

Action of Primary and Secondary Amines on Trihalogenated Esters¹

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The reactions of a series of trichloro- and trifluoroacetates with primary and secondary amines were investigated at room temperature. When the trichlorinated esters were treated with primary amines, acyl-oxygen cleavage occurred predominantly. A haloform-type cleavage took place when the same esters were treated with secondary amines. Trifluorinated esters were found to yield exclusively amides regardless of the amine used. In the trichloroacetate series the order of decreasing acyl-oxygen cleavage with *n*-butylamine was found to be: $C_6H_5O > CH_2=CHO > CH_3O \cong C_2H_5O > (CH_3)_3CO > C_6H_5CH_2O$. When the same esters were treated with piperidine the order of decreasing acyl-oxygen cleavage was found to be: $C_6H_5O > CH_2=CHO > CH_2=CHCH_2O \cong C_6H_5CH_2O > (CH_3)_3CO > CH_3O \cong C_2H_5O$. Steric hindrance in both the ester and the amine influenced the type of cleavage that occurred. Solvents such as acetonitrile or dioxane increased the per cent of haloform-type cleavage while carbon tetrachloride induced exclusive acyl-oxygen cleavage. The infrared carbonyl stretching frequencies of all esters, amides, and carbamates prepared in this study were measured with a precision of ± 2 cm^{-1} .

Primary amines were found to react with ethyl trichloroacetate to yield predominantly amides, while secondary amines reacted with the same ester to yield predominantly carbamates.³ Similar results were obtained when methyl trichloroacetate was treated with a secondary amine.⁴ On the other hand, ethyl trifluoroacetate reacted with both primary and secondary amines to yield exclusively amides.⁵ These reactions appeared to be of sufficient interest to warrant further study. The primary purpose of this investigation was to determine the influence of the alkoxide portion of the trihalogenated ester on the type of cleavage that occurred and to measure the extent of acyl-oxygen cleavage as compared to the haloform-type of cleavage. Another objective of this work was to study the reactions of several trifluoroacetates in order to ascertain that only acyl-oxygen cleavage occurred regardless of the nature of the ester.

The study of the reactions of trihalogenated acetates with primary and secondary amines involved the preparation of a series of trichloro- and trifluoroacetates in which the alkoxyl portion of the ester was varied to include electron-repelling, electron-withdrawing, and sterically hindered groups. All of these esters were treated with a primary amine, *n*-butylamine, and a secondary amine, piperidine, respectively, first in the absence of solvents and then in the presence of polar and nonpolar solvents. It was hoped that a systematic study of the possible factors which could affect the types of cleavage observed would lead to a better understanding of these reactions.

The separation and isolation of all the products formed in some reactions was hampered by the fact that these compounds were held together by strong polar interactions which were not broken by distillation. The complete separation and identification of the reaction mixtures was finally accomplished through the right combination of extraction methods, column chromatography, gas-liquid chromatography and infrared spectroscopy.

Experimental

Materials.—All of the compounds used in this investigation were carefully purified. If the compounds were new or if the values in the literature did not agree with our values, the compounds were analyzed.⁶

All amines were purified by first drying them over potassium hydroxide pellets for 1 week, removing the drying agent by filtration and distilling the filtrate through a 30-cm. column, 2 cm. in diameter, packed with glass helices. All solvents were purified by standard methods until their physical constants agreed with the literature values. The purity of the compounds used in this investigation was also checked by gas-liquid chromatography.

Trifluoro- and trichloroacetic acid were purchased from Matheson, Coleman and Bell. Tribromoacetic acid was purchased from Aldrich Chemical Co. Trichloroethoic acid was prepared by the reaction of trichloroacetyl chloride and hydrogen sulfide in the presence of dry aluminum chloride, yield 80%, b.p. 44° (3 mm.), n_D^{25} 1.5262, lit. b.p. 57° (11 mm.).⁷ Since no index of refraction could be found in the literature, an elemental analysis was carried out to ascertain the purity of the product.

Anal. Calcd. for C_2HCl_3OS : C, 13.39; H, 0.56; Cl, 59.19; S, 17.87. Found: C, 13.39; H, 0.59; Cl, 59.07; S, 18.14.

t-Butyl thioltrichloroacetate was prepared by the reaction of isobutylene with trichloroethoic acid, yield 85%, b.p. 68° (2 mm.), n_D^{25} 1.5055.

Anal. Calcd. for $C_8H_9Cl_3SO$: C, 30.60; H, 3.85; Cl, 45.17; S, 13.62. Found: C, 30.72; H, 3.96; Cl, 45.39; S, 13.46.

p-Acetamidophenyl trichloroacetate was prepared by the reaction of *p*-hydroxyacetanilide and trichloroacetyl chloride, yield 70%, m.p. 174°.

Anal. Calcd. for $C_{10}H_8Cl_3NO_2$: C, 40.49; H, 2.70; N, 4.72; Cl, 35.91. Found: C, 40.36; H, 2.47; N, 4.84; Cl, 35.72.

All amides and carbamates were prepared by standard synthetic routes.

Trichloroacetanilide was prepared by the reaction of trichloroacetyl chloride and aniline in dry benzene, yield 90%, m.p. 95°, lit. m.p. 95–97°.⁸ Phenyl 1-piperidine carboxylate was prepared by the reaction of phenyl chloroformate and piperidine in dry benzene solution, yield 88%, m.p. 80°, lit. m.p. 80°.⁹

N-*n*-Butyl phenyl carbamate was prepared by the reaction of *n*-butylamine and phenyl chloroformate in dry benzene, yield 98.5%, b.p. 146–148° (2 mm.).

Anal. Calcd. for $C_{11}H_{15}NO_2$: C, 68.37; H, 7.82; N, 7.25. Found: C, 68.54; H, 8.08; N, 7.44.

The retention times of the compounds studied by gas-liquid chromatography and the conditions used for their isolation are listed in Table I. The physical constants and analytical data for new esters, amides, and carbamates are also reported in Table I.

Gas-Liquid Chromatographic Analysis.—A Burrell K₁ Kromotog was employed using a 250-mm. column, 12 mm. in diameter containing 15% silicone oil on Chromosorb regular 30–60 mesh

(1) Abstracted in part from the Ph.D. dissertation of A. C. Pierce, University of Pennsylvania, 1962.

(2) Recipient of W. T. Taggart and E. F. Smith Memorial Scholarships, 1961–1962.

(3) M. M. Joullié and A. R. Day, *J. Am. Chem. Soc.*, **76**, 2990 (1954).

(4) Y. Ury and M. Paty, *Compt. rend.*, **262**, 3812 (1961).

(5) M. M. Joullié, *J. Am. Chem. Soc.*, **77**, 6662 (1955).

(6) All microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn.

(7) J. I. Cunneen, *J. Chem. Soc.*, 141 (1947).

(8) E. Votocěk and J. Burda, *Ber.*, **43**, 1006 (1915).

(9) P. Cazeneuve and Moreho, *Compt. rend.*, **125**, 1107 (1897).

TABLE I
 GAS-LIQUID CHROMATOGRAPHIC DATA

Compound	t_R^a	He flow, ml./min.	Column, ^b temp., °C.
Esters			
$F_3C_2O_2C_2H_5$	0.75	120	210
$F_3C_2O_2C(CH_3)_3$	0.75	120	225
$F_3C_2O_2CH_2C_6H_5^c$	2.31	100	213
$F_3C_2O_2C_6H_5$	1.8	120	210
$Cl_3C_2O_2CH_3$	2.8	78	210
$Cl_3C_2O_2C_2H_5$	2.75	120	210
$Cl_3C_2O_2C(CH_3)_3$	2.0	120	217
$Cl_3C_2O_2CH_2CH=CH_2^d$	3.8	78	200
$Cl_3C_2O_2CH_2C_6H_5$	24.6	120	225
$Cl_3C_2O_2C_6H_5$	14.3	120	210
$Cl_3C_2O_2CH=CH_2$	2.3	78	200
$Cl_3C_2OSCH_3$	1.6	160	245
Amides			
$F_3C_2ONHC_4H_9-n$	3	85	210
$F_3C_2ONC_6H_{10}$	4.8	85	210
$F_3CON(C_2H_5)_2$	1.6	120	217
$Cl_3C_2ONHC_4H_9-n$	14.6	85	210
$Cl_3C_2ONC_6H_{10}$	16.4	120	223
$Cl_3C_2ON(C_2H_5)_2$	2.5	160	245
$C_6H_{10}NCHO$	4.8	85	210
	6.7	78	200
Carbamates			
$n-C_4H_9NHCO_2C_2H_5$	3.8	150	215
$n-C_4H_9NHCO_2CH_2C_6H_5^f$	32.0	120	220
$C_6H_{10}NCO_2CH_3$	5.7	78	200
$C_6H_{10}NCO_2C_2H_5$	4.7	120	223
	6.9	75	195
$C_6H_{10}NCO_2CH_2CH=CH_2^g$	6.7	78	200
$C_6H_{10}NCO_2CH_2C_6H_5^h$	4.0	85	210

^a Retention time (t_R) in minutes. ^b Silicone oil (15%) on Chromosorb, 30-60 regular mesh, 250 mm. × 12 mm. ^c Prepared by direct esterification in a 2:1 ratio of acid to alcohol, yield 82%, b.p. 178° (760 mm.), 50-52° (5 mm.), n_D^{25} 1.4380, d_4^{25} 1.2419. *Anal.* Calcd. for $C_8H_7F_3O_2$: C, 52.94; H, 3.43; F, 27.94. Found: C, 53.17; H, 3.68; F, 27.79. ^d Prepared by direct esterification in a 1:3 ratio of acid to alcohol, yield 60%, b.p. 76° (15 mm.), n_D^{25} 1.4645, d_4^{25} 1.378. *Anal.* Calcd. for $C_8H_5O_2Cl_3$: C, 29.47; H, 2.45; Cl, 52.33. Found: C, 29.60; H, 2.48; Cl, 52.53. ^e Prepared by adding trichloroacetyl chloride to an ether solution of methanethiol and triethylamine, yield 70%, b.p. 44° (3 mm.), n_D^{25} 1.5249. *Anal.* Calcd. for $C_3H_3Cl_3SO$: C, 18.62; H, 1.56; Cl, 54.97; S, 16.57. Found: C, 18.89; H, 1.63; Cl, 54.76; S, 16.41. ^f Prepared by the reaction of *n*-butylamine and benzyl chloroformate in dry benzene; yield 99%; b.p. 149-150° (3 mm.), n_D^{25} 1.5050, d_4^{25} 1.037. *Anal.* Calcd. for $C_{12}H_{17}NO_2$: C, 69.53; H, 8.27; N, 6.76. Found: C, 69.61; H, 8.32; N, 6.53. ^g Prepared by the reaction of allyl alcohol and phosgene in dry benzene, yield 90%, b.p. 93-94° (7 mm.), n_D^{25} 1.4720, d_4^{25} 1.022. *Anal.* Calcd. for $C_9H_{15}NO_2$: C, 63.90; H, 8.87; N, 8.28. Found: C, 63.80; H, 8.80; N, 8.15. ^h Prepared by the reaction of piperidine and benzyl chloroformate in dry benzene, yield 94%, b.p. 140° (3.5 mm.), n_D^{25} 1.5285, d_4^{25} 1.0867. *Anal.* Calcd. for $C_{13}H_{17}NO_2$: C, 71.23; H, 7.76; N, 6.39. Found: C, 71.38; H, 7.61; N, 6.27.

packing at various temperatures and various rates of helium flow. Although several other columns were tried, they did not resolve the components of the mixtures to the extent of silicone oil on Chromosorb and this packing was used throughout the study in spite of the fact that it decomposed small amounts of unchanged benzyl trichloroacetate into chloral and benzaldehyde.

Peak areas were measured with an Otts planimeter Type 31. The area of an unknown volume of a known compound was compared with the relative area of a known volume of the compound and this ratio multiplied by 100 was assumed to be the per cent yield of the compound. This method is limited to a precision of $\pm 3-5\%$.

Identification of the compounds of a mixture was carried out by comparing the retention time of the compound under investi-

gation to the retention time of an authentic sample and by addition of an authentic specimen to the reaction mixture in varying amounts (*i.e.*, 20:80; 50:50; 80:20).

The reactions of methyl and ethyl trichloroacetate with *n*-butylamine and piperidine were studied by gas-liquid chromatography and infrared spectroscopy, since previous investigations of these reactions did not report yields.

Infrared Analysis.—The infrared spectra of the compounds studied were measured as carbon tetrachloride solutions on a Perkin-Elmer Model 421 double-beam spectrophotometer. Matched sodium chloride cells 1.0 mm. in thickness were employed. All absorption bands in the 1900-1600-cm.⁻¹ region were read from the meter. The infrared carbonyl stretching frequencies of the trihalogenated acids, esters, amides, and carbamates are listed in Table II. Beer's law curves were constructed for each of the esters listed and were essentially linear. It was observed that known concentrations of amide or carbamate, in carbon tetrachloride solution, had the same per cent absorbance ($\% A = \log_{10} (I_0/I) \times 100$). The absorbance of the carbonyl stretching bands of 0.05 *M* carbon tetrachloride solutions of the amide and carbamate did not change upon mixing the two compounds. Absorbance in the infrared was used as a method to estimate the per cent of amide and carbamate in a reaction mixture and was found to be precise to $\pm 3-5\%$. Equimolar amounts of reactants, either in the absence or presence of a solvent, were allowed to stand for 24 hr. before the mixtures were analyzed by infrared spectroscopy. The reactions of *t*-butyl trichloroacetate and methyl thioltrichloroacetate with *n*-butylamine and piperidine as well as the reaction of benzyl trichloroacetate and aniline were studied by infrared spectroscopy only. The reactions of ethyl trichloroacetate and ethyl trifluoroacetate with diethylamine were studied by infrared spectroscopy over a 3-day period. In the case of ethyl trifluoroacetate the yield of amide was 60% after 5 min., 80% after 1 hr., 100% after 24 hr. In the case of ethyl trichloroacetate the yield of carbamate was 8% after 1 hr., 20% after 24 hr. and 60% after 3 days.

Isolation of Products.—Equimolar amounts of benzyl trifluoroacetate and benzyl and phenyl trichloroacetates were treated with equimolar amounts of *n*-butylamine and piperidine, respectively, and allowed to stand at room temperature for 24 hr. Phenyl trifluoroacetate, vinyl and allyl trichloroacetates were treated with piperidine only, under the same conditions.

A typical separation of reaction products will be illustrated by the isolation of products from the reaction of benzyl trichloroacetate and piperidine. Cooled piperidine (4.25 g., 0.05 mole) was added gradually to a cooled solution of 40 ml. of hexane containing benzyl trichloroacetate (12.67 g., 0.05 mole). A white solid precipitated after 2.5 hr. This solid was removed by filtration and shown to be piperidine hydrochloride, m.p. 244°. The reaction mixture was allowed to stand for 9 days and during this time an oily layer separated from the hexane solution. The hexane insoluble layer was dissolved in benzene, made neutral to Hydriion pH paper by washing with sodium bicarbonate solution and dried over magnesium sulfate. The hexane soluble layer was also neutralized in the same way, dried over magnesium sulfate and the hexane removed in a rotary evaporator. The residual oil was then extracted for 12 hr. in a liquid-liquid extractor with hexane. The residual insoluble oil was combined with the previous hexane insoluble layer and the resulting mixture distilled in a molecular still, b.p. 75° (0.2 mm.), n_D^{25} 1.5280. The distillate proved to be the carbamate, yield 35%. This product was identified by comparing its physical constants and infrared spectrum to those of an authentic sample of this material prepared by a standard synthetic method.

The solvent was removed from the hexane soluble fraction, the residue dissolved in 25 ml. of petroleum ether (b.p. 100-115°) and poured into a column (2 in. × 2 ft.) packed with ground calcium chloride which had been diluted with alumina in a 1:2 ratio. The column was eluted with a total of 2.36 l. of chloroform. Each time the chloroform was removed in a rotary evaporator. The residues were combined, dissolved in absolute ethanol, and addition of ice to the ethanol solution caused a solid to precipitate, yield 29%, m.p. 44-45°. This solid was shown to be *N*-trichloroacetyl piperidine by comparing its physical constants and infrared spectrum to those of an authentic sample of this compound.

The products of the reaction of phenyl trichloroacetate with *n*-butylamine or piperidine were separated by column chromatography using a strong cation-exchange resin (Amberlite IR 120) in the sodium form. The products were eluted with distilled

TABLE II

INFRARED CARBONYL STRETCHING FREQUENCIES OF TRIHALOGENATED ACIDS, ESTERS, AMIDES, AND CARBAMATES, ± 2 CM.⁻¹

Compounds	$\nu_{\max}^{\text{C=O}}$ CCl ₄	Compounds	$\nu_{\max}^{\text{C=O}}$ CCl ₄	$\nu_{\max}^{\text{C=O}}$ CH ₃ CN
Acids				
F ₃ C ₂ O ₂ H	1779	F ₃ C ₂ ONHC ₄ H ₉ - <i>n</i>	1736	
Cl ₃ C ₂ O ₂ H	1750	F ₃ C ₂ ONC ₅ H ₁₀	1694	1684
Cl ₃ C ₂ OSH ^a	1721	F ₃ C ₂ ON(C ₂ H ₅) ₂	1690	
Br ₃ C ₂ O ₂ H	1734	Cl ₃ C ₂ ONHC ₄ H ₉ - <i>n</i>	1724	1708
Esters				
F ₃ C ₂ O ₂ C ₂ H ₅	1789	Cl ₃ C ₂ ONHC ₆ H ₅	1728	
F ₃ C ₂ O ₂ CH ₂ C ₆ H ₅	1787	Cl ₃ C ₂ ONC ₅ H ₁₀	1682	1669
F ₃ C ₂ O ₂ C(CH ₃) ₃	1781	Carbamates		
F ₃ C ₂ O ₂ C ₆ H ₅	1802	<i>n</i> -C ₄ H ₉ NHCO ₂ C ₂ H ₅	1727	1710
Cl ₃ C ₂ O ₂ CH ₃	1773	<i>n</i> -C ₄ H ₉ NHCO ₂ CH ₂ C ₆ H ₅	1728	
Cl ₃ C ₂ O ₂ C ₂ H ₅	1769	<i>n</i> -C ₄ H ₉ NHCO ₂ C ₆ H ₅	1752	1734
Cl ₃ C ₂ O ₂ CH ₂ CH=CH ₂	1769	C ₆ H ₁₀ NCO ₂ CH ₃	1703	
Cl ₃ C ₂ O ₂ CH ₂ C ₆ H ₅	1769	C ₅ H ₁₀ NCO ₂ C ₂ H ₅	1698	1686
Cl ₃ C ₂ O ₂ C(CH ₃) ₃	1764	C ₅ H ₁₀ NCO ₂ CH ₂ CH=CH ₂	1699	
Cl ₃ C ₂ O ₂ CH=CH ₂	1782	C ₅ H ₁₀ NCO ₂ CH ₂ C ₆ H ₅	1699	
Cl ₃ C ₂ O ₂ C ₆ H ₅	1789	C ₅ H ₁₀ NCO ₂ C ₆ H ₅	1721	1704
Cl ₃ C ₂ O ₂ C ₆ H ₄ NHCOCH ₃	1776	C ₆ H ₅ NHCO ₂ CH ₂ C ₆ H ₅	1739	
Cl ₃ C ₂ OSCH ₃ ^b	1699			
Cl ₃ C ₂ OSC ₂ H ₅ ^c	1703			
Cl ₃ C ₂ OSC(CH ₃) ₃ ^d	1702			
Br ₃ C ₂ O ₂ C ₂ H ₅	1757			

^a $\nu_{\max}^{\text{C-S}}$ 1059 cm.⁻¹ in CCl₄. ^b $\nu_{\max}^{\text{C-S}}$ 1032 cm.⁻¹ in CCl₄. ^c $\nu_{\max}^{\text{C-S}}$ 1031 cm.⁻¹ in CCl₄. ^d $\nu_{\max}^{\text{C-S}}$ 1032 cm.⁻¹ in CCl₄.

water and benzene. The benzene extracts were dried over magnesium sulfate and distilled *in vacuo* after removal of the drying agent. Almost quantitative yields of amides were recovered by this method. Phenol was recovered by acidifying the aqueous extracts.

In the reaction of vinyl trichloroacetate and *n*-butylamine, the acetaldehyde formed was isolated as its 2,4-dinitrophenylhydrazone.

The products of the other reaction mixtures were also separated by distillation *in vacuo*, column chromatography and liquid-liquid extraction. All products were identified by comparing their physical constants and infrared spectra to those of authentic samples. The same reaction mixtures were also analyzed by gas-liquid chromatography and infrared spectroscopy.

Although attempts were made to isolate the *t*-butyl carbamates formed in the reactions of *t*-butyl trichloroacetate with amines, they could not be isolated. Infrared data supported the existence of these compounds since reactions in which they were suspected to exist showed peaks characteristic of carbamates. The analytical data also suggested that these compounds were present in the reaction mixtures but they decomposed when their purification was attempted.

Tests.—In most reactions both acyl-oxygen and haloform-type cleavages occurred to an appreciable extent so that yields and identification of products could be determined by more than one method. However, in some cases, one of the cleavages occurred so slightly that chemical separation was impossible. Detection of the cleavage products by gas-liquid chromatographic analysis was complemented with chemical tests for the presence of an alcohol, thioalcohol or chloroform. The presence of an alcohol was tested with ceric nitrate reagent prepared by the standard method.¹⁰ The presence of a thioalcohol was tested with a 1% solution of sodium nitroprusside.¹¹

A test for chloroform has been devised by Fujiwara.¹² The test has been modified to be used as a test for fluoroform and any source of haloforms or halocarbenes. A few drops of the mixture suspected of containing a haloform is added to a 10% solution of sodium hydroxide (3 ml.) and 2 ml. of pyridine. If the resulting mixture turns pink to bright blue-red in color within 1-2 min. of vigorous shaking, at room temperature, a haloform is present.

(10) R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "The Systematic Identification of Organic Compounds," 4th ed., John Wiley and Sons, Inc., New York, N. Y., 1956, p. 110.

(11) N. D. Cheronis and J. B. Entrikin, "Semimicro Qualitative Organic Analysis," 2nd ed., Interscience Publishers, Inc., New York, N. Y., 1960, p. 275.

(12) K. Fujiwara, *Sitz. Nat. Ges. Rostock*, **6**, 33 (1916); *Chem. Abstr.*, **11**, 3201 (1917).

If no color change occurs, the mixture is heated on a steam bath for 1 min. If a pink to bright red-blue color appears, a source of halocarbene is present. The color may be due to the reaction of a dihalocarbene with pyridine although no direct evidence is available for this assumption. The intensity of the color is proportional to the concentration of the haloform or source of haloform or halocarbene present.

The modified Fujiwara test was particularly useful to detect chloroform in the reaction products of *p*-acetamidophenyl trichloroacetate and piperidine.

Discussion

Infrared Spectra.—The carbonyl stretching frequencies of methyl, ethyl, vinyl, and phenyl acetate were measured in carbon tetrachloride.¹³ The $\nu_{\text{C=O}}$ maxima for these esters were found to be 1750, 1742, 1763, and 1769 cm.⁻¹, respectively, in agreement with the predicted increased double bond character of the carbonyl group.

The inductive effect of the trihalomethyl group on the carbonyl group of an ester may be estimated from a comparison of the carbonyl stretching frequencies of ethyl trifluoroacetate, ethyl trichloroacetate, and ethyl tribromoacetate with ethyl acetate. The substitution of a trihalomethyl group for a methyl group results in an increase in the carbonyl stretching frequency of 47 cm.⁻¹ for the trifluoromethyl group, 27 cm.⁻¹ for the trichloromethyl group, and 15 cm.⁻¹ for the tribromomethyl group. The increase in carbonyl stretching frequency due to the trihalomethyl group is also dependent on the alkoxy or aryloxy group of the ester. The smallest differences between the carbonyl stretching frequencies of an acetate, a trifluoroacetate, and a trichloroacetate are observed in the case of phenyl esters which absorb at 1769, 1802, and 1789 cm.⁻¹, respectively. The fact that the phenyl esters have the highest carbonyl stretching frequencies shows that the carbonyl group in these esters has the greatest double bond character. This indicates

(13) H. W. Thompson and D. A. Jameson, *Spectrochim. Acta*, **13**, 236 (1958).

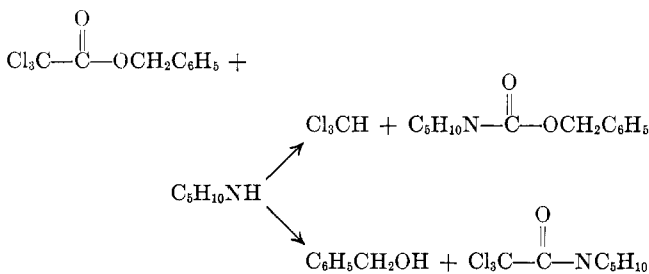
that the phenyl group is acting as an electron-withdrawing group. This is in agreement with the views of Bellamy.¹⁴ Further support for the fact that the phenyl group is acting as an electron-withdrawing group is given by the carbonyl stretching frequency of *p*-acetamidophenyl trichloroacetate which is 1776 cm.⁻¹. The introduction of an electron-donating group in the *para* position of the phenyl group lowers the carbonyl stretching frequency by 13 cm.⁻¹.

The carbonyl stretching frequencies of allyl, benzyl and ethyl trichloroacetates are the same, lower than the frequency of the corresponding methyl ester but higher than the frequency of the *t*-butyl ester. The similarity in carbonyl stretching frequencies of the allyl, benzyl, and ethyl esters makes correlation between Taft's σ^* and carbonyl frequency of no significance in this study. Allyl and ethyl difluoronitroacetates have also been reported to have the same carbonyl stretching frequency.¹⁵ The carbonyl stretching frequencies of methyl and *t*-butyl trichloroacetate are found at the expected positions for the decreased and increased electron repelling effect of a methyl and *t*-butyl group, respectively, as compared to an ethyl group.

Interestingly the carbonyl stretching frequencies of the carbamates follow the same trend as those of the esters when the amino substituent is kept constant and the alkoxy group varied.

The carbonyl stretching frequencies of a number of trichlorothiol esters prepared were found to be lower than those of their oxygen analogs. This is in agreement with the previous findings¹⁶ and has been attributed to the ability of the *d* orbitals of sulfur to accommodate the electrons of oxygen by *pd* hybridization and thus decrease the double bond character of oxygen.¹⁷ The effect of the alkyl groups in the thiol esters is small compared to the effect resulting from the hybridization of the sulfur atom. The expected increase in the C—S stretching frequency accompanies the decreased carbonyl stretching frequency.

Cleavage Reactions.—The reactions of all trifluorinated esters with primary and secondary amines were found to yield amides exclusively. However, the reactions of trichlorinated esters with the same amines yielded either amides or carbamates predominantly. In some cases the reactions were rather complex because of the formation of several products. A typical example is the reaction of benzyl trichloroacetate and piperidine in which both acyloxygen cleavage and a haloform-type



of cleavage occurred. In addition to these products, piperidine hydrochloride, *N*-formylpiperidine, and benzaldehyde were identified. Piperidine hydrochloride and *N*-formylpiperidine were found to arise from the reac-

tion of piperidine and the chloroform formed.¹⁸ Amine hydrochlorides were side products in all of the reactions that involved a haloform-type cleavage. Although some of the benzaldehyde formed could have come from unchanged benzyl trichloroacetate, experiments were devised to show that benzaldehyde can also be formed from the oxidation of benzyl alcohol. Some benzaldehyde was formed in all the reactions that yielded benzyl alcohol. The separations of all the products, although tedious, were finally accomplished by the methods described in the experimental section. Reactions which involved exclusive or predominant acyl-oxygen cleavage were immediately exothermic while those with piperidine involved a deepening in color prior to the observed evolution of heat.

The cleavage reactions studied and the relative per cent acyl-oxygen cleavage are shown in Table III.

TABLE III
CLEAVAGE REACTIONS STUDIED AND RELATIVE % ACYL-OXYGEN CLEAVAGE^a

Ester	Amine	% Acyl-oxygen cleavage \pm 5		
		No solvent	CCl ₄	CH ₃ CN
F ₃ C ₂ O ₂ R ^b	<i>n</i> -C ₄ H ₉ NH ₂	100		
F ₃ C ₂ O ₂ R	C ₆ H ₁₀ NH	100		
Cl ₃ C ₂ O ₂ CH ₃	<i>n</i> -C ₄ H ₉ NH ₂	92		
Cl ₃ C ₂ O ₂ CH ₃	C ₆ H ₁₀ NH	8		
Cl ₃ C ₂ O ₂ C ₂ H ₅	<i>n</i> -C ₄ H ₉ NH ₂	92	100 ^c	0
Cl ₃ C ₂ O ₂ C ₂ H ₅	C ₆ H ₁₀ NH	8	100 ^d	0
Cl ₃ C ₂ O ₂ C(CH ₃) ₃	<i>n</i> -C ₄ H ₉ NH ₂	84		
Cl ₃ C ₂ O ₂ C(CH ₃) ₃	C ₆ H ₁₀ NH	29		
Cl ₃ C ₂ O ₂ CH ₂ C ₆ H ₅	<i>n</i> -C ₄ H ₉ NH ₂	58		
Cl ₃ C ₂ O ₂ CH ₂ C ₆ H ₅	C ₆ H ₁₀ NH	42		
Cl ₃ C ₂ O ₂ CH ₂ CH=CH ₂	C ₆ H ₁₀ NH	43		
Cl ₃ C ₂ O ₂ CH=CH ₂	<i>n</i> -C ₄ H ₉ NH ₂	98		
Cl ₃ C ₂ O ₂ CH=CH ₂	C ₆ H ₁₀ NH	98		
Cl ₃ C ₂ O ₂ C ₆ H ₅ ^e	<i>n</i> -C ₄ H ₉ NH ₂	100	100	95
Cl ₃ C ₂ O ₂ C ₆ H ₅	C ₆ H ₁₀ NH	100		73

^a The % acyl oxygen is approximately equivalent to the yield of amide formed. Unless otherwise noted the remaining % is equivalent to the yield of carbamate formed. These values are obtained from gas-liquid chromatographic data and are roughly equivalent to the actual yields obtained by chemical methods.
^b R = C₂H₅, CH₂C₆H₅, C(CH₃)₃, C₆H₅.
^c Unchanged ester, 50%.
^d Unchanged ester, 3%.
^e The % of acyl-oxygen cleavage was 71 in dioxane and 66 in ethyl ether.

The fact that trifluorinated esters undergo only acyl-oxygen cleavage is consistent with the chemical behavior of the trifluoromethyl group as compared to the trichloromethyl group. The energies of activation for the decarboxylations of sodium trifluoroacetate and sodium trichloroacetate in ethylene glycol were found to be 42 and 36.6 kcal./mole, respectively.¹⁹ The relative rates of formation of carbanions by haloforms were studied by Hine and co-workers.²⁰ These authors found that α -halogen substituents facilitate carbanion formation in the order I ~ Br > Cl > F. The observed data was ascribed to a combination of inductive effects, polarizability and *d*-orbital resonance of the halogens involved although the importance of *d*-orbital resonance as a factor in explaining the reactivity of deuterated haloforms could not be assessed. Hine and co-workers suggested that polarizability was probably the most

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important factor to be considered in explaining the rates of carbanion formation in the deuterated haloforms.

The fission of a carbon chain which occurs with trichloromethyl carbonyl compounds to yield chloroform has also been observed with the trifluorinated analogs which yield fluoroform under the same conditions.²¹ The same carbon-carbon fission has been noted with higher perfluoroalkyl aldehydes and ketones.^{21a,22} A similar cleavage was observed during the reaction of ethyl trifluoroacetate, perfluoropropionate and perfluorobutyrate with sodium ethoxide.²³

In the present study, acyl-oxygen cleavage should always predominate in either type of ester according to average bond energy considerations. However, a haloform-type of cleavage becomes a competing reaction for the trichlorinated esters but not the trifluorinated esters. This is in accord with the reported differences between chlorine and fluorine^{19,20} although these differences are not always apparent under the ordinary conditions of the haloform cleavage.²¹⁻²⁴

The esters of trichloroacetic acid reacted with *n*-butylamine to give decreasing acyl-oxygen cleavage in the following order: $C_6H_5O > CH_2 = CHO > CH_3O \cong C_2H_5O > (CH_3)_3CO > C_6H_5CH_2O$. The order for decreasing acyl-oxygen cleavage when the same esters were reacted with piperidine was $C_6H_5O > CH_2 = CHO > CH_2 = CHCH_2O \cong C_6H_5CH_2O > (CH_3)_3CO > CH_3O \cong C_2H_5O$.

Exclusive acyl-oxygen cleavage was found to occur with phenyl trichloroacetate regardless of the amine group. This is in agreement with the greater rate of aminolysis of phenyl acetate as compared with methyl acetate.²⁵ The observed order of decreasing acyl-oxygen cleavage suggested a correlation between the preferred conformation of these esters and their reactivities toward amines. Courtauld models of the trihalogenated esters show that the distance between the alkoxide oxygen and the closest hydrogen to it is greater in the case of phenyl trichloroacetate than in the case of benzyl trichloroacetate. The steric hindrance presented to the

alkoxide oxygen by the R group attached to it may also be estimated by examining the *E_s* values of some of the alkyl groups involved.²⁶ Steric hindrance to the oxygen of the alkoxy portion of the ester by the groups attached to it appears to be related to the decrease in the percent of acyl-oxygen cleavage. This steric hindrance may increase the steric strain in the transition state or interfere with adjacent groups in such a way as to increase the free energy of activation of the system.

Acyl-oxygen cleavage was found to predominate when the reactions were carried out in carbon tetrachloride regardless of the amine employed. The haloform-type cleavage was increased by using more polar solvents such as acetonitrile, ethyl ether, and dioxane. Carbon tetrachloride has the least ionizing ability of all the solvents studied and favors ion-pairs.²⁷ This solvent would be most conducive to an oriented, low entropy transition state. Electrostatic attractions involving hydrogen bonds between the ester and amine could be more feasible in this solvent. Polar solvents would favor more dissociation of reactive species, less orientation would be possible and the entire system would have higher entropy. A polar intermediate would be more readily stabilized in polar solvents than in carbon tetrachloride.

Although the importance of the amine has not been widely studied during the course of this investigation, it would seem that acyl-oxygen cleavage decreases with the increasing nucleophilicity of the amine used.

Secondary amines yield predominantly carbamates when treated with ethyl trichloroacetate. In contrast with the reactions which involve acyl-oxygen cleavage, reactions which yield carbamates are very slow when a sterically hindered amine is used. The reaction of diethylamine with ethyl trichloroacetate is much slower than the reaction of this ester with unhindered amines. A comparison of the rate of reaction of diethylamine with ethyl trifluoroacetate and ethyl trichloroacetate shows that this amine reacts much faster with ethyl trifluoroacetate than ethyl trichloroacetate. Sterically hindered amines raise the energy requirements of the transition state of the haloform-type cleavage.

Although the experimental data available indicate that acyl-oxygen cleavage involves a lower entropy transition state than the haloform-type of cleavage, it is not possible at this time to postulate mechanisms which would explain the different behavior of primary and secondary amines toward trihalogenated esters any better than those already postulated.⁵

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