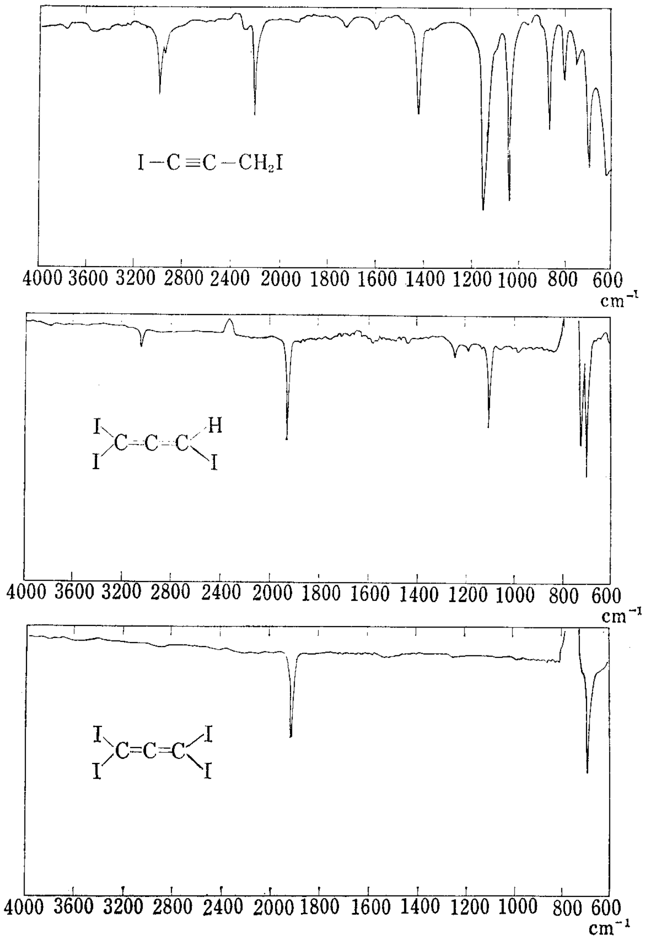

Fig. 1. Infrared Spectra of Ⅱ (liquid film), Ⅲ, Ⅳ (in CCl$_4$)

The experimental results mentioned above combined with the results of the elemental analyses confirmed the structures, Ⅱ, Ⅲ and Ⅳ. Further chemical evidences for the structures, Ⅲ and Ⅳ are provided by the results of the oxygenolytic solvolysis of them as described below.

Reaction Mechanism in the Formation of Tri- and Tetraiodoallene (III and IV) from 1,3-Diiodopropyne (II)

[*3] The number of the hydrogen in one molecule of Ⅲ was determinated as follows. The NMR spectrum of a mixture of Ⅲ and a reference compound (XⅢb) (molar ratio 3:1) in CCl$_4$ showed two sharp singlet signals of equal integrated intensity at 4.55 and 6.12 τ. A single solution of XⅢ in CCl$_4$ gave a singlet signal at 6.12 τ. The NMR spectra of Ⅲ, Ⅳ and XⅢb were taken on Varian Associates A-60 recording spectrometer and others on JNM-C-60 recording spectrometer (Japan Electron Optics Laboratory Co., Ltd.), at 60 Mc. with tetramethylsilane as internal standard.

1) F. Kai, S. Seki: This Bulletin, **13**, 1374 (1965).

2) J.H. Wotiz, D.E. Mancuso: J. Org. Chem., **22**, 207 (1957).

As shown in Chart 2, from consideration of the well-known reactions concerning acetylene-allene rearrangement, it can be noted that the three-carbon acetylenic system (Ⅴ)3) with an electro-negative group X is favored for the prototropic rearrangement under relatively mild reaction conditions to afford the corresponding substituted allene (Ⅶ). 3-Halo-1-propynes which are expected to be activated for theabove prototropic rearrangement by the electron-withdrawing effect of the halogen atom, however, react with various bases to give the ordinary substitution products, 2-propynyl-alcohols4), -ethers5), -thioethers6) or -amines7) Now, if a stronger cationoid reagent $Y^{\oplus}$ which reacts in alkaline medium exist in the reaction of Ⅴ or 3-halo-1-propynes with bases, it is highly expected that attacking of $Y^{\oplus}$ on the carbanion (Ⅵ) occures to give the substituted allene (Ⅷ).

On the other hand, haloethynyl compounds are known to be dehalogenated by the action of strong nucleophiles*4,8) to regenerate the parent ethynyl compounds. The reaction is to be understood in a concept that an attack of a nucleophile on the positive halogen9) of the haloethynyl compound removes the halogen as hypohalogenous acid, alkyl hypohalite10) or presumably as sulfenyl halide. Hypohalogenous acid and alkyl hypohalite are considered to be able to react as iodonium cation (corresponds to $Y^{\oplus}$) donors. The occurrance of the two kinds of the reactions, formation of Ⅵ and deiodination from Ⅱ or Ⅲ is quite probable under the reaction conditions in the formation of Ⅲ or Ⅳ from Ⅱ or Ⅲ, respectively.

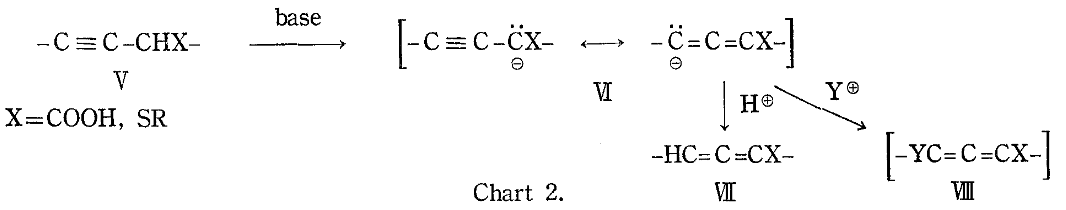

Chart 2.

The above consideration leads to the reaction mechanism presented in Chart 3. The fundamental aspect of it is supported by the following experimental results. First, it can be shown from the reactions in Chart 1 that the combined action of iodine and potassium hydroxide has the same iodinating effect as the combined action of Ⅱ (or Ⅲ) and potassium hydroxide. Secondly, in the convertion of Ⅱ to Ⅲ with potassium hydroxide, about 0.6 moles of potassium hydroxide were consumed to give a by-product (Ⅻ) which was characterized by the qualitative test for terminal acetylene*5 and converted to methyl 3-iodo-2-propynyl ether (Ⅺ). Therefore, it is apparent that about one half mole of Ⅱ was actually dehalogenated and converted to Ⅺ through Ⅻ.

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*4 The reaction occurs quite easily in many iodoethynyl compounds by treating with KOH in hot alcohol. Thiolate anion, a more strong nucleophile, removes the iodine in protic solvents at room temperature practically in a moment (Unpublished work by the authors).

*5 See experimental part.

3) E.R.H. Jones, C.H. Whitham, M.C. Whiting: J. Chem. Soc., **1954**, 3201; L. Crombie, A.G. Jacklin: *Ibid.*, **1955**, 1740; G. Pourcelot, P. Cadiot, A. Willemart: Compt. rend., **252**, 1630 (1961).

4) G.F. Hennion, J.J. Sheehan, D.E. Maloney: J. Am. Chem. Soc., **72**, 3542 (1950).

5) G.F. Hennion, D.E. Maloney: *Ibid.*, **73**, 4735 (1951).

6) G. Pourcelot, *et al.*: Reference 3).

7) G.F. Hennion, K.W. Nelson: J. Am. Chem. Soc., **79**, 2142 (1957); G.F. Hennion, R.S. Hanzel: *Ibid.*, **82**, 4908 (1960); N.R. Easton, R.D. Dillard, W.J. Doran, M. Livezey, D.E. Morrison: J. Org. Chem., **26**, 3772 (1961).

8) V. Grignard, H, Perrichon: Ann. chim., **5**, 5 (1926); R. Truchet: *Ibid.*, **16**, 309 (1931); M. Julia, J.M. Surzur: Compt. rend., **238**, 1130 (1954).

9) C.J. Wilson, H.H. Wenzke: J. Am. Chem. Soc., **56**, 2025 (1934).

10) J.F. Arens: Recueil Trav. chim. Pays-Bas, **82**, 183 (1963).

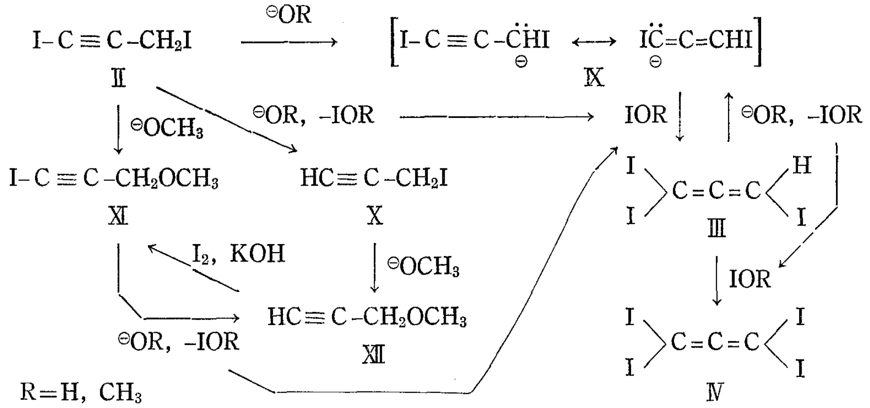

Chart 3.

Two different routes, one *via* X and another *via* Ⅺ, are equally probable in the formation of Ⅻ. Perhaps they are concurrent. The extra-ordinary high yield (at least 95%) in the reaction, I→Ⅳ, which involves the step, Ⅲ→Ⅳ, in which the yield was at best 72%, suggests the presence of the inverse reaction, X→Ⅱ.

Concernig the transporter of the iodine, there are three possible iodinating reagents, hypoiodous acid, hypodite ion and methyl hypoiodite, although methyl hypoiodite is considered most plausible when sodium methoxide in methanol was used. However, in the aqueous medium these three reagents are considered to exist under equillibriums with each other. For this reason, to decide an actual iodinating reagent is difficult in case of the aqueous medium.

Other possible intermediates, 1,1-diiodopropyne and triiodpropyne, are thought not to be completely ruled out in the formation of Ⅲ, although neither experimental nor strong theoretical support for one of them is available at present.

Oxygenolytic Solvolysis of Tri- and Tetraiodoallene

Ⅲ and Ⅳ are very unstable compounds and readily oxidized with atmospheric oxygen at room temperature to decompose into black materials. They can be stored unchanged for months under nitrogen at room temperature.

When the autoxidation of Ⅳ was carried out in a stirred alcoholic or aqueous tetrtahydrofuran solution at room temperature, the reaction occurred smoothly releasing molecular iodine. Dilution of the reaction mixture with water yielded alkyl triiodoacrylate (XⅢb,c) or triiodoacrylic acid (XⅢa) depending on each solvent, respectively. The reaction in aqueous tetrahydrofuran proceeded much slower than in alcohol. The structures of the products (XⅢa~c) were confirmed through the direct comparisons with the authentic specimens synthesized from alkyl iodopropiolates (XIVb,c) or iodopropiolic acid (XIVa) by addition of iodine. XIVa~c were synthesized by the well-known Nefś method.[11]

On the other hand, the same oxygenolytic solvolysis of Ⅲ, the molecular of which is unsymmetric in contrast with Ⅳ, gives a mixture out of at least two compounds which result surely from the oxidation of the different carbon atoms, C_1 and C_3. Thus, as shown in Chart 4, the reaction of Ⅲ in 70% aqueous tetrahydrofuran gave *cis*-2,3-diiodoacrylic acid (XVa) and triiodoacrolein (XVI) in a molar ratio 0.25:0.51[*6] (total yield 76%). Quite analogously, the reaction of Ⅲ in methanol gave methyl *cis*-2,3-diiodoacrylate (XVb) and XVI in a molar ratio 0.32:0.62[*6] (total yield 94%). The stereospcificity toward *cis* in the formation of XVa,b is quite remarkable and its origin

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[*6] The ratio varied to some extent depending on the reaction conditions. The yields are based on the IR-spectroscopically pure materials.

11) J. U. Nef : Ann., **308**, 323 (1899).

is discussed below. In connection with this reaction, the stereochemistry of 2,3-diiodoacrylic acid and its ester has been first established.

The structures of XVa,b and XVI were confirmed as follows. The analytical values and the melting point[12] of XVI led to the structure, triiodoacrolein, almost without doubt. In was confirmed further by the following experimental results. XVI gave the 2,4-dinitrophenyl hydrazone, m.p. 219~220° (decomp.). The infrared absorption spectrum of XVI in carbon tetrachloride showed only one C-H streching absorption band at 2845 cm^{-1} of the aldehyde group and a carbonyl absorption band at 1700 cm^{-1}. Furthermore, convertion of XVI to triiodoacrylic acid (XVa) was succeeded by the oxidation with hydrogen peroxide in a mixture of conc. nitric acid, ethanol and water.

The acid (XVa), $C_3HO_2I_2$, m.p. 109~111.5°, was converted to iodopropiolic acid (XIVa) by treating with warm aqueous sodium hyroxide that is the same reaction condition as in the well-known synthesis of XIVa from 2,3-diiodoacrylic acid[13] (XVIII) by Nef.[11] The infrared absorption spectra of XVa and XVIII are different but quite resemble each other (Fig. 2). The mixed melting point of XVa and XVIII was depressed remarkably. Methylation of XVa with diazomethane gave the methyl ester, $C_4H_4O_2I_2$, as an oil which was identical to the methyl ester (XVb) obtained from the autoxidation of III in

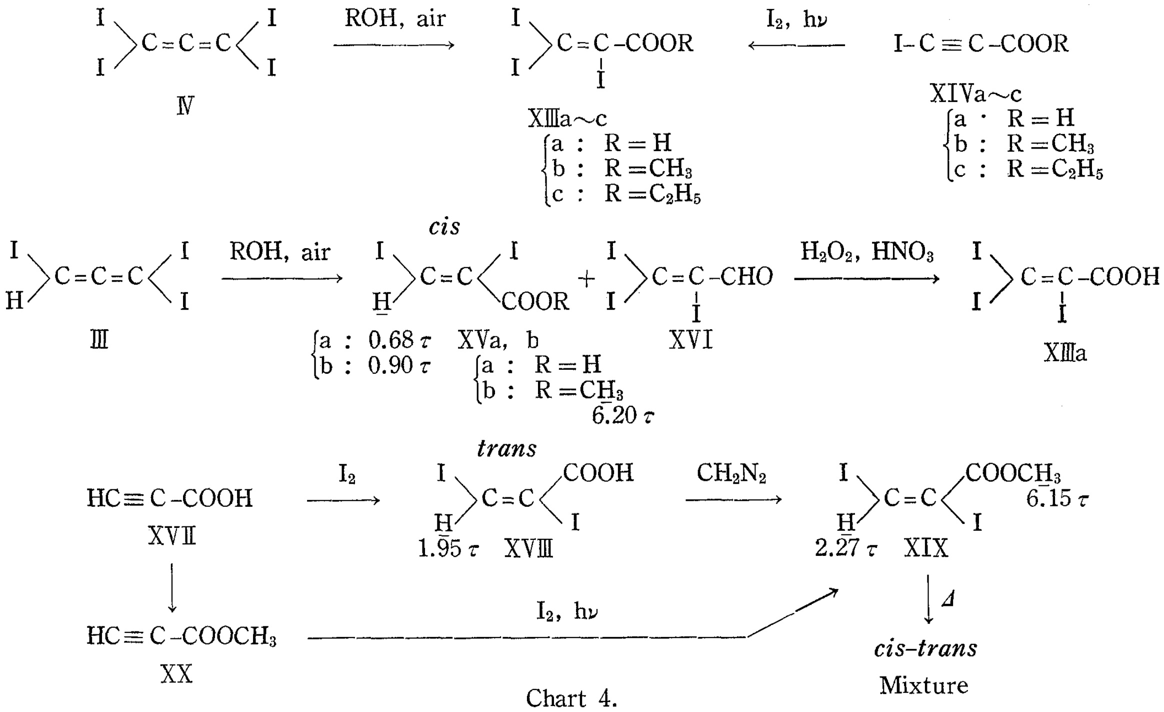

Chart 4.

methanol. The methyl ester (XVb) differed from the authentic methyl 2,3-diiodoacrylate (XIX), m.p. 37.5~38.5°, synthesized from XVIII by methylation with diazomethane or from methyl propiolate[14] by addition of iodine. A known isomer of diiodoacrylic acid, 3,3-diiodoacrylic acid,[15] m.p. 133°, differed from XVa on the direct comparison.

From the experimental results above mentioned, *cis*(or *trans*)-2,3-diiodoacrylic acid and methyl *cis*(or *trans*)-2,3-diiodoacrylate are assigned for XVa and XVb, respectively. The *cis-trans* configurations of XVa,b, XVIII and XIX were determined from the nuclear magnetic resonance spectra as shown in Chart 4. The chemical

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12) J. Grard: Compt. rend., **189**, 541, 925 (1929).
13) B. Homolka, F. Stolz: Ber., **18**, 2282 (1885).
14) C.K. Ingold: J. Chem. Soc., **1925**, 1203.
15) K. Nishida, I. Masuda: J. Pharm. Soc. Japan, **54**, 1097 (1934).

shifts of the proton signals are written under the protons marked with underlines. The chemical shift of the β-olefinic proton of the *cis*-acid (XVa) and the *cis*-methyl ester (XVb) appeared at lower field each by 1.27 and 1.37 parts per million due to the anisotropic effect of the *cis*-carbonyl group[16] than that of the *trans*-isomers, XVIII and XIX.

Thermal *trans*-*cis* isomerization of XIX occurred when it was boiled for one minute. Purification of the isomerisate by alumina chromatography gave a *cis*-*trans* isomeric mixture with a *cis*-*trans* ratio 3:5 which was determined from the intensities of two signals due to the *cis*- and *trans*-vinyl proton in the nuclear magnetic resonance spectrum. The infrared absorption spectrum of the isomeric mixture showed five characteristic "*cis*-bands" in addition to the bands due to tne *trans*-isomer (XIX).

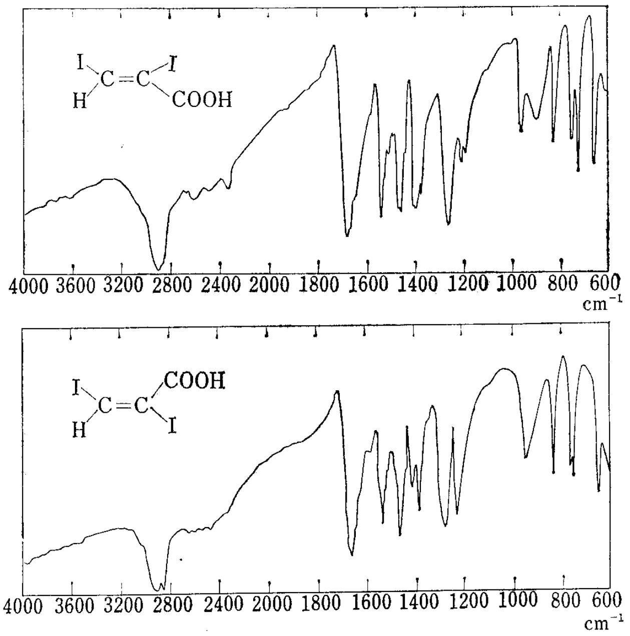

Fig. 2. Infrared Spectra of XVa and XVIII (both in nujol)

Reaction Mechanism of the Oxygenolytic Solvolysis

Tetrachloro- and tetrabromoethylene have been known to be oxidized to the corresponding trihaloacetyl halide by several workers.[11,17] Nef assumed in the classical work[11] that the reaction would have proceeded through an intermediate, "Dihalogenacetyliden" which would have been oxidized to the corresponding dihaloketene followed by the halogen addition to give trihaloacetyl halide.

If the first step of the oxygenolysis of III and IV is supposed to be 1,2-isomerization of the iodine or α-elimination of iodine or hydrogen iodide, vinyl carbenes of the types (XXIa~c), or vinylidene carbenes of the types (XXIIa,b) can be assumed quite formally as possible intermediates. Oxidation of the carbenes with atmospheric oxygen or iodine addition to the resulting ketene analogues can explain the formation of di- or triiodoacryloyl iodide which would give the final product, XV or XIII, respectively. However, if XXIIa,b are the actual intermediates, the same product, one of the alkyl triiodoacrylates or triiodoacrylic acid is expected to form from both III and IV, because both the same intermediate (XXIIa) and excess iodine exist in the reaction medium. But it was not the case in the reaction of III and IV. Reaction of IV in the presence of added hydrogen iodide in methanol did not give XVI. For these reasons, intermediacy of XXIIa,b seems implausible.

On the other hand, III and IV did not react with olefines, *e.g.*, styrene, cyclohexene or 2,3-dimethyl-2-butene, without giving the cyclopropane compounds. Moreover, it is not to be believed that the hypothetic carbenes, XXIa~c, or XXIIa,b can react with atmospheric oxygen exclusively without giving any insertion product with the solvent. Therefore, intermediacy of these carbenes seems quite implausible.

Frankel, *et al.*[17] isolated tetrachloroethylene oxide as an intermediate in the photochemical oxidation of tetrachloroethylene with oxygen in the presence of chlorine

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[16] L.M. Jackman, R.H. Wiley: Proc. Chem. Soc., **1958**, 196; *Idem*: J. Chem. Soc., **1960**, 2886; A.N Kurtz, W.E. Billups, R.B. Greenlee, H.F. Hamil, W.T. Pace: J. Org. Chem., **30**, 3141 (1965).

[17] R. Dickinson, J. Leermakers: J. Am. Chem. Soc., **54**, 3852 (1932); D.M. Frankel, C.E. Johnson, H.M. Pitt: J. Org. Chem., **22**, 1119 (1957).

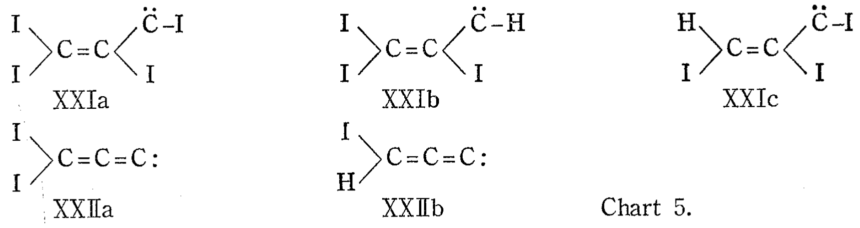

Chart 5.

and showed that tetrachloroethylene oxide easily isomerized to trichloroacetyl chloride or methyl trichloroacetate, the former on heating or treating with sulfuric acid and the latter on treating with methanol containing mercuric chloride.

Isomerization of various epoxides to aldehydes, ketones or corresponding carbonyl compounds, with 1,2-alkyl, -hydride, or -acetoxy shift is well known.[18] Allenes are known to be rapidly attacked by organic hydroperoxides to give the epoxides.[19] On the other hand, it can be expected that epoxide formation from polyiodoallenes would be favored by the electron-donating effect[20] of the iodine.

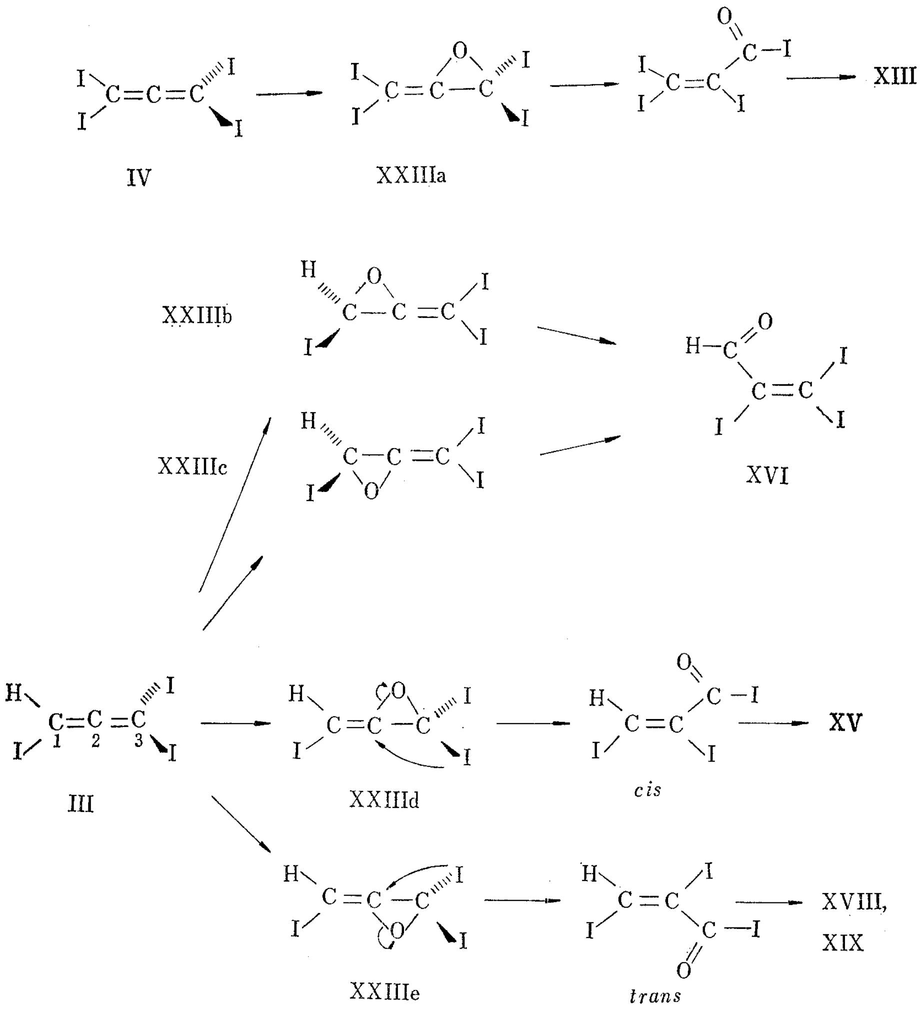

Chart 6.

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[18] R.E. Parker, N.S. Isaacs: Chem. Rev., **59**, 737 (1959); A. Rosowsky: "The Chemistry of Heterocylic Compounds"; Heterocyclic Compounds with Three- and Four-membered Rings, Part 1, 231, Interscience Publishers (1964).

[19] V.I. Pansevich-Kolyada, Z.B. Idelčhik: Zhur. Obscheĭ Khim., **24**, 1617 (1954) (through C.A., **49**, 12428 (1955)).

[20] B.M. Lynch, K.H. Pausacker: J. Chem. Soc., **1955**, 1525; Y. Ogata, I. Tabushi: J. Am. Chem. Soc., **83**, 3440 (1961).

Thus, as shown in Chart 6, assumption of the formation of the epoxides (XXⅢa∼d) and their isomerization to the corresponding acryloyl iodides or triiodoacrolein provides a more rational interpretation for the oxygenolytic solvolysis of Ⅲ and Ⅳ. The steric hindrance by the iodine atoms in Ⅲ and Ⅳ may cause the following order in the ease of the epoxide formation, XXⅢb,c∼XXⅢd>XXⅢa>XXⅢe, which can be suggested by the yields of the final products, XVI, XVa XⅢa. In the epoxidation of Ⅲ with atmospheric oxygen, four epoxides, XXⅢb∼e are possible to form, because the molecule of Ⅲ has four different sites for the epoxide linkage as shown in Chart 6. However, steric hindrance by the three iodine atoms would remarkably decrease the formation of XXⅢe. The *cis*-stereospecificity in the formation of XV would be, thus, attributed to the preferential formation of XXⅢd to XXⅢe and the isomerization of XXⅢd in which C_3-iodine atom would rearrange on C_2-atom from the opposite side to the epoxide oxygen. If the electronic effects by the substituents affecting the ease of the epoxide formation is not so much different between Ⅲ (especially at the site, C_2-C_3) and Ⅳ, probability of the attack by oxygen to result XXⅢe from Ⅲ should be about one fourth of that to result XXⅢa from Ⅳ, because Ⅳ has four sites for the epoxide linkage to result XXⅢa, while Ⅲ has only one isosteric site for the formation of XXⅢe. This also suggests that the formation of XXⅢe would be much slower than that of XXⅢd, because it is apparent from the experimental results that the formation of XⅢa is much slower than that of XVa.

Experimental*7

1,3-Diiodopropyne (II)——To a solution of I (20 g.) in 200 ml. of MeOH were added 42.7 g. of finely powdered iodine with ice-cooling. To the mixture was added slowly a solution of KOH (11 g.) in 60 ml. of MeOH-H_2O (9:1) with stirring and keeping the temperature between 10∼25°. The dropping of KOH solution took about 2 hr. The resulting reaction mixture was cooled on ice and the separated inorganic salt was filtered off. The filtrate was concentrated *in vacuo* to 50 ml., added with powdered KI (20 g.) and 50 ml. of EtOH then allowed to stand with ice-cooling for 1 hr. The inorganic salt precipitated was filtered off. The filtrate was added with ice-water (200 ml.) and extracted with ether (200 ml.). The ether-extract was washed with H_2O, dried over anhyd. Na_2SO_4 and evaporated *in vacuo* to leave an oil which was fractionally distilled in reduced pressure. A colorless oil, 28.4 g. (yield 58%), $b.p_{0.025}$ 47∼48°, was obtained as the main fraction. IR ν_{max}^{liquid} cm^{-1}: 2200 (-C≡C-), 2990, 2945, 1415 (-CH_2-). *Anal.* Calcd. for $C_3H_2I_2$: C, 12.35; H, 0.69; I, 86.96. Found: C, 12.18; H, 1.05; I, 86.80.*8

Triiodoallene (III)——a) From Ⅱ by the action of KOH: To a solution of Ⅱ (5 g.) in 40 ml. of MeOH was added a solution of KOH (1 g.) in 10 ml. of MeOH-H_2O (8:2). The mixture was warmed at 60° for 20 min. After the solvent was removed *in vacuo*, the residue (yellow crystals) was washed with H_2O and recrystallized from MeOH to give yellow plates, m.p. 80∼82° (decomp.), 3.05 g. (82.5% based on Ⅱ, calcd. according to the equation presented in Chart 3). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3050 (C-H), 1928 (C=C=C), 1243, 1104, 722, 700. NMR (CCl_4): 4.55 τ (singlet, $\underline{H}IC=C=$). *Anal.* Calcd. for C_3HI_3: C, 8.63; H, 0.24; I, 91.13. Found: C, 8.97; H, 0.16; I, 91.40.*8

b) From Ⅱ with Iodine and KOH: To a solution of Ⅱ (2.0 g.) in 30 ml. of MeOH were added a solution of KOH (1.0 g.) in 10 ml. of MeOH-H_2O (9:1) and powdered iodine (1.74 g.) all at once. The solution was warmed at 60° for 10 min. with occational stirring. The most solvent was removed *in vacuo* to separate a yellow solid, m.p. 76∼78°, 2.0 g. (70%), which was recrystallized from MeOH to give yellow plates of m.p. 80∼82°. The IR spectrum of this material was completely identical to that of Ⅲ obtained in experiment a) and the mixed melting point showed no depression.

c) From I without isolation of Ⅱ: To a mixture of I (20 g.) and powdered iodine (42.8 g.) in 200 ml. of MeOH was added slowly a solution of KOH (18.85 g.) in 110 ml. of MeOH-H_2O (9:1) with stirring and keeping the temperature between 20∼25°. When 66 ml. of the solution of KOH were added over 2 hr., dropping was stopped and the reaction mixture was cooled on ice and filtered. The filtrate was concentrated to 50 ml., added with 200 ml. of EtOH, cooled on ice and filtered. The filtrate was added with 30 ml. of H_2O and allowed to stand in a freezer at −20° overnight. Yellow crystals separated were collected, washed

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*7 Melting points are uncorrected. Infrared spectra were taken on a Koken Model DS 401G Infrared Spectrometer. The IR bands of Ⅲ, Ⅳ, XV, XVI, XVⅢ, XIX presented are all of the main bands.

*8 Obtained from the $NaBH_4$ reduction.

with cold MeOH and H_2O and dried *in vacuo* over P_2O_5. Yellow plates of m.p. 80～82°, 19.2 g. were obtained. On addition of H_2O (50 ml.) to the mother liquor, more 4.2 g. of Ⅲ were obtained. Total yield 23.4 g. (67%, based on I, calcd. according to the equation in Chart 3).

Tetraiodoallene (IV)——a) From Ⅲ with iodine and KOH : To a solution of Ⅲ (1.0 g.) and KOH (0.27 g.) in 20 ml. of MeOH was added 0.607 g. of powdered iodine with stirring and keeping the temperature at 20°. The reaction mixture was added with 20 ml. of H_2O and allowed to stand at 5° overnight. Yellow crystals separated were collected and washed with cold MeOH and H_2O. Yellow prisms, of m.p. 91～92° (decomp.), 0.89 g., were obtained. Recrystallization from MeOH gave pure yellow crystals of m.p. 93～94° (decomp.). IR $\nu_{\max}^{\mathrm{CCl_4}}$ $\mathrm{cm^{-1}}$: 1915 (C=C=C), 694. IR $\nu_{\max}^{\mathrm{KBr}}$ $\mathrm{cm^{-1}}$: 1905 (C=C=C), 723, 700. *Anal.* Calcd. for C_3I_4 : C, 6.63; I, 93.37. Found : C, 6.89; H, 0.51; I, 93.00,[*8] 92.94.

b) From I without isolation of Ⅱ and Ⅲ : To a solution of I (20 g.) in 200 ml. of MeOH suspended with 42.7 g. of powdered iodine, added slowly a solution of KOH (20 g.) in 100 ml. of MeOH-H_2O (9:1). When about one half of the solution of KOH was added and the color of iodine disappeared, addition of KOH was stopped and 20 g. of powdered KI were added to the solution, then it was cooled on ice. The reaction mixture was filtered, added with the residual solution of KOH and warmed at 60° with occational stirring for 30 min. The solution was cooled at 20°, suspended with 42.7 g. of powdered iodine and added slowly with a solution of KOH (20 g.) in 80 ml. of MeOH-H_2O (8:1) with stirring at 20～25°. When the color of iodine disappeared, addition was stopped and the solution was stored at −20° for 17 hr. Yellow crystals separated were collected and washed with cold MeOH and H_2O to yield Ⅳ, 18.0 g., m.p. 91～92° (decomp.). From the filtrate, on addition of H_2O (200 ml.), more 24.5 g. of Ⅳ, m.p. 91～92° (decomp.), were obtained. Total yield 42.5 g. (95%). This was analytically pure and showed m.p. 93～94° (decomp.) after recrystallization from MeOH, CCl_4 or AcOH.

c) From Ⅱ with KOH : A solution of Ⅱ (1.0 g.) and KOH (0.25 g.) in 17 ml. of MeOH was allowed to stand at 20° for 5 min. and then at 0° for 17 hr. The solution was neutralized with 1*N* HCl and diluted with 10 ml. of H_2O. The yellow precipitates were filtered, washed with H_2O and suspended into 5 ml. of MeOH, then allowed to stand at 5° for 2 days. The suspension was filtered and the yellow crystals were washed with a small amount of cold MeOH and H_2O. Yield 0.23 g., m.p. 89～91° (decomp.). The IR spectrum of this material was completely identical with that of the standard compound obtained in experiment a) or b) and no depression of mixture melting point was observed.

d) From Ⅲ with KOH : A solution of Ⅲ (1.0 g.) and KOH (0.4 g.) in 30 ml. of MeOH was warmed at 60° for 1 hr. The solution was poured on 30 ml. of ice-water and the separated oil soon solidified. This was collected and washed with cold MeOH and H_2O. Yield 0.2 g. m.p. 90～91° (decomp.). This material was identical with the standard Ⅳ on the direct comparison.

Sodium Borohydride Reduction of II, III and IV——To a solution of the sample balanced correctly (100～200 mg.) in 20 ml. of EtOH was added 100～200 mg. of $NaBH_4$ in small portions with ice-cooling and stirring. The solution was warmed at 50° for 30 min. Then, 30 ml. of H_2O and 100 ml. of conc. HCl were added carefully to the solution with ice-cooling and stirring. After addition of 3 ml. of $CHCl_3$, the iodide ions were titrated with a 0.05*M* standard solution of KIO_3. The results obtained are given at the analytical data.

3-Iodo-2-propynyl Ether (XI)[21)]——a) From Ⅲ : A solution of Ⅲ (5.0 g.) in 40 ml. of MeOH was warmed at 60° for 20 min. During the reaction, a reflux condenser and a trap cooled in MeOH-dry ice mixture were attached to the vessel. All of the volatile materials was then distilled *in vacuo* (10 mm. Hg) and condensed into the trap. The condensate was distilled again *in vacuo* (13 mm. Hg) at 40°. Most of the volatile materials collected in the trap and a few ml. of the liquid were let to remain undistilled. On testing the terminal acetylene with aqueous ammoniacal cuprous chloride solution prepared from CuCl and $(NH_4)_2CO_3$, the condensate precipitated green Cu^{I}-acetylide. 1.7 g. of powdered iodine were added to the condensate and a solution of KOH (0.7 g.) in 10 ml. of MeOH-H_2O (9:1) was then added dropwise with stirring at 20～25°. The reaction mixture was poured on ice-water and extracted with ether. Ether-extract was washed with H_2O, dried over anhyd. Na_2SO_4 and evaporated *in vacuo*. The residue was fractionally distilled to give 0.75 g. of colorless oil, $\mathrm{b.p_{0.3}}$ 30～31°, as the main fraction. Comparison of the IR and NMR spectra comfirmed the identity of this material with the authentic Ⅺ prepared in the following experiment b).

b) From I : A solution of KOH (5 g.) in 30 ml. of MeOH was slowly to a solution of I (10 g.) in 60 ml. MeOH with stirring and cooling on ice. The solution was allowed to stand at room temperature for 30 min., then warmed at 55～60° for 30 min. The precipitated KBr was filtered off and the filtrate was suspended with 21.4 g. of powdered iodine and added dropwise with a solution of KOH (5 g.) in 30 ml. of MeOH-H_2O (9:1). The reaction mixture was diluted with H_2O, extracted with ether, and the extract was washed with H_2O, dried over anhyd. Na_2SO_4 and evaporated *in vacuo*. The residue was fractionally distilled to give a colorless liquid, 5.0 g., $\mathrm{b.p_{1.8}}$ 38～39°. $\nu_{\max}^{\mathrm{liquid}}$ $\mathrm{cm^{-1}}$: 2190 (-C≡C-). NMR (in CCl_4) : 5.84 τ (2H, -$\underline{H}$-less CH_2-O-), 6.69 τ (3H, $C\underline{H}_3O$-). *Anal.* Calcd. for C_4H_5IO : C, 24.50; H, 2.57. Found : C, 24.84; H, 2.61.

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21) Lespieau : A. chim., [7], **11**, 274; Synthesized by iodination of the Ag-acetylide (through Beilsteins Handbuch der Organischen Chemie, **1**, 455).

Triiodoacrylic Acid (XIIIa)——a) From Ⅳ : A solution of Ⅳ (1.0 g.) in 50 ml. of tetrahydrofuran-H_2O (7:3) was put into a 500 ml. open flask and was stirred on a magnetic stirrer at 20∼25° for 10 days. The solvent was removed *in vacuo* and the residue was extracted with 5 ml. of 0.1*N* NaOH. The extract was acidified with 1*N* HCl to separate crystals (270 mg., m.p. 205∼207°, decomp.) which were recrystallized from MeOH to yield colorless plates of m.p. 207°(decomp.). This material was proved to be identical with the authentic specimen (experiment b)) from comparison of the IR spectra and the mixed melting point (no depression). The MeOH-insoluble material (300 mg.) was unreacted Ⅳ.

b) From iodopropiolic acid (XIVa) : To a solution of XIV[11] (1 g.) in 40 ml. of CCl_4 was added 1.3 g. of powdered iodine. The suspension was irradiated with a tungsten lamp (500 W) with occational stirring for 4 hr. After the color of iodine was almost disappeared, the solvent was removed *in vacuo* to yield 2.2 g. of almost colorless crystals of m.p. 205∼207°(decomp.). After recrystallization it showed m.p. 207°(decomp.), (from MeOH).

Methyl Triiodoacrylate (XIIIb)——a) From Ⅳ : A solution of Ⅳ (2.0 g.) in 50 ml. of MeOH was put into an open 300 ml. flask and it was allowed to stand at 20∼25° with occational stirring for 17 hr. The iodine separated was titrated with 1*N* $Na_2S_2O_3$ (0.6 ml. were consumed.). The solvent was removed *in vacuo* and the residue was washed with water to give colorless crystals (1.3 g.) m.p. 83∼85°. Recrystallization from MeOH gave colorless plates, 0.8 g., m.p. 85∼86°. IR $\nu_{\max}^{\text{KBr}}$ cm^{-1} : 3000, 2945, 1431 (CH_3); 1707, 1260 (ester). NMR (in CCl_4) : Singlet at 6.12 τ ($COOC\underline{H}_3$). *Anal.* Calcd. for $C_4H_3O_2I_3$: C, 10.35; H, 0.65; I, 82.20. Found : C, 10.29; H, 0.53; I, 82.99.

b) From methyl iodopropiolate (XIVb) : A solution of XIXb[22,23] (0.3 g.) in 5 ml. of $CHCl_3$ suspended with 0.36 g. of powdered iodine was irradiated a tungusten lamp (500 W) with occational stirring. After 10 min., most iodine disappeared. Removal of the solvent gave crude XⅢb, 0.65 g., which was recrystallized from MeOH. m.p. 85∼86°. Yield 0.55 g. This material was proved to be identical with XⅢb obtained in experiment a) from the IR spectra and the mixed melting point (no depression).

Ethyl Triiodoacrylate (XIIIc)——a) From Ⅳ : A solution of Ⅳ (2.0 g.) in 50 ml. of MeOH was allowed to stand in an open flask at 20∼25° for 2 days. The solution was added with 150 ml. of H_2O and allowed to stand at 5° for 24 hr. The precipitating crystals were collected and washed with H_2O. (1.25 g., m.p. 62∼64°). Recrystallization from MeOH-H_2O (1:1) gave colorless needles, 0.5 g., m.p. 65.5∼66.5°). IR $\nu_{\max}^{\text{KBr}}$ cm^{-1} : 2985, 2960, 2820, 2900, 2860, 1475, 1465, 1445, 1394, 1375 (-CH_2CH_3); 1705, 1240 (ester). *Anal.* Calcd. for $C_5H_5O_2I_3$: C, 12.55; H, 1.05. Found : C, 12.11; H, 1.42.

b) From ethyl iodopropiolate (XIVc) : This was prepared from XIVc[23,24] by the same method as in the preparation of XⅢb from XIVb. From 0.3 g. of XIVc was obtained 0.62 g. of crude XⅢc, m.p. 63∼65°, which was recrystallized from MeOH-H_2O (1:1) to give coloress needles, m.p. 65.5∼66.5°. This material was proved to be identical with XⅢc obtained in experiment a) from the IR spectra and the mixed melting point (no depression).

Triiodoacrolein (XVI)[*9] **and *cis*-2,3-Diiodoacrylic Acid (XVa) from III**——A solution of Ⅲ (3.0 g.) in 70 ml. of tetrahydrofuran-H_2O (7:3) was allowed to stand in an open flask (500 ml.) at 20∼30° with occational stirring for 3 hays. Removal of the solvent *in vacuo* gave reddish crystalline solid which was extracted with cold MeOH (5 ml.). Yellow powder which is hardly soluble in cold MeOH weighed 1.6 g. (m.p. 127∼129°, practically pure XVI, 0.6 moles from 1 mole of Ⅲ). Recrystallization from MeOH gave large yellow crystals of m.p. 129∼130°. IR $\nu_{\max}^{\text{CCl}_4}$ cm^{-1} : 2845, 1695 (aldehyde); 1508, 1370, 1070. *Anal.* Calcd. for C_3HOI_3 : C, 8.32; H, 0.23. Found : C, 8.66; H, 0.80.

2,4-Dinitrophenyl hydrazone : Orange plates from MeOH, m.p. 219∼220°(decomp.). *Anal.* Calcd. for $C_9H_5O_4N_4I_3$: C, 17.61; H, 0.82; N, 9.30. Found : C, 17.71; H, 0.99; N, 9.41.

The MeOH-extract was evaporated to dryness and extracted with 8 ml. of 5% $NaHCO_3$ in H_2O. The extract was acidified with 1*N* HCl to separate colorless needles (XVa) of m.p. 105∼108°, yield 0.57 g. (0.25 moles from 1 mole of Ⅲ). Two recrystallizations from CCl_4 gave colorless needles of m.p. 109∼111.5°. IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1} : 3100∼2300 broad, 1680 (-COOH), 1542, 1402, 1274, 1211, 1195, 961, 901, 828, 754, 729, 660. NMR (in $CDCl_3$) : 0.68 τ ($\underline{H}IC{=}CI$-), 0.30 τ ($COO\underline{H}$, disappeared in $CDCl_3$-D_2O). *Anal.* Calcd. for $C_3H_2O_2I_2$: C, 11.16; H, 0.62; I, 78.62. Found : C, 11.20; H, 0.85; I, 78.79.

XIVa from XVa——A solution of XVa (100 mg.) in 3 ml. of 10% NaOH-H_2O was heated at 60° for 30 min. The solution was acidified with 2*N* HCl at 0° and extracted with 50 ml. of H_2O. The ether-extract was washed with 5 ml. of H_2O, dried over anhyd. Na_2SO_4, and evaporated to dryness. The crystalline residue (20 mg.) was recrystallized from cyclohexane, to give colorless prisms of m.p. 141∼142° (decomp.). This compound was proved to be identical with the authentic specimen[11] from the direct comparison (IR spectrum and mixture melting point). IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1} : 2160 (-C≡C-), 2700∼2300, 1657∼1600 (COOH).

XVI and Methyl *cis*-2,3-Diiodoacrylate (XVb) from III——A solution of Ⅲ (2.0 g.) in 50 ml. of MeOH

[*9] Grard[12] synthesized XVI *via* different routes which mainly consist of iodination of the Grignard reagent of propiolaldehyde diethylacetal and hydrolysis of it.

22) I. Muirhead : Ann. Appl. Biol., **36**, 250 (1949).

23) A. Baeyer : Ber., **18**, 2269 (1885).

24) S. Seki, K. Umemura, H. Ogawa, F. Kai : Japan. Pat., 25034 (1964) (An improved method of preparation).

was stirred in an open flask at 20~25° for 2 days. The solution was evaporated *in vacuo* to dryness and the crystalline residue was extracted three times with each 5 ml. of ether. The residue was washed with cold MeOH to yield 1.28 g. of XVI (0.62 moles from 1 mole of III), m.p. 129~130°(recrystallized from MeOH). Identity with the XVI obtained in the preceding experiment was confirmed from the IR spectra and the mixed melting point.

The above ether-extracts were washed with 5% $NaHCO_3$ solution in H_2O, dil. $Na_2S_2O_3$ solution in H_2O and finally with H_2O one after another. After drying over anhyd. Na_2SO_4, the solvent was removed *in vacuo* to give an oil (0.51 g.) which was dissolved in CCl_4 and chromatographed on Al_2O_3. Elution with CCl_4 gave a colorless oil, 0.4 g. This was identical with the methyl ester (XVb) obtained from XVa by methylation with diazomethane.[25] IR $\nu_{\max}^{\text{liquid}}$ cm^{-1}: 3036, 2845, 2835, 1726, 1712, 1550, 1537, 1437, 1240, 1193, 1023, 923, 887, 825, 774, 730, 667, 652. NMR (in CCl_4): 0.90 τ (1H, $\underline{H}IC=CI-$); 6.20 τ (3H, $-COOC\underline{H}_3$). *Anal.* Calcd. for $C_4H_4C_2I_2$: C, 14.21; H, 1.19. Found: C, 14.53; H, 1.27.

Methyl *trans*-2,3-Diiodoacrylate (XIX)——a) From *trans*-2,3-Diiodoacrylic acid (XVIII): XVIII was prepared according to Homolka and Stolz[13] in a good yield. Two recrystallizations from CCl_4 and one more recrystallization from cyclohexane gave colorless crystals of m.p. 102~103°. IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1}: 3100~2300 (broad), 1666, 1538, 1410, 1275, 1225, 940, 826, 748, 639. NMR (in $CDCl_3$): 1.95 τ ($\underline{H}IC=CI-$), -0.47 τ ($-COO\underline{H}$, disappeared in $CDCl_3$-D_2O).

XVIII was methylated with diazomethane according to the ordinary method.[25] From 0.9 g. of XVIII was obtained 0.79 g. of a colorless oil (XIX) which soon solidified, m.p. 37.5~38.5°(unchanged on recrystallization from CCl_4). IR $\nu_{\max}^{\text{liquid}}$ cm^{-1}: 3036, 2845, 2835, 1725, 1553, 1436, 1268, 1204, 1173, 993, 881, 820, 778, 623. NMR (in CCl_4): 2.27 τ (1H, $\underline{H}IC=CI-$); 6.15 τ (3H, $COOC\underline{H}_3$). *Anal.* Calcd. for $C_4H_4O_2I_2$: C, 14.21; H, 1.19. Found: C, 14.43; H, 1.37.

b) From methyl propiolate (XX): A solution of XX[14] (1.0 g.) in 50 ml. of CCl_4 was added with 1.5 g. of powdered iodine and stirred with ultraviolet irradiation at 25~30° for three days. The solvent was removed *in vacuo* to give an oil which soon solidified, 2.45 g. Recrystallization from CCl_4 gave colorless crystals of m.p. 37.5~38.5°. The IR and NMR spectrum of the material before recrystallization were identical with those of XIX prepared in experiment a).

H_2O_2-HNO_3 Oxidation of XVI——A solution of XVI (400 mg.) in a mixture of 30% H_2O_2 (4 ml.), conc. HNO_3 (d=1.38, 1 ml.) and EtOH (20 ml.) was warmed at 75° for 30 min. The solution was concentrated *in vacuo* almost to dryness then added with H_2O (30 ml.) and evaporated *in vacuo* to dryness. The residue (slight yellowish solid) was extracted with 1 ml. of 2N KOH and filtered. The extract was acidified with 1N HCl to separate crystals which were collected, washed with cold H_2O and recrystallized from MeOH-H_2O to give colorless plates of m.p. 207°(decomp.), 70 mg. The alkali-insoluble yellow solid was unreacted XVI, 100 mg. IR spectrum of the acid was completely identical with that of the authentic XIIIa and no melting point depression was observed on admixture with the authentic XIIIa.

Thermal Isomerization of XIX——0.5 g. of XIX were boiled over a burner for 1 min. The reddish-black oil was dissolved into 20 ml. of CCl_4 and chromatographed on Al_2O_3 packed with CCl_4 to give a colorless eluate. The total eluate was evaporated *in vacuo* to yield a mixture of XIX and XVb as a colorless oil, 0.35 g. IR $\nu_{\max}^{\text{liquid}}$ cm^{-1}: Five characterisic *cis* bands appeared at 1537, 1240, 1023, 922 and 730 in addition to the bands of the parent (XIX). NMR (in CCl_4): 0.90 τ (*cis* $\underline{H}IC=CI-$), 2.27 τ (*trans* $\underline{H}IC=CI-$), 6.15 τ (*cis* $-COOC\underline{H}_3$), 6.20 τ (*trans* $-COOC\underline{H}_3$), all singlets of relative integrated intensity, 3:5:9:15, respectively. *Anal.* Calcd. for $C_4H_4O_2I_2$: C, 14.21; H, 1.19. Found: C, 14.58; H, 1.43.

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Summary

Synthesis of tri- and tetra-iodoallene (III and IV) from 3-bromo-1-propyne (I) was described. III and IV are very susceptible to autoxidation and both the autoxidation and a solvolysis occurred in aqueous tetrahydrofuran or alcohols to afford the following products depending on the solvents. The reaction of III in aqueous tetrahydrofuran gave triiodoacrolein (XVI) and *cis*-2,3-diiodoacrylic acid (XVa). The reaction of III in methanol gave XVI and methyl *cis*-2,3-diiodoacrylate (XVb). The reaction of IV in

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[25] Org. Syntheses, Coll. Vol., II, 165 (1948).

aqueous tetrahydrofuran, methanol, or ethanol gave triiodoacrylic acid (XIIIa), methyl triiodoacrylate (XIIIb) or ethyl triiodoacrylate (XIIIc), respectively.

The formation of III from 1,3-diiodopropyne (II) by the action of alkali was well explained in terms of intermediate formation of the allenic carbanion (IX) followed by the iodination of IX with the hypoiodite resulted from the ethynyl iodine of III.

A reaction mechanism involving the intermediate formation of the epoxides (XXIII) and their isomerization to the corresponding carbonyl compounds with the 1,2-iodide shift gave a good explanation proposed for the oxygenolytic solvolysis of III and IV.

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155. **Daisuke Satoh and Mieko Horie**: Studies on Digitalis Glycosides. XXV.[*1] Preparation of $14\beta,15\beta$-Epoxycardenolides from Odoroside H and Digitoxin.[*2]

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Several epoxycardenolides, having the epoxide ring at $7\beta,8\beta$-,[1] $8\beta,14\beta$-,[2] $11\beta,12\beta$-[3] and $16\alpha,17\alpha$-[4] positions were found in plants as glycosides, while those at $14\alpha,15\alpha$- and $14\beta,15\beta$-,[5~9] and $16\beta,17\beta$-[10] positions were only synthesized and have never been known as glycosides. In the previous paper,[6] the preparation of 3β-hydroxy-$14\beta,15\beta$-epoxy-5β-card-20(22)-enolide was reported. This paper is concerned with the preparation of glycosides possessing $14\beta,15\beta$-epoxide as aglycone.

Digitoxigenin-β-D-monodigitaloside diacetate (odoroside H diacetate, Ib)[11,12] was treated with thionyl chloride in pyridine to give 14-anhydrodigitoxigenin-β-D-monodigitaloside diacetate (IIc), $C_{34}H_{48}O_9$, m.p. 218~221°. A mild hydrolysis of IIc with 2% hydrochloric acid in a mixture of chloroform and methanol (1:3) afforded 14-anhydrodigitoxigenin-β-D-monodigitaloside (IIa), $C_{30}H_{44}O_7$, m.p. 209~212°, and its monoacetate (IIb), $C_{32}H_{46}O_8$, m.p. 250~255°. The compounds (IIb) and (IIc) had been prepared by Reichstein and his co-workers[11] from odoroside H monoacetate (Ia) by

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[*1] Part XXIV. D. Satoh, M. Horie, J. Morita: This Bulletin, **14**, 613 (1966).

[*2] A part of this work has been reported in brief in the review entitled "Studies on the Constituents of *Digitalis purpurea* L Leaves" published in Ann. Rept. Shionogi Res. Lab., **14**, 14 (1964).

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