

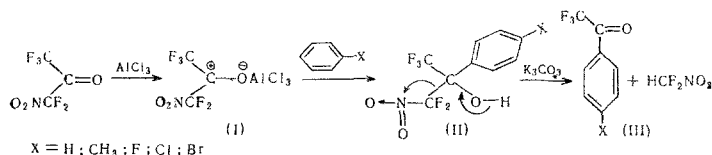
REACTIONS OF POLYFLUORO KETONES
WITH AROMATIC COMPOUNDS

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Polyfluoro ketones undergo electrophilic addition reactions with difficulty [1, 2], and these reactions have therefore been little studied. We here report an investigation of the reactions of fluorinated ketones with aromatic compounds.

Hexafluoroacetone (HFA) and pentafluoronitroacetone (PFNA) readily react with aromatic compounds in presence of aluminum chloride with formation of the corresponding alcohols* (see below, Tables 1 and 2).

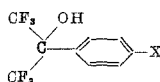


Reaction with unsubstituted benzene and particularly with toluene goes under much milder conditions than reaction with halobenzenes. In accord with the scheme given above, PFNA reacts with greater difficulty than HFA †: from a mixture of equimolecular amounts of HFA, PFNA, and chlorobenzene we obtained only p-chloro- α,α -bistrifluoromethylbenzyl alcohol. The presence of the difluoronitromethyl group, which

*The condensation of HFA with benzene and with ethylbenzene in presence of AlCl₃ at 100° and above has been described in a patent [3]. Recently there has also appeared a report on the analogous synthesis of substituted benzyl alcohols from HFA without description of the experiments [4]. Hexafluorocyclobutanone reacts with benzene at room temperature [5].

†With nucleophilic reagents PFNA reacts more vigorously than HFA [6].

TABLE 1. Alcohols



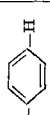
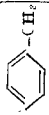
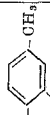
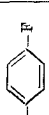
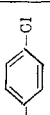
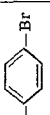
X	Conditions of formation	Properties	Yield, %
H	20°, 10—12 h	B.p. 51—53°(6 mm); n_D^{25} 1,4151 *	56,3
CH ₃	—50 ÷ —30°, 15 min	B.p. 69—70°(6 mm); n_D^{20} 1,4234; d_4^{20} 1,4166;	67,0
F	20°, 10—12 h	B.p. 55—56°(6 mm); n_D^{25} 1,4301	62,6 †
Cl	20°, 10—12 h	B.p. 68—70°(6 mm)	71,0
Br	20°, 10—12 h	B.p. 78—80°(6 mm)	57,0 ‡

*[3] gives: b.p 50° (10 mm); n_D^{25} 1.4128.

†Found %: C 41.3; H 1.87; F 50.84. C₉H₅OF₇. Calculated %: C 40.57; H 2.01; F 50.70.

‡Found %: C 33.39; H 1.55; F 35.35. C₉H₅OF₆Br. Calculated %: C 33.4; H 1.54; F 35.38.

TABLE 2. Alcohols $\text{CF}_3\text{C}(\text{OH})(\text{Ar})\text{O}_2\text{NCF}_2$ Ketones $\text{CF}_3\text{C}(\text{O})(\text{Ar})$

Ar	Conditions of formation	Properties	Yield, %	Found				Yield, %	Properties	Found			
				MR	C, %	H, %	N, %			F, %	MR	C, %	H, %
	20° 10-12 h	B.p. 70-73° (6 mm) n_D^{20} 1.4449 d_4^{20} 1.4982	78, 0	47, 05 47, 96	39, 38 39, 9	2, 46 2, 22	5, 37 5, 17	34, 81 35, 1	36, 02 37, 15	55, 11 55, 17	3, 1 2, 9	33, 44 32, 76	
	from -50 to -30° 15 min	B.p. 76-77° (2 mm) n_D^{20} 1.4511 d_4^{20} 1.4653	73, 3	52, 43 52, 3	42, 02 42, 1	2, 27 2, 80	5, 06 4, 91	32, 75 33, 33	—	57, 27 57, 5	3, 6 3, 72	30, 78 30, 30	
		B.p. 102, 5-103° (7 mm) n_D^{20} 1.4540 d_4^{20} 1.2038	59, 0	—	43, 46 44, 2	3, 32 3, 35	—	32, 15 31, 8	45, 21 46, 85	59, 35 59, 46	—	28, 28 28, 27	
	20° 10-12 h	B.p. 81-82° (6 mm) n_D^{20} 1.4349 d_4^{20} 1.5800	63, 5	48, 1 47, 57	37, 02 37, 00	1, 75 1, 73	—	40, 43 39, 31	—	50, 03 50, 00	1, 96 2, 08	40, 18 39, 6	
	150°, 5 h	B.p. 95-96° (6 mm) n_D^{20} 1.4652 d_4^{20} 1.5848	69, 5	53, 7 53, 37	34, 65 35, 35	1, 74 1, 8	4, 8 4, 68	31, 44 31, 09	—	45, 98 46, 00	1, 97 1, 91	27, 57 27, 33	
	150°, 5 h	B.p. 98-99° (3 mm) n_D^{20} 1.4830 d_4^{20} 1.7753	24, 3	56, 31 56, 6	30, 7 30, 85	1, 4 1, 43	4, 0 4, 1	27, 78 27, 14	—	37, 64 37, 94	1, 47 1, 58	23, 1 22, 52	

*[14] gives: b.p. 152° (730 mm); n_D^{20} 1.4583; d_4^{20} 1.2790.

†[15] gives: b.p. 92° (37.5 mm); n_D^{20} 1.4693; d_4^{20} 1.2304.

‡Under the action of 10% KOH in the cold 2,2,2-trifluoroacetophenones are converted into the corresponding p-substituted benzoic acids.

**[16] gives b.p. 182-184°.

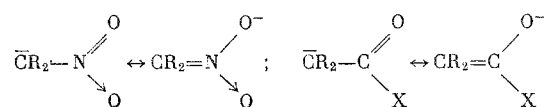
is more electronegative than the trifluoromethyl group [7], probably makes the first stage of the reaction — the formation of the carbonium ion (I) — more difficult.

The difluoronitromethyl group in the benzyl alcohols (II) is readily eliminated at 90–100° in presence of a catalytic amount of potassium carbonate with formation of the corresponding 2,2,2-trifluoroacetophenones (III). In our experiments the over-all yields of the ketones (III) averaged at 60%, so that this synthesis of fluorinated substituted acetophenones can be regarded as a preparative method of synthesis along with the known Friedel-Crafts and Grignard syntheses [8]. An analogous case of the elimination of a difluoronitromethyl group has also been found in fluorinated aliphatic alcohols [6].

The breakdown of tertiary alcohols usually requires relatively severe conditions [9]. Tertiary alcohols containing electronegative trifluoromethyl groups can be broken down only by the pyrolysis of their alkali-metal derivatives [10]. When fluorinated alcohols contain, apart from trifluoromethyl groups, considerably less electronegative phenacyl, ethoxycarbonyl, or 2-methylpropenyl groups [11], the latter are eliminated exclusively [6, 12].

The attempt which we undertook to bring about the breakdown of α,α -bistrifluoromethylbenzyl alcohols was unsuccessful, even in boiling with 40% KOH, whereas α -(difluoronitromethyl)- α -(trifluoromethyl)benzyl alcohols are broken down on dissolution in 10% KOH, even at room temperature. Fluorine-free tertiary nitro alcohols also readily break down in an alkaline medium with formation of a nitroalkane and a ketone [13].

The above discussion indicates that the ease and course of the breakdown of tertiary alcohols are determined not so much by the electronegative character of the groups, as by the stability of the carbanions eliminated, which is determined by resonance of the type



The ketones (III) formed in the "haloform" breakdown of the alcohols (II) readily lose haloform in their turn with formation of the corresponding benzoic acids [14], which was made use of by us for the determination of the position of the substituent in the aryl group. The structure of p-methyl- α,α -bistrifluoromethylbenzyl alcohol* was also proved by its oxidation to α -hydroxy- α,α -bistrifluoromethyl-p-toluic acid.

EXPERIMENTAL

Preparation of Benzyl Alcohols (II) (Typical Method). An equimolecular mixture of the fluorinated ketone and the aromatic hydrocarbon containing a catalytic amount of anhydrous aluminum chloride was kept in a sealed tube until separation into layers no longer occurred. The reaction mixture was then decomposed with 20% HCl and water, extracted with ether, and vacuum-distilled. The conditions and results of the experiments are given in Tables 1 and 2.

Reaction of a Mixture of Hexafluoroacetone and Pentafluoronitroacetone with Aromatic Compounds. A mixture of 0.02 mole of HFA, 0.02 mole of PFNA, 0.017 mole of chlorobenzene, and 0.3 g of AlCl_3 was kept in a sealed tube at room temperature for 12 h. After treatment in accordance with the typical procedure, from the reaction mixture we isolated 3.01 g of p-chloro- α,α -bistrifluoromethylbenzyl alcohol. PFNA was extracted completely in the form of the hydrate, b.p. 115–120°.

An analogous experiment conducted with the mixture of ketones (0.02 mole of each) and 0.018 mole of toluene (12 h at between –58 and –32°) led to a mixture of p-methyl- α,α -bistrifluoromethylbenzyl alcohol (2.46 g, 50%) and α -(difluoronitromethyl)-p-methyl- α -(trifluoromethyl)benzyl alcohol (0.89 g, 12%).

Isolation of p-Methyl- α,α -bistrifluoromethylbenzyl Alcohol in the Preparation of Hexafluoro-2,2-di-p-tolylpropane. A mixture of 0.435 mole of toluene, 0.213 mole of HFA, and 75 g of HF was heated in a metal ampule for 12 h at 180–183°. After the evaporation of HF

*p-Methyl- α,α -bistrifluoromethylbenzyl alcohol is also formed as an intermediate product in the synthesis of hexafluoro-2,2-di-p-tolylpropane and is converted into the latter when heated with toluene in presence of HF. This fact confirms the view expressed earlier on the mechanism of the formation of 2,2-diarylhexasfluoropropanes [1].

the mixture was steam-distilled. The distillate was extracted with ether, and the extract was dried and vacuum-distilled. We obtained 4.3 g (7%) of p-methyl- α,α -bistrifluoromethylbenzyl alcohol and 43.78 g (62.2%) of hexafluoro-2,2-di-p-tolylpropane [2].

Oxidation of p-methyl- α,α -bistrifluoromethylbenzyl Alcohol. A mixture of 3 g of p-methyl- α,α -bistrifluoromethylbenzyl alcohol and 12 ml of 20% HNO_3 was heated for 7.5 h at 180-185°. We obtained 2.81 g (81%) of α -hydroxy- α,α -bistrifluoromethyl-p-toluic acid, m.p. 121-123° (mixture of heptane and benzene). Found %: C 41.25; H 2.16; F 38.99. $\text{C}_{10}\text{H}_6\text{O}_3\text{F}_6$. Calculated %: C 41.7; H 2.08; F 39.6.

Preparation of Hexafluoro-2,2-di-p-tolylpropane from p-Methyl- α,α -bistrifluoromethylbenzyl Alcohol. A mixture of 0.01 mole of p-methyl- α,α -bistrifluoromethylbenzyl alcohol, 0.012 mole of toluene, and 5 ml of HF was heated at 180-183° for 10 h. The residue remaining after the evaporation of HF was washed with warm water and crystallized from methanol. We obtained 1.81 g (58.4%) of a product of m.p. 80-82°, identical to the hexafluoro-2,2-di-p-tolylpropane prepared from HFA and toluene [2].

Breakdown of α -(Difluoronitromethyl)- α -(trifluoromethyl)benzyl Alcohols (Typical Method). The (difluoronitromethyl)(trifluoromethyl)benzyl alcohol was introduced into a Claisen flask, and a catalytic amount of potassium carbonate was added. When the mixture was heated in a boiling water bath, difluoronitromethane distilled off; b.p. 42-43° ([17] gives b.p. 42°). It was identified by gas-liquid chromatography. The residue was vacuum-distilled. The yields of the corresponding 2,2,2-trifluoroacetophenones were 81-96%.

Reaction of α -(Difluoronitromethyl)- α -(trifluoromethyl)benzyl Alcohol with KOH. 8 ml of 10% KOH was added gradually at room temperature to 1.2 g of α -(difluoronitromethyl)- α -(trifluoromethyl)benzyl alcohol. After 1 h the reaction mixture was treated with dilute HCl and extracted with ether. We obtained 0.84 g (69%) of a liquid of b.p. 33-34° (5 mm) and $n_D^{19.5}$ 1.4560, identical to 2,2,2-trifluoroacetophenone.

CONCLUSIONS

1. By the condensation of hexafluoroacetone and pentafluoronitroacetone with aromatic hydrocarbons the corresponding substituted benzyl alcohols were synthesized. It was shown that in this reaction pentafluoronitroacetone is less active than hexafluoroacetone.

2. In α -(difluoronitromethyl)- α -(trifluoromethyl)benzyl alcohols the difluoronitromethyl group is readily eliminated with formation of the corresponding ketones.

3. p-Methyl- α,α -bistrifluoromethylbenzyl alcohol is an intermediate product in the synthesis of hexafluoro-2,2-di-p-tolylpropane.

LITERATURE CITED

1. I. L. Knunyants, N. P. Gambaryan, Ch'eng Ch'in-yün, and E. M. Rokhlin, *Izv. AN SSSR, Otd. khim.n.*, **1962**, 684.
2. I. L. Knunyants, N. P. Gambaryan, B. R. Livshits, and L. A. Simonyan, *Authors' Declaration (USSR)*, No. 864550/23-4 of November 4, 1963.
3. D. C. England, *French Patent* 1,325,204 (1963); *Chem. Abstrs.*, **59**, 11339 (1963).
4. S. Farah, E. E. Gilbert, E. S. Jones, and J. P. Sibilia, *Abstracts of Papers Presented at the 148 Meeting, ACS, Division of Fluorine Chemistry, September 1964*, 23 K.
5. D. C. England, *J. Amer. Chem. Soc.*, **83**, 2205 (1961).
6. N. P. Gambaryan, E. M. Rokhlina, and Yu. V. Zeifman, *Izv. AN SSSR, Ser. khim.*, **1965**, 1466.
7. I. L. Knunyants and B. L. Dyatkin, *Izv. AN SSSR, Ser. khim.*, **1964**, 923.
8. A. E. Pavlath and A. J. Leffler, *Aromatic Fluorine Compounds*, Reinhold Publishing Corp., New York (1962).
9. D. J. Cram, L. K. Gaston, and H. Jäger, *J. Amer. Chem. Soc.*, **83**, 2183 (1961).
10. I. L. Knunyants, Yu. A. Cherburkov, and Yu. V. Makarov, *Izv. AN SSSR, Otd. khim. n.*, **1961**, 1471.
11. V. A. Pal'm, *Uspekhi khimii*, **30**, 1069 (1961).
12. I. L. Knunyants, Ch'eng Ch'in-yün, and N. P. Gambaryan, *Zh. Vses. khim. obshch. im. D. I. Mendeleeva*, **5**, 112 (1960).

13. P. Souchay and S. Deswarte, *Compt. rend.*, 255, 688 (1962).
14. J. H. Simons and E. O. Ramler, *J. Amer. Chem. Soc.*, 65, 389 (1943).
15. J. Park, H. A. Brown, and J. R. Lacher, *J. Amer. Chem. Soc.*, 75, 709 (1951).
16. A. Kaluszyner, *J. Organ. Chem.*, 25, 473 (1960).
17. I. L. Knunyants, A. V. Fokin, and V. A. Komarov, *Zh. Vses. khim. obshch. im. D. I. Mendeleeva*, 7, 709 (1962).