PERFLUORO KETONE IMINES*

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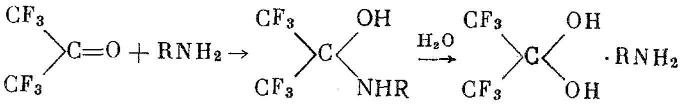
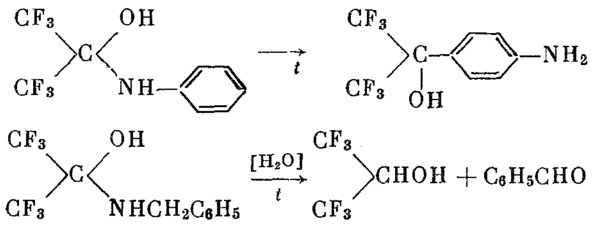
A peculiar feature of fluorinated ketones is the formation of completely stable products of addition at the carbonyl group with nucleophilic reagents, in particular amines. On the other hand, the further transformations of the adducts, which in the case of nonfluorinated ketones lead to products of the complete replacement of the carbonyl oxygen (e.g. to imines, oximes, and hydrazones), are difficult. The effect of a single perfluoroalkyl group on the carbonyl carbon atom is insufficient to suppress the formation of the usual derivatives. Thus, 1,1,1-trifluoroacetone forms an oxime and 2,4-dinitrophenylhydrazone in the normal way [1]. Analogous derivatives have been obtained for 1,1,1-trifluoro-3-phenylacetone [2] and a number of perfluoro aldehydes. In agreement with this we found that the anil of trifluoroacetone is formed directly from aniline and trifluoroacetone (see below). However, when there are two perfluoroalkyl groups these reactions, which require the heterolytic cleavage of a C–O bond, do not occur and the direct synthesis of the "usual" derivatives of perfluoro ketones is therefore impossible.

The reaction of hexafluoroacetone with amino compounds† leads to relatively stable geminal amino alcohols, which do not undergo spontaneous dehydration. These amino alcohols are extremely sensitive to traces of moisture, which give products that can be isolated in the form of quite stable amine salts of hexafluoroacetone hydrate. The dianiline salt of hexafluoroacetone hydrate [5] is of this type; this can be conveniently used for the identification of hexafluoroacetone. With isobutylamine and benzylamine the reaction leads to monoamine salts of hexafluoroacetone hydrate:



$(R{=}C_6H_5CH_2,\ CH_2CH(CH_3)_2)$

By the reaction of hexafluoroacetone with hydroxylamine the hydroxylamine salt of hexafluoro-2-(hydroxyamino)-2-propanol is obtained [6]. Attempts to dehydrate the amino alcohols have not been successful. When heated, geminal arylamino alcohols are rearranged into ar-amino-α,α-bistrifluoromethylbenzyl alcohols [7], and benzylamino alcohols are converted by oxidation-reduction into 1,1,1,3,3,3-hexafluoro-2-propanol and benzaldehyde derivatives [8]:



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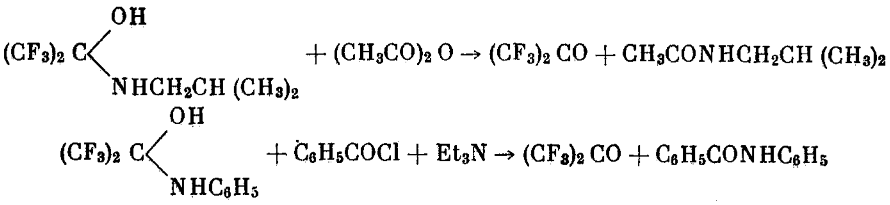
† Under the action of ammonia and of amines, including benzylamine, perfluoro-4-heptanone [3] and pentafluoronitroacetone [4] undergo haloform breakdown.

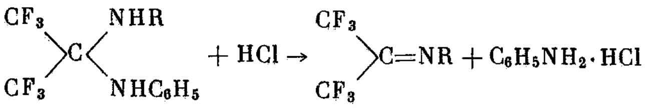
We were unable to obtain imines by the action of dehydrating agents on the amino alcohols. Thus, the action of acetic anhydride on hexafluoro-2-(isobutylamino)-2-propanol and of benzoyl chloride in presence of triethylamine on 2-anilinohexafluoro-2-propanol led to hexafluoroacetone and the corresponding amide:



$$(CF_3)_2C\begin{matrix}OH\\ NHCH_2CH(CH_3)_2\end{matrix} + (CH_3CO)_2O \rightarrow (CF_3)_2CO + CH_3CONHCH_2CH(CH_3)_2$$

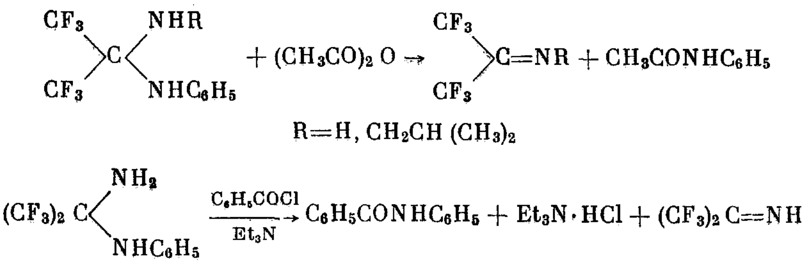
$$(CF_3)_2C\begin{matrix}OH\\ NHC_6H_5\end{matrix} + C_6H_5COCl + Et_3N \rightarrow (CF_3)_2CO + C_6H_5CONHC_6H_5$$

For the preparation of hexafluoroacetone imines it was necessary to develop a number of special methods [9]. One of these consists in the cleavage of N-alkylhexafluoro-N'-phenyl-2,2-propanediamine with hydrogen chloride in ether:



$$\begin{matrix}CF_3\\ CF_3\end{matrix}C\begin{matrix}NHR\\ NHC_6H_5\end{matrix} + HCl \rightarrow \begin{matrix}CF_3\\ CF_3\end{matrix}C{=}NR + C_6H_5NH_2\cdot HCl$$

It was found that this cleavage can be affected by other electrophilic reagents—acetic anhydride or a mixture of benzoyl chloride and triethylamine:

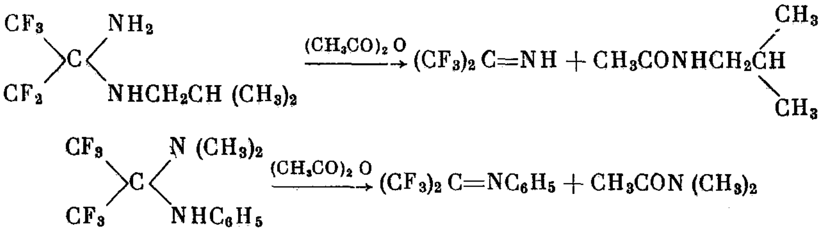


$$\begin{matrix}CF_3\\ CF_3\end{matrix}C\begin{matrix}NHR\\ NHC_6H_5\end{matrix} + (CH_3CO)_2O \rightarrow \begin{matrix}CF_3\\ CF_3\end{matrix}C{=}NR + CH_3CONHC_6H_5$$

$$R{=}H,\ CH_2CH(CH_3)_2$$

$$(CF_3)_2C\begin{matrix}NH_2\\ NHC_6H_5\end{matrix} \xrightarrow[Et_3N]{C_6H_5COCl} C_6H_5CONHC_6H_5 + Et_3N\cdot HCl + (CF_3)_2C{=}NH$$

A peculiar feature of the breakdown is that of the two bases present in the geminal diamine, it is the weaker that is eliminated (aniline). It was of interest to determine whether the elimination of the weaker base is general or is characteristic only for derivatives of hexafluoro-2,2-propanediamine in which one of the nitrogen-attached substituents is phenyl. For this purpose we subjected hexafluoro-N-isobutyl-2,2-propanediamine [9] and hexafluoro-N,N-dimethyl-N'-phenyl-2,2-propanediamine to the cleavage treatment. The latter was prepared by the addition of dimethylamine to the anil of hexafluoroacetone.*

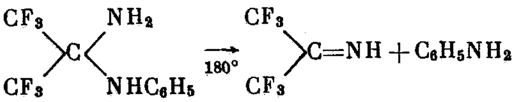


$$\begin{matrix}CF_3\\ CF_3\end{matrix}C\begin{matrix}NH_2\\ NHCH_2CH(CH_3)_2\end{matrix} \xrightarrow{(CH_3CO)_2O} (CF_3)_2C{=}NH + CH_3CONHCH_2CH\begin{matrix}CH_3\\ CH_3\end{matrix}$$

$$\begin{matrix}CF_3\\ CF_3\end{matrix}C\begin{matrix}N(CH_3)_2\\ NHC_6H_5\end{matrix} \xrightarrow{(CH_3CO)_2O} (CF_3)_2C{=}NC_6H_5 + CH_3CON(CH_3)_2$$

In both cases the breakdown led to the regeneration of the original imine. The data available at present do not permit us to establish the general rules governing the cleavage of hexafluoro-2,2-propanediamine derivatives.

Another method, particularly convenient for the preparation of the imine of hexafluoroacetone, consists in the pyrolysis of hexafluoro-N-phenyl-2,2-propanediamine:



$$\begin{matrix}CF_3\\ CF_3\end{matrix}C\begin{matrix}NH_2\\ NHC_6H_5\end{matrix} \xrightarrow[180^\circ]{} \begin{matrix}CF_3\\ CF_3\end{matrix}C{=}NH + C_6H_5NH_2$$

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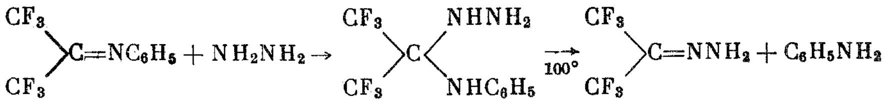
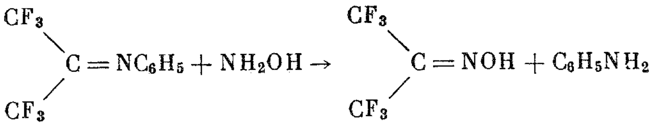
*It is interesting that diethylamine does not react with the anil of hexafluoroacetone at 100°, probably as a result of steric hindrance. On the other hand, the imine of hexafluoroacetone, which is in general more active than the anil, combines, with diethylamine under the same conditions.

This method made it possible to obtain the oxime* and hydrazone of hexafluoroacetone. By the reaction of hydrazine with the anil of hexafluoroacetone under mild conditions an additión product can be isolated, and this breaks down when heated:



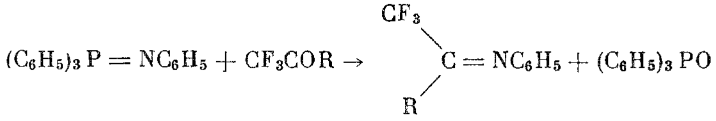
Hydroxylamine does not react with the anil of hexafluoroacetone at room temperature, but at 100° the direct formation of the oxime occurs:



Both the oxime and the hydrazone of hexafluoroacetone were isolated as azeotropic miztures with ether. When the oxime is treated with sulfuric acid it does not undergo Beckmann rearrangement, but only decomposes with formation of hexafluoroacetone.† A third method consists in the reaction of hexafluoroacetone with P,P,P-triphenylphosphine imides [6, 9]:

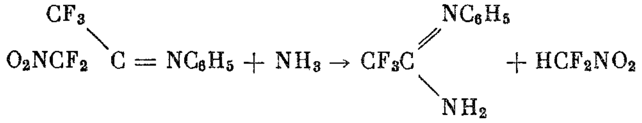
$$(C_6H_5)_3P = NR + (CF_3)_2CO \rightarrow (CF_3)_2C = NR + (C_6H_5)_3PO$$
$$R = H,\ C_6H_5$$

We carried out this reaction with trifluoroacetaldehyde, trifluoroacetone, and pentafluoronitroacetone and obtained the anils of the corresponding carbonyl compounds:



$$R = H,\ CH_3,\ CF_2NO_2$$

As in the case of hexafluoroacetone, reaction went considerably more readily than with nonfluorinated aldehydes and ketones [11]. The anil of trifluoroacetaldehyde, like the anil of chloral,‡ polymerizes rapidly in ethereal solution and in the pure state. However, we succeeded in reducing it to the corresponding amine without isolating it from the reaction mixture. It was considered to be of interest to prepare the products of the addition of ammonia and amines to the anil of pentafluoronitroacetone, but in this case the reaction was complicated by haloform breakdown:



Pentafluoronitroacetone itself undergoes haloform breakdown just as readily [4]. In particular, this fact makes it impossible to prepare its imine from P,P,P-triphenylphosphine imide.

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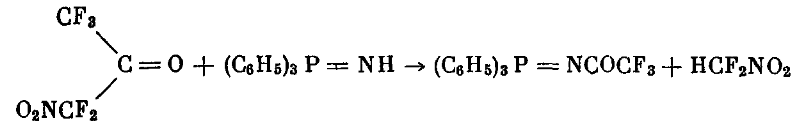
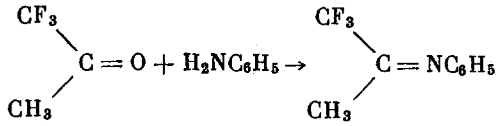
* Hexafluoroacetone oxime was prepared recently by an independent method—by the reduction of heptafluoro-2-nitropropane [10].

† The same occurs with the hydroxylamine salt of hexafluoro-2-(hydroxyamino)-2-propanol [6].

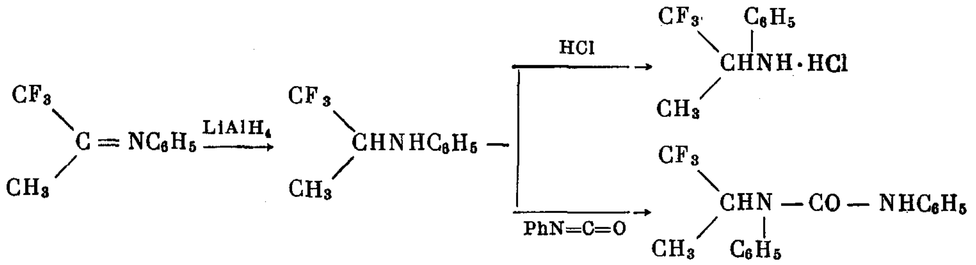
‡ The anil of chloral was prepared by Kresze [12] from N-phenylsulfimine and chloral. The author did not state that, after being distilled from the reaction mixture, this compounds rapidly polymerize, as we found it to do when we reproduced his experiments.



As already stated, we prepared the anil of trifluoroacetone also from aniline and trifluoroacetone:



The anil of trifluoroacetone, unlike the anil of hexafluoroacetone, is unable to combine with such nucleophilic reagents as ammonia, amines, and alcohol. Its reduction leads to N-(2,2,2-trifluoro-1-methylethyl)aniline:



Unlike N-[2,2,2-trifluoro-1-(trifluoromethyl)ethyl]aniline [9], in which basic properties are completely absent (it does not dissolve in concentrated sulfuric acid, does not form a hydrochloride with dry hydrogen chloride, and does not react with phenyl isocyanate at 180°C), N-(2,2,2-trifluoro-1-methylethyl)aniline forms the usual derivatives.

EXPERIMENTAL

Reaction of hexafluoroacetone with amines. Aniline. Aniline was cooled while an equimolecular amount of hexafluoroacetone was passed in. Toward the end of the reaction the mass solidified. We obtained an unstable amino alcohol of m.p. 42-49° (a mixture with the dianiline salt of hexafluoroacetone hydrate melted at 24-35°), which when left in air was converted into the dianiline salt of hexafluoroacetone hydrate, m.p. 64-66°, undepressed by admixture of a known sample [5]. 4.5 g of hexafluoroacetone was passed into 3.2 g of aniline in 20 ml of dry ether, and then 4.8 g of benzoyl chloride and 3.5 g of triethylamine were added. The liberation of hexafluoroacetone was observed. On the next day the precipitate formed was filtered off, washed with water, and crystallized from alcohol. We obtained 5.5 g (80%) of benzanilide.

Isobutylamine. 6 g of hexafluoroacetone was passed into 2.5 g of isobutylamine with cooling. An oil was obtained, which when left in air was converted into the isobutylamine salt of hexafluoroacetone hydrate, m.p. 80-91° (from heptane). Found: C 32.62; H 5.0; F 42.98; N 5.31%. $C_7H_{13}F_6NO_2$. Calculated: C 32.8; H 4.68; F 44.5; N 5.45%.

3.5 g of acetic anhydride was added to the amino alcohol, and when the exothermic reaction had stopped the mixture was heated in a water bath. We obtained 4.3 g (72%) of hexafluoroacetone. By fractionation of the residue we isolated 2.7 g (69%) of N-isobutylacetamide, b.p. 225-228°.

Benzylamine. When equimolecular amounts of benzylamine and hexafluoroacetone were mixed, an amino alcohol was formed as an oil, which when left in air was converted into the benzylamine salt of hexafluoroacetone hydrate, m.p. 84-85° (from hexane). Found: F 39.54%. $C_{10}H_{11}F_6NO_2$. Calculated: F 39.9%. Regarding the transformations of the amino alcohol on heating see [8].

Hexafluoro-N,N-dimethyl-N'-phenyl-2,2-propanediamine. Excess of dimethylamine was passed into 7.6 g of the anil of hexafluoroacetone. On the next day fractionation gave 7.7 g (85%) of the diamine; b.p. 59-62° (6 mm); m.p. 29-30°. Found: F 39.86; N 9.85%. $C_{11}H_{12}F_6N_2$. Calculated: F 39.9; N 9.78%. A mixture of 7 g of the anil of hexafluoroacetone and 2 g of diethylamine was heated in a sealed tube for 5 h at 100°. By fractionation we recovered 5.9 g (80%) of unchanged anil.

N,N-Diethylhexafluoro-2,2-propanediamine. A mixture of 2.2 g of the imine of hexafluoroacetone and 1 g of diethylamine was heated in a sealed tube for four hours at 100°. Fractionation gave 1.4 g (45%) of the diamine; b.p. 67-69° (90 mm), n_D^{21} 1.3572, d_4^{21} 1.257. Found: F 47.4%; MR 41.51. $C_7H_{12}F_6N_2$. Calculated: F 47.9%; MR 41.72.

Breakdown of hexafluoro-2,2-propanediamine and its N-derivatives. A mixture of 3.2 g of hexafluoro-2,2-propanediamine and 3.8 g of acetic acid was boiled for one hour in a water bath. In a trap cooled to −50° we collected 2.2 g (80%) of the imine of hexafluoroacetone. From the residue, after treatment with ether, we isolated 0.65 g (65%) of acetamide.

10.3 g of hexafluoro-N-phenyl-2,2-propanediamine was mixed with 4.1 g of acetic anhydride. On the next day the imine of hexafluoroacetone was distilled from the mixture. We obtained 4.8 g (72%) of the imine. The solid residue was identified as acetanilide. A solution of 1.9 g of hexafluoro-N-phenyl-2,2-propanediamine, 1.1 g of benzoyl chloride, and 0.7 g of triethylamine in 30 ml of ether was allowed to stand. After one week the precipitate of triethylamine hydrochloride was filtered off. The residue remaining after the removal of ether was crystallized from alcohol. We obtained 0.9 g (65%) of benzanilide.

5 g of hexafluoro-N-isobutyl-N'-phenyl-2,2-propanediamine was mixed with 1.6 g of acetic anhydride. On the next day by fractionation we isolated a fraction of b.p. 85-119°, which was washed with sodium bicarbonate solution and with water and dried with magnesium sulfate. After redistillation we obtained 1.9 g (55%) of the isobutylimine of hexafluoroacetone, b.p. 86-89° [9].

4.8 g of hexafluoro-N-isobutyl-2,2-propanediamine was mixed with 2.1 g of acetic anhydride. On the next day 2.8 g (85%) of the imine of hexafluoroacetone was driven from the mixture. In the residue, by thin-layer chromatography on unbound alumina, we detected N-isobutylacetamide.

A mixture of 5 g of hexafluoro-N,N-dimethyl-N'-phenyl-2,2-propanediamine and 1.8 g of acetic anhydride was heated at 100° for one hour. The mixture was poured into water, and the oil precipitated was extracted with ether. N,N-Dimethylacetamide was shown to be present in the aqueous layer by thin-layer chromatography. The ether extract was washed with sodium bicarbonate solution and dried. By fractionation we obtained 3.6 g (86%) of the anil of hexafluoroacetone.

[1-Anilino-2,2,2-trifluoro-1-(trifluoromethyl)]hydrazine. 8.2 g of the anil of hexafluoroacetone was added with stirring and cooling with ice water to 1 g of hydrazine. We obtained 8.5 g (92%) of the substituted hydrazine, m.p. 75-77° (from aqueous alcohol). Found: F 41.56; N 15.46%. $C_9H_9F_6N_3$. Calculated: F 41.75; N 15.40%.

Hexafluoroacetone hydrazone. A solution of 8.1 g of the anil of hexafluoroacetone and 1.1 g of hydrazine in 20 ml of alcohol was boiled for one hour. The mixture was poured into 100 ml of water and extracted with ether. The ether extracts were washed with 1 : 10 hydrochloric acid, water, calcium chloride solution, and again water. The solution was dried with magnesium sulfate and fractionated. We obtained 3.3 g (50%) of the azeotropic mixture of the hydrazone and ether, b.p. 91-95°. Found: C 24.75; H 2.24; F 56.98%. Calculated for an azeotropic mixture containing 10% of ether: C 24.48; H 2.35; F 56.9%. Infrared spectrum: 1620 cm^{-1} (C = N bond).

Hexafluoroacetone oxime. A mixture of 7.4 g of the anil of hexafluoroacetone and 1 g of hydroxylamine was heated for 11 h at 100°. The mixture was dissolved in ether, and the solution was washed with hydrochloric acid (1 : 5) and dried. Fractionation gave 4.3 g of the azeotropic mixture of the oxime and ether; b.p. 97-102°; 45-47° (75 mm); n_D^{20} 1.3224; d_4^{20} 1.194. Found: C 32.41; H 3.9; F 47.15%. Calculated for an azeotropic mixture containing 27% of ether: C 32.02; H 4.05; F 46.98%. Its identity with the oxime prepared by the method given in [10] was shown by gas-liquid chromatography.

2.4 g of the azeotropic mixture of hexafluoroacetone oxime and ether was added with cooling to 4 ml of concentrated sulfuric acid contained in a flask fitted with a reflux condenser connected to a trap cooled to −78°. In the course of 90 min the bath temperature was raised from 80 to 135°. In the trap we collected 1.3 g (80%) of hexafluoroacetone, identified as the dianiline salt of its hydrate.

Anil of pentafluoronitroacetone. 25 g of pentafluoronitroacetone was added to a suspension of 47.3 g of P,P,P-triphenylphosphine imide in 200 ml of ether. On the next day the precipitate of triphenylphosphine oxide was filtered off. Fractionation of the filtrate gave 28 g (80%) of the anil; b.p. 52-54° (4 mm); n_D^{23} 1.421; d_4^{23} 1.421. Found: C 39.97; H 1.75; F 35.7%; MR 50.39. $C_9H_5F_5N_2O_2$. Calculated: C 40.3; H 1.80; F 35.4%; MR 49.2.

2,2,2-Trifluoro-N'-phenylacetamidine. Excess of ammonia was passed into 12.8 g of the anil of pentafluoronitroacetone. After treatment with carbon tetrachloride we obtained 6.5 g (72%) of the amidine, m.p. 77-78°. Found: C 50.92; H 3.8; F 31.49; N 15.33%. $C_8H_7F_3N_2$. Calculated: C 51.0; H 3.72; F 30.3; N 14.9%. Infrared spectrum: 1670 cm^{-1} (C = N bond).

P,P,P-Triphenyl-N-(trifluoroacetyl)phosphine imide. 7.2 g of pentafluoronitroacetone was added to 10.3 g of P,P,P-triphenylphosphine imide in 30 ml of diglyme. The residue remaining after the removal of solvent was recrystallized from methanol. We obtained 3.7 g (27%) of the acylimide, m.p. 160-161°. Found: C 64.35; H 4.13; F 15.58; N 3.75%. $C_{20}H_{15}F_3NOP$. Calculated: C 64.32; H 4.03; F 15.28; N 3.73%. Infrared spectrum: 1650 cm^{-1} (C—O group), 1410 cm^{-1} (P = N bond).

Anil of trifluoroacetaldehyde. This was prepared analogously to the anil of pentafluoronitroacetone. It slowly polymerizes in ethereal solution at 0°. In the pure state [b.p. 157-159°, 64-67° (2 mm)] it polymerizes with liberation of heat with formation of a solid polymer. Found: F 32.85; N 7.85%. $C_8H_8F_3N$. Calculated: F 32.95; N 8.08%. On treatment of an ethereal solution of the anil of trifluoroacetaldehyde with lithium aluminum hydride we obtained N-(2,2,2-trifluoroethyl)aniline, b.p. 73-74° (10 mm). Found: F 31.24; N 8.39%. $C_8H_8F_3N$. Calculated: F 32.5, N 8.02%.

Anil of trifluoroacetone. 13 g of trifluoroacetone was added with cooling to a solution of 10 g of aniline in 30 ml of benzene. After two days the solution was washed with hydrochloric acid (1 : 10) cooled to 0° and with water, and it was dried with magnesium sulfate. Fractionation gave 5 g (25%) of the anil; b.p. 43-45° (5 mm); n_D^{20} 1.4706; d_4^{20} 1.169. Found: C 57.95; H 4.69; F 30.13%; MR 44.23. $C_9H_8F_3N$. Calculated: C 57.76; H 4.28; F 30.44%; MR 43.26.

5 g of trifluoroacetone was added to a suspension of 15.7 g of N,P,P,P-tetraphenylphosphine imide in 50 ml of ether. On the next day the precipitate of triphenylphosphine oxide was filtered off. By the fractionation of the filtrate we isolated 4 g (48%) of the anil of trifluoroacetone, b.p. 58-60° (10 mm).

N-(2,2,2-Trifluoro-1-methylethyl)aniline. 5 g of the anil of trifluoroacetone was added to a stirred suspension of 0.8 g of lithium aluminum hydride in 50 ml of ether. Stirring was continued for two hours. On the next day the mixture was decomposed with water and treated with concentrated alkali; the ether layer was separated. By fractionation we obtained 3 g (60%) of the amine; b.p. 75-77° (10 mm), n_D^{20} 1.4761; d_4^{20} 1.196. Found: C 57.29; H 5.47; F 30.3%; MR 44.58. $C_9H_{10}F_3N$. Calculated: C 57.25; H 5.3; F 30.1%; MR 44.18.

N-(2,2,2-Trifluoro-1-methylethyl)aniline hydrochloride sublimes at 105-115° (in a sealed capillary). Found: Cl 15.55%. $C_9H_{11}F_3NCl$. Calculated: Cl 15.76%.

1,3-Diphenyl-1-(2,2,2-trifluoro-1-methylethyl)urea. 0.61 g of N-(2,2,2-trifluoro-1-methylethyl)aniline was mixed with 0.38 g of phenyl isocyanate. After two weeks the semisolid mass was dissolved in 20 ml of benzene and boiled for four hours. The solid residue remaining after benzene had been distilled off was recrystallized from heptane. We obtained 0.7 g (70%) of the urea, m.p. 88-89°. Found: N 9.13%. $C_{16}H_{15}F_3N_2O$. Calculated: N 9.09%.

SUMMARY

1. With amino compounds hexafluoroacetone forms relatively stable gemical amino alcohols, which do not undergo dehydration.

2. A number of special methods were developed for the preparation of hexafluoroacetone imines; these were based on the decomposition of hexafluoro-2,2-propanediamine derivatives.

3. Trifluoroacetaldehyde, 1,1,1-trifluoroacetone, and pentafluoronitroacetone imines were prepared by Staudinger's reaction, and a number of their reactions were studied.

LITERATURE CITED

1. H. P. Braendlin and E. T. McBee, "Advances in Fluorine Chemistry," (London, 1963), p. 1.
2. W. R. Nes and A. Burger, J. Amer. Chem. Soc., 72, 5410 (1950).
3. M. Hauptstein and R. A. Braun, J. Amer. Chem. Soc., 77, 4930 (1955).
4. I. L. Knunyants and A. V. Fokin, Izv. AN SSSR. Ser. khim., in the press.
5. I. L. Knunyants, Ch'en Ch'ing-yün, N. P. Gambaryan, and E. M. Rokhlin, Zh. VKhO im. Mendeleeva, 5, 114 (1960).

6. I. L. Knunyants, Ch'en Ch'ing-yün, N. P. Gambaryan, and E. M. Rokhlin, Zh. VKhO im. Mendeleeva, 1962, 684.
7. I. L. Knunyants, E. M. Rokhlin, N. P. Gambaryan, Yu. A. Cheburkov, and Ch'en Ch'ing-yün, Khim. nauka i prom -st^1, 4, 802 (1959).
8. I. L. Knunyants and N. P. Gambaryan, Izv. AN SSSR. Ser. khim., in the press.
9. Yu. V. Zeifman, N. P. Gambaryan, and I. L. Knunyants, Dokl. AN SSSR, 153, 1334 (1963).
10. I. L. Knunyants, B. L. Dyatkin, L. S. German, V. A. Komarov, and I. N. Rozhkov, Zh. VKhO im. Mendeleeva, 8, 709 (1963).
11. H. Staudinger and E. Hauser, Helv. chim. acta, 4, 874 (1921).
12. R. Albrecht, G. Kresze, and B. Mlakar, Chem. Ber., 97, 483 (1964).