Photochemical α-Chlorination of Fatty Acid Chlorides by Thionyl Chloride

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Upon chlorination of long and intermediate chain fatty acid chlorides in refluxing thionyl chloride exposed to visible and ultraviolet light, the orientation of chlorine was primarily to the α position. The more intense the light source, the more rapid the reaction, and the same reaction in the dark or in ambient light affords no more than a trace of α-chloro-substituted products. The rate of α-chlorination is appreciably accelerated in the presence of benzoyl peroxide, whereas mineral acid causes the rate to decrease very little. It is proposed that the reaction is photochemical and takes place in the liquid phase according to the following course. Irradiation of boiling thionyl chloride with intense visible or ultraviolet light causes it to slowly decompose to chlorine along with other products. α-Chloro acid chlorides are subsequently produced by a Hell–Volhard–Zelinsky type chlorination of the enol of the acyl chloride.

Fatty acids can be halogenated by one of two mechanisms: hydrogen abstraction by free radicals[1,2] or addition to the enol[3] form of the acid halide (Hell–Volhard–Zelinsky method[4]). The hydrogen abstraction method leads to the α-halo acid plus halo substitution in various other positions along the carbon chain. Bromination according to the Hell–Volhard–Zelinsky method yields only α-bromo acid,[4] whereas chlorination by the same procedure leads not only to α-chloro acid but to chlorination in various other positions[5] in appreciable amounts. Thionyl chloride is ordinarily employed to convert fatty acids into their acid chlorides or anhydrides and, as a solvent, it is one of a number of reagents used to facilitate α-halogenation of carboxylic acid chlorides. When fatty acid chlorides are treated with thionyl chloride in the presence of tertiary amines, a number of unusual products are obtained: α-chloro, α,β-unsaturated, and α-chlorosulfenyl acids.[6]

We wish to report a new reaction of thionyl chloride on fatty acids. When long and intermediate chain length fatty acids are treated with boiling thionyl chloride in the presence of strong visible or ultraviolet light, in the absence of base, a high percentage of α-chloro fatty acid is formed along with a small amount of α,α-dichloro substituted product.

The more intense the light source, the faster the reaction. The effect of light intensity on the rate of α-chlorination is indicated in Table I. A number of experiments were carried out to show that this reaction was light mediated and not merely brought about by the heat of the system, the results of which are summarized in Table II. When lauroyl chloride was heated under reflux by a heating mantle with thionyl chloride in the dark for 25 hr, only methyl laurate was detected by glc after esterification. In ambient light under the same conditions, 8.0% of α-chlorinated product was found. Upon exposure to a 1000-W tungsten lamp for the same period of time a yield of 84% methyl α-chlorolaurate was obtained. When the reaction flask was kept under reflux and shielded from the light rays of this lamp but not from its heat, 3.2% of α-chlorinated product was formed, whereas 0.2% of α-chlorolauric ester was detected when the reaction flask was not heated and shielded from the light rays of the lamp but not its heat. If a mixture of lauroyl and thionyl chlorides is kept under reflux and exposed to the rays of a 1000-W light source where the air space between the light source and reaction flask is cooled to <40°, 81.2% of methyl α-chlorolaurate is found.

TABLE I

EFFECT OF LIGHT INTENSITY ON RATE OF α-CHLORINATION OF LAUROYL CHLORIDE BY THIONYL CHLORIDE UNDER REFLUX[a]

Light source	Time, hr	Methyl laurate, %	Methyl α-chlorolaurate, %	Methyl α,α-dichlorolaurate, %
Ambient light	5	100		
200 W[b]	5	98.6	1.4	
300 W[b]	5	97.0	3.0	
500 W[b]	5	94.0	6.0	
1000 W[b]	5	63.0	37.0	1.0
Uv[c]	0.58	0.91	90.0	4.1

[a] Composition of mixture determined by converting acid chlorides into methyl esters followed by glc analysis. [b] Tungsten bulb. [c] Reference 9.

TABLE II

IMPORTANCE OF VISIBLE LIGHT FOR THE α-CHLORINATION OF LAUROYL CHLORIDE IN REFLUXING THIONYL CHLORIDE[a]

Light source	Methyl laurate, %	Methyl α-chlorolaurate, %	Methyl α,α-dichlorolaurate, %
Dark	100		
Ambient light	92.0	8.0	
1000 W[b,c]	4.4	84.0	11.6
1000 W[b,d]	86.4	3.2	10.4
1000 W[b,e]	99.8	0.2	
1000 W[b,f]	4.4	81.2	14

[a] Reaction time, 25 hr; products detected as methyl esters by glc. [b] Tungsten bulb. [c] Vapor temp, 146°. [d] Flask covered to keep out light but not heat of lamp; vapor temp, 94°. [e] Same as c without refluxing; vapor temp, 87°. [f] Cool air space between reaction flask and light source, $T < 40°$; vapor temp, 131°.

The addition of benzoyl peroxide, a free radical initiator, markedly accelerates the rate of chlorination of lauroyl chloride, whereas the addition of sulfuric acid decreases the rate of reaction very little, as seen in Figure 1. Upon the addition of a catalytic amount of benzoyl peroxide to myristoyl chloride, the rate of α-chlorination was also appreciably accelerated.

It was established that the α-chlorination was not intramolecular, by refluxing lauroyl chloride in the

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(1) M. S. Kharasch, and H. C. Brown, *J. Amer. Chem. Soc.*, **62**, 925 (1940).

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(3) H. B. Watson, *Chem. Rev.*, **7**, 173 (1930).

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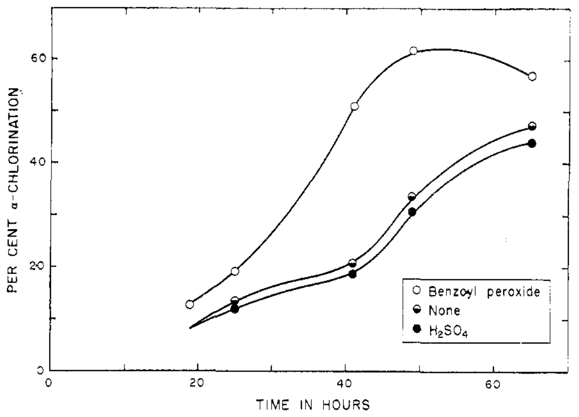

Figure 1.—Effect of benzoyl peroxide and sulfuric acid on the rate of α-chlorination of lauroyl chloride in boiling thionyl chloride illuminated by a 500-W tungsten lamp.

TABLE III

CHLORINATION OF 10-UNDECENOYL CHLORIDE BY REFLUXING THIONYL CHLORIDE[a]

Time, hr	Methyl undecenoate, %	Methyl 9,10-dichloro-undecanoate, %	Methyl 2,9,10-trichloroundecanoate, %	Methyl 2,2,9,10-tetrachloroundecanoate, %
17	100			
53	64.7	35.4		
78	28.1	55.0	16.9	
126		30.4	51.8	17.8

[a] Light source, 500-W tungsten lamp, products detected as methyl esters by glc.

TABLE IV

CHLORINATION OF 9,10-DICHLOROUNDECANOYL CHLORIDE BY REFLUXING THIONYL CHLORIDE[a]

Time, hr	Methyl 9,10-dichloro-undecanoate, %	Methyl 2,9,10-trichloro-undecanoate, %	Methyl 2,2,9,10-tetrachloroundecanoate, %
17	100		
53	69.6	16.1	14.3
78	57.4	20.6	18.7
126	33.6	44.0	22.4

[a] Light source, 500-W tungsten lamp; products detected by glc.

presence of strong visible light (500 W) for 48 hr. Only starting material was detected by glc. In order to verify that thionyl chloride does decompose into chlorine, we reacted 10-undecenoyl chloride with thionyl chloride according to our procedure, and a number of products were detected by glc. To identify these different peaks in the chromatograms, the undecenoic acid was chlorinated across the double bond according to standard procedures and subjected to thionyl chloride and light. The principal products were characterized by glc and mass spectrometry. The experiment shows that, when refluxing thionyl chloride is exposed to strong light, it decomposes to significant quantities of chlorine. This is in contrast to the thermal decomposition of thionyl chloride which only begins to dissociate at its boiling point.[7] The initial product formed, when 10-undecenoic acid chloride is exposed to thionyl chloride and light, is the 10,11-dichloro acid chloride and, with time, the 2,10,11-trichloro acid chloride becomes the major product. These data are summarized in Tables III and IV.

To demonstrate that the rate of α-chlorination is dependent on the vapor volume, a number of experiments were carried out varying the volume of the vapor phase. The results shown in Table V indicate that the greater the vapor volume, the faster the rate of α-chlorination.

TABLE V

EFFECT OF VAPOR VOLUME ON RATE OF α-CHLORINATION OF LAUROYL CHLORIDE BY REFLUXING THIONYL CHLORIDE[a]

Volume of flask, ml	Methyl laurate, %	Methyl α-chlorolaurate, %	Methyl α,α-dichlorolaurate, %
100	78.8	9.5	11.6
500	74.2	15.5	10.4
1000	64.3	20.4	15.2
5000	6.8	73.0	20.2

[a] Light source, 500-W tungsten lamp; reaction time 67 hr; products detected as methyl esters by glc.

That chlorination took place principally in the α position was demonstrated as follows. The mass spectrum of methyl α-chlorolaurate was characterized by peaks at *m/e* 248 (parent) and *m/e* + 2 250 (presence of Cl), which was approximately one third of that of the 248 peak. There was also a large 213 peak showing the loss of chlorine (P − 35). The base peak was *m/e* 108 ($ClCH{=}C(OH)OCH_3$), whereas methyl laurate, or any monochloro methyl laurate other than α, has a base peak of *m/e* 74 ($CH_2{=}C(OH)OCH_3$). The mass spectrometric data were similarly consistent for the α-chlorinated long chain fatty acid methyl esters of 10,11-dichloroundecanoic, myristic, palmitic, and stearic acids. Nmr data provided confirming evidence of α-chlorination by showing the presence of a triplet at *ca.* δ 4.3 (J = 6 Hz) which integrated for one α proton in the pure product. The nmr spectra of the chlorinated stearic and palmitic acids also showed only one α proton. Methyl laurate and methyl α-chlorolaurate were also identified and quantitated by glc and compared with authentic samples.[8] Elemental analyses and boiling points of some of the chlorinated fatty acids are listed in Table VI. A number of other fatty acids have been studied under these reaction conditions, and the results are summarized in Table VII. It shows that other long chain fatty acid chlorides, such as myristoyl, palmitoyl, and stearoyl, can be similarly α-chlorinated. By controlling the time of reaction, the rate of formation of side products can be minimized. Upon treating lauroyl chloride for 36 hr, the yield of α-chloro compound decreased while the yield of α,α-dichloro compound increased, and, after 96 hr, the

TABLE VI

METHYL ESTERS OF α-CHLORO FATTY ACIDS

Methyl ester	Registry no.	Bp, °C[a]	Formula[c]
α-Chlorolauric	33422-27-4	140 (8 mm)[b]	$C_{13}H_{25}O_2Cl$
α-Chloropalmitic	41753-98-4		$C_{17}H_{33}O_2Cl$
α-Chlorostearic	41753-99-5		$C_{19}H_{37}O_2Cl$
α,α-Dichlorolauric	33422-25-2	262	$C_{13}H_{24}O_2Cl_2$

[a] Analytical sample. [b] Lit.[8] bp 136–139° (8 mm). [c] Satisfactory analytical data (±0.4% for C, H, Cl, O) were reported for all compounds listed in the table: Ed.

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[7] N. V. Sidgwick, "The Chemical Elements and Their Compounds," Vol. II, Oxford University Press, London, 1950, p 931.

[8] H. H. Guest and C. M. Goddard, Jr., *J. Amer. Chem. Soc.*, **66**, 2074 (1944).

TABLE VII

α-CHLORINATION OF LONG CHAIN FATTY ACIDS[a]

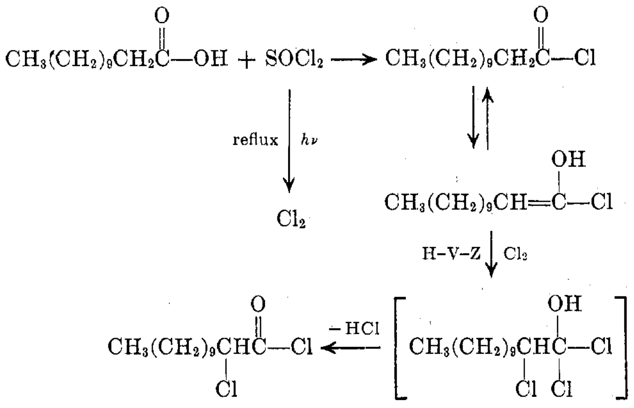
Fatty acid	Methyl ester, %	Methyl α-chloro ester, %	Methyl α,α-dichloro ester, %
Lauric	5.3	82.1	12.6
Myristic	3.2	84.6	12.2
Palmitic	4.3	90.0	5.7
Stearic	13.7	86.3	

[a] Light source, 1000-W tungsten lamp, 14 cm from pot; reaction time, 24 hr; products detected as methyl esters by glc.

yield of α,α-dichloro compound increased to over 60%. If the reaction time was reduced to 18 hr, the per cent of α-chloro product was increased to 91, while the dichloro product decreased to 5.1%.

It appears that the reaction is photochemical and takes place in the liquid phase proceeding by the mechanism shown in Scheme I. Thionyl chloride is decomposed in the vapor phase by heat and light into elemental chlorine among other products. The chlorine subsequently adds to the enol form of the acid chloride by a Hell–Volhard–Zelinsky reaction to finally yield α-chloro fatty acid chloride as a principal product. Enolization of fatty acid chlorides is enhanced by the presence of thionyl chloride.[5a] Since benzoyl peroxide is not volatile, its effect on increasing the rate of α-chlorination seems to be in accelerating the decomposition of thionyl chloride in the liquid phase. The increased rate of α-chlorination due to increased head space over the liquid phase is obviously due to the photodecomposition of greater volumes of thionyl chloride vapor in the unit of time, the products of which dissolve in the liquid phase. Finally, since the vapor pressures of the higher fatty acid chlorides are quite low at the boiling point of thionyl chloride, it would be reasonable to expect the chlorination reaction to take place in the liquid phase.

SCHEME I



Experimental Section

Boiling points are uncorrected. Mass spectra were run on a Hitachi RMU-6E single-focusing mass spectrometer. All nmr data were obtained on a Jeolco JMN-C-60HL spectrometer. Separations were carried out on a Varian Aerograph 1200 gas chromatograph, fitted with a flame ionization detector. The column used was 5 ft × 1/8 in. o.d. stainless steel tube packed with 3% QF-10065 on Chromosorb W, with a flow rate of nitrogen of 25 ml/min. The fatty acid esters were chromatographed isothermally at a column temperature of 150° for 2 min and programmed at 12°/min to 210°, and a Varian Aerograph Autoprep Model 700 was used for preparative fractionation.

Chlorination of Fatty Acids Using Visible Light.—To a round bottom flask, fitted with a reflux condenser and thermometer, were added 0.5 g of fatty acid and 10 ml of reagent grade thionyl chloride. The mixture was refluxed in the presence of a light source for a given period of time, after which an excess of anhydrous methanol was introduced and refluxing continued overnight. The reaction mixture was evaporated to dryness and the products identified by glc. Preparative samples were obtained using liquid chromatography and preparative glc.

Chlorination of Lauroyl Chloride Using Ultraviolet Light.—The reaction was carried out in a reaction vessel fitted with a quartz immersion well and a Hanovia high-pressure quartz mercury 450-W lamp.[9] Lauric acid (0.5 g) in 30 ml of reagent grade thionyl chloride was heated under reflux in the presence of the ultraviolet light. When the quartz immersion well was water cooled, the reaction was completed in 2 hr with the vapor temperature reaching 165°. When the quartz immersion well was not water cooled, the reaction was completed in 35 min, and the vapor temperature reached 230°. The composition of the product of the water-cooled reaction was 2% starting material, 73% α-chloro and 7% α,α-dichloro product, and 18% tarry material. For the reaction that was not water cooled, the composition of products was 0.9% starting material, 88% α-chloro and 4.6% α,α-dichloro product, and 6.5% tarry material.

Registry No.—Lauric acid, 143-07-7; thionyl chloride, 7719-09-7.

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[9] This lamp emits approximately 30% in the ultraviolet portion of the spectrum, 18% in the visible, and the remainder in the infrared.