

bromine atoms from equation 3. This suggests that the active entity responsible for the chain reaction may not be the bromine atom but a free radical of the type $\cdot\text{BrO}_2$. The latter is a possibility which we are keeping in mind.

From the standpoint of the thesis developed in this paper, an attractive explanation is at once available to account for the fact that cyclopropylamine does not react with bromine, although the ring is easily cloven by nitrous acid.⁹ The amino group is an inhibitor in reactions involving bromine atoms. The stability of the ring, therefore, is to be ascribed to the chain-breaking mechanism of the amino group, rather than to the inherently greater stability of the ring in cyclopropylamine. The same explanation applies to the resistance toward cleavage of cyclopropyl cyanide.^{5c} The effect of groups on the stability of the cyclopropane ring is, therefore, not necessarily related to ease of cleavage of the ring with bromine.

The oxygen effect in the reaction of hydrogen bromide and cyclopropane, when the latter is used in large excess, is readily correlated with our bromine atom chain mechanism. The free bromine atoms are formed by equations 1 or 2. The formation of normal propyl bromide by the chain mechanism is indicated by equations 4 and 6, by a different mechanism in equation 9.

The ineffectiveness of light and oxygen on the rate of reaction of equimolecular quantities of hydrogen bromide and cyclopropane is suggestive of an ionic mechanism different from an atom or

free-radical chain reaction. Furthermore, the fact that substances such as thiocresol, catechol, acetic acid, and water have an accelerating effect lends some support to the idea that the mechanism is ionic in character. These substances are all capable of combining with a proton and thereby causing dissociation of the hydrogen bromide molecule into a bromide ion and a positively charged fragment. The cleavage of the cyclopropane ring by ions would not be expected to be photochemical. The accelerating effect of hydroxylic compounds indicates that the contribution of an atom mechanism to the rate of reaction is insignificant in concentrated hydrogen bromide solutions.

Summary

1. The reaction of bromine with a ten-fold excess of cyclopropane is greatly accelerated by the combined effect of oxygen and light.

2. The reaction of hydrogen bromide with a ten-fold excess of cyclopropane is greatly accelerated by oxygen and only slightly accelerated by light.

3. Organic peroxides have an effect similar to that of oxygen.

4. A chain mechanism involving bromine atoms is suggested for each addition reaction.

5. The addition of hydrogen bromide to an equivalent quantity of cyclopropane is not significantly affected by oxygen or light, but is accelerated by hydroxylic compounds. For this effect a competing non-atomic mechanism is suggested.

(9) Kishner, *Chem. Zentr.*, **73**, 11, 579 (1901); **76**, I, 1703 (1905).

CHICAGO, ILLINOIS

RECEIVED MAY 22, 1939

[CONTRIBUTION FROM THE GEORGE HERBERT JONES LABORATORY OF THE UNIVERSITY OF CHICAGO]

Chlorinations with Sulfuryl Chloride. I. The Peroxide-Catalyzed Chlorination of Hydrocarbons

BY M. S. KHARASCH AND HERBERT C. BROWN¹

In the past the use of sulfuryl chloride as a chlorinating agent has depended upon the dissociation of the compound, under the experimental conditions, into its components—sulfur dioxide and chlorine. That is, the sulfuryl chloride served as a source of *molecular* chlorine, and it has been used almost exclusively for the chlorination of aromatic nuclei in the presence of halogen carriers.²

The utilization of sulfuryl chloride in this way offers little advantage over the use of gaseous chlorine; for this reason sulfuryl chloride has not been generally adopted in the laboratory for carrying out such chlorinations.

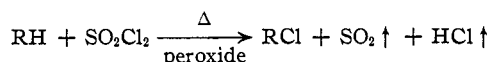
In the course of investigations on the chemical properties of free radicals in solution, which are now being carried out in this Laboratory, it was found that in the presence of certain catalysts (such as organic peroxides) sulfuryl chloride can serve as a source of chlorine *atoms*. Using this procedure,

(1) Eli Lilly Fellow, 1938-39.

(2) (a) Tohl and Eberhard, *Ber.*, **26**, 2940 (1893); (b) Silberrad, *J. Chem. Soc.*, **119**, 2029 (1921); (c) **121**, 1015 (1922); (d) Silberrad, Silberrad and Parke, *ibid.*, **127**, 1724 (1925).

it is possible to chlorinate *in the dark* many types of compounds (paraffin hydrocarbons, side-chains of aromatic hydrocarbons, aliphatic acids, aldehydes, and ketones, etc.) far more rapidly and conveniently than is possible by the use of elementary chlorine and light.³

General Procedure



The sulfuryl chloride is mixed with the compound to be chlorinated (Note 1) in a round-bottomed flask, and a small amount of benzoyl peroxide (Note 2) is added (0.001 to 0.005 mole of peroxide per mole of sulfuryl chloride). The flask is connected to an efficient reflux condenser (Note 3), preferably by a ground-glass joint, and the entire mixture is refluxed gently. Evolution of gases (hydrogen chloride and sulfur dioxide) begins at once. When these gases are no longer given off, the reaction is complete (Note 4). The reaction mixture is fractionated without further treatment (Note 5).

As previously stated (Note 3), the yields obtainable by this method vary with the efficiency of the reflux condenser. Without using any particular precautions, yields of 80% (based on the available chlorine utilized) are obtained easily. If a trap kept at -10° is connected to the condenser, and the trapped material is returned to the reaction flask periodically, the yields can be made quantitative.

Notes

(1) The molar ratio of sulfuryl chloride to organic compound which is used depends upon the same factors that operate in ordinary chlorinations: relative cost of materials, ease of separation of the higher chlorinated products, etc. In this work, we have usually used a large excess of hydrocarbon in carrying out the chlorination because in most of the preparations we were interested primarily in observing the point of attack of the reagent, not in obtaining the maximum possible yield.

(2) Benzoyl peroxide was used in most of this work. Most other peroxides tested (*e. g.*, lauroyl peroxide) act similarly. On the other hand, ascaridole gives poor results. Apparently, it decomposes far too rapidly to be used as a catalyst in this reaction.

(3) In this paper the chlorination of hydrocarbons is discussed. The chlorination of many types of oxygen derivatives by this method is under investigation, and the results will be reported shortly.

(3) The yield of product depends upon the efficiency of the reflux condenser. An inefficient condenser permits the gases evolved to carry off an appreciable quantity of the volatile reactants.

(4) The progress of the reaction is followed easily if the gases evolved are led through a gas wash bottle connected by tubing to the top of the reflux condenser. The time required to carry out a reaction varies with the compound to be chlorinated, the rate of heating, and the amount of peroxide added; however, in most cases, the reaction can be completed in from one to two hours for reaction mixtures which contain one mole of sulfuryl chloride, one to three moles of hydrocarbon, and 0.002 mole of peroxide.

(5) The results reported in this paper were obtained with the use of a short fractionating column, 25 cm. in length, the inner tube of which (9 mm.) was packed with a spiral of no. 18 silver wire coiled to two turns per centimeter.

Chlorination of Paraffin Hydrocarbons

The study of the action of sulfuryl chloride on paraffin hydrocarbons and their halogen derivatives has been neglected almost completely. The only report in the literature dealing with this subject is a patent covering the chlorination of methane with sulfuryl chloride at 300° in the presence of a catalyst such as carbon.⁴

In the absence of catalysts and light, sulfuryl chloride does not react with cyclohexane⁵ to an appreciable extent at temperatures as high as its boiling point. Even in the presence of light, the chlorination of the hydrocarbon with sulfuryl chloride is very slow. For example, a mixture of the two compounds, strongly illuminated⁶ and refluxed, reacts no more than 25% in six hours.

Most of the materials whose catalytic activity was investigated affect the rate of chlorination but slightly. In contrast, the effect of a trace of peroxide is amazing. The addition of 0.001 mole of benzoyl peroxide to the reaction mixture causes *complete reaction in from fifteen to thirty minutes in the dark*. The results of these studies are listed in Table I.

In these experiments, 0.6 mole of the hydrocarbon and 0.2 mole of sulfuryl chloride were refluxed, usually for six hours unless the reaction was complete before that time.

(4) McKee and Salls, U. S. Patent 1,765,601 (1930).

(5) Cyclohexane was selected because of its simple structure and availability, and its reactions with sulfuryl chloride under various conditions were studied intensively.

(6) A 300-watt lamp, placed 10 cm. from the flask, was used to illuminate the reaction mixture.

The extent of reaction was calculated from the amount of chlorocyclohexane isolated upon fractionation of the reaction mixture. Except where stated otherwise, the reaction was carried out with complete exclusion of light.

TABLE I
CHLORINATION OF CYCLOHEXANE WITH SULFURYL
CHLORIDE

Catalyst	Reaction time, hours	Yield, %
CuCl, 0.2 mole	6	20
S, 0.01 mole	6	0
I, 0.01 mole	6	0
PCl ₅ , 0.01 mole	6	5
Slow stream HCl	3	0
Slow stream SO ₂	3	0
Slow stream O ₂	3	0
No catalyst	6	0
Animal carbon, 5 g.	6	30
No catalyst, light ^a	6	25
Animal carbon, 5 g., light	6	75 ^b
Benzoyl peroxide, 0.001 mole	1/2	80
Lauroyl peroxide, 0.001 mole	1/4	80

^a For intensity of light, see footnote 6. ^b Reaction was not complete in less than six hours.

The study of the chlorination of a number of paraffin hydrocarbons and their halogen derivatives was undertaken to determine the generality of this method of chlorination and to compare the results thus obtained with those reported for the photochemical chlorination of these compounds with chlorine gas.

In general, the results are similar. Secondary hydrogen atoms are substituted by chlorine more readily than primary, and the presence of a halogen substituent increases the difficulty of further substitution. This deactivating effect is especially strong upon the carbon atom holding the substituent,⁷ and decreases with increasing distance from it.

The experimental results are summarized in Table II.

Chlorination of Side-Chains in Aromatic Hydrocarbons

As stated previously, the use of sulfuryl chloride as a chlorinating agent has been restricted largely to the chlorination of aromatic nuclei in the presence of halogen carriers.² However, the isolation of benzyl chloride from the chlorination of toluene has been reported several times. Dubois⁸

(7) The presence of two or more chlorine atoms upon a carbon atom completely prevents further substitution on that carbon atom by this method. Thus, neither chloroform nor *sym*-tetrachloroethylene could be chlorinated. That this inactivity is not due to the presence of inhibitors is shown by the fact that these compounds can be used as solvents in the chlorination of other substances.

(8) Dubois, *Bull. acad. roy. Belg.*, **42**, 126 (1876).

reports that toluene and sulfuryl chloride react slowly at 115° to form benzyl chloride and chlorotoluene, and Wohl⁹ patented the preparation of benzyl chloride in 50% yield by the action of sulfuryl chloride on toluene at 130°. Tohl and Eberhard^{2a} state that a refluxing mixture of toluene and sulfuryl chloride does not react. More recently, this statement has been questioned, and it has been reported that toluene and sulfuryl chloride do react in the dark at the temperature of reflux.^{2d}

We find that pure peroxide-free toluene shows no sign of reaction with sulfuryl chloride after six hours of refluxing in the dark. In the light,⁶ however, a slow reaction takes place which is not complete in less than seven hours.¹⁰ Benzyl chloride is formed. In the presence of a small amount of added peroxide, a vigorous reaction occurs in the dark and nearly quantitative yields of benzyl chloride can be obtained in fifteen minutes. In the presence of excess sulfuryl chloride further chlorination of the side-chain occurs and benzal chloride is formed. The introduction of a third chlorine atom into the side-chain either does not take place or occurs so slowly that for all practical purposes the reaction may be neglected. For example, a mixture of benzal chloride, sulfuryl chloride, and benzoyl peroxide was refluxed for twenty hours without any reaction being observed. This result is a confirmation of the conclusion previously drawn from the inertness of *sym*-tetrachloroethane and chloroform: the accumulation of two chlorine atoms upon a carbon atom prevents further substitution upon that atom (by this method of chlorination).

Derivatives and homologs of toluene are chlorinated readily by sulfuryl chloride and peroxide with but few exceptions. Thus *p*-chlorotoluene, ethylbenzene, isopropylbenzene, etc., are easily and smoothly chlorinated in the side chain. On the other hand, neither *o*-nitrotoluene nor *p*-nitrotoluene can be chlorinated in this way.

Diphenylmethane is another compound which does not undergo the peroxide-catalyzed chlorination with sulfuryl chloride. Furthermore, this compound strongly inhibits the reaction between sulfuryl chloride and cyclohexane. This inhibitory ability must be a property of the substance itself; careful purification of the hydrocarbon does not alter its behavior.

(9) Wohl, German Patent 139,552 (1903); 160,102, 162,394 (1905).

(10) The reaction mixture contained 0.6 mole of toluene and 0.2 mole of sulfuryl chloride.

TABLE II
CHLORINATION OF ALIPHATIC HYDROCARBONS AND THEIR HALOGEN DERIVATIVES

Compound chlorinated	Moles taken			Reacn. time, hr.	Yield chlor. prod., % ^a	Products ^b % Compound	°C.	B. p. Mm.	n _D ²⁰
	Compound	SO ₂ Cl ₂	Peroxide						
Cyclohexane	0.8	0.6	0.001	1.5	100	72 Chlorocyclohexane	66-68	62	1.462
						28 Dichlorocyclohexane			
Cyclohexane	1.8	.6	.001	1.5	98	89 Chlorocyclohexane			
						11 Dichlorocyclohexane			
n-Heptane	3.0	.75	.001	1.0	90	15 1-Chloroheptane	156-159		1.428
						85 s-Chloroheptane			
n-Propyl chloride	0.6	.2	.002	4.0	85	60 1,2-Dichloropropane	96-99		
						40 1,3-Dichloropropane	121-125		
n-Butyl chloride	2.5	1.0	.001	3.0	85	25 1,2-Dichlorobutane	121-123		1.441
						50 1,3-Dichlorobutane	131-133		1.444
						25 1,4-Dichlorobutane	77-79	62	1.455
						No 1,1-Dichlorobutane			
Propylene chloride	10.0	2.5	.005	1.5	80	15 1,1,2-Trichloropropane	131-133		
						48 1,2,2-Trichloropropane	122-124		
						37 1,2,3-Trichloropropane	155-158		
						70 1,2,2-Trichloroethane	113-114		1.4708
Ethylene chloride	0.3	0.3	.002	2.5					
sym-Tetrachloroethane	.2	.4	.002	6.0	None				
Chloroform	.22	.2	.005	3.0	None				
n-Propyl bromide	3.0	.75	.001	2.5	90	50 1-Bromo-2-chloropropane	116-117		1.4746
						30 1-Bromo-3-chloropropane	68-70	62	1.4950
						20 Higher b. unidentified			
						No n-Propyl chloride			

^a The total yield was calculated from the chlorinated reaction mixture before separation into the individual components. ^b Yields are calculated from the rectification graphs.

This method of chlorination with sulfuryl chloride promises to be of special value in the chlorination of side-chains of aromatic hydrocarbons containing reactive nuclei. The photochemical chlorination of the side-chains of such molecules usually leads to impure products due to simultaneous nuclear substitution. By the use of sulfuryl chloride and a peroxide, however, it is possible, in some cases, to prevent entirely the chlorination of the nucleus and obtain a pure product, containing halogen in the side-chain only.

For example, the chlorination of the side-chain of *m*-xylene with chlorine gas and sunlight to form *m*-xylyl chloride is accompanied by the formation of at least 10% of 4-chloro-*m*-xylene under the most favorable conditions.¹¹ The separation of the two products by fractionation is difficult. Chlorination of *m*-xylene with sulfuryl chloride and peroxides yields only *m*-xylyl chloride. The purity of the product was ascertained from the refractive index, and a comparison of the analytical data for side-chain and total halogen. In spite of reports to the contrary,^{2a} pure sulfuryl chloride and *m*-xylene do not react at the reflux temperature¹² of the mixture.

(11) King and Merriam, *Proc. Nova Scotian Inst. Sci.*, **18**, 276 (1933-34); *C. A.*, **29**, 8214 (1935).

(12) The difficulties encountered in proving this fact illustrate the extreme caution needed in working with peroxide-catalyzed reactions. A test run which was made in the dark with *m*-xylene and sulfuryl chloride in the absence of added peroxides showed a vigorous reaction. The product formed, however, was *m*-xylyl chloride, not the 4-chloro-*m*-xylene which nuclear chlorination would have pro-

duced. *t*-Butylbenzene is another compound whose chlorination is better effected by the use of sulfuryl chloride than by the ordinary photochemical method. As a matter of fact, the side-chain of this hydrocarbon is so unreactive toward the halogens that it is impossible to obtain the halogen derivatives directly. Conditions under which reaction occurs with the halogens lead only to nuclear substitution products.¹³ However, by the use of a peroxide and sulfuryl chloride, the side-chain can be chlorinated with ease.

On the other hand, the nuclei of fluorene and β -methyl-naphthalene are extremely reactive, and the reaction, to produce nuclear substitution products,¹⁴ occurs so readily that the method cannot be used for the chlorination of the side-chains of these molecules.

The experimental results are summarized in Table III.

Experimental Part

Materials.—The sulfuryl chloride was obtained in large quantities from the Hooker Electrochemical Company. The other materials used in this work were chiefly Eastman Kodak Co. chemicals or commercial products. Several of the substances used were prepared by standard methods.

The reagents were tested and found to be peroxide free. Further investigation disclosed that the solvent (acetone) which had been used to rinse the reaction flask, was the source of the peroxide impurity.

(13) Salibil, *Chem. Zig.*, **35**, 97 (1911); *Chem. Zentr.*, **I**, 1581 (1911).

(14) The products formed in the reaction between sulfuryl chloride and such reactive hydrocarbons will be reported in a later communication.

TABLE III
 CHLORINATION OF SIDE-CHAINS OF AROMATIC HYDROCARBONS

Compound chlorinated	Moles taken			Reacn. time, hr.	Yield chlor. prods., % ^a	Products ^b Compound	Physical constants		
	Cpd.	SO ₂ Cl ₂	Per-oxide				°C.	B. p.	Mm.
Toluene	0.6	0.2	None,	7.0		75 Benzyl chloride	96-99	62	1.5390
			light						
Toluene	.4	0.2	0.0003	0.25		80 Benzyl chloride			
Toluene	.4	1.6	.003 ^c	6.0	85	10 Benzyl chloride			
						90 Benzal chloride	104-105	30	1.5503
Benzal chloride,	.2	0.4	.002	20	None				M. p.
<i>p</i> -Chlorotoluene	.4	.2	.001	0.25		70 <i>p</i> -Chlorobenzyl chloride	114-117	30	29 ^d
Ethylbenzene	.8	.2	.001	0.25	85	Chiefly α -chloroethylbenzene	90-93	30	
Isopropylbenzene + 0.75 mole of benzene	1.5	.3	.001	1.5	95	90 α -Chlorocumene			
						10 β -Chlorocumene	95-99	21	
<i>m</i> -Xylene + 0.7 mole of carbon tetrachloride	1.0	.3	.001	0.5		80 <i>m</i> -Xylyl chloride	101-102	30	1.5345
<i>m</i> -Xylene + 0.3 mole of carbon tetrachloride	0.2	.1	None	6.0	None				
<i>t</i> -Butylbenzene	.6	.3	0.001	0.2		70 β -Chloro- <i>t</i> -butylbenzene	119-120	30	1.5253
<i>o</i> -Nitrotoluene	.6	.2	.001	2.0		No chlorination but decomposition of SO ₂ Cl ₂			
<i>p</i> -Nitrotoluene	.2	.4	.005	4.0		No chlorination but decomposition of SO ₂ Cl ₂			
Diphenylmethane	.2	.22	.002	2.0		Less than 20% chlorination and decomposition of SO ₂ Cl ₂			
Fluorene	.3	.1	None	Reacn. on warming		Nuclear chlorination			
β -Methylnaphthalene	.3	.1	None	Reacn. on warming		Nuclear chlorination			

^{a,b} See notes on Table II. ^c Added in three equal portions at one-hour intervals.

n-Propyl bromide and *n*-butyl chloride were synthesized according to the general procedures described in "Organic Syntheses." Diphenylmethane was prepared by the action of aluminum amalgam on benzyl chloride and benzene.¹⁵ *t*-Butylbenzene was prepared conveniently by the treatment of a mixture of 40 moles of benzene and 4 moles of *t*-butyl chloride with 10-15 g. of aluminum chloride for four hours at room temperature. The yield of purified product was 80%.

Although in the experiments reported in this paper the materials were purified by distillation or recrystallization before use, such purification is not necessary: the commercial products undergo this peroxide-catalyzed chlorination readily. In some cases in which impure materials were used, an inhibition period of from fifteen to thirty minutes was observed. However, no noticeable diminution of the yield occurred. It appears that the impurities which cause the inhibition are removed or deactivated by continued refluxing with sulfuryl chloride and peroxides.

Solvents.—The use of a solvent or a diluent is advantageous in a few cases, as in the chlorination of solid materials and in lowering the reaction temperature,¹⁶ so the applicability of a number of solvents was tested.

(15) *Org. Syntheses*, **15**, 34 (1934).

(16) The solution must be kept refluxing throughout the reaction so that the vapors of the boiling solution may keep the oxygen of the air, which strongly inhibits the reaction, away from the reaction mixture. By using a low-boiling solvent, it is possible to accomplish this at a lower temperature and thus minimize the possibilities of secondary reactions of sulfuryl chloride with the compound.

A mixture containing 0.3 mole of toluene, 0.2 mole of sulfuryl chloride, and 0.3 mole of the solvent (diluent in this case) was treated with 0.001 mole of benzoyl peroxide and refluxed. The course of the reaction was followed by the rate of evolution of the gases, and by the loss in weight of the reaction flask.

The following solvents were found applicable: methylene chloride (40°), chloroform (61°), carbon tetrachloride (77°), benzene (80°), chlorobenzene (132°), and *o*-dichlorobenzene (180°).

Carbon tetrachloride was used in the chlorination of a number of aromatic hydrocarbons (Table III).

Chlorination of Aliphatic Hydrocarbons.—The chlorination of the aliphatic hydrocarbons and their halogen derivatives when treated with sulfuryl chloride and peroxides according to the general procedure outlined, proceeds smoothly, and the experimental conditions in the individual cases need not be described. However, it may be worthwhile to call attention to the following observation. The chlorination of volatile compounds (*e. g.*, *n*-propyl chloride, b. p. 46.8°) is rather slow, due to the slow rate of decomposition of the benzoyl peroxide at the temperature of reflux. This rate can be increased in two ways—by using a less stable peroxide (*e. g.*, lauroyl peroxide) or by raising the boiling point of the reaction mixture. The latter can be accomplished most conveniently in the laboratory by adding a suitable diluent of relatively high boiling point (chlorobenzene or *o*-dichlorobenzene).

Chlorination of Side-Chains.—The chlorination of the side-chains of aromatic hydrocarbons according to the general procedure also proceeds smoothly in most cases. However, certain of the preparations require special techniques or raise points of interest, and therefore should be discussed further.

Toluene reacts readily when an excess of the hydrocarbon is treated with benzoyl peroxide and sulfuryl chloride. The identity of the chief product was established as benzyl chloride by preparing the quaternary ammonium salt with dimethylaniline (m. p. 115–116°). On the other hand, when the hydrocarbon is treated with an excess (1:4) of sulfuryl chloride, the reaction does not go to completion, but ceases after only two parts of the sulfuryl chloride have been utilized to form benzal chloride. In order to determine the cause of this inactivity the following experiments were carried out.

In a 200-cc. round-bottomed flask were placed 36.8 g. of toluene (0.4 mole), 54.0 g. of sulfuryl chloride (0.4 mole), and 0.5 g. of benzoyl peroxide (0.002 mole). Upon refluxing this mixture a vigorous reaction took place, complete in less than half an hour. Another portion of sulfuryl chloride (0.4 mole) and benzoyl peroxide (0.002 mole) was added, and the refluxing was continued. In this case, the reaction required three hours to reach completion. No further reaction was observed after a third portion of sulfuryl chloride and peroxide was added and the treatment was repeated. The product isolated was benzal chloride.

Benzal chloride (Eastman Kodak Co.) was distilled under reduced pressure, and a fraction boiling between 104–105° at 30 mm. was collected. A reaction mixture made up of 32.2 g. of this material (0.2 mole), 54.0 g. of sulfuryl chloride (0.4 mole), and 0.5 g. of benzoyl peroxide (0.002 mole) was refluxed for twenty hours. The loss in weight of the flask was less than 10% of the theoretical. The reaction mixture was fractionated, but beyond the fact that the last portion of the reaction mixture distilled up to 108° (30 mm.), no evidence of reaction was observed.

In a flask were placed 18.4 g. of toluene (0.2 mole), 16.1 g. of benzal chloride (0.1 mole), and 27.0 g. of sulfuryl chloride (0.2 mole). Benzoyl peroxide was added (0.002 mole), and the mixture was refluxed. Reaction began at once, and was complete in twenty minutes.

These experiments indicate that the inability of sulfuryl chloride to chlorinate toluene completely to benzotrichloride must be due to the inactivity of benzal chloride toward the reagent, and not to any chain-breaking property of the molecule.

The chlorination of **ethylbenzene** yields the α -chloro derivative as shown by the ease of hydrolysis of the compound isolated, and by the

formation of acetophenone by the action of cupric nitrate upon the compound.¹⁷ A small amount of β -chloroethylbenzene is probably formed also, but its presence could not be demonstrated by the method used.¹⁸

In a sealed tube were placed 14.0 g. of chloroethylbenzene (0.1 mole), and 20 g. of pyridine (0.25 mole). The mixture was heated at 115–120° for six hours. The tube was then opened, and the styrene and excess pyridine were removed under reduced pressure. The residue was extracted twice with an alcohol-ether mixture. However, the quaternary ammonium salt of β -chloroethylbenzene could not be isolated.

The chlorination of **isopropylbenzene** also indicates that the substitution of chlorine in the side-chain takes place predominantly at the α -position. In this case, the analysis of the reaction mixture is simplified by the fact that the α -chloro derivative is a tertiary chloride, readily decomposed by heating into an olefin and hydrogen chloride.

The reaction was carried out according to the general procedure. In order to minimize disubstitution, a 5:1 ratio of hydrocarbon to sulfuryl chloride was used (1.5 mole cumene, 0.3 mole sulfuryl chloride). Benzene was used as a solvent to keep the temperature moderate throughout the reaction. After the reaction was complete, the benzene and excess isopropylbenzene were carefully removed under reduced pressure (21 mm.). The weight of the residual liquid indicated a yield of 95%. This material was refluxed under reduced pressure until hydrogen chloride was no longer given off, and was then fractionated. β -Phenylpropylene passed over between 59 and 62° (21 mm.). Between 95 and 100°, 2.5 g. of β -chloroisopropylbenzene was collected. This represents approximately 10% of the total product.

***t*-Butylbenzene** was prepared by the Friedel-Crafts synthesis. The measurement of the refractive index of the product (n_D^{20} 1.4927) and its unreactivity toward bromine demonstrate the absence of alpha hydrogen atoms, and establish the purity of the product.

The hydrocarbon, 5.0 g., was treated with 1 cc. of a 5% solution of bromine in carbon tetrachloride. The mixture was illuminated by a 300-watt lamp for twenty-four hours. No reaction was evident.

In another experiment, the hydrocarbon was treated with bromine and ascaridole,¹⁹ but no reaction occurred.

Chlorination of the hydrocarbon with sulfuryl chloride proceeded with a rapidity that is especially surprising in view of the general unreactivity.

(17) Fischer and Schmitz, *Ber.*, **39**, 2210 (1906). The acetophenone was identified in the form of its phenylhydrazone.

(18) α - and β -chloroethylbenzene cannot be separated by fractionation.

(19) Kharasch, Margolis, White and Mayo, *THIS JOURNAL*, **59**, 1405 (1937).

tivity of the side-chain toward other reagents. A product was isolated by fractionation (b. p. 119–120° at 30 mm., n_D^{20} 1.5253) which was identified as β -chloro-*t*-butylbenzene by the preparation of the anilide of β,β -dimethylhydrocinnamic acid,²⁰ m. p. 122–123°.

The action of **diphenylmethane** toward sulfuryl chloride is different from that of any of the other hydrocarbons whose chlorinations have been described. Not only is this compound incapable of undergoing the usual peroxide-catalyzed reaction with sulfuryl chloride, but it is capable of inhibiting the chlorination of other hydrocarbons by this method.

It is probable that this peculiar action is not due to the hydrocarbon itself, but to some product formed by a reaction of sulfuryl chloride with the compound. When diphenylmethane is mixed with sulfuryl chloride (no peroxide added), and the mixture is permitted to stand at room temperature, the originally clear solution becomes cloudy within a few minutes, reddening upon longer standing. After some time (one to three days), a red oil separates.

In a round-bottomed flask were placed 33.6 g. of diphenylmethane (0.2 mole), 30 g. of sulfuryl chloride (0.22 mole), and 0.5 g. of benzoyl peroxide (0.002 mole). The mixture was refluxed. No evolution of gas occurred during the first thirty minutes, but the solution became red in color. Upon continued refluxing, a slow reaction occurred, as was shown by the gas given off. Examination disclosed that this gas contained free chlorine, indicating decomposition of the sulfuryl chloride. After three hours, reaction had ceased. The reaction mixture was fractionated under reduced pressure. It consisted chiefly of unchanged diphenylmethane. Less than 20% of the product distilled in the temperature range of benzhydryl chloride (156–162 at 13 mm.). No sulfuryl chloride was recovered; it was probably completely dissociated into sulfur dioxide and chlorine.

A number of other experiments were carried out in which the conditions (temperature, solvents, peroxide, ratio of reagents, etc.) were altered, but with the same result. Since sulfuryl chloride is ordinarily stable under the conditions used in these experiments, the dissociation of the reagent must be due to the catalytic action of some substance formed in the reaction mixture.

The following experiment illustrates the inhibiting effect of diphenylmethane on the chlorination of other hydrocarbons.

(20) The general procedure recommended by Underwood and Gale, *THIS JOURNAL*, **58**, 2117 (1934), was followed with one exception. The Grignard reagent could not be prepared with the usual commercial magnesium activated according to the procedure recommended. Using sublimed magnesium and a crystal of iodine, the reaction occurred without difficulty.

Two reaction mixtures were made up. Both contained 5 g. of sulfuryl chloride and 5 g. of toluene plus a few grains of benzoyl peroxide. To one was added 5 cc. of chlorobenzene; to the other, 5 cc. of diphenylmethane. The flasks containing the mixture were placed in a hot-water bath simultaneously. The first mixture reacted vigorously while the second showed no signs of reaction after two hours.

Triphenylmethane, however, is chlorinated without difficulty.

In a reaction flask were placed 8.4 g. of triphenylmethane (0.033 mole), 13.5 g. of sulfuryl chloride (0.1 mole), and 0.1 g. of lauroyl peroxide (0.0005 mole). The mixture was refluxed for thirty minutes. The excess sulfuryl chloride was removed, and the reaction product was twice recrystallized from ligroin (90–100°). There was isolated 5.7 g. of material, m. p. 111–112°, which was identified as triphenylmethyl chloride by the fact that the melting point of a mixture with a known sample of triphenylmethyl chloride was not depressed.

The **nitrotoluenes** do not undergo the peroxide-catalyzed reaction with sulfuryl chloride. This inactivity is probably due to inhibitory (chain-breaking) properties of the nitro groups. For example, the chlorination of cyclohexane is slowed down markedly by the addition of a small amount of *p*-nitrotoluene.

Inhibition of the Reaction.—It has been pointed out that the reaction between sulfuryl chloride and hydrocarbons is markedly catalyzed by small amounts of peroxides.²¹ The reaction is equally sensitive to small quantities of other substances. For example, the addition of iodine or sulfur, in moderate excess over the amount of peroxide added, will completely inhibit the reaction. A slow stream of oxygen through the reaction mixture also inhibits the reaction.¹⁶ A number of substances were tested for their effect on the reaction.

A mixture of 168 g. of cyclohexane (2.0 moles) and 270 g. of sulfuryl chloride (2.0 moles) was made up. To 21.9 g. of this mixture (containing 0.1 mole each of cyclohexane and sulfuryl chloride) there was added 0.001 mole of benzoyl peroxide and 0.01 mole of the substance whose inhibitory properties were being tested. The mixture was refluxed for one hour (unless the reaction was complete before that time), and the extent of the reaction was estimated from the loss in weight of the reaction flask.

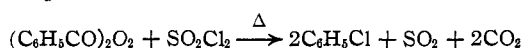
Under these conditions, the following substances inhibit the reaction: iodine, sulfur, *p*-nitrotoluene, thionyl chloride, phosphorus trichloride, and isoamyl nitrite. A slow stream of oxygen passing

(21) We have not made any attempt as yet to measure the smallest quantity of peroxide capable of completely chlorinating one mole of hydrocarbon. In one experiment, however, 0.0003 mole of benzoyl peroxide was sufficient catalyst to chlorinate completely one mole of toluene.

through the reaction mixture also prevents reaction.

On the other hand, the addition of acetyl chloride, acetic acid, and benzophenone has no noticeable effect upon the rate of the reaction.

Reaction of Benzoyl Peroxide with Sulfuryl Chloride.—In developing the mechanism of this reaction between sulfuryl chloride and hydrocarbons to be described later in this paper, it became of interest to study the action of benzoyl peroxide on sulfuryl chloride itself. It was found that at 70–80° benzoyl peroxide reacts slowly with sulfuryl chloride to form chlorobenzene, according to the equation

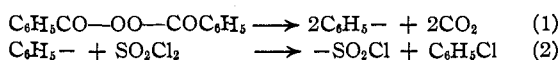


Sulfuryl chloride (0.4 mole) and benzoyl peroxide (12.1 g., 0.05 mole) were placed in a round-bottomed flask, and 0.4 mole of benzene was added as a diluent. The mixture was refluxed for twenty-four hours, and then fractionated; chlorobenzene, 8.0 g., was isolated (b. p. 128–131°), and identified by means of its nitration product, 2,4-dinitrochlorobenzene (m. p. 50–51°). Since the amount of chlorobenzene isolated represents 70% of the theoretical yield, it is evident that the equation above represents the main reaction. A few grams of higher-boiling material was also formed. This was fractionated under reduced pressure and the presence of benzoic acid and diphenyl demonstrated. These are the usual products of the decomposition of benzoyl peroxide in benzene.²²

Mechanism of the Reaction

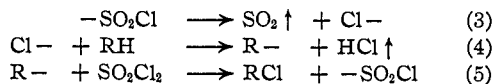
It is evident that this reaction between sulfuryl chloride and hydrocarbons has those characteristics which are commonly ascribed to chain reactions. Among these properties, the most significant is probably the sensitivity of the reaction to small traces of other substances—the rate is increased tremendously by small amounts of peroxides, and completely inhibited by small quantities of sulfur, iodine, and oxygen. Furthermore, the similarity of the results obtained in this reaction with those obtained by photochemical chlorination is also significant, and points to an identical reactive intermediate—the chlorine atom.

The decomposition of peroxides to form free radicals appears to be well established.²³ These free phenyl radicals are known to remove halogen from molecules containing reactive halogen. Based upon these facts, the following chain mechanism for this reaction is advanced tentatively.

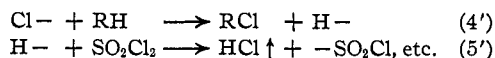


(22) Lippmann, *Monatsh.*, **7**, 522 (1886).

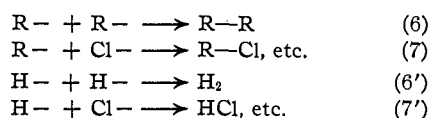
(23) Hey and Waters, *Chem. Rev.*, **21**, 186 (1937).



It may be that the reaction proceeds through an alternative mechanism involving a direct attack of the chlorine atom upon the hydrocarbon, forming the alkyl chloride and liberating a *hydrogen atom* to carry on the chain. This mechanism, which we consider very unlikely, may be indicated as follows:



The chain could be broken by the following steps

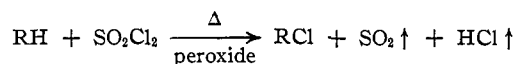


In addition, traces of impurities could break the chain by combining with the reactive intermediates, the atoms or free radicals. Those substances which have been shown capable of inhibiting the reaction probably operate in this manner.

These considerations indicate why peroxides are effective catalysts in this reaction. Furthermore, they suggest that any substance capable of removing a chlorine atom from sulfuryl chloride should also catalyze the reaction between sulfuryl chloride and organic compounds. This conclusion has been verified in a number of cases.²⁴ However, benzoyl peroxide remains the most convenient catalyst for general use in this reaction.

Summary

1. A trace of an organic peroxide induces a reaction between sulfuryl chloride and organic compounds



By the use of this procedure, it is possible to chlorinate *in the dark* many types of organic compounds more rapidly and conveniently than can be done by the use of elementary chlorine and light.

2. The study of the chlorination by this method of cyclohexane, *n*-heptane, *n*-propyl chloride, *n*-butyl chloride, ethylene chloride, propylene chloride, *sym*-tetrachloroethylene, chloroform, and *n*-propyl bromide leads to the following generalization: (a) Substitution takes place on a secondary carbon atom in preference to a primary. (b) A second chlorine atom tends to substitute as

(24) These results will be reported in a later communication.

far from the first chlorine atom as possible. (c) Substitution of a second chlorine atom upon a carbon atom already holding a halogen substituent is difficult; a third chlorine atom cannot be introduced. (d) A bromine substituent is not displaced.

3. The chlorination of side-chains of aromatic hydrocarbons proceeds readily as shown by a study of the chlorination of toluene, *p*-chlorotoluene, ethylbenzene, isopropylbenzene, *t*-butylbenzene, *m*-xylene, and triphenylmethane. The study of the chlorination of toluene, with an excess of sulfuryl chloride, reveals that in this case also the substitution of chlorine upon a carbon atom ceases with the introduction of the second chlorine atom. Both ethylbenzene and isopropylbenzene chlorinate chiefly in the alpha posi-

tion of the side-chain. Diphenylmethane and the nitrotoluenes cannot be chlorinated by this method.

4. This method of chlorination is of particular value for the chlorination of side-chains in molecules containing reactive nuclei. Thus, *m*-xylene is chlorinated in the side-chain without the simultaneous formation of any nuclear-substituted products; and *t*-butylbenzene reacts readily to form β -chloro-*t*-butylbenzene, a compound which cannot be prepared by the direct action of chlorine upon the hydrocarbon.

5. The characteristics of the reaction indicate that the slow decomposition of the peroxide at the reaction temperature initiates a chain reaction involving chlorine atoms.

CHICAGO, ILLINOIS

RECEIVED MAY 24, 1939

[CONTRIBUTION FROM THE GATES AND CRELLIN LABORATORIES OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY, No. 711]

The Magnetic Properties of Myoglobin and Ferrimyoglobin, and their Bearing on the Problem of the Existence of Magnetic Interactions in Hemoglobin

BY DONALD S. TAYLOR

Myoglobin, or muscle hemoglobin, was first isolated in crystalline form by Theorell,^{1a} who showed that it is very similar to hemoglobin but that it has certain important differences. The minimum molecular weight calculated from the iron analysis is 17,000,^{1a} a value agreeing with that calculated from hemoglobin analyses. Theorell^{1b} investigated the sedimentation velocity of crystallized myoglobin, and found two components, with molecular weights of 34,000 for the principal one and 68,000 for the secondary one. A re-determination by Polson² in the same laboratory gave the value 17,000, leading to the conclusion that there is only one iron atom, and therefore only one heme group per molecule. The oxygen saturation curve found for myoglobin^{1c} is a rectangular hyperbola rather than a sigmoid curve as is found for hemoglobin. It has a much higher affinity for oxygen than hemoglobin has^{1e} and thus acts as an oxygen reservoir for the muscle. Its oxygen

equilibrium is much less affected by change in acidity than is that of hemoglobin.^{1e} Myoglobin forms compounds analogous to those of hemoglobin, and is very easily oxidized to brown ferrimyoglobin³ (metamyoglobin). The absorption spectra^{1c} of myoglobin and its derivatives are very similar to those of the analogous hemoglobin substances, but the band positions are slightly shifted.

The magnetic studies of myoglobin are then of interest for the information they give about the structural chemistry of the myoglobin series, and also for the opportunity offered to make a comparison between this series in which the hemes are located on individual molecules (or at least are physico-chemically independent as judged by the oxygen equilibrium study^{1e}) and the hemoglobin series in which there are four hemes per molecule with a large physico-chemical interaction effect (calculated to be about 6000 calories per mole according to the theoretical analysis of the oxygen equilibrium by Pauling⁴). In particular this comparison should shed light on the question as to

(1) H. Theorell, *Biochem. Z.*, (a) **252**, 1 (1932); (b) **268**, 47 (1934); (c) **268**, 55 (1934); (d) **268**, 64 (1934); (e) **268**, 73 (1934).

(2) T. Svedberg, *Nature*, **139**, 1051 (1937). Note added in proof: Dr. Theorell has informed us in a private communication that Polson worked with cow myoglobin, so that the reported differences from values obtained by Theorell on horse myoglobin may be real. However, the discussion or conclusions given here are not changed by this new information.

(3) The nomenclature adopted here is analogous to that proposed by Pauling and Coryell⁵ for hemoglobin substances.

(4) L. Pauling, *Proc. Natl. Acad. Sci.*, **21**, 186 (1935).