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THE ACIDIC PROPERTIES OF FLUORINE-CONTAINING ALCOHOLS, HYDROXYLAMINES AND OXIMES

B. L. Dyatkin, E. P. Mochalina and I. L. Knunyants
Institute of Organo-Element Compounds, Academy of Sciences, Moscow, USSR

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Abstract—The pK_a of a number of fluorine-containing alcohols, hydroxylamines and oximes have been measured and compared. A linear dependence of the pK_a of alcohols upon the sum of the Taft induction constants σ^* of substituents at the carbinol carbon atom has been established. Tertiary perfluoroalcohols compare in their acidic properties with carboxylic acids. Dissociation constants of hydroxylamines $(CF_3)_xCH_{3-x}NHOH$ are close to the dissociation constants of trifluoromethylcarbinols containing the same number of trifluoromethyl groups. The acidity of oximes is about 300 times as great as that of corresponding hydroxylamines.

High electronegativity of the fluorine atom and a great —I-effect of perfluoroalkyl groups connected with it facilitate protonization of the neighbouring hydrogen atom and sharply increase acidic properties of fluoro-organic compounds as compared with the corresponding non-fluorinated analogues. This phenomenon can be observed in various classes of compounds, e.g. carboxylic acids, sulphonic acids and hydrocarbons. Although, for the series of acids[1-3] and hydrocarbons[4] systematic quantitative data have been obtained making it possible to evaluate the influence of the number of fluorine atoms and their position on the dissociation constant, the information concerning other classes is non-systematic and mainly of a qualitative character.

The problem concerning the acidic properties of the fluorinated alcohols is complicated. The fact, that the introduction of fluorine increases the acidity of alcohols had been pointed out by Swarts[5] and was confirmed later, although the view concerning the acidity of $CF_3CH(OH)CH_3$ given by Swarts proved to be exaggerated.

It was shown[6] that the dissociation constant of carbinols, containing one perfluoroalkyl group is in the order of 3 to 4 times higher than the dissociation constant of ordinary alcohols. For $(C_3F_7)_2CHOH$ it was shown[7] that the introduction of a second perfluoroalkyl radical leads to a further increase in the acidity. As to tertiary perfluoroalkylcarbinols of the type $R_fR_f'R_f''COH$, they have been described only recently. Although in 1953 it was reported[8] that such alcohols are formed when

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[1] H. J. Emeléus, R. N. Haszeldine and R. C. Paul, *J. Chem. Soc.* 563 (1955).

[2] A. L. Henne and C. J. Fox, *J. Amer. Chem. Soc.* **73**, 2323 (1951); **75**, 5750 (1953); **76**, 479 (1954).

[3] E. T. McBee, O. R. Pierce and D. C. Smith, *J. Amer. Chem. Soc.* **76**, 3722 (1954).

[4] S. Andreades, *J. Amer. Chem. Soc.* **86**, 2003 (1964).

[5] F. Swarts, *Bull. Soc. Chim. Belg.* **38**, 99 (1929).

[6] A. L. Henne and R. L. Pelley, *J. Amer. Chem. Soc.* **74**, 1426 (1952).

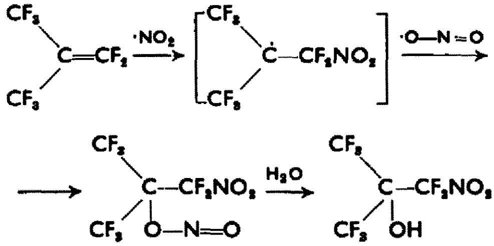
[7] A. L. Henne and W. C. Francis, *J. Amer. Chem. Soc.* **75**, 991 (1953).

[8] R. N. Haszeldine, *J. Chem. Soc.* 1748 (1953).

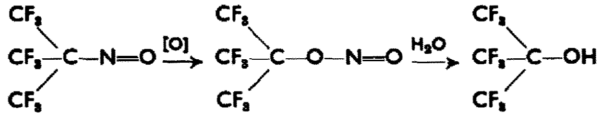
perfluoroalkyl magnesium iodides react with esters of perfluorocarboxylic acids, neither constants, nor analytical data were given. Other authors did not observe the formation of tertiary perfluoroalcohols by this reaction.[9] The report on the synthesis of $(C_3F_7)_3COH$ by reacting C_3F_7Li with $C_3F_7COOC_2H_5$ also proved to be erroneous.[10]

It was shown later,[11] in this case that with solvent participation, the initially formed perfluoroketone $(C_3F_7)_2C{=}O$ is reduced to the secondary alcohol $(C_3F_7)_2CHOH$. Nevertheless, in handbooks and surveys[12,13] the values of the dissociation constants of perfluorinated tertiary alcohols are cited, viz., $3\cdot10^{-10}$ and $1\cdot10^{-10}$ for $(CF_3)_3COH$ and $(C_3F_7)_3COH$, respectively, and thus the concept developed that the order of the acidity of tertiary perfluoroalcohols is the same as that of phenols.

The first described representative of this class of compounds—nitroperfluoro-t-butyl alcohol—was obtained by us by nitration of perfluorosiobutylene with nitrogen dioxide.[14]



This compound is an acid (pK_a = 3·9), stronger than acetic acid (pK_a = 4·7), a fact which did not agree with the available data. Therefore, it was of interest to synthesize the perfluoro-t-butyl alcohol $(CF_3)_3COH$ and compare its acidity with the acidic properties of other perfluoroalkyl carbinols. The perfluoro-t-butyl alcohol was obtained by oxidation of t-nitrosoperfluoroisobutane and subsequent hydrolysis of the nitrite formed.[15]



This alcohol has pronounced acidic properties. It can be titrated using phenolphtalein, and has a pK_a = 5·4, i.e. it is 10,000 times stronger than previously reported. Its acidity, therefore, compares with that of nitroperfluoro-t-butyl alcohol.

In order to ascertain the influence exerted by an accumulation of perfluoroalkyl groups at the carbinol carbon atom upon the dissociation constant, we compared the

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[9] A. L. Henne and W. C. Francis, *J. Amer. Chem. Soc.* **75**, 992 (1953).

[10] O. R. Pierce, E. T. McBee and G. F. Judd, *J. Amer. Chem. Soc.* **76**, 474 (1954).

[11] E. T. McBee, C. W. Roberts and S. G. Curtis, *J. Amer. Chem. Soc.* **77**, 6387 (1955).

[12] M. Hudlický, *Chemie Organických Sloučenin Fluoru* (*Chemistry of Organic Fluorine Compounds*) Praha (1958).

[13] A. M. Lovelace, D. A. Rausch and W. Postelnek, *Aliphatic Fluorine Compounds*. N.Y. and London (1957).

[14] I. L. Knunyants, A. V. Fokin, B. L. Dyatkin and V. A. Komarov, *ZhVKhO imeni Mendeleeva* **8**, 239 (1963); *Izv. Akad. Nauk USSR, Chem. Ser.* 1425 (1964).

[15] I. L. Knunyants and B. L. Dyatkin, *Izv. Akad. Nauk USSR, Chem. Ser.* 923 (1964).

acidity of tertiary perfluroralcohols with that of hexafluoroisopropyl alcohol (bis-trifluoromethyl carbinol) $(CF_3)_2CHOH$ and trifluoroethyl alcohol (trifluoromethyl carbinol) CF_3CH_2OH and found that the pK_a values of these alcohols are 9·3 and 12·8, respectively.† The values obtained for pK_a are given in Table 1. The dependence of pK_a upon the sum of σ^* substituents is a straight line expressed by Equation 1.

TABLE 1

Alcohol	CF_3CH_2OH	$(CF_3)_2CHOH$	$(CF_3)_3COH$	$(CF_3)C(OH)CF_2NO$
$\Sigma\sigma^*$	2·6	5·2	7·8	8·8
pK_a	12·8	9·3	5·4	3·9

$$pK_a = -1{\cdot}44\,\Sigma\sigma^* + 16{\cdot}67 \text{ (Eq. 1)}$$

Thus, hexafluoroisopropyl alcohol has the same order of acidity as phenol, whereas tertiary perfluoroalcohols, as regards their acidic properties, compare with carboxylic acids.

The recent work of Middleton and Lindsay[18] confirms our results. They investigated acidic properties of dodecafluoropinacol $(CF_3)_2C(OH)C(OH)(CF_3)_2$ and hydrates of perfluoroketones $R_fR_f'C(OH)_2$. These compounds behave as monobasic acids and can be regarded as tertiary alcohols. The pK_a values obtained[18] are in close agreement with the values calculated in accordance with Equation I (Table 2).

TABLE 2

		HYDRATES OF FLUORINATED KETONES $R_fR_f'C(OH)_2$			
Compound	Dodecafluoropinacol	$(CF_3)_2$	$(CF_2Cl)_2$	$(CF_2H)_2$	CF_2Cl, CF_2H
pK_a according to [18]	5·95	6·58	6·67	8·79	7·90
pK_a as calculated by Equation 1	5·7‡	7·0	6·6	8·5	7·9

‡ Dodecafluoropinacol was obtained earlier in our Laboratory by N. P. Gambaryan *et al.*, who employed another method. According to their data, pK_a of this compound is 5·7.[19]

Similarly, the acidic properties of fluorine-containing hydroxylamines are greatly influenced by the introduction of perfluoroalkyl substituents to the carbon carrying the functional group. A series of hydroxylamines e.g. CH_3CH_2NHOH, $(CF_3)_2CHNHOH$ and $(CF_3)_3CNHOH$ as well as oximes of trifluoroacetaldehyde $CF_3CH{=}NOH$ and hexafluoroacetone $(CF_3)_2C{=}NOH$, were prepared by the reduction of the corresponding nitro- and nitroso-compounds. Hydroxylamines are usually regarded as bases and oximes display both slight acidic and basic properties. The fluorinated hydroxylamine derivatives prepared by us have strongly pronounced acidic properties (Table 3).

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† The value of pk_a = 12·8 for CF_3CH_2OH agrees with the data cited in literature. viz., 12·43[16] and 12·37.[17] The value of pK_a = 9·3 for $(CF_3)_2CHOH$ was recently confirmed.[18]

[16] C. W. Roberts, E. T. McBee and C. E. Hathaway, *J. Org. Chem.* **21**, 1369 (1956).

[17] P. Ballinger and F. A. Long, *J. Amer. Chem. Soc.* **81**, 1050 (1959).

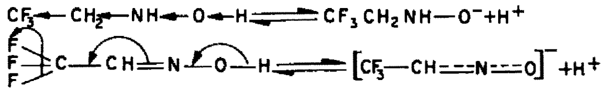
[18] W. J. Middleton and R. V. Lindsey, *J. Amer. Chem. Soc.* **86**, 4948 (1964).

[19] N. P. Gambaryan, Yu. A. Cheburkov and I. L. Knunyants, *Izv. Akad. Nauk USSR, Chem. Ser.* 1526 (1964).

TABLE 3

Compound	CF_3CH_2NHOH	$(CF_3)_2CHNHOH$	$(CF_3)_3CNHOH$	$CF_3CH{=}NOH$	$(CF_3)_2C{=}NOH$
pK_a	11·3	8·5	5·8–6·0	8·9	6·0

As it can be seen from Table 3, the acidity of hydroxylamines is similar to that of alcohols containing the same number of trifluoromethyl groups. In the case of oximes, they are about 300 times more acidic than hydroxylamines. This may be accounted for, first of all, by the mesomeric stabilization of the corresponding anion, as well as by the easier influence of trifluoromethyl groups via the double carbon–nitrogen bond:



The dependence of the pK_a values of alcohols, hydroxylamines and oximes upon $\Sigma\sigma^*$ of substituents is plotted in Fig. 1.

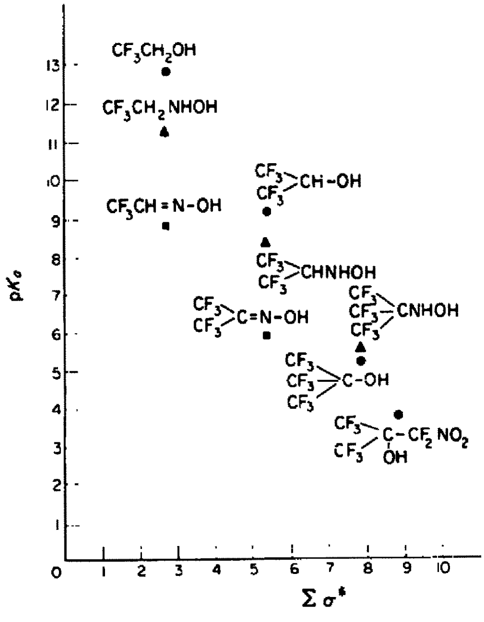


FIG. 1.

EXPERIMENTAL

Trifluoroethyl alcohol. The commercial product was purified by distillation. B.p. 74°.

Hexafluoroisopropyl alcohol was obtained by reducing hexafluoroacetone with $NaBH_4$.[20] B.p. 57°.

Perfluoro-t-butyl alcohol was obtained by reacting $(CF_3)_3C{-}N{=}O$ with N_2O_4 with subsequent hydrolysis; b.p. 45°.[15]

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[20] I. L. Knunyants and M. P. Krasouskaya, *Author's Certificate of the USSR.* No. 138604, July 21 (1960).

Nitroperfluoro-t-butyl alcohol was obtained by reacting N_2O_4 with perfluoroisobutylene and subsequent hydrolysis; b.p. 88·5°.[14]

Hexafluoroacetone oxime, b.p. 69–70°, was obtained by reducing $(CF_3)_2CFNO_2$ with hydrogen over Pd-black.[21]

Trifluoroethylhydroxylamine, m.p. 80–81°, *hexafluoroisopropylhydroxylamine*, b.p. 46–47° at 71 mm Hg, *perfluoro-t-butylhydroxylamine*, b.p. 94–95°, and *trifluoroacetatealdehyde oxime*, b.p. 49° at 200 mm Hg were obtained by hydrogenation over Pd-black of $CF_3CH_2NO_2$, $(CF_3)_2CHNO_2$, $(CF_3)_3C—NO$ and CF_3CFHNO_2, respectively.

The details of the synthesis of these compounds will be published elsewhere.

pK_a *Measurements* were carried out in water at 25° by means of potentiometric techniques for all the compounds except $(CF_3)_3CNHOH$, whose acidity was evaluated approximately by measuring the conductivity of aqueous solutions at 25°. It was assumed that the anion mobility, being greater than zero, did not exceed that of inorganic anions.

[21] I. L. Knunyants, B. L. Dyatkin, L. S. German, I. N. Rozhkov and V. A. Komarov, *ZhVKhO 'meni Mendeleeva* **8**, 709 (1963).