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ACIDITIES OF SOME FLUORINE SUBSTITUTED C–H ACIDS

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SUMMARY

Acidities of some fluorinated hydrocarbons, R_FH, have been estimated by polarographic method. Polarographic data on electrochemical reduction of $(R_F)_2Hg$ have been correlated with rate constants of hydrogen isotopic exchange in R_FH in methanol.

Investigation of the fluorinated hydrocarbons towards the metallation and hydrogen isotopic exchange reactions showed that such compounds usually display relatively high acidity. Recently the works have been published on determination of the kinetic acidities of some fluorine-containing alkanes[1], bicycloalkanes[2], arenes[3,4], ethylenes[5] and acetic esters[6]. These studies indicate that under mild conditions the polyfluorinated compounds readily enter the hydrogen isotopic exchange even in a diluted sodium methoxide methanolic solution. The acidity of a fluorinated C–H acid may both increase or decrease if fluorine is directly bonded to the carbon atom which becomes a carbanion center after the proton splitting. When the generating carbanion has an sp^3 configuration (*i.e.* that of its starting C–H acid) the inductive effect of fluorine stabilizes the carbanion and thus affords the stronger C–H acid as compared to a non-fluorinated compound. In the case of a planar sp^2 configuration of the carbanion generated in the course of the C–H acid dissociation, the unfavourable fluorine lone electron pairs effect on the adjacent carbanion center decreases the acidity of the compound. This has been observed by Hine[6] for α-fluorinated acetic esters. In a general, no prediction can be made regarding wether the acidity of a C–H acid will increase or decrease with introduction of fluorine at the α-position, since the carbanions generated have rehybridization states different from the sp^3 of the starting C–H acid. An experimental determination of the acidities of various fluorinated compounds is thus of theoretical interest.

In the present work we studied the acidities of some fluorinated compounds and other derivatives with electron-attracting groups. In estimating the acidities of the compounds we used a polarographic method which has been earlier described in our work[7]. This method is based on relation between the hydrocarbon (RH) acidities and the parameters of polarographic reduction of the respective organomercury compounds, R_2Hg[7].

$$\Delta(\alpha \cdot n_a \cdot E_{\frac{1}{2}}) = \rho \cdot \Delta pK_a$$

where $E_{\frac{1}{2}}$ is the half-wave potential of R_2Hg, α is the transfer coefficient, pK_a is the RH acidity, ρ is a constant depending on the nature of the solvent.

Polarograms of the organomercury compounds were taken at 25° in anhydrous dimethylformamide (DMF) with 0.1 *M* tetra-n-butylammonium perchlorate as a supporting electrolyte. The half-wave potentials and slopes of polarographic waves from which the $\alpha \cdot n'_a$ values were estimated (n_a is the number of electrons in the potential determining step) were found using the Heyrovsky $E - i/(i_d - i)$ plots (where i is the current at a potential E, i_d is the limiting diffusion current). The results are shown in Table 1 with the organomercury compounds arranged in an order of the decreasing negative $E_{\frac{1}{2}}$ values.

TABLE 1

THE POLAROGRAPHICAL PARAMETERS FOR THE ELECTROCHEMICAL REDUCTION OF SOME ORGANOMERCURY COMPOUNDS R_2Hg

DMF, 0.1 *M* $(C_4H_9)_4NClO_4$, 25°.

No.	R in R_2Hg	Concn. (mmole/l)	$-E_{\frac{1}{2}}{}^a$ (V)	$\alpha \cdot n_a$	$-\alpha \cdot n_a \cdot E_{\frac{1}{2}}$	pK_a
1	$CH_2{=}CH$	0.2	2.62	0.72	1.88	36.5^b
2	C_6H_5	0.2	2.61	0.66	1.82	37^b
3	$C_6H_5CH_2$	0.2	2.17	0.76	1.65	35^b
4	*p*-Carboranyl	0.02	1.78	0.90	1.60	33^c
5	$C_6H_5C{\equiv}C$	0.1	1.75	0.32	0.56	18.5^b
6	$CF_2{=}CF$	0.26	1.70	0.49	0.83	20^d
7	*m*-Carboranyl	0.02	1.48	0.60	0.89	21^c
8	$CF_2COOC_2H_5$	0.1	1.48	0.66	0.98	25^d
9	CF_3	0.25	1.47	0.74	1.09	25.5^d
10	$C_6H_5SO_2CH_2$	0.1	1.37	0.69	0.95	27^e
11	CH_2COOCH_3	0.1	1.34	0.68	0.91	24^f
12	$CHFCOOC_2H_5$	0.1	1.17	0.74	0.87	21^d
13	C_6F_5	0.1	1.15	0.48	0.55	23^f
14	$(CF_3)_2CH$	0.1	1.04	0.87	0.90	22^d
15	$CFClCOOC_2H_5$	0.01	1.02	0.68	0.69	18^d
16	$(CF_3)_2CF$	0.1	0.94	1.02	0.95	22.5^d
17	*o*-Carboranyl	0.02	0.75	0.80	0.60	16^c
18	Cyclo-C_5H_5	0.2	0.59	1.04	0.61	15.5^b
19	$CH(CF_3)COOC_2H_5$	0.12	0.59	(0.50)	(0.30)	$16^{d,g}$
20	CN	0.05	0.54	0.91	0.49	12^h
21	$CF(CF_3)COOC_2H_5$	0.2	0.48	(0.39)	(0.19)	$14^{d,g}$
22	CCl_3	0.02	0.46	1.02	0.47	15^d
23	$C(CF_3)_2COOC_2H_5$	0.1	0.45	1.02	0.46	14^d
24	CBr_3	0.2	0.16	0.90	0.15	9^d
25	$(CF_3)_3C$	0.1	−0.01	0.53	−0.01	7^d

[a] *vs.* SCE. [b] The pK_a's from MSAD scale[8]. [c] See ref.[9]. [d] The pK_a's were first determined in the present work. [e] In dimethyl sulfoxide[10]. [f] See ref. 7. [g] Assigned on the basis of the half-wave potentials (see text). [h] The pK_a of HCN was determined by potentiometric titration with tetra-n-butylammonium hydroxide in DMF.

Using the data of Table 1 the product $\alpha \cdot n_a \cdot E_{\frac{1}{2}}$ (characterizing the reduction rate of R_2Hg at $E = 0$ *vs.* SCE) *vs.* the pK_a's of the corresponding C–H acids was derived (Fig. 1). For such a purpose a choice was made of the following C–H acids: (1) hydrogen cyanide, its pK_a was determined by potentiometric acid–base titration in

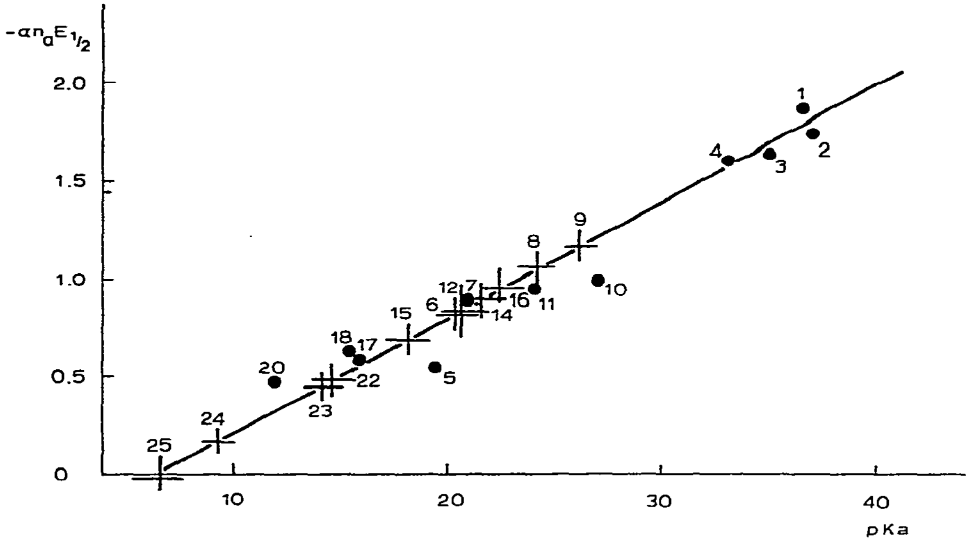

Fig. 1. The parameters of polarograhic reduction of the organomercury compounds R_2Hg *vs.* the $\mathrm{p}K_a$'s (MSAD scale) of the respective RH hydrocarbons. The point numbers correspond to those of the compounds in Table 1.

DMF and this value was equal to 12, (2) phenylacetylene, cyclopentadiene, toluene and benzene, whose acidities are known from the MSAD scale[8]; (3) *o*-, *m*-, and *p*-carboranes, methyl acetate and pentafluorobenzene whose acidities were determined in our earlier work[7,9] based on the MSAD scale; (4) phenyl methyl sulfone for which $\mathrm{p}K_a = 27$ (in dimethyl sulfoxide)[10]. Through these points a calibration curve was drawn. The values $\alpha \cdot n_a$ and $E_{\frac{1}{2}}$ were experimentally determined for the fluorinated organomercury compounds. Thus we were able to estimate the acidities for a number of the fluorine-containing C–H acids and, besides, for chloroform and bromoform. The $\mathrm{p}K_a$'s of these compounds are listed in the last column of Table 1. These values correspond to the acidities of the fluorine-containing C–H acids in the MSAD scale.

Acidities of $HCH(CF_3)COOC_2H_5$ and $HCF(CF_3)COOC_2H_5$ (see compounds 19 and 21 in Table 1) were estimated from the half-wave potentials since their polarographic waves are distorted. Thus it was rather difficult to define the values $\alpha \cdot n_a$.

It follows from the data of Table 1 that the haloform acidities increase in the order

$$HCF_3 < HCCl_3 < HCBr_3$$

which is reverse to that expected from the halogen inductive effects and might be explained by the *d*-orbital participation [11]. Of all haloforms, fluoroform is the least strong acid, since its resonance structure involving the *d*-orbital participation, *i.e.* contribution of the structure with the tenth electron valence shell of halogen, is impossible.

Acidities of the substituted acetic esters increase in the following sequence:

$$CF_2HCOOC_2H_5 < CH_3COOCH_3 < CH_2FCOOC_2H_5 < CHFClCOOC_2H_5$$

Acidity of ethyl fluoroacetate is by 3 $\mathrm{p}K_a$ units higher than that of methyl acetate

(Table 1). Ethyl difluoroacetate, however, even the weaker acid in comparison to unsubstituted methyl acetate. Thus one fluorine atom in the molecule of acetic ester increases the acidity whereas two fluorine atoms decrease the acidity of the compound. These results are in agreement with the Hine data on the hydrogen isotopic exchange in these compounds[7]. In methanol at 35° the rate of hydrogen–deuterium exchange in methyl fluoroacetate is two times faster while in methyl difluoroacetate 5000 times slower than in methyl acetate. Hence the introduction of fluorine as a substituent at the α-position of C–H acid may increase or decrease the equilibrium constant of the carbanion (having sp^2 configuration) formation but there is certain contradiction to what can be expected from the halogen inductive effect. As it follows from the data of Table 1, chlorine at the α-position is more preferable to stabilize the carbanions than the fluorine atom (*cf.* $R = CF_2COOC_2H_5$ and $CFCl\text{-}COOC_2H_5$ in compounds 8 and 15, Table 1).

Absence of correlation between the acidities of some fluorinated hydrocarbons and the fluorine inductive effect are illustrated by the following series of increasing acidity (Table 1):

$$(CF_3)_2CH_2 \sim (CF_3)_2CFH < (CF_3)_3CH$$

Introduction of fluorine at the position 2 of hexafluoropropane has no effect on its acidity while the effect of trifluoromethyl group whose inductive effect is comparable to that of the fluorine atom[12] is very strong (Table 1). Much larger effect on acidity of the CF_3 group as compared to the fluorine atom (which is often explained as a "negative hyperconjugation" of CF_3[1], see however ref.2) follows also from the fact that the acidities of CH_3COOCH_3 and $CH_2(CF_3)COOC_2H_5$ differ by 8pK_a units whereas in CH_3COOCH_3 and $CH_2FCOOC_2H_5$ the difference is only 3 pK_a units (Table 1).

As it was already mentioned, some papers concerning kinetics of the base-

TABLE 2

COMPARISON OF THE POLAROGRAPHIC REDUCTION PARAMETERS FOR SOME ORGANOMERCURY COMPOUNDS R_2Hg (Methanol, 0.1 *M* $(C_4H_9)_4NClO_4$, 25°, concentration of R_2Hg 10^{-4} mole/l) with the constants of hydrogen isotopic exchange of the respective C–H acids RH in the system CH_3OH/CH_3ONa.

No.	R in R_2Hg or RH	Polarography in R_2Hg			Isotopic exchange		
		$-E_{\frac{1}{2}}{}^{a}$ (V)	$\alpha \cdot n_a$	$\alpha \cdot n_a \cdot E_{\frac{1}{2}}$	log k	Temp. (°C)	Ref.
1	$CF_2{=}CF$	1.46	0.56	0.82	−4.3	33	5
2	CF_3	1.33	0.69	0.92	−6.9	75	1
3	C_6F_5	1.12	0.45	0.50	-1.1^b	35	4
4	$CF_2COOC_2H_5$	1.09	0.64	0.70	-5.1^c	35	6
5	$(CF_3)_2CF$	1.00	0.70	0.70	-1.6^b	35	1
6	CH_2COOCH_3	0.83	0.69	0.57	−2.9	35	6
7	$CHFCOOC_2H_5$	0.68	0.67	0.46	-2.6^c	35	6
8	CCl_3	0.35	0.67	0.23	−1.0	33	5
9	$(CF_3)_3C$	0.34	0.77	0.26	0	−29	1
10	$CH(C_6H_5)COOC_2H_5$	0.22	0.98	0.22	-0.4^c	35	6

[a] *vs.* SCE. [b] Extrapolation to 35° is based on the known ΔH values. [c] Constants for methyl esters.

catalyzed hydrogen isotopic exchanges of the fluorine-containing C–H acids have appeared. A majority of these reactions were conducted in methanol with sodium methylate as a base.

Table 2 shows the logs of the rate constants for the hydrogen isotopic exchange reactions of some fluorine-containing compounds measured in MeOH/MeONa. If for these series the Brönsted principle is valid than the logs of the exchange reaction rate constants should correspond to the relative acidities of the compounds in methanol. In order to make comparison of the data published for the constants of the hydrogen isotopic exchange with the data on the acidities of some fluorinated acids determined with polarographic method, we found the parameters of the polarographic reduction of some organomercury compounds in methanol. These parameters are shown in Table 2.

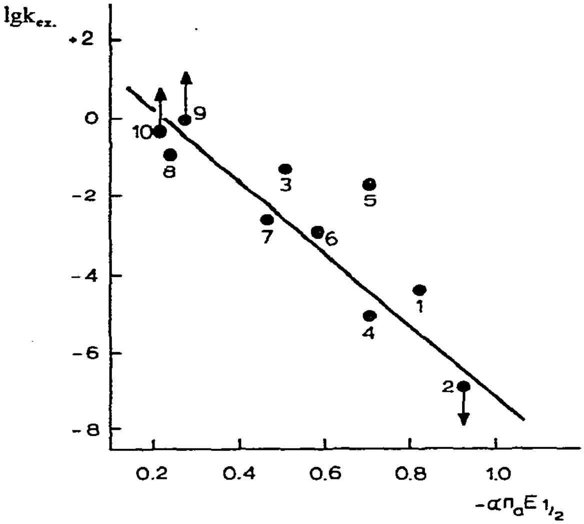

Fig. 2. The parameters of polarographic reduction of the compounds R_2Hg *vs.* the logs of the hydrogen isotopic exchange rate constants in methanol. The point numbers correspond to those of the compounds in Table 2.

Fig. 2 shows the logs of the rate constants of the hydrogen isotopic exchange *vs.* the values of $\alpha \cdot n_a \cdot E_{\frac{1}{2}}$ (Table 2) of the respective fluorine-containing organomercury compounds. A satisfactory correlation is observed between these parameters.

EXPERIMENTAL

Polarographic technique and purification of the solvents are described earlier[7].

The fluorine-containing organomercury compounds were synthesized as described[13]..

REFERENCES

1 S. Andreades, *J. Amer. Chem. Soc.*, 86 (1964) 2003.
2 A. Streitwieser and D. Holts, *J. Amer. Chem. Soc.*, 89 (1967) 692.
3 A. I. Shatenstein, *Advan. Phys. Org. Chem.*, 1 (1963) 162.

4 A. Streitwieser, J. A. Hudson and F. Mares, *J. Amer. Chem. Soc.*, 90 (1968) 648.
5 D. Daloze, H. J. Viehe and J. Chiurdojlu, *Tetrahedron Lett.*, (1969) 3925.
6 J. Hine, L. G. Mahone and C. L. Liotta, *J. Amer. Chem. Soc.*, 89 (1967) 5911.
7 K. P. Butin, I. P. Beletskaya, A. N. Kashin and O. A. Reutov, *J. Organometal. Chem.*, 10 (1967) 197.
8 D. Cram, *Fundamentals of Carbanion Chemistry*, Academic Press, New York, 1965.
9 A. N. Kashin, K. P. Butin, V. I. Stanko and I. P. Beletskaya, *Izv. Akad. Nauk SSSR*, (1969) 1917.
10 F. J. Bordwell and R. H. Imes, *J. Amer. Chem. Soc.*, 89 (1967) 3905.
11 W. Kirmse, *Carbene Chemistry*, Academic Press, New York, 1964.
12 R. Taft, in *Steric Effects in Organic Chemistry*, 1960, Chapter 13.
13 V. V. Polishchuk, L. S. German and I. L. Knunyants, *Avtorskoe Svidetel'stvo No. 256771. Bull. Izobretenii*, (1969) (35) 27.