

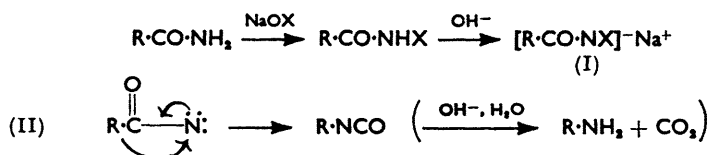
## 7. Perfluoroalkyl Derivatives of Nitrogen. Part V.\* The Mechanism of the Hofmann Reaction with Amides containing Electronegative Groups.†

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The Hofmann reaction with a perfluoro-amide  $R_F \cdot CO \cdot NH_2$  can show a duality of mechanism to give high yields (85—95%) of either  $R_F X$  ( $X = Cl$  or  $Br$ ) or  $R_F \cdot NCO$ . The bromo-compound, for example, is formed by elimination of isocyanate ion from  $R_F \cdot CO \cdot NBr^-$  in a solvent of high dielectric constant, whereas pyrolysis of the anhydrous salt  $[R_F \cdot CO \cdot NBr]^- Na^+$  gives  $R_F \cdot NCO$  with intermediate formation of  $R_F \cdot CO \cdot \ddot{N}:$ . The results are correlated with those from Curtius and Arndt-Eistert reactions. A mechanism is proposed for the reaction of  $YZ$  with a silver salt  $R \cdot CO_2 Ag$  derived from a strong carboxylic acid (the Simonini reaction) to give  $AgY$ ,  $CO_2$ , and  $RZ$  ( $YZ = Cl, Br, I, NOCl$ , or  $NO_2Cl$ ).

It is suggested that the Hofmann reaction with  $\alpha$ -keto-acids,  $\alpha$ -halogeno-acids, 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<sup>1</sup> involves an intramolecular rearrangement to give the isocyanate. 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 isocyanate :



There is ample evidence<sup>2,3</sup> 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 isocyanate.

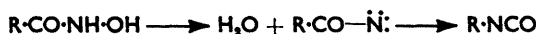
\* Part IV, *J.*, 1956, 3428. † For a preliminary report see *Chem. and Ind.*, 1956, 1050.

<sup>1</sup> Hofmann, *Ber.*, 1881, 14, 2725.

<sup>2</sup> For a review see Wallis and Lane, "Organic Reactions," Vol. III, Wiley, New York, 1946, p. 267.

<sup>3</sup> 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:



Curtius rearrangement of an acyl azide:

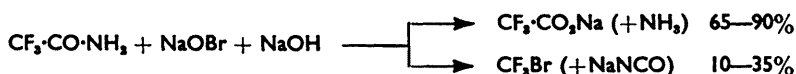


Arndt-Eistert (Wolff) rearrangement of a diazo-ketone:



It has been reported that perfluoro-amides  $\text{R}_\text{F}\cdot\text{CO}\cdot\text{NH}_2$  ( $\text{R}_\text{F}$  = perfluoroalkyl) fail to undergo the Hofmann reaction: trifluoroacetamide is said to yield hexafluoroethane,<sup>4</sup> whereas heptafluorobutyramide gave bromoheptafluoropropane (with sodium hypobromite) or heptafluoropropane (with sodium hypoiodite).<sup>5</sup> The supposed formation of hexafluoroethane was accepted by Husted and Kohlhasse,<sup>5</sup> 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  $\text{CF}_3$  and  $\text{C}_2\text{F}_5$  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  $\text{NaOX}$  with a perfluoro-amide  $\text{R}_\text{F}\cdot\text{CO}\cdot\text{NH}_2$  can show a duality of mechanism, and gives a high yield (85–95%) of either  $\text{R}_\text{F}\text{X}$  ( $\text{X} = \text{Cl}$  or  $\text{Br}$ ) or  $\text{R}_\text{F}\cdot\text{NCO}$  depending on the reaction conditions.

The reaction of trifluoroacetamide with sodium hypobromite was first investigated. Under the conditions reported in the literature,<sup>4</sup> 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<sup>4</sup> 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  $\text{CF}_3\text{Br}$  (149) and  $\text{C}_2\text{F}_6$  (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:



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:



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



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  $\text{R}_\text{F}\text{Br}$ .

Reaction of heptafluorobutyramide with sodium hypobromite in presence of an excess

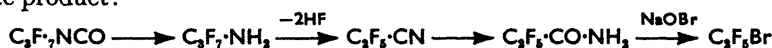
<sup>4</sup> Gryszkiewicz-Trochimowski, Sporzynski, and Wnuk, *Rec. Trav. chim.*, 1947, **66**, 426.

<sup>5</sup> Husted and Kohlhasse, *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%),  $NH_3$  (10%), and  $C_3F_7 \cdot CO_2Na$  (10%). Formation of  $R_FBr$  thus predominates over hydrolysis to give sodium heptafluorobutyrate and ammonia. The formation of sodium cyanate should be particularly noted. That the normal Hofmann reaction to give the *isocyanate*  $C_3F_7 \cdot NCO$  does not occur is shown by the failure to detect this volatile compound or its hydrolysis products  $C_2F_5 \cdot CN$ ,  $C_2F_5 \cdot CO \cdot NH_2$ , or  $C_2F_5 \cdot CO_2NH_4$ . A perfluoroalkyl *isocyanate* such as heptafluoro-*n*-propyl *isocyanate* is known <sup>6</sup> 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.* : <sup>6</sup>



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



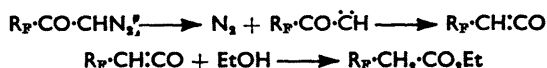
The failure to isolate a perfluoro-amine from the reaction of sodium hypobromite with a perfluoro-amide thus cannot be taken as evidence that the Hofmann rearrangement has failed, although the failure to isolate the known decomposition products of the amine makes it very unlikely that the *isocyanate*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

The absence of heptafluoropropane as product is also noteworthy, since Husted and Kohlhasse <sup>5</sup> reported it as a product from the action of sodium hypiodate 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 ( $C_3F_7 \cdot CO_2Na \longrightarrow C_3F_6 + NaF + CO_2$ ). These conditions cannot be regarded as normal for a Hofmann reaction, and neither heptafluoropropane nor hexafluoropropene 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  $R_F \cdot NCO$ .

The Curtius reaction <sup>6</sup> of a perfluoroacyl halide proceeds normally under correct conditions and gives the *isocyanate* in good yield; this shows that the intermediate,  $R_F \cdot CO \cdot \dot{N}:$ , once formed, can rearrange to  $R_F \cdot NCO$  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; <sup>7</sup> trifluoro-diazoacetone, 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, <sup>7</sup> 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 :

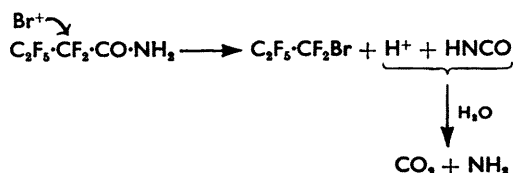


<sup>6</sup> Barr and Haszeldine, *J.*, 1956, 3428.

<sup>7</sup> Brown and Musgrave, *J.*, 1953, 2087.

The success of the Curtius and the Arndt-Eistert reaction clearly shows that the failure to obtain an *isocyanate* (or its subsequent products) by the Hofmann reaction with perfluoro-amides is caused by failure to produce  $R_F \cdot CO \cdot \dot{N}$ : 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:

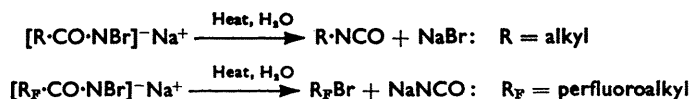


This route was found preferable to the earlier method<sup>8</sup> of treating the amide with silver oxide and bromine in trifluoroacetic acid solution. Bromoheptafluoropropane is not produced by pyrolysis of the *N*-bromo-amide at temperatures up to 200°, or when an aqueous solution of the *N*-bromo-amide 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 *isocyanate*.

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  $[R_F \cdot CO \cdot \text{NX}]^- \text{Na}^+$  clearly must precede liberation of  $R_F \text{Br}$ . 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,  $[\text{C}_3\text{F}_7 \cdot \text{CO} \cdot \text{NBr}]^- \text{Na}^+$ , is a white solid which infrared spectroscopic examination shows to be free from N-H bonds. *N*-Bromoalkylamides usually give only unstable salts, few of which have been isolated,<sup>2,9</sup> 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  $[R_F \cdot CO \cdot \text{NX}]^- \text{Na}^+$  to lose  $\text{X}^-$  to give  $R_F \cdot CO \cdot \dot{N}$ : must thus be the reason for the change in mechanism of the Hofmann reaction:



The separation of halide ion from  $[\text{R} \cdot \text{CO} \cdot \text{NX}]^-$  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

<sup>8</sup> Park, Gerjovich, Lycan, and Lacher, *J. Amer. Chem. Soc.*, 1952, **74**, 2189.

<sup>9</sup> Mauguin, *Ann. Chim. (France)*, 1911, **22**, 297.

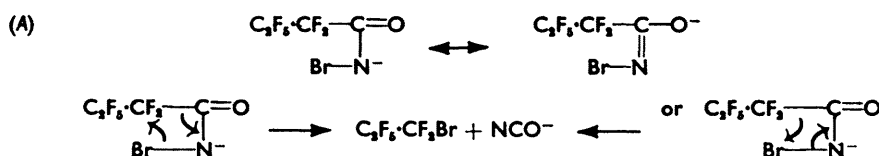
when electron-releasing groups (Me, OMe) are present in the aromatic ring, and slower when electron-attracting groups (CN, NO<sub>2</sub>) are in the ring;<sup>10</sup> the ease of the Hofmann reaction is thus inversely related to the dissociation constant of the acid from which the amide is derived. The failure of bromine to separate from R<sub>F</sub>·CO·N<sup>-</sup>Br 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·N<sub>3</sub> → R·CO·N<sup>·</sup> + N<sub>2</sub>; R·CO·CHN<sub>3</sub> → R·CO·CH<sup>·</sup> + N<sub>3</sub>), 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 electron-attracting groups such as CO<sub>2</sub>H, CN, or NO<sub>2</sub> are in the molecule,<sup>11</sup> and the excellent yields readily obtained when R = perfluoroalkyl.<sup>6</sup>

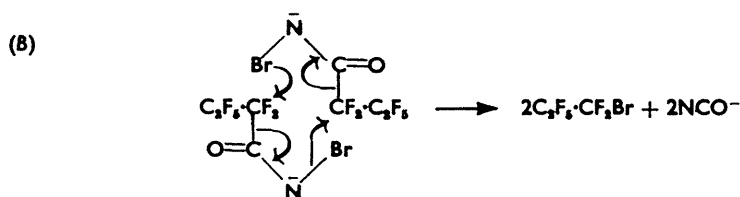
An alternative mechanism must be proposed for the Hofmann reaction with perfluoroamides, the essential step of which is R<sub>F</sub>·CO·N<sup>-</sup>Br → R<sub>F</sub>Br + NCO<sup>-</sup>. Attack of bromide ion or of bromine cation on the α-carbon atom of the ion is unlikely in view of the high yields of R<sub>F</sub>Br obtained by heating [R<sub>F</sub>·CO·NBr]<sup>-</sup>Na<sup>+</sup> in water alone; if bromide ion were lost from the R<sub>F</sub>·CO·N<sup>-</sup>Br 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<sub>F</sub>·CO·NH<sub>2</sub> and sodium hypobromite would be necessary in order to obtain bromine cation, and if this hydrolysis occurred, the yield of R<sub>F</sub>Br is unlikely to be over 90%, yet such yields were readily obtained.

A two-stage process involving intermediate R<sub>F</sub><sup>-</sup> ions is also unlikely, since such fluorocarbanions are known<sup>12</sup> 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.*;

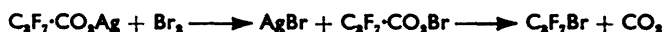


The related bimolecular reaction is less probable :



The 1 : 3-shift of R<sub>F</sub> from carbon to bromine (A) will be facilitated by the marked positive character of the bromine and the negative R<sub>F</sub> 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.* :



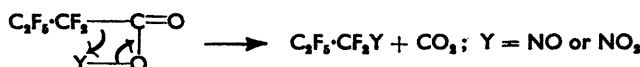
<sup>10</sup> Hauser and Renfrow, *J. Amer. Chem. Soc.*, 1937, **59**, 121, 2308; Bright and Hauser, *ibid.*, 1939, **61**, 618.

<sup>11</sup> Smith, "Organic Reactions," Vol. III, Wiley, New York, 1946, p. 267.

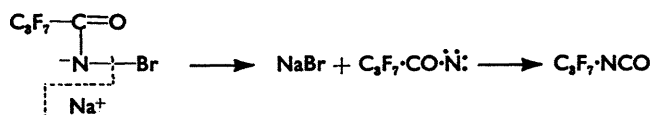
<sup>12</sup> See Haszeldine, "Fluorocarbon Derivatives," Roy. Inst. Chem. Monograph, 1956, for references.



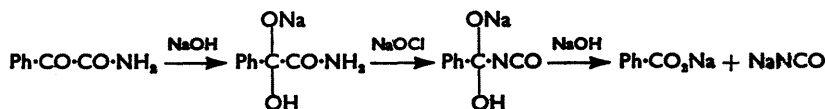
Perfluoroalkyl nitroso- and nitro-compounds are similarly formed by treatment of the silver salt of the acid with nitrosyl or nitryl chloride, with  $R_F \cdot CO \cdot O \cdot NO$  or  $R_F \cdot CO \cdot O \cdot NO_2$  as intermediates,<sup>14</sup> e.g. :


$$\text{C}_6\text{F}_5\cdot\text{CO}\cdot\text{NHI} \longrightarrow \text{I}^+ + \text{C}_6\text{F}_5\cdot\text{CO}\cdot\text{NH}_2 \xrightarrow{\text{OH}^-} \text{C}_6\text{F}_5\cdot\text{CO}_2\text{Na}$$

The above elimination of cyanate ion from  $R_F \cdot CO \cdot NX$  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  $R_F \cdot CO \cdot \bar{N}X$  ion, *e.g.*, as in the crystal lattice of the anhydrous salt, then at a suitable temperature, reaction to yield  $NaX$  and the intermediate  $R_F \cdot CO \cdot \dot{N}$ : and thence  $R_F \cdot NCO$  should not be impossible. This prediction was adequately confirmed by preparation of heptafluoropropyl isocyanate in 83% yield when the *anhydrous* salt  $[C_3F_7 \cdot CO \cdot NBr]^- Na^+$  was heated to  $170^\circ$ :

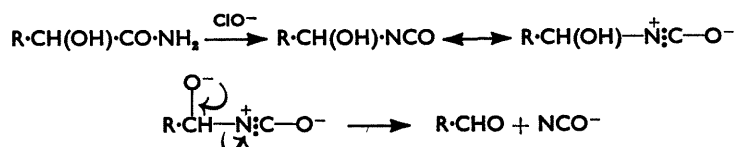


A perfluoroalkyl group is extremely electronegative, and it is to be expected that amides containing other negative groups will show similar behaviour. Examples can be found in the literature, but they are few and a general study is merited in this field. Benzoylformamide yields sodium benzoate (80%)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

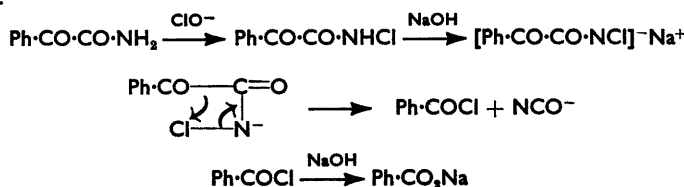


<sup>16</sup> Rinkes, *Rec. Trav. chim.*, 1920, **39**, 200; 1926, **45**, 819; 1929, **48**, 960.

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

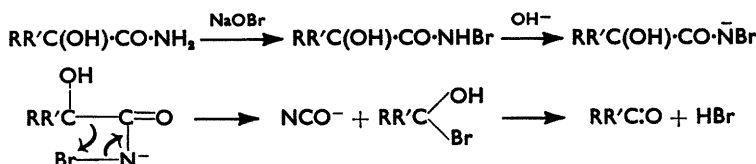


The carbonyl group is electron-attracting, like a perfluoroalkyl group, and a similarity between them in causing apparently anomalous reactions has been noted earlier.<sup>20</sup> It is likely that an intermediate such as  $\text{Ph}\cdot\text{CO}\cdot\text{CO}\cdot\text{N}^+\text{Cl}$  would lose chloride in aqueous solution only with difficulty, and an alternative reaction scheme analogous to (4) above is therefore now suggested :



The parallel thus drawn between  $\alpha$ -keto-compounds and perfluoroalkyl compounds extends to the Curtius reaction. Keto-azides derived from  $\alpha$ -keto-acids rearrange normally,<sup>11</sup> thus revealing that  $\text{R}\cdot\text{CO}\cdot\text{CO}\cdot\text{N}^+\text{:}$ , once produced, can rearrange just like  $\text{R}_\text{F}\cdot\text{CO}\cdot\text{N}^+\text{:}$ .

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



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



We suggest that Kishner's <sup>21</sup> isolation of 2 : 2-dibromopropane and acetone from the reaction of  $\alpha$ -bromoisobutyramide with sodium hypobromite exemplifies this reaction :



Control of pH will clearly be necessary if *gem*.-dihalides are to be isolated, and Stevens and Coffield's <sup>22</sup> 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

<sup>17</sup> Arcus and Prydal, *J.*, 1954, 4018.

<sup>18</sup> Weerman, *Annalen*, 1913, 401, 1.

<sup>19</sup> Arcus and Greenwood, *J.*, 1953, 1937.

<sup>20</sup> Haszeldine and Leedham, *J.*, 1952, 3483; 1954, 1261.

<sup>21</sup> Kishner, *J. Russ. Phys. Chem. Soc.*, 1905, 37, 103, 106; *Zentralbl.*, 1905, 76, I, 1219, 1220.

<sup>22</sup> Stevens and Coffield, *J. Amer. Chem. Soc.*, 1951, 73, 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  $\text{CBrF}_3$ : *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  $\text{CBrF}_3$ : *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  $\text{C}_3\text{BrF}_7$ : *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–pyridine–chloroform, and the cyanate was determined in an 80% aliquot part by conversion into dicarbamoylhydrazine,  $\text{NH}_2\cdot\text{CO}\cdot\text{NH}\cdot\text{NH}\cdot\text{CO}\cdot\text{NH}_2$  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.,<sup>23, 17</sup> 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<sup>-2</sup> mm., to give *N*-bromoheptafluorobutyramide (21.5 g., 75%) (Found: C, 16.6; H, 0.4; N, 4.6. Calc. for  $\text{C}_4\text{HONBrF}_7$ : C, 16.5; H, 0.3; N, 4.7%), m. p. 78–79°. Husted and Kohlhas<sup>5</sup> 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

<sup>23</sup> 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  $C_3BrF_7$  : *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.  $C_4ONBrF_7Na$  requires C, 15.3; N, 4.5%) as a white solid; N–H and –OH bands were absent from the 3  $\mu$  region of its spectrum, and this is consistent with the formula  $[C_3F_7CO\cdot NBr]^-Na^+$ .

*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 Hypiodite.*—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 trifluoriodomethane 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<sup>–2</sup> 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 isocyanate (0.131 g., 83%) (Found : *M*, 210. Calc. for  $C_4ONF_7$  : *M*, 211). The infrared spectrum of the isocyanate was identical with that of a known sample,<sup>6</sup> 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

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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.

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