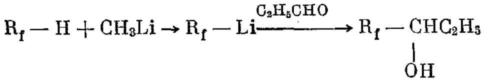
# MOBILITY OF HYDROGEN ATOMS IN MONO-H-POLYFLUOROALKANES AND RELATED COMPOUNDS

## COMMUNICATION 2. 2H-HEXAFLUORO-2-(TRIFLUOROMETHYL)PROPANE IN THE MICHAEL REACTION*

I. L. Knunyants, S. T. Kocharyan,
and E. M. Rokhlin

UDC 542.95 + 661.723-16

In view of the known proton mobility of hydrogen atoms in mono-H-polyfluoroalkanes [2] it could be expected that these compounds would be able to undergo the reactions characteristic for compounds containing an active methylidyne group. However, up to now there has been no significant information in the literature on the application of the mobility of hydrogen atoms in mono-H-polyfluoroalkanes in synthesis. We can refer only to the synthesis of the secondary alcohols (I) from propionaldehyde and 1H- and 2H-heptafluoropropanes (II) via the corresponding organolithium compounds (III) [2]:

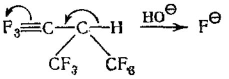


$$\underset{\text{(II)}}{R_f-H} + CH_3Li \rightarrow \underset{\text{(III)}}{R_f-Li} \xrightarrow{C_2H_5CHO} \underset{\text{(I)}}{R_f-\underset{OH}{\underset{|}{C}}HC_2H_5}$$

$$R_f = CF_3CF_2CF_2 \text{ or } (CF_3)_2CF$$

However, the alcohols (I) were obtained in low yields and in the form of difficultly separable mixtures with other reaction products.

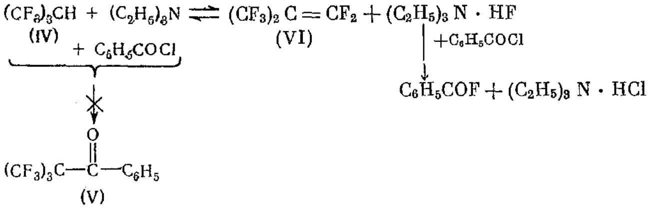
The accumulation of perfluoroalkyl groups raises the acidity of mono-H-polyfluoroalkanes, but also facilitates the elimination of fluorine atoms in the form of ions under the action of bases. Thus, 2H-hexafluoro-2-(trifluoromethyl)propane (IV) (pK ≈ 11) is very readily split under the action of alkalies [2]:



(IV)

To bring compounds of the type of 2H-hexafluoro-2-(trifluoromethyl)propane into reaction at the active methylidyne group (Michael reaction, aldol condensation, C-acylation, etc.) it is necessary to choose a basic catalyst such that it will polarize the C—H bond sufficiently without bringing about the mineralization of fluorine atoms.

We have shown previously that under the action of triethylamine 2H-hexafluoro-2-(trifluoromethyl)-propane is dehydrofluorinated reversibly and that the equilibrium is very much on the side of the formation of the original reactants [1]. It could be hoped, therefore, that triethylamine would be found to be a suitable catalyst for the condensation reactions of 2H-hexafluoro-2-(trifluoromethyl)propane. However, an attempt to use triethylamine as a catalyst in the C-acylation of 2H-hexafluoro-2-(trifluoromethyl)-propane was not successful: in the reaction with benzoyl chloride, instead of the expected ketone (V), perfluoroisobutene (VI) was formed as a result of the displacement of the equilibrium to the right [1]



---

* For communication 1 see [1].

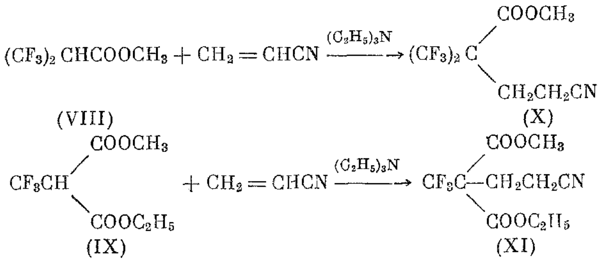
Institute of Heteroorganic Compounds, Academy of Sciences of the USSR. Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 6, pp. 1057-1062, June, 1966. Original article submitted December 13, 1965.

However, in the present work we have shown that triethylamine can be used successfully as a catalyst in the Michael reaction in the case of 2H-hexafluoro-2-(trifluoromethyl)propane and related compounds. It was found that in presence of triethylamine 2H-hexafluoro-2-(trifluoromethyl)propane adds at the double bond of acrylic systems — acrylonitrile, methyl acrylate, and acrolein. In this way we obtained 5,5,5-trifluoro-4,4-bistrifluoromethylvaleronitrile (VIIa), methyl 5,5,5-trifluoro-4,4-bistrifluoromethylvalerate (VIIb), and 5,5,5-trifluoro-4,4-bistrifluoromethylvaleraldehyde (VIIc):

$$\underset{\text{(IV)}}{(CF_3)_3CH} + CH_2=CH-X \xrightarrow{(C_2H_5)_3N} \underset{\text{(VII)}}{(CF_3)_3CCH_2CH_2X}$$

$$\text{(VII): a) } X = CN; \quad \text{b) } X = COOCH_3; \quad \text{c) } X = CHO$$

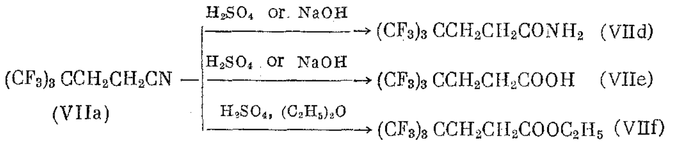
3,3,3-Trifluoro-2-(trifluoromethyl)propionic and (trifluoromethyl)malonic esters (VIII) and (IX) react analogously with greater ease, which confirms that alkoxycarbonyl groups have a stronger activating action than perfluoroalkyl groups. The cyanoethylation of the esters (VIII) and (IX) leads to the corresponding 2-cyanoethyl derivatives (X) and (XI):



$$\underset{\text{(VIII)}}{(CF_3)_2CHCOOCH_3} + CH_2=CHCN \xrightarrow{(C_2H_5)_3N} \underset{\text{(X)}}{(CF_3)_2C(COOCH_3)CH_2CH_2CN}$$

$$\underset{\text{(IX)}}{CF_3CH(COOCH_3)(COOC_2H_5)} + CH_2=CHCN \xrightarrow{(C_2H_5)_3N} \underset{\text{(XI)}}{CF_3C(COOCH_3)(COOC_2H_5)-CH_2CH_2CN}$$

By the hydrolysis of 5,5,5-trifluoro-4,4-bistrifluoromethylvaleronitrile (VIIa) we obtained the corresponding amide (VIId) and acid (VIIe). Ethyl 5,5,5-trifluoro-4,4-bistrifluoromethylvalerate (VIIf) was obtained by heating the nitrile with concentrated sulfuric acid in presence of diethyl ether.

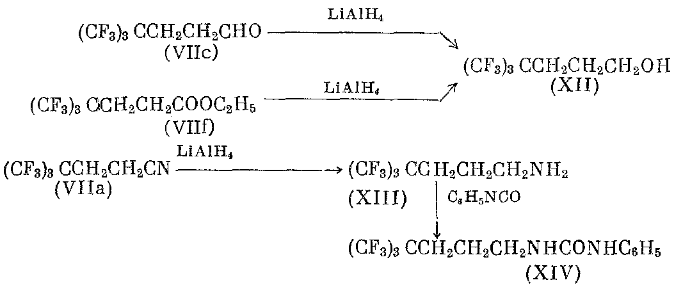


$$\underset{\text{(VIIa)}}{(CF_3)_3CCH_2CH_2CN} \xrightarrow{H_2SO_4 \text{ or } NaOH} (CF_3)_3CCH_2CH_2CONH_2 \ \text{(VIId)}$$

$$\xrightarrow{H_2SO_4 \text{ or } NaOH} (CF_3)_3CCH_2CH_2COOH \ \text{(VIIe)}$$

$$\xrightarrow{H_2SO_4,\ (C_2H_5)_2O} (CF_3)_3CCH_2CH_2COOC_2H_5 \ \text{(VIIf)}$$

Reduction of the aldehyde (VIIc) or ester (VIIf) led to 5,5,5-trifluoro-4,4-bistrifluoromethyl-1-pentanol (XII), and reduction of the nitrile (VIIa) led to 5,5,5-trifluoro-4,4-bistrifluoromethylpentylamine (XIII), which was characterized in the form of the corresponding substituted phenylurea (XIV):

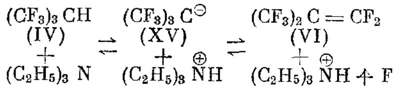


$$\underset{\text{(VIIc)}}{(CF_3)_3CCH_2CH_2CHO} \xrightarrow{LiAlH_4} \underset{\text{(XII)}}{(CF_3)_3CCH_2CH_2CH_2OH} \xleftarrow{LiAlH_4} \underset{\text{(VIIf)}}{(CF_3)_3CCH_2CH_2COOC_2H_5}$$

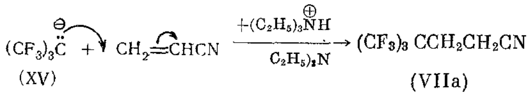
$$\underset{\text{(VIIa)}}{(CF_3)_3CCH_2CH_2CN} \xrightarrow{LiAlH_4} \underset{\text{(XIII)}}{(CF_3)_3CCH_2CH_2CH_2NH_2} \xrightarrow{C_6H_5NCO} \underset{\text{(XIV)}}{(CF_3)_3CCH_2CH_2CH_2NHCONHC_6H_5}$$

Thus, in its application to 2H-hexafluoro-2-(trifluoromethyl)propane the Michael reaction opens up fairly wide possibilities in the synthesis of various compounds containing the perfluoro-t-butyl group.

As regards the mechanism of this reaction, it may be supposed that it is effected with intermediate formation of the carbanion (XV), which reacts at the activated double bond:

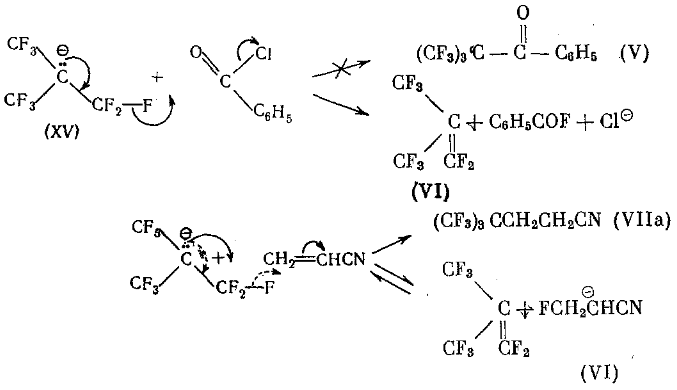


$$\underset{\text{(IV)}}{(CF_3)_3CH} + (C_2H_5)_3N \rightleftharpoons \underset{\text{(XV)}}{(CF_3)_3C^{\ominus}} + (C_2H_5)_3\overset{\oplus}{N}H \rightleftharpoons \underset{\text{(VI)}}{(CF_3)_2C=CF_2} + (C_2H_5)_3\overset{\oplus}{N}H + F^{\ominus}$$



$$\underset{\text{(XV)}}{(CF_3)_3\overset{\ominus}{C}} + CH_2=CHCN \xrightarrow[(C_2H_5)_3N]{+(C_2H_5)_3\overset{\oplus}{N}H} \underset{\text{(VIIa)}}{(CF_3)_3CCH_2CH_2CN}$$

However, in reaction with benzoyl chloride the same carbanion does not give the corresponding ketone (V), but loses a fluoride ion and is converted into perfluoroisobutene (VI) [1]. This can be explained either by steric hindrance to the approach of the benzoyl chloride molecule to the carbanion (XV) from the side of the tertiary carbon atom, or on the view that, under the conditions of the reaction, the reaction of the fluoride ion with benzoyl chloride is irreversible, in contrast to the addition of the fluoride ion to the activated double bond of the acrylic system:



In the future we intend to study the mechanisms of these reactions and the behavior of the 2H-hexafluoro-2-(trifluoromethyl)propane—triethylamine system under various conditions.

## EXPERIMENTAL

5,5,5-Trifluoro-4,4-bistrifluoromethylvaleronitrile (VIIa). A mixture of 26 g of 2H-hexafluoro-2-(trifluoromethyl)propane, 6 g of acrylonitrile, and 2.8 g of triethylamine was heated in a sealed tube in a boiling water bath for 77 h. By distillation of the mixture we isolated 20.5 g (66%) of 5,5,5-trifluoro-4,4-bistrifluoromethylvaleronitrile; b.p. 80-81° (55 mm); m.p. ~ 25°. Found %: N 5.09; F 62.64. $C_7H_4F_9N$. Calculated %: N 5.12; F 62.63. NMR spectrum (internal standard hexamethyldisiloxane): $\delta$ $CH_2$ 2.5 (singlet).

5,5,5-Trifluoro-4,4-bistrifluoromethylvaleraldehyde (VIIc). A mixture of 5.5g of 2H-hexafluoro-2-(trifluoromethyl)propane, 1.4 g of acrolein, and 0.35 g of triethylamine was left overnight in a sealed tube at 0°. On the next day vacuum distillation gave 1.5 g (20%) of 5,5,5-trifluoro-4,4-bistrifluoromethylvaleraldehyde; b.p. 50-53° (40 mm). Found %: F 61.87. $C_7H_5F_9O$. Calculated %: F 61.95.

In addition, distillation of the residue gave 2 g of a high-boiling mixture of unidentified condensation products; b.p. 92-96° (2 mm).

Methyl 5,5,5-Trifluoro-4,4-bistrifluoromethylvalerate (VIIb). A mixture of 7.5 g of 2H-hexafluoro-2-(trifluoromethyl)propane, 2.8 g of methyl acrylate, and 1.5 g of triethylamine was heated in a sealed glass tube in a boiling water bath for 20 days. Distillation gave 3.1 g (30%) of methyl 5,5,5-trifluoro-4,4-bistrifluoromethylvalerate; b.p. 63-64° (33 mm). Found %: F 55.53. $C_8H_7F_9O_2$. Calculated %: F 55.88.

The ester (VIIb) was also formed in the methylation of 5,5,5-trifluoro-4,4-bistrifluoromethylvaleric acid (VIIe) with diazomethane.

Methyl 4-Cyano-2,2-bistrifluoromethylbutyrate (X). A mixture of 10 g of methyl 3,3,3-trifluoro-2-(trifluoromethyl)propionate (VIII) [3], 2.5 g of acrylonitrile, and 1.1 g of triethylamine was heated in a boiling water bath for 15 h, and we obtained 6 g (50%) of the nitrile (X); b.p. 72-74° (3 mm). Found %: N 5.38; F 43.30. $C_8H_7F_6NO_2$. Calculated %: N 5.32; F 43.34.

Ethyl Methyl (2-Cyanoethyl)(trifluoromethyl)malonate (XI). A mixture of 9 g of ethyl methyl (trifluoromethyl)malonate (IX) [1], 2.2 g of acrylonitrile, and 0.73 g of triethylamine was heated in a boiling water bath for 7.5 h, and we obtained 5 g (45%) of the nitrile (XI); b.p. 125-127° (3 mm). Found %: N 5.39; F 21.84. $C_{10}H_{12}F_3NO_4$. Calculated %: N 5.20; F 21.34.

5,5,5-Trifluoro-4,4-bistrifluoromethylvaleric Acid (VIIe) and Its Amide (VIId). a) A mixture of 3 g of 5,5,5-trifluoro-4,4-bistrifluoromethylvaleronitrile (VIIa), 3 ml of water, 3 ml of concentrated sulfuric acid, and 3 ml of glacial acetic acid was heated for 4.5 h in a boiling water bath, and the mixture was then poured into 200 ml of cold water. The precipitate formed was reprecipitated from its solution in sodium bicarbonate solution by the addition of dilute hydrochloric acid. We obtained 2.63 g (82%) of 5,5,5-trifluoro-4,4-bistrifluoromethylvaleric acid (VIIe), m.p. 82-83° (from benzene). Found %: C 28.76; H 1.91; F 58.69. $C_7H_5F_9O_2$. Calculated %: C 28.76; H 1.71; F 58.56.

b) A mixture of 1 g of 5,5,5-trifluoro-4,4-bistrifluoromethylvaleronitrile (VIIa) and 2.5 ml of concentrated sulfuric acid was heated at 140-170° for 1 h, cooled, and poured in cold water. The precipitate formed was washed with water and then extracted with sodium bicarbonate solution and with ether. Acidification of the bicarbonate solution gave 0.19 g (18%) of 5,5,5-trifluoro-4,4-bistrifluoromethylvaleric acid (VIIe). The ether extract was evaporated, and the residue consisted of 0.6 g (55%) of 5,5,5-trifluoro-4,4-bistrifluoromethylvaleramide (VIId), m.p. 89-90° (from benzene). Found %: N 5.32; F 58.75. $C_7H_6F_9NO$. Calculated %: N 4.81; F 58.76.

c) A mixture of 1 g of 5,5,5-trifluoro-4,4-bistrifluoromethylvaleronitrile (VIIa), 0.4 g of KOH, 0.4 ml of water, and 5 ml of alcohol was boiled for 3.5 h, and the mixture was evaporated in air on a clock glass. The residue was treated with sodium bicarbonate solution. As a precipitate we obtained 0.25 g (23.5%) of the amide (VIId), m.p. 88-89° (from benzene); a mixture with the sample prepared by the method (b) melted without depression. By acidification of the bicarbonate solution we obtained 0.4 g (37.4%) of 5,5,5-trifluoro-4,4-bistrifluoromethylvaleric acid (VIIe), m.p. 81-82° (from benzene), undepressed by admixture of the samples prepared by the methods (a) and (b).

It was shown by titration that, when 5,5,5-trifluoro-4,4-bistrifluoromethylvaleronitrile was boiled with alcoholic KOH, 5-6% of its fluorine was eliminated in the form of fluoride ion.

Ethyl 5,5,5-Trifluoro-4,4-bistrifluoromethylvalerate (VIIf). A mixture of 2 g of 5,5,5-trifluoro-4,4-bistrifluoromethylvaleronitrile (VIIa), 4 ml of diethyl ether, and 12 ml of concentrated sulfuric acid was heated under reflux at 140-165° for 5 h. Vacuum distillation (about 25 mm, bath temperature up to 180°) gave an impure product, which was washed with water and dried with anhydrous magnesium sulfate. Distillation gave 1.2 g (51%) of ethyl 5,5,5-trifluoro-4,4-bistrifluoromethylvalerate; b.p. 67-68° (25 mm); $n_D^{24}$ 1.3428. Found %: C 33.71; H 3.10; F 53.40. $C_9H_9F_9O_2$. Calculated %: C 33.75; H 2.84; F 53.44.

5,5,5-Trifluoro-4,4-bistrifluoromethyl-1-pentanol (XII). A solution of 2.5 g of ethyl 5,5,5-trifluoro-4,4-bistrifluoromethylvalerate in 5 ml of dry ether was added slowly with vigorous stirring to a suspension of 0.56 g of lithium aluminum hydride in 10 ml of dry ether. When the exothermic reaction subsided, the mixture was boiled for 2 h. It was cooled, and with stirring 10 ml of moist ether, 3 ml of water, and 15 ml of 10% sulfuric acid were added successively. The ether layer was separated, the residue was extracted with ether, and the combined ether extracts were dried with magnesium sulfate. Distillation gave 2 g (91%) of 5,5,5-trifluoro-4,4-bistrifluoromethyl-1-pentanol; b.p. 77-78° (35 mm). Found %: C 29.98; H 2.54; F 61.47. $C_7H_7F_9O$. Calculated %: C 30.21; H 2.52; F 61.51. Phenylcarbamate, m.p. 64° (from a mixture of benzene and heptane). Found %: N 3.85; F 42.86. $C_{14}H_{12}F_9NO_2$. Calculated %: N 3.53; F 43.07.

Analogously, from 2 g of 5,5,5-trifluoro-4,4-bistrifluoromethylvaleraldehyde (VIIc) and 0.15 g of lithium aluminum hydride we obtained 0.97 g (48%) of 5,5,5-trifluoro-4,4-bistrifluoromethyl-1-pentanol; m.p. 60-62° (15 mm); the phenylcarbamate melted without depression in admixture with the sample described above.

5,5,5-Trifluoro-4,4-bistrifluoromethylpentylamine (XIII). A solution of 4 g of 5,5,5-trifluoro-4,4-bistrifluoromethylvaleronitrile (VIIa) in 6 ml of dry ether was added gradually with vigorous stirring and cooling to a suspension of 0.57 g of lithium aluminum hydride in 27 ml of dry ether. After 10 min with stirring and cooling 1.5 ml of water, 1.5 ml of 20% NaOH solution, and 3 ml of water were added successively. The ether layer was separated, the residue was extracted with ether, and the combined ether extracts were dried with magnesium sulfate. Distillation gave 0.8 g (19%) of impure 5,5,5-trifluoro-4,4-bistrifluoromethylpentylamine (XIII), b.p. about 45-51° (6 mm).

From 0.6 g of unpurified (XIII) and 0.24 g of phenyl isocyanate we obtained 0.45 g (53%) of 1-phenyl-3-(5,5,5-trifluoro-4,4-bistrifluoromethylpentyl)urea (XIV), m.p. 163-164° (from a mixture of acetone and benzene). Found %: N 7.09; F 43.10. $C_{14}H_{13}F_9N_2O$. Calculated %: N 7.07; F 43.18.

## CONCLUSIONS

For the first time the proton mobility of hydrogen atoms in mono-H-polyfluoroalkanes due to the electron-attracting action of perfluoroalkyl groups was applied in synthesis. By Michael reactions with 2H-hexafluoro-2-(trifluoromethyl)propane various derivatives of 5,5,5-trifluoro-4,4-bistrifluoromethylvaleric acid were prepared, and from these a number of compounds containing the perfluoro-t-butyl group were synthesized.

Michael reactions were also conducted with 3,3,3-trifluoro-2-(trifluoromethyl)propionic and (trifluoromethyl)malonic esters.

## LITERATURE CITED

1. I. L. Knunyants, S. T. Kocharyan, Yu. A. Cheburkov, M. D. Bargamova, and E. M. Rokhlin, Dokl. AN SSSR 165, 827 (1965).
2. S. Andreades, J. Amer. Chem. Soc. 86, 2003 (1964).
3. I. L. Knunyants, L. S. German, and B. L. Dyatkin, Izv. AN SSSR. Otd. khim. n. 1956, 1353.