Notes

Amide Hydrofluoroborates

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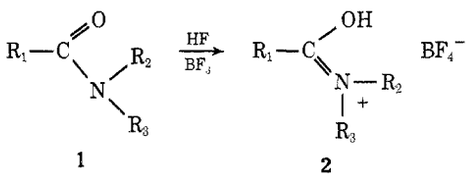
We have found that aliphatic amides (**1a–d**) react with anhydrous HF and BF_3 to give stable, isolable amide hydrofluoroborates (**2a–d**) in 40–60% yield.[2] Compounds **2a–d** were typically prepared by dissolving the amide in liquid HF at 0–15°, bubbling in BF_3, and allowing the mixture to stand for 30 min at 15–20°. They were isolated by removal of excess HF and BF_3 and purified by recrystallization.



1 **2**

a, $R_1 = C_{17}H_{35}$; $R_2 = CH_3$; $R_3 = H$
b, $R_1 = C_{17}H_{35}$; $R_2 = CH_3$; $R_3 = CH_3$
c, $R_1 = C_{15}H_{31}$; $R_2 = n\text{-}C_4H_9$; $R_3 = H$
d, $R_1 = C_7H_{15}$; $R_2 = n\text{-}C_4H_9$; $R_3 = H$

The structures of these compounds have been established by spectral data and by elemental analysis (see Experimental Section). For example, *N*-*n*-butylpalmitamide hydrofluoroborate (**2c**) shows ir bands at 3300 [OH or $(=NHR)^+$] and 1680 cm^{-1} [$(>C=N<)^+$], compared to absorptions of 3455 (–NH) and 1660 cm^{-1} (>C=O) for the starting amide. The nmr spectrum of **2c** shows two downfield singlets at 10.15 (OH) and 9.12 ppm [$(=NHR)^+$]. In addition, a quartet centered at 3.52 [$(>C=NHCH_2CH_2-)^+$] and a triplet at 2.75 ppm [$-CH_2CH_2C(=NHR)^+OH$] are in agreement with the amide hydrofluoroborate structure.[3] These data are indicative of protonation on oxygen, which has been noted in previous studies of amides in strongly acidic media.[4] The stereochemistry at the quaternary nitrogen in **2a**, **c**, and **d** is not known.

Amide hydrofluoroborates are quantitatively reconverted to the corresponding amides by treatment with H_2O and undergo partial decomposition on heating. However, they appear to be indefinitely stable in the absence of H_2O at room temperature.

In contrast to the above results, *N*-methylstearamide (**1a**) does not form stable salts with HF alone or upon treatment with HCl in CH_2Cl_2. Reaction of **1a** with BF_3 alone in CH_2Cl_2 results in the formation of a hygroscopic complex.[5] In the case of stearamide (R_1 = $C_{17}H_{35}$; $R_2 = R_3 = H$), reaction with HF and BF_3 yields a less stable salt, which could not be successfully separated from the starting amide. Apparently, the unsubstituted amide is less basic than either **1a** or **1b**.

Experimental Section

All reactions were performed in a graduated polyethylene bottle with an inlet tube for attachment to HF and BF_3 cylinders[6] and an exit tube protected by Drierite. The ratio of liquid HF to amide in the preparation of **2a–c** is important, since the use of a larger amount of HF results in a different reaction pathway.[7] Caution: To avoid toxicity and severe burns in the handling of HF, appropriate safety precautions should be taken.

***N*-Methylstearamide Hydrofluoroborate (2a).**—Liquid HF (6 ml) was condensed into the vessel containing *N*-methylstearamide (**1a**) (3.0 g, 0.0101 mol) at 0°. Anhydrous BF_3 was then admitted into the mixture at a moderate bubbling rate for 5 min with occasional warming to maintain solution. The mixture was allowed to stand at 15° for 30 min. Excess HF and BF_3 were removed in a stream of N_2, and the resulting solid residue was recrystallized from CH_2Cl_2 to give **2a**: 1.8 g (48%); mp 66–70° dec; ir ($CHCl_3$) 3300, 2920, 2860, 1685, 1070 cm^{-1}; nmr ($CDCl_3$) 9.45 (1 H, s), 8.75 (1 H, s), 3.10 (3 H, d), 2.72 (2 H, t), 1.4–0.9 ppm (33 H, m).

Anal. Calcd for $C_{19}H_{40}NOBF_4$: C, 59.23; H, 10.47; N, 3.64; F, 19.72. Found: C, 59.32; H, 10.31; N, 3.56; F, 19.54.

***N*,*N*-Dimethylstearamide Hydrofluoroborate (2b).**—*N*,*N*-Dimethylstearamide (2.0 g, 0.0064 mol) was suspended in liquid HF (3 ml) at 10° and anhydrous BF_3 was admitted at a moderate bubbling rate for 10 min at 10°. The mixture was then warmed briefly to achieve complete solution. After the solution had stood at 0° for 30 min, the excess HF and BF_3 were removed and the residue was crystallized from methylene chloride–hexane (1:1) to give **2b**: 1.5 g (59%); mp 61–65° dec; ir ($CHCl_3$) 3480, 2920, 2860, 1670, 1070 cm^{-1}; nmr ($CDCl_3$) 9.38 (1 H, s), 3.40 (3 H, br s), 2.85 (2, H, t), 1.8–0.9 ppm (33 H, m).

Anal. Calcd for $C_{20}H_{42}NOBF_4$: C, 60.15; H, 10.61; N, 3.51. Found: C, 60.35; H, 10.90; N, 3.30.

***N*-*n*-Butylpalmitamide Hydrofluoroborate (2c).**—*N*-*n*-Butylpalmitamide (**1c**) (3.0 g, 0.0096 mol) was dissolved in liquid HF (4 ml) at 0° and BF_3 was bubbled in at a moderate rate for 5 min. The solution was then allowed to stand at 0–15° for 30 min. The excess HF and BF_3 were removed and the crude product was recrystallized from CH_2Cl_2–hexane (3:1) to yield **2c** (hygroscopic): 1.5 g (40%); mp 55–59° dec; ir ($CHCl_3$) 3300, 2930, 2860, 1680, 1070 cm^{-1}; nmr ($CDCl_3$) 10.15 (1 H, s), 9.12 (1 H, s), 3.52 (2, H, q), 2.75 (2 H, t), 1.9–0.7 ppm (36 H, m).

Anal. Calcd for $C_{20}H_{42}NOBF_4$: C, 60.15; H, 10.60; N, 3.51. Found: C, 59.96; H, 10.42; N, 3.33.

***N*-*n*-Butyloctanamide Hydrofluoroborate (2d).**—*N*-*n*-Butyloctanamide (**1d**) (2.0 g, 0.01 mol) was dissolved in liquid HF (2 ml) at 0°. The usual procedure was then followed leaving an oily residue, which was dissolved in boiling CH_2Cl_2/hexane (1:1). On cooling, **2d** separated as an oil which was isolated, filtered to remove a very small amount of inorganic solid, and freed from residual solvent *in vacuo* at 20°. This treatment yielded 1.7 g of **2d** (58%): ir ($CHCl_3$) 3300, 2930, 2860, 1680, 1070 cm^{-1};

(1) Agricultural Research Service, U. S. Department of Agriculture.

(2) Certain other examples of isolation of amide salts have been reported. For example, see (a) E. H. White, *J. Amer. Chem. Soc.*, **77**, 6215 (1955); (b) R. Gompper and P. Altreuther, *Z. Anal. Chem.*, **170**, 205 (1959).

(3) The corresponding quartet and triplet in *N*-*n*-butylpalmitamide occur at 3.30 and 2.25 ppm, respectively.

(4) (a) D. M. Brouwer and J. A. van Doorn, *Tetrahedron Lett.*, 3339 (1971); (b) G. A. Olah, A. M. White, and D. H. O'Brien, *Chem. Rev.*, **70**, 580 (1970), and references cited therein.

(5) See E. L. Muetterties and E. G. Rochow, *J. Amer. Chem. Soc.*, **75**, 490 (1953), for previous examples.

(6) Commercial research grade BF_3 and HF were used directly.

(7) Long-chain aliphatic amides undergo chain-cleavage reactions under these conditions. We will report this in detail separately.

nmr ($CDCl_3$) 11.15 (1 H, s), 9.12 (1 H, s), 3.52 (2 H, q), 2.74 (2 H, t), 2.0–0.6 ppm (20 H, m).

Anal. Calcd for $C_{12}H_{26}NOBF_4$: C, 50.20; H, 9.13; N, 4.88. Found: C, 50.47; H, 9.33; N, 5.01.

Registry No.—2a, 36955-98-3; 2b, 36994-06-6; 2c, 36989-94-3; 2d, 36989-95-4.

Reactivity of Hydroxamic Acids. Correlation with the Two-Parameter Taft Equation

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The problem of the separation of polar, steric, and resonance effects has recently been reviewed,[1] and further testing of the range of applicability of the empirical equations as well as the assumptions underlying them deserve further testing. The two-parameter eq 1 suggested by Taft[1,2] for use with aliphatic compounds correlates the data reported below for the acidic hydrolysis of a series of aliphatic hydroxamic acids. ρ^* and δ are constants to be determined for each reaction and set of reaction conditions and represent the susceptibility of the reaction system to polar and steric effects, respectively. σ^* and E_s are polar and steric substituent constants, respectively, characteristic of each substituent and are tabulated in the literature.[1,2]

$$\log k = \rho^*\sigma^* + \delta E_s + \log k_0 \quad (1)$$

The kinetics of amide hydrolysis have been studied extensively; nevertheless, uncertainties remain, especially for the acid-catalyzed reactions.[3] Three reports, to our knowledge, of kinetic studies of hydrolysis of the related hydroxamic acids exist; two report results for benzohydroxamic acid and a few of its derivatives at moderate[4] to very high acidities[5] and the third,[6] results for acetohydroxamic acid at very low acidity (pH >0.7). Table I reports results for the acidic dependence of the hydrolysis rate of propionohydroxamic acid at moderate acidities.

TABLE I

RATE CONSTANTS FOR PROPIONOHYDROXAMIC ACID HYDROLYSIS IN AQUEOUS *p*-TOLUENESULFONIC ACID AT 50.2° AND IONIC STRENGTH AT 0.494 *M*

$[H^+]$,[a] *M*	$10^5 k_{obsd}$[b]	$10^4 k_{obsd}/[H^+]$
0.494	22.0	4.45
0.247	9.88	4.00
0.124	5.27	4.25
		Av 4.23

[a] *p*-Toluenesulfonic acid. [b] Average pseudo-first-order rate constant, sec^{-1}.

The results of Table I are represented by eq 2, *i.e.*,

$$k_{obsd} = k_2[H^+] \quad (2)$$

the reaction is first order in catalytic acid and also in the hydroxamic acid. Equation 2 is consistent with the accepted bimolecular mechanism (eq 3 and 4) for acidic hydrolysis of benzohydroxamic acid[4,5] and amides[3] at moderate acidity. This mechanism requires k_2 to be a product of an equilibrium constant and a second-order rate constant.[4]

$$RCONHOH + H^+ \rightleftharpoons R\overset{+}{C}(OH)NHOH \quad (3)$$

$$R\overset{+}{C}(OH)NHOH + H_2O \longrightarrow \text{products} \quad (4)$$

Equation 1 should be applicable to the hydrolysis of acyl compounds following the bimolecular mechanism.[1,2] Table II lists the experimental results and log k calculated from eq 5 with the parameters determined by the method of least squares.[7] The reference substituent is methyl.

TABLE II

HYDROLYSIS RATES OF HYDROXAMIC ACIDS IN 0.249 *N* AQUEOUS *p*-TOLUENESULFONIC ACID AT 50.5°

Hydroxamic acid	Registry no.	$10^5 k_1$[a]	$10^5 k_2$[b]	$-\log k_2$	$-\log k_2$ (calcd)[c]
Aceto-	1113-25-3	11.0	44.2	3.355	3.438
Propiono-	2580-63-4	11.2	45.0	3.347	3.434
Isobutyro-	22779-89-1	3.92	15.7	3.804	3.608
Pivalo-	29740-67-8	2.17	8.71	4.060	4.126
Phenylaceto-	5330-97-2	4.27	17.1	3.767	3.726

[a] Pseudo-first-order rate constant, sec^{-1}. [b] Second-order rate constant, l. mol^{-1} sec^{-1}, $k_1/0.249$. [c] Calculated from eq 5.

$$\log k = -0.409\sigma^* + 0.526E_s - 3.438 \quad (5)$$

Equation 5 reproduces the log k values within 1 to 5% over a σ^* range of 0.515 (from phenylaceto, 0.215, to *tert*-butyl, −0.30) and an E_s range of 1.54 (from methyl, 0.00, to *tert*-butyl, −1.54). The coefficient of multiple regression[7] is 0.920. Neither σ^* nor E_s individually provide satisfactory correlation of the log k values. A log k *vs.* σ^* plot is quite scattered while a log k *vs.* E_s plot is a curve.

These results show that polar and steric effects are of comparable magnitude in the acid-catalyzed hydrolysis of hydroxamic acids. This result is in contrast to the acidic hydrolysis of amides and esters which shows very little or no dependence on polar effects.[1,2,8] The Taft steric substituent constants, E_s, implicitly allow for hyperconjugative effects.[9] A somewhat improved correlation for acidic hydrolysis

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(7) D. A. Leabo, "Basic Statistics," 3rd ed, Richard D. Irvin, Inc., Homewood, Ill., 1968, Chapter 14.
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(9) C. K. Hancock, E. A. Meyers, and B. J. Yager, *J. Amer. Chem. Soc.*, **83**, 4211 (1961).