[Contribution from the Rohm and Haas Company, Redstone Arsenal Research Division]

THE REACTION OF TRICHLOROETHYL NITRATE WITH SECONDARY AMINES[1]

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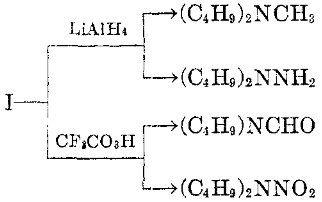
In connection with other work, we have observed an interesting reaction between trichloroethyl nitrate and secondary aliphatic amines. Upon admixture of the two reactants at ice-bath temperatures, an instantaneous, highly exothermic reaction occurs producing chloroform and a mixture of the nitrosamine and dialkylformamide corresponding to the secondary amine employed.

$$Cl_3CCH_2ONO_2 + 2\ R_2NH \rightarrow CHCl_3 + R_2NNO + R_2NCHO + H_2O$$

In all the reactions studied the formamide and nitrosamine formed an inseparable mixture and were identified through their oxidation and reduction products. After the mixture's components had been established conclusively it was possible to determine the amount of each component present by quantitative infrared analysis of the mixture. By this method, the yields of formamides and nitrosamines were found to be 90–95% and 80%, respectively.

The reaction of trichloroethyl nitrate and di-*n*-butylamine is typical. These two compounds reacted within 15 minutes at 0–5° to produce a dark red solution. Distillation of this solution at atmospheric pressure yielded chloroform as evidenced by its boiling point, index of refraction, and infrared spectrum. The residue was distilled *in vacuo* to yield a bright yellow oil (I). This product at first appeared to be homogeneous as indicated by a sharp and reproducible boiling point, but satisfactory analytical data could not be obtained from it. Upon reduction of the oil (I) with lithium aluminum hydride, two amines, dibutylmethylamine and *unsym*-dibutylhydrazine, were obtained. Both were identified by comparison of their infrared spectra with those of authentic samples. Oxidation of the oil (I) with peroxytrifluoroacetic acid (1) yielded a mixture of dibutylnitramine and dibutylformamide. These reactions are summarized in Scheme **A**.

A.



From these reactions it is clear that the oil (I) is a mixture of two compounds, one of which contains a nitrogen-nitrogen bond and is the precursor of the hydrazine and nitramine, and a second which possesses a nitrogen-carbon bond and is the precursor of dibutylmethylamine. This latter compound is certainly

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dibutylformamide. It is reduced by lithium aluminum hydride to the tertiary amine, but is unaffected by the peroxy acid. Its presence in the oily reaction product (I) explains the strong band at 1642 cm^{-1} in the infrared spectrum of this oil since the amide carbonyl band of authentic dibutylformamide is also at 1642 cm^{-1}.

The other component of the mixture must be dibutylnitrosamine which was oxidized to the nitramine and reduced to the hydrazine. Further proof of the nitrosamine's existence in the original oil (I) was obtained upon saturation of an ethereal solution of that oil with dry hydrogen chloride. Dibutylnitrosamine hydrochloride precipitated as a white solid, from which the nitrosamine could be regenerated by treatment with alkali. Unfortunately all the nitrosamine could not be removed by this method and the amide could not be obtained in a pure state.

In a recent study of the solvolysis of nitrate esters, Baker and Easty (2) suggested three paths whereby such reactions may occur: (a) nucleophilic attack at the *alpha*-carbon with displacement of nitrate ion; (b) abstraction of an *alpha*-hydrogen atom with subsequent decomposition to a carbonyl compound and nitrite ion; and (c) *beta*-hydrogen abstraction leading to olefin formation.

(a) $B\colon + RCH_2CH_2ONO_2 \rightarrow RCH_2CH_2B + NO_3^-$

(b) $B\colon + RCH_2CH_2ONO_2 \rightarrow BH + RCH_2\overset{-}{C}HONO_2 \rightarrow RCH_2CHO + NO_2^-$

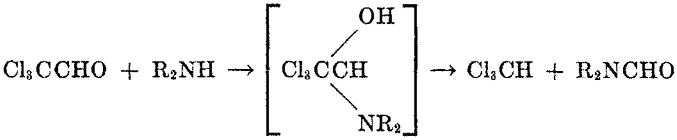
(c) $B\colon + RCH_2CH_2ONO_2 \rightarrow BH + R\overset{-}{C}HCH_2ONO_2 \rightarrow RCH{=}CH_2 + NO_3^-$

Any attempt to suggest a course for the reaction of trichloroethyl nitrate and secondary amines must account for three products: chloroform, the nitrosamine, and the formamide. Since none of these products can be produced *via* route (a), and (c) is precluded by the structure of the nitrate, path (b) may be used to interpret the reaction. A possible reaction path is presented in equations 1–4.

1. $R_2NH + Cl_3CCH_2ONO_2 \rightarrow R_2NH_2^+ + Cl_3C\overset{-}{C}HONO_2$

2. $Cl_3C\overset{-}{C}HONO_2 \rightarrow Cl_3CCHO + NO_2^-$

3. $R_2NH_2^+ + NO_2^- \rightarrow R_2NNO + H_2O$

4. 

$$Cl_3CCHO + R_2NH \rightarrow \left[Cl_3C\,CH{\begin{smallmatrix} OH \\ NR_2 \end{smallmatrix}} \right] \rightarrow Cl_3CH + R_2NCHO$$

The decomposition of a nitrate ester to a carbonyl compound and nitrite ion has been observed to a small extent with simple alkyl nitrates (2). It is not surprising that this mode of reaction becomes the predominant one in this negatively-substituted nitrate. The reaction of chloral with amines to produce formamides and chloroform has recently been the subject of a general investigation (3). It has been shown to be a very rapid, exothermic reaction from which high yields of the amide may be obtained.

The proposed mechanism predicts that the nitrosamine and formamide should be present in 1:1 ratio in the reaction product. Quantitative infrared analysis of the oil (I) shows that the formamide-nitrosamine ratio is actually about 1.2:1. A similar examination of the analogous product from the reaction of piperidine with trichloroethyl nitrate showed that the same ratio in this reaction mixture was also approximately 1.2:1.

EXPERIMENTAL[2]

Trichloroethyl nitrate. To 105 g. of mixed acid prepared from 42 g. of nitric acid and 63 g. of sulfuric acid at 10° was added 14.9 g. (0.1 mole) of freshly distilled trichloroethanol. The reaction was not noticeably exothermic. The solution was allowed to warm to room temperature and was stirred for 30 minutes. The mixture was quenched in 500 ml. of a crushed ice-water mixture and the product was extracted with three 100-ml. portions of methylene chloride. The combined extracts were washed with water and dried over magnesium sulfate. The solvent was evaporated under reduced pressure and the residue was distilled *in vacuo* to yield 12.1 g. (63%) of trichloroethyl nitrate, b.p. 44–45°/8.2 mm., n_D^{20} 1.4713.

Anal. Calc'd for $C_2H_2Cl_3NO_3$: C, 12.36; H, 1.04; N, 7.26.
Found: C, 13.28; H, 1.26; N, 7.34.

Reaction of trichloroethyl nitrate and di-n-butylamine. This procedure is typical of those employed with the following secondary amines: piperidine, morpholine, dimethylamine, diethylamine and diisopropylamine.

To 25.8 g. (0.2 mole) of di-*n*-butylamine contained in an Erlenmeyer flask immersed in an ice-bath was added very slowly 19.4 g. (0.1 mole) of trichloroethyl nitrate. Efficient stirring was maintained with a magnetic stirrer. A dark red mixture resulted which was stirred at room temperature for 15 minutes after addition was complete. Distillation of the reaction mixture at atmospheric pressure yielded 6.9 g. (57%) of chloroform, b.p. 60–62°, n_D^{20} 1.4454. The residue was distilled *in vacuo* to yield 26.4 g. of a bright yellow oil (I), b.p. 62–64°/0.2 mm., n_D^{20} 1.4465. Quantitative infrared analysis (see method below) of this mixture showed that it contained 14.1 g. (90%) of dibutylformamide and 12.3 g. (78%) of dibutylnitrosamine.

Reaction of trichloroethyl nitrate with piperidine. Following the method described above, from 17 g. (0.2 mole) of piperidine and 19.4 g. (0.1 mole) of trichloroethyl nitrate there was obtained 6.8 g. (57%) of chloroform and 15.9 g. of yellow oil, b.p. 55–56°/0.7 mm., n_D^{20} 1.4898. Infrared analysis of this oil showed that it contained 8.9 g. (94%) of N-formylpiperidine and 7.0 g. (78%) of nitrosopiperidine.

Reduction of trichloroethyl nitrate-dibutylamine product (I). A solution of the yellow oil (I) in 50 ml. of dry ether was added to a slurry of 4.0 g. (0.105 mole) of lithium aluminum hydride in 200 ml. of dry ether. This mixture was heated under reflux for two hours and then decomposed with 10% sodium hydroxide solution. The layers were separated and the aqueous layer was extracted several times with ether. The ether extracts were combined and dried over magnesium sulfate. The solvent was evaporated and the residue was fractionated *in vacuo*.

The first fraction consisted of dibutylmethylamine, b.p. 49–50°/10 mm., n_D^{20} 1.4182. Two conflicting reports of the properties of dibutylmethylamine are in the literature. Westphal and Jerchel (4) reported the following constants for the product obtained from the reaction of *n*-butyl chloride with methylamine: b.p. 53–54°/11 mm., n_D^{20} 1.418. Emerson and Uraneck (5) claimed to have produced the amine by the hydrogenation of a mixture of nitromethane and *n*-butyraldehyde, and they reported the following constants: b.p. 155–163°, n_D^{20} 1.4302.

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[2] All melting points and boiling points are uncorrected. We are indebted to Miss Annie Smelley for the microcombustion data.

Since the product obtained from this reduction appeared to be the same as that obtained by Westphal and Jerchel, a methiodide was prepared to substantiate its proposed structure. The melting point of this derivative (148–149°) was not depressed upon admixture with the same derivative prepared from authentic dibutylmethylamine. The authentic amine was prepared in two ways as described below.

The second fraction from the reduction consisted of *unsym*-dibutylhydrazine, b.p. 66–67°/10 mm., n_D^{20} 1.4340. When treated with phenylisothiocyanate (6), it was converted to its phenylthiourea, m.p. 70.5–71° (from ethanol).

Anal. Calc'd for $C_{15}H_{25}N_3S$: C, 64.47; H, 9.02; N, 15.04.
Found: C, 64.88; H, 9.33; N, 14.97.

Admixture of this derivative with the phenylthiourea of authentic *unsym*-dibutylhydrazine (see below) caused no depression of the melting point. In addition the infrared spectra of both of these amines were identical with those of the authentic samples.

Dibutylmethylamine. A solution of 8.0 g. (0.05 mole) of dibutylformamide (7) in 50 ml. of dry ether was added to a slurry of 5.0 g. (0.13 mole) of lithium aluminum hydride in 200 ml. of dry ether. The mixture was heated under reflux for two hours, decomposed with alkali, and extracted with ether. The extracts were dried, the solvent evaporated, and the residue distilled to yield 4.8 g. (67%) of dibutylmethylamine, b.p. 49–51°/10 mm., n_D^{20} 1.4178. When treated with methyl iodide, it yielded a methiodide, m.p. 149–150° (from ethanol and ethyl acetate).

Anal. Calc'd for $C_{10}H_{24}NI$: C, 42.11; H, 8.48.
Found: C, 41.94; H, 8.11.

This amine, b.p. 50–50.5°/10 mm., n_D^{20} 1.4179, was also prepared by the reaction of dibutylamine with methyl iodide. Its methiodide melted at 147–149°.

Dibutylhydrazine. A solution of 7.9 g. (0.05 mole) of dibutylnitrosamine in 50 ml. of ether was added to a slurry of 5.0 g. (0.13 mole) of lithium aluminum hydride in 100 ml. of dry ether. Upon decomposition and distillation, dibutylhydrazine was obtained as a colorless liquid, b.p. 66–67°/10 mm., n_D^{20} 1.4342; yield 5.0 g. (77%). Its *phenylthiourea* melted at 70–71°.

Oxidation of trichloroethyl nitrate-dibutylamine product (I). To a solution of peroxytrifluoroacetic acid (1) prepared from 2.6 g. (0.075 mole) of 90% hydrogen peroxide and 50 ml. of trifluoroacetic acid was added, with stirring, 8.6 g. of the oil (I) at room temperature. The mixture was warmed at 45° for an hour and then quenched in ice-water. The mixture was extracted with methylene chloride and the extracts were washed with sodium bicarbonate solution and dried over magnesium sulfate. Upon evaporation of the solvent and distillation of the residue, two fractions were obtained.

The first consisted of dibutylformamide, b.p. 62–63°/0.1 mm., n_D^{20} 1.4446 [lit. (7): b.p. 76–78°/0.25 mm., n_D^{20} 1.4435]. Its infrared spectrum was identical with that of authentic dibutylformamide prepared from dibutylamine and formic acid.

The second fraction consisted of dibutylnitramine, b.p. 91–92°/0.6 mm., n_D^{20} 1.4562 [lit. (8): b.p. 129–130°/11 mm., n_D^{25} 1.4557]. Its infrared spectrum was identical with that of authentic dibutylnitramine prepared by the oxidation of dibutylnitrosamine with peroxytrifluoroacetic acid.

Infrared analysis of nitrosamine-formamide mixtures. Standard solutions of dibutylformamide, dibutylnitrosamine, N-formylpiperidine, and nitrosopiperidine were prepared in carbon tetrachloride. Synthetic mixtures containing both components of each system in known concentrations and solutions of the distilled reaction products were prepared in similar fashion.

Spectra of the carbon tetrachloride solutions of the pure compounds were obtained from a Perkin-Elmer Model 21 infrared spectrophotometer. Few bands appeared suitable for analysis because of the great similarity between the spectra of the nitrosamine and the corresponding formamide. The following were chosen: dibutylformamide, 1393 cm^{-1}; dibutylnitrosamine, 1357 cm^{-1}; N-formylpiperidine, 1393 cm^{-1}; nitrosopiperidine, 1095 cm^{-1}.

A Perkin-Elmer 12C spectrophotometer was used for the absorption measurements. Since frequency and slit settings were quite critical, the instrument was set for 100% transmission with carbon tetrachloride in the 0.1-mm. cell and the per cent transmission of each solution was then determined in the same cell at that frequency without further change of instrument settings. The procedure was repeated at the second frequency. The per cent transmission at the two pertinent frequencies could be determined for eight solutions in less than an hour. During this period instrument drift was negligible. Since the apparent extinction coefficients of the dibutylformamide-dibutylnitrosamine system were constant within 2%, concentrations were calculated from the additive form of Beer's law. The N-formylpiperidine-nitrosopiperidine system yielded optical density *vs* concentration plots of considerable curvature which necessitated calculating concentrations by the method of successive graphical approximations.

A synthetic mixture which contained 0.184 g. of dibutylformamide and 0.235 g. of dibutylnitrosamine in 10 ml. of carbon tetrachloride was found by analysis to contain 0.182 g. of dibutylformamide and 0.235 g. of dibutylnitrosamine. A mixture prepared from 0.156 g. of N-formylpiperidine and 0.158 g. of nitrosopiperidine showed on analysis 0.154 g. of the formamide and 0.153 g. of the nitrosamine. These check solutions thus indicated that the analytical method was satisfactory. In similar fashion 0.302 g. of the reaction product of trichloroethyl nitrate and dibutylamine was shown to contain 0.161 g. of dibutylformamide and 0.141 g. of dibutylnitrosamine. From 0.041 g. of the piperidine-trichloroethyl nitrate product there was obtained by analysis 0.023 g. of N-formylpiperidine and 0.018 g. of the nitrosamine.

SUMMARY

The reaction of trichloroethyl nitrate with secondary aliphatic amines has been shown to yield chloroform and a mixture of the nitrosamine and formamide corresponding to the amine employed. This reaction has been interpreted in the light of mechanisms proposed for the solvolysis of nitrate esters.

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