Chlorination by Sulfuryl Chloride. II[1]. *Action of Sulfuryl Chloride on the Methylenedioxy-ring*

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(Received December 25, 1961)

In the first part of this series[1], the author reported on the action of sulfuryl chloride on aromatic aldehyde (including anisaldehyde) in the presence of benzoyl peroxide. The reaction resulted in the formation of the corresponding acid chlorides by the attack of chlorine on aldehydic hydrogen. At the same time, the author noticed that the reaction with phenolic aldehyde usually leads to nuclear chlorination, the aldehydic hydrogen being intact. The investigation of this type of reaction has now been extended to an aromatic aldehyde, such as piperonal, with etheric linkage.

The reaction of sulfuryl chloride on piperonal has already been reported on in a patent[2]. On heating at 130°C, the reaction proceeded to give dichloropiperonal, which afforded protocatechualdehyde on being hydrolyzed. Later investigation by Weisse[3] indicated that no reaction took place by heating, but that, after the substance had been allowed to stand for two days at room temperature, only nuclear chlorination occurred, the methylenedioxy bridge being intact.

A survey has now also been made using methyl piperonylate and 1, 2-methylenedioxy-4-nitrobenzene in the presence of benzoyl peroxide in order to see which of the reactions, nuclear chlorination or cleavage of the ethereal ring, would occur preferentially.

Results and Discussion

To confirm Weisse's findings, piperonal and sulfuryl chloride were heated without a solvent. After hydrolysis with water, 6-chloropiperonal (89%) and protocatechualdehyde (8%) were obtained, showing that mainly nuclear chlorination had occurred. When carbon tetrachloride was used as a solvent, complete recovery of the starting material resulted.

Following the procedure of the previous paper[1], piperonal was heated in benzene with two moles of sulfuryl chloride in the presence of benzoyl peroxide. On treatment of the reaction products with aniline, protocatechuic anilide, not piperonyl anilide, was obtained. An attempt was made to isolate the chlorinated product by distillation under reduced pressure. However, polymerization occurred as a result of the heat, and the attempt failed to obtain any pure substance.

Moreover, piperonal was submitted to the reaction with one or two moles of sulfuryl chloride, followed by hydrolysis with water. The results, shown in Table I, indicate that protocatechualdehyde and protocatechuic acid are the reaction products and that no 6-chloropiperonal, a nuclear substitution product, is detectable. The quantitative formation of protocatechuic acid with two moles of sulfuryl chloride indicates that one mole of the reagent attacks the methylenedioxy bridge and the other the aldehyde group. It is also clear that the chlorination occurred first at the methylenedioxy bridge and then at the aldehyde group, since no piperonylic acid is formed in a benzene solution.

The chlorination of the methylenedioxy-ring and its cleavage has been studied. The dichloro-compound is considered to be produced by chlorination with phosphorous chloride[4,5], thionyl chloride[5], sulfur chloride[2,3,6] or gaseous chlorine[7], and its hydrolysis is assumed to proceed through the cyclic carbonate, as is shown in the following scheme:

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[1] M. Arai, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zasshi*), **81**, 1450 (1960).

[2] German Pat. 165727 (1906).

[3] K. Weisse, *Ber.*, **43**, 2605 (1910).

[4] R. Fittig and I. Remsen, *Ann.*, **159**, 128 (1871); H. Pauly, *Ber.*, **40**, 3096 (1907); P. Hoering and F. Baum, ibid., **41**, 1914 (1908).

[5] G. Barger, *J. Chem. Soc.*, **93**, 563 (1908).

[6] H. Pauly, *Ber.*, **42**, 417 (1907).

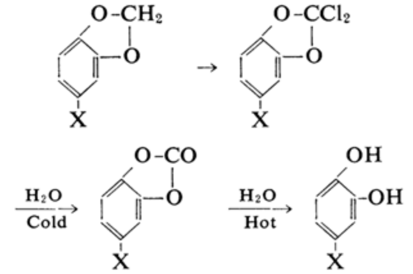
[7] L. Schmidt, *Chem. Zentr.*, **1914**, II, 1080; **1921**, II, 358.

TABLE I. CHLORINATION OF PIPERONAL BY SULFURYL CHLORIDE[a)]

Exp. No.	Reactants			React. time. hr.	Products, %[b)]		
	Piperonal mol.	SO_2Cl_2 mol.	Solvent ml.		Protocatechuic acid	Protocatechualdehyde	Piperonylic acid
1	0.01	0.01	C_6H_6, 15	6	30 (60)	36	
2	0.01	0.02	C_6H_6, 15	8	90	8 (4)	
3	0.01	0.01	CCl_4, 15	48	54 (108)	8	4
4	0.01	0.02	CCl_4, 15	48	98		

a) In the presence of benzoyl peroxide at 85°C.

b) Based upon the amount of piperonal used, and the numerical values in parentheses are based upon the amount of SO_2Cl_2.



As had been reported by the author[1)], chlorination by sulfuryl chloride is a radical chain reaction. Therefore, the intermediate is assumed to be a monochloro-compound. In Experiment 3), piperonylic acid was formed, and the yield of protocatechuic acid was greater than that expected from the amount of sulfuryl chloride. This result suggests a further radical reaction of piperonal and carbon tetrachloride during the reaction.

In order to confirm this cleavage reaction, methyl piperonylate was heated in benzene with sulfuryl chloride in the presence of benzoyl peroxide. After distillation of the solvent, the chlorinated product was hydrolyzed with water to give methyl protocatechuate quantitatively. The titration curve (Fig. 1) of the mother liquor for hydrolysis indicates that the liquor contains two kinds of acids, the one being stronger in acidity than the other. The latter was identified as formic acid by the formation of *p*-bromophenacyl ester (Kubota and Matsuura's method[8)]), and the former must be hydrochloric acid formed by the decomposition of the monochloro compound I. Consequently, the entire course of the reaction should be depicted as follows:

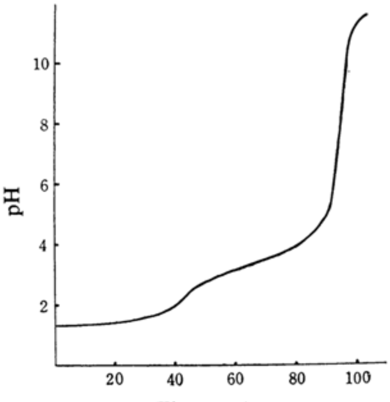
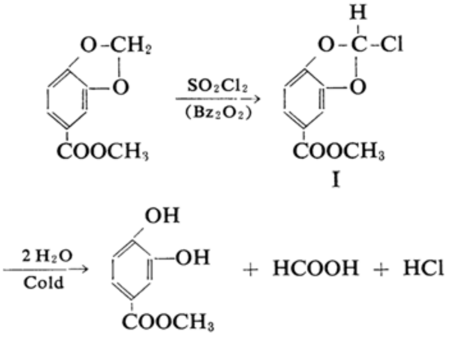


Fig. 1. Titration curve of the mother liquor for the hydrolysis of chlorinated products of methyl piperonylate by 0.1 N NaOH (f=0.985).



This reaction sequence was also supported by the quantitative isolation of viscous fuming oil, b.p. 101~101.5°C/0.15 mmHg, which yielded methyl protocatechuate on the addition of water, and an equivalent number of chloride ions (Mohr's method). The infrared absorption spectrum of the oil (Fig. 2) lacks the peaks to be expected at 2780, 925, 720 cm^{-1} judging from the methylenedioxy group in the starting substance, while it exhibits a newly developed broad peak at 705 cm^{-1} attributable to the C–Cl bond.

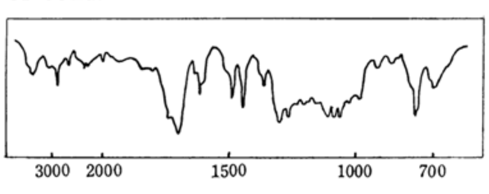


Fig. 2. Infrared absorption spectrum of chlorinated methyl piperonylate (I).

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8) T. Kubota and T. Matsuura, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zassi*), 72, 482 (1951).

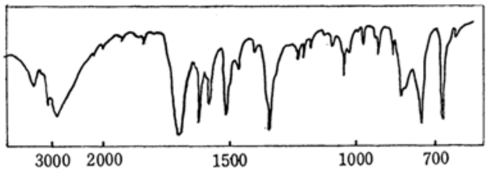
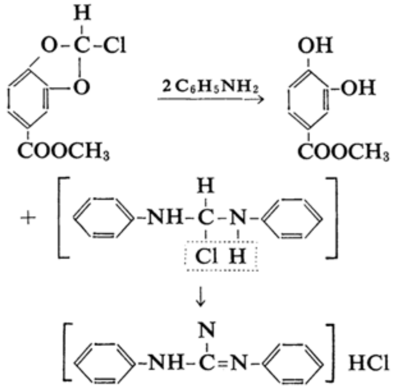


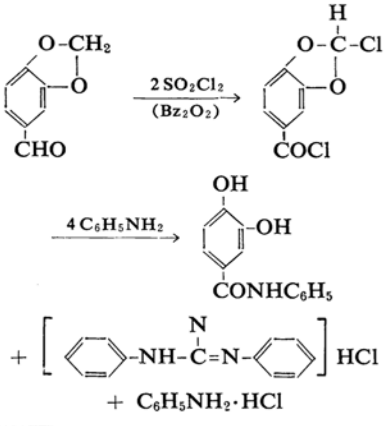
Fig. 3. Infrared absorption spectrum of *N, N'*-diphenylformamidine (II) hydrochloride.

Treatment of the oil with aniline gave a colorless featherly crystalline substance, $C_{13}H_{18}N_2Cl\cdot H_2O$, m. p. 253°C, besides methyl protocatechuate. The infrared absorption spectrum of this substance shows a strong absorption at $1700\,cm^{-1}$ ($\nu_{C=N}$), suggesting the hydrochloride of compound II.



II

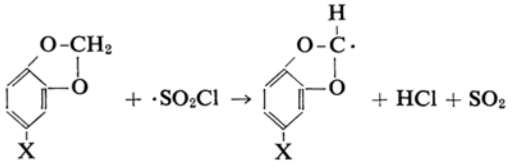
The free base II, m. p. 139°C, has an absorption maximum at 274 mμ. The value[9] for *N, N'*-diphenylformamidine supports the figure of II. The imide II was also obtained, together with protocatechuic anilide, by the reaction of two moles of sulfuryl chloride on piperonal, followed by treatment with aniline.



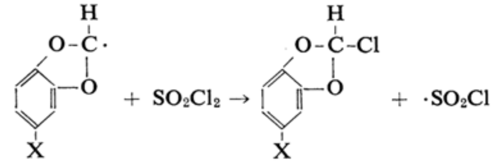
Further chlorination of the oil I was attempted under the same conditions, but the inertness of the tertiary hydrogen of I for chlorination by stlfuryl chloride was recognized upon obtaining *N, N'*-diphenylformamidine hydrochloride by treatment with aniline.

In another experiment, a similar chlorination of 4-nitromethylenedioxy-benzene was carried ont. The quantitative formation, 4-nitrocatechol, was recognized after treatment with water, though the reaction rate was rather small.

From the results mentioned above, the mechanism of this chlorination is shown to be as follows;



III



IV

The chlorosulfonyl radical ($\cdot SO_2Cl$), formed by the reaction of sulfuryl chloride and benzoyl peroxide, attacks the methylenedioxy group and abstracts a hydrogen atom to produce the radical III, hydrogen chloride and sulfur dioxide. The radical III stabilizes by abstracting a chlorine atom from sulfuryl chloride to form the compound IV and the chlorosulfonyl radical, completing a radical chain. The preference for the chlorosulfonyl radical over the chlorine atom for the first step of the chain reaction is based on the fact that the dichloro-compound, which should have resulted from the reaction of the molecular chlorine[7], was not produced in this reaction. It is quite natural to assume that the chlorosulfonyl radical is not capable of attacking compound IV, but is capable of attacking only the methylenedioxy group of the starting substance in preference to decomposing to sulfur dioxide and a chlorine atom.

Experimental

Reaction of Piperonal and Sulfuryl Chloride.— 1) In the Absence of Benzoyl Peroxide.—*a*) *Without a Solvent*.—A mixture of 1.50 g. of piperonal and 2.70 g. of sulfuryl chloride was heated under reflux in an oil bath at 105~110°C for 2 hr., with moisture excluded. After the mixture had been cooled, water (20 ml.) was added to the reaction mixture, which was then made alkaline and extracted with ether. The evaporation of ether gives 1.65 g.

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[9] L. Claisen, *Ann.*, **287**, 366 (1895); Brit. Pat. 353138 (1930); French Pat. 717145 (1932); W. Bradley and I. Wright, *J. Chem. Soc.*, **1956**, 640; R. N. Roberts and R. H. De. Walfe, *J. Am. Chem. Soc.*, **76**, 2411 (1954).

of colorless needles, which were recrystallized from ethanol to 6-chloropiperonal, m. p. 115°C (Found: C, 52.39; H, 2.68%). An alkali-soluble part gives, by separation with toluene, 0.11 g. of plates which give a dark green coloration with ferric chloride. The 2,4-dinitrophenylhydrazone of this compound, m. p. 273°C, (Found: N, 17.54%), coincides with that of protocatechualdehyde.

b) *In Carbon Tetrachloride*.—The same reaction was carried out in carbon tetrachloride (10 ml.). After refluxing for 10 hr., the starting material was completely recovered and identified as 2,4-dinitrophenylhydrazone.

2) **In the Presence of Benzoyl Peroxide.**—In an atmosphere of dry nitrogen, piperonal and sulfuryl chloride (1 or 2 equiv.) were heated at 85°C in benzene or carbon tetrachloride in the presence of benzoyl peroxide (1% of the amount of sulfuryl chloride) until the evolution of hydrogen chloride ceased. After evaporation of the solvent, the product was decomposed by the addition of a small amount of water, and the resultant mixture was fractionated with benzene. Protocatechuic acid was obtained from the insoluble part and protocatechualdehyde from the benzene-layer, as is shown in Table I.

3) **Treatment with Aniline.**—The same reaction was carried out using more than 2 mol. of sulfuryl chloride. After the solvent was removed, a solution of 4 mol. of aniline in ether was added to the resultant viscous oil. A vigorous reaction took place, and an yellow solid was separated out. The solid was washed with 5% hydrochloric acid and recrystallized from dilute methanol to give colorless prisms, m. p. 166~167°C. The solid was identified with protocatechuanilide by the melting point test, and gave a dark green color with ferric chloride (Found: N, 6.01%).

The yellow solid described above was treated with 5% of an aqueous solution of sodium hydroxide, filtered, and washed with a small amount of ether. The crystals remaining were recrystallized from benzene-peteroleum ether to give colorless needles, m. p. 139°C. The compound obtained was identified as *N,N'*-diphenylformamidine, obtained from methyl piperonylate, by the mixed-melting point test (vid. Fig. 3).

Reaction with Methyl Piperonylate. — In an atmosphere of nitrogen, 0.90 g. (0.005 mol.) of methyl piperonylate, an equivalent of sulfuryl chloride and 10 mg. of benzoyl peroxide were heated in 10 ml. of benzene at 85°C for 6 hr. in an oil bath. After the complete evaporation of the solvent in vacuo at 80°C, the addition of cold water (ca. 1.5 ml.), the filtration of the separated crystal and, washing with cold water, 0.82 g. of colorless crystals were obtained. Recrystallization from water gave methyl protocatechuate, m. p. 134°C, in a 97.6% yield. Dark green on conbination with ferric chloride (Found: C, 57.08; H, 4.76%). The filtrate and washing were combined and titrated with 0.1 N of an aqueous solution of sodium hydroxide (titration curve: Fig. 1). After adjusting the pH value to 7, the titrated solution was evaporated to dryness, and the residue was triturated with absolute ethanol (50 ml.) and absolute methanol (5ml.). The alcoholic solution was treated with *p*-bromophenacyl bromide, giving *p*-bromophenacyl formate as colorless plates, m. p. 100°C.

The same reaction was carried out using 4.50 g. of methyl piperonylate at 85°C for 15 hr. The reaction mixture was distilled in vacuo to give a viscous liquid, b. p. 101~101.5°C/0.15 mmHg, in a quantitative yield (The infrared absorption spectrum is shown in Fig. 2). On standing in the air, the liquid decomposed to give methyl protocatechuate.

Found: Cl, 16.22 (Mohr's method). Calcd. for $C_9H_7O_4Cl$; Cl, 16.53%.

After evaporation of the solvent, a solution of 2 mol. of aniline in ether was added, drop by drop, to the reaction mixture under cooling. The precipitate formed was filtered. Methyl protocatechuate was obtained quantitatively from the ether-layer, and feathery crystals, m. p. 253°C, were obtained after recrystallization of the precipitate from water. The infrared absorption spectrum of the latter indicates that the product is *N, N'*-diphenylformamidine hydrochloride, as is shown in Fig. 3.

Found: C, 62.39; H, 6.13; N, 11.34. Calcd. for $C_{13}H_{13}N_2Cl \cdot H_2O$; C, 62.24; H, 6.25; N, 11.17%.

After treatment of the hydrochloride with 5% of an aqueous solution of sodium hydroxide, the free base was obtained as colorless needles, m. p. 139°C.

Found: N, 14.57. Calcd. for $C_{13}H_{12}N_2$; N, 14.28%.

Reaction with 4-Nitromethylenedioxybenzene.—4-Nitromethylenedioxybenzene (0.64 g.) was submitted to the reaction described above with an equivalent amount of sulfuryl chloride. After the decomposition with water, the reaction mixture gave yellow needles, m. p. 176°C (4-nitrocatechol melts at 175°C[10]). The needles gave a dark green color when treated with ferric chloride solution.

Found: N, 9.17. Calcd. for $C_6H_5O_4N$; N, 9.03%.

The author wishes to express his gratitude to Professor Mamoru Yamaguchi of Tohoku University for his constant guidance in the course of this work. He also wishes to thank the members of Professor Fujise's laboratory of the Faculty of Science for their microanalyses.

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[10] E. Bamberger and M. Czerkis, *J. prakt. Chem.*, (2), **68**, 480 (1903).