7. Perfluoroalkyl Derivatives of Nitrogen. Part V.* The Mechan ism of the Hofmann Reaction with Amides containing Electronegative Groups.[†]

By D. A. BARR and R. N. HASZELDINE.

The Hofmann reaction with a perfluoro-amide R_{F} ·CO·NH₂ can show a duality of mechanism to give high yields (85–95%) of either $R_{F}X$ (X = Cl or Br) or R_{F} ·NCO. The bromo-compound, for example, is formed by elimination of *iso*cyanate ion from R_{F} ·CO·NBr⁻ in a solvent of high dielectric constant, whereas pyrolysis of the anhydrous salt $[R_{F}$ ·CO·NBr]⁻Na⁺ gives R_{F} ·NCO with intermediate formation of R_{F} ·CO·NBr]⁻Na⁺ correlated with those from Curtius and Arndt-Eistert reactions. A mechanism is proposed for the reaction of YZ with a silver salt R·CO₂Ag derived from a strong carboxylic acid (the Simonini reaction) to give AgY, CO₂, and RZ (YZ = Cl₂, Br₂, I₂, NOCl, or NO₂Cl).

It is suggested that the Hofmann reaction with α -keto-acids, α -halogenoacids, and other acids containing electronegative groups, as well as the Weerman reaction of hydroxy-amides, also proceeds by intramolecular

ejection of cyanate ion from an intermediate ion of type $R \cdot CO \cdot NX$ (X = Cl or Br).

THE Hofmann degradation of amide to amine ¹ involves an intramolecular rearrangement to give the *iso*cyanate. The reaction of the hypohalite with the amide yields an N-halogeno-amide, which with alkali gives a salt (I); loss of the N-halogen as halide ion gives the intermediate (II) which rearranges to the *iso*cyanate:

There is ample evidence 2,3 that, as in many other molecular rearrangements, the migrating group in (II) never leaves the vicinity of the atoms concerned. The loss of halide ion from the salt (I) may well overlap, or be simultaneous with, the migration of R from carbon to nitrogen and the electron rearrangement to give the *iso*cyanate.

- * Part IV, J., 1956, 3428. † For a preliminary report see Chem. and Ind., 1956, 1050.
- ¹ Hofmann, Ber., 1881, 14, 2725.
- ¹ For a review see Wallis and Lane, "Organic Reactions," Vol. III, Wiley, New York, 1946, p. 267.
 ³ Arcus and Kenyon, J., 1939, 916; Noyes and Potter, J. Amer. Chem. Soc. 1915, 37, 189; Wallis and Moyer, *ibid.*, 1933, 55, 2598; Kenyon and Young, J., 1941, 265.

Production of an unstable intermediate in which one atom has only six electrons in its valency shell also occurs during other molecular arrangements involving 1: 2-shifts :

Lossen rearrangement of a hydroxamic acid :

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Curtius rearrangement of an acyl azide :

R•CO--N₂ ----→ N₂ + R•CO---Ń: ----→ R•NCO

Arndt-Eistert (Wolff) rearrangement of a diazo-ketone :

It has been reported that perfluoro-amides $R_F \cdot CO \cdot NH_3$ ($R_F = perfluoroalkyl$) fail to undergo the Hofmann reaction : trifluoroacetamide is said to yield hexafluoroethane,⁴ whereas heptafluorobutyramide gave bromoheptafluoropropane (with sodium hypobromite) or heptafluoropropane (with sodium hypoiodite).⁵ The supposed formation of hexafluoroethane was accepted by Husted and Kohlhase,⁵ who concluded that there was a sharp break in properties between trifluoroacetamide and pentafluoropropionamide which was " a change in kind and not in degree of reactivity." Consideration of the reactions of fluorine compounds in general, and of the mechanism of the Hofmann reaction in particular, made these results irreconcilable to us; we do not consider that this sharp change in kind between CF₃ and C₂F₅ compounds occurs in fluorine chemistry, though there is often a difference in reaction rate. Both reactions have therefore been re-investigated, and it is now clear that the reaction of a hypohalite NaOX with a perfluoro-amide $R_F \cdot CO \cdot NH_3$ can show a duality of mechanism, and gives a high yield (85–95%) of either $R_F X$ (X = Cl or Br) or $R_F \cdot NCO$ depending on the reaction conditions.

The reaction of trifluoroacetamide with sodium hypobromite was first investigated. Under the conditions reported in the literature,⁴ the only volatile product was bromotrifluoromethane spectroscopically uncontaminated by even a trace of hexafluoroethane. Variation of the conditions enabled the yield of bromotrifluoromethane to be increased to 35% by use of short reaction times. The reported identification ⁴ of the volatile product as hexafluoroethane in unspecified yield rested only on vapour-density measurements, and since there is little difference in molecular weight between CF_3Br (149) and C_2F_6 (138), or in their boiling points, it is probable that the compound obtained by the earlier workers was in fact bromotrifluoromethane and not hexafluoroethane. Amides containing negative groups are readily hydrolysed, and hydrolysis of the trifluoroacetamide to sodium trifluoroacetate accounts for the missing material :

$$CF_{3} \cdot CO \cdot NH_{3} + NaOBr + NaOH \longrightarrow CF_{3} \cdot CO_{3}Na (+NH_{3}) 65-90\%$$

$$CF_{3} \cdot CO_{3}Na (+NH_{3}) 65-90\%$$

$$CF_{3} \cdot CO_{3}Na (+NH_{3}) 65-90\%$$

Cyanate is decomposed to ammonia and Carbondioxide only in acid solution.

The possibility that bromotrifluoromethane is produced by a reaction between sodium trifluoroacetate and sodium hypobromite :

$$CF_3 \cdot CO_3 Na \xrightarrow{NaOBr} CF_3 \cdot CO_3 Br \xrightarrow{Heat} CF_3 Br + CO_3$$

formally analogous to the known reaction carried out under anhydrous conditions :

$$CF_{s} \cdot CO_{s}Ag \xrightarrow{Br_{s}} CF_{s} \cdot CO_{s}Br \xrightarrow{Heat} CF_{s}Br + CO_{s}$$

was eliminated by the failure of sodium hypobromite and sodium trifluoroacetate to give volatile products when heated together. Hydrolysis of the amide thus does not precede formation of R_FBr .

Reaction of heptafluorobutyramide with sodium hypobromite in presence of an excess

- ⁴ Gryszkiewicz-Trochimowski, Sporzynski, and Wnuk, Rec. Trav. chim., 1947, 66, 426.
- ⁵ Husted and Kohlhase, J. Amer. Chem. Soc., 1954, 76, 5141.

of alkali, and under conditions suitable for minimum hydrolysis, *i.e.*, hot solution with short reaction time, gives only $C_3F_7Br(81\%)$, NaNCO (80%), NH₃ (10%), and $C_3F_7CO_2Na$ (10%). Formation of R_FBr thus predominates over hydrolysis to give sodium hepta-fluorobutyrate and ammonia. The formation of sodium cyanate should be particularly noted. That the normal Hofmann reaction to give the *iso*cyanate C_3F_7 ·NCO does not occur is shown by the failure to detect this volatile compound or its hydrolysis products C_2F_5 ·CO·NH₂, or C_2F_5 ·CO₂NH₄. A perfluoroalkyl *iso*cyanate such as hepta-fluoro-*n*-propyl *iso*cyanate is known ⁶ to be hydrolysed readily by water to give, *via* the amine, the nitrile, and the amide and ammonium salt of the fluoro-acid containing one less carbon atom in the perfluoroalkyl group. Thus even if the Hofmann reaction proceeded normally with a perfluoroalkylamide, the product, in the alkaline medium prevailing, would be the sodium salt of the shorter-chain acid, *e.g.*: ⁶

$$C_3F_7$$
·NCO \xrightarrow{NaOH} C_2F_5 ·CO₃Na + 2F⁻ + CO₃ + NH₃

Careful examination showed that sodium pentafluoropropionate was not a product. The absence of bromopentafluoroethane also suggests that pentafluoropropionamide is not an intermediate product:

$$C_3F_7NCO \longrightarrow C_3F_7NH_3 \longrightarrow C_2F_6CN \longrightarrow C_3F_6CONH_3 \longrightarrow C_3F_6Br$$

The failure to isolate a perfluoro-amine from the reaction of sodium hypobromite with a perfluoro-amide thus cannot be taken as evidence that the Hofmann rearrangement has failed, although the failure to isolate the known decomposition products of the amine makes it very unlikely that the *iso*cyanate is produced as intermediate.

The absence of heptafluoropropane as product is also noteworthy, since Husted and Kohlhase ⁵ reported it as a product from the action of sodium hypoiodite with heptafluorobutyramide. Heptafluoropropane is in fact produced only when the amide is heated vigorously with extremely concentrated or semi-solid sodium hydroxide and results from the decarboxylation of concentrated sodium heptafluorobutyrate. Hexafluoropropene is often formed under these conditions also, by the known thermal decomposition of the anhydrous sodium salt (C_3F_7 ·CO₂Na $\longrightarrow C_3F_6$ + NaF + CO₂). These conditions cannot be regarded as normal for a Hofmann reaction, and neither heptafluoropropane nor hexa-fluoropropene is a relevant product in the reaction under consideration.

Consideration of the various steps of the Hofmann reaction reveals at what stage the normal course of the reaction is changed by the presence of the strongly negative group in the amide to give R_FBr rather than R_FNCO .

The Curtius reaction ⁶ of a perfluoroacyl halide proceeds normally under correct conditions and gives the *iso*cyanate in good yield; this shows that the intermediate, R_{F} ·CO·N; once formed, can rearrange to R_{F} ·NCO even when R_{F} = perfluoroalkyl. The driving force of this rearrangement may be presumed to arise from the tendency of the electronically deficient nitrogen atom to acquire electrons from the neighbouring carbon atom. It is interesting that in this instance the driving force is not diminished, to such an extent that rearrangement fails to occur, by the strongly electronegative perfluoroalkyl group also attached to the carbon.

The Arndt-Eistert reaction also proceeds normally with fluoro-acids; ⁷ trifluorodiazoacetone, for example, decomposes smoothly in ethanolic solution to give ethyl $\beta\beta\beta$ -trifluoropropionate. The mechanism of this reaction was not discussed by Brown and Musgrave,⁷ but it clearly involves the rearrangement of an intermediate similar to $R_FCO\cdot\dot{N}$: to give the keten, which then reacts with ethanol to give the ester :

$$\begin{array}{ccc} R_{F} \cdot CO \cdot CHN_{a}, & & & \\ R_{F} \cdot CO \cdot CH_{a}, & & \\ R_{F} \cdot CH: CO + EtOH - & & \\ R_{F} \cdot CH_{a} \cdot CO_{a}Et \end{array}$$

⁶ Barr and Haszeldine, J., 1956, 3428.

⁷ Brown and Musgrave, J., 1953, 2087.

The success of the Curtius and the Arndt-Eistert reaction clearly shows that the failure to obtain an *iso*cyanate (or its subsequent products) by the Hofmann reaction with per-fluoro-amides is caused by failure to produce $R_{\mathbf{F}}$ ·CO·N: as intermediate under the conditions used.

Heptafluorobutyramide fails to yield bromoheptafluoropropane when heated with aqueous bromine, and a direct reaction of the type

thus does not occur.

N-Bromoheptafluorobutyramide was prepared by reaction of bromine with silver heptafluorobutyramide:

$$C_{3}F_{7}$$
·CO·NH₃ $\xrightarrow{Ag_{3}O}$ $C_{3}F_{7}$ ·CO·NHAg $\xrightarrow{Br_{3}}$ $C_{3}F_{7}$ ·CO·NHBr

This route was found preferable to the earlier method ⁸ of treating the amide with silver oxide and bromine in trifluoroacetic acid solution. Bromoheptafluoropropane is not produced by pyrolysis of the N-bromo-amide at temperatures up to 200° , or when an aqueous solution of the N-bromo-amide is heated under reflux; bromine and heptafluorobutyramide are the products from the last reaction. An unsuccessful attempt was made to remove hydrogen bromide from the anhydrous N-bromo-amide by heating it with anhydrous ferric chloride, and so produce the *iso*cyanate.

Only when heated with aqueous alkali does the N-bromo-amide yield bromoheptafluoropropane (92%), cyanate (69%), ammonia (2%), and sodium heptafluorobutyrate (0.5%), and the formation of the salt $[R_F \cdot CO \cdot NX]^-Na^+$ clearly must precede liberation of R_FBr . The high yield of bromoheptafluoropropane shows that an excess of brominating agent, *e.g.*, an excess of sodium hypobromite, is not essential for the final decomposition into bromoheptafluoropropane. The increase in yield compared with that obtained from the original amide and sodium hypobromite (81%) is caused by decrease in the hydrolysis side-reaction.

The hydrogen atom in N-bromoheptafluorobutyramide is strongly acidic and can be titrated with aqueous base. The anhydrous salt, $[C_3F_7\cdot CO\cdot NBr]^-Na^+$, is a white solid which infrared spectroscopic examination shows to be free from N⁻H bonds. N-Bromo-alkylamides usually give only unstable salts, few of which have been isolated,^{2,9} and the influence of the perfluoroalkyl group is clearly apparent. An aqueous solution of sodium N-bromoheptafluorobutyramide yields bromoheptafluoropropane (91%) and cyanate when heated; presence of additional bromide ion or bromine cation is thus not necessary for the production of bromoheptafluoropropane essentially quantitatively.

The failure of $[R_F \cdot CO \cdot NX] - Na^+$ to lose X⁻ to give $R_F \cdot CO \cdot \dot{N}$; must thus be the reason for the change in mechanism of the Hofmann reaction :

$$[R \cdot CO \cdot NBr]^{-}Na^{+} \xrightarrow{\text{Heat}, H_{a}O} R \cdot NCO + NaBr: R = alkyl$$
$$[R_{F} \cdot CO \cdot NBr]^{-}Na^{+} \xrightarrow{\text{Heat}, H_{a}O} R_{F}Br + NaNCO: R_{F} = perfluoroalkyl$$

The separation of halide ion from $[R \cdot CO \cdot NX]^-$ is probably the key and rate-controlling step during the Hofmann reaction with normal amides, since the rate of decomposition of substituted benzamides, and hence presumably the rate of rearrangement, is more rapid

⁸ Park, Gerjovich, Lycan, and Lacher, J. Amer. Chem. Soc., 1952, 74, 2189.

⁹ Mauguin, Ann. Chim. (France), 1911, 22, 297.

when electron-releasing groups (Me, OMe) are present in the aromatic ring, and slower when electron-attracting groups (CN, NO₂) are in the ring; ¹⁰ the ease of the Hofmann reaction is thus inversely related to the dissociation constant of the acid from which the

amide is derived. The failure of bromine to separate from R_{F} ·CO·NBr as bromide can be attributed to the strongly electronegative perfluoroalkyl group, and the Hofmann reaction with perfluoroalkylamides represents an extreme of behaviour.

The Curtius and the Arndt-Eistert reaction, by contrast, involve loss of a neutral molecule (nitrogen) in the key stage (R·CO·N₃ \rightarrow R·CO·N[:] + N₂; R·CO·CHN₃ \rightarrow $R \cdot CO \cdot CH + N_2$), rather than loss of an ion, and such a process will clearly be considerably less sensitive to the electron-attracting demands of the group R. This is in accord with the only slight change in yield or rate observed in the Curtius reaction when electronattracting groups such as CO₂H, CN, or NO₂ are in the molecule,¹¹ and the excellent yields readily obtained when R = perfluoroalkyl.⁶

An alternative mechanism must be proposed for the Hofmann reaction with perfluoroamides, the essential step of which is $R_F \cdot CO \cdot NBr \longrightarrow R_F Br + NCO^-$. Attack of bromide ion or of bromine cation on the α -carbon atom of the ion is unlikely in view of the high yields of R_FBr obtained by heating $[R_F \cdot CO \cdot NBr]$ -Na⁺ in water alone; if bromide ion were

lost from the $R_{\mathbf{F}}$ CO·NBr ion, there appears to be little reason why the normal rearrangement to isocyanate should not follow. Initial partial hydrolysis of the salt to give the amide R_F·CO·NH, and sodium hypobromite would be necessary in order to obtain bromine cation, and if this hydrolysis occurred, the yield of $R_{\rm F}Br$ is unlikely to be over 90%, yet such yields were readily obtained.

A two-stage process involving intermediate $R_{\mathbf{F}}^{-}$ ions is also unlikely, since such fluorocarbanions are known ¹² to abstract hydrogen from solvents or lose fluoride to give an olefin, and neither heptafluoropropane nor hexafluoropropene is among the products.

The most probable mechanism involves intramolecular ejection of a cyanate ion, e.g.;

The related bimolecular reaction is less probable :

(B) $\begin{array}{c} Br \\ \bullet CF_{3} \\ \bullet CF_{3}$

The 1: 3-shift of R_F from carbon to bromine (A) will be facilitated by the marked positive character of the bromine and the negative R_F group.

Cyanate ion is isoelectronic with carbon dioxide, and the above reaction (A) is, not surprisingly, closely related to the decarboxylation with simultaneous halogenation of silver salts under anhydrous conditions (the Simonini reaction), e.g., :

$$C_sF_{7}$$
·CO_sAg + Br_s \longrightarrow AgBr + C_sF_{7} ·CO_sBr \longrightarrow C_sF₇Br + CO_s

¹⁰ Hauser and Renfrow, J. Amer. Chem. Soc., 1937, 59, 121, 2308; Bright and Hauser, ibid., 1939, **61**, 618.

Smith, "Organic Reactions," Vol. III, Wiley, New York, 1946, p. 267.
 See Haszeldine, "Fluorocarbon Derivatives," Roy. Inst. Chem. Monograph, 1956, for references.

and we propose an analogous mechanism :

$$\begin{array}{ccc} C_2F_5\cdot CF_3 & \hline & C = O \\ \downarrow & \downarrow \land \mid \\ Br & O \end{array} \longrightarrow C_2F_5\cdot CF_2Br + CO_3 \end{array}$$

Perfluoroalkyl nitroso- and nitro-compounds are similarly formed by treatment of the silver salt of the acid with nitrosyl or nitryl chloride, with R_{F} ·CO·O·NO or R_{F} ·CO·O·NO₂ as intermediates, 14 e.g. :

Such reactions are possible only when Y is made relatively positive by the inductive pull of $R_{\rm F}$. In this connection it is noteworthy that although the chloro-compound $R_{\rm F}$ Cl can be prepared from the perfluoro-amide, attempts to prepare the perfluoroiodoalkane $R_{\mathbf{F}}$ I by reaction of the perfluoro-amide with sodium hypoiodite failed, and hydrolysis to the sodium salt of the acid predominates, e.g.:

$$C_{3}F_{7}$$
·CO·NHI -----> I⁺ + $C_{3}F_{7}$ ·CO·NH₃ ----> $C_{3}F_{7}$ ·CO₃Na

<u>____</u>

probably since the iodine has insufficient positive character for the 1: 3-shift to occur in an ionising solvent, though Hofmann¹⁵ noted that sodium hypoiodite did not produce methylamine from acetamide.

The above elimination of cyanate ion from R_R•CO•NX involves the free ion in a polar solvent such as water, and the sodium ion plays no essential part in the reaction. Clearly, however, if the sodium ion is deliberately kept in proximity to the

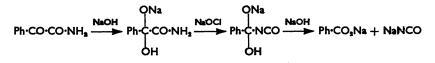
 R_{F} CO·NX ion, e.g., as in the crystal lattice of the anhydrous salt, then at a suitable temperature, reaction to yield NaX and the intermediate R_{F} ·CO·N: and thence R_{F} ·NCO should not be impossible. This prediction was adequately confirmed by preparation of heptafluoropropyl isocyanate in 83% yield when the anhydrous salt $[C_8F_7 \cdot CO \cdot NBr] - Na^+$ was heated to 170°:

$$C_{3}F_{7} - C = 0$$

 $-N - Br - N = NaBr + C_{3}F_{7} \cdot CO \cdot N: - C_{3}F_{7} \cdot NCO$
 Na^{+}

The reaction of a hypohalite NaOX with a perfluoro-amide R_{P} ·CO·NH₃ can thus be controlled to give high yields of either $R_F X$ (X = Cl or Br) or $R_F NCO$.

A perfluoroalkyl group is extremely electronegative, and it is to be expected that amides containing other negative groups will show similar behaviour. Examples can be found in the literature, but they are few and a general study is merited in this field. Benzoylformamide yields sodium benzoate (80%) and sodium cyanate (75%) rather than benzoyl isocyanate or its expected hydrolysis products when treated with sodium hypochlorite,¹⁶ and it was suggested that the reaction involved :



¹³ Haszeldine, Nature, 1951, 168, 1028; J., 1951, 585; 1952, 4259, 3490.
¹⁴ Haszeldine and Jander, J., 1953, 4172.
¹⁵ Hofmann, Ber., 1882, 15, 411.

¹⁶ Rinkes, Rec. Trav. chim., 1920, 39, 200; 1926, 45, 819; 1929, 48, 960.

More recently ¹⁷ the reaction has been interpreted as analogous to the Weerman ¹⁸ reaction with hydroxy-amides, for which the following was proposed : ¹⁹

$$\begin{array}{ccc} R \cdot CH(OH) \cdot CO \cdot NH_{2} & \stackrel{CIO^{-}}{\longrightarrow} R \cdot CH(OH) \cdot NCO & & R \cdot CH(OH) - \dot{N}_{1}^{+}C - O^{-} \\ & & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & &$$

The carbonyl group is electron-attracting, like a perfluoroalkyl group, and a similarity between them in causing apparently anomalous reactions has been noted earlier.²⁰ It is

likely that an intermediate such as Ph·CO·CO·NCl would lose chloride in aqueous solution only with difficulty, and an alternative reaction scheme analogous to (A) above is therefore now suggested :

$$Ph \cdot CO \cdot CO \cdot NH_{2} \xrightarrow{CIO^{-}} Ph \cdot CO \cdot CO \cdot NHCI \xrightarrow{NaOH} [Ph \cdot CO \cdot CO \cdot NCI]^{-}Na^{+}$$

$$Ph \cdot CO - - C = O$$

$$Ph \cdot CO - - C = O$$

$$Ph \cdot CO CI + NCO^{-}$$

$$Ph \cdot CO CI \xrightarrow{NaOH} Ph \cdot CO_{2}Na$$

The parallel thus drawn between a-keto-compounds and perfluoroalkyl compounds extends to the Curtius reaction. Keto-azides derived from α -keto-acids rearrange normally,¹¹ thus revealing that R·CO·CO·N:, once produced, can rearrange just like R_F·CO·N.

The Weerman reaction of hydroxy-amides can similarly be re-interpreted as

$$RR'C(OH) \cdot CO \cdot NH_{a} \xrightarrow{NaOBr} RR'C(OH) \cdot CO \cdot NHBr \xrightarrow{OH^{-}} RR'C(OH) \cdot CO \cdot \overline{N}Br$$

$$OH$$

$$RR'C \xrightarrow{C=0} \xrightarrow{OH} NCO^{-} + RR'C \xrightarrow{OH} Br \xrightarrow{RR'C:O + HBr}$$

$$Br \xrightarrow{N-} N^{-}$$

The reaction of α -halogeno-amides with hypohalite should provide a general route to gem.-dihalogeno-compounds and thence to ketones, aldehydes, or olefins :

$$RR'CY \cdot CO \cdot NH_2 \xrightarrow{NaOX} RR'CYX + NCO^-$$
; X = Cl or Br; Y = F, Cl, or Br

We suggest that Kishner's²¹ isolation of 2:2-dibromopropane and acetone from the reaction of a-bromoisobutyramide with sodium hypobromite exemplifies this reaction :

$$Me_{a}CBr \cdot CO \cdot NBr^{-} \longrightarrow NCO^{-} + Me_{a}CBr_{a} \xrightarrow{OH^{-}} Me_{a}CO$$

Control of pH will clearly be necessary if gem.-dihalides are to be isolated, and Stevens and Coffield's ²² isolation of ketones (40-70%), but not of dihalides, by the Kishner reaction can be attributed to the strongly alkaline conditions used.

EXPERIMENTAL

Reaction of Trifluoroacetamide with Sodium Hypobromite.-Trifluoroacetamide (1.02 g., 9.0 mmoles) and bromine (1.6 g., 10.0 mmoles) were dissolved in cold 10% aqueous sodium hydroxide (5 ml.), and the mixture was then added to a solution of sodium hydroxide (1.7 g.) in water

- ¹⁷ Arcus and Prydal, J., 1954, 4018. ¹⁸ Weerman, Annalen, 1913, **401**, 1.
- ¹⁹ Arcus and Greenwood, J., 1953, 1937.
- ²⁰ Haszeldine and Leedham, J., 1952, 3483; 1954, 1261.
 ⁸¹ Kishner, J. Russ. Phys. Chem. Soc., 1905, 37, 103, 106; Zentralbl., 1905, 76, I, 1219, 1220.
- ²² Stevens and Coffield, J. Amer. Chem. Soc., 1951, 78, 103.

(5 ml.) at 60—70°. The volatile products were condensed in a trap cooled by liquid oxygen, washed with 50% aqueous sulphuric acid to remove ammonia, and distilled *in vacuo*, to give bromotrifluoromethane (0.95 mmole, 11%) (Found : M, 145. Calc. for CBrF₃: M, 149). Comparison of the infrared spectrum of the bromo-compound with that of the known specimen confirmed its identity, and showed the complete absence of hexafluoroethane.

In a second experiment, sodium hydroxide (4.8 g., 120 mmoles) was dissolved in water (14 ml.) and cooled to 0°, and bromine (3.48 g., 24.0 mmoles) was added dropwise with shaking. When the solution was no longer red, trifluoroacetamide (2.26 g., 20 mmoles) in water (6 ml.) was added, and after being stirred (5 min.) the mixture was heated rapidly to reflux temperature. The volatile products were washed with aqueous hydrochloric acid and aqueous sodium hydroxide, then fractionated *in vacuo*, to give only bromotrifluoromethane (6.9 mmoles, 35%) (Found : M, 147. Calc. for CBrF₃ : M, 149) identified by means of its infrared spectrum. Sodium trifluoroacetate present in the aqueous solution accounted for the missing material.

Reaction of Sodium Trifluoroacetate with Sodium Hypobromite.—A solution of sodium trifluoroacetate (1.36 g., 10.0 mmoles) in water (15 ml.) was heated under reflux and a solution of sodium hypobromite prepared at 0° from sodium hydroxide (20 g.) and bromine (16 g.) in water (50 ml.) was added during 30 min. Refluxing was maintained for a further 40 min. but failed to yield any volatile products.

Reaction of Heptafluorobutyramide with Sodium Hypobromite.—The hypobromite solution was prepared at 0° from sodium hydroxide (10.0 g., 250 mmoles), water (15 ml.) and bromine (1.6 g., 10 mmoles) during 30 min. The amide (1.92 g., 9 mmoles), suspended in water (20 ml.), was then added and the mixture stirred for 10 min., then heated rapidly to reflux temperature. Effervescence was apparent for *ca.* 2 min., then smooth boiling set in. After a further 15 min. the volatile products were pumped into a cooled trap and distilled *in vacuo*, to give bromoheptafluoropropane (1.82 g., 81%) (Found : M, 248. Calc. for C₃BrF₇ : M, 249) identified by means of its infrared spectrum, and a fraction (0.9 mmole; 10%) (M, 17) readily absorbed by acid and shown by qualitative tests to be ammonia.

The aqueous solution gave a positive test for cyanate with copper sulphate-pyridinechloroform, and the cyanate was determined in an 80% aliquot part by conversion into dicarbamoylhydrazine, $NH_2 \cdot CO \cdot NH \cdot NH \cdot CO \cdot NH_2$ as follows. Sodium sulphite (0.5 g.) and 20% aqueous sulphuric acid were added, care being taken not to acidify the solution, which was then cooled; the sodium sulphate which separated was filtered off and discarded. Semicarbazide hydrochloride (0.78 g., 7.0 mmoles) was added to the ice-cold solution, then N-sulphuric acid dropwise to pH 3—4, and the solution was boiled (20 min.) to give a white precipitate which was filtered off, shaken with N-sodium carbonate (20 min.), then water, and dried. The m. p. of the dried solid was 252° (lit., ²³, ¹⁷ 249°).

Attempted Reaction of Heptafluorobutyramide with Bromine.—The amide (0.213 g., 1.0 mmole), water (20 ml.), and bromine (0.48 g., 3.0 mmoles) were heated under reflux for 30 min., and the evolved gases were condensed in a trap cooled by liquid oxygen. Distillation showed that only bromine had been evolved.

Synthesis of N-Bromoheptafluorobutyramide.—Heptafluorobutyramide (42 g., 197 mmoles), dry silver oxide (22.3 g., 96 mmoles), and anhydrous ether (200 ml.) were heated under reflux (48 hr.), to give a greyish-brown mass. Ether (2 l.) was then added, only unchanged silver oxide remaining undissolved. Filtration and evaporation to dryness of the ethereal extract gave a white solid which was heated at 60° in vacuo to remove by sublimation the unchanged heptafluorobutyramide (20 g.). The residual solid was silver heptafluorobutyramide (32.0 g., 98% based on amide used), m. p. 240° (decomp.).

The silver salt (31·2 g., 98 mmoles) was dissolved in trifluoroacetic acid (150 ml.), and bromine (16·0 g., 100 mmoles) in trifluoroacetic acid (200 ml.) was added dropwise with stirring (2 hr.). Removal of the silver bromide and evaporation of the solvent at 40—45° (4 hr.) gave a crude solid which was kept in an evacuated desiccator over solid sodium hydroxide for 24 hr. to remove residual acid, then sublimed at 80—85°/10⁻² mm., to give *N*-bromoheptafluorobutyramide (21·5 g., 75%) (Found : C, 16·6; H, 0·4; N, 4·6. Calc. for C₄HONBrF₇ : C, 16·5; H, 0·3; N, 4·7%), m. p. 78—79°. Husted and Kohlhase ⁵ report m. p. 78—79·2°.

Reactions of N-Bromoheptafluorobutyramide.—(a) Attempted thermal decomposition. The bromo-compound (0.292 g., 1.0 mmole) was heated stepwise in an oil-bath. It melted at *ca*. 80°, but no further change was apparent until 130° when it began to darken; bromine was

28 Jacini, Gazzetta, 1937, 67, 715.

evolved at 160°, and at 180° the liquid appeared to boil. The only volatile product evolved during the total heating period was bromine, and no further change was apparent at higher temperatures.

(b) With hot water. The bromo-amide (0.146 g., 0.5 mmole) and water (20 ml.) gave an acid solution which slowly liberated bromine vapour when heated under reflux. Some of the bromo-amide sublimed into the water-condenser. Examination of the volatile products which passed through the condenser and collected in a trap cooled by liquid oxygen showed them to contain only bromine and a small amount of water.

(c) With aqueous sodium hydroxide. Sodium hydroxide (10 g., 0.25 mole) was dissolved in water (35 ml.) and bromoheptafluorobutyramide (2.92 g., 10 mmoles) was added to the cooled stirred solution, which was then heated rapidly to reflux temperature. The solution effervesced for *ca.* 2 min. then boiled smoothly. After 15 min. the volatile products were pumped into a cooled trap, then distilled *in vacuo*, to give bromoheptafluoropropane (2.28 g., 92%) (Found : M, 249. Calc. for C₂BrF₇ : M, 249) and ammonia (0.2 mmole, 2%).

A quarter of the residual solution used for cyanate determination gave 0.203 g. (69%) of dicarbamoylhydrazine. The remaining solution was acidified with 25% sulphuric acid and distilled to a small volume, the condensate being collected in a flask containing silver carbonate. The excess of silver carbonate was removed, and the water was evaporated under reduced pressure; extraction of the solid with ether followed by evaporation of the ethereal solution gave silver heptafluorobutyrate (0.01 g., 0.5%), identified by means of its infrared spectrum and uncontaminated by silver pentafluoropropionate.

(d) With anhydrous ferric chloride. The bromo-compound (0.146 g., 0.5 mmole) and anhydrous ferric chloride (0.162 g., 1.0 mmole), heated at 50°, gave a viscous liquid which evolved brown fumes. Examination of the material which condensed in a trap attached showed it to contain only bromine.

Sodium N-Bromoheptafluorobutyramide.—N-Bromoheptafluorobutyramide (5.84 g., 20 mmoles) in water (40 ml.) required the addition of 19.6 ml. of N-sodium hydroxide at 5—10° to achieve neutrality. The filtered solution, evaporated to dryness at 30—40°/5 mm., gave sodium N-bromoheptafluorobutyramide (6.20 g., 99%) (Found : C, 15.5; N, 4.5. C₄ONBrF₇Na requires C, 15.3; N, 4.5%) as a white solid; N-H and -OH bands were absent from the 3 μ region of its spectrum, and this is consistent with the formula [C₈F₇·CO·NBr]-Na⁺.

Decomposition of Sodium N-Bromoheptafluorobutyramide in Aqueous Solution.—The sodium salt (0.235 g., 0.75 mmole) and water (10 ml.) were heated to 100° during 10 min. without evolution of gas. The liquid boiled with foaming, and steadily evolved gas, which was collected in an attached trap cooled by liquid oxygen. Foaming ceased after 10 min. and heating was continued for a further 10 min. Fractionation of the volatile product gave only bromoheptafluoropropane (0.169 g., 91%) (Found : M, 249), identified by means of its infrared spectrum. Cyanate ion was determined in the residual aqueous solution by the dicarbamoylhydrazine method described earlier.

Reaction of Trifluoroacetamide with Sodium Hypoiodite.—Iodine (6.1 g., 24 mmoles) was added to ice-cold sodium hydroxide (4.8 g., 120 mmoles) in water (14 ml.), and the mixture was stirred until the brown colour disappeared (1 hr.). The amide (2.26 g., 20 mmoles) in water (6 ml.) was added with stirring (5 min.) and the temperature then raised rapidly to the b. p. After 15 min. under reflux the only volatile reaction product was ammonia (0.158 g., 46%) (Found : M, 18), and in particular trifluoroiodomethane was absent.

Pyrolysis of Sodium N-Bromoheptafluorobutyramide.—The salt (0.235 g., 0.75 mmole) in a flask attached by means of tubing to a trap cooled in liquid oxygen was heated at 10^{-4} mm. in an oil-bath. No decomposition occurred below 150°, but reaction was detectable at 165° and rapid at 170°. Further increase in temperature up to 200° failed to cause further change. Non-condensable gas was not formed. Fractionation of the volatile product *in vacuo* showed it to be heptafluoro-*n*-propyl *iso*cyanate (0.131 g., 83%) (Found : M, 210. Calc. for C₄ONF₇: M, 211). The infrared spectrum of the *iso*cyanate was identical with that of a known sample,⁶ and bromoheptafluoropropane was not present. The residual solid from the reaction was readily soluble in water; bromide, but not cyanate, ion was present.

Reaction of N-Iodoheptafluorobutyramide with Sodium Hydroxide.—Silver heptafluorobutyramide (0.175 g., 0.58 mmole) and iodine (0.153 g., 0.6 mmole), mixed in a mortar, gave a pale yellow odourless solid. This was added to 10% aqueous sodium hydroxide (30 ml.) under reflux, and after 10 min. examination was made of any volatile material which had condensed in an attached trap cooled in liquid oxygen; only a small amount of water was present. Cyanate ion was absent from the residual solution which contained sodium heptafluorobutyrate.

One of us (D. A. B.) is indebted to Imperial Chemical Industries Limited, Plastics Division, for a maintenance grant.

UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE.

[Received, June 29th, 1956.]