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THE REACTION OF DICHLOROCARBENE WITH AMINES*

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Abstract—Dichlorocarbene reacts with secondary amines to give the derived formamide. With tertiary amines, amides are obtained which are the result of rearrangements and Hofmann eliminations in an intermediate nitrogen ylid. In one case, trimethylamine, a compound was obtained whose analysis and properties are consistent with those expected for α,α,β-trichloroethyldimethylamine, V.

THE intermediacy of dichlorocarbene in the basic hydrolysis of chloroform first suggested in 1862 by Geuther[1] has now been convincingly demonstrated by the kinetic results obtained by Hine[2] and by the structural evidence presented by Doering and Hoffmann[3]. The carbylamine test for primary amines, discovered in 1870 by Hofmann[4], has been interpreted as the reaction of dichlorocarbene with the amine by Nef[5] and later by Hine[2]. Recently Smith and Kalenda[6], in the preparation of various substituted isonitriles, reported the isolation of a small amount of 3-diethylaminopropylformamide when 3-diethylaminopropylamine was treated with chloroform and potassium hydroxide. These authors attribute the formation of the amide product to the hydrolysis of the dichloromethylamine intermediate resulting from the addition of dichlorocarbene to the primary amine. Thus, the dichloromethylamine intermediate in the case of primary amines generally proceeds to the isonitrile but may give the formamide derivative in some cases.

The object of this study was to determine the nature of the products, if any, resulting from the reaction of dichlorocarbene with secondary and tertiary amines. A series of secondary amines was treated under conditions where it has been clearly established[3] that dichlorocarbene is produced. A benzene solution of chloroform was added, dropwise, to stirred mixtures of the amine, benzene, and potassium t-butylate. Precautions were taken to exclude water prior to, and during the reaction. The reactions proceeded smoothly to give varying yields of the derived formamide. Diethylamine, dimethylamine, diphenylamine, and piperidine were treated in the manner described to give diethylformamide, dimethylformamide, diphenylformamide, and N-formylpiperidine, respectively. Yields varied from 31 per cent in the piperidine case to 0·3 per cent in the case of diphenylamine. The poor yield from diphenylamine can be attributed to its very weak basicity. The reactions were invariably accompanied by the production of large quantities of brown polymeric material. When the reactions were carried out without using benzene as solvent for the chloroform and

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[1] A. Geuther, *Liebigs Ann.* **123**, 121 (1862).

[2] J. Hine, *J. Amer. Chem. Soc.* **72**, 2438 (1950).

[3] W. E. Doering and A. K. Hoffmann, *J. Amer. Chem. Soc.* **76**, 6162 (1954).

[4] A. W. Hofmann, *Ber. Dtsch. Chem. Ges.* **3**, 767 (1870).

[5] J. U. Nef, *Liebigs Ann.* **298**, 367 (1897).

[6] P. A. S. Smith and N. W. Kalenda, *J. Org. Chem.* **23**, 1599 (1958).

potassium t-butylate, the yield of amide was reduced and the amount of polymeric material produced was increased. Likewise, carrying out the reaction at room temperature led to reduced yields.

The reaction probably proceeds by an attack of dichlorocarbene on the amine to give the expected dichloromethylamine intermediate, I, such as has been postulated by Smith and Kalenda[6]. This intermediate then proceeds to the observed amide under the reaction conditions or work-up.

$$R_2NH + :CCl_2 \rightarrow R_2\dot{N}-CCl_2^- \rightarrow R_2N\ CCl_2H$$

$$\text{H}$$

$$R_2N-CCl_2H \rightarrow R_2N-CHO$$

Since preliminary publication of these results Frankel *et al.*[7] have published similar results and have expressed agreement with the mechanism presented above.

Attempts to isolate the dichloromethylamine intermediate were unsuccessful. Dichloromethylamines are not known in the pure state although they have been suggested as intermediates by several authors. Thus, Hinkel and Watkins[8] have claimed the formation of dichloromethylamine itself (formamidodichloride) by treating hydrogen cyanide with hydrogen chloride. The presence of the amine is suggested by its condensation with nitrobenzaldehydes to give, eventually, nitrobenzylidenebisformamides. The initial condensation product between the nitrobenzaldehyde and dichloromethylamine could not be isolated. These same authors claim the formation of acetamidodichloride, from the action of hydrogen chloride on acetonitrile, as unpublished work, Recently, however, Janz and Danyluk[9] made a similar study but these authors favor a nitrilium salt structure, [CH_3CNH^+ $ClHCl^-$], for the crystalline compound formed. They indicate that no evidence was found for the acetamidodichloride structure.

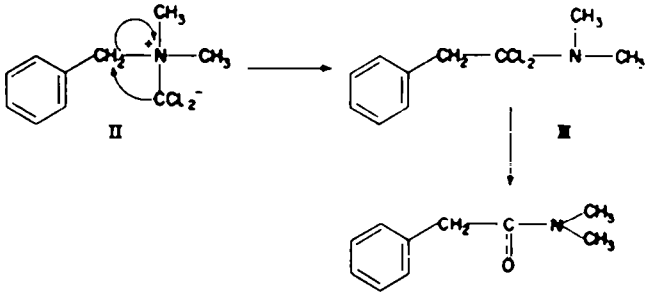
Wallach[10–12] and von Braun[13,14] have postulated the formation of amidodichlorides when amides are treated with phosphorus pentachloride. The amidodichlorides were not isolated, however. Stephen and Bleloch[15] have isolated the hydrochloride of N-phenylbenzamidodichloride as large yellow prisms. Hallman[16] reported the formation of dimethylbenzamidodichloride when dimethylbenzamide was treated with phosgene. The author described this product as unstable and deliquescent.

In view of the reported instability of the dichloromethylamines it seems reasonable to assume that this intermediate was hydrolyzing to the observed amide, despite precautions taken to exclude water during the reaction.

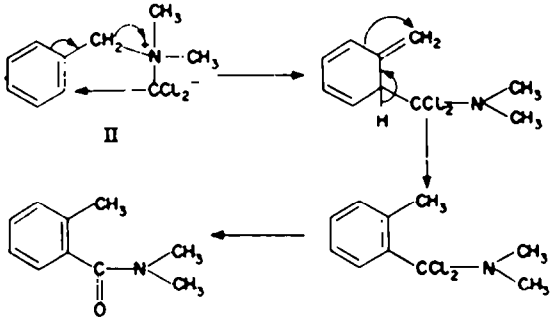
When diethylamine, aqueous sodium hydroxide and sodium formate were placed together under the conditions of the reaction, no amide was formed. Thus the trivial explanation involving prior basic hydrolysis of the chloroform to formate, followed by reaction with amine to give amide, is precluded.

[7] M. B. Frankel, H. Feuer and J. Bank, *Tetrahedron Letters* No. 7, 5 (1959).
[8] L. E. Hinkel and T. I. Watkins, *J. Chem. Soc.* 647 (1944).
[9] G. J. Janz and S. D. Danyluk, *J. Amer. Chem. Soc.* **81**, 3850 (1959).
[10] O. Wallach, *Liebigs Ann.* **237**, 251 (1887).
[11] O. Wallach, *Liebigs Ann.* **214**, 193 (1882).
[12] O. Wallach, *Liebigs Ann.* **184**, 1 (1877).
[13] J. von Braun, *Ber. Dtsch. Chem. Ges.* **37**, 2678 (1904).
[14] J. von Braun and J. Weismantel, *Ber. Dtsch. Chem. Ges.* **55**, 3165 (1922).
[15] H. Stephen and W. Bleloch, *J. Chem. Soc.* 886 (1931).
[16] F. Hallmann, *Ber. Dtsch. Chem. Ges.* **9**, 846 (1876).

When tertiary amines were subjected to the conditions described above a variety of products was observed depending upon the structure of the amine used. Benzyldimethylamine reacted to give N,N-dimethylphenylacetamide and dibenzyl. Formation of the amide product is most likely due to a Stevens rearrangement of the initially-formed nitrogen ylid. This rearrangement, first reported by Stevens *et al.*[17], involves a 1,2 shift of a methyl, benzyl, substituted benzyl, phenacyl, allyl, or 3-phenylpropargyl group in quarternary ammonium ions. Migration of a benzyl group in the initial ylid, II, formed by addition of dichlorocarbene to benzyldimethylamine, followed by hydrolysis of the amidodichloride, III, could explain the observed product.



The ylid, II, presumably also could undergo a rearrangement of the type reported by Sommelet[18]. Such a rearrangement involves attack in the aromatic nucleus *ortho* to the substituent followed by rearomatization of the intermediate exomethylene compound. The hydrolyzed product of such a rearrangement in this case would be N,N-dimethyl-O-toluamide. None of this product could be detected in the reaction mixture.



Whether a particular quarternary ammonium ion will undergo the Stevens or Sommelet rearrangement, or both, seems to depend on the base and conditions used. Benzyltrimethylammonium, benzhydryltrimethylammonium and dibenzyldimethylammonium ions are all known to give Stevens or Sommelet rearrangements depending on the conditions.[19-22] Phenyl lithium, hydroxide or methoxide tended to give

[17] T. S. Stevens, E. M. Creighton, A. B. Gordon and M. McNicol, *J. Chem. Soc.* 3193 (1928).
[18] M. Sommelet, *C.R. Acad. Sci., Paris.* **205**, 56 (1937).
[19] G. Wittig, R. Mangold and G. Felletschin, *Liebigs Ann.* **560**, 116 (1948).
[20] C. K. Ingold and E. D. Hughes, *J. Chem. Soc.* 69 (1933).
[21] T. Thomson and T. S. Stevens, *J. Chem. Soc.* 1932 (1932).
[22] S. W. Kantor and C. R. Hauser, *J. Amer. Chem. Soc.* **73**, 4122 (1951).

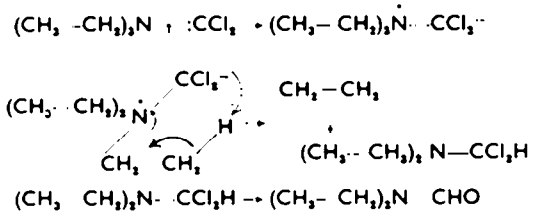
Stevens rearrangements, while sodamide in liquid ammonia favored Sommelet rearrangements.

The formation of products analgous to the dibenzyl product isolated has been observed by other workers. Thus, Stevens *et al.*[23] found that when phenacyl-*p*-nitrobenzyldimethylammonium bromide was treated with base the rearrangement product, *ω*-dimethylamino-*ω*-*p*-nitrobenzylacetophenone, was obtained, along with *p*-nitrotoluene and *p,p'*,-dinitrodibenzyl. Likewise, Wittig *et al.* [19] upon treating benzhydryltrimethylammonium bromide with phenyl lithium obtained tetraphenylethane in addition to the Stevens and Sommelet rearrangement products.

Previous work on the mechanism of the Stevens rearrangement[17,24-28] indicates that an ylid is formed which rearranges with migration of a group from nitrogen to carbon. In some cases apparently, elimination of this group as an anion can occur. Protonation of the anion can then give the corresponding hydrocarbon. Alternatively alkylation of this anion by another quarternary ammonium ion[22,29] can give the observed coupling products. The ammonium cation left by this elimination would be expected to give a carbonyl containing product on work up. Such a product has been isolated.[22]

The formation of dibenzyl in the reaction between benzyldimethylamine and dichlorocarbene can be explained using these steps. The initially formed ylid, II, can eliminate a benzyl anion which can then be benzylated by the quarternary salt formed when the ylid is protonated. t-Butyl alcohol may act as a source of protons to give this quarternary salt.

When triethylamine was treated with chloroform and potassium t-butylate two amide products were obtained. The products were separated by gas chromatography and were identified as diethylformamide, (15·2%) and N,N,-diethyl-α-chloropropionamide, (12·2%). The formation of diethylformamide is most likely due to a *β*-elimination in the initially-formed ylid, IV, followed by hydrolysis of the diethyldichloromethylamine.



IV

Weygand *et al.*[30], in an investigation of the Hofman degradation of quarternary ammonium salts using isotopic hydrogen have found that an α hydrogen can be abstracted initially which, in turn, can abstract the *β* hydrogen leading to olefin formation. The ylid, IV, is, therefore, expected to decompose, at least partially, to give the observed diethylformamide.

[23] T. S. Stevens, W. W. Spedden, E. T. Stiller and T. Thomson, *J. Chem. Soc.* 2119 (1930).
[24] T. S. Stevens and B. A. Hems, *J. Chem. Soc.* 856 (1937).
[25] T. S. Stevens and T. Thomson, *J. Chem. Soc.* 69 (1932).
[26] T. S. Stevens and T. Thomson, *J. Chem. Soc.* 55 (1932).
[27] T. S. Stevens and J. L. Dunn, *J. Chem. Soc.* 1926 (1932).
[28] T. S. Stevens, *J. Chem. Soc.* 2107 (1932).
[29] H. R. Snyder, C. W. Smith and J. M. Stewart, *J. Amer. Chem. Soc.* **66**, 200 (1944).
[30] F. Weygand, H. Daniel and H. Simon, *Chem. Ber.* **91**, 1691 (1958).

The other product shows the infrared spectrum of an amide. The nuclear magnetic resonance spectrum (NMR) of this compound is shown in Fig. 1.

When the sample is heated and its NMR spectrum retaken then two groups peaks of at 6·77 and 8·90* collapse to a quadruplet and a triplet, respectively (Spectrum 2b in Fig. 1). These peaks are assigned to the methylene and methyl groups of a diethyl-substituted amide.

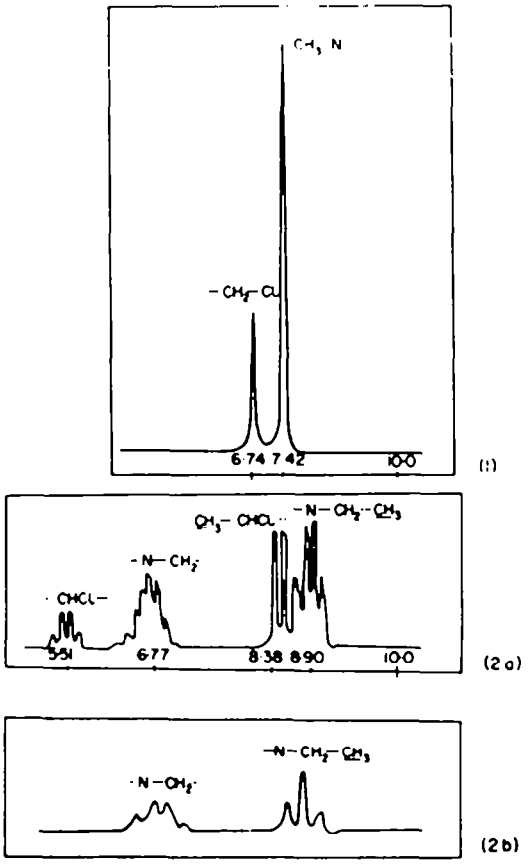


FIG. 1. Nuclear magnetic resonance spectra. (1) V in CS_2, (2a) α-Chlorodiethylpropionamide in CCl_4 at room temperature, (2b) 8·90 and 6·77 peaks of XIII at ca. 80°. Chemical shift values are in p.p.m. relative to tetramethylsilane (– 10·0 p.p.m.).

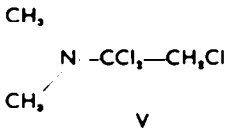
There is restricted rotation about the C–N bond because of amide resonance and at room temperature the two ethyl groups attached to the nitrogen atom are non-equivalent.[31,32] When the amide is heated the barrier to rotation is passed rapidly, the diethylamino group rotates freely and the two ethyl groups become equivalent leading to a single ethyl group spectrum. The spectrum also has a doublet at 8·38 and a quadruplet at 5·51 which are assigned to the remaining methyl group and the α hydrogen of N,N-diethyl-α-chloropropionamide, respectively.

* NMR values given are chemical shifts in p.p.m. with tetramethylsilane = 10·00 p.p.m.

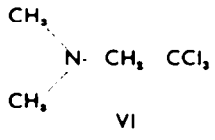
[31] W. D. Phillips, *J. Chem. Phys.* **23**, 1363 (1955).

[32] H. S. Gutowsky and C. H. Holm, *J. Chem. Phys.* **25**, 1228 (1956).

Trimethylamine was liquified at $-20°$ and then treated as described previously. In this case, the evaporative distillation used to separate the crude reaction product from tars produced in the reaction was characterized by the production of an acidic gas and the sublimation of a tan-colored solid. The solid sublimate was resublimed several times and could be obtained as a pale yellow solid. This solid turned brown upon standing. It decomposed at ca. 185°. The reaction also gave a liquid product, V, $C_4H_8NCl_3$, which could be distilled at reduced pressure and had b.p. 50·5° (11 mm). When distillation was attempted at atmospheric pressure the liquid decomposed rapidly giving off an acidic gas. The NMR spectrum of the pure compound (Fig. 1) was very simple, consisting of two sharp peaks in an approximate three to one ratio. These peaks had τ values of 7·42 and 6·74 for the stronger and weaker peaks, respectively. When the solid product of the reaction was treated with aqueous base it gave a liquid whose infrared spectrum was identical with that of the liquid product. When a benzene solution of V was treated with aqueous silver nitrate an immediate, copious, white precipitate was formed. The product of this reaction had a gas phase chromatography retention time which was identical with that for authentic N,N-dimethyl-α-chloroacetamide. The infrared spectrum of a sample of this component was superimposable on that of authentic N,N-diethyl-α-chloroacetamide. On the basis of the evidence given the liquid product, V, appears to be a chloro-amine. The solid product obtained is undoubtedly the hydrochloride of this amine, the HCl being produced by partial decomposition of V during distillation. The infrared spectrum of V indicates that it is a tertiary amine since there is no NH absorption. Since the NMR spectrum indicates that the compound has only two kinds of protons and these in a three to one ratio, only structures V and VI would seem to warrant consideration for the chloroamine. Compound VI would not be expected to react with silver nitrate.



V



VI

Compound V, on the other hand, should react with aqueous silver nitrate to give N,N-dimethyl-α-chloroacetamide the observed product. On the basis of the evidence given the amine isolated is believed to be, V, α,α,β-trichloroethyldimethylamine.

The mechanism for the formation of V from trimethylamine is undoubtedly the same as that for the formation of N,N-diethyl-α-chloropropionamide in the triethylamine reaction. However, V, does not appear to hydrolyze to the amide as readily. An attempt to prepare an authentic sample of this amine from the amide and phosphorus pentachloride failed.

No final conclusion about the mechanisms of the last two reactions described can be drawn at this time. However, certain aspects of the reaction deserve comment. Apparently an α,α,β trichloro amine is formed in each case, but hydrolyzed during work-up in the triethylamine reaction. It may be noted that this is the expected result of a Stevens rearrangement where the product has been chlorinated. The ultimate source of this extra chlorine must be chloroform. In strong base, the most

likely mechanism for chlorination is "positive halogen transfer",[33 41] which is nucleophilic displacement on halogen. The halogen donor may be chloroform itself or some reaction product. t-Butyl hypochlorite may well be the actual chlorinating agent as suggested[42] in explanation of a reaction performed under similar conditions.

Since no normal product of the Stevens rearrangement is obtained, and since the chlorination is specific, it may be that the chlorination occurs at a stage before the rearrangement; however, elimination of HCl from the normal Stevens product followed by chlorination of the resulting eneamine has not been ruled out. Further work, which may illuminate the mechanism, is in progress.

EXPERIMENTAL*

Reaction of chloroform, potassium t-butylate, and diethylamine. The reaction of potassium metal (23·5 g, 0·6 mole) and 0·6 l. dried (distilled from calcium hydride) t-butyl alcohol was carried out with stirring at room temp in a 1 l. three-necked flask equipped with a reflux condenser and drying tube and kept under a slight positive pressure of prepurified nitrogen. After the potassium had completely dissolved, excess t-butyl alcohol was removed by distillation. The dry powder remaining was further dried at 160–170° at 1-2 mm for 6 hr. To a slurry of the dried powder with 350 ml dry benzene was added 100 ml (71·0 g, 0·97 mole) diethylamine which had been carefully fractionated. The flask contents were stirred in a dry ice-trichloromethylene bath maintained at ca. 5–10°. A solution of 33·1 ml (47·9 g, 0·4 mole) chloroform in 100 ml dry benzene was added, dropwise, to the stirred reaction mixture. When all the chloroform solution had been added the dark brown mixture was allowed to warm to room temp and stirred for an additional 0·5 hr. The reaction mixture was concentrated *in vacuo*. Ether was added to the dark residue to precipitate potassium chloride which was filtered off and washed with ether. The filtrate was transferred to a distillation apparatus. After removal of ether, benzene, and t-butyl alcohol a fraction was obtained at 64° and 10 mm. The infrared spectrum of this material was superimposable with that of authentic diethylformamide; lit.[43] b.p. 177-179° (760 mm). Yield was 9·0 g (22·5% based on chloroform).

When this preparation was carried out at room temp or without using benzene as solvent the yield was reduced to ca. 10-15%.

When the amine is treated with sodium formate no amide is produced. To a solution of 17·7 g (0·24 mole) diethylamine in 100 ml benzene was added 10 g (0·15 mole) sodium formate and the mixture stirred at room temp for 4 hr. After adding 100 ml NaOH, (10% aqueous solution) stirring was continued for an additional hour. The benzene layer was separated off and concentrated to ca. 10 ml. An infrared spectrum of the residue showed no amide present.

Reaction of dimethylamine, chloroform, and potassium t-butylate. A slurry was made of benzene and potassium t-butylate, produced by dissolving 38·3 g (0·98 mole) potassium metal in 600 ml t-butyl alcohol and removing excess alcohol. Chloroform (117·5 g, 0·98 mole) in benzene solution was added dropwise to a stirred mixture of the slurry and 11·0 g (0·24 mole) dimethylamine in a 1 l., three-necked flask equipped with a dry ice condenser. The flask was cooled to ca. -10° in a dry ice-trichloroethylene bath. When chloroform addition was complete the reaction mixture was allowed to warm to room temp and was stirred for an additional 0·5 hr. The reaction mixture was extracted

* All melting and boiling points are uncorrected. Infrared spectra were taken with a Perkin-Elmer Corporation model 21 recording infrared spectrophotometer. Nuclear magnetic resonance spectra were taken with a Varian Associates 60 mc. high resolution nuclear magnetic resonance spectrometer. Gas chromatograms were run on a Wilkins Instrument and Research Aerograph model A-90-C gas chromatograph. Analyses were performed by Schwarzkopf Microanalytical Laboratory, Woodside 17, N.Y.

[33] M. Ballester, C. Molinet and J. Rosa, *Tetrahedron* **6**, 109 (1959).
[34] R. Altschul and P. D. Bartlett, *J. Org. Chem.* **5**, 623 (1940).
[35] J. E. Leffler, *J. Amer. Chem. Soc.* **75**, 3598 (1953).
[36] M. F. Hawthorne, *J. Amer. Chem. Soc.* **77**, 5739 (1955).
[37] H. Finkelstein, *Ber. Dtsch. Chem. Ges.* **43**, 1528 (1910).
[38] J. V. Backus, R. W. West and M. A. Whitely, *J. Chem. Soc.* 359 (1921).
[39] R. Willstätter and V. Hottenroth, *Ber. Dtsch. Chem. Ges.* **37**, 1775 (1904).
[40] M. Weizmann and J. Edlitz, *Bull. Soc. Chim. Fr.* **53**, 1495 (1933).
[41] A. Perret and R. Perrot, *Bull. Soc. Chim. Fr.* **1**, 1547 (1934).
[42] W. E. Parham, F. C. Loew and E. E. Schweizer, *J. Org. Chem.* **24**, 1900 (1959).
[43] O. Wallach, *Liebigs Ann.* **214**, 271 (1882).

with 300 ml water and the aqueous layers backwashed with ether. The combined ether and benzene solutions were dried over magnesium sulfate. The ether and benzene were distilled out *in vacuo*. The dark residue was distilled in an evaporative still. The fraction boiling from 80–165° at 20 mm was redistilled through a fractional column. Dimethylformamide (2·03 g, 11·3%) distilled out at 59° (19 mm). The infrared spectrum of the product was superimposable with that of an authentic sample of dimethylformamide.

Reaction of piperidine, chloroform, and potassium t-butylate. To a slurry of potassium t-butylate, prepared from 34·2 g (0·87 mole) potassium metal and 200 ml benzene was added 86·2 g (1·01 mole) of redistilled piperidine. The reaction flask was cooled to ca. 5° in a dry ice-trichloroethylene bath. A solution of 47·9 g (0·4 mole) chloroform in 100 ml benzene was added, dropwise, to the stirred reaction mixture. When addition was complete, the reaction mixture was allowed to warm to room temp and was stirred for an additional 0·5 hr. The benzene solution was concentrated *in vacuo* and ether added to precipitate potassium chloride. The potassium chloride was filtered off and washed well with ether. The combined benzene and ether solutions were distilled *in vacuo*. After removal of ether, benzene and t-butyl alcohol the amide distilled at 80° (3 mm), lit.[44] b.p. 108° (14–15 mm). Yield was 14·0 g (31%). The infrared spectrum of the product was identical to that of an authentic sample of N-formyl piperidine prepared by refluxing piperidine with formic acid.

Reaction of diphenylamine, chloroform, and potassium t-butylate. A solution of 28·9 g (0·24 mole) chloroform in 80 ml benzene was added, dropwise, at room temp, to a slurry of 200 ml benzene and 5·74 g (0·051 mole) potassium t-butylate to which had been added 6·9 g (0·041 mole) redistilled diphenylamine. When addition of the chloroform solution was complete, 100 ml water was added and stirring was continued at room temp for an additional hour. The benzene layer was separated and concentrated by distillation *in vacuo*.

A portion (ca. 21 ml) of the dark, crude residue was placed on a column of alumina (ca. 100 g). Elution with benzene : ether; 9:1 gave a solid whose infrared spectrum was identical to that of an authentic sample of diphenylformamide. Yield, by quantitative infrared measurement, was 0·028 g (0·34%).

The authentic sample was prepared by refluxing 24·9 g (0·14 mole) diphenylamine with 18·3 g (4·0 mole) formic acid for 144 hr. The reaction mixture was then poured into water. The white crystals obtained were filtered off and recrystallized from ethanol water, m.p. 68·5°.

Reaction of triethylamine, chloroform, and potassium t-butylate. To a slurry of alcohol-free potassium t-butylate, prepared by dissolving 34·4 g (0·88 mole) potassium metal in t-butyl alcohol, and 400 ml benzene, was added 31 ml (22·4 g, 0·22 mole) triethylamine. The amine had been carefully fractionated through a column packed with metal helices. To the stirred flask contents, cooled to 5°, was added, dropwise, a solution of 70·8 ml (106 g, 0·88 mole) chloroform in 400 ml benzene. The flask contents were stirred at room temp for an additional 0·5 hr following addition of the chloroform solution. The dark reaction mixture was then washed with water and the aqueous layers backwashed with ether. The combined ether benzene solution was dried with magnesium sulfate. The dried solution was concentrated by distillation *in vacuo*. The dark, viscous residue was transferred to an evaporative still. After removal of most of the benzene and t-butyl alcohol, all the remaining volatile material was collected as a second fraction. Analysis of this fraction by gas phase chromatography showed the presence of two major products. One of the products had the same retention time as authentic diethylformamide. Its infrared spectrum was superimposable with that of authentic diethylformamide. Yield was 3·4 g (15·2%). The second component had a longer retention time than diethylformamide. Its infrared spectrum indicated the presence of a disubstituted amide. The NMR spectrum of this compound had a quartet at 5·51, a complex peak at 6·77, methyl peaks at 8·38, and a complex peak at 8·90. When heated, the peaks at 6·77 and 8·90 became a quartet and triplet, respectively. The behavior of the peaks at 6·77 and 8·90 is strong evidence for the presence of a diethyl-substituted amide. The quartet at 5·51 and the methyl peaks at 8·38 are assigned to the methine and remaining methyl protons of N,N-diethyl-α-chloro-propionamide, respectively. Yield was 4·38 g (12·15%). (Found: C, 51·6; H, 8·74; Cl, 21·6; N, 8·58. Calc. for $C_7H_{14}ClNO$: C, 51·4; H, 8·62; Cl, 21·7; N, 8·56%).

Reaction of benzyldimethylamine, chloroform, and potassium t-butylate. To a slurry of alcohol-free potassium t-butylate (from 32·8 g, 0·84 mole potassium metal) and 500 ml benzene was added 28·6 g (0·21 mole) benzyldimethylamine. The amine was prepared from the reaction of benzyl

[44] O. Wallach, *Liebigs Ann.* **237**, 251 (1887).

chloride and dimethylamine; b.p. 81·5–82·5° (23 mm). Chloroform (100·5 g, 0·84 mole), in benzene solution, was added, with stirring, to the cooled reaction mixture. When addition of the chloroform solution was complete, the dark reaction mixture was allowed to warm to room temp and was stirred for an additional hour. The mixture was extracted with 200 ml water and the aqueous layers backwashed with ether. The ether–benzene solution was dried with magnesium sulfate. The dark solution was concentrated *in vacuo*. The thick, dark oil obtained was transferred to an evaporative still and all volatile material collected. The final stages of this distillation were characterized by the sublimation of a pale yellow solid. The gas phase chromatogram of the distillate showed the presence of two major components and several minor components. One of the major components had a retention time identical to that for authentic dibenzyl. Its NMR spectrum and infrared spectrum were identical to those for authentic dibenzyl. A sample of the material obtained by gas phase chromatography was resublimed; m.p. and mixed m.p. 53·5°. Yield was 2·34 g (12·2%), from gas chromatogram peak area. The second major component had retention time identical to that for authentic N,N-dimethylphenylacetamide. The infrared spectrum of this component was superimposable with that of authentic N,N-dimethylphenylacetamide. A sample of this material was recrystallized from ether at low temperature. It had m.p. and mixed m.p. 38–40° (Kofler block). Yield was 1·1 g (3·19%), from gas chromatogram peak area. All efforts to separate the mixture of minor components present by gas chromatography and distillation were fruitless. None was present in isolable quantity.

The authentic N,N-dimethylphenylacetamide was prepared from the reaction of the acid chloride and dimethylamine. To 4·0 g (0·029 mole) phenylacetic acid was added 25 ml (41·5 g, 0·35 mole) thionyl chloride. The mixture was refluxed for 4 hr and then poured cautiously into an ice-cold solution of dimethylamine in water. The solution was made basic with aqueous sodium hydroxide. It was extracted with ether and the ether solution dried with magnesium sulfate. The ether was distilled off to give a yellow oil. The product was purified by gas phase chromatography and by three recrystallizations from ether at low temp, m.p. 38–40°.

Reaction of trimethylamine, chloroform, and potassium t-butylate. A slurry was prepared from 300 ml benzene and alcohol-free potassium t-butylate (from 35·2 g, 0·9 mole potassium metal) and cooled to ca. 10°. Trimethylamine (13·3 g, 0·23 mole) was added and the stirred mixture treated, dropwise, with a solution of chloroform (107·5 g, 0·9 mole) in benzene. When addition of the chloroform solution was complete the dark brown reaction mixture was allowed to warm to room temp and stirred for an additional 0·5 hr. The reaction mixture was extracted with water and the aqueous layers backwashed with ether.

After drying with magnesium sulfate the solution was concentrated *in vacuo*. The thick dark residue was transferred to an evaporative still and all volatile material removed *in vacuo*. During the final stages of this distillation there was considerable fuming in the still and a solid material (A) formed on the still cold finger. A portion of the distillate was transferred to a Piros–Glover Spinning band column and redistilled. After removal of benzene and t-butyl alcohol, a colorless liquid distilled at 50·5° (16 mm). Total yield was 2·32 g (5·73%, includes small amount of this material present as hydrochloride). When this distillation was attempted at atm press. complete decomposition of the product occurred. The distillate had a sweet, pleasant odor and lost HCl slowly on standing. I.R. (CS_2) 3·56 (m), 7·1(s), 8·75(m), 9·11(m), 9·39(s), 9·81(m), 10·19(s), 11·64(m), 12·90 13·00(s), 14·10–14·15(s). The NMR spectrum of this liquid had a sharp peak at 7·42 and one at 6·74 in an approximate 3:1 ratio, respectively.

When a benzene solution of 0·201 g (0·00114 mole) of this liquid product was treated with an aqueous solution of silver nitrate (5·81 g, 0·0342 mole) an immediate, copious white precipitate was produced. The reaction mixture was stirred at room temp (magnetic stirrer) for 0·5 hr. The benzene layer was separated off and the aqueous layer extracted 3 times with ether. The organic layers were combined and concentrated by distillation on the steam bath. The residue which contained a strong skin irritant was analyzed by gas phase chromatography. In addition to solvent peaks the residue showed the presence of one major component which had a retention time identical to that of N,N-dimethyl-α-chloroacetamide. The infrared spectrum of this product was superimposable with that of authentic N,N-dimethyl-α-chloroacetamide. Yield of the amide from gas chromatogram peak area was 0·072 g (52%).

The liquid product gave a picrate of *α,α,β-trichloroethyldimethylamine*, m.p., 134–136°. (Found: C, 29·6; H, 2·73; N, 13·8; Cl, 26·2. $C_{10}H_{11}N_4Cl_3O_7$ requires: C, 29·8; H, 2·97; N, 13·9; Cl, 25·9%).

The solid material (A) which sublimed during the course of the evaporative distillation was

resublimed 3 times to give almost white crystals which turned brown upon standing. The crystalline solid decomposed at 185°, with discoloration beginning at 170° (Hershberg appartus used with bath heated to 150° before insertion of sample). When treated with aqueous sodium hydroxide this solid gave a liquid whose infrared spectrum was identical to that of the liquid product. In addition a small amount of an amide (shown by infrared analysis) was produced in the base treatment.

The authentic N,N-dimethyl-α-chloroacetamide was prepared from the reaction of chloroacetyl chloride and dimethylamine. To 24·2 g (0·25 mole) α-chloroacetic acid was added 18·1 ml (30·0 g, 0·25 mole) thionyl chloride and the mixture refluxed for 1·5 hr. The resulting reaction mixture was allowed to cool and dissolved in 100 ml anhydrous ether. This solution was added, dropwise, with stirring, to a solution of 33·3 ml (22·5 g, 0·5 mole) dimethylamine in 100 ml anhydrous ether at 20°. When addition was complete the reaction was allowed to warm to room temp and stirred for an additional hour. The reaction mixture was extracted with dil, aqueous HCl. The ether layer was then extracted with dil, aqueous NaOH. The resulting ether solution was dried with magnesium sulfate. The ether was distilled off on the steam bath to give a yellow oil. This oil was distilled *in vacuo* to give 9·0 g (29%) of N,N-dimethyl-α-chloroacetamide, b.p. 71° (2 mm), lit.[44] b.p. 98·5 99·5° (11 mm). The product was a strong skin irritant.

An attempt to obtain α,α,β-trichloroethyldimethylamine by treatment of authentic N,N-dimethyl-α-chloroacetamide with phosphorous pentachloride gave no isolable product. To 0·28 g (0·0023 mole) N,N-dimethyl-α-chloroacetamide in 30 ml benzene was added 0·97 g (0·005 mole) phosphorous pentachloride. The reaction mixture was refluxed for 1·5 hr during which time it gradually darkened, finally becoming dark brown. The reaction mixture was allowed to cool and was then poured over cracked ice. The acidic reaction mixture was extracted with ether and then made basic with aqueous sodium hydroxide and reextracted. The ether solutions were dried with magnesium sulfate and the ether evaporated off. Both fractions gave a dark brown oil. Gas phase chromatograms of these oils showed only solvent peaks.

[44] W. A. Jacons and M Heidelberger, *J. Biol. Chem.* **21**, 148 (1915).