1. A study of fluorinated acids and aldehydes. 2. The chlorofluorination of pyridine

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1. A STUDY OF FLUORINATED ACIDS AND ALDEHYDES.

2. THE CHLOROFLUORINATION OF PYRIDINE.

I wish to express my indebtedness to Dr. W.K.R. Musgrave under whose supervision this work was carried out and also to the Department of Scientific and Industrial Research and the Northumberland Education Committee for maintainance grants during the period of research.

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The Arndt-Eistert Synthesis.

Application of the Arndt-Eistert Synthesis to trifluoro and trichloracetic acids gave rise to the corresponding halogenated propionic acids or their derivatives (ethyl esters, amides and anilides), thus demonstrating the possibility of using the synthesis for the ascent of a homologous series of halogenated carboxylic acids. Though the yields of the halogenated diazoketones compared favourably with those obtained from normal carboxylic acids, the percentage conversion of these diazoketones to the halogenated propionic acids or their derivatives was, in most cases, quite low so the over-all yields from the syntheses were not as great as those normally obtainable from an unsubstituted aliphatic carboxylic acid series. The yields from trichloroacetic acid were higher than those from trifluoroacetic acid but the stabilities of the fluorinated products were greater than those of the chlorinated analogues.

The Rosenmund Reaction.

Since no successful applications of the Rosenmund Reduction to fluorinated aliphatic acid chlorides has previously been reported, this reduction was applied, in the

vapour phase, to trifluoroacetyl chloride in an endeavour to produce trifluoroacetaldehyde. The product consisted of a mixture of the aldehyde, a solid polymer of the aldehyde and fluoral hydrate and thus indicated the possibility of using this method for the preparation of fluorinated aliphatic aldehydes.

Halogenation of Pyridine.

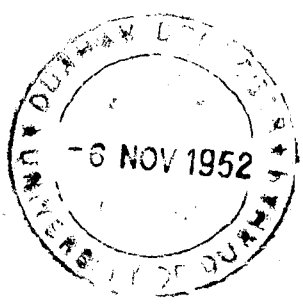
The reaction between chlorine trifluoride and pyridine in carbon tetrachloride solution with cobaltous fluoride as catalyst in the presence of anhydrous potassium fluoride, led to the formation of 2-fluoropyridine, chlorofluoro addition compounds of pyridine and organic tar. There was no experimental evidence for any break down of the pyridine ring system; more evidence is required to prove conclusively whether or not there was any reaction between the chlorine trifluoride and the solvent.

Analytical.

A volumetric procedure was devised whereby the fluorine, chlorine and nitrogen content of organic compounds could be accurately determined. The compounds were fused with sodium and the resultant fusion solutions titrated for fluoride, chloride and cyanide. Fluorine was

estimated by titration with thorium nitrate and the cyanide determined by application of Liebig's Method in ammoniacal solution. Removal of the cyanide by addition of formaldehyde and then the addition of excess silver nitrate allowed the chloride to be estimated by a back-titration procedure.

An Investigation of the Lower Members of the Series of Halogenated Aliphatic Carboxylic Acids.



Introduction.

At the time when this investigation was first undertaken very few fluorinated aliphatic carboxylic acids had been prepared and it was therefore considered worth while to synthesis a few members of the series $CF_3(CH_2)_nCOOH$ so as to compare their various properties. In conjunction with this work a parallel set of investigations were also to be carried out using the acid series $CCl_3(CH_2)_nCOOH$ so that comparisons could be drawn with the fluorinated analogues.

Aliphatic fluorinated carboxylic acids containing the trifluoromethyl group ($-CF_3$) were chosen for investigation since the stability of the $-CF_3$ group is more marked than that of the $>CF_2$ and $\rightarrow CF$ groups, this being shown by the fact that the oxidation of an organic compound containing the $-CF_3$ group, if the stabalising effect of the group on the rest of the molecule can be overcome, is an excellent procedure for the preparation of trifluoroacetic acid (Swarts, Bull. Acad. roy. Belg., 8, 343, 1922; Henne et. al. J.A.C.S., 918, 1945). In addition it has also been observed that the $-CF_3$ group is more stable in aliphatic compounds than aromatic compounds, for example the $-CF_3$ group in benzotrifluoride can be hydrolysed by concentrated hydrobromic acid. (Swarts, Bull. Acad. roy. Belg., 6, 389,

1920). A final illustration of the great stability of the $-CF_3$ group lies in the properties of fluoroform (CHF_3), which shows no change when heated to 1,150°C with potassium iodide. Oxidising agents have little effect on it eg., nitric acid either alone or with concentrated sulphuric acid, and oxides of nitrogen or silver nitrate, have no action in 15 days at 150°C. (Sidgwick, Chemical Elements and their Compounds, Vol. II, p. 1126).

Taking these observations into consideration it appeared therefore that the $-CF_3$ group would be sufficiently stable to resist attack by reagents used to prepare the fluorinated acids and later to examine their properties by the preparation of suitable derivatives. It was expected however that the fluorinated acids would be more stable than their chlorinated analogues for in acids of the type CH_3CCl_2COOH the chlorine is rather labile and the same effect may occur in acids of the $CCl_3(CH_2)_nCOOH$ series.

If these halogenated acids could be prepared in sufficient quantities it was then hoped to convert them to suitable acid derivatives, from whence the corresponding series of halogenated aldehydes could be obtained by one or other of the standard preparative procedures.

The first member (trifluoro and trichloroacetic acid) of each of the homologous series of halogenated carboxylic acids can be readily obtained in the pure state and so they were used as the starting materials, in an attempt to ascend the halogenated acid series. There are four possible methods available for the ascent of series and each is outlined below:-

(1) $RCOOH \longrightarrow RCOCl \longrightarrow RCHO \longrightarrow RCH_2OH \longrightarrow RCH_2Br \longrightarrow RCH_2CN \longrightarrow RCH_2COOH.$

(2) $RCOOH \longrightarrow RCOCl \longrightarrow RCH_2OH \longrightarrow RCH_2Br \longrightarrow RCH_2CN \longrightarrow RCH_2COOH.$

(3) $RCOOH \longrightarrow RCOCl \longrightarrow RCOCN \longrightarrow RCOCOOH \longrightarrow RCH_2COOH.$

(4) $RCOOH \longrightarrow RCOCl \longrightarrow RCOCHN_2 \longrightarrow RCH_2COOH.$

The method illustrated by the last sequence of reactions (4) is known as the Arndt-Eistert Synthesis and a survey of the literature by Backmann & Struve (Organic Reactions, Vol. I., p. 38) showed that, though it had been applied to a wide range of aliphatic, aromatic and heterocyclic carboxylic acids, it had not been applied to any perhalogenated aliphatic carboxylic acids. The yields, normally 50% - 80% of those theoretically possible, are higher than those obtainable by the other methods. In

addition, since there are fewer stages, the working time is less and thus the method is most attractive especially when only small amounts of material are available. Each of the other methods involves reduction at one stage or another while the Arndt-Eistert Synthesis does not, so there would be no interference with the halogenated groups (especially the $-CCl_3$ group) on this account and furthermore while methods (1), (2) and (3) lead only to the next higher homologous acid the Arndt-Eistert Synthesis can be adapted to yield not only the homologous acid but several of its derivatives (ester, amide or anilide). Finally the practibility of using this method for the ascent of an acid series has been demonstrated by previous workers for in several cases two methylene groups have been added to the chain of an acid by carrying out two successive syntheses (Plentl and Bogert, J. Org. Chem., 6, 669, 1941 and Backmann et al., J.A.C.S., 62, 2250, 1940; ibid., 62, 2750, 1940).

The evidence thus tends to show that the Arndt-Eistert Synthesis would be the most advantageous method to apply to trifluoro and trichloroacetic acids in an attempt to build up the series of halogenated aliphatic carboxylic acids.

The Mechanism of the Arndt-Eistert Synthesis.

This synthesis, as previously indicated, is a three-step process which, when applied to an organic carboxylic acid, results in the formation of the next higher homologue or a derivative of the homologous acid (ester, amide or anilide).

Stage I.

The acid is converted to the acid chloride by any one of the standard methods:-

$$RCOOH \longrightarrow RCOCl.$$

Stage II.

The acid chloride is converted into a diazoketone by treatment with an excess of diazomethane and the over-all reaction mechanism can be represented as below:-

$$RCOCl + 2CH_2N_2 \longrightarrow RCOCHN_2 + CH_3Cl + N_2$$

Investigations of the interaction of diazomethane with acid chlorides were carried out by Arndt et al., (B., 60, 1364, 1927; ibid., 61, 1122 and 1949, 1928), and also by Robinson and Bradley (J.C.S., 1310, 1928), who showed that the slow addition of an acid chloride to a cold solution of an excess of diazomethane yielded the diazoketone in

high yield. On the other hand Nierenstein et al., (J.C.S., 107, 1491, 1915; J.A.C.S., 47, 1728, 1925; ibid., 52, 1504, 1930) showed that the addition of diazomethane to an excess of an acid chloride resulted in the formation of an ω-chloromethyl-ketone ($RCOCH_2Cl$) and not the diazoketone. Arndt and co-workers and Bradley and Schwarzenback (J.C.S., 2904, 1928) postulated a series of reactions which would explain these differing results in the following manner:-

(1) $RCOCl + CH_2N_2 \longrightarrow RCOCHN_2 + HCl$

(2) $CH_2N_2 + HCl \longrightarrow CH_3Cl + N_2$

(3) $RCOCHN_2 + HCl \longrightarrow RCOCH_2Cl + N_2$

Provided there is a sufficient excess of diazomethane present then all the hydrogen chloride formed in reaction (1) will be destroyed in reaction (2) thus the primary product will be a diazoketone, if however there is insufficient diazomethane present to react with all the hydrogen chloride formed then the excess hydrogen chloride will react with the diazoketone to form the ω-chloromethyl-ketone (3). The results of Nierenstein and his co-workers can then be explained by reaction (3) since in their experiments there was an excess of acid chloride

present, which would result in the formation of excess hydrogen chloride and hence the formation of the ω-chloromethylketone.

Groups capable of reacting with diazomethane such as the phenolic, aldehydic, active methylene and α and β unsaturated carbonyl groups, might interfere with the production of a diazoketone but only a few acid chlorides containing these groups have been studied eg., a high yield of diazoketone was obtained from 4-fluorenone-carboxylic acid chloride although fluorenone itself reacts with diazomethane (Backmann and Skeehan, J.A.C.S., 62, 2687, 1940), while 2-hydroxy-3-naphthoyl chloride yielded the diazoketone without methylation of the hydroxyl group (Krzikalla and Eistert, J. prakt. Chem., 143, 50, 1935). It is not however certain that the acid chloride group, in compounds containing other active groups, will react preferentially with diazomethane but it was hoped, in the case of the halogenated acids, that the known stability of the $-CF_3$ group would be sufficient to withstand attack by diazomethane and that the $-CCl_3$ group would also prove resistant to attack by this reagent.

Stage III.

In this last stage of the synthesis the diazoketone

is rearranged, with the loss of nitrogen, in the presence of suitable reagents and a catalyst (usually colloidal silver). In the presence of water, an alcohol, ammonia or an amine the diazoketone rearranges to form an acid, an ester, an amide or an anilide respecfively:-

$$RCOCHN_2 + H_2O \longrightarrow RCH_2COOH + N_2$$

$$RCOCHN_2 + R'OH \longrightarrow RCH_2COOR' + N_2$$

$$RCOCHN_2 + NH_3 \longrightarrow RCH_2CONH_2 + N_2$$

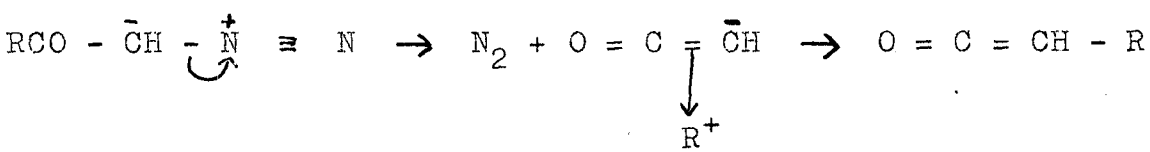
$$RCOCHN_2 + R'NH_2 \longrightarrow RCH_2CONHR' + N_2$$

The conversion of a diazoketone to form the derivatives of an acid was discovered by Wolff (Ann., 394, 25, 1912) and this stage of the synthesis is known as the Wolff Rearrangement but, since he prepared the diazoketones by a complex series of reactions, the rearrangement had no aynthetic value until the diazoketones were found to be readily obtainable from acid chlorides and diazomethane by the investigations of later workers (Arndt et al., and Robinson and Bradley).

After their investigations into the formation of diazoketones Arndt and Eistert correlated their results with the investigations of Wolff and showed that the three-step process constituted a new method for lengthening a carbon chain by one methylene group. They then carried out

the procedure on a variety of organic carboxylic acids (B., 68, 200, 1935) thus proving it to be capable of general application in the conversion of organic carboxylic acids to their next higher homologues and it was through this work that the process became associated with their names, thus becoming known as the Arndt-Eistert Synthesis or Arndt-Eistert Homologation Process.

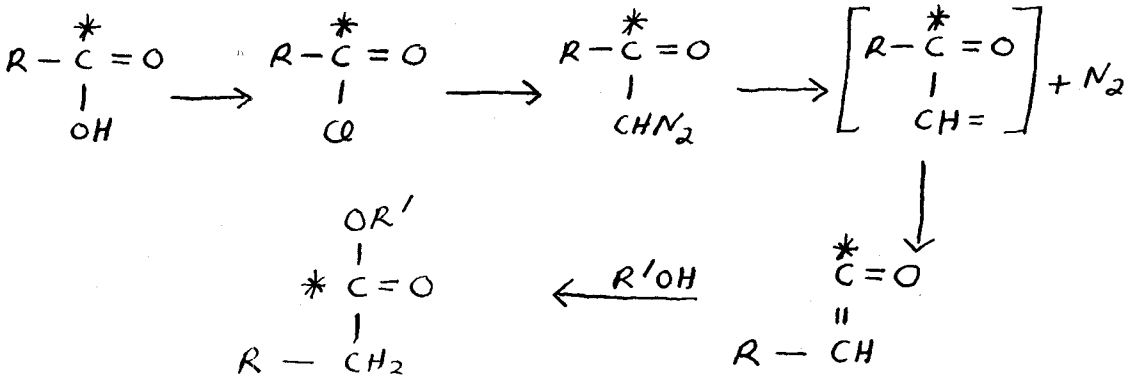
The rearrangement of a diazoketone resembles formally the rearrangement of acyl azides and very probably takes place by a similar mechanism (Dewar, Electronic Theory of Organic Chemistry, p. 222) the nitrogen being eliminated and a short lived radical produced, which rearranges to form the corresponding ketene (Waters, Physical Aspects of Organic Chem., p. 418).



The ketene then reacts with water, an alcohol, ammonia or an amine to form the desired reaction product. A similar type of reaction mechanism was postulated by Eistert (B., 68, 208, 1935) which can be represented as follows:-

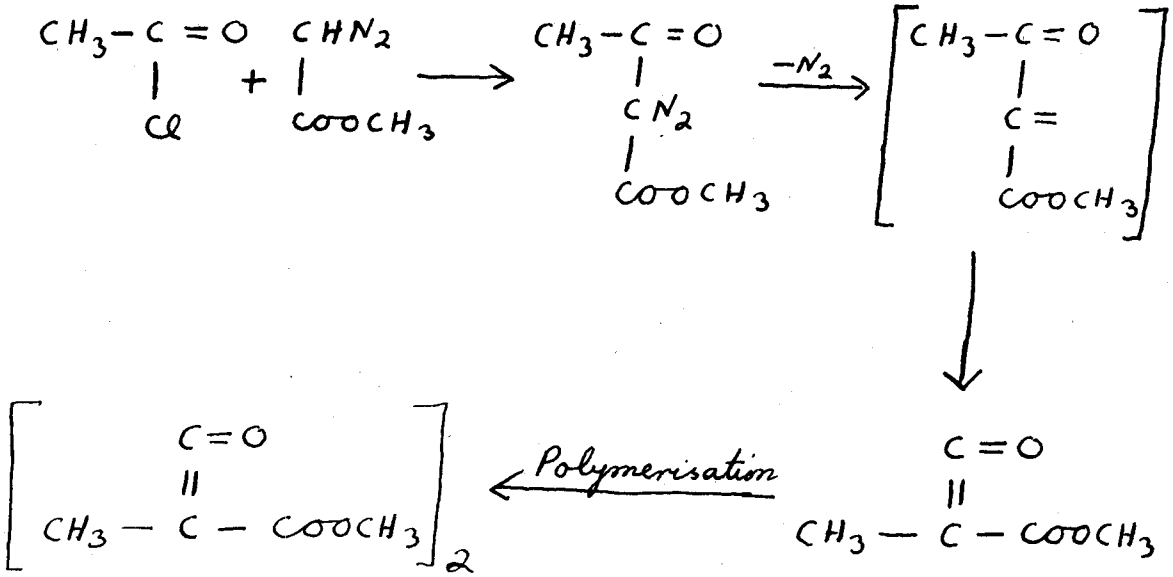
$$RCOCHN_2 \longrightarrow N_2 + [RCOCH=] \longrightarrow RCH = C = O$$

while Hugget et al., (J.A.C.S., 64, 3043, 1942) showed that this type of reaction involving ketene formation would readily explain the type of products formed under the varying experimental conditions. From the equation:-



the carbonyl carbon atom of the starting acid becomes the carbonyl carbon atom in the final product i.e. the newly introduced carbon atom occupies the alpha position. Hugget and co-workers proved this to be the case by using heavy C^{13} for the carbonyl carbon atom in benzoic acid and then converting the benzoic acid to phenylacetic acid by application of the Arndt-Eistert synthesis. The heavy isotope was then detected in the carbonyl group of the phenylacetic acid and this was confirmed by decarboxylation. Additional evidence for this type of reaction was provided by the isolation of a few intermediate ketenes (Schroeter,

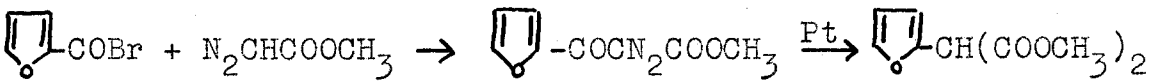
B., 49, 2704, 1916), though normally they are converted into acid derivatives by the water, alcohol etc., present in the reaction mixtures. Here the diazoketones were formed by the interaction of an acid chloride with the diazoacetic ester eg.:-



The metal catalyst used in the Wolff Rearrangement is considered to accelerate the conversion of the diazoketone for if the catalyst is absent no rearrangement occurs and the product is a derivative of the ketone eg., if diazoacetophenone is heated with water at 70°C - 80°C benzoyl carbinol is formed:-

$$C_6H_5COCHN_2 + H_2O \longrightarrow C_6H_5COCH_2OH + N_2$$

while the presence of silver catalyst causes rearrangement to phenylacetic acid (Wolff, Ann., 394, 25, 1912; Arndt and Amende B., 61, 1122, 1928). Wolff also found that powdered silver did not catalyse the decomposition of diazoacetone in the presence of ammonia but that a rapid reaction occurred if silver oxide or silver nitrate was added, thus tending to show that the catalyst must be colloidally dispersed. Arndt and Eistert (B., 68, 200, 1935) found that even with very pure diazoketones a small amount of reduction of the silver salts took place, which would account for the production of the desired catalyst. On a few occasions powdered copper of platinum have been used as catalysts but silver oxide is almost universally employed. An example of the use of a platinum catalyst is the conversion of the diazoketone prepared from α-furoyl bromide and methyl diazoacetate to dimethyl-α-furylmalonate;-



as carried out by Reichstein and Morsman (Helv., 17, 1119, 1934).

The Wolff-Rearrangement of α-diazoketones using

methanol and silver oxide has been reported by Newman and Beal (J.A.C.S., 72, 5163, 1950) as erratic and capable of giving large variations in yield. They developed a new procedure in which the catalyst was a solution of silver benzoate in triethylamine and when a few mls. of this was added to a solution of an α-diazoketone in methanol at room temperature, nitrogen was evolved and silver precipitated. The methyl esters on separation were said to give duplicatable yields in reasonable quantity (methyl phenyl acetate 82%, methyl p-methoxyphenylacetate 84%, methyl hydrocinnamate 70%). If the diazoketones react sluggishly at room temperature they recommend replacing the methanol by t-butyl alcohol and heating eg., obtained t-butyl-p-nitro phenylacetate in 57% yield. However since this procedure only applies to the formation of methyl and t-butyl esters it was decided in the present work to use the silver oxide method since its use, together with the appropriate reagents, gives a wider choice of derivatives for the final product. Furthermore a survey of the literature (Backmann and Struve, Organic Reactions, 1, p. 55 - 62), showed that the use of silver oxide to rearrange diazoketones in an alcoholic solution gives rise to the appropriate esters in yields equally as good as those claimed

by Newman and Beal, who used the new technique on a limited number of diazoketones, none of which had been obtained from the acid chlorides of short chain aliphatic carboxylic acids.

General Experimental Procedures.

The following general procedures used for the preparation of diazoketones and their subsequent rearrangement to acids or acid derivatives, have been suggested (Idem. ibid.) as a result of investigations by previous workers in this field and it was by the application of these techniques that it was hoped to prepare the higher halogenated aliphatic carboxylic acids.

Since the acid chlorides must be added to an excess of diazomethane in order to cut the formation of ω-chloromethylketones to a minimum, an ethereal solution of the acid chloride (1 mole.) is usually added, with stirring, to a cold ethereal solution of diazomethane (3 moles.). The evolution of nitrogen occurs during the addition and in the case of most aliphatic acid chlorides the reaction appears complete immediately after the addition but it is usual to allow the mixture to stand for an hour or two. With aromatic and less reactive acid chlorides the mixture is allowed to stand for several hours

(10 - 24). The diazoketones, isolated by evaporation of the ether, are satisfactory for rearrangement without further purification and most are quite stable under normal conditions, though a small minority tend to decompose on standing.

The addition of silver oxide to a hot solution of a diazoketone dissolved in an anhydrous alcohol yields the ester of the homologous acid but there is an appreciable variation in the rates at which different diazoketones rearrange to form esters and times varying from one hour to twenty-four hours may be required to complete the conversion. The completion of the reaction can however be detected by treatment of a sample of the solution with concentrated hydrochloric acid, when the evolution of nitrogen indicates the presence of unchanged diazoketone (Eistert, B., 69, 1074, 1936).

Anilides can be prepared by the gradual addition of a diazoketone to boiling aniline or by heating a solution of the diazoketone and aniline in ethyl alcohol or dioxane containing a small quantity of aqueous silver nitrate.

To prepare an acid amide a 10% - 20% aqueous

solution of ammonia containing a little silver nitrate is added to the warm solution of a diazoketone in dioxane; or anhydrous gaseous ammonia can be passed into a cold solution of the diazoketone in ethyl alcohol containing a small amount of silver oxide.

Finally the conversion of a diazoketone to the homologous acid can be carried out by slowly adding a dioxane solution of a diazoketone to a warm solution of silver nitrate and sodium thiosulphate or to a suspension of silver oxide in dilute thiosulphate solution. However a review of average yields obtainable by the Arndt-Eistert Synthesis shows that the homologous acid is often formed from the diazoketone in a lower yield than the corresponding ester, amide or anilide and consequently, if the acid is required, it would often seem to be advantageous to prepare one of these derivatives and then to hydrolyse it to the desired acid.

In order to become familiar with the experimental techniques involved in carrying out the synthesis several standard preparations were undertaken involving the use of both aliphatic and aromatic carboxylic acids before the synthesis was actually applied to the halogenated aliphatic carboxylic acids. The experiments carried out involved

(a) the conversion of benzoyl chloride to phenylacetamide (Arndt and Eistert, B., 68, 200, 1935) and to ethyl phenylacetate (Application of general procedure), (b) acetyl chloride to propionamide and ethyl propionate (Arndt, Eistert and Amende, B., 61, 1949, 1928), (c) α-naphthoyl chloride to ethyl-α-naphthoylacetate (Arndt and Eistert, B., 200, 1935) and finally (d) the bishomologation of adipyl chloride to suberic acid diamide (Walker, J.C.S., 1304, 1940). The results obtained are tabulated below:-

Table I.

Starting Material	Yield of Diazoketone %	Final Product	% Overall yield from acid chloride
Benzoyl chloride	90.0	Phenyl acetamide	20.0
Benzoyl chloride	82.3	Ethyl phenylacetate	57.6
Acetyl chloride	68.5	Propionamide	33.6
Acetyl chloride	68.0	Ethyl propionate	37.0
Naphthoyl chloride	93.1	Ethyl-α-naphthoyl acetate	59.0
Adipyl chloride	63.5	Suberic acid diamide	61.8

The results agreed substantially with those quoted in the literature and tended to show that, though in all cases the yields of diazoketones were moderately high, the best were obtained from aromatic acid chlorides. In addition the diazoketones from the low membered aliphatic acid chlorides were liquids while those from the aromatic series were solids. The over-all yields from the acid chlorides to the homologous acid derivatives varied considerably and it seemed that the final percentage yield depended on the type of derivative formed. Since the choice of derivative to give the best yield depends on the particular diazoketone under consideration it can only be determined experimentally as no set rules are followed.

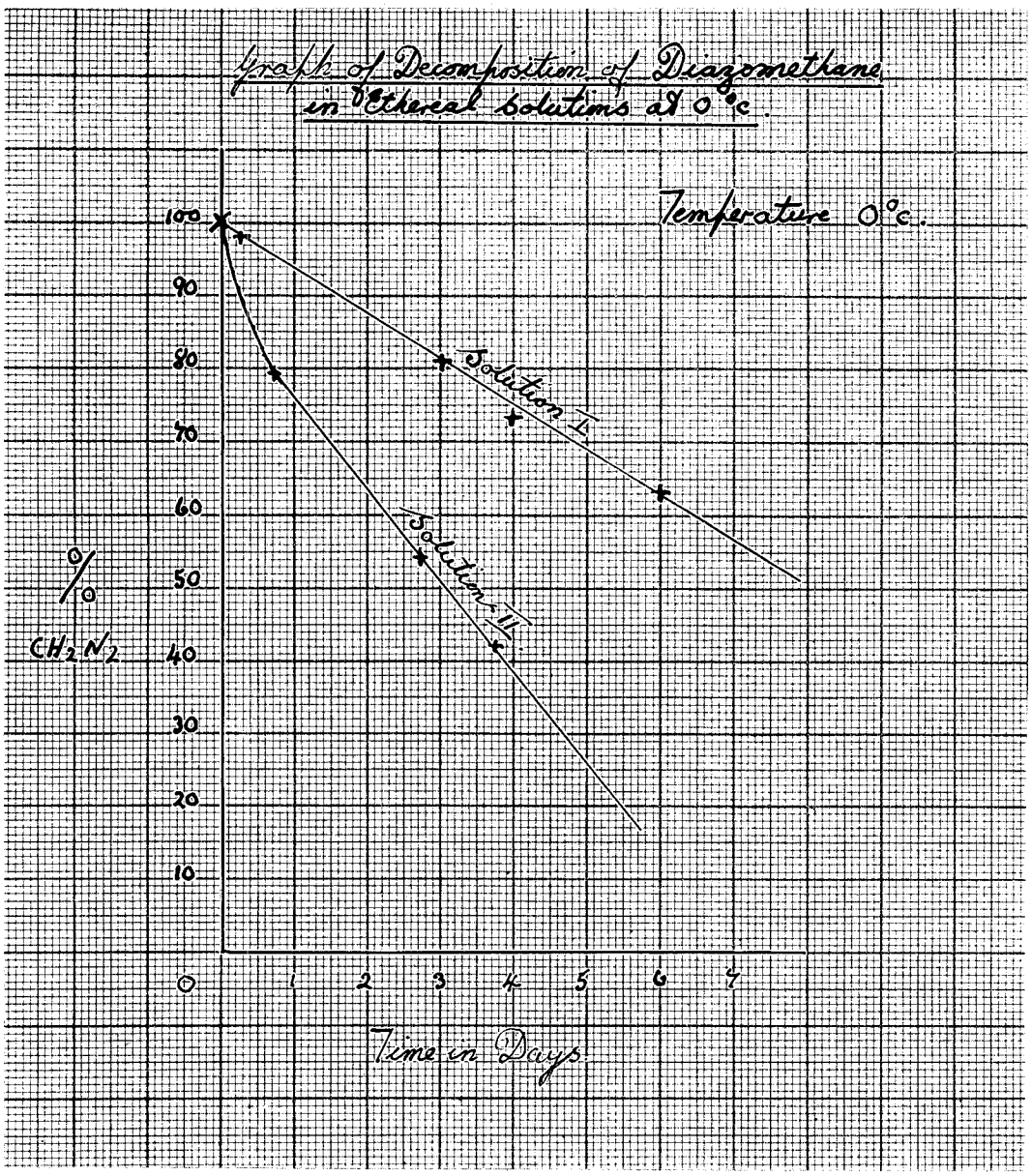
With the previously discussed theoretical and practical techniques borne in mind the synthesis was then applied to the halogenated aliphatic carboxylic acids.

Application of the Arndt-Eistert Synthesis to Halogenated Aliphatic Carboxylic acids.

Commercially pure trichloroacetic acid was converted to the acid chloride by heating the acid with phosphorus trichloride in a Carius Tube. This method was found to give a better yield of pure trichloroacetyl chloride than

the procedure of Delacre (C.Z., 1, 1197, 1902), who refluxed these reactants together on a water bath for two days. Trifluoroacetic acid was prepared either by the permanganate oxidation of trifluorotrichloropropene (Henne et al., J.A.C.S., 918, 1945) or by the dichromate oxidation of m-aminobenzotrifluoride (Swarts, Bull. Acad. roy. Belg., (5), 8, 343, 1922), and was then converted to trifluoroacetyl chloride by the method of Henne and co-workers (J.A.C.S., 70, 1968, 1948) involving treatment with benzoyl chloride. Both the trifluoro and trichloroacetyl chlorides were purified by distillation before being reacted with diazomethane and were kept as dry as possible since any hydrolysis produces the free acids, which would react with the diazomethane and be converted to the methyl esters, thus reducing the yield of any diazoketones formed as well as contaminating the products. For the same reason the apparatus employed for the synthesis must be kept dry. In addition the presence of moisture would destroy some of the diazomethane and if its concentration in solution was lowered below a critical value the addition of acid chloride would result in the production of ω-chloromethylketones as a further side reaction.

The diazomethane was prepared from acetamide via α-nitrosomethylurea (Amstutz and Meyers, Organic Synthesis Vol. II and Arndt, Organic Synthesis, 15, 4, 1935). The advantages of applying this method are that the diazomethane is obtained in an ethereal solution at 0°C and can be used as such without further need of purification. Also ethereal solutions of diazomethane are relatively safe to handle at temperatures approaching 0°C, while diazomethane itself is explosive in the gaseous state. The concentration of the diazomethane in these ethereal solutions was estimated by titration with benzoic acid (Marshall and Acree, B., 2323, 1910) but care must be taken since diazomethane is extremely toxic and repeated exposure, even to low concentrations, causes increased sensitivity to it (Sunderman et al., Am. J. Medical Sci., 195, 469, 1938). A series of titrations carried out on sample solutions over a period of days showed that the solutions were best used as soon as they were prepared since the concentration of diazomethane fell sharply as time progressed (see graph), though this drop in concentration could be lessened by standing the solution over potassium hydroxide pellets to remove any traces of water with which the diazomethane gradually reacts.



Methods employed to convert trifluoro and trichloro-acetyl chlorides to their respective diazoketones were based on that of Arndt and Amende (B., 61, 1122, 1926) for the preparation of diazoacetone from acetyl chloride. In

each case the acid chloride was observed to react immediately and vigorously with cold ethereal solutionsof diazomethane but, though in the case of trifluoroacetyl chloride the reaction appeared complete as soon as the addition ended, the reaction with trichloroacetyl chloride continued for an appreciable time afterwards. The solutions were allowed to stand overnight and the excess ether then removed under suction at room temperature. Vacuum distillation of the residues gave good yields of trichlorodiazoacetone (88%) but poor yields of trifluorodiazoacetone (20%). Since, however, the trifluorodiazoacetone has a low boiling point it seemed possible that it was being lost during removal of the ether under suction. Further experiments were therefore undertaken in which the excess ether was removed by distillation under normal pressure at 35°C through a column packed with Fenske helices. Vacuum distillation of the residue then gave much higher yields of trifluorodiazoacetone (62.5%) thus substantiating the previous conclusions. The yield of trifluorodiazoacetone was also found to depend on the rate at which the trifluoroacetyl chloride was distilled into the ethereal diazomethane solution and best results were obtained when the rate of distillation did not exceed 11 gm.

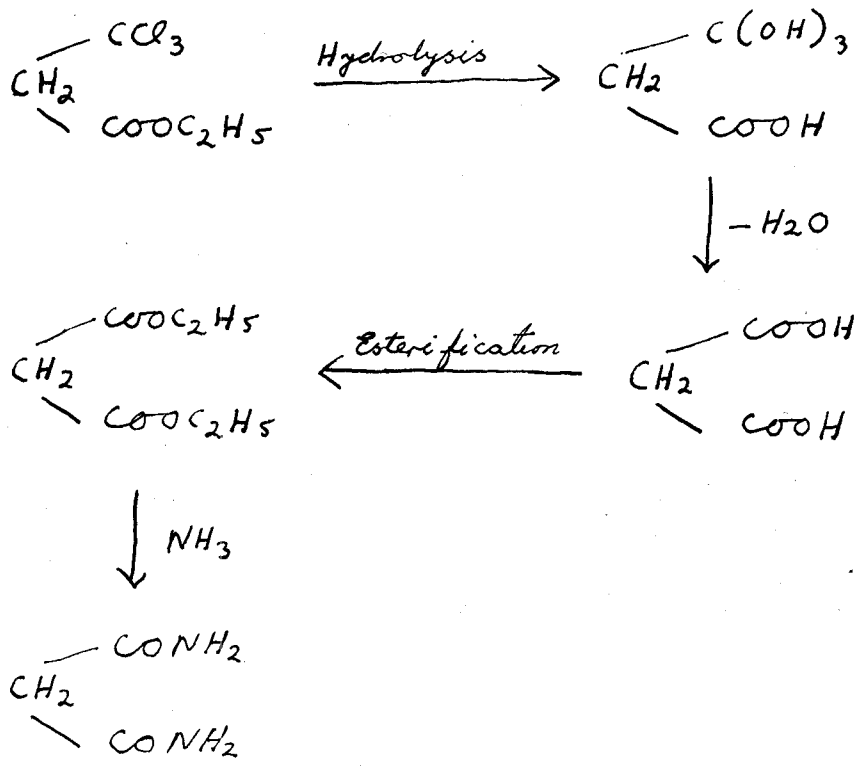
of acid chloride per hour. Both diazoketones appear to be quite stable at room temperature and could be distilled under reduced pressure without appreciable decomposition, but distillation at normal pressures was not attempted since it is known that diazoacetone itself explodes under these conditions (Wolff, Ann., 394, 25, 1912). The residue left behind after the distillation of trifluorodiazoacetone yielded two higher boiling fractions analyses of which showed the presence in each of fluorine, chlorine and nitrogen but no characterisation was possible, thus no light could be shed on the exact types of side reaction taking place simultaneously with the production of the diazoketones.

Having successfully prepared the required diazoketones the next step in the investigations was the application of the Wolff Rearrangement to these compounds in an attempt to prepare the trihalogenated propionic acids or their derivatives (esters, amides or anilides) in reasonable yields. Since however in many cases the esters or amides can be obtained in higher yields than the corresponding free acids (Backmann and Struve, Organic Reactions, 1, 49) it was decided first of all to attempt the conversion of trifluoro and trichlorodiazoacetone to the ethyl esters of

trifluoro and trichloropropoinic acids respectively.

The method employed in each case was to treat a hot solution of the diazoketone in absolute alcohol with an alcoholic slurry of dry silver oxide and then to reflux the mixture for several hours before distilling off the excess alcohol and fractionating the residue. The addition of silver oxide was carried out over a period since the observations of Arndt and Eistert (B., 69, 1805, 1936) showed that best results are obtained by this gradual addition rather than by adding the slurry in bulk. Vacuum distillation of the residues, after removal of the excess alcohol, yielded the desired esters. It was observed, as in the case of the formation of the diazoketones, that though both the initial halogenated diazoketones underwent the same type of reaction the yield of the chloro ester was substantially higher than that of the fluorinated analogue (ethyl trifluoropropinate 40.5% and ethyltrichloropropionate 73.7%). Though analyses of the compounds confirmed them as being the desired esters it was decided, in addition, to carry out equivalent weight determinations for further identification. The determinations, carried out by alkaline hydrolyses, worked normally on ethyl tri-

fluoropropionate as would be expected since the esters of fluorocarbon acids are readily hydrolysed while the fluorine atoms are stable to hydrolyses and can withstand refluxing with dilute aqueous base for long periods without formation of fluoride ions (Simons, Fluorine Chemistry, 1, 48), but with ethyl trichloropropionate a result approximating to one quarter of the calculated value was obtained. Tests carried out on the hydrolysis mixture revealed the presence of large quantities of free chloride ion and so it seemed that four equivalents of alkali had reacted with one equivalent of the ester, thus causing hydrolyses of both the ester and the trichloromethyl groups, with the subsequent production of free chloride ion in the hydrolysis mixture. This was confirmed by further experiments in which small quantities of malonic ester were isolated from the products of hydrolysis. Here the reaction scheme was that on treatment with aqueous alkali the hydrolysed trichloromethyl group would spontaneously lose the elements of water to give malonic acid which would subsequently be esterified and the resulting ester converted to the readily characterised malonamide.



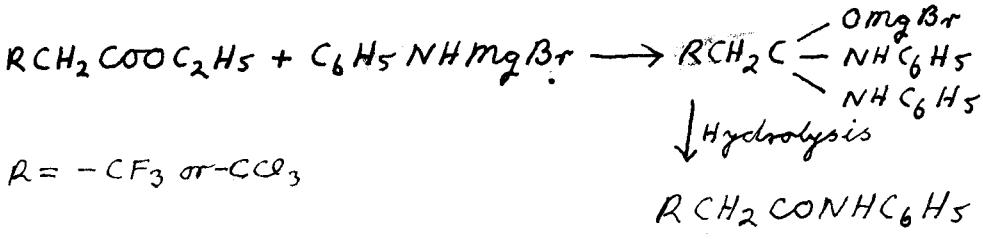
Equivalent weight determinations carried out by acid hydrolyses yielded the theoretical result.

Rearrangement of the respective diazoketones in cold absolute alcohol with dry gaseous ammonia and silver oxide gave rise to the formation of trichloro and trifluoro-propionamide in small yields. Both compounds were found to sublime quite readily and were purified by this means. An accurate analyses could not however be carried out on the trifluoropropionamide since it was deliquescent so it was hydrolysed to ammonium trifluoropropionate, which was

quite stable and gave the correct analyses figures after purification by sublimation. Since treatment of an ester with liquid ammonia often gives the corresponding amide (Fernelius and Bowmann, Chem. Rev., 26, 23, 1940) attempts were made to prepare the halogenated amides from ethyl trichloro and ethyl trifluoropropionates. Under these conditions ethyl trifluoropropionate gave rise to the corresponding ammonium salt but it was subsequently discovered that the liquid ammonia used was damp and so the amide formed in the reaction must have been hydrolysed to the ammonium salt. Thus the effect runs parallel with the observations of Gilman and Jones (J.A.C.S., 65, 1458, 1943), who found that during the preparation of trifluoroacetamide the presence of moisture readily caused hydrolyses resulting in the formation of ammonium trifluoroacetate. Similar experiments carried out with ethyl trichloro-propionate gave some ammonium chloride but no amide. Here, as in the case of the equivalent weight determinations carried out by alkali hydrolyses, the reagent used in an attempt to replace the ester grouping appeared to attack the trichloromethyl group with the subsequent production of chloride ion and thence ammonium chloride. A similar effect was observed if the ester was treated with

concentrated aqueous ammonia for a brown syrup gradually formed which could not be recrystallised, while tests carried out on the reaction solution again showed the presence of appreciable quantities of free chloride ion.

To return to the Wolff Rearrangement of trifluoro-diazoacetone it was found possible to convert the diazoketone to the anilide of trifluoropropionic acid by heating it in dioxane solution with aniline and silver nitrate; a procedure based on that used by Arndt and Eistert (B., 68, 200, 1935) for the preparation of anthraquinone-2-acetanilide. The yield in this conversion was low (9%) but the crystalline product isolated analysed correctly, while the melting point of the pure compound agreed with that obtained by Henne and co-workers (J.A.C.S., 72, 3370, 1950), who prepared it directly from the trifluoropropionic acid. Further attempts to prepare the anilides of trifluoro and trichloropropionic acids by application of the Grignard Reaction to ethyl trifluoro- and ethyl trichloropropionate in the following manner:-



were unsuccessful although application of this procedure to ethyl trichloroacetate resulted in the formation of trichloroacetanilide in moderate yields. The use of higher molecular weight amines in the formation of the Grignard Reagent, with which the esters were treated, did not lead to any improvement in the method.

Finally, for the conversion of diazoketones to the homologous free acids, Walker (J.C.S., 1304, 1940) found that treatment of a hot suspension of silver oxide in aqueous sodium thiosulphate with a dioxane solution of a diazoketone gave good results. However, application of this method to trifluorodiazoacetone gave only very poor yields of trifluoropropionic acid, which was identifiable both by analyses and boiling point determinations. However the sodium salt of this acid could be obtained in good yield by hydrolyses of ethyl trifluoropropionate or ammonium trifluoropropionate and this can be obtained in a pure anhydrous state by extraction with absolute alcohol after the procedure of Henne and co-workers (J.A.C.S., 918, 1945) for the isolation of pure anhydrous sodium trifluoroacetate.

The reaction between the sodium salts of carboxylic

acids and benzyl thiuronium chloride has been examined and recommended as a quick and efficient means of identifying acids (Donleavy, J.A.C.S., 58, 1004, 1936 and Viebel et al. Bull. Soc. chim. Fr., 5, 1153, 1938, ibid., 6, 1434, 1939), the high molecular weight of this reagent and the low solubility of its salts makes it possible to obtain a high yield from a small amount of acid. These S-benzyl thiuronium salts have been prepared for the chlorinated acetic acids (Vogel, A Text Book of Organic Chem., p. 361) but not for the fluorinated series and so the method was first applied to sodium trifluoroacetate and a crystalline S-benzyl thiuronium salt produced before successfully applying the same procedure to the sodium salt of trifluoro-propionic acid. Other crystalline derivatives prepared were the anilinium salts of the two acids concerned, the method used being based on a procedure similar to that suggested by Campbell (Qualitative Org. Chem., p. 89, McMillan & Co. Ltd., 1946). These derivatives formed very easily and the equivalent weight of each could be estimated by simple alkali titration procedures. Attempts to form the p-nitrobenzyl ester of trifluoropropionic acid from sodium trifluoropropionate and p-nitrobenzyl bromide yielded no conclusive results. A crystalline compound was

obtained, which had a different melting point from the p-nitrobenzyl bromide but analyses showed that it contained approximately half the fluorine required of the desired ester of trifluoropropionic acid. Recrystallisation from various solvents led to no improvement so it was considered probable that the compound obtained was a mixture of the two substances crystallising out simultaneously.

On the basis of the results obtained during these investigations it appears that the application of the Arndt-Eistert Synthesis to halogenated aliphatic carboxylic acids, as exemplified by trifluoro and trichloroacetic acids, is a practicable possibility. The corresponding diazoketones are obtained in good yields so proving that the trifluoro and trichloromethyl groups are stable to attack by diazomethane, these compounds were isolated as mobile liquids and appeared quite stable under normal conditions for they could be stored for several days without apparent decomposition. Though the yields of diazoketones are not so high as those generally obtainable from normal aromatic carboxylic acid chlorides they compare very favourably with those obtained in the aliphatic series eg. trichlorodiazoketone 88% and trifluorodiazoacetone

62.5% as against diazoacetone 68%. [This result for diazoacetone was obtained by the method of Arndt and Amende (B., 61, 1122, 1928), who do not quote their own yields.]. When they undergo the Wolff Rearrangement the diazoketones yield the homologous halogenated propionic acids or derivatives of these acids but the percentage conversion of the diazoketones to these various products shows a marked variation, as illustrated in Table II:-

Table II.

Diazoketone	Isolated Products	% Conversion	% Conversion from Acid Chloride.
CF_3COCHN_2	$CF_3CH_2COOC_2H_5$	40.5	25.30
CCl_3COCHN_2	$CCl_3CH_2COOC_2H_5$	73.7	65.00
CF_3COCHN_2	$CF_3CH_2CONH_2$	13.5	8.45
CCl_3COCHN_2	$CCl_3CH_2CONH_2$	5.3	4.65
CF_3COCHN_2	$CF_3CH_2CONHPh$	9.0	5.62
CF_3COCHN_2	CF_3CH_2COOH	Traces	—

In each halogenated series the conversion of the diazoketones to the esters of the homologous propionic acids gave by far the best results though, comparatively, the yield of ethyl trichloropropionate is much higher than that of the fluorinated analogue. The conversion to the acid amides and, in the case of trifluorodiazoacetone, to trifluoropropionanilide gave low results while the formation of the homologous trifluoropropionic acid was very poor indeed. These results therefore tend to confirm the general statement applicable to the Wolff Rearrangement, that conversion of a diazoketone to the homologous ester or amide generally gives rise to higher yields than conversion to the homologous free acid. Normally when applying the Arndt-Eistert Synthesis to aromatic and aliphatic carboxylic acids the over-all yields obtainable are between 50% and 80% but in the case of the halogenated aliphatic carboxylic acids the over-all yields were on the whole well below the minimum of these values. Ethyl trichloropropionate proved an exception since in this case the over-all yield was 65%.

Since the homologous esters are formed in the highest yields it would appear that in any attempts to ascend higher in the acid series by means of successive Arndt-Eistert

Syntheses it would be best to proceed via the esters, which would then need to be converted to the acid chlorides. The various experiments carried out on these esters, however, showed that while the trifluoromethyl group is quite stable the trichloromethyl group can be readily hydrolysed. Thus it is doubtful whether the conversion of trichloropropionic ester to trichlorobutyric ester could be carried out with a reasonable over-all yield. There seems no doubt however that, given sufficient quantities of trifluoroacetic acid, it should be possible to proceed to the formation of any of the higher homologues. However, since the building up of sufficient quantities of ethyl trifluoropropionate with which to ascend the series further would take an appreciable length of time, it was decided to investigate instead the preparation of the corresponding fluorinated aldehydes, by one or other of the standard preparative techniques.

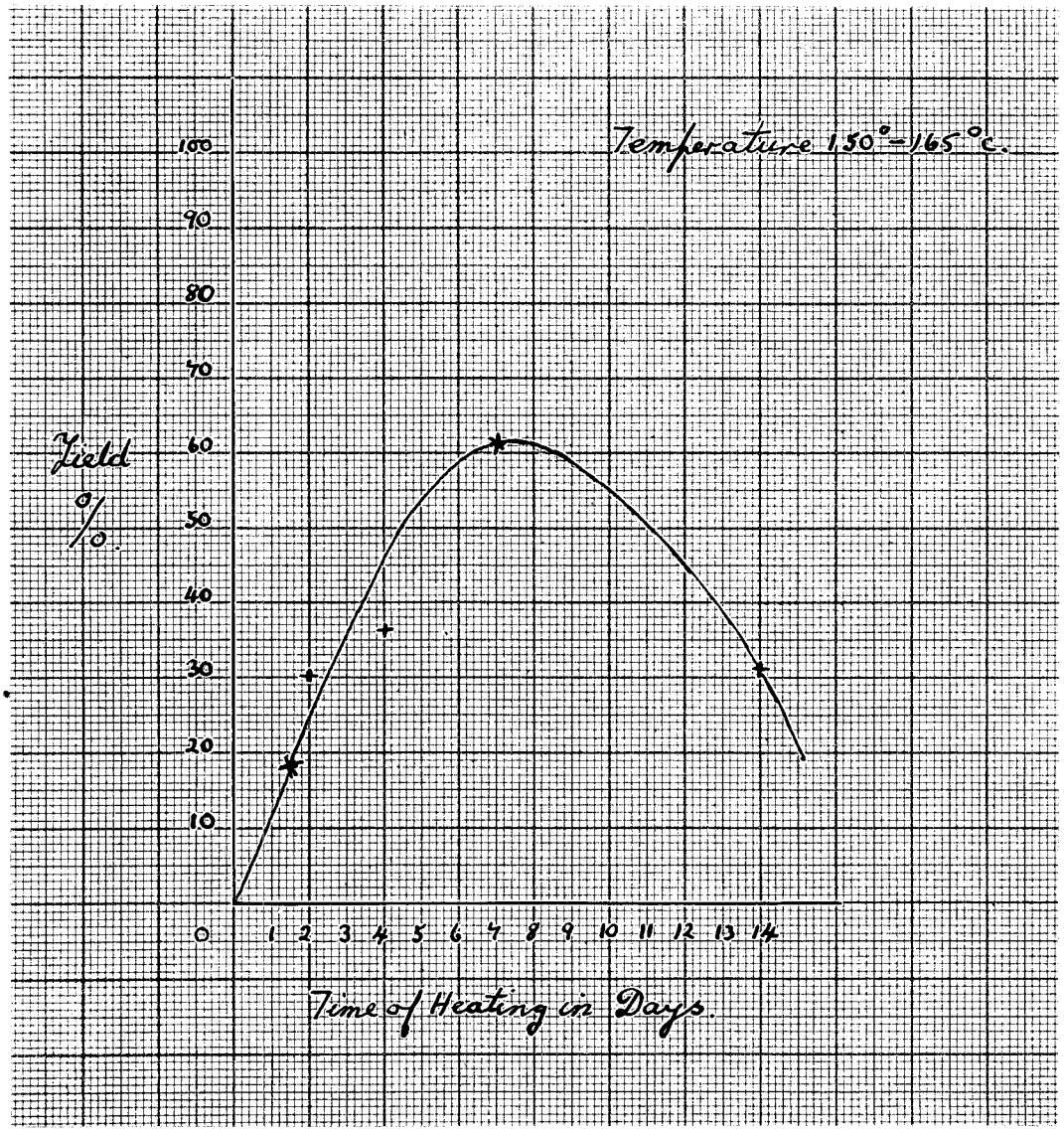
Experimental.

Preparation of Trichloroacetyl chloride.

Trichloroacetic acid purified by distillation was poured while still molten, into a Carius Tube and sealed up with slightly more than the calculated quantity of phosphorus trichloride. After heating in a furnace for a specified time at a carefully controlled temperature the tube was cooled, opened and the resultant dark liquid reaction mixture distilled from a small Claisen Flask up to a bath temperature of 200°C. Fractionation of this distillate through an eight inch column packed with Fenske helices yielded pure trichloroacetyl chloride B.P. 118°C. A series of experiments were carried out to ascertain the optimum conditions for maximum yields of the acid chloride and the results so obtained tabulated below:-

CCl_3COOH gm.	PCl_3 ml.	Time of Heating hrs.	Temperature Degrees C.	Yield gm.	Yield %
58.0	11.0	32	150	12.1	19.3
64.0	11.4	48	150	21.5	30.3
62.0	11.0	96	140	25.3	36.8
77.5	14.4	168	165	52.8	61.5
76.0	13.1	336	165	26.8	31.8

The maximum yield (61.5%) was reached after heating at 165°C for 168 hrs. and any longer period of heating resulted in a sharp fall in the yield of the desired product (see graph) accompanied by a corresponding increase in the amount of apparent decomposition.



C_2OCl_4 Requires Cl = 78.01%

Found Cl = 77.9%

Preparation of Trichlorodiazoacetone.

Trichloroacetyl chloride (15 gm., 0.083 mole) dissolved in anhydrous ether (100 ml.) was gradually added to a consfantly stirred solution of diazomethane (0.21 mole) in absolute ether (600 ml.) cooled at 0°C. An immediate and vigorous reaction occurred with the evolution of nitrogen and, as this effect was observed for a considerable time after the addition of the acid chloride had been completed, the solution was allowed to stand overnight at room temperature before the excess ether was removed under reduced pressure at 20°C. This left a small volume of an orange-yellow liquid which on vacuum distillation, with the receiver cooled in an ice-salt mixture, gave trichlorodiazoacetone as a pale yellow mobile liquid B.P.$_{1.0}$ 60°C. Yield 13.6 gm. (88% of theory).

$C_3HOCl_3N_2$ Requires Cl = 56.5%

Found Cl = 56.7%

Preparation of Trifluorodiazacetone.

Trifluoroacetyl chloride (11.7 gm., 0.089 mole) was slowly distilled into a constantly stirred ice cold ethereal solution (600 ml.) of diazomethane (0.22 mole.). As in the case of the addition of trichloroacetyl chloride an extremely vigorous reaction set in accompanied by nitrogen evolution but here the reaction ceased as soon as all the acid chloride had been distilled in. After standing for several hours and attaining room temperature the excess ether was removed by distillation through an eight inch column packed with Fenske helices, on a very slow stream of air, while the bath temperature was maintained at 35°C. Vacuum distillation of the residue at room temperature, with the receiver cooled in an alcohol-drikold bath, yielded trifluorodiazoacetone as a pale yellow to a colourless mobile liquid B.P.$_{1.0}$ 25°C. Yield 7.5 gm. (62.5% of theory). As in the preparation of diazoacetone (Arndt and Amende, B., 61, 1122, 1928) it was observed that if the trifluorodiazoacetone was allowed to remain in the alcohol-drikold bath for a prolonged period then colourless crystals began to separate from the liquid.

$C_3HOF_3N_2$ Requires F = 41.3%

Found F = 41.2%

In the following experiments involving the use of silver oxide, this reagent was prepared by the addition of 2N. sodium hydroxide to a solution of 20% aqueous silver nitrate (20 ml.) until precipitation was just complete. The crude precipitated oxide was then filtered under suction, washed with water until free of alkali, washed several times with absolute alcohol, sucked dry and made into a slurry with the desired volume of absolute alcohol.

Preparation of Ethyl 3,3,3 Trichloropropionate.

A slurry of dry silver oxide in absolute alcohol (50 ml.) was gradually added, over a period of ¾hr., to a well stirred solution of trichlorodiazoacetone (13.63 gm.) in absolute alcohol (200 ml.) heated to 70°C. During the addition evolution of nitrogen occurred and gradual reduction of the silver took place. When the addition of the alcoholic slurry had been completed the reaction mixture was refluxed at 110°C for 29 hrs. after which a little animal charcoal was introduced and this was followed by a further ¼ hr. refluxing. The mixture was then filtered, while still warm, through a Whatman No. 50 paper and the excess alcohol removed from the filtrate by

distillation at atmospheric pressure. The desired ethyl trichloropropionate was obtained from the residue by vacuum distillation as a pale yellow, slightly viscous liquid B.P.$_{14}$ 97°C. n_D^{20} 1.5140. Yield 10.98 gm. (73.7% of theory).

$C_5H_7O_2Cl_3$ Requires Cl = 51.8%

Found Cl = 51.8%

Preparation of Ethyl β,β,β Trifluoropropionate.

A solution of trifluorodiazoacetone (7 gm.) in absolute alcohol (150 ml.) was constantly stirred at a temperature of 65°C and treated over a period of ½ Hr. with a slurry of silver oxide in absolute alcohol (40 ml.). On completion of the addition, during which nitrogen was evolved and some reduction of the silver took place, the temperature was raised to 84°C and the mixture refluxed for 18 hrs. It was then treated with animal charcoal for one hour, cooled, and filtered as in the previous experiment. The excess alcohol was carefully distilled off through an eight inch column packed with Fenske helices with a bath temperature of 92°C. When the refractive index

of the distillate showed a change from that of pure ethyl alcohol the residue was transferred to a small Claisen Flask and, after removal of the last traces of alcohol, distilled in vacuo. with the receiver cooled in an alcohol-drikold bath. The product, ethyl trifluoropropionate (3.106 gm., 40.4% of theory), was obtained as a colourless mobile liquid B.P.$_{12}$ 50°C, n_D^{21} 1.3940.

$C_5H_7O_2F_3$ Requires F = 36.5%

Found F = 36.4%

Equivalent Weight Determinations of the Halogenated Esters.

The equivalent weight determinations were first carried out by alkaline hydrolyses and back titration of the excess alkali with standard acid.

a) Ethyl trifluoropropionate (0.209 gm.) heated for 4 hr. at 105°C with approximately 0.5 N. sodium hydroxide (25 ml.) while a blank experiment containing only 25 ml. of alkali was heated under identical conditions. The amount of alkali present in each case was then determined by titration with N. sulphuric acid.

Blank titration = 13.21 ml. N. H_2SO_4

Titration on Ester solution = 11.90 ml. N. H_2SO_4

Titration Difference = 1.31 ml. N. H_2SO_4

$\therefore$ Equivalent of Ester = $0.209 \times \frac{1000}{1.31}$

= 159

$C_5H_7O_2F_3$ Requires Equiv. Wt. = 156

Found Equiv. Wt. = 159 and 152

b) With ethyl trichloropropionate results averaging one quarter of the calculated value were obtained

Wt. of ester taken = 0.254 gm.

Blank titration = 10.4 ml. N. H_2SO_4

Titration on Ester solution = 5.8 ml. N. H_2SO_4

Titration Difference = 4.6 ml. N. H_2SO_4

$\therefore$ Equivalent of Ester = $0.254 \times \frac{1000}{4.6}$

= 55

Repeated estimations gave results of the same order i.e. 56 and 53 instead of the calculated value of 205.5. However acidification of the hydrolysis solutions with

dilute nitric acid followed by treatment with silver nitrate solutions showed the presence of large quantities of free chloride ion. Thus under the experimental conditions employed the trichloromethyl group, as well as the ester grouping, must be attacked by the alkali.

Equivalent weight determinations carried out by acid hydrolyses did not lead to hydrolyses of the trichloromethyl group and gave results as near the theoretical value as the experimental errors of the method would allow.

$C_5H_7O_2Cl_3$ Requires Equiv. Wt. = 205.5

Found Equiv. Wt. = 209

Preparation of Malonamide from Ethyl Trichloropropionate.

Ethyl trichloropropionate (5 gm.) was refluxed for 3 hrs. at 110°C with an excess of an aqueous solution of sodium hydroxide (7.8 gm. in 300 ml.) and the resultant homogenous solution allowed to stand overnight to ensure complete hydrolyses. The solution was then neutralised with N. hydrochloric acid, the amount of acid required showing that roughly 93% hydrolyses had occurred.

The resultant neutral solution was then evaporated to dryness and the mixture of sodium salts left was heated for 39 hrs. at 88°C with absolute alcohol (200 ml.) containing concentrated sulphuric acid (6 ml.). This treatment converted any sodium malonate to the ethyl ester. On cooling, the mixture was neutralised with sodium ethoxide and the sodium salts so precipitated were removed by filtration and centrifuging, the latter being necessary since part of the precipitate was extremely finely divided. Removal of the excess alcohol by distillation at atmospheric pressure left a small residue of dark liquid, which on vacuum distillation yielded a colourless liquid B.P.$_{17}$ 94°C, which was thought to be malonic ester. Yield 0.34 gm. (9.25% of theory). Treatment of this with liquid ammonia and one crystal of ammonium chloride as catalyst (Fellinger and Audrieth, J.A.C.S., 60, 579, 1938) yielded, after slow evaporation of the ammonia, small quantities of a white crystalline solid. This after recrystallisation from hot water gave malonamide, melting point 170°C, yield 0.037 gm. (14.2% of theory).

Preparation of ~~333~~ Trichloropropionamide.

A slurry of dry silver oxide in absolute alcohol

(50 ml.) was added to a vigorously stirred solution of trichlorodiazoacetone (9.253 gm.) in absolute alcohol (200 ml.). The mixture was cooled in an ice bath and dry gaseous ammonia bubbled in for 1½ hrs. after which time the ice bath was removed and the mixture allowed to attain room temperature (20°C). Ammonia was then passed for a further 1½ hrs. at room temperature before treating the mixture with a small quantity of animal charcoal followed by refluxing at 100°C until all the excess ammonia had been expelled. Filtration, followed by distillation of the excess alcohol at atmospheric pressure, gave a brown solid which was found to sublime at 150°C under reduced pressure (8 mm.) to yield white crystals (0.46 gm., 5.27% of theory) of trichloropropionamide.

$C_3H_4OCl_3N$ Requires Cl = 60.3%, N = 7.9%

Found Cl = 60.1%, N = 7.9%

Preparation of 3,3,3 Trifluoropropionamide.

Using a solution of trifluorodiazoacetone (5.481 gm.) in absolute alcohol (150 ml.) the experiment was carried out as detailed in the previous preparation. The solid, left on removal of the excess alcohol, sublimed slightly at

160°C under 20 mm. pressure but the bulk formed a liquid which on vacuum distillation gave 0.684 gm. of a colourless liquid B.P.$_{12}$ 130°C. This liquid crystallised to a white compound on standing at r oom temperature but on exposure to the air was found to be quite deliquescent so that accurate analysis could not be carried out. Assuming this to be the required amide it was treated for several hours with the calculated quantity of warm dilute hydrochloric acid in an attempt to hydrolyse it to the corresponding ammonium salt of trifluoropropionic acid. On evaporating the hydrolyses solution to dryness a white solid was obtained, which was purified by sublimation and found to be quite stable under normal conditions. Accurate analyses carried out on this compound proved it to be ammonium trifluoropropionate and this showed that the initial product was trifluoropropionamide. Yield of ammonium salt 0.7 gm., 12.4% of theoretical conversion from trifluorodiazoacetone.

$C_3H_6O_2F_3$ N. Requires F = 39.3%, N = 9.6%

Found F = 39.1%, N = 9.7%

Preparation of β,β,β Trifluoropropionanilide.

The procedure adopted in this experiment was adapted

from that used by Arndt and Eistert (B., 68, 200, 1935) for the preparation of anthroquinone-2-acetanilide.

A solution of aniline (15 ml.) and silver nitrate (20 ml. of 10% aqueous solution) in dioxane (150 ml.) was constantly stirred at room temperature and gradually treated with trifluorodiazoacetone (7.65 gm.). Gas evolution occurred and as soon as the addition of diazoketone was completed the temperature of the reaction mixture was raised to 115°C over a 2 hr. period and maintained there for 15 hrs. in order to complete the reaction. The hot reaction mixture was then filtered under suction through a Whatman No. 50 paper to remove silver residues and the filtrate charcoaled. On refiltering, while still hot, a pale brown filtrate was obtained from which a white compound separated on cooling. To obtain a further quantities of this compound the liquid volume was reduced to one-third by distillation and filtration then gave 1.5 gm. of crude product which on recrystallisation from alcohol yielded pure β trifluoropropionanilide. M.P. 118°C. Yield 1.0 gm. (8.9% of theory).

$C_9H_8OF_3N$ Requires F = 28.1%

Found F = 27.9%

The melting point obtained agreed with that found by

Henne, Pelley and Alm (J.A.C.S., 72, 3370, 1950), who prepared the anilide directly from trifluoropropionic acid.

Preparation of βββ Trifluoropropionic Acid.

The procedure was based on the investigations of Walker (J.C.S., 1304, 1940) concerning the conversion of diazoketones to the homologous free acids.

A solution of trifluorodiazoacetone (6.128 gm.) in warm dioxane (166 ml.) was added to a constantly stirred suspension of freshly prepared silver oxide (11.7 gm.) in aqueous sodium thiosulphate (18.4 gm. in 420 ml.) maintained at 75°C. After 1½ hrs. at this temperature the mixture was allowed to cool and stand overnight before removing the residue by filtration. The filtrate was acidified with dilute nitric acid and extracted several times with ether (6 x 50 ml.) the extract being dried over anhydrous calcium chloride. Fractionation of the extracts at normal pressure left, after removal of the ether and dioxane, a dark residue which on distillation from a small Claisen Flask yielded a very small quantity of a colourless liquid B.P. 140°C. This liquid had strong acidic properties and the analyses figures proved it to be trifluoropropionic acid.

$C_3H_3O_2F_3$ Requires F = 44.5%

Found F = 44.6%

Preparation of Ammonium Trifluoropropionate.

Ethyl trifluoropropionate (1 gm.) plus two crystals of ammonium chloride as catalyst were placed in a Dewar flask and treated with an excess of liquid ammonia. The flask was closed by a soda lime tube and the excess ammonia allowed to evaporate slowly. There remained some white crystals plus a little brown syrup and after filtering off the crystals the syrup was again treated with liquid ammonia and ammonium chloride but no further amounts of a crystalline derivative was obtained. The crystalline derivative was insoluble in alcohol or ether but was purified by sublimation under reduced pressure (136°C at 21 mm.) and found to be ammonium trifluoropropionate (0.5 gm. 61.5% of theory). Normally treatment of an ester with liquid ammonia and ammonium chloride as catalyst gives rise to the corresponding amide (Fernelius and Bowmann, Chem. Rev., 26, 23, 1940) but since the liquid ammonia used was found to be damp it was concluded that the amide originally formed had been

hydrolysed to the ammonium salt. [cf. the preparation of trifluoroacetamide (Gilman and Jones, J.A.C.S., 65, 1458, 1943)].

$C_3H_6O_2F_3N$. Requires N = 9.6%

Found N = 9.7%

Preparation of Sodium 3,3,3 Trifluoropropionate.

a) Ethyl trifluoropropionate (1 gm.) was refluxed with the calculated quantity of dilute sodium hydroxide (64.2 ml. of 0.1N.) until a homogeneous solution was formed, This was cooled, neutralised with hydrochloric acid (0.1N.) and evaporated to dryness. The residue was refluxed with absolute alcohol (100 ml.) and filtered while hot. Evaporation of the alcohol left the white, anhydrous sodium salt of the trifluoropropionic acid (0.7 gm., 73% of theory).

$C_3H_2O_2F_3Na$ Requires F = 38.0%

Found F = 38.0%

During the later part of the procedure it is essential to exclude all traces of moisture or the salt is not obtained as a white anhydrous solid, for like sodium trifluoroacetate it is rather deliquescent.

b) Ammonium trifluoropropionate (0.94 gm.) was boiled with the calculated quantity of aqueous sodium hydroxide (65 ml. of 0.1N) until no more ammonia was evolved. The solution was then neutralised and treated as in method (a) whereupon (0.93 gm. of 96% of theory) pure sodium trifluoropropionate was obtained.

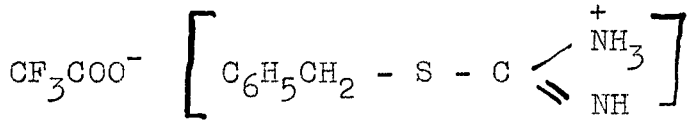
$C_3H_2O_2F_3Na$ Requires F, = 38.0%

Found F = 38.1%

Preparation of the S-benzyl Thiuronium Salts of Trifluoroacetic and Trifluoropropionic Acids.

a) A few drops of methyl orange were added to a solution of trifluoroacetic acid (1.14 gm., 0.01 mole) in water (10 ml.) and the solution neutralised with N. sodium hydroxide followed by acidification with one drop of 2N. hydrochloric acid. This was then cooled in ice water and added to a similarly cooled solution of benzyl thiuronium chloride (2 gm.) in water (10 ml.). An immediate precipitate was obtained but the precipitation was completed by cooling the mixture at $0^{o}C$ for two days. The white crystalline precipitate was filtered off under

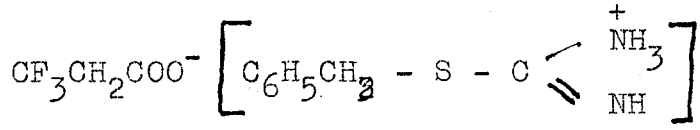
suction, repeatedly recrystallised from absolute alcohol and finally yielded 0.25 gm. of a pure crystalline compound, which melted sharply at 173°C and proved to be the benzyl thiuronium salt of trifluoroacetic acid.



$C_{10}H_{11}O_2F_3N_2S$ Requires F = 20.36%

Found F = 20.56%

b) A solution of sodium trifluoropropionate (0.5gm.) dissolved in water (6.6 ml.) and acidified with one drop of 2N. hydrochloric acid was added to a solution of benzyl thiuronium chloride (0.66 gm.) in water (3.3 ml.). A crystalline compound gradually began to separate out and as in the previous experiment the precipitation was completed by cooling at 0°C for two days. Filtration and recrystallisation from alcohol yielded 0.07 gm. of the benzyl thiuronium salt of trifluoropropionic acid M.P. 176°C.



$C_{11}H_{13}O_2F_3N_2S$ Requires F = 19.4%

Found F = 19.6%

Preparation of the Aniline Salt of Trifluoroacetic Acid..

Analar aniline (1.25 gm.) was dissolved in anhydrous ether (3 ml.) and gradually added to a solution of trifluoroacetic acid (1.54 gm.) in anhydrous ether (3 ml.). A slight evolution of heat occurred and after standing for several minutes a white crystalline solid separated out. Filtration followed by recrystallisation from rectified spirits yielded 0.97 gm. (34% of theory) of the crystalline aniline salt of trifluoroacetic acid. M.P. 121° - 122°C.

$$CF_3COO^- \; H_3\overset{+}{N}C_6H_5$$

$C_8H_8O_2F_3N$. Requires F = 27.54%

Found F = 27.4%

The molecular weight of the salt was determined by dissolving a weighed sample (0.25 gm.) in water (20 ml.) and titrating with standard sodium hydroxide (0.1016N.) using phenolphthalein as indicator.

Sodium hydroxide titre = 11.68 ml.

∴ Molecular weight = $0.25 \times \frac{1000}{11.68 \times 0.1016}$

= 210.7

Calculated Value = 207.

Preparation of the Aniline Salt of Trifluoropropionic Acid.

A solution of sodium trifluoropropionate (0.35 gm.) in water (20 ml.) was acidified with normal hydrochloric acid (6 ml.) and then exhaustively extracted with ether (20 x 12 ml.). The ethereal extract was dried over anhydrous magnesium sulphate and the excess ether distilled off until the volume was reduced to 2 ml. To this was added anilar aniline (0.25 ml.) and the solution allowed to stand for 48 hours at $0^{o}C$. A small quantity of a white solid separated which, after filtering under suction and recrystallising from rectified spirits, yielded 0.12 gm. of a white crystalline compound of M.P. $116^{o}C$.

A molecular weight determination was carried out as in the previous experiment (p. 54.)

Weight of sample taken = 0.10 gm.

Sodium hydroxide (0.1016N.) titre = 4.41 ml.

$\therefore$ molecular weight = $0.1 \times \frac{1000}{0.1016 \times 4.41}$

= 223.2

This result shows the product to be the aniline salt of trifluoropropionic acid.

$C_9H_{10}O_2F_3N$ Requires M.W. = 221.0

Found M.W. = 223.2

Fluorinated Aliphatic Aldehydes.

Introduction.

Up to the present time the preparation of very few fluorinated aliphatic aldehydes have been reported although the aldehydes corresponding to trifluoroacetic and trifluoropropionic acids have both been obtained, trifluoroacetaldehyde by reduction of trifluoroacetonitrile with lithium aluminium hydride at low temperatures (Henne, Pelley and Alm, J.A.C.S., 72, 3370, 1950) or by oxidative nitration of 1,1,1-trifluoropropane (Shechter and Conrad, J.A.C.S., 72, 3371, 1950), while trifluoropropionaldehyde was obtained by dichromate oxidation of trifluoropropyl alcohol (Henne, Pelley and Alm, J.A.C.S., 72, 3370, 1950). In addition to these, two higher membered aliphatic aldehydes have been reported (Abstracts, Am. Chem. Soc., 116th meeting, Atlantic City, 1949, p. 10 K), trifluorobutyraldehyde by treatment of the compound $CF_3CH_2CH_2MgX$ with ethyl orthoformate (McBee) and heptafluorobutyraldehyde during the reduction of heptafluorobutyric acid to the corresponding alcohol (Husted and Ahlbrecht). The boiling points of the trifluorinated aldehydes are substantially the same as those of the corresponding unfluorinated aldehydes except for trifluoroacetaldehyde which boils approximately 40°C below acetaldehyde. With regard to the

successful preparation of trifluoroacetaldehyde carried out by Henne and co-workers it is of interest to note that Friedman (Atlantic City 1949, p. 5 M) recommends the reduction of nitriles as a general procedure for the preparation of aldehydes.

The products obtainable by carrying out the Arndt-Eistert Synthesis under varying experimental conditions are a free carboxylic acid, its ester, amide or anilide and so the general methods available for converting these types of compound to the corresponding aldehydes were first reviewed. Application of reduction processes to free carboxylic acids or esters do not readily yield aldehydes, though in the case of acids the conversion may be effected by passing the vaporised acid, mixed with formic acid, over titanium dioxide at elevated temperatures. With acetic acid and its homologues yields of 50% have been obtained but if thoria is used as a catalyst the yields are smaller (Sabatier and Mailhe, Compt. rend., 154, 561, 1912). Formation of aldehydes from acid amides is possible by reduction of the amides using hydrogen and a catalyst (usually platinum) but the yields are poor. The conversion of acid anilides to aldehydes can be brought about by treatment with phosphorus pentachloride to yield the

imino chloride, which can react with stannous chloride under suitable conditions to form an azomethine the hydrolysis of which gives rise to the desired product (Sonn and Müller, B., 52, 1927, 1919):-

$$RCONHPh \longrightarrow RCCl = NPh \longrightarrow R - CH = NPh \longrightarrow RCHO + PhNH_2$$

Straudinger (B., 41, 2217, 1908) described a similar type of reaction of limited application for the reduction of anilides to aldehydes:-

$$RCONHPh \longrightarrow RCCl = NPh \longrightarrow R - C(=NPh)(MgCl) \longrightarrow RCH = NPh \longrightarrow RCHO + PhNH_2$$

These types of reaction were however considered unsuitable for the preparation of trifluorinated aldehydes since Henne and co-workers (J.A.C.S., 72, 3370, 1950) have observed that a mixture of formic and trifluoroacetic acids did not react on manganous oxide at high temperatures until decomposition set in, while trifluoroacetamide was reduced to the alcohol with hydrogen and a platinum catalyst and broke down completely with sodium in liquid ammonia. Furthermore though the use of trifluoroacetanilide has not

been reported it is possible that an imino chloride would not be formed under the influence of phosphorus pentachloride since trifluoroacetonitrile does not form an imine in the Stephens Reduction (Henne et al., loc. cit.), the structure of which would be very similar to that of an imino chloride. Thus it appeared expedient to investigate the formation of aldehydes from other types of fluorinated compounds.

The reduction of acid chlorides to the corresponding aldehydes can be carried out by hydrogen in the presence of a catalyst (usually supported palladium) and this method has been applied with success to a wide range of acid chlorides, (Rosenmund et al., B., 51, 585, 1918, ibid., 54, 425, 2038, 2088, 1921; ibid., 55, 2360, 1922; ibid., 56, 1481, 1923.) and is now generally known as the Rosenmund Reduction. Henne and co-workers (J.A.C.S., 72, 3370, 1950) reported that trifluoroacetyl chloride did not react in the Rosenmund Reduction or was reduced directly to the alcohol but no further details are given and since this reduction process can be carried out in the liquid or vapour phase with different types of catalyst with or without the presence of a regulator, a wide range of experimental techniques are available. For this reason

it was concluded that application of the Rosenmund Reduction to trifluoroacetyl chloride might still offer a possibility of obtaining trifluoroacetaldehyde in reasonable yields.

The Mechanism of the Rosenmund Reduction.

The basis of the method is the selective hydrogenation of an acid chloride in the presence of a suitable catalyst (supported palladium) to form the corresponding aldehyde:-

$$RCOCl + H_2 \longrightarrow RCHO + HCl$$

It is essential however that the aldehyde must be capable of withstanding reduction under the conditions necessary for its formation from the acid chloride or it will be further reduced to the alcohol and even to the hydrocarbon:-

$$RCHO + H_2 \longrightarrow RCH_2OH$$

$$RCH_2OH + H_2 \longrightarrow RCH_3 + H_2O$$

If this further reduction does occur then the alcohol and water so formed can react with the acid chloride thus resulting in the production of an ester and acid anhydride respectively:-

$$RCOCl + RCH_2OH \longrightarrow RCOOCH_2R + HCl$$

$$RCOCl + H_2O \longrightarrow RCOOH + HCl$$

$$RCOCl + RCOOH \longrightarrow (RCO)_2O + HCl$$

Rajahn and Fahr (Ann., 434, 252, 1923) state that the formation of the acid anhydride, as shown above, is an important side reaction in the reduction of heterocyclic acid chlorides if traces of oxygen and water are present in the hydrogen used. Another type of side reaction found during the reduction of many heterocyclic acid chlorides and also in the formation of aldehydes from p-anisoyl chloride (Rosenmund, Zetzsche and Heise, B., 54, 638, 1921) and 2-naphthoyl chloride (Hershberg and Cason, Org. Syntheses, 21, 84, 1941) is the reductive removal of the acid chloride group to form the hydrocarbon:-

$$RCOCl + H_2 \longrightarrow RH + HCl + CO$$

In practice the reduction is usually carried out by bubbling hydrogen through a hot solution of the acid chloride in xylene or toluene in which the catalyst is suspended. Palladised barium sulphate (2% - 5% Pd) has been most frequently used as catalyst and the ratio of catalyst to acid chloride is usually 1 to 10. The barium sulphate can be replaced by other carriers such as charcoal,

calcium carbonate or kieseleguhr (Rosenmund, B., 54, 425, 1921; Rajahn and Seitz, Ann., 437, 279, 1924; Waser, Helv. Chim. Acta., 8, 117, 1925), while osmium, platinum and nickel have been used instead of palladium (Weygand and Meusel, B., 76, 503, 1943; Rosenmund, B., 51, 585, 1918). The investigations of Rosenmund and Zetzsche (B., 54, 625, 1921) showed that the presence of a regulator mixed with the catalyst could prevent further reduction of the aldehyde to the alcohol etc., consequently special attention has since been paid to the development of suitable regulators most of which contain sulphur. In many cases however the use of a regulator is not required, while in others their use seems to be definitely disadvantagous, thus whether or not a regulator is required can only be determined by experiment for any particular case. The most widely used regulator is thioquinanthrene (quinoline-S) and usually 10 mg./gm. of catalyst has been found quite satisfactory (Hershberg and Cason, Org. Syntheses, 21, 84, 1941).

A limited number of acid chlorides have been converted to the aldehydes by carrying out the reduction in the vapour phase and good yields of benzaldehyde and isovaleraldehyde were obtained by Fröschl and Danoff

(J. prakt. Chem., 144, 217, 1936), who passed the acid chlorides over palladised asbestos at temperatures approaching 200°C. However phenylethyl alcohol and ethyl benzene were obtained from phenylacetyl chloride, while succinyl chloride gave butyrolactone. By operating at reduced pressure with nickel, nickel chloride and platinum as catalysts Escourrou (Bull. soc. chim. Fr., (5), 6, 1173, 1939) reduced higher aliphatic and aromatic acid chlorides but there appears to be no advantage in adopting such a procedure. On the whole it appears therefore that by far the greatest number of investigations have been carried out in the liquid phase but since trifluoroacetyl chloride has a boiling point of -27°C it was considered expedient to attempt a vapour phase Rosenmund Reduction in preference to a liquid phase technique.

In conclusion it thus appears that the Rosenmund Reduction is generally applicable to the preparation of aliphatic and aromatic monoaldehydes from the corresponding acid chlorides and though the yields vary considerably most acid chlorides gave yields of over 50% while yields of 80% can occasionally be obtained. With the acid chlorides of dibasic acids however the reduction often gives poor yields of the dialdehydes but in most cases this appears due

to polymerisation of the products during isolation and purification (Rosenmund et al., B., 54, 2888, 1921; ibid., 55, 609, 1922). A final advantage of this method is that no variation in yield with the quantity of reactants employed was observed when the method was used with small quantities of acid chlorides or on a preparative scale (Hershberg and Cason, Org. Syntheses, 21, 84, 1941) and this is of importance since the available quantity of fluorinated acid chloride was quite small.

Application of the Rosenmund Reduction to Fluorinated Acid Chlorides.

First of all, in order to gain experience in the experimental techniques employed during the vapour phase reduction of acid chlorides, the work of Fröschl and Danoff (J. prakt. Chem., 144, 217, 1936) was repeated and good yields (80%) of benzaldehyde obtained from benzoyl chloride.

The trifluoroacetyl chloride required for reduction was prepared from trifluoroacetic acid and benzoyl chloride (Henne et al., J.A.C.S., 70, 1968, 1948) in preference to the action of phosphoros trichloride on barium trifluoroacetate (Simons and Ramler, J.A.C.S., 65, 389,

1943) since it is known that traces of phosphorus compounds in an acid chloride can retard, or even prevent, any reduction from taking place (Zetzsche and Arndt, Helv. Chim. Acta., 8, 591, 1925; ibid., 9, 173, 1926). In addition to this Fröschl and Danoff, in their work on the vapour phase reduction of acid chlorides, stress the point that the acid chlorides must be free from traces of sulphur containing compounds, in which case the use of a regulator, such as quinoline-S, would be definitely disadvantageous. It is essential therefore that the fluorinated acid chloride must be perfectly free from compounds containing these elements before attempting reduction to the corresponding fluorinated aldehyde.

The apparatus used in these investigations was a modified version of that developed by Fröschl and Danoff (loc. cit.) and the catalyst employed (palladised asbestos, 2.5% to 2.8% Pd.) was prepared as described by these investigators. The apparatus, catalyst, and acid chloride were kept as dry as possible so as to prevent any hydrolysis taking place, since the formation of free trifluoroacetic acid would result in sidereactions occuring with a subsequent decrease in the amount of aldehyde produced. In addition the aldehyde would be contaminated

with undesirable materials.

Reduction of the trifluoroacetyl chloride was found to proceed smoothly and rapidly, while the progress of the reaction could be followed by titration, with standard alkali, of the hydrogen chloride formed during the process:-

$$CF_3COCl + H_2 \rightarrow CF_3CHO + HCl$$

Though a small quantity of free trifluoroacetaldehyde was produced the bulk of the reaction product was obtained as a solid polymer from which the aldehyde was liberated on application of heat. This affect agreed with the observations of Schechter and Conrad (J.A.C.S., 72, 3371, 1950), who found that trifluoroacetaldehyde polymerised to a waxy resin, which readily decomposed into the aldehyde when heated. In addition to these products a quantity of fluoral hydrate was isolated and purified by sublimation (c.f., Henne et al., J.A.C.S., 72, 3370, 1950). The formation of this compound must have been due to the presence of small quantities of moisture in the cooled receivers, from the asbestos used as a carrier for the catalyst. The asbestos was baked before use but it was most difficult to remove the last traces of moisture since trifluoroacetaldehyde forms a hydrate with great ease (Henne et al., loc. cit.). Both the aldehyde and the

hydrate were characterised by analyses and by the formation of the crystalline 2.4-dinitrophenylhydrazone (Henne et al., loc. cit.; Schechter and Conrad, loc. cit.).

The results obtained in this investigation tend to contradict the statement of Henne, Pelley and Alm (J.A.C.S., 72, 3370, 1950) that trifluoroacetyl chloride does not react in the Rosenmund Reduction or is reduced directly to the alcohol, but since they give no details as to the conditions under which they attempted the reduction it is impossible to compare any differences in the techniques employed. However, as has been previously pointed out, there are a large number of possible variations in the experimental conditions under which a Rosenmund Reduction can be carried out, so the failure of Henne and his co-workers to reduce trifluoroacetyl chloride to trifluoroacetaldehyde could be attributed to the fact that they did not get the correct combination of experimental conditions necessary for the reduction to take place.

When the trifluoromethyl group is not adjacent to the carbonyl group contentional methods can be used for the preparation of fluorinated aldehydes eg., CF_3CH_2CHO by dichromate oxidation of $CF_3CH_2CH_2OH$ (Henne et al., loc.

cit.) and $CF_3CH_2CH_2CHO$ by treatment of $CF_3CH_2CH_2MgX$ with ethyl orthoformate (McBee, loc. cit.). Thus, since trifluoroacetaldehyde can be obtained by application of the Rosenmund Reduction to trifluoroacetyl chloride, there appears to be no reason why the higher fluorinated aliphatic aldehydes should not be prepared by carrying out the same procedure on the corresponding fluorinated acid chlorides.

Experimental.

Preparation of Trifluoroacetaldehyde.

Hydrogen from a cylinder was led through a flow-meter at a constant rate (14 l/hr.) and bubbled through two wash bottles, the first containing potassium permanganate solution and the second dilute aqueous potassium hydroxide. From thence it was led through two large calcium chloride towers and two horizontal calcium chloride tubes. The pure dry hydrogen then passed over the surface of liquid trifluoroacetyl chloride (11 gm.) contained in a tube cooled in an alcohol-drikold bath. By lowering this bath the acid chloride was gradually evaporated (over a period of 1 hr.) and the mixture of hydrogen and vapour passed into a preheater, which consisted of a small flask (100 ml.) carrying inlet and outlet tubes together with a thermometer and which was heated in an oil bath at 170°C. The hot gaseous mixture was then fed directly into a pyrex glass tube (length 36 inches, internal diameter 0.7 inch) packed with palladised asbestos as catalyst, the temperature of which was carefully maintained at a constant value (205°C) by winding it with an electric heater. The reaction tube led into two receivers, each cooled in an alcohol-drikold bath, where the products of the reaction collected. The

exit gases consisting of excess hydrogen and hydrogen chloride formed in the reaction then passed through a calcium chloride tube before being bubbled through water, containing methyl orange as indicator, where the hydrogen chloride was titrated with standard alkali. Finally the residual hydrogen was fed into the open air. After completion of the experiment, hydrogen was passed for a further hour to sweep out the apparatus, and titration of the hydrogen chloride with alkali indicated, according to the following equation:-

$$CF_3COCl + H_2 \rightarrow CF_3CHO + HCl$$

that 61% of the theoretical amount of hydrogen chloride had been produced during the operations.

The products of the reaction collected in the receivers as a white solid and, as such, could not be unchanged trifluoroacetyl chloride since it would be a liquid at the temperatures concerned. On attaining room temperature the solid formed a pale yellow liquid (Vol. 5 ml., Wt. 6 gm.) which on further treatment proved to be a mixture of trifluoroacetaldehyde, a polymer of the aldehyde and fluoral hydrate.

The trifluoroacetaldehyde, which boils at -18°C

(Shechter and Conrad, J.A.C.S., 72, 3371, 1950), was completely removed from the mixture by bubbling a slow stream of nitrogen through it at room temperature and collecting the distillate in a drikold cooled receiver (Vol. 0.75 ml., Wt. 1 gm., 12.3% yield). The colourless distillate, as expected, rapidly evaporated at room temperature but did not readily evaporate when cooled in an efficient ice-salt freezing mixture. It rapidly reduced ammoniacal silver nitrate and if it was allowed to absorb moisture a white solid gradually formed, which could be readily sublimed at 50°C thus showing it to be fluoral hydrate (Henne et al., J.A.C.S., 72, 3370, 1950):-

$$CF_3CHO + H_2O \longrightarrow CF_3CH(OH)_2$$

Analysis of the distillate confirmed it to be the desired trifluoroacetaldehyde.

C_2HOF_3	Requires	F	= 58.17%
	Found	F	= 58.0%

While bubbling dry nitrogen to isolate the trifluoroacetaldehyde the exit gases were passed through water containing methyl orange as indicator and were found to contain hydrogen chloride. This was titrated with standard alkali so bringing the total amount of hydrogen chloride produced in the reaction up to 90% of the

theoretical value. It appeared therefore that approximately 30% of the hydrogen chloride formed must be trapped in the drikold cooled receivers along with the reaction products.

After removal of the trifluoroacetaldehyde the residue formed a brown solid on standing at room temperature. On warming, this solid gradually melted to form a brown liquid and a colourless liquid distillate (3.1 gm., 38.1% yield) was collected in a drikold cooled receiver. Even when the bath temperature was raised as high as 92°C the distillation temperature did not exceed room temperature and this fact was consistent with the brown solid being a polymer of trifluoroacetaldehyde for it is known that the aldehyde easily polymerises to a waxy resin which, upon heating, readily decomposes into the aldehyde (Shechter and Conrad, J.A.C.S., 72, 3371, 1950). The liquid distillate evaporated rapidly at room temperature, readily reduced ammoniacal silver nitrate and absorbed moisture forming a white solid which could be sublimed at 50°C and proved to be fluoral hydrate. These properties together with an analysis proved the low boiling liquid to be trifluoroacetaldehyde and therefore the original solid must have been a solid polymer of the aldehyde. Analyses

carried out on the aldehyde and aldehyde hydrate gave the following results:-

C_2HOF_3	Requires	F	= 58.17%
	Found	F	= 58.1%
$C_2H_3O_2F_3$	Requires	F	= 49.2%
	Found	F	= 49.1%

The solid residue remaining after removal of the polymer was found to sublime at 50°C to yield a white crystalline solid (1.1 gm., 11.4% of theory) which analysed as pure fluoral hydrate:-

$C_2H_3O_2F_3$	Requires	F	= 49.2%
	Found	F	= 49.2%

Finally there remained a small volume of dark liquid which did not sublime and could be distilled at a bath temperature of 110°C, though no true distillation temperature was obtained due to the small quantities involved (0.2 gm.). This liquid analysed as slightly impure fluoral hydrate but this is improbable and it is most likely some type of decomposition product or polymer. Thus the overall yield of aldehyde was approximately 62%.

Preparation of the 2.4-dinitrophenylhydrazone of Fluoral.

Fluoral hydrate (0.2 gm.) was dissolved in 6N. sulphuric acid (66 ml.) containing 2.4-dinitrophenylhydrazine (0.66 gm.) and the resultant solution allowed to stand for two days. During this time an orange-yellow compound crystallised out which, after filtration and recrystallisation from aqueous alcohol, yielded 0.1 gm. of an orange crystalline compound M.P. 150°C. This was the desired 2.4-dinitrophenylhydrazone of fluoral (c.f. Henne et al., J.A.C.S., 72, 3370, 1950; Shechter and Conrad, ibid., p. 3371.) and was obtained in 20.8% yield.

$C_8H_5O_4F_3N_4$ Requires F = 20.5%

Found F = 20.4%

Further samples of this compound were obtained by bubbling the trifluoroacetaldehyde through a solution of 2.4-dinitrophenylhydrazine in 6N. sulphuric acid (c.f., Shechter and Conrad, loc. cit.)

The Chlorofluorination of Pyridine.

Introduction.

As yet little attention has been paid to the use of interhalogen compounds as fluorinating agents in organic chemistry, though iodine pentafluoride is known to be a mild fluorinating agent capable of replacing halogens, but not hydrogen, by fluorine (Sharpe, Quart. Reviews, 4, 127, 1950) and bromine trifluoride has been used to fluorinate hexachlorobenzene, carbon tetrachloride and carbon tetraiodide (McBee et al., Ind. Eng. Chem., 39, 378, 1947; Nutting and Petrie, U.S.P., 1961622, 1934; Emeleus et al., J.C.S., 2188, 1948). So far no controlled reactions have been reported using chlorine monofluoride, bromine monofluoride or bromine pentafluoride. Previous to the investigations of Ellis and Musgrave (J.C.S., 3608, 1950), concerning the halogenation of benzene with chlorine trifluoride, no detailed reports were available for the controlled reactions of this reagent with organic materials but it had been stated that in such reactions both fluorine and chlorine were introduced into the molecule (Porter, Chem. Eng., 55, No. 4, 102, 1948; Burnett and Banks, Chem. Soc. Symposium on Fluorine Chem., Nov. 1949), while Haszeldine (Private Communication to Sharpe, loc. cit.) indicated that the vapour phase fluorination of benzene and toluene with chlorine trifluoride led to both addition and substitution products.

The controlled reaction of chlorine trifluoride with benzene in carbon tetrachloride solution (Ellis and Musgrave, loc. cit.) showed the main process to be one of substitution leading to the formation of both fluorobenzene and chlorobenzene, while small amounts of addition compounds, thought to be chlorofluorocyclohexanes, - cyclohexenes and - cyclohexadienes, were also produced. Various catalysts were used during these investigations but cobaltous fluoride proved to be the most efficient. Thus taking cobaltous fluoride as an example the formation of fluorobenzene, by the usual ionic process, was postulated in the following manner:-

$$ClF_3 + 2CoF_2 \longrightarrow 2CoF_3 + ClF \text{ ----------(1)}$$

$$ClF_3 + CoF_3 \longrightarrow F^+ + CoF_4^- + ClF \text{ ---------(2)}$$

The formation of chlorobenzene was explained by the chlorinating action of chlorine monofluoride (Bigelow et al., J.A.C.S., 62, 267, 1940; Ind. Eng. Chem., 39, 360, 1947). Since chlorine monofluoride is also produced in the conversion of the catalyst to the trivalent state (1) and also in a secondary reaction between chlorine trifluoride and the solvent (3&4), the fact that the chlorobenzene was produced in higher molecular proportion than fluorobenzene

could be readily accounted for:-

$$ClF_3 + CCl_4 \longrightarrow CCl_3F + 2ClF \text{ ----------(3)}$$

$$ClF_3 + CCl_3F \longrightarrow CCl_2F_2 + 2ClF \text{ ----------(4)}$$

In the direct fluorination of organic compounds elementary fluorine fails to give aromatic substitution products since it is difficult to remove an electron so as to form the positive ion and the aromatic nucleus is attacked by an atomic chain mechanism, first by addition to form the saturated hexafluoride and then by substitution of the hydrogen atoms in this compound (Bigelow et al., J.A.C.S., 72, 2411, 1950).

In view of the fact that the action of chlorine trifluoride on benzene gave rise to aromatic substitution products and that the effect of this reagent on heterocyclic compounds had not been described, investigations were begun by Beaty (Ph.D. Thesis) using pyridine as a typical example of a conjugated heterocyclic ring system. This work showed, as in the case of benzene, that the main reaction was one of substitution giving rise to 2-fluoropyridine and 3-chloropyridine. The use of various catalysts (CoF_2, $CoCl_2$, AgF, TlF and SbF_3) was investigated and the yields of substitution products were found to be greater than those obtained in uncatalysed experiments, provided that

anhydrous potassium fluoride was added to the reaction mixture so removing any hydrogen fluoride produced during the reaction, and preventing the formation of pyridinium salts, which were said to react with chlorine trifluoride so resulting in ring fission. As with benzene, the use of cobaltous fluoride gave rise to the greatest yield of substitution compounds but the actual ratio of fluoro to chloropyridine appeared to depend to some extent on the nature of the catalyst employed.

The present series of experiments were undertaken in order to complete the investigation of the reaction between chlorine trifluoride and pyridine in carbon tetrachloride solution. Firstly by varying the experimental conditions so as to ascertain the effect on the yields of substitution products. Secondly, since Beaty did not report the formation of any addition compounds, the presence of which could be expected by analogy with the benzene experiments, attempts would be made to isolate and characterise any such compounds as were produced. Lastly it was hoped to devise experiments to indicate whether or not any ring fission took place during the reaction, which would result in the production of volatile fluorinated compounds such as nitrogen trifluoride, carbon

tetrafluoride and halogenated hydrocarbons.

It is quite possible that ring fission could occur, at least to a limited extent, for during the direct fluorination of heterocyclic compounds ring degradation often occurs with the elemination of the heterocyclic atom and the formation of volatile fluorinated materials. The electrolysis of pyridine in anhydrous hydrogen fluoride led to the formation of perfluoropentane and nitrogen trifluoride (Simons, J. Electrochem. Soc., 95, 47, 1949), while the fluorination of pyridine either by the cobaltic fluoride method or a catalytic method resulted in fission of the C-N bond (Haszeldine, J.C.S., 1966, 1950). Here the elimination of nitrogen from the pyridine ring was demonstrated by isolation of the straight chain fluorocarbon C_5F_{12} and other compounds in which c-c bond fission had occurred were also present in the reaction products but not isolated. Similar processes when applied to 2:6-lutidine (Haszeldine, J.C.S., 1638, 1950) resulted in the isolation of small quantities of perfluoro-2:6-dimethyl piperidine but the bulk of the products boiled below room temperature and were believed to be fluorocarbons, nitrogeneous compounds, eg., CF_3NF_2 and $(CF_3)_2NF$ together with nitrogen trifluoride formed by dissruption of the ring. Fluorination of quinoline (Montgomery and Smith, J.C.S., 258, 1952) also

gives rise to a mixture of perfluorohydrocarbons due to extensive degradation and finally Montgomery and Smith (loc. cit.) have shown that fluorination of thionaphthen in the vapour phase with cobalt trifluoride leads to complete elimination of sulphur. Thus the direct fluorination of heterocyclic compounds leads to ring fission with elimination of the heterocyclic atoms and fluorination of the hydrocarbon fragments.

The Reaction of Pyridine with Chlorine Trifluoride.

The previous investigations undertaken by Beaty (Ph.D. Thesis) were all carried out at $0^{o}C$ and so, in order to determine the effect of small increases of temperatures on the yields of substitution products, a series of experiments were performed at room temperature (approximately $20^{o}C$).

In these experiments the pyridine was dissolved in an excess of carbon tetrachloride and treated with a controlled amount of gaseous chlorine trifluoride at such a rate that tests carried out on the exit gases failed to show the presence of chlorine trifluoride, hydrogen fluoride or hydrogen chloride. Cobaltous fluoride was used as catalyst while anhydrous potassium fluoride was present to remove any hydrogen fluoride formed during the reaction thus preventing the formation of pyridinium salts. It was

observed that, during the course of the experiments, a considerable evolution of heat occurred so the actual temperature of the reaction mixture must have been appreciably higher than room temperature (about 40°C).

The liquid reaction products were in each case shaken with anhydrous potassium fluoride to ensure complete removal of any hydrogen fluoride and then a rapid reduced pressure distillation removed the excess solvent thus giving rise to two fractions, (a) predominantly carbon tetrachloride and (b) pyridine derivatives.

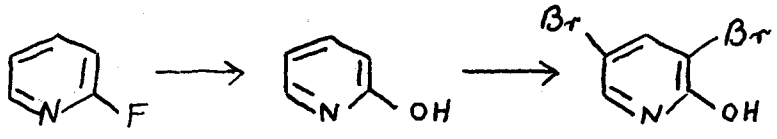
Since 2-fluoropyridine distils in carbon tetrachloride under reduced pressure the carbon tetrachloride fractions were analysed for combined fluorine. In this manner an estimate of the amount of 2-fluoropyridine produced in the reactions could be obtained (Table I). The pyridine derivatives, concentrated in the second fraction, appeared to be mainly addition compounds.

In all the experiments listed in Table I the pyridine was dissolved in carbon tetrachloride (500 ml.) with cobaltous fluoride (10 gm.) as catalyst, while anhydrous potassium fluoride (60 gm.) was present to remove any hydrogen fluoride formed during the reaction.

Table I.

	Pyridine gm.	ClF_3 gm.	ClF_3 flow rate gm./hr.	2-fluoropyridine Yield gm.	2-fluoropyridine Yield %	Pyridine derivative fraction. gm.
1.	50	35	14.0	12.9	21.0	26.3
2.	50	32	12.3	11.8	19.2	30.4
3.	50	29	11.2	14.0	22.7	28.0
4.	50	34	13.6	12.7	20.7	29.7

In order to verify the fact that it was 2-fluoropyridine present in the carbon tetrachloride fractions, samples of these fractions were distilled, at atmospheric pressure, through an electrically controlled column packed with nickel turnings and by this means samples of 2-fluoropyridine were isolated. Further verification was obtained by converting the 2-fluoropyridine to the readily characterisable solid 3.5-dibromo-2-hydroxypyridine:-



The fractions containing the concentrated pyridine derivatives (Table I, column VII), which appeared to be mainly addition compounds, were found to turn rapidly black on standing due to decomposition. This being the case it was decided to carry out a rapid reduced pressure fractionation of the products, using a small Claisen flask, in an attempt to isolate and analyse the various components before decomposition made any characterisation impossible. Results obtained by this procedure are shown in Table II.

Each distillation yielded three fractions (a,b and c) and attempts were made to analyse these products for fluorine, chlorine and nitrogen. No reasonable results could be obtained from the higher boiling fractions (c) owing to their rapid decomposition at room temperature, with the evolution of hydrogen fluoride. Accurate analytical figures were given by the lower boiling fractions (a and b), since they were slower to decompose, and it was possible to estimate their approximate molecular structure (Table II, column VII). These showed them to be chlorofluoro addition compounds of pyridine and in no case was there any 3-chloropyridine detected (c.f. Beaty loc. cit.). The fractions obtained in each experiment were not identical,

Table II.

Expt.	Fraction	Yield gm.	Appearance	B.P.	Action on $KMnO_4$ & Br_2, aq.	Possible Formula
				14mm.		
1.	a	6.60	Pale brown	47°C	Rapidly decol.	$C_5H_4NFCl_2$
	b	2.26	Blue-green	75°C	" "	$C_5H_4NFCl_2$
	c	0.93	Pale brown	>75°C	" "	——
	Tar.	8.50	Black	—	——	——
				12mm.		
2	a	6.44	Pale yellow	37°-40°C	Slowly decol.	$C_{10}H_6N_2F_2Cl$
	b	1.48	Colourless	54°-56°C	Rapidly "	$C_{10}H_7N_2F_3Cl_2$
	c	1.76	Pale brown	65°-70°C	" "	——
	Tar.	7.00	Black	—	——	——
				19mm.		
3	a	3.20	Brown	29°-30°C	Decolourised	C_5H_4NFCl
	b	2.04	Pale brown	37°-38°C	Rapidly decol.	$C_5H_4NF_2Cl$
	c	0.96	Colourless	48°-51°C	" "	——
	Tar.	6.00	Black	—	——	——

there being variations of physical appearance, boiling point and estimated molecular formula. This effect may be due to slight variations in the initial halogenation processes giving rise to slightly different addition products.

In each of the previous experiments it was found, after shaking the reaction products with additional anhydrous potassium fluoride and filtering, that the volume of the filtrate was only 80% of the initial starting volume of carbon tetrachloride plus pyridine. Similarly from tables I and II the amount of organic material isolated was approximately 60% by weight of the pyridine initially employed. Thus investigations were undertaken to account for these losses for, though part must have been due to absorption by the potassium fluoride and cobaltous fluoride, there was the possibility of reaction between the pyridine or carbon tetrachloride and the chlorine trifluoride so leading to the formation of volatile products, which would be lost under the reaction conditions hitherto employed.

Firstly, by carrying out blank experiments, an average value of the amount of liquid absorbed by the potassium

fluoride and cobaltous fluoride present in the reaction mixture was determined. The experimental apparatus was then modified so that the exit gas, instead of escaping into the atmosphere, was passed through a trap containing solid potassium fluoride for removal of hydrogen fluoride and then through two receivers the first cooled in drikold and the second in liquid nitrogen, by means of which it was hoped to condense any volatile products produced during the reaction. To reduce absorption still further the reaction products were not shaken with extra potassium fluoride (1 gm. mol.) as previously but filtered immediately. This led not only to a larger volume of filtrate but also to the collection of quantities of an organic tar (approximately 10 ml.), which in preceeding runs must have been prevented from filtering by the large excess of potassium fluoride present. Attempted vacuum distillation of this product led to decomposition with the evolution of hydrogen fluoride so no characterisation was possible. This tar however did account for a large part of the loss of organic material previously noted and in each case there appeared to be further quantities intimately mixed with the solid fluorides but the actual amounts were inestimable.

In each experiment the cooled receivers were allowed to attain room temperature, while any gas expelled was collected in an aspirator over water and the volume noted. The receiver cooled in drikold always contained some liquid which was invariably shown to be carbon tetrachloride. The results are collected in Table III.

Table III.

	N_2 flow rate l/hr.	ClF_3 gm.	ClF_3 flow rate gm/hr.	Volume of filtrate ml.	Volume absorbed by KF & CoF_2 ml.	CCl_4 in drikold receiver. ml.	Vol. loss on 550ml. ml.	Volume of gas collected. ml.
1	10	33	12.4	467	40	17	26	—
2	10	34	13.5	465	40	15	30	550
3	10	34	15.5	458	40	21	31	500
4	5	35	7.8	470	40	10	30	3000

Consideration of Table III shows the loss of liquid in each experiment to average 30 ml. i.e. 5.5% of the initial volume but it was impossible to give an estimate of the amount held in the trap containing solid anhydrous potassium fluoride.

In experiment (1) the gases were not collected in an aspirator but were bubbled directly through bromine to test for unsaturated materials. Though the liquid nitrogen cooled receiver contained a small amount of a volatile liquid, the gas produced had no reaction whatsoever with the bromine and so excluded the presence of unsaturated products. The volume of gas collected in experiments (2) and (3) could nearly all be accounted for by expansion on warming the receivers to room temperature but samples were analysed using a standard Orsat gas analyses apparatus. These analyses showed the gas samples to consist mainly of inert gas together with small quantities of oxygen and traces of carbon dioxide. Experiment (4) yielded larger volumes of gas due to the fact that, as in experiment (1), the nitrogen cooled receiver contained some volatile liquid. Analyses carried out agreed substantially with those obtained in experiments (2) and (3) but owing to the large increase in volume of the gas collected it was thought possible that the inert portion, in addition to nitrogen, may have contained nitrogen trifluoride and halogenated saturated hydrocarbons formed by break down of the pyridine during the reaction with chlorine trifluoride.

Since the alkali metals, when heated just above their

melting points, react with nitrogen trifluoride (Simons, Fluorine Chemistry, 1, p. 86, Academic Publishers Inc., New York, 1950) to give nitrogen and alkali fluorides, a sample of the gas from experiment (4), freed from traces of oxygen and moisture, was condensed in a Carius tube and fused with sodium at a temperature slightly higher than the melting point of the metal. Tests carried out on the resultant fusion mixture disclosed the presence of chloride but merely traces of fluoride. Further samples were then fused for longer periods at temperatures considerably in excess of the melting point of sodium but the results were in no way altered. These results tended to show therefore that there was no nitrogen trifluoride present in the gas for under the conditions employed reaction would have occurred with the sodium so resulting in the formation of appreciable quantities of fluoride. Furthermore, since nitrogen trifluoride is produced during the direct fluorination of pyridine owing to degradative processes (Simons, loc. cit., Haszeldine, loc. cit.) it would appear that no degradation occurs during its reaction with chlorine trifluoride and this reaction must therefore be much milder than that involving fluorination with fluorine, cobaltic fluoride or hydrogen fluoride (Idem Ibid). There

is however the possibility of a slight reaction taking place between the carbon tetrachloride solvent and the chlorine trifluoride leading to the formation of chlorofluoromethanes. This could be expected since the temperature of the reaction mixture rises to 40°C during the experiments and it is known that carbon tetrachloride itself when treated with chlorine trifluoride at this temperature and under similar conditions gives rise to monofluorotrichloro and difluorodichloromethane (Ellis, Ph.D. Thesis). Since these volatile liquids require high temperatures to ensure their complete fusion with sodium, temperatures much higher than those used in the previous Carium tube fusions, it was possible that it was the incomplete fusion of these materials which led to the detection of appreciable quantities of chloride but merely traces of fluoride in the previous experiments. However as the greatest volume of gas was collected in the experiment where the lowest nitrogen and chlorine trifluoride flow rates were employed (Table III, experiment 4) further investigations will be required to verify this possibility. Large volumes of the gas need to be collected and condensed so that the resultant liquid could be distilled through a low temperature fractionation column and the products analysed.

The results so far obtained from the investigation of the reaction between pyridine and chlorine trifluoride in carbon tetrachloride solution, show the formation of 2-fluoropyridine, chlorofluoro addition compounds of pyridine and organic tar. These products were formed in sufficient quantities to account for practically all the pyridine employed and there was additional evidence to indicate that no degradation of the pyridine occurred, thus the reaction was much milder than the direct fluorination of pyridine undertaken by other workers. Though the pyridine reacted preferentially with the chlorine trifluoride there was the possibility of a limited reaction between the latter reagent and the carbon tetrachloride solvent but further experimental evidence is required to determine this point conclusively.

Experimental.

The complete apparatus employed in the investigations is illustrated in diagram I. The nitrogen flowmeter, made of pyrex glass with the top half capilliary tubing, contained carbon tetrachloride as the manometric liquid and the calibration was such that the nitrogen flow-rate was $2\frac{1}{2}$l./hr./cm. difference between the liquid levels. Gaseous chlorine trifluoride was passed through a special flowmeter made partly of metal and partly of pyrex glass tubing (diagram IV). The nickel rod was a sliding fit into the nickel tube and using carbon tetrachloride as the manometric liquid a flow-rate of 5 gm. chlorine trifluoride/hr./cm. difference in the liquid levels was obtained. Gas tight glass to metal joints were obtained as shown in diagram V and the use of neoprene washers is recommended owing to their stability to attack by chlorine trifluoride. On the whole this type of flowmeter was found to be highly satisfactory, it had a high sensitivity and allowed a constant flow-rate when once in operation. Both the reaction vessel (diagram II) and the hydrogen fluoride trap (diagram III) were cylindrical mild steel vessels and each carried copper inlet and outlet tubes. The lower portion of each vessel had a knife edge round the rim while the lids had a ring of lead let into their undersides so that when the two portions were

DIAGRAM I

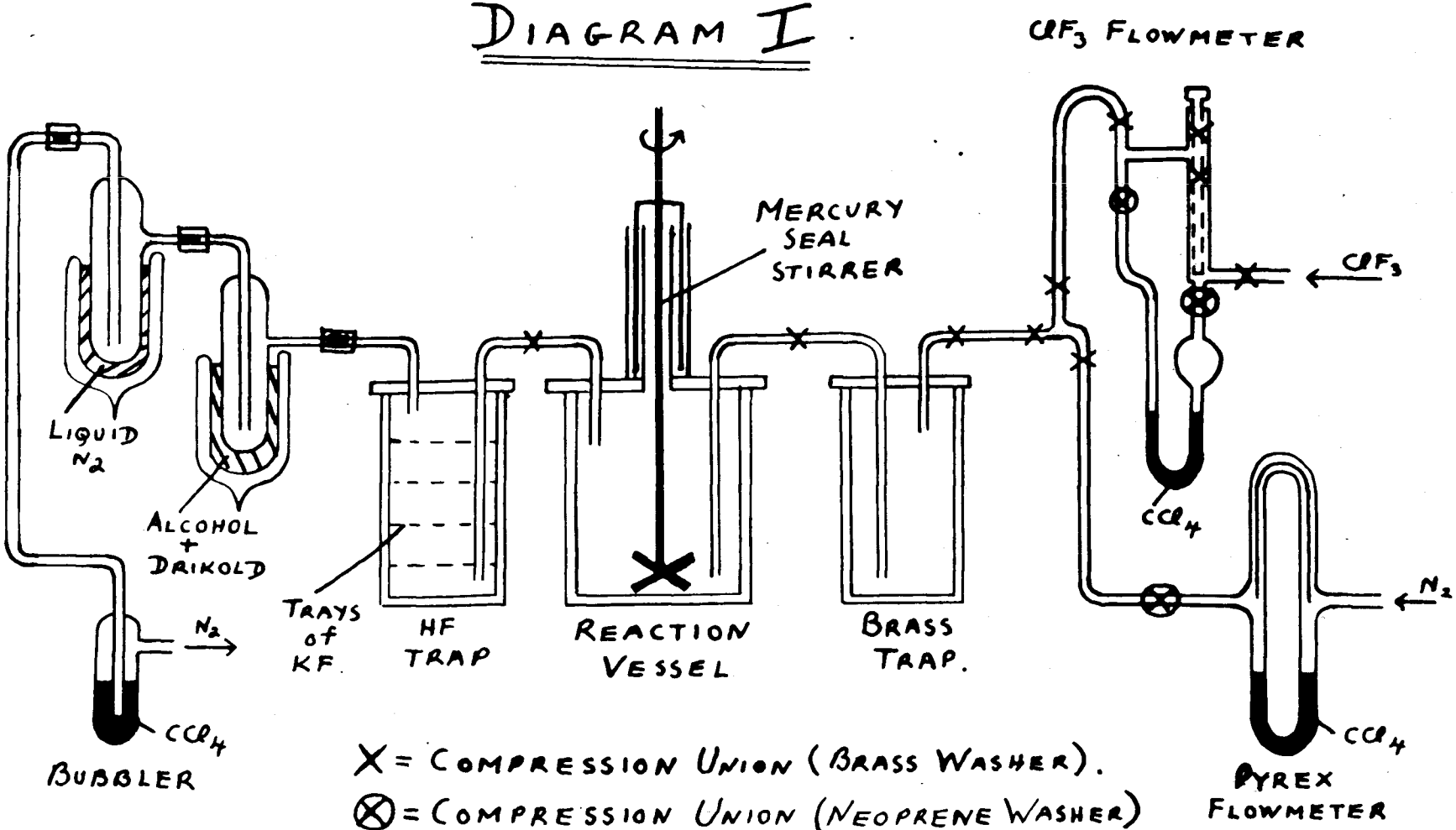
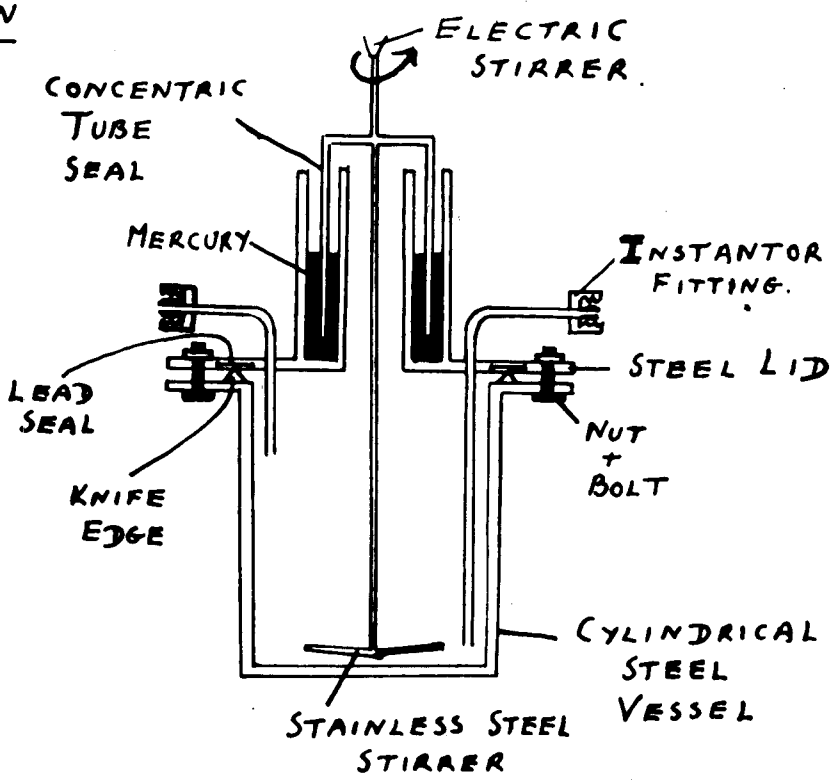

CF_3 FLOWMETER
MERCURY SEAL STIRRER
CF_3
LIQUID N_2
ALCOHOL + DRIKOLD
N_2
CCl_4
BUBBLER
TRAYS of KF
HF TRAP
REACTION VESSEL
BRASS TRAP.
CCl_4
N_2
CCl_4
PYREX FLOWMETER
X = COMPRESSION UNION (BRASS WASHER).
⊗ = COMPRESSION UNION (NEOPRENE WASHER).
■ = RUBBER CONNECTION.

DIAGRAM II

REACTION VESSEL

ELEVATION



PLAN

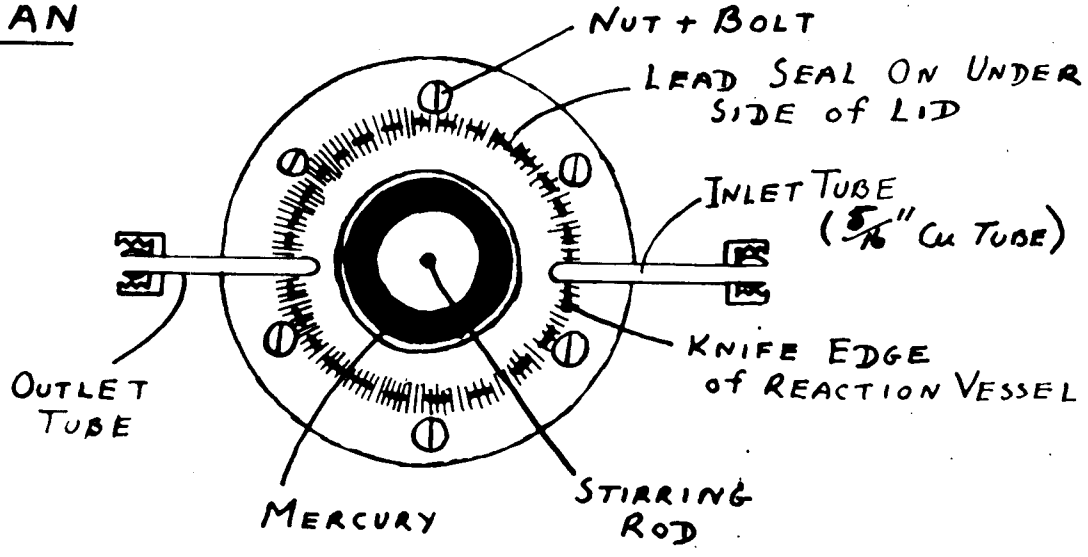
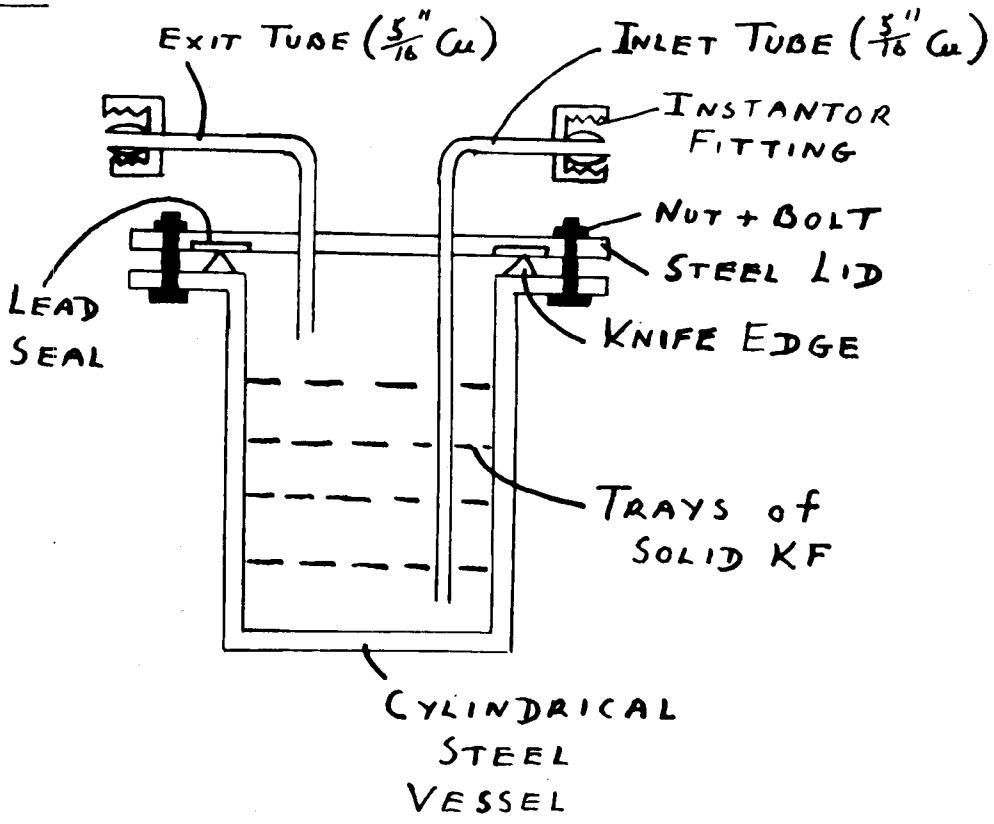


DIAGRAM III

HF. TRAP

ELEVATION



PLAN

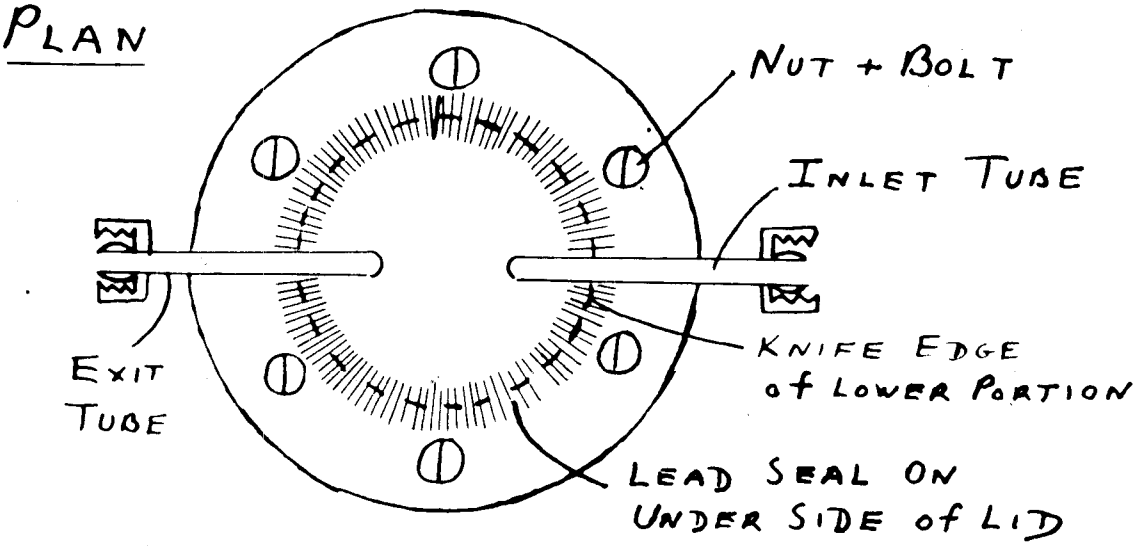


DIAGRAM IV

ClF_3 FLOWMETER

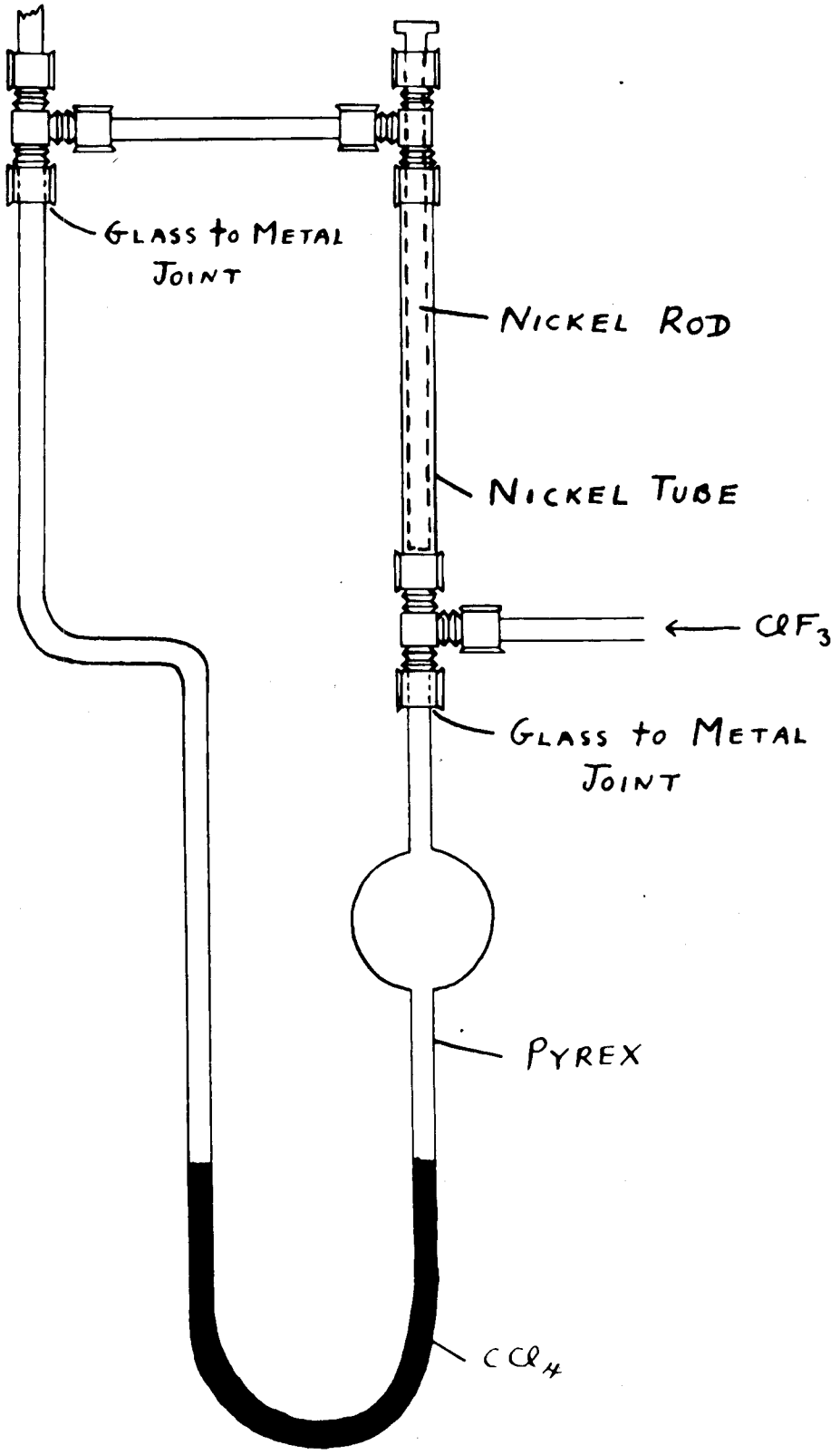
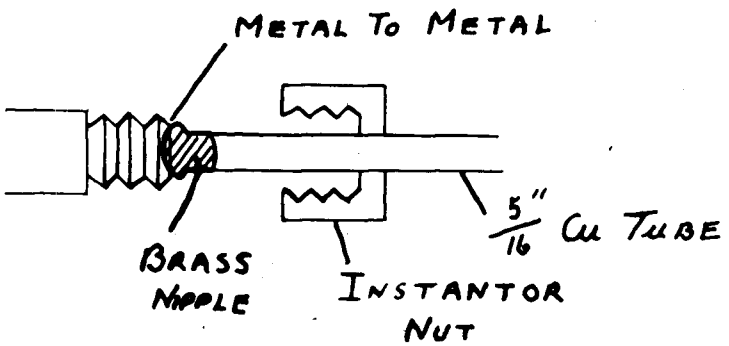


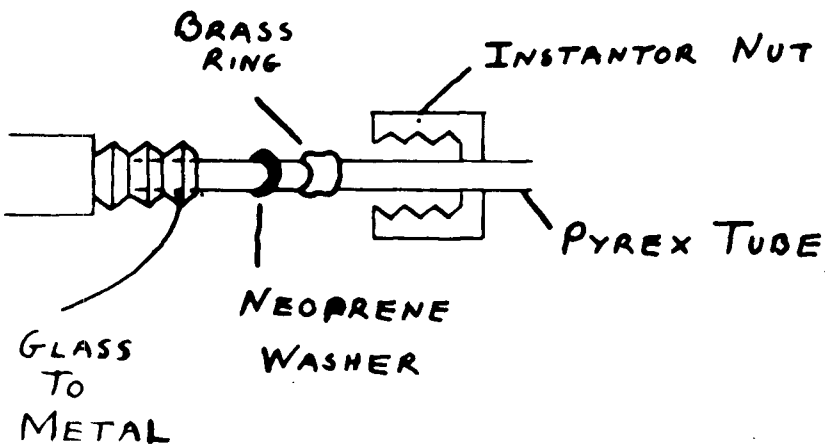
DIAGRAM V

METAL TO METAL JOINT



COMPRESSION UNION WITH BRASS NIPPLE

GLASS TO METAL JOINT.



COMPRESSION UNION WITH NEOPRENE WASHER

bolted together the knife edge bit into the lead ring and thus produced a gas tight seal. In addition the reaction vessel was fitted with a mercury sealed stirring device, while the hydrogen fluoride trap was fitted with perforated trays on which to carry solid anhydrous potassium fluoride. The brass trap between the flowmeters and the reaction vessel was included in case, during the course of an experiment, any liquid tended to suck back out of the reaction vessel. All the metal to metal joints between the various component parts of the apparatus were as shown in diagram V and found to be perfectly gas tight. Both the drikold and liquid nitrogen cooled receivers fitted beyond the hydrogen fluoride trap were made of pyrex glass and fitted into Dewar flasks. They were connected to the apparatus by rubber connections and the outlet from the nitrogen cooled receiver was connected to a bubbler filled with carbon tetrachloride. This procedure served the double purpose of indicating whether or not there was a blockage in the apparatus and of preventing any atmospheric oxygen condensing into the cooled receiver.

In all the experiments the initial reaction mixture

consisted of pyridine (50 gm.) dissolved in carbon tetrachloride (500 ml.) together with cobaltous fluoride (10 gm.) as catalyst and anhydrous potassium fluoride (60 gm.) with which to remove any hydrogen fluoride formed during the reaction. This mixture was vigerously stirred and into it was passed gaseous chlorine trifluoride diluted with nitrogen. The gaseous mixture was fed in at a controlled rate and when the ratio of pyridine to chlorine trifluoride reached 1 mole to $\frac{1}{2}$ mole then the supply of the latter gas was cut off and nitrogen was blown through the apparatus to ensure that all the chlorine trifluoride was swept into the reaction vessel. During the course of these experiments the temperature of the reaction mixture rose from room temperature to approximately 40°C and so indicated that considerable quantities of heat were always evolved. It is essential that the apparatus must be dry and all reagents anhydrous or an explosion may occur when the chlorine trifluoride is introduced.

The first series of investigations concerned the formation of 2-fluoropyridine together with chlorofluoro addition compounds of pyridine and during these experiments the exit gases from the reaction vessel were allowed to escape into the atmosphere, being tested with

starch iodide paper, a moist glass rod and silver nitrate solution for traces of halogens, hydrogen fluoride, and hydrogen chloride respectively, but in no case were these gases detected. In the second series of experiments however the aim was to ascertain whether or not any break down of the pyridine occurred, with the formation of gaseous products, thus in these cases the complete apparatus (diagram I) was employed in attempts to condense any volatile products contained in the exit gases issuing from the reaction vessel.

Series I.

Chlorine trifluoride (32 gm.) was passed into the vigorously stirred reaction mixture over a period of approximately three hours with a nitrogen stream of 10l./hr. After blowing nitrogen through the apparatus for an additional ½ hour the reaction mixture was poured onto anhydrous potassium fluoride (100 gm.) and shaken for two hours to remove any remaining traces of hydrogen fluoride. During this period the colour of the solid material changed from dark green to black and the colour of the solution from pale orange to yellow-brown. On filtering the mixture, the volume of the filtrate was 454 ml. i.e. a loss of 96 ml. on the initial volume of

liquid in the reaction vessel. The residue was washed with additional carbon tetrachloride and the combined filtrate and washings (660 ml.) rapidly distilled under reduced pressure to remove the excess carbon tetrachloride, using two receivers in series the first cooled in alcohol-drikold mixture and the second in liquid nitrogen. The carbon tetrachloride distilled off as a colourless liquid (volume 598 ml.) at 40°C under 80 mm. pressure and left behind a red liquid residue (volume 25 ml.) which contained pyridine derivatives, so the total loss of liquid during the distillation was 37 ml.

Since 2-fluoropyridine distils in carbon tetrachloride solution under reduced pressure the solvent fraction was analysed for combined fluorine after tests had shown the absence of free fluoride ion. A sample was fused with sodium and the resultant fusion solution titrated for fluoride:-

Weight of sample fused = 0.2326 gm.

$\frac{N}{20}$ Thorium nitrate titre = 0.6 ml.

This result indicated 11.3 gm. of 2-fluoropyridine in 598 ml. of carbon tetrachloride solution. To verify this figure 500 ml. of the solution were distilled down to

100 ml. using an electrically controlled fractionating column packed with nickel turnings and having a theoretical platage value of 28 with a take off ratio of one in thirty. This concentrated solution turned yellow on standing, an effect characteristic of 2-fluoropyridine solutions, and a sample (0.264 gm.) on fusion gave a N/20 thorium nitrate titre of 2.88 ml. thus indicating 9.53 gm. of 2-fluoropyridine in the solution. Taking into account decomposition during the distillation process and the time of standing this figure agreed substantially with that previously obtained.

In order to prove conclusively that it was 2-fluoropyridine present in the carbon tetrachloride a sample (500 ml.) of the concentrated solution was fractionated through an electrically controlled, 35 cm. distillation column packed with Fenske helices until the volume was reduced to 4 ml. This liquid residue was dark yellow in colour N_D^{20} 1.4687 as against N_D^{20} 1.4678 for 2-fluoropyridine (Roe and Hawkins, J.A.C.S., 69, 2443, 1947). Further distillation from a small blaisen flask yielded:-

a) a small quantity of impure carbon tetrachloride

b) 1 gm. of 2-fluoropyridine B.P. 128. N_D^{20} 1.4677.

c) 0.7 gm. of tar.

This showed that although the amount of 2-fluoropyridine in the carbon tetrachloride could be estimated by titration, its isolation involved a large amount of decomposition so that the actual amount isolated was much lower than that estimated.

The remaining 50 mls. of concentrated carbon tetrachloride solution were refluxed with concentrated hydrochloric acid for $8\frac{1}{2}$ hours at 100°C. and after cooling, the resultant acid layer was separated off and neutralised with concentrated sodium hydroxide solution. On addition of excess bromine water a white precipitate was obtained, which was filtered off, recrystallised from water and yielded 0.35 gm. of a white crystalline compound of melting point 208°C. This was 3.5-dibromo-2-hydroxypyridine and confirmed the presence of 2-fluoropyridine in the carbon tetrachloride solution.

To return to the red liquid residue (25 ml.) left after removal of the carbon tetrachloride solution by reduced pressure distillation, it was found that decomposition rapidly set in turning the liquid black in

colour. In an attempt to characterise the components of this liquid, before decomposition occurred to any great extent, the liquid was rapidly distilled from a small Claisen flask and the following fractions collected in receivers cooled in an alcohol-drikold freezing mixture:-

1) B.P.$_{12}$ 20°-30°C	Weight 14.1 gm.	Colourless liquid N_D^{20} 1.4650
2) B.P.$_{12}$ 37°-40°C	Weight 6.44 gm.	Pale yellow liquid N_D^{20} 1.4770
3) B.P.$_{12}$ 54°-56°C	Weight 1.145 gm.	Colourless liquid. N_D^{20} 1.4840
4) B.P.$_{12}$ 65°-70°C	Weight 1.455 gm.	Pale brown liquid Decomposes with evolution of HF
5) Residual tar	Weight 7.00 gm.	

Fraction I, which solidified at the temperature of the alcohol-drikold bath, was slightly impure carbon tetrachloride and had no effect on dilute permanganate solution or bromine water. Fraction 2 however slowly decolourised these reagents while fractions 3 and 4

rapidly decolourised them, so showing the three liquids to be addition compounds. Analyses were carried out on fractions 2 and 3 for chlorine, fluorine and nitrogen but this procedure could not be followed with fraction 4 since it rapidly decomposed with the evolution of hydrogen fluoride:-

Fraction 2.	F = 14.82%	Fraction 3	F = 17.9%
	Cl = 13.39%		Cl = 20.79%
	N = 11.27%		N = 9.122%

These figures indicate the compounds to be addition compounds of the form $C_{10}H_4N_2F_2Cl$ and $C_{10}H_7N_2F_3Cl_2$ respectively but no absolute identification was possible. Fraction 1 was analysed for combined fluorine and a sample (0.1205 gm.) after fusion gave a N/20 thorium nitrate titre of 0.84 ml. so indicating 0.4525 gm. 2-fluoropyridine/ 14.1 gm.

The total organic material recovered in this experiment was 28.1 gm. and consisted of 2-fluoropyridine (11.75 gm., 19% yield), chlorofluoro addition compounds of pyridine (9.337 gm.) and organic tar (7.0 gm.) and thus represented 56.2% by weight of the initial pyridine employed.

Several similar experiments were carried out, the results of which are collected in Tables I and II (pages 84 and 86).

Series II.

Here the complete apparatus (diagram I) was employed.

The reaction mixture was treated with chlorine trifluoride (35 gm.), diluted with a nitrogen stream of 4 l/hr., over a period of $4\frac{1}{2}$ hours and the apparatus was then swept out with nitrogen for a further $\frac{1}{2}$ hour. Filtration of the reaction mixture yielded an orange liquid (458 ml.) on the surface of which was a layer of organic tar (12 ml.). Thus the apparent loss of liquid during the reaction was 80 ml. However blank experiments showed that a mixture of potassium fluoride (60 gm.) and cobaltous fluoride (10 gm.), which is present in the actual reaction mixture, was capable of absorbing 40 ml. of liquid when added to a solution of pyridine (50 gm.) in carbon tetrachloride (500 ml.) and so taking this into account the loss of liquid during the reaction was reduced to 40 ml. The organic tar was

separated off but attempts to distil it under reduced pressure led to decomposition with the evolution of hydrogen fluoride.

The receiver cooled in an alcohol-drikold bath was allowed to attain room temperature and the gas evolved (130 ml.) was collected over water in an aspirator. There remained in the receiver a small volume of a colourless liquid (10 ml.) and this boiled at 77°C (N_D^{20} 1.4618) so proving it to be pure carbon tetrachloride. Allowing for this further quantity of carbon tetrachloride the loss of liquid during the halogenation process was further reduced to 30 ml. The receiver cooled in liquid nitrogen contained an appreciable quantity of a colourless volatile liquid and on attaining room temperature 3700 ml. of gas were collected in the aspirator. In this case there was no liquid residue left in the receiver.

A sample of this gas (100 ml.) was analysed in a standard Orsat gas analyses apparatus and found to consist of inert gas (89.7%), oxygen (9.9%) and carbon dioxide (0.4%).

To ascertain whether or not the inert portion of the gas contained nitrogen trifluoride and saturated

halogenated hydrocarbons, formed by break down of the pyridine during the reaction, further analyses were carried out. A further sample of the gas was bubbled through alkaline pyrogallol to remove any oxygen and passed over phosphorus pentoxide to remove traces of moisture, it was then condensed in a Carius tube, cooled in liquid nitrogen, containing metallic sodium. The tube was then heated in a furnace for 1¼ hours at 110° - 115°C and the resultant fusion mixture worked up as in a normal sodium fusion. Titration of samples of the fusion solution with thorium nitrate and silver nitrate showed the absence of fluoride but amounts of chloride, equivalent to a titre of 4.5ml. of N/20 $AgNO_3$, were detected. The experiment was repeated but the tube was fused for 18 hours at 450°C and here traces of fluoride (equivalent to 0.6 ml. N/20 $Th(NO_3)_4$) were detected as well as chloride (equivalent to 9.1 ml. of N/20 $AgNO_3$).

Since only minute quantities of fluoride were detected it was unlikely that the gas contained any nitrogen trifluoride since under the fusion conditions employed the gas would react vigorously with the sodium to yield nitrogen and sodium fluoride (Simons, Fluorine Chemistry, 1, p. 86). The gas may however have

contained traces of chlorofluoromethanes formed by reaction between the carbon tetrachloride solvent and the chlorine trifluoride, for these compounds require much higher temperatures than those hitherto employed in order to bring about complete fusion with the sodium. This could explain the detection of appreciable quantities of chloride but merely traces of fluoride, however more experimental evidence is required to prove this point absolutely.

Other experiments were carried out under similar conditions and the results are listed in Table III (page 89).

A N A L Y T I C A L

S E C T I O N.

The Volumetric Determination of Fluorine, Chlorine and Nitrogen in Organic Compounds.

Introduction.

To enable complete characterisation of the products obtained in the halogenation of pyridine with chlorine trifluoride, an analytical method was required whereby the fluorine, chlorine and nitrogen content of these compounds could be accurately determined. Assuming that the fluorine, chlorine and nitrogen can be quantitatively converted to sodium fluoride, chloride and cyanide respectively, by fusing samples of the compounds with metallic sodium in a Nickel bomb, the simplest procedure would be by means of volumetric determinations involving the titration of fluoride, chloride and cyanide in the resultant fusion solutions.

Accurate methods for estimating the fluorine and chlorine content of organic chlorofluoro compounds, by fusing these compounds with sodium followed by titration of the fluoride and chlorine in the fusion solutions, have been known for some time: Musgrave and Smith (with Tatlow J.C.S. 1949, 3026). In these methods the fluoride is titrated with thorium nitrate and the chloride with silver nitrate using sodium alizarin sulphonate and dichlorofluorescein respectively as indicators. If however cyanide is present in the fusion solutions the chloride estimation becomes impracticable owing to the formation of silver cyanide,

though the fluoride titration remains unimpaired.

Beaty (Ph.D. Thesis) has stated that the sodium fusion method can be extended to compounds containing fluorine, chlorine and nitrogen, the fluorine being estimated as above, while the cyanide is estimated by titration with silver nitrate until permanent turbidity is produced i.e. Liebig's Method. A figure for the combined cyanide plus chloride content was said to be obtained by precipitating the chloride and cyanide as their silver salts with excess silver nitrate and then back titrating the residual silver nitrate with potassium bromide. From the cyanide and cyanide plus chloride figures, the chloride content could then be obtained by difference. Application of this method to the products derived from the halogenation of pyridine, however, gave inaccurate results. Firstly the cyanide titration, as stated, is carried out in solutions approximately 0.25N. in sodium hydroxide and it was found that an accurate end point was extremely difficult to obtain. It appeared that under these conditions of alkalinity the precipitation of silver oxide took place, obscuring the end point and so giving low titration figures. Secondly when the figure for cyanide was taken from that for the cyanide plus chloride it was found that often the resulting chloride

figure had a negative value i.e. the potassium bromide titration was indicating that the amount of silver nitrate left after reaction with the cyanide and chloride was greater than the amount originally added, which is of course an impossible state of affairs. Consequently after repeated attempts the method was rejected and a method capable of giving accurate results was devised as described below.

Since methods are available for the determination of fluoride in the presence of chloride and cyanide; and chloride separately in the presence of fluoride, the problem resolved itself into the separate estimation of chloride and cyanide when present together in solutions also containing fluoride. Consideration of this problem showed three main avenues of approach:-

a) Since the cyanide ion is capable of forming complexes with a wide variety of reagents, there was the possibility of forming some complex whereby the cyanide would be completely removed from solution so leaving the chloride to be determined by one of the standard volumetric procedures.

b) Liebig's method of estimating cyanide by

titrating with silver nitrate until permanent turbidity is produced, is not affected by the presence of halides since all silver salts, except the sulphide, are readily soluble in an excess of a solution of an alkali cyanide. Therefore, even though the method did not work in sodium hydroxide solution, there remained the alternative of trying to obtain good results in neutral solutions either by titrating until permanent turbidity is produced in the normal way or by using diphenyl carbazide to indicate the end point. Another variation that appeared possible was to carry out the titration in ammoniacal solution with potassium iodide as indicator, for here silver iodide is precipitated at the end point and it is much easier to observe than the turbidity obtained in the straight forward titration.

c) It is possible in gravimetric analyses to determine chloride or cyanide accurately by precipitating them quantitatively as their silver salts. In a solution of cyanide and

chloride it ought therefore to be possible, by the addition of excess silver nitrate, to cause quantitative precipitation of both silver chloride and silver cyanide. Back titration of the excess silver nitrate should then give an over-all figure for the combined chloride and cyanide in solution. If the actual amount of one of the ions is known by methods a) or b) then by difference the amount of the other ion can be determined.

With these considerations in view investigations were undertaken to devise a method by which the fluorine, chloride and nitrogen content of an organic compound could be determined to within $\pm$0.2% of the theoretical value.

The Determination of Chloride in the presence of Cyanide and Fluoride.

In a solution containing chloride and cyanide the latter ion can be completely removed by the addition of formaldehyde Graham, (J. Assoc. Official Agr. Chem. 10, 150, 1927, see Am. Abstracts, 2352, 1927) with which it reacts to form hexamethylene tetramine Kohn (M. 20, 904 see

Beilstein I, 565). The free chloride is then reacted with an excess of silver nitrate and the residual silver nitrate determined by titration with standard thiocyanate solution i.e. Volhard's Method. Using standard solutions of chloride plus cyanide experiments were carried out to ascertain the conditions necessary for the complete removal of the cyanide by formaldehyde, followed by titration of the chloride with silver nitrate. With actual fusion solutions the concentration of fluoride, chloride and cyanide would be approximately N/100 and in order to get a titration figure of reasonable magnitude the silver nitrate, used to estimate the chloride, would have to be of similar strength. At this dilution the reddish-brown colouration given at the end point of the Volhard Method, due to the formation of the complex thiocyanate ion, is unsatisfactory and so, instead of adding excess silver nitrate, it was decided first of all to attempt direct titration of the chloride using some adsorption indicator to give a sharp end point.

Dichlorofluorescein was chosen first for in neutral solutions this indicator can be used down to 0.0005N.Cl^-. T.B. Smith (Analytical Processes p. 161.). Standard sodium chloride was titrated with silver nitrate using this indicator and then various quantities of formaldehyde, cyanide, fluoride and alcohol were added to ascertain their

individual and combined effects on the titration. The results obtained are tabulated below:

Table I.

	NaCl. 0.025N. ml.	KCN. 0.0768N. ml.	EtOH. ml.	HCHO. 0.10N. ml.	NaF. 0.10N. ml.	$AgNO_3$. 0.10N. ml.
1.	10.0	-	-	-	-	5.02
2.	10.0	-	-	1.0	-	5.02
3.	10.0	-	-	2.0	-	5.01
4.	10.0	-	-	3.0	-	5.01
5.	10.0	-	-	4.0	-	5.01
6.	10.0	2.0	-	1.0	-	No end point
7.	10.0	2.0	-	2.0	-	5.01
8.	10.0	2.0	-	2.0	-	5.01
9.	10.0	2.0	-	2.0	2.0	5.02
10.	10.0	2.0	0.2	2.0	2.0	5.02
11.	10.0	2.0	0.4	2.0	2.0	5.01

Results 1-5 indicated that the presence of formaldehyde did not affect the titration. Solutions 6-11 were made up containing 1 ml. of 2N. sodium hydroxide and then neutralised to phenolphthalein with 2N. nitric acid

before titrating, so showing that the actual alkaline fusion solutions could be neutralised with no adverse effects. That formaldehyde completely destroyed the cyanide present was illustrated in results 7-11 and, where no clear end point was obtained as in 6, it was assumed that there was insufficient formaldehyde present to destroy all the available cyanide. The presence of fluoride and traces of alcohol in solutions 9, 10 and 11 showed no tendency to interfere and this is especially important since alcohol is used to destroy the excess sodium in the quantitative fusions and traces persist in the final fusion solutions even after evaporation. Also appreciable quantities of alcohol have been observed to interfere when dichlorofluorescein is used in a normal chloride estimation.

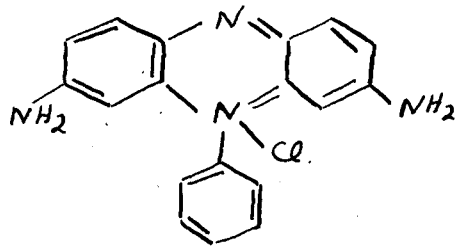
From the above results it appeared practicable to apply this method to actual fusion solutions. Samples (approx. 0.1 gm.) of pure o-chloro-nitrobenzene, sealed in glass capsules, were fused and the resultant fusion solutions, after evaporation, were each made up to a standard volume (100 ml.). Formaldehyde (2 ml.) was added to 10 ml. aliquots which were then neutralised to phenolphthalein with 2N. nitric acid and titrated with N/20 silver nitrate using three drops of dichlorofluorescein as

indicator. However in no case could an end point to any of these titrations be obtained. Returning to standard solutions it was found that in the same way no end point could be obtained if traces of sodium silicate were present. It was considered to be quite possible that traces of this were present after fusion with sodium in a glass capsule and evaporation of the fusion solution in a glass beaker in the presence of sodium hydroxide. A solution was therefore made up containing water (150 ml.), alcohol (50 ml.), 2N. sodium hydroxide (4 ml.) and N./10 sodium chloride (10 ml.) and evaporated down under conditions similar to the fusion solutions. Titrations carried out on this yielded correct results and therefore no traces of silicate could have been obtained from the glass evaporation vessel. Further samples of o-chloro-nitrobenzene were then fused in a nickel capsule but again no end point was discernable when the fusion solutions were titrated and this removed any possibility that traces of silicate were being introduced by fusing in glass capsules.

If the fusion solutions were titrated in slightly acid, instead of neutral solutions, the dichlorofluorescein gave a gradual colour change from green to pink but no sharp end point was obtained so it was decided to carry out

the titrations in distinctly acid solution. Dichlorofluorescein is a weak acid and can be used with a pH. as low as four but to carry out the titration of chloride in highly acid solutions basic dyes are best used since they are more highly ionized under these conditions. Bearing this in mind the use of Phenosafranine was investigated since it can be used in solutions up to 0.3N. in nitric acid T.B.Smith (Analytical Processes p. 164) and, at the equivalent point, the colour of the precipitate changes sharply from red to blue. When Phenosafranine was tested out on standard chloride solutions, which were 0.3N. in nitric acid and contained various quantities of formaldehyde, cyanide, fluoride and alcohol, as in the case of dichlorofluorescein (Table I), a violet colour spread throughout the solution obscuring the expected colour change on the precipitate. This effect appeared to be due to the presence of excess formaldehyde in the titration solution for if a sample of standard chloride solution, made 0.3N. in nitric acid, was titrated with silver nitrate the Phenosafranine gave a clear colour change on the precipitate at the correct titration figure but if then a small amount of formaldehyde was added the precipitate and solution turned violet. Thus it appeared that the formaldehyde was reacting with the free amino

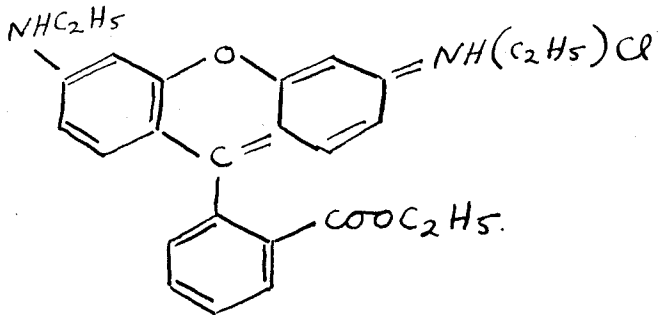
groups present in the dye:-



so altering its nature and causing the observed violet colouration. Attempts were made to destroy any excess formaldehyde by the addition of ethylamine to the titration solution before the phenosafranine was introduced but, although the presence of ethylamine itself did not interefere, a violet colouration still prevented any estimation from taking place.

In the previous methods the technique employed has been to destroy any cyanide with an excess of formaldehyde followed by direct titration of the chloride with silver nitrate in the presence of an acid or basic adsorption indicator. This technique having been so far without success an experimental procedure based on Volhard's Method was then devised in the following manner. If the cyanide was destroyed with formaldehyde as before, the chloride could then be precipitated with an excess of silver nitrate and, provided that the residual silver nitrate could be

accurately determined, a figure for the chloride content would result. Adapting the procedure of Vogel (Qnant. Inorg. Analy. p. 95.) the titration of the residual silver nitrate could be readily carried out with bromide as the precipitating agent and Rhodamine 6G. as indicator. A sharp end point is given, the precipitate turning violet, in solutions up to 2N. in nitric acid, though 0.3N. is preferable T.B. Smith (Analytical Processes p. 451). The basic indicator Rhodamine 6G.:-



has no free amino groups and should not therefore on that account react with excess formaldehyde as in the case of phenosafranine, which has two amino groups in the molecule.

Now in the estimation of chloride by Volhard's Method there are two equilibria during the titration of the excess silver ions with thiocyanate Vogel (Quant. Inorg. Anal. p. 92) i.e. :-

$$Ag^+ + Cl^- \rightleftharpoons AgCl$$

$$Ag^+ + CNS^- \rightleftharpoons AgCNS$$

The two sparingly soluble salts will be in equilibrium with the solution hence:-

$$\frac{[Cl^-]}{[CNS^-]} = \frac{SAgCl}{SAgCNS} = \frac{1.2 \times 10^{-10}}{7.1 \times 10^{-13}} = 170$$

When all the excess silver ion has reacted the excess of CNS^- may react with silver chloride, since silver thiocyanate is the less soluble salt, until the ratio $\frac{[Cl^-]}{[CNS^-]}$ in solution is 170

$$AgCl + CNS^- \rightleftharpoons AgCNS + Cl^-$$

This takes place before reaction occurs with the ferric ions in the solution and so there will be a considerable titration error, which can be prevented by the removal of silver chloride.

In an attempt to estimate excess silver nitrate with potassium bromide and Rhodamine 6G. as outlined above, a similar type of effect must be taken into consideration. Here the two equilibria during the titration of excess silver with bromide will be:-

$$Ag^+ + Cl^- \rightleftharpoons AgCl$$

$$Ag^+ + Br^- \rightleftharpoons AgBr$$

and again two sparingly soluble salts will be in equilibrium with the solution hence:-

$$\frac{[Cl^-]}{[Br^-]} = \frac{S\ Ag\ Cl}{S AgBr} = \frac{1.2 \times 10^{-10}}{3.5 \times 10^{-13}} = 343$$

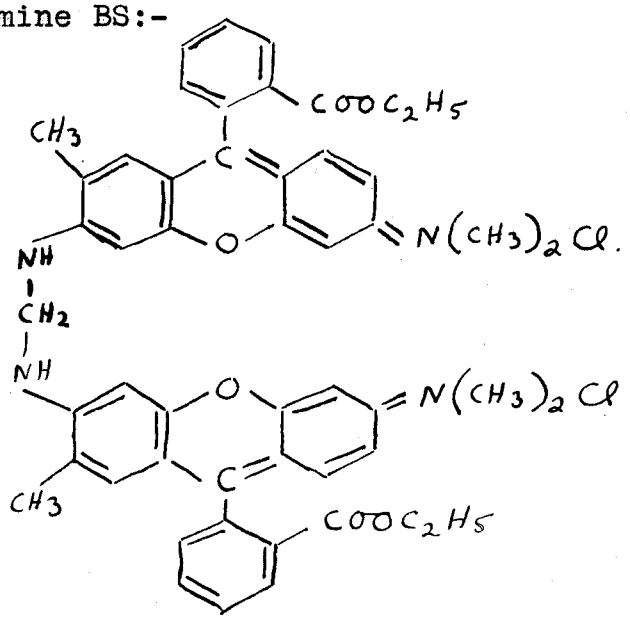
After all the excess silver ion has reacted the excess of bromide may react with silver chloride, as the silver chloride is the most soluble salt, until the ratio $\frac{[Cl^-]}{[Br^-]}$ is 343.

$$AgCl + Br^- \rightleftharpoons AgBr + Cl^-$$

The ratio $[Cl^-]/[Br^-]$ is much greater than the ratio $[Cl^-]/[CNS^-]$ obtained in the Volhard Method so the titration error could be correspondingly greater and therefore care would be needed to remove the precipitated silver chloride from solution before titration of the excess silver nitrate. The most effective method would be to filter off the precipitate and then back titrate filtrate and washings, though coagulation of the precipitate before back titration (by boiling or addition of ether or nitrobenzene thus making it more difficult to set up an equilibrium) should be almost as effective.

This method of chloride estimation having been proved possible in theory, it was then applied to synthetic

solutions of chloride plus cyanide in order to test its practical possibilities. As there was no Rhodamine 6G. readily available another dye of the same series was used. This was Rhodamine BS:-



which like Rhodamine 6G. has no free amino groups in its structure and should not be effected by formaldehyde. 10 ml. samples of silver nitrate (N/100), made 0.3N. in nitric acid, were titrated with potassium bromide (N/100) using three drops of Rhodamine BS. (0.05% aqueous solution) as indicator and in each case a sharp end point was obtained, which was as good as that described for Rhodamine 6G. Various amounts of formaldehyde were then added to the standard chloride solution to see if it affected the indicator but in each case an excellent titration figure was

obtained showing that formaldehyde in no way impaired the properties of Rhodamine BS, (see Table II). It was found expedient, however, to carry out the titration as rapidly as possible for the indicator began to turn blue 10 - 12 minutes after starting to add the potassium bromide whether or not the titration was complete.

Table 2.

$AgNO_3$ 0.01015N. ml.	Concentrated HNO_3 ml.	Rhodamine BS No. of drops	HCHO 0.10N. ml.	KBr 0.0256N. ml.
10.12	0.2	3.0	-	4.04
10.12	0.2	3.0	-	4.05
10.12	0.2	3.0	1.0	4.05
10.12	0.2	3.0	2.0	4.04
10.12	0.2	3.0	3.0	4.04

To approximate to the concentrations of fluoride, chloride and cyanide present in actual fusion solutions, a synthetic solution was prepared being 0.01007N. in sodium

chloride, 0.01025N. in sodium fluoride and 0.01032N. in potassium cyanide. The method employed to estimate the chloride was then as follows:-

Add formaldehyde (2 ml.) to an aliquot (10.12 ml.) of solution and neutralize to phenolphthalein with 2N. nitric acid. Then add concentrated nitric acid (2 ml.) and 0.05N. silver nitrate (10.12 ml.). Filter through a Whatman Number 50 paper and make filtrate and washings up to a standard volume (100.5 ml.). Aliquots (10.12 ml.) plus 3 drops of Rhodamine BS. were then titrated with potassium bromide (0.0256N.) and a titre of 1.60 ml. was obtained. In the following calculation it was assumed that 100.5 ml. of original standard solution were obtained by fusing 0.13 gm. of organic compound, in order to get a percentage figure for the chlorine content and compare it with the calculated value.

Calculated Value.

10.12 ml. of 0.01007N. NaCl = 2.038 ml. of 0.05N. $AgNO_3$

$$\text{Chlorine content} = \frac{2.038 \times 0.05 \times 35.46 \times 100 \times 100.5}{1000 \times 0.13 \times 10.12}$$

$$= \underline{27.61\%}.$$

Determined Value.

KBr titre = 1.60 ml.

Equivalent to amount of excess silver nitrate in 10.12 ml. aliquot of original solution. $= 1.6 \times \frac{0.0256}{0.05} \times \frac{100.5}{10.12}$ ml.

$= 8.132$ ml. $AgNO_3$.

thus silver nitrate used by Cl^- = 10.12 - 8.132 ml.

$\therefore$ = 1.988 ml.

$\therefore$ Chlorine content $= \frac{1.988 \times 0.05 \times 35.46 \times 100 \times 100.5}{1000 \times 0.13 \times 10.12}$

= 26.93%.

The result obtained was 0.67% lower than the calculated value and was beyond the desired $\pm$0.2% margin of error but the method was then applied to fusion solutions, to see if the same degree of accuracy could be obtained, before attempting to make the method more accurate. Samples of o-chloro-nitrobenzene (22.54% chlorine) were fused and after evaporation the fusion solutions were in each case made up to a standard volume (100.5 ml.). 10.12 ml. aliquots were then treated with formaldehyde, nitric acid, and silver nitrate, and titrated with potassium bromide as in the case of the standard solution.

(1) Weight of sample 0.1740 gm.

KBr titre on 10.12 ml. aliquot is 1.53 ml.

Excess $AgNO_3$ in 10.12 ml. aliquot of original fusion solution. $= 1.53 \times \frac{0.0256}{0.05} \times \frac{100.5}{10.12}$ ml.

$= 7.776$ ml.

$AgNO_3$ required by Cl^- $= 10.12 - 7.776$ ml. $= 2.344$ ml.

Chlorine content $= \frac{2.344 \times 0.05 \times 35.46 \times 100 \times 100.5}{1000 \times 0.1740 \times 10.12}$

$= \underline{23.71\%}$.

(2) Weight of sample = 0.1534 gm. Chlorine content = 24.84%

(3) Weight of sample = 0.1121 gm. Chlorine content = 24.50%

(4) Weight of sample = 0.1369 gm. Chlorine content = 24.17%

The results gave figures for the chlorine content which were from 1.17% to 2.3% higher than the calculated value. Consideration of the titration figures, illustrated above, however showed that a very small error in the amount of silver nitrate added to the aliquot of fusion solution or in the final potassium bromide titration figure, would have an exaggerated effect on the final figure for the chlorine content. For example, in fusion I, if instead of 2.344 ml. the amount of silver nitrate used by the Cl^- had been 2.228 ml., the result would have been correct i.e. a difference of 0.116 ml.

of silver nitrate make an error of 1.17% in the final results. This figure represented an increase of only 0.022 ml. in the KBr titration figure and was within the limits of experimental error. Since in two stages of the method 10 ml. aliquots were taken from volumes of 100 ml., any error became multiplied one hundredfold and so, in order to get more accurate results, larger aliquots would have to be taken and/or the concentrations of the reagents reduced in order to improve the sensitivity of the final bromide titration. The effect of increasing the aliquot of solution taken was tried first. A sample of o-chloro-nitrobenzene was fused and the solution finally made up to a standard volume (100 ml.). A 50 ml. aliquot of this was treated with formaldehyde (10 ml.), nitric acid (1 ml.) and excess silver nitrate (10 ml.) as usual, but after filtering, the filtrate and washings were evaporated down to a small volume and then made up to 50 ml. The whole of this solution was then titrated with potassium bromide and gave a figure for the chlorine content still 2.06% higher than the calculated value. This tended to show that the size of the aliquot taken was not the most critical factor in the estimation and that even though the multiplication factor was further reduced by titrating the total filtrate and washings, after evaporation and making up to a convenient volume, the method was still

insufficiently accurate. A further attempt was made, using a synthetic solution, to increase the accuracy of the method by taking a large aliquot (50 ml.), titrating the filtrate and washings without evaporating or making up to a standard volume; and also by reducing the strength of the silver nitrate and potassium bromide to approximately N./100. Assuming for the purpose of calculation that 100 ml. of synthetic solution was produced by fusing a certain weight (0.16 gm.) of organic compound, this procedure gave results of 22.33% to 22.35% chlorine as against a calculated value of 22.36%. These figures are practically identical with the calculated value so it appeared that under these conditions the errors in the method were sufficiently reduced to give results well within the required $\pm$0.2% margin of error. This procedure was then applied to fusion solutions of o-chloro-nitrobenzene (22.54% chlorine) with the following results:-

I. Weight of sample = 0.1239 gm. Chlorine content = 22.48%

II. Weight of sample = 0.1458 gm. Chlorine content = 22.45%

III. Weight of sample = 0.1376 gm. Chlorine content = 22.45%

Compared with the theoretical value of 22.54% these results represent a maximum error of 0.09% which shows the method to be emminently suitable when applied to fusion

solutions of organic compounds containing chlorine, fluorine and nitrogen.

It was found that, if the silver chloride was not filtered off, the results obtained were still within $\pm$0.2% of the theoretical value. In view of the calculation concerning the interaction of silver chloride and Br^- ion, from which one would expect a more inaccurate titration figure than this, it seems probable that the silver chloride was extremely well coagulated and so virtually removed from solution, there being no time for it to react before the excess bromide in solution caused the indicator change. However it was still considered best to remove the silver chloride by filtration and so to eliminate any possible source of error in the titration figures.

In view of the results put forward the estimation of chloride in fusion solutions which also contain fluoride and cyanide can be summarized as follows:-

Fuse 0.1 to 0.2 gm. of the organic compound and, after evaporation, make the fusion solution up to a standard volume (100 ml.). Treat half of the solution with N/10 aqueous formaldehyde (10 ml.) and neutralise to phenolphthalein with 2N. nitric acid. Then add concentrated nitric acid (2ml.) followed by an excess of N/100 silver nitrate. Filter

off the silver chloride using a Whatman Number 50 paper and wash the precipitate several times with small quantities of distilled water. Finally titrate the filtrate and washings with N/100 potassium bromide using 6 drops of Rhodamine BS. (0.05% aqueous solution) as indicator.

The Attempted Determination of Cyanide in the presence of Chloride and Fluoride.

Since the method devised for the estimation of chloride, in the presence of cyanide and fluoride, gave accurate results the next stage in the problem was to investigate the methods for determining the cyanide content of similar solutions.

As previously stated the titration of cyanide with silver nitrate (Liebig's method) did not give accurate results when carried out in solutions approximately 0.25N. in sodium hydroxide, but it was still considered possible that accurate results could be obtained if the method was applied to neutral or ammoniacal solutions. Here it was hoped to get an accurate end point by titrating with silver nitrate until permanent turbidity was obtained, as in the usual manner, or by addition of a suitable indicator; diphenyl carbazide in neutral, or potassium iodide in ammoniacal solution.

The theory of the reaction in neutral and ammoniacal solutions was investigated in order to ascertain their suitability for quantitative estimations of cyanide and to calculate what titration errors could be expected:

(1) Neutral solutions.

When silver nitrate is gradually added to a solution of an alkali cyanide a white precipitate first forms but this redissolves owing to the formation of a soluble complex cyanide:-

$$AgNO_3 + 2KCN. \rightleftharpoons K.[Ag(CN)_2] + KNO_3 \quad .....(1)$$

or $$Ag^+ + 2CN^-. \rightleftharpoons [Ag(CN)_2]^- \quad .....(2)$$

Completion of the above reaction is indicated when further addition of silver nitrate yields the insoluble silver argentocyanide:-

$$Ag^+ + [Ag(CN.)_2]^- \longrightarrow Ag[Ag(CN.)_2] \quad .....(3)$$

The formation of permanent turbidity therefore indicates the end point of the reaction. Application of the Law of Mass Action to equation (2) gives the dissociation or instability constant of the complex at normal temperatures. Vogel (Quant. Inorg. Anal. p. 23):-

$$\frac{[Ag^+]\ [CN^-]^2}{[Ag(CN)_2^-]} = 1.0 \times 10^{-21} \quad \ldots\ldots\ldots\ldots\ldots\ldots(4)$$

As an illustration, if an amount of potassium cyanide equivalent to 10 ml. of 0.1N. silver nitrate is used and the volume at the end point is 100 ml., then the concentration of the complex $K[Ag(CN.)_2]$ will be 0.01 molar. Then at this point any silver ion and cyanide ion present in solution will be due to the dissociation of the complex. At the stoichiometric point:-

$$[CN.^-] = 2[Ag^+] = 2\alpha$$

therefore $1.0 \times 10^{-21} = \frac{[Ag^+][CN^-]^2}{[Ag\ (CN)_2^-]} = \frac{(\alpha) \times (2\alpha)^2}{0.01}$

and so $[Ag^+] = 1.36 \times 10^{-8}$ and $[CN^-] = 2.72 \times 10^{-8}$

From Smith (Anal. Processes p. 248) the solubility product:-

$$[Ag^+][Ag(CN)_2^-] = 2.25 \times 10^{-12} \quad \ldots\ldots\ldots\ldots\ldots(5)$$

therefore precipitation of the complex will occur when,

$$[Ag^+] > \frac{2.25 \times 10^{-12}}{[Ag(CN)_2^-]} > \frac{2.25 \times 10^{-12}}{0.01} > 2.25 \times 10^{-10}$$

Since the $[Ag^+]$ at the theoretical end point is 1.36×10^{-8} precipitation will occur just before this but the titration difference is so small (0.0002 ml.) that it can be neglected and in any case the theoretical end point will be

exceeded in order to produce sufficient precipitate to be visible. In theory, therefore, this method should be capable of accurate results but one practical difficulty would be to see when permanent turbidity was first produced.

Using diphenyl carbazide as indicator, the end point is marked by the colour of the indicator changing from pink to pale violet. In dilute solutions (ca. 0.01N.) this change takes place on the colloidal precipitate before opalescence is visible, Vogel (Quant. Inorg. Anal. p. 327.), while in 0.1N. solutions the change is observed on the precipitated silver argentocyanide.

(2) Ammoniacal solutions.

If an ammoniacal solution of cyanide is titrated with silver nitrate solutions using potassium iodide as indicator, the silver argentocyanide is not precipitated as it is readily soluble in ammonia:-

$$Ag\left[Ag(CN.)_2\right] + 4NH_4OH \longrightarrow 2\left[Ag(NH_3)_2\right]CN. + 4H_2O \quad ...(6)$$

and at the end point sparingly soluble silver iodide will be precipitated since the cyanide, in which it is soluble, is no longer present in solution.

$$2\left[Ag(NH_3)_2\right]CN + 2KI + 4H_2O \longrightarrow 2AgI + 2KCN. + 4NH_4OH \quad ..(7)$$

The instability constant of the complex cation $\left[Ag(NH_3)_2\right]^+$ is:-

$$\frac{[Ag^+][NH_3]^2}{[Ag(NH_3)_2^+]} = 7 \times 10^{-8} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots(8)$$

and its relatively large value compared with that for the argentocyanide anion shows the amine to be the less stable complex and therefore when silver nitrate is added to the mixture of cyanide and ammonia, the greater part will form the negative complex ion but the end point of the titration may be influence to a perceptible extent by a considerable quantity of ammonia. Smith (Analytical Processes p. 250).

This influence can be illustrated by the following examples:-

Suppose volume of solution = 100 ml. and $[NH_3] = 0.2$

Then $[\text{Total cyanide}] = 0.02 = 2[Ag(CN.)_2^-] + [CN.^-]$ ....(9)

a) at equivalence point

Total silver $= 0.01 = [Ag(CN.)_2^-] + [Ag(NH_3)_2^+] + [Ag^+]$..(10)

therefore $[Ag(CN.)_2^-] \gg [Ag(NH_3)_2^+] \gg [Ag^+]$

From (9) and (10) $[CN^-] \doteqdot 2[Ag(NH_3)_2^+]$

Put $[Ag(NH_3)_2^+] = \alpha$ and substitute (8)

$$[Ag^+] = 1.75 \times 10^{-6}\alpha$$

substitute this value into (4) and assume that $[Ag(CN)_2^-] \doteqdot 0.01$ i.e. neglect $[CN.^-]$ therefore,

$$10^{-21} = \frac{(1.75 \times 10^{-6}\alpha)(2\alpha)^2}{0.01}$$

then $\alpha = \left[Ag(NH_3)_2^+\right] = 1.13 \times 10^{-6}$

$2\alpha = \left[CN^-\right] = 2.26 \times 10^{-6}$

$1.75 \times 10^{-6}\alpha = \left[Ag^+\right] = 1.97 \times 10^{-11}$

$\left[Ag(CN.)_2^-\right] = 0.01 - \frac{1}{2}\left[CN^-\right] = 0.01 - 1.13 \times 10^{-6}$

These are the concentrations at the ideal end point.

(b) <u>At an actual end point when no special indicator is used</u>:-

From (5) $\left[Ag^+\right] = \frac{2.25 \times 10^{-12}}{0.01} = 2.25 \times 10^{-10}$

substitute this value in (8) whence $\left[Ag(NH_3)_2^+\right] = 1.3 \times 10^{-4}$

substituting the value for $\left[Ag^+\right]$ in (4), $\left[CN^-\right] = 2.1 \times 10^{-7}$

therefore $\left[Ag(CN.)_2^-\right] = 0.01 - 0.5\left[CN^-\right] = 0.01 - 1.1 \times 10^{-7}$

From (10):-

$$\left[\text{Total } Ag^+\right] = (0.01 - 1.1 \times 10^{-7}) + 1.3 \times 10^{-4} + 2.25 \times 10^{-10}$$

The difference between this and the ideal value of 0.01 is then:-

$$-1.1 \times 10^{-7} + 1.3 \times 10^{-4} + 2.25 \times 10^{-10} = 1.3 \times 10^{-4}$$

Hence the result will be 1.3% too high, due almost entirely to the fact that $\left[Ag(NH_3)_2^+\right] \gg$ than at equivalence points.

(c) <u>At the actual end point when KI is used as indicator</u>:-

Suppose at end point $[I^-] = 0.1$

then $[Ag^+] = \frac{ks}{[I^-]} = \frac{10^{-16}}{10^{-1}} = 10^{-15}$

Hence from (8) $[Ag(NH_3)_2^+] = 5.7 \times 10^{-10}$

and from (4) $[CN^-] = 10^{-4}$ (assume $[Ag(CN)_2^-] = 0.1$)

$[Ag(CN)_2^-] = 0.01 - 5 \times 10^{-5}$

The error in this case is $-5 \times 10^{-5} + 5.7 \times 10^{-10} + 10^{-15} = .5 \times 10^{-4}$ in 0.01 i.e. -0.5% (0.05 ml. in a 10 ml. titration, which is about experimental error). In practice, however, it will be less than this because a small quantity of extra silver nitrate will be required to produce a visible precipitate of silver iodide. No appreciable error is therefore caused by the presence of ammonia and its presence is advantageous because the precipitate, which tends to form when the titration is nearing completion, redissolves more readily than does the silver argentocyanide in the original method.

The previous calculations having shown that theoretically good results can be obtained by applying Liebig's Method

to neutral or ammoniacal solutions of alkali cyanides, experiments were carried out on solutions containing fluoride, chloride and cyanide to test the practical possibilities of the method.

A solution was made up containing sodium chloride (0.01002N.), sodium fluoride (0.0100N.) and potassium cyanide (0.01078N.) and aliquots (10 ml.) titrated with silver nitrate (0.01004N.). For the purpose of obtaining a figure for the calculated nitrogen content and comparing it with the experimental values obtained, it was assumed that 100 ml. of this solution were obtained by fusing 0.15 gm. of an organic compound.

10.11 ml. of 0.01078N. KCN. $\equiv$ 5.429 ml. of 0.01004N. $AgNO_3$

therefore calculated Nitrogen content $= \frac{5.429 \times .01004 \times 28 \times 100 \times 100}{1000 \times .15 \times 10.11}$

$= \underline{10.07\%}$

a) Straight forward titration of this solution, which is very slightly alkaline due to the alkali cyanide, with silver nitrate until permanant turbidity was produced gave titration figures averaging 0.1 ml. lower than the calculated value of 5.429 ml. This gave a figure of 9.879% for the nitrogen content, which is 0.191% too low and since this represented the extreme limit of accuracy

desired in the estimation i.e. ±0.2% it was necessary to try diphenyl carbazide as indicator, in an attempt to get a sharper end point. When this indicator was used, however, the results did not improve as it was found difficult to ascertain with accuracy the exact point at which the indicator gave the colour change from pink to violet.

The difficulty in obtaining a sharp end point lies in the fact that silver cyanide is often precipitated in a curdy form, which does not readily redissolve and this obscures the end point tending to give a premature turbidity so leading to low titration figures.

b) To try and overcome this effect the titration solution was made ammoniacal with ammonium hydroxide and a small quantity of potassium iodide added as indicator. The end point of the titration was indicated by the precipitation of silver iodide, which proved much easier to detect than the previous permanent turbidity and so led to improved results.

Aliquots (10 ml.) of solution were treated with 6N. ammonium hydroxide (2 ml.) and N/10 potassium iodide (2 drops) before titrating with silver nitrate (0.01004N.)

until a permanant precipitate of silver iodide was detected.

Table III.

Silver Nitrate titre. ml.	% Nitrogen Content	% Variation from Calculated value of 10.07 %
5.45	10.1	0.03
5.48	10.16	0.09
5.47	10.14	0.07
5.48	10.16	0.09

Since the results obtained were all well within the $\pm$0.2% margin of error, the method was then applied to actual fusion solutions of o-chloro-nitrobenzene (8.888% nitrogen). As for the chloride estimation, samples of the compound (approximately 0.1 gm.) were sealed in glass capsules, fused with excess sodium in a nickel bomb and after evaporation the resultant fusion solutions made up to standard volumes (100 ml.). Aliquots (10 ml.) were neutralised with 2N.HNO_3 and then treated as in the case of the standard solution and gave the following results:-

Table IV.

Wt. of cpd. taken. gm.	Calculated silver nitrate titration. ml.	Observed Titration ml.	%Nitrogen Content.	%Variation from Calculated value of 8.888 %
0.1099	3.478	1.67	4.268	4.62
0.1355	4.289	2.40	4.979	3.909
0.1910	6.046	3.00	4.416	4.472

In each case a titration figure was obtained which indicated a nitrogen content approximately 50% of the calculated value and the end points were not distinct but were marked by a blue opalescence in the titration solution, which gradually turned to a yellow precipitate as more silver nitrate was added. Variation of the amounts of ammonium hydroxide and potassium iodide added to the solution did not improve the results so it was concluded that:-

a) There was some substance present in the fusion solutions which was either causing a premature end point to the silver nitrate titration or reacting with the cyanide and so removing part of it from solution.

b) The sodium fusion did not give quantitative conversion of the nitrogen, in the organic compound, to cyanide. When samples of the synthetic solution, containing traces of sodium silicate, were treated as before, titration figures of 5 ml. silver nitrate were obtained i.e., the titration figure was lowered by 0.45 ml. to 0.48 ml. so giving a nitrogen content of approximately 9.0 % as against the calculated value of 10.07%. It seemed therefore that traces of silicate could not be responsible for the 50% error when the method was applied to fusion solution; this is confirmed by tests carried out during the chloride estimation which showed that little or no silicate was obtained by fusing the organic compound in glass capsules and evaporating the fusion solution down in glass beakers. To prove this, aliquots (10 ml.) of the fusion solutions were neutralised with 2N. nitric acid and then an excess of 2N. nitric acid (2 ml.) was added. The solution was then distilled to dryness, so leaving behind any silicate, borate etc., and the distillate, after neutralising with 2N. sodium hydroxide, was treated as before and titrated with silver nitrate. The same blue opalscence was observed in each case and the

titration figures substantially agreed with those previously obtained so showing that silicate was not causing the low results. It would seem from this that either something in the fusion solution was reacting with the cyanide or that the nitrogen was not completely converted to cyanide, for any other interfering substance would be left behind when the solutions were distilled to dryness. Before investigating this problem further it was considered expedient to attempt to devise an overall method for determining cyanide plus chloride, from which the cyanide value could be obtained by difference, since as has already been seen the chloride content could be accurately obtained.

The Attempted Determination of Cyanide plus Chloride in the presence of Fluoride.

The proposed method, by which it was hoped to obtain a value for the combined chloride plus cyanide content of fusion solutions, was basically the same as that employed to determine chloride in the presence of fluoride and cyanide. By omitting the formaldehyde, which would remove the cyanide, the addition of excess silver nitrate should result in the quantitative precipitation of silver chloride

and silver cyanide. Back titration of the residual silver nitrate with bromide should therefore give a figure for the combined chloride plus cyanide present in the solutions.

If the precipitated silver salts are left in contact with the solution, there will be three equilibria during the titration of excess silver ion with potassium bromide:-

$$Ag^+ + Cl^- \rightleftharpoons AgCl$$
$$Ag^+ + CN^- \rightleftharpoons AgCN$$
$$Ag^+ + Br^- \rightleftharpoons AgBr$$

and the insoluble salts will be in equilibrium with the solution hence:-

$$\frac{[Cl^-]}{[Br^-]} = \frac{SAgCl}{SAgBr} = \frac{1.2 \times 10^{-10}}{3.5 \times 10^{-13}} = 343$$

$$\frac{[CN^-]}{[Br^-]} = \frac{SAgCN}{SAgBr} = \frac{2.8 \times 10^{-12}}{3.5 \times 10^{-13}} = 8.3$$

When the excess silver ion has reacted, then the excess bromide can react with AgCl until the ratio $[Cl^-] / [Br^-]$ in solution is 343 and with AgCN until the ratio $[CN^-] / [Br^-]$ is 8.3.

$$AgCl + Br^- \rightleftharpoons AgBr + Cl^- \quad \ldots\ldots\ldots\ldots (1)$$

$$AgCN + Br^- \rightleftharpoons AgBr + CN^- \quad \ldots\ldots\ldots\ldots (2)$$

Under these conditions one would expect a considerable titration error, larger than that theoretically possible in the chloride estimation where reaction (1) only takes place, so once again to avoid any titration errors the precipitate should be removed from solution before titrating with bromide. Vogel (Quant. Inorg. Anal. p. 92). A standard solution was prepared containing sodium chloride (0.01002N.), sodium fluoride (0.01028N.) and potassium cyanide (0.01078N.) with which to investigate the proposed method. First of all, to ascertain what magnitude of titration error could be expected if the precipitate was not removed from solution, the following technique was adopted.

An aliquot (10.11 ml.) of solution was neutralised to phenolphthalein with 2N. nitric acid, concentrated nitric acid (1 ml.) and excess silver nitrate (25.2 ml.) was then added. The solution was then titrated with potassium bromide (0.01276N.) using 3 drops of Rhodamine BS as indicator. The observed titre was 5.05 ml. of potassium bromide.

In the following calculation and in all subsequent

calculations involving standard solutions, it was assumed that 100 ml. of original solution was obtained by fusing 0.16 gm. of an organic compound.

Theoretical Nitrogen Content.

10.11 ml. 0.01002 N. NaCl ≡ 10.11 ml. 0.01002 N. $AgNO_3$

10.11 ml. 0.01076 N. KCN ≡ 10.86 ml. 0.01002 N. $AgNO_3$

Excess $AgNO_3$ added = = 25.2 ml.

therefore $AgNO_3$ required to precipitate total chloride plus cyanide = 20.96 ml.

∴ Titratable residue = 4.24 ml. $AgNO_3$ ≡ 3.329 ml. KBr

$$\text{Nitrogen content} = \frac{10.86 \times .01002 \times 14 \times 100 \times 100}{1000 \times 0.16 \times 10.11}$$

$$= \underline{9.419\ \%}$$

Experimental Nitrogen Content.

KBr titre = 5.05 ml. ≡ 6.433 ml. $AgNO_3$

∴ Silver nitrate required to precipitate chloride plus cyanide = 25.2 - 6.433 ml.

= 18.767 ml.

Assuming that the chloride reacts with the theoretical amount of silver nitrate (as shown by the results obtained

in the chloride estimation) then:-

$AgNO_3$ required to precipitate total cyanide = 18.767 - 10. 11 ml.

= 8.66 ml.

$$\text{Nitrogen Content} = \frac{8.66 \times .01002 \times 14 \times 100 \times 100}{1000 \times 0.16 \times 10.11}$$

= 7.509 %.

The low results obtained indicated that it was essential to remove the precipitate before titrating the solution, as was predicted by the theoretical consideration, but since good results have been obtained, without filtration, in the chloride estimation it appeared that the error was due to the presence of silver cyanide only. It is possible that the reaction:-

$$AgCN + Br^- \rightleftharpoons AgBr + CN^-$$

goes with a greater velocity than the reaction:-

$$AgCl + Br^- \rightleftharpoons AgBr + Cl^-$$

due perhaps to the silver cyanide being in a more colloidal state than the silver chloride, and thus causing an appreciable titration error before the indicator colour change.

A second aliquot was similarly treated but the solution

was filtered through a Whatman Number 50 Paper and the precipitate washed with small quantities of distilled water. When the filtrate and washings were titrated with potassium bromide a titre of 4.0 ml. was obtained which gave a nitrogen content of 8.664 %. This was a distinct improvement but was still 0.775% too low and since this method of filtration yielded excellent results in the chloride estimation, then the error must be due to traces of colloidal silver cyanide passing through the filter. Assuming this to be solely responsible for the titration error various methods of coagulating the precipitate, before filtering, were investigated. In each case 10.0 ml. aliquots of solution were used and 30 ml. of excess silver nitrate were added.

Table V.

	Method of coagulating precipitate.	KBr titre ml.	% Nitrogen Content.	% Variation from calculated value of 9.419 %
1.	1 ml. Nitrobenzene added.	8	8.64	0.779
2.	5 ml. ether added	7.92	8.73	0.689
3.	Solution heated and then cooled.	7.92	8.73	0.689

These results showed a little improvement but were still too low to make the method practicable for accurate analyses. Different methods of filtration were tried next - a) filter through a thick charcoal pad based on a No. 50 filter paper. b) filter through a No. 4 sintered glass crucible, with and without an asbestos pad. The results showed no great improvement whether or not ether and nitrobenzene were used to coagulate the precipitate before filtering, values obtained varied from 8.53% to 8.64% for the nitrogen content, i.e. 0.889% to 0.779% lower than the calculated value.

Since the above variations in the filtering technique and the coagulation of the precipitate with ether or nitrobenzene did not lead to improved results, other modifications in the method were desired. Vogel (Quant. Inorg. Anal. p. 475 and 578) states that, if the precipitate is washed with pure water it may become colloidal and pass through the filter, so washing with a suitable electrolyte (0.01 N., nitric acid) is recommended. Also, to precipitate silver cyanide, the cold solution of an alkali cyanide should be treated with an excess of silver nitrate faintly acidified with nitric acid.

Bearing these recommendations in mind the procedure was modified accordingly and gave results 0.619% lower than the calculated value for the nitrogen content and represented a slight improvement on the previous values obtained. Still in the belief that traces of colloidal silver cyanide, passing through the filter into the titration solution, were responsible for the titration error, the method was applied to a solution of pure potassium cyanide (0.01007 N.). 10 ml. aliquots were used and the results obtained gave a nitrogen content of 8.56% as against the calculated value of 8.878% i.e. 0.318% too low. This was a definite improvement on the results obtained from solutions of fluoride, chloride and cyanide but since the amount of silver cyanide passing through the filter cannot be of a constant value, then slight variations are bound to occur. Further aliquots were treated with silver nitrate but were made up to a standard volume (50 ml.) before filtering and an aliquot (25 ml.) of the filtrate titrated with bromide. This removed the neccessity of washing the precipitate and so it was hoped to cut down the possibility of colloidal silver cyanide passing through the filter. A result of 8.896% was obtained for the nitrogen content which agreed to within 0.018% of the calculated value, since this was

well within the desired ± 0.2% margin of error the method was applied to a synthetic solution containing sodium chloride (0.01002 N.), sodium fluoride (0.01028 N.) and potassium cyanide (0.01003 N.), which had a calculated nitrogen content of 8.861%. A series of results were obtained which averaged a constant of 0.3% lower than the calculated value and the use of ether or nitrobenzene to help coagulation of the precipitate, before filtration, did not increase the percentage. accuracy.

In further attempts to increase the efficiency of the filtration four thicknesses of number 50 paper were used and here results averaged 0.221% below the calculated value. Finally the use of six thicknesses of filter paper gave figures of 8.816%, 8.95%, 8.976%, 8.869% and 8.923% for the nitrogen content, all of which were within ±0.2% of the calculated value (8.861%) so the filter must now be capable of retaining practically all of the colloidal silver cyanide. The variation between the maximum and minimum values obtained (0.115%) was thought to be due in part to the acidity of the solutions, in which the bromide titrations were carried out (approximately 0.3 N. in nitric acid) for the acidity used was that recommended for Rhodamine 6 G. T.B. Smith (Analytical Processes, p. 251) and it may not

be the best value when using Rhodamine B S. A series of estimations were therefore carried out in which the pH of the titration solution (25 ml.) was considerably varied, and gave the following results. (Shown in Table 6)

All estimations gave results within $\pm$0.2% of the correct value but the most accurate results were obtained when 0.4 ml. of concentrated nitric acid were added to the titration solution (25 ml.). Allowing 1 drop from the burette to have a volume of 0.03 ml. then, from the table, 1. drop in the titration will make a difference of approximately 0.06% in the final nitrogen content for a titration of 2.5 ml. Thus if the titration figure were considerably increased by adding more excess silver nitrate, there would be a larger margin of error possible in the titration figure before an appreciable change could be detected in the final nitrogen content.

From the preceeding results the method was considered sufficiently accurate to apply to actual fusion solutions in the following manner:-

Make the fusion solution up to a standard volume (100 ml.) and neutralise aliquots (10 ml.) to phenolphthalein with 2N. nitric acid. Add an excess of silver nitrate (0.10 N.), slightly acidified with nitric acid (0.2 ml. conc. HNO_3/100 ml. $AgNO_3$) and make solution

Table VI.

Calculated nitrogen content = 8.861%.

Amount of concentrated HNO_3 added to titration solution (25ml.) ml.	KBr titre ml.	Nitrogen Percentage	% Variation from calculated value.
0.0	2.65	8.748	- 0.113
0.0	2.69	8.686	- 0.175
0.1	2.66	8.730	- 0.131
0.1	2.67	8.720	- 0.141
0.2	2.65	8.748	- 0.113
0.2	2.65	8.748	- 0.113
0.3	2.61	8.861	- 0.045
0.3	2.63	8.782	- 0.079
0.4	2.60	8.835	- 0.026
0.4	2.58	8.869	+ 0.008
0.4	2.53	8.950	+ 0.089
0.4	2.53	8.923	+ 0.062
0.4	2.60	8.835	- 0.026
0.5	2.53	8.950	+ 0.089
0.5	2.55	8.923	+ 0.062

up to a standard volume (50 ml.). Filter the solution but do not wash the precipitate and titrate an aliquot (25 ml.) of the filtrate, after the addition of concentrated nitric acid (0.4 mls.), with potassium bromide (0.10 N.) using 3 drops of Rhodamine B S (0.5% aqueous solution) as indicator.

The method was applied to fusion solutions obtained from three types of organic compound:-

a) Those containing nitrogen only.
e.g. p. nitraniline (N = 20.29%)

b) Those containing nitrogen and chlorine,
e.g. o-chloro-nitrobenzene (N = 8.888%, Cl = 22.54%)

c) Those containing nitrogen, chlorine and fluorine
e.g. the compound $C_{11}H_9O_2NClF_3$ (N = 5.008%, Cl = 12.7%, F = 20.39%)

In each case, knowing the amount of compound fused, the quantity of silver nitrate required to give total precipitation of cyanide or cyanide plus chloride was calculated and an excess of silver nitrate added so as to give a final bromide titre of approximately 5 ml. The nitrogen content of each compound so determined, was in each case well below the theoretical value.

Table VII.

Compound fused.	Weight of sample gm.	Nitrogen Content %	
		Calculated	Found
p.nitraniline	0.1364	20.29	12.7
o-chloro nitro benzene	0.1809	8.888	5.76
	0.1854	8.888	5.166
	0.2479	8.888	5.516
$C_{11}H_9O_2NClF_3$	0.1841	5.008	4.392
	0.1937	5.008	4.260

The percentage chloride was then estimated in o-chloro nitrobenzene and the chloride and fluoride estimated in $C_{11}H_9O_2NClF_3$ and the results obtained were within 0.1% of the calculated values so showing that there was no fault in the actual sodium fusions. Since p.nitraniline and $C_{11}H_9O_2NClF_3$ were solids and did not therefore require fusing in a glass capsule it appeared that traces of sodium silicate or borate were not responsible for the low results.

The o-chloro nitrobenzene was melted, introduced into a glass capsule and then fused and since the results obtained in this case are of the same degree of error then the preceeding statement is merely further substantiated. With any one compound the results obtained by treating several aliquots of the same fusion solution are practically identical but vary from that obtained from other fusion solutions of the same compound. This tends to show that the error lies in the actual fusion, where perhaps complete conversion of nitrogen to cyanide does not occur, or in the evaporation of the fusion solution where possibly some cyanide is lost since these stages are the only ones which can not be carried out under exactly identical conditions. It was also observed that, when adding concentrated nitric acid before titrating with bromide, there was a brisk effervescence as though considerable quantities of carbonate were present in the titration solution. This effect did not occur with standard synthetic solutions but as yet no mechanism could be postulated to explain this difference satisfactorily. The results obtained with $C_{11}H_9O_2NClF_3$ indicated that the percentage error falls rapidly when the nitrogen content

is fairly low (approximately 5%) so it was possible that the method devised by Beaty (Ph.D. Thesis) gave good results on compounds with a low nitrogen content but was not satisfactory when applied to compounds with a larger nitrogen percentage (approximately 10% - 20%).

Tests were next carried out, using synthetic solutions, to see if the evaporation of the fusion solutions resulted in a loss of cyanide and if so to find by how much the final figures were thrown out. A solution was made up containing N/10 sodium chloride (10 ml.). N/10 sodium fluoride (10 ml.), N/10 potassium cyanide (10 ml.), alcohol (100 ml.), 2N. sodium hydroxide (10 ml.) and water (200 ml.) and evaporated down in a glass beaker in a similar manner to that employed with fusion solutions. After evaporation the solution (approximately 30 ml.) was made up to a standard volume (100 ml.). This made the strength of the respective ions in solution 0.01 N. and gave a calculated nitrogen content of 8.8%, while estimations carried out on the solution gave an experimental value of 6.9% so showing that the presence of alcohol and/or the actual evaporation had caused a drop of 1.9% in the final nitrogen content. The experiment was repeated several times without alcohol and it was found that the results obtained varied from

1.9% to 2.3% lower than the calculated value. This must therefore be due to loss of cyanide during evaporation, whether or not alcohol is present, and must depend to some extent on the time taken to evaporate the solution down. The results showed a drop of approximately 2% in 9% and so would not account for all the descrepancy found in actual fusion solutions, where the drop was approximately 8% in 20% and 3.5% in 9% but if this error could be eliminated a substantial improvement would result. A possible mechanism for the loss of cyanide, which takes place on evaporation of the fusion solution, is that the cyanide hydrolyses to sodium formate, oxalate and carbonate. (Gmelin Handbook of Inorganic. Chem. 21, 796). The complete hydrolyses of aqueous sodium cyanide solutions:-

$$2NaCN + 4H_2O \longrightarrow 2NH_3 + Na_2CO_3 + H_2 + CO + 46.2 \text{ Kg.cals.}$$

goes in the following temperature stages:-

1) $100^{\circ}C - 200^{\circ}C.\ 2NaCN + 4H_2O \longrightarrow 2NH_3 + 2NaHCO_2 + 64 \text{ Kg.cals.}$

2) $200^{\circ}C - 360^{\circ}C.\ 2NaHCO_2 \longrightarrow Na_2C_2O_4 + H_2 - 3 \text{ Kg.cals.}$

3) over $400^{\circ}C.\ Na_2C_2O_4 \longrightarrow Na_2CO_3 + CO - 14.8 \text{ Kg.cals.}$

since the evaporation of the fusion solutions takes place at $100^{\circ}C$ reaction (1) would be the primary effect but over the period necessary to complete the evaporation reactions

(2) and (3) may occur to a limited extent. This would also explain in part the effervescence observed when concentrated nitric acid was added to the titration solutions for reaction (3) results in the production of carbonate.

From these results it was decided not to evaporate down the fusion solutions as before but to destroy excess sodium with a minimum of alcohol, wash the bomb with a minimum of water and then to warm the solution gently for a few minutes before filtering and making the filtrate and washings up to a standard volume (150 ml.). This meant that the estimations would have to be carried out in the presence of appreciable quantities of alcohol so experiments were undertaken to ascertain the effect of alcohol on the estimation. 10 ml. aliquots of a synthetic solution of chloride, cyanide and fluoride were treated with amounts of alcohol up to 10 ml. and it was found that the estimation still gave results well within the $\pm$0.2% margin of error.

Since the presence of alcohol did not have an adverse effect on the estimation, a sample of o-chloro nitrobenzene was fused and after treating as described the fusion solution was made up to 150 ml. When the estimation was applied to aliquots (10 ml.) of this solution the results

gave a value of 6.45% for the nitrogen content as against the theoretical value of 8.888%. This was a considerable improvement on results previously obtained with this compound and could only be due to the fact that in the previous cases a substantial quantity of cyanide has been lost during evaporation of the fusion solutions. Here however in order to carry out the chloride estimation and so get the nitrogen content by taking this value from the combined chloride plus cyanide figures, an aliquot of the fusion solution had to be evaporated down since in the presence of alcohol the formaldehyde added did not remove all the cyanide present and so high results for the chloride figures were obtained leading to very low figures for the nitrogen content.

Consideration of the organic compounds, which had so far been fused and found to give low nitrogen figures, showed that in each case there was oxygen in the molecule either in the form of a nitro group or as a carboxyl group. It was therefore thought possible that, during the sodium fusion, some oxygen combined with the nitrogen to form traces of cyanate so cutting down the amount of cyanide formed and leading to low nitrogen figures. If this were the case it would also account for traces of carbonate in

the resultant fusion solution since an aqueous solution of cyanate decomposes on standing, faster by warming, to form sodium carbonate and ammonia (Gmelin Handbook of Inorganic Chem. 21, 799). The reaction goes according to the equation:-

$$4NaCNO + 6H_2O \longrightarrow 2Na_2CO_3 + (NH_4)_2CO_3 + CO(NH_2)_2$$

and as more carbonate is formed the reaction increases in velocity. Though the reaction is said to be greatly reduced by the presence of alkali hydroxide, which would be present in the fusion solutions, it was thought possible that the reaction would occur at least to a limited extent.

To test this assumption compounds were fused which did not contain oxygen and the fusion solutions were worked up without evaporation and then the nitrogen content estimated. (See Table VIII). The aniline and pyridine estimations gave results 2.1% to 2.57% below theoretical while the aniline hydrobromide gave a result within the $\pm$0.2% margin of error. Since the aniline and pyridine are liquids they were fused in glass capsules while the solid aniline hydrobromide was fused without the use of glass, this being the only difference it was concluded that the presence of glass during the fusion had an adverse effect

Table VIII.

Compound fused.	Nitrogen Content %.		
	Calculated	Found.	Error %
Aniline	15.05	12.48	2.57
	15.05	12.55	2.50
Pyridine	17.72	15.45	2.27
	17.72	15.61	2.11
Aniline hydrobromide	8.046	8.034	0.012
	8.046	8.866	0.180

on the production of cyanide. It was also observed that the precipitate, obtained by treatment of an aliquot of the fusion solution with excess silver nitrate, was yellow in the case of aniline and pyridine. This latter effect was put down to some reaction caused by having glass present when aniline and pyridine were originally fused. Also when nitric acid was added to the titration solutions in no case was a vigorous effervescence observed so showing that the production of carbonate had been greatly reduced. Since correct results for the nitrogen content

were obtained with aniline hydrobromide it was, as a matter of interest, decided to apply Liebig's Method to an aliquot of the fusion solution to see what results would be given now that the effects, due to evaporation of the fusion solution and the presence of oxygen in the compound fused, had been eliminated. An aliquot (10 ml.) of the fusion solution was treated with 6N. ammonium hydroxide (7 ml.) and N/10 potassium iodide (2 drops) and then titrated with N/100 silver nitrate until permanent turbidity was obtained, the titre yielded a value of 8.136% for the nitrogen content which was only 0.09% higher than the theoretical value. Thus it indicated that, when the method had been previously applied to fusion solutions of o-chloro nitrobenzene, it had been the production of cyanate and the partial hydrolyses of the cyanide formed, which had caused the low results. Application of this method to the fusion solutions of aniline and pyridine yielded results which were approximately 1.1% below the theoretical nitrogen figure and so were nearly 1.0% higher than the results obtained by the bromide back titration method.

Samples of aniline and pyridine were next fused in nickel capsules to remove any effect due to the presence of

glass and the back titration method yielded results of 13.24% and 15.9% respectively for the nitrogen content, which were slightly higher than those obtained when glass capsules were used. Liebig's method, however, yielded results of 15.08% and 17.18% respectively which were well within the margin of error desired of the experiment ($\pm$0.2) so it appeared that Liebig's method could now be successfully applied to fusion solutions of organic compounds when the compounds contained no oxygen in their structure and the fusions were carried out in nickel capsules.

Since the results were still too low when the back titration method was used and the precipitated silver cyanide was still of a yellow colour it was concluded that the effect was not totally due to the presence of glass as previously stated but the copper washer used to seal the bomb during fusion was in some way giving traces of a complex with the cyanide so causing the low results. It was also found that if a dilute solution of copper sulphate was treated with a dilute solution of potassium cyanide until the blue colour was discharged, then addition of silver nitrate yielded a precipitate which had a definite yellow colouration and might be due to a complex of the form $Ag_3[Cu(CN)_4]$. If a soluble copper complex of the

type $Na_3[Cu(CN)_4]$ were formed during the sodium fusion then the addition of silver nitrate would give rise to $Ag_3[Cu(CN)_4]$ which would only require $3Ag^+$ per $[Cu(CN)_4]^{3-}$ and so less silver nitrate would be required than if the following reaction were taking place:-

$$AgNO_3 + NaCN \longrightarrow AgCN + KNO_3$$

Other possible types of complex are $Na[Cu(CN)_2]$ and $Na_2[Cu(CN)_3]$ which tend to form at high dilutions. Sidgwick (Chem. Elements and their Compounds, Vol. I, p. 133). That aniline hydrobromide yielded good nitrogen figures when a copper washer was used, could be explained by the fact that being solid it fused in the lower part of the bomb and so did not come into intimate contact with the washer, while the liquids aniline and pyridine vapourised and so came into intimate contact with the surface of the washer where some interaction could possibly occur during the fusion with molten sodium. To bear this out it was observed in practice that, the fused mass obtained from the hydrobromide was caked in the bottom of the bomb leaving the surface of the copper quite clean, while after fusion of the liquids considerable quantities of the fused masses adhered to the surface of the copper washers. To test this idea samples of aniline were fused in a nickel capsule

using a nickel washer and the results obtained for the nitrogen content rose to 14.35% i.e. 0.7% below the theoretical value, but the error was still too large to permit the use of the method for accurate analyses. However the precipitated silver cyanide now appeared white and was in no way tinged with yellow as in previous estimations. It may be that nickel from the bomb itself forms a nickel-cyanide complex to a very small extent and that this causes the errors in the estimations but it would be rather surprising if this were actually the case. If a nickel complex did form however it could be expected to be of the type $Na_2[Ni(CN)_4]$. Sidgwick (Chem. Elements and their Compounds, Vol. II. p. 1438) the dissociation constant of which:-

$$K = \frac{[Ni(CN)_4^{--}]}{[Ni^{++}][CN^-]^4} = 5.6 \times 10^{-13}$$

shows it to be quite stable i.e. if concentration of nickel complex is normal that of free Ni^{2+} would be 2.8×10^{-3}N.

From the results obtained it would seem that a source of error arises when the fusion mixtures come into intimate contact with the copper washer of the bomb. Since the tendency of copper to form complexes is so strong that it will dissolve in concentrated potassium cyanide solution

with the evolution of Hydrogen, Sidgwick (Chem. Elements and their Compounds, Vol. I, p. 133) it seems reasonable to suppose the formation, in very small amounts, of a copper complex under the fusion conditions. However, this does not furnish a complete explanation of the experimental observations since, even with a copper washer, the estimation of cyanide in a fusion solution by Liebig's Method gives accurate results although none of the reagents used appear capable of decomposing a copper cyanide complex.

Whilst no doubt, answers to the two problems:-

a) The effect on the fusion of the material of which the bomb was made.

b) The effect of the copper washer

could be determined by carrying out experiments in which the materials of the bomb and washer were varied, it was felt, since the original aims of the investigation had been fulfilled and good methods had been evolved for the determination of chloride and nitrogen in fusion solutions that time would now be more profitable spent on further fluorination studies rather than proceeding further with this investigation.

The methods of obtaining the nitrogen content of

an organic compound, which does not contain oxygen, can be summarised as follows:-

Fuse a sample of the compound (0.1 to 0.2 gm.) with sodium in a nickel bomb using either a copper or nickel washer. Destroy the excess sodium with a minimum of alcohol and wash the bomb well with a minimum of distilled water. Warm the fusion solution for a few minutes then cool, filter, and make the filtrate and washings up to a standard volume (150 ml.).

a) Liebig's Method.

Use a copper or nickel washer for the fusion.

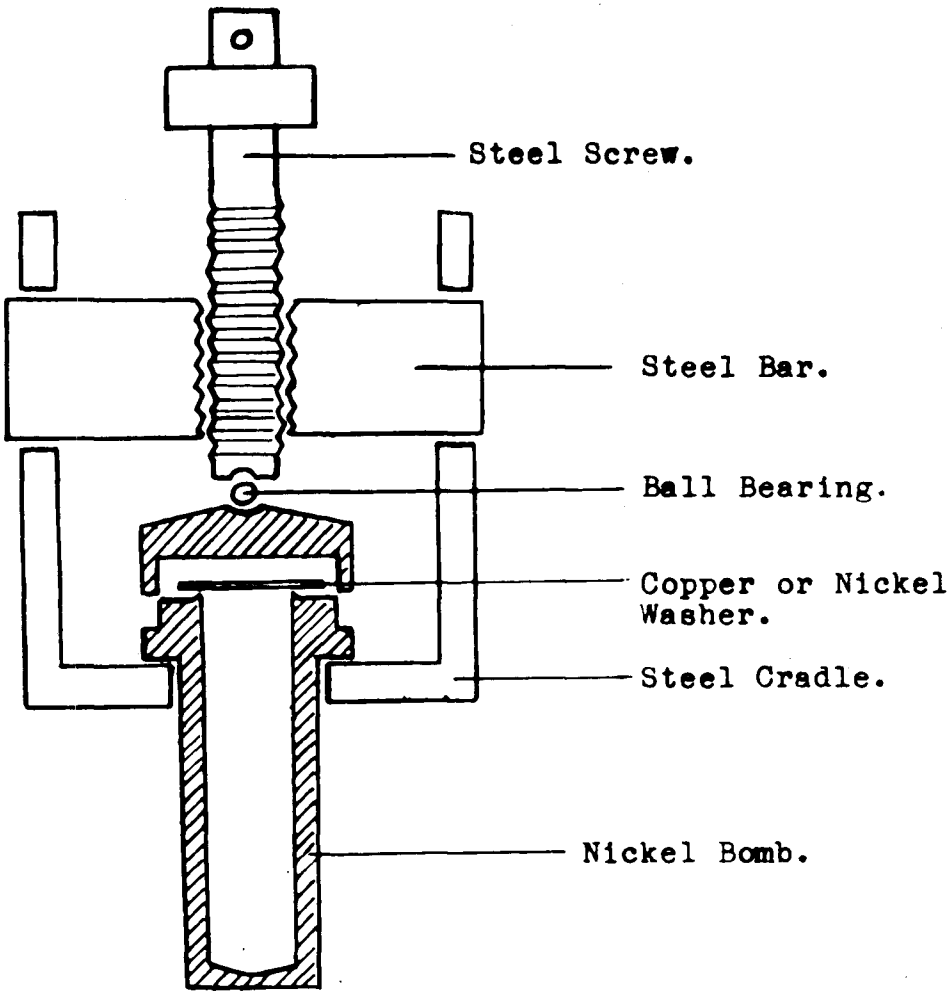
Treat an aliquot (25 ml.) of the fusion solution with 6N. ammonium hydroxide (7 ml.), N/10 potassium iodide (2 drops) and titrate with silver nitrate (0.01N.) until a permanent turbidity of silver iodide is obtained. Results obtainable are within $\pm$0.2% of the theoretical value so making the method eminently suitable for accurate analyses.

b) The back-titration method.

This method in its present form is only capable of giving results to within -0.7% of the theoretical value.

Fuse compounds using a nickel washer.

Nickel Bomb for Sodium Fusions.



Take an aliquot of the fusion solution (10 ml.), neutralise to phenolphthalein with 2N. nitric acid and add an excess of silver nitrate (0.01N.) slightly acidified with nitric acid (0.02 ml. conc. HNO_3/100 ml. $AgNO_3$). Make the solution up to a standard volume (50 ml.) and filter through six thicknesses of Whatman No, 50 Paper. Titrate an aliquot (25 ml.) of the filtrate, plus concentrated nitric acid (0.4 ml.), with potassium bromide (0.01N) using 3 drops of Rhodamine B.S. as indiactor. This result gives a figure for the silver nitrate equivalent to the total cyanide or total cyanide plus chloride in the solution. In the latter case the chloride content, as separately estimated, must be taken from the combined result so yielding the nitrogen content.

The methods so devised were applied to the products from the Halogentation of Pyridine with Chlorine Trifluoride and were found capable of giving good results for the estimation of the fluoride, chloride and nitrogen content of these compounds as in no case oxygen was present in their structure.

I N D E X.