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THE OXIDATION OF TRIETHYLAMINE BY TRICHLOROACETYL CHLORIDE

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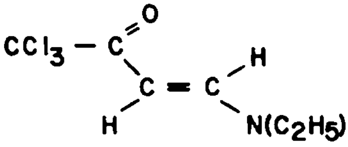
Abstract—The reaction of trichloroacetyl chloride with triethylamine is found to produce a β-acylenamine by oxidation of the tertiary amine to diethylvinylamine, then acylation. Evidence is obtained which indicates that the enamine is formed by an elimination reaction of the initially formed addition complex. A slower reaction occurred with 1,4-diazabicyclo[2.2.2]octane but the product was shown to have resulted from a Von Braun type of ring opening. The NMR and IR spectra of the β-acylenamine provide evidence that it possesses a *trans* substituted double bond and an exclusive s-*cis* conformation.

WE WISH to report the observation of an unexpected reaction between triethylamine and trichloroacetyl chloride. This reaction occurred during the attempted trichloroacetylation of a secondary amine in the presence of one equivalent of triethylamine. Subsequently, it was found that trichloroacetyl chloride and triethylamine, in methylene chloride, underwent a smooth reaction to produce the compound I in yields of up to 44% under the optimum conditions of 1 hr of reaction time at room temperature. Other solvents, temperatures and varying concentrations were tried without improving the yield.

The structure of I was assigned as shown on the basis of NMR evidence which indicated the presence of an N,N-diethyl group and a vinyl group, mass spectral evidence for the presence of three chlorines and a mol wt of 243, and IR evidence for a trichloroacetyl group. Proof of the structure was obtained by the successful synthesis of I by an alternate route. Diethylvinylamine was formed by the reaction of diethylamine with acetaldehyde in benzene.[1] Then *in situ* acylation[2] by the addition of trichloroacetyl chloride gave I, albeit in only a 5% yield of isolated product.



I

It was also found I could be prepared in poor yield (5%) using trichloroacetic anhydride in the place of trichloroacetyl chloride. Reaction of trifluoroacetic anhydride with triethylamine gave no evidence for the formation of any β-acylenamine. The production of a β-acylenamine by the reaction of trichloroacetyl chloride with

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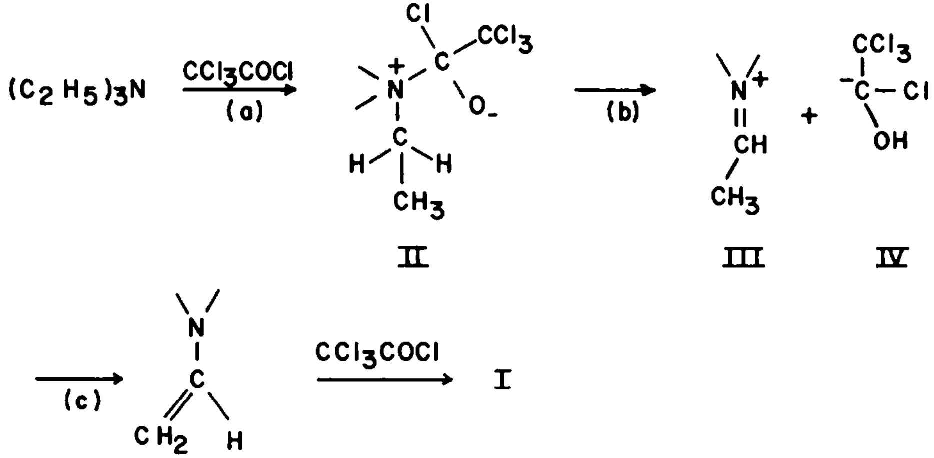
triethylamine appears to be without precedent* and we have therefore investigated the mechanism of this unusual oxidation reaction.

Mechanistic consideration. Both ionic and free radical pathways must be considered for the reaction in question. The possibility of a radical reaction was first investigated. When scrupulously purified reactants were brought together either in the dark, or in an atmosphere free from oxygen, the rate of the reaction was not visibly affected. When styrene was added at the beginning of the reaction it could be isolated unchanged after completion of the unimpeded reaction. These observations, while not conclusive, provide a strong indication that the free radical pathway is not involved.[4]

Since an oxidation had occurred we then sought evidence for some reduction product in the reaction mixture. The following products were considered possible on sometimes dubious mechanistic grounds; carbon monoxide, chloroform, dichloroketene or products resulting therefrom, and trichloroacetaldehyde. Careful examination of the gaseous atmosphere in a closed reaction vessel by mass spectrometry failed to reveal any trace of carbon monoxide but did reveal the presence of small amounts (<1%) of ethylene and N,N-diethyltrichloroacetamide. An examination of all distillable components of the reaction mixture by NMR showed only one proton containing product which was readily identified as trichloroacetaldehyde by its chemical shift of τ 1.00 and was confirmed by observation of a band at 1759 cm^{-1} in its IR spectrum. From the intensity of this band the yield of aldehyde in the distillate was estimated to be 25% (±10%). No evidence for dichloroketene or a derivative thereof could be detected spectroscopically.

These findings lead us to propose the most likely mechanism for this reaction as shown in Scheme I.

SCHEME I



The reaction of a nucleophile with an acid halide is generally believed to form an initial addition product similar to the intermediate formed by nucleophilic attack at an ester carbonyl. Specific infrared evidence for the latter intermediate is available in the reaction of ethoxide ion with ethyl trifluoroacetate[5]. By analogy, it would seem reasonable to expect that the intermediate II will be readily formed in step (a). IR

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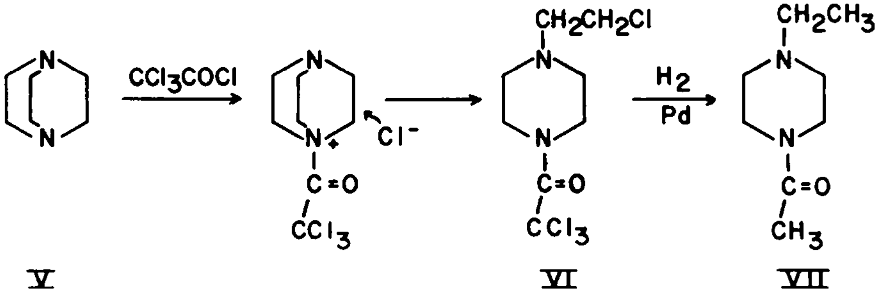
* A formally similar pair of reactants, dichloroacetyl chloride and triethylamine have very recently been reported to yield trichlorovinyl dichloroacetate, via acylation of an enolate anion[3].

evidence for II was sought but no change in the spectrum of trichloroacetyl chloride could be seen on addition of triethylamine. Step (b) of the proposed scheme could be a concerted cyclic process involving abstraction of the proton alpha to nitrogen and a synchronous C—N bond cleavage. Alternatively a two step process involving a nitrogen ylid might be operative. Finally in (c) loss of a proton from III gives the enamine while in IV proton migration to carbon and loss of chloride ion produces chloral.*

This mechanism of oxidation is similar to several which have become accepted for other amine oxidations in the sense that an addition, then an elimination reaction occurs. Such a sequence is proposed for amine oxidation by nitrous acid,[8] bromine[9] and mercuric acetate.[10] The unusual aspect of our proposed mechanism is the necessity to employ carbon as a leaving group. Nevertheless in this case the carbanion bears three electronegative substituents which would provide excellent stability as is found for trichloromethyl carbanion. The formation of trace amounts of ethylene and N,N-diethyltrichloroacetamide can also be accounted for on the basis of the intermediate II. Attack by the oxy anion of II on a β hydrogen in a concerted fashion would give these observed products.

An oxidation which would test the validity of the proposed mechanism was carried out on 1,4-diazabicyclo[2.2.2]octane or DABCO (V). The proposed mechanism predicts this amine to be inert, since the formation of an iminium salt at the bridge head of a bicyclic ring is prohibited by Bredt's rule.[11] When a mixture of DABCO and trichloroacetyl chloride were allowed to stand for one day, it was found that a reaction had occurred. However the reaction was not an oxidation but a degradation, the product (in 5% yield) being N-2-chloroethyl-N′-trichloroacetyl piperazine (VI). The elemental analysis, IR and NMR spectra of VI are all consistent with the assigned structure (see experimental for details of NMR). The mass spectrum showed a parent peak at *m/e* 292 and had M + 2, M + 4, M + 6 and M + 8 peaks in an intensity ratio typical of a tetrachloro compound.[12] Reduction of VI using a palladium catalyst gave a liquid VII whose NMR spectrum showed the presence of a Me and an Et group both of which were absent in VI. From this data we conclude that the chlorines are present in VI as CCl_3 and CH_2-CH_2-Cl functions. On the basis of the NMR indication of eight methylene protons as well as one methyl and one Et group, structure VII can be assigned to the hydrogenation product. A chemical proof by synthesis was not undertaken. The DABCO reaction is summarized in Scheme II.

SCHEME II



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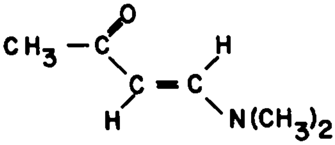
* A referee pointed out that the reaction might involve a direct hydride abstraction as has been observed with $\mathrm{R\overset{+}{C}O}$.[6,7] Such a mechanism seems unlikely for the unactivated trichloroacetyl chloride.

In this scheme, because the oxidation is prohibited by the geometry of the bicyclic amine, a von Braun type[13] of degradation occurs although at a much slower rate than the oxidation of triethylamine.

The possibility that oxidation of a tertiary amine might be a general reaction with trichloroacetyl chloride has not been adequately explored. We did try the reaction on the monocyclic tertiary amine, N-methylpyrrolidine. Examination of the product by NMR indicated that a β-acylenamine had been formed but only in a very small yield (less than 5%). Since this product showed a pronounced instability, optimum conditions were not sought. Other potential uses of this reaction with tertiary amines are being examined.

IR spectral properties of I. A potassium bromide dispersion of I showed strong CO and C—C double bond absorptions at 1663 and 1575 cm^{-1} respectively. The corresponding peaks and proof of their assignments in the IR (C_2Cl_4 solvent) of VIII 4-N,N-dimethylamino-3-buten-2-one[14], are reported to occur at 1673 and 1586 cm^{-1}. In the same paper the occurrence of a third band at 1623 in the spectrum of VIII was shown to be due to the carbonyl absorption of the s-*trans* rotamer. Additional studies on β-acylenamines of fixed geometry confirmed this assignment[15]. We can therefore conclude with confidence that the band at 1663 cm^{-1} in I is due to an s-*cis* CO absorption. The shift to slightly lower wave number for this band in I compared with VIII, in spite of the presence of three alpha chlorines, is probably due to the increased resonance interaction in I (see the following discussion of NMR) and the difference in media.

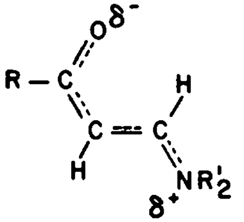


VIII

NMR spectral properties of I. The spectrum of I in $CDCl_3$ contained absorption peaks at τ 2·32 (doublet of spacing 12·5 c/s, area 1), τ 4·54 (doublet of spacing 12·5 c/s, area 1), τ 7·63 (quintet of spacing 6·8 c/s, area 4), τ 8·72 (triplet of spacing 6·8 c/s, area 3), and τ 8·77 (triplet of spacing 6·8 c/s, area 3). The strongly coupled AX pattern for two protons at low field is typical of two vicinal olefinic protons *trans* to one another on a double bond to which a nitrogen is attached.[16] The high field quintet can be interpreted as arising from two nonequivalent methylene quartets which fortuitously overlap. This assignment was corroborated by the observation that the two quartets separated as the temperature was lowered below 0°. The two triplets represent the Me absorption of the two Et groups.

In all, the spectrum of I was examined over a temperature range of −90 to +95°. It had already been reported that rotation about the N—C_4 bond in VIII is strongly hindered, the coalescence temperature for the non-equivalent Me's being about 0° in trichloroethylene.[16] In addition the C_2—C_3 bond was found to have a large barrier to rotation. The coalescence temperature for interconversion of *s-cis* and *s-trans* rotamers was found to be about −50° (the authors failed to report the exact values).

The behaviour of I was notably different in that no barrier to rotation could be detected for the C_2—C_3 bond, presumably because the *s-trans* form of I is too unstable. The barrier to rotation about N—C_4 is appreciably larger in I than in VIII, the coalescence being observed at +40° in I. The difference in barriers cannot be assessed exactly due to the inaccuracy of the reported measurement for VIII and the fact that two quartets are coalescing in I. Nevertheless we have estimated the barrier to be about 2 kcal greater in I.* This increase can be attributed to an increase in resonance energy for IXa over IXb as a result of the electronegative stabilization effect of the three chlorines.



IX a: R = CCl_3, R' = CH_2CH_3
b: R = R' = CH_3

EXPERIMENTAL

All m.ps and b.ps are corrected. The NMR spectra were recorded on a Varian HA-100 NMR spectrometer. The IR spectra were measured using a Beckman IR-8 spectrometer. The mass spectral analyses were performed using an Hitachi–Perkin Elmer RMU-6D spectrometer.

Trichloroacetyl chloride. We have found that the trichloroacetyl chloride prepared by the method of Carre and Libermann[18] is very difficult to separate completely from pyridine. Although Gerrard and Thrush[19] observed no reaction between trichloroacetic acid and thionyl chloride at toom temp, the following procedure was found suitable.

To a flask containing 30 g (0·184 mole) trichloroacetic acid was added 50 g (0·420 mole) $SOCl_2$. The mixture was heated under reflux for 6 days. The excess $SOCl_2$ was distilled off at atm press through a Vigreaux column. The trichloroacetyl chloride then distilled over, b.p. 116–117°. A total of 14·5 g (0·0795 mole) was obtained, yield 43%.

Both the residue and the $SOCl_2$ distillate were used in a second reaction along with fresh $SOCl_2$ and acid. The two batches of trichloroacetyl chloride were combined and distilled once more on a vacuum line.

4-N,N-*Diethylamino*-1,1,1-*trichloro*-3-*buten*-2-*one*(I). To a soln of 1 g (5·5 mmole) trichloroacetyl chloride in 50 ml CH_2Cl_2 was slowly added 2g (19·8 mmole) Et_3N. During the addition the reaction flask was cooled in a water bath at 20°. After standing for 1 hr the contents of the flask were washed twice with 1N HCl. The CH_2Cl_2 soln was then dried over $MgSO_4$, filtered and concentrated under reduced press (16 mm). The residual brown syrup was extracted several times with heptane and the heptane extracts were treated with Norite A. Concentration of the filtrate gave 295 mg (1·2 mmole) of I, m.p. 55·5–57°. The yield based on the stoichiometric requirement of two moles of trichloroacetyl chloride was 44%. (Found: C, 39·24; H, 4·86. $C_8H_{12}NOCl_3$ requires C, 39·29; H, 4·95).

The same reaction has been carried out in $CHCl_3$ and with neat reactants and in each case poorer yields were obtained. When Ac_2O was used as the oxidizing agent a 5% yield of I was isolated. In contrast trifluoroacetic anhydride gave no reaction. The course of the reaction was unaffected by the presence of 0·5 equiv styrene or sulfur. In addition the effect of varying the temp from −70° to + 50° was investigated. Above 50° the reaction mixture rapidly turned black, while below zero, no product was

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* From the relation $k=(\pi\Delta\nu/2)$ at T_C[17], we have calculated the barrier in I to be 16·1 kcal. From an estimate of $T_C=0°$ for VIII, the barrier is calculated to be 13·8 kcal.

formed during an hr period. The best yield occurred at room temp. The product (I) showed an instability to both heat and light. It began to decompose when heated above 90°. It is insoluble in dilute acid or base but soluble in conc HCl. The mass spectrum of I showed a parent peak at *m/e* 243 and M + 2, M + 4 and M + 6 peaks in the intensity ratios typical of a compound containing three Cl atoms.[12]

Synthesis of I *from acetaldehyde.* To a soln of 1·6 g (2·2 mmole) Et_2NH in 50 ml benzene was added 0·8 g (1·8 mmole) acetaldehyde. After the soln had turned cloudy, 2 g (11 mmoles) trichloroacetyl chloride was added while the soln was stirred and cooled in an ice bath. After 5 min the benzene soln was washed with 1N HCl, dried and concentrated under reduced press. The residue was extracted with heptane. The heptane extracts were distilled under a pressure of 0·07 mm to remove all diethyl trichloroacetamide. The residue in the pot, after recrystallization from heptane amounted to 32 mg of a solid, m.p. 55·5°–57° which had IR and NMR spectra which were identical to those of I.

Reaction in the dark under a nitrogen atmosphere. A total of 10 g (0·099 mmole) Et_3N was distilled under a N_2 into a flask fitted with a pressure-equalized dropping funnel and an outlet tube. Then 5 g (0·027 mole) of trichloroacetyl chloride was distilled into the dropping funnel, under N_2 which was maintained throughout the reaction. The acid chloride was then slowly added to the cooled flask which was kept in the dark throughout the reaction. The same work up as employed in the preceding experiment gave a 41% yield of I.

Mass spectrometric analysis of gaseous reaction products. A pressure-equilibrated dropping funnel containing 2·5 g (13·7 mmole) trichloroacetyl chloride was fitted to a 3-necked flask containing 5 g (49·5 mmole) Et_3N. A dry-ice condenser and He inlet were also attached to the flask. The flask was evacuated, then He introduced, and the process was repeated several times. The pressure was finally reduced to 3 mm Hg, then the system was closed to both the evacuation line and the He source. The trichloroacetyl chloride was then added to the Et_3N and after 10 min of reaction time, any gases were condensed in a bulb cooled by liquid N_2. The contents of this bulb were then introduced into a mass spectrometer through its gas inlet system. No CO at *m/e* 28·01 could be detected, but a noticeable peak at *m/e* 28·05 could be seen. In a control experiment using the same apparatus and procedure but using an amount of HCOOH and H_2SO_4 which would produce 7 mmoles CO, a readily observable CO peak (above background) could be seen.

Spectroscopic examination of volatile reaction products. The distillate of all volatile components present at the end of reaction was examined by NMR and IR spectrscopy. The NMR spectrum showed a sharp singlet at τ 1·00. The IR spectrum of a solution of the distillate in dichloromethane showed a band at 1759 cm^{-1}, the same position as exhibited by a soln of authentic chloral. From the intensity of this band it is estimated that a 25% (± 10%) yield of chloral is present in the distillate. (The poor accuracy of this estimate is due to a sluggish response in our spectrometer at this time).

The residue after distillation was dissolved in ether and a portion of this soln analyzed by mass spectrometry. The spectrum revealed the presence of N,N-diethyltrichloroacetamide in the soln, as proven by comparison with the spectrum of an authentic sample of the amide.[20]

Attempted oxidation of 1,4-*diazabicyclo*[2.2.2]*octane*(V). To a soln of 5 g (0·045 mole) of V in 50 ml CH_2Cl_2 was added in two portions 11 g (0·061 mole) trichloroacetyl chloride in 25 ml CH_2Cl_2. The reaction was allowed to stand for 20 hr. The solid which had precipitated was filtered off and the filtrate was evaporated leaving 2·8 g residue. The residue was washed with heptane, the heptane was then decolorized with Norite A and, after filtration, concentrated. From the concentrate 0·8 g of a solid, m.p. 73·5–75·5° was obtained. The NMR of a soln of this material in $CDCl_3$ showed multiplets at τ 6·17 (a 4-proton triplet), τ 6·45 (a 2-proton triplet), τ 7·40 (a 4-proton triplet), and at τ 7·74 (a 2-proton triplet). The mass spectrum showed a parent peak at *m/e* 292 and the isotope cluster typical of a compound containing four chlorines. The IR of this solid showed a strong CO at 1675 cm^{-1}. Based on these data the structure VI was assigned. (found: C, 32·79; H, 4·20. $C_8H_{12}N_2OCl_4$ requires: C, 32·68; H, 4·12).

Reduction of VI. A soln of 300 mg (1·02 mmole) of VI in 50 ml MeOH containing 1 g KOH pellets and 1 g 10% Pd-C in a pressure bottle was shaken on a Parr hydrogenation apparatus at 42 psi for 3 hr. After filtration of the soln the filtrate was diluted to 150 ml with water and extracted several times with $CHCl_3$. The extracts were dried over $MgSO_4$, filtered, and concentrated on a rotary evaporator. The liquid residue, 146 mg was tentatively identified as N-acetyl-N′-ethylpiperazine. The mass spectrum of the product showed a parent peak at *m/e* 156. The IR spectrum showed a strong band at 1650 cm^{-1} and the NMR spectrum consisted of a triplet at τ 9·00 ($J = 6·75$ c/s, 3 protons), a singlet at τ 8·01 (3 protons), a complex multiplet at τ 7·66 (6 protons) and two triplets at τ 6·60 and 6·44 both having $J = 5·0$ c/s and representing two protons each. A satisfactory analysis of this product, which discolored on standing could not be obtained.

Attempted oxidation of N-*methylpyrrolidine*. A soln of 2 g (25 mmole) of N-methylpyrrolidine in 25 ml CH_2Cl_2 was slowly added to 1 g (5·5 mmole) trichloroacetyl chloride in 10 ml CH_2Cl_2. After 10 min, the reaction mixture was worked up as described previously and gave 98 mg of a syrup. The NMR of this material showed the presence of a compound possessing an unsplit vinyl proton at 2·29. Attempts at purification of the product were thwarted by its instability.

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