described by Robertson and Sandrock.[7] The acid chloride was obtained in 84% yield, bp 74–78° (19 mm), lit.[7] 74–78° (19 mm).

t-Butylperoxy α-Carbethoxyisobutyrate.—A solution of 1.3 g (7.3 mmoles) of α-carbethoxyisobutyryl chloride in 15 ml of petroleum ether was added slowly to a suspension of 1.4 g (11 mmoles) of potassium *t*-butyl peroxide[8] in 20 ml of petroleum ether at room temperature. After stirring for 3 more hr at room temperature, 10 ml of water was added and stirring was resumed for 15 min. The organic layer was removed and washed successively with 10% sulfuric acid, 10% sodium carbonate solution, and cold water until neutral. The petroleum ether solution was dried over anhydrous magnesium sulfate and evaporated *in vacuo* at room temperature. The product, an oil, was purified by passing it through a column of Florosil. Infrared analysis showed absorption at 5.62 and 5.75 μ characteristic of the peroxy ester carbonyl group and the ester carbonyl group, respectively. Peroxide content by iodometric titration was 93%, yield 0.40 g (1.7 mmoles), 24%.

Anal. Calcd for $C_{11}H_{20}O_5$: C, 56.88; H, 8.68. Found: C, 57.07; H, 8.77.

Kinetic Measurements.—The procedure used in the kinetic measurements was that described by Bartlett, Benzing, and Pincock.[9]

(8) N. Kornblum and P. de la Mare, *J. Am. Chem. Soc.*, **74**, 3081 (1952).

The peroxy esters were shown to obey Beer's law at the concentrations used in the kinetic measurements.

Product Studies.—The methods used for the study of the products of the thermal decomposition of the peroxy ester in cumene were modeled after those described by Bartlett and co-workers.[9]

The nonvolatile residue was separated into dicumyl and a carbonyl-containing material by chromatography on silica gel. The carbonyl-containing material could not be further divided or purified by chromatography. Solution of this material in benzene followed by evaporation of the benzene left a clear lacquer, whereas similar treatment with pentane left a white solid. Neither the solid nor the lacquer had a distinct melting point. These properties, similar to those observed for previously isolated polyesters,[2] suggested the carbonyl containing material was a polyester.

t-Butylperoxy isobutyrate[2] was carefully decomposed at 85° in the absence of solvent and the solid residue, the polyester described and characterized by Milas,[1] was recrystallized from ethanol. The infrared spectrum of this polyester of α-hydroxyisobutyric acid ($CHCl_3$) was identical in all its features with that of the carbonyl-containing material described above.

(9) P. D. Bartlett, F. P. Benzing, and R. E. Pincock, *ibid.*, **82**, 1762 (1960).

Polar, Steric, and Solvent Effects in the Cleavage Reactions of Trichloro- and Tribromoacetates with Primary and Secondary Amines[1,2]

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The reactions of a series of trichloro- and tribromoacetates with primary and secondary amines were investigated both in the absence and in the presence of solvents. All primary amines reacted with ethyl trichloroacetate to give predominantly amides while secondary amines yielded products which resulted from both acyl oxygen and haloform cleavages. The extent of acyl oxygen cleavage was dependent upon the geometry rather than the basicity of the amine. The reactions of *n*-butylamine with various tribromoacetates gave products which resulted from both types of cleavage. Exclusive acyl oxygen was never observed in these reactions. The reactions of piperidine with methyl and ethyl tribromoacetates in the absence or presence of solvents gave predominantly a haloform cleavage. Several side reactions were noted. Possible mechanisms are discussed for the side and main reactions that occur when trihalogenated esters are treated with amines.

Trifluoroacetates[4–6] are known to undergo aminolysis when treated with either primary or secondary amines. Trichloroacetates[4,6,7] react with primary amines to yield predominantly amides but with secondary amines carbamates are the major products. From these studies, it is obvious that the action of amines on trihalogenated esters may cleave these esters in two different ways. These cleavages appeared to be of sufficient interest to warrant further investigation.

The first objective of the present study was to examine the role of the amine. The second objective was to synthesize and examine the reaction of four esters of particular interest: β,β,β-trifluoroethyl, β,β,β-trichloroethyl, and β,β,β-tribromoethyl trichloroacetates and also ethyl dichlorofluoroacetate. The third and last objective was to synthesize a few tribromoacetates and to study their reactions with *n*-butylamine and piperidine. Gas–liquid partition chromatography was used extensively for both the qualitative and quantitative analyses of the reaction mixtures. The reactions of tribromoacetates with amines proved to be more complex than the same reactions with trichloroacetates and the separation and identification of all products was a laborious operation.

(1) Abstracted from the Ph.D. dissertation of R. H. Yocum, University of Pennsylvania, 1965.

(2) Presented before the Division of Organic Chemistry, First Middle Atlantic Regional Meeting of the American Chemical Society, Philadelphia, Pa., Feb 3, 1966, p 111.

(3) Recipient of E. F. Smith Memorial Scholarships, 1963–1965.

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

(5) M. M. Joullié, *ibid.*, **77**, 6662 (1955).

(6) A. C. Pierce and M. M. Joullié, *J. Org. Chem.*, **28**, 658 (1963).

(7) Y. Ursy and M. Paty, *Compt. Rend.*, **252**, 3812 (1961).

Experimental Section[8]

Materials.—All of the compounds used in this investigation were analytically pure. Analytical data was obtained for all new compounds and compounds whose physical constants did not agree with those in the literature. All solvents were purified by standard methods until their physical constants agreed with literature values. Purity of liquids was checked by gas–liquid partition chromatography. Amines were purified by allowing them to stand over potassium hydroxide pellets for 3 days, removing the pellets, and distilling the filtrate through a 30-cm column, 2 cm in diameter, packed with glass helices.

Tribromoacetyl Bromide.—This compound was prepared by an improved method. Tribromoacetic acid (44.6 g, 0.15 mole),

(8) Melting points were determined in a Thomas–Hoover capillary melting point apparatus. Microanalyses were carried out by Galbraith Laboratories, Knoxville, Tenn., and by Dr. A. Bernhardt, Max Planck Institute, 433 Mulheim (Ruhr), West Germany. Infrared spectra were determined on a Perkin-Elmer double-beam Model 521 recording spectrophotometer. All spectra were run as carbon tetrachloride solutions using 0.211-mm matched sodium chloride cells. Refractive indices were recorded on an Abbe 3L refractometer.

TABLE I
ANALYTICAL AND PHYSICAL DATA FOR NEW ESTERS, AMIDES, AND CARBAMATES

Compound	Yield, %	Bp, °C (mm)	n^tD	d_t^t	$\nu_{C=O}$, cm^{-1}	Formula	Analysis, % Carbon Calcd	Carbon Found	Hydrogen Calcd	Hydrogen Found	Nitrogen Calcd	Nitrogen Found	Bromine Calcd	Bromine Found	Chlorine Calcd	Chlorine Found
$CCl_3CO_2CH_2CF_3$	69	58–58.5 (27)	21.2	19	1785	$C_4H_2Cl_3F_3O_2$[a]	19.57	19.66	0.82	1.01	...	...	...	...	43.34	43.19
			1.3980	1.5649												
$CCl_3CO_2CH_2CCl_3$	72	66 (0.25)[b]	23	21.5	1781	$C_4H_2Cl_6O_2$	16.29	16.47	0.68	0.81	...	...	...	...	72.16	72.22
			1.4925	1.6617												
$CCl_3CO_2CH_2CBr_3$	86.5	98 (0.5)[c]	...	...	1779	$C_4H_2Br_3Cl_3O_2$	11.22	11.36	0.48	0.65	...	...	55.99	55.89	24.84	24.75
$CBr_3CO_2CH_2CH=CH_2$	11	...	24.7	...	1754	$C_5H_5Br_3O_2$	17.83	17.90	1.50	1.44	...	...	71.17	71.17	...	...
			1.5456													
$CBr_3CO_2C_4H_9$	44	63–64.5[d]	...	...	1767	$C_8H_9Br_3O_2$	25.77	25.70	1.35	1.24	...	...	64.30	64.11	...	...
$CBr_3CO_2C(CH_3)_3$	63	74.2–75[d]	...	...	1743	$C_6H_9Br_3O_2$	20.42	20.45	2.57	2.59	...	...	67.94	68.24	...	...
$CBr_3CONHC_4H_9$-n	74	44–45[d]	...	...	1691	$C_6H_{10}Br_3NO$	20.48	20.62	2.86	3.00	3.98	3.95	68.13	68.29	...	...
					1494											
$CBr_3CONHC_6H_{11}$	63	90–91.5[d]	...	...	1691	$C_8H_{12}Br_3NO$	25.42	25.47	3.20	3.32	3.71	3.76	63.44	63.25	...	...
					1498											
$CCl_3CONHC_6H_{11}$-n	65	40–41[d]	...	...	1720	$C_7H_{12}Cl_3NO$	36.16	36.40	5.20	5.36	6.02	5.96	...	...	45.74	45.64
					1508											
n-$C_5H_{11}NHCO_2C_2H_5$	80.3	70 (0.55)	20.5	...	1722	$C_8H_{17}NO_2$	60.38	60.52	10.69	10.71	8.81	8.94	...	...	...	...
			1.4337		1501											

[a] *Anal.* Calcd: F, 23.23. Found: F, 23.26. [b] Lit. bp 109° (10 mm): R. Dworzak, *Monatsch*, **47**, 11 (1926). [c] Mp 34.4–35.4°. [d] These values represent melting points.

phosphorus tribromide (19.0 g, 0.07 mole), and xylene (175 ml) were heated for 4 hr at the boiling point of the solvent. The turbid reaction mixture was poured over asbestos. The resulting clear liquid was distilled under reduced pressure to give 37.0 g (68.5%) of tribromoacetyl bromide, bp 40–43° (0.8 mm), $n^{18.6}$D 1.6158 [lit.[9] bp 88–90° (12 mm)].

Esters of Trichloroacetic Acid.—These esters (Table I) were prepared by treating trichloroacetyl chloride with the corresponding alcohols, in either ether or benzene, in the presence of triethylamine or pyridine.

Esters of Tribromoacetic Acid.—Methyl and ethyl tribromoacetates were prepared by an improved synthesis illustrated with the preparation of methyl tribromoacetate. Methanol (48.1 g, 1.50 moles) was cooled to 0° and saturated with anhydrous hydrogen chloride. Tribromoacetic acid (29.7 g, 0.01 mole) was added to the saturated solution at 0°. The temperature was allowed to rise to room temperature. After 18 hr, the reaction was poured over ice and extracted with three 100-ml portions of ether and the ether solution was neutralized, washed with water, and dried over magesium sulfate. Distillation under reduced pressure yielded 25.7 g (83%) of methyl tribromoacetate, bp 79–81° (4.7 mm), $n^{19.5}$D 1.5568, $d_{23.3}^{22.3}$ 2.5031, $\nu_{C=O}^{CCl_4}$ 1756 cm^{-1}.

Ethyl tribromoacetate was prepared by the same method, yield 60%, bp 56–58° (0.5 mm) [lit.[10] bp 65–69° (2 mm)], $n^{21.5}$D 1.5390 (lit.[11] n^{18}D 1.5437), d_{20}^{20} 2.2331 (lit.[11] d_{20}^{20} 2.230), $\nu_{C=O}^{CCl_4}$ 1752 cm^{-1}.

Allyl tribromoacetate was prepared by the reaction of silver tribromoacetate and allyl bromide.

Phenyl tribromoacetate was prepared by the reaction of tribromoacetyl bromide with phenol, in anhydrous benzene, and in the presence of triethylamine.

t-Butyl tribromoacetate was prepared by bubbling isobutylene through a solution of tribromoacetic acid and carbon tetrachloride which contained a few drops of concentrated sulfuric acid.

Amides.—All amides were prepared by treating tribromoacetyl bromide with an excess of the corresponding amine in benzene.

Carbamates.—All carbamates were prepared by treating ethyl chloroformate with an excess of the corresponding amine in benzene.

Oxamides.—All oxamides were prepared from ethyl oxalate and an excess of the corresponding amine.

Gas–Liquid Partition Chromatographic Analysis.—Gas–liquid partition chromatography was used for the qualitative and quantitative analysis of the reaction mixtures. The analyses were carried out using a gas chromatograph (F and M Model 700) equipped with a thermal conductivity detector, W-2 filaments, and a Model 240 linear temperature programmer was employed using a 8-ft column, 0.25 in. in diameter containing either 10% Dow 550 silicone oil on Chromosorb W (60–80 mesh) or 10% Carbowax 20 M on Chromosorb W (60–80 mesh). Often a combination of these columns was required to achieve best results. Because of the wide boiling point range of the reaction mixtures temperature programming was a necessity. The areas under the peaks were integrated with a disk chart integrator, Model 201-B, and the integration read to ±2 units. All reactions were performed in 25-ml erlenmeyer flasks containing the ester and sealed with rubber septums. The amines were injected into the flask in microliter quantities over a period of time and at room temperature. The reactions were placed in the dark for approximately 24 hr and then subjected to gas–liquid partition chromatographic analysis. Reproducibility was 2–3%.

Results and Discussion

The results of the reactions of ethyl trichloroacetate with various primary and secondary amines, in the absence of solvents are shown in Table II. The reactions of ethyl trichloroacetate with piperidine,[4,6] morpholine,[4] and pyrrolidine[4] had been carried out previously but because of the different method of quantitative analysis used in this investigation, these reactions were repeated so that legitimate comparisons could be made between these reactions and the other reactions

(9) W. Steinkopf, W. Mieg, and J. Herold, *Ber.*, **53B**, 1147 (1920).
(10) A. Magnani and S. McElvain, *J. Am. Chem. Soc.*, **60**, 2211 (1938).
(11) I. M. Heilbron, "Dictionary of Organic Compounds," 2nd ed, Oxford University Press, New York, N. Y., 1953, p 543.

TABLE II

CLEAVAGE REACTIONS OF ETHYL TRICHLOROACETATE WITH PRIMARY AND SECONDARY AMINES

Amine	Acyl oxygen cleavage, %	Haloform cleavage, %	Q^a	Unreacted ester, %
n-Butylamine	96.8 ± 2.0	2.3 ± 0.1	98.8	...
n-Amylamine	97.2 ± 2.4	1.6 ± 0.2	98.3	...
n-Hexylamine	99.1 ± 2.4	1.3 ± 0.2	99.0	...
Benzylamine	96.5[b]	0	100.0	...
Cyclopropylamine	95[b]	0	100.0	...
Piperidine	2.6 ± 0.4	89.8 ± 1.9	2.8	2.5 ± 0.2
Morpholine	9.3 ± 0.7	72.9 ± 0.7	11.2	14.7 ± 1.0
Pyrrolidine	44.9 ± 1.5	51.4 ± 1.0	46.6	2.1 ± 0.2
Aziridine	46.5 ± 0.2	0	100.0	48.8
Diethylamine[c]	13.0 ± 0.4	68.6 ± 0.4	16.0	14.8 ± 0.2

[a] Q represents the relative per cent acyl oxygen cleavage as compared to the per cent haloform type of cleavage. [b] These values are based on yields of recrystallized products. [c] Diethyl carbonate was found as one of the products of this reaction (5.4 ± 0.2%).

carried out in this study. The amides were eluted at such long retention times that reproducible chromatograms could not be obtained for the amides. For this reason, the amount of alcohol present was equated to the moles of amides since the alcohol and amides were formed in equimolecular quantities.

A study of Table II reveals that primary amines give predominantly amides when treated with ethyl trichloroacetate while secondary amines give different amounts of amides and carbamates. The haloform-type cleavage appears to increase with the increasing steric requirements of the secondary amine. No relationship could be observed between the dissociation constants of the secondary amines used and the mode of ester cleavage.

The reaction of ethyl trichloroacetate and diethylamine took 40 days to go to completion. A slow side reaction which involved ethanol and either the ester or carbamate yielded a small amount of diethyl carbonate.

In the reaction of aziridine with ethyl trichloroacetate a large amount of unreacted ester was noticed. This observation suggested that half of the aziridine was taking part in a side reaction. This reaction could be either the polymerization of the aziridine before it reacted with the ester or the attack of the resulting N-trichloroacetylaziridine by unreacted aziridine. The

$$CCl_3CO_2C_2H_5 + HN\langle \longrightarrow CCl_3CON\langle + C_2H_5O^-$$

$$CCl_3CON\langle + HN\langle \longrightarrow CCl_3CONHCH_2CH_2N\langle$$

latter possibility seems plausible since the electron-withdrawing effect of the trichloroacetyl group would enhance the reactivity of the aziridine ring toward nucleophiles.

The reactions of β,β,β-trihaloethyl trichloroacetates with *n*-butylamine were studied to determine the effect of the different β,β,β-trihaloethyl groups. In the absence of solvents, β,β,β-trifluoroethyl and β,β,β-trichloroethyl trichloroacetate reacted with *n*-butylamine to form amides in quantitative yields. β,β,β-Tribromoethyl trichloroacetate and *n*-butylamine in acetonitrile also gave exclusive acyl oxygen cleavage although polar solvents are known to favor a haloform-type cleavage. Ethyl trichloroacetate under the same conditions gave 92% of a haloform-type cleavage.[6]

β,β,β-Trifluoroethyl trichloroacetate was treated with piperidine to give a 95% yield of amide. Under the same conditions ethyl trichloroacetate gave a 90% yield of carbamate.[6]

The reaction of ethyl dichlorofluoroacetate with piperidine was carried out to determine the effect of replacing one of the chlorine atoms in ethyl trichloroacetate by fluorine. The dichlorofluoromethyl group is more electron withdrawing than the trichloromethyl group and should impart less steric hindrance in the vicinity of the carbonyl group of the ester. Exclusive acyl oxygen cleavage was observed. The reaction of ethyl dichloroacetate and piperidine also resulted in exclusive acyl oxygen cleavage.[5] On the other hand, ethyl trichloroacetate gives predominantly a haloform-type cleavage under the same conditions. Thus substitution of a chlorine by a fluorine or hydrogen atom totally changes the site of cleavage. This suggests that it is the size or stability of the anion formed rather than the electron-withdrawing effect of the group attached to the ester group which determines the type of cleavage which will occur.

The last part of this investigation involved the study of the reactions of tribromoacetates with primary and secondary amines. This study was complicated by the fact that these esters were not commercially available and that the few methods of preparation reported did not give good yields of products. Also the reaction mixtures were more complex than those resulting from the reactions of amines with trichloroacetates.

The reactions of *n*-butylamine with various tribromoacetates exhibited both types of cleavage (Table III). Exclusive acyl oxygen cleavage was never observed. The reaction of methyl tribromoacetate with *n*-butylamine yielded predominantly amide but the yield of carbamate was almost twice that obtained in the reaction of methyl trichloroacetate with the same amine. A small amount of methyl dibromoacetate was also formed in this reaction but the yield was so small that an accurate measurement was impossible.

The reaction of *n*-butylamine with ethyl tribromoacetate was more complex. The exact amount of N-*n*-

$$CBr_3CO_2C_2H_5 + n\text{-}C_4H_9NH_2 \longrightarrow CBr_3CONHC_4H_9 + C_2H_5OH + CHBr_3 + n\text{-}C_4H_9NHCO_2C_2H_5 + C_4H_9\overset{+}{N}H_3\bar{B}r + CHBr_2CO_2C_2H_5 + CHBr_2CONHC_4H_9$$

butyl dibromoacetamide could not be estimated because, like all amides, this compound was eluted at such a long retention time that reproducible chromatograms could not be obtained. By a process of elimination the yield of this product was estimated to be 5–8%. When the same reaction was carried out in acetonitrile, the amount of carbamate formed increased. The amounts of unreacted ester and dibromoacetate also increased. The latter increase suggests that the formation of this compound depends upon either a charged attacking species or a charged intermediate. The use of an excess of amine had no effect on the original path of the reaction. However, an additional product, N,N-di-*n*-butyloxamide, was formed in about 8–9% yield. A reasonable path for the formation of this compound may be shown as follows. In the presence of excess

TABLE III

REACTIONS OF TRIBROMOACETATES WITH *n*-BUTYLAMINE

R in CBr_3CO_2R	Solvent	Acyl oxygen cleavage, %	Haloform cleavage, %	Dibromoacetate, %	Unreacted ester, %
CH_3	...	81.1	14.9	~1–2	...
C_2H_5	...	61.2 ± 2.0	24.0 ± 2.0	1.6 ± 0.2	5.4 ± 0.6
C_2H_5	CH_3CN	45.0 ± 1.0	32.5 ± 2.0	14.9 ± 0.1	9.1 ± 0.13
$CH_2CH{=}CH_2$	...	86.7	13.3	...	...
C_6H_5	CCl_4	81.3	19.7	...	...
C_2H_5[a]	CCl_4	...	39.0 ± 1.2	11.3 ± 0.2	35.5 ± 0.8

[a] With piperidine.

$$CBr_3CONHC_4H_9 + C_4H_9NH_2 \rightleftharpoons R\overset{+}{N}HCBr_2CONHR + \underset{H}{}$$

$$Br^- \xrightarrow{RNH_2} RNHCBr_2CONHR + R\overset{+}{N}H_3$$

I

$$I + HOH \longrightarrow HBr + RNHC(Br)CONHR \longrightarrow$$

II

$$RNHCCNHR + HBr$$

amine the tribromoamide could react to give intermediate I which could react with the moisture from the atmosphere to give the oxamide. If this path is correct one would expect a larger quantity of *n*-butylamine hydrobromide than in the reaction involving an equimolecular quantity of amine and this was observed. Further evidence for this path was given by the reaction of N-cyclohexyltribromoacetamide with cyclohexylamine. A 13% yield of oxamide was isolated from the reaction mixture. The reaction was repeated in the presence of hydroquinone and under nitrogen with no detectable decrease in the yield of N,N-dicyclohexyloxamide.

The reaction of phenyl tribromoacetate with *n*-butylamine was carried out in carbon tetrachloride but exclusive acyl oxygen cleavage was not observed. This is in contrast to the reaction of phenyl trichloroacetate with the same amine which gave exclusive acyl oxygen cleavage.[6]

The analysis of the products formed in the reaction of ethyl tribromoacetate with piperidine, in carbon tetrachloride, was difficult. In addition to the products shown in Table III, ethyl bromide, chloroform, bromotrichloromethane, and chlorodibromomethane were formed but could not be determined accurately because they were present in small amounts. The yield of N-dibromoacetylpiperidine also could not be determined accurately. The formation of ethyl dibromoacetate and N-dibromoacetylpiperidine presents an interesting problem. Parrot and Paty[12] have reported that N-bromoacetylpiperidine was one of the products formed in the reaction of methyl tribromoacetate with piperidine in anhydrous ether. They did not isolate the bromoamide but isolated bromoacetic acid after treating the reaction mixture with dilute hydrochloric acid. They suggested that the bromoamide resulted from the action of methanol and piperidine on N-tribromoacetylpiperidine to give formaldehyde, N-bromoacetylpiperidine, and hydrogen bromide.

To explain the formation of our products we treated ethanol with ethyl tribromoacetate. No reaction occurred until some amine was added to the reaction mixture. Then the formation of ethyl dibromoacetate was observed. When the same reagents were mixed in a sealed vial with an outlet tube immersed in a solution of 95% ethanol containing *p*-nitrophenylhydrazine and the reaction vial was warmed slightly, the formation of the *p*-nitrophenylhydrazone derivative of acetaldehyde was observed. From these results and the data reported by Parrot and Paty the following path appears reasonable for the formation of the dibromo compounds.

$$C_2H_5OH + CBr_3CO_2C_2H_5 \rightleftharpoons CH_3CH_2\overset{+}{O}CBr_2CO_2C_2H_5 + \underset{H}{}$$

$$\bar{B}r \xrightarrow{NH} \overset{+}{N}H_2\bar{B}r + CH_3C(H)-O-CBr_2CO_2C_2H_5 \longrightarrow$$

$$CHBr_2CO_2C_2H_5 + CH_3CHO$$

The formation of N-dibromoacetylpiperidine could occur in the same manner.

The reaction of methyl tribromoacetate and piperidine in carbon tetrachloride gave essentially the same products as the reaction of ethyl tribromoacetate with the same amine in the same solvent. Chloroform, bromotrichloromethane, bromoform, methyl dibromoacetate, carbon tetrabromide, methylpiperidine N-carboxylate, di- and tribromoacetylpiperidines, and unreacted ester were identified. The main difference between the two reactions is the absence of chlorodibromomethane and presence of chloroform and carbon tetrabromide in the methyl tribromoacetate mixture. The reaction of methyl tribromoacetate with piperidine, in anhydrous ether, yielded the same products as the reaction in carbon tetrachloride except for the absence of chloroform and bromotrichloromethane.

The different halogenated methanes found in these reactions are probably due to halogen exchange between the bromoform or tribromomethyl anion and the carbon tetrachloride. Forbes and Anderson[13] found a random distribution of halogen atoms when certain pairs of halogen-substituted methanes were heated with a catalyst such as potassium chloride and partially hydrolyzed aluminum chloride. Although no heat was applied to the reactions studied, they were exothermic. Another possibility is that this interchange could have been catalyzed by piperidine hydrobromide or the material of the chromatographic column or the heat applied during the gas-chromatographic analysis. The tribromomethyl anion would be more susceptible to this haloform exchange than bromoform and if this anion is

(12) J. Parrot and M. Paty, *Compt. Rend.*, **256**, 2415 (1963).

(13) G. S. Forbes and H. H. Anderson, *J. Am. Chem. Soc.*, **67**, 1914 (1945).

formed it is possible that this reaction could occur without a catalyst.

Conclusions

From the results obtained in the present and past investigations certain trends are apparent in determining the site of cleavage of trihalogenated esters by amines.

(1) As the halogens in the trihalogenated methyl group of the ester go from fluorine to chlorine and then bromine, an increase in carbamate formation is observed.

(2) More sterically hindered amines favor the haloform-type cleavage while less sterically hindered amines favor acyl oxygen cleavage.

(3) Polar solvents favor the haloform-type cleavage while nonpolar solvents favor acyl oxygen cleavage.

(4) The degree of acyl oxygen cleavage increases with the increasing electron-withdrawing power of the group present in the alkoxy portion of the ester and the ability of this group to stabilize itself as a leaving group.

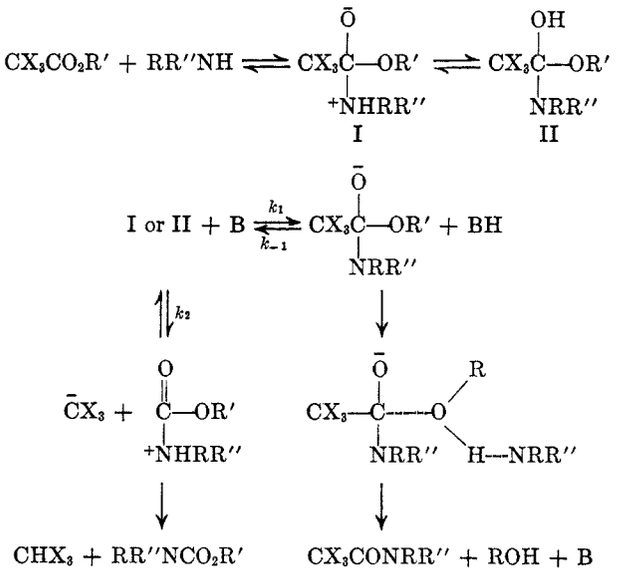
The first trend appears to be due to the increase in stability of the trihalomethyl group and/or the increase in the size of this group as one goes from fluorine to bromine. This statement is supported by recalling the reactions of ethyl trichloroacetate, ethyl dichloroacetate, and ethyl dichlorofluoroacetate with piperidine. If electron-withdrawing power of the trihalogenated group were important one would expect carbamate formation from ethyl dichlorofluoroacetate. The fact that the stability of the anion appears to be important suggests the formation of a trihalogenated methyl anion in the course of the reaction. The formation of small quantities of bromotrichloromethane, chlorodibromomethane, etc., in some of these reactions supports the existence of an anion as an intermediate in these reactions.

The second trend seems to indicate that the mechanism of these reactions might involve general base catalysis.

The effect of solvents on these reactions is in agreement with the fact that the formation of a trihalogenated methyl anion would be favored by a polar solvent. Acyl oxygen cleavage, on the other hand is favored by a nonpolar solvent. This suggests that the rate-determining step in this cleavage involves a transition state which has no significant charge separation.

The results obtained in the study of the cleavage reactions of trihalogenated esters with amines are consistent with the mechanism proposed by Bunnett and Davis[14] for the aminolysis of esters involving general base catalysis.

The first step in the reaction of trihalogenated esters with amines is the same as postulated for other esters.



The next step decides the site of cleavage. If this step involves general base catalysis, sterically hindered amines will prevent it. In the case of normal esters this results in a decrease in the rate of aminolysis. In the case of trihalogenated esters a competing reaction can occur because of the leaving ability of the CCl_3 and CBr_3 groups. As steric hindrance increases k_1 becomes smaller, k_2 becomes larger, and more carbamate is formed. Sterically hindered amines favor k_2. In the reactions of piperidine, morpholine, and diethylamine with ethyl trichloroacetate, the haloform-type cleavage predominates over the acyl oxygen cleavage. Jencks and Carriulo have shown that piperidine and morpholine cannot take part in general base catalysis in the aminolysis of phenylacetate.[15] This would account for the large quantities of carbamate formed when these amines are treated with ethyl trichloroacetate. The stability of the $\bar{C}X_3$ anion also favors k_2 and this anion should be stabilized further in polar solvents. The transition state shown for acyl oxygen cleavage would be favored in nonpolar solvents. Steric hindrance in the alkoxy group of the ester should also affect the transition state and increase k_{-1}. The ability of an alkoxy group to leave could facilitate or hinder this reaction path.

In conclusion, we have shown that although aminolysis of trihalogenated esters probably follows the same basic mechanism established for the aminolysis of simple esters, the introduction of the trihalomethyl group gives rise to an important side reaction and some minor side reactions. Thus aminolysis of trihalogenated esters is not a simple reaction and caution is in order before utilizing these reactions for synthetic purposes or attempting to obtain reliable kinetic data on these reactions.

(14) J. Bunnett and G. Davis, *J. Am. Chem. Soc.*, **82**, 665 (1960).

(15) W. P. Jencks and J. Carriulo, *ibid.*, **82**, 678 (1960).