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^{13}C NMR Chemical Shift Displacements and $^{13}C-^{19}F$ Coupling Constant Changes Induced by Interaction of Weak Bases and Trifluoroacetic Acid. Determination of Basicity Parameters

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The ^{13}C NMR shift displacements of 1-butyl derivatives dissolved in tetrachloromethane induced by addition of trifluoroacetic acid provide information about the relative basicity of C–O, C=O, C–S, and C=S groups in esters. The 1-butyl derivatives induce changes in the ^{13}C NMR shift and in the $^{13}C-^{19}F$ coupling constant of the trifluoroacetic acid. These changes run parallel with basicity. Insertion of the data in a generalized linear free energy relationship renders values for the basicity parameter β of the butyl derivatives. β-Values for a carboxylic acid and a sulfide is reported for the first time.

The ^{13}C NMR signals of alcohols, ethers and esters dissolved in tetrachloromethane are displaced on addition of trifluoroacetic acid.[1,2] The structure-dependent and stereoselective shift displacements seem to be the result of association between the acidic proton and oxygen lone pairs rather than protonation. The shift displacements can be used for calculation of association constants. Assuming that proclivity to form hydrogen bonds run parallel to basicity the association constants provide a measure of basicity. In this way, the relative basicity of alcohols and of ethers was estimated. Estimation of the relative basicity of esters was hampered by the presence of two basic sites.

The interaction of other functional groups with trifluoroacetic acid has now been studied by measuring the trifluoroacetic acid induced ^{13}C NMR shift displacements of a series of n-butyl derivatives as well as the simultaneous changes in the ^{13}C NMR shift and $^{13}C-^{19}F$ coupling constants of the trifluoroacetic acid.

RESULTS AND DISCUSSION

The ^{13}C NMR shift displacements of a series of n-butyl derivatives in 1 M solution in tetrachloromethane resulting from addition of 1 mole-equivalent of trifluoroacetic acid are shown in Table 1.* The titration curves of pentanal, 2-hexanone, and 1-pentanoic acid are

* 1-butylamine is not included in the data since 1-butyl-ammonium tetrafluoroacetate separated before the NMR measurements could be completed.

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Table 1. ^{13}C NMR chemical shift displacements of 1-butyl derivatives in 1 M solution in tetrachloromethane containing 1 mol-equivalent of trifluoroacetic acid.

X in substrate Bu^n-X[a]	Carbon atom						
	in n-butyl group						
	1	2	3	4	Me or CF_3	C=O	1 (corrected)[b]
Bu^n[c]	0.07	0.00	0.08	0.17			–
Cl[d]	−0.03	0.12	0.10	0.17			−0.10
$CH=CH_2$[e]	0.11	0.08	0.08	0.18			0.04
$SCOCF_3$[f]	−0.04	0.19	0.14	0.14	0.09	−0.97	−0.11
SH[g]	0.03	0.21	0.10	0.16			−0.04
$OCOCF_3$[f]	−0.53	0.17	0.17	0.21	0.09	−0.72	−0.60
SCSMe[f]	−0.18	0.22	0.09	0.22	0.31	−1.75	−0.25
NCS[f]	0.10	0.20	0.10	0.23			0.03
COOH[h]	0.16	0.19	0.18	0.33		−1.45	0.09
OCSMe[f]	−0.60	0.13	0.10	0.18	0.17	−1.42	−0.67
NO_2[f]	−0.16	0.10	0.19	0.26			−0.23
SMe[g]	0.24	0.34	0.09	0.52	0.29		0.17
SCOMe[i]	−0.60	0.65	0.15	0.32	0.18	−7.90	−0.67
CHO[j]	0.32	0.22	0.18	0.36		−7.82	0.25
COMe[k]	−0.42	−0.03	0.25	0.41	0.16	−10.01	−0.49
OH[l]	−1.15	1.21	0.40	0.49			−1.22
OCOMe[m]	−1.95	0.51	0.27	0.36	−0.02	−4.82	−2.02
OMe[n]	−0.63	1.20	0.49	0.41	0.51		−0.70
SO_2Me[f]	0.02	0.40	0.31	0.46	0.35		−0.05
CN[j]	0.49	0.09	0.29	0.31	CN: −0.28		0.42

[a] The ^{13}C NMR spectra were assigned following the references given. [b] Correction means C-1 shift displacement of substrate minus C-4 shift displacement of n-octane. [c] Grant, D.M. and Paul, E.G. *J. Am. Chem. Soc. 86* (1964) 2984. [d] Bruker 13–C Data Bank Vol. 1. [e] Couperus, P.A., Clague, A.D. and van Dongen, J.P. *Org. Magn. Reson. 8* (1976) 426. [f] See Experimental. [g] Barbarella, G., Dembech, P., Gahbera, A. and Fava, A. *Org. Magn. Reson. 8* (1967) 108. [h] Hagen, R. and Roberts, J.D. *J. Am. Chem. Soc. 91* (1969) 4504. [i] Hall, C.M. and Wemple, J. *J. Org. Chem. 42* (1977) 2118. [j] Hawkes, G.F., Herweg, K. and Roberts, J.D. *J. Org. Chem. 39* (1974) 107. [k] Breitmayer, E., Haas, G. and Volter, W. Atlas of C–13 NMR Data. [l]Roberts, J.D., Weigert, F.J., Kroschwitz, J.I. and Reich, H.J. *J. Am. Chem. Soc. 92* (1970) 1338. [m] Dorman, D.E., Bauer, D. and Roberts, J.D. *J. Org. Chem. 40* (1975) 3729. [n]Konno, C. and Hikino, H. *Tetrahedron 33* (1976) 325.

shown in Fig. 1. It is seen that the correction for the effects of the specific interaction between trifluoroacetic acid and the alkyl residue is necessary in order to obtain converging curves with the shape expected if progressive formation of a 1:1 adduct occurs.[2]

Shift displacements of significant magnitude may be a useful and simple aid for signal assignments, structure determinations, conformational analysis, assessment of the distribution of rapidly interconverting conformers, and estimation of the relative basicity of series of alkyl derivatives with a common substituent as demonstrated for alcohols, ethers, and esters.[1,2] As expected, however, hydrogen bonding ability runs parallel with proton-transfer basicity only within closely related compounds having similar binding sites.[3,4] Thus the shift displacement of C-1 in pentanal (up-field), 2-hexanone (down-field), and 1-butanol (more down-field) does not reflect the fact that 2-hexanone is considered to be the strongest of the bases.[5–7]

Also in conflict are the decreasing carbonyl carbon shift displacements of 2-hexanone, pentanal, and pentanoic acid with the derived equilibrium constants K, characterizing the

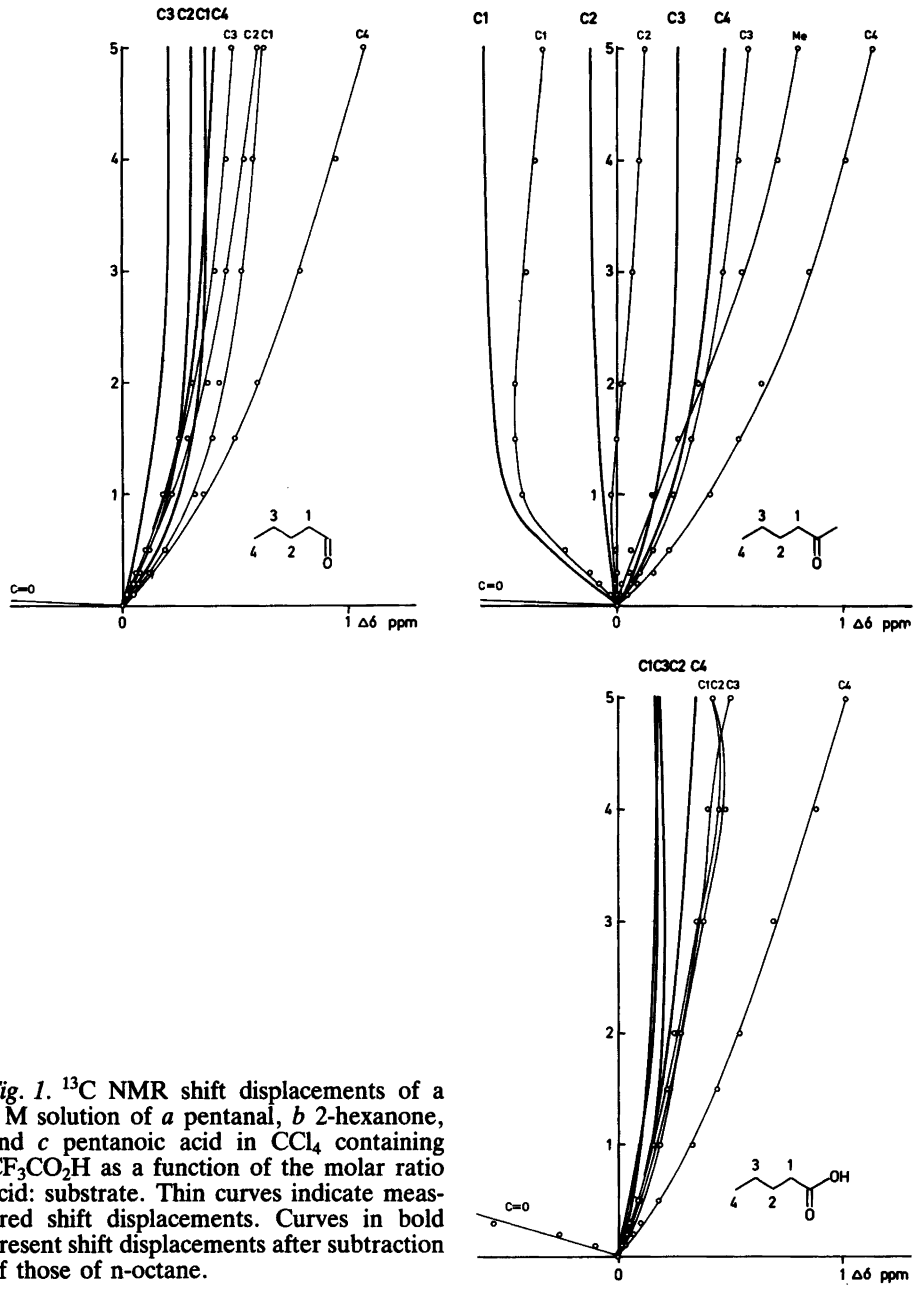

Fig. 1. ^{13}C NMR shift displacements of a 1 M solution of *a* pentanal, *b* 2-hexanone, and *c* pentanoic acid in CCl_4 containing CF_3CO_2H as a function of the molar ratio acid: substrate. Thin curves indicate measured shift displacements. Curves in bold present shift displacements after subtraction of those of n-octane.

extent of hydrogen bonding[2], which decreases in the order hexanone (K=50.0), pentanoic acid (K=20.3), and pentanol (16.7).

Nor do the shift displacements of ester and thio ester carbon atoms provide a measure for relative basicity, but the ratio between shift displacements of oxygen and sulfur analogues is fairly constant and the displacements reflect the relative negative charge at the oxygen and

Table 2. ^{13}C NMR chemical shifts and $^{13}C-F$ coupling constants of trifluoroacetic acid in a 1 M solution in tetrachloromethane containing 1 mole- equivalent of a 1-butyl derivative.

X in substrate Bu^n-X	$\delta_{C=O}$	δ_{CF_3}	$^1J_{CF}$	$^2J_{CF}$
No substrate	163.55	114.80	283.3	45.3
Bu^n	163.47	114.79	283.6	43.0
Cl	163.04	114.80	283.6	43.2
$CH=CH_2$	163.01	114.83	285.1	43.3
$SCOCF_3$	162.09	114.89	283.8	44.1
SH	162.03	114.91	284.7	43.2
$OCOCF_3$	161.58	114.93	284.7	43.2
SCSMe	161.43	114.98	284.9	43.0
NCS	162.26	114.98	285.2	43.2
COOH	162.72	115.04	285.3	42.6
OCSMe	160.69	115.08	284.1	42.2
NO_2	160.38	115.05	285.4	42.7
SMe	160.35	115.05	285.1	42.2
SCOMe	159.11	115.27	284.9	42.2
CHO	159.22	115.28	286.3	42.6
COMe	158.72	115.34	286.5	43.6
OH	160.45	115.39	285.6	42.1
OCOMe	158.81	115.39	286.5	41.7
OMe	158.69	115.44	285.8	41.8
SO_2Me	158.65	115.31	285.4	41.6
CN	158.65	115.30	285.9	41.9

Table 3. Known or estimated solvatochromic parameters for n-butyl derivatives.[a]

X in Bu^n-X	Type of substrate[b]	π^*	α	β
Bu^n	NHB	−0.08	0	0
$CH=CH_2$	NHB	0.13[c]	0	
$OCOCF_3$	HBA	0.19[d]	0[d]	
COOH	HBA−D	0.64[e]	1.12[e]	
NO_2	HBA	0.85[f]	0.22[f]	
SMe	HBA	0.39[c]	0[g]	
CHO	HBA	0.63[c]	0[h]	0.41[i]
COMe	HBA	0.67[j]	0.06[j]	0.50[k]
OH	HBA−D	0.47	0.79	0.88
OCOMe	HBA	0.46	0	0.45[l]
OMe	HBA	0.24[m]	0[m]	0.46[m]
SO_2Me	HBA	0.98[n]	0[n]	
CN	HBA	0.71[o]	0.19[p]	0.31[p]

[a] Values taken from Ref. 9. δ and $\xi=0$ for all compounds listed except n-butanol and n-butyl methyl ether ($\xi=0.20$) and 1-nitrobutane and pentanonitrile (ξ not known). δ_H values are given in Ref. 11. [b] NHB=non hydrogen-bond donor, HBA=hydrogen-bond acceptor, HBA−D=hydrogen-bond acceptor and donor. Trifluoroacetic acid is a HBD=hydrogen-bond donor. [c] Value calculated from $\mu=4.3$ $\pi^*-0.1$ [12] in which μ is the dipole moment. These are given in Ref. 13. [d–p] Values estimated from those of [d] ethyl trifluoroacetate, [e] acetic acid, [f] nitromethane, [g] other sulfur HBA compounds, [h] aromatic aldehydes, [i] butanal, [j] 2-butanone, [k] 2-pentanone, [l] ethyl acetate, [m] di-n-butyl ether, [n] sulfolane, [o] butanonitril, [p] acetonitrile.

sulfur atoms in ester C–O, C–S, C=O, and C=S groups.

The interaction between butyl derivative and trifluoroacetic acid also causes displacements of the trifluoroacetic acid carbon signals and changes in the one and two-bond C–F coupling constants (Table 2). This allows an unequivocal comparison of the butyl derivatives. The trifluoroacetic acid carbonyl carbon shift is the parameter most sensitive to interaction (range 4.9 p.p.m., up-field). The range of the displacement of the CF_3 signal is only 0.6 p.p.m. (down-field). The ranges of the one and two-bond C–F coupling constant changes are 3.2 Hz (increase) and 3.6 Hz (decrease).

The substrate induced changes of the shifts and C–F coupling constants obviously provide some qualitative information about the relative basicity of the substrates. Thus, the relative displacement of the carbonyl carbon shift agrees with the following facts: (i) alkanes, alkenes, and alkyl chlorides are very weak bases[5,6]; (ii) thioles are weaker bases than the corresponding alcohols[7]; (iii) methanethiole and 1-butanol are weaker bases than their methyl derivatives[7,8]; (iv) aldehydes are weaker bases than ketones[7]; (v) 2-hexanone is a weaker base than 1-butanol[5,6]; (vi) ethyl acetate is a weaker base than diethyl ether.[5,6] Moreover, the data suggest that thiol esters are weaker bases than their oxygen analogues, that trifluoroacetates are weaker bases than acetates, and that thionoesters are weaker bases than their oxygen analogues. The latter suggestions cannot be confirmed since other basicity measurements of these functional groups do not seem to have been reported. The displacement of the CF_3 signal and changes in C–F coupling constants roughly follow the same trends. Exceptions may be explained by uncertainties due to the smaller range in the displacement of these parameters.

In order to get quantitative information from the substrate induced changes in the trifluoroacetic acid shifts and coupling constants these were treated in terms of the Taft–Kamlet generalized linear solvation energy relationship:[9]

$$XYZ=XYZ_0+s(\pi^*+d\delta)+a\alpha+b\beta+h\delta_H+e\xi \quad (1)$$

π^*, α, β, δ_H, and ξ are the solvatochromic parameters and β is the basicity parameter. s,d,a,b,h, and e are the coefficients measuring the relative susceptibility of the indicated free energy property XYZ to the solvatochromic parameters. In the present case the substrate is equivalent to the solvent and trifluoroacetic acid equivalent to the indicator in the original treatise[9]. XYZ is the trifluoroacetic acid shift or coupling constant observed.

Since all substrates are 1-butyl derivatives, a treatment in these terms may give solvatochromic parameters characteristic of the functional groups. The characterization of the substrates are given in Table 3. In all cases the indicator acts as a HBD acid and the substrates as HBA bases giving rise to type-A hydrogen bonding.[10]

In order to extract maximum information from the displacement data a stepwise analysis was performed as described by Taft and Kamlet.[9] The trifluoroacetic acid shift observed in the absence of substrate was used as the XYZ_0-value. Next, the coefficients s, a, b, and e were determined by insertion in eqn. (1) of XYZ, trifluoroacetic acid carbonyl carbon shifts in the presence of substrates, for which the parameters π, α, β, and ξ are known or can be estimated with reasonable accuracy (Table 3). Thus, insertion of π^* of octane ($\delta=\alpha=\beta=h=\xi=0$) gives s. With s known, b can be determined by insertion of π^* and β of 1-butyl acetate ($\delta=\alpha=h=\xi=0$). Continuing in this way e can be calculated by insertion of the known parameters of 1-butyl methyl ether ($\delta=\alpha=h=0$). Finally, a is found using the known parameters of 1-butanol ($\delta=h=0$). The calculated system coefficients are given in Table 4.

Table 4. Calculated coefficients for eqn. (1).

Coefficient	Trifluoroacetic acid parameter used for calculation			
	$\delta_{C=O}$	δ_{CF_3}	$^1J_{CF}$	$^2J_{CF}$
s	1.00	0.13	−3.75	−28.75
a	8.08	−0.73	−4.98	−11.89
b	−11.56	1.18	10.94	37.39
e	1.09	0.33	−8.17	−33.99

In order to determine unknown or to confirm literature values of the basicity parameter β the XYZ_o, *s*, *a*, *b* and *e* values were inserted in eqn. (1) for compunds with known π^*, α, and ξ-values (Table 3). The β-value found (Table 5) for 2-hexanone ($\delta=h=\xi=0$) agrees well with that estimated (Table 3). So do the β-value for pentanal, ($\delta=h=\xi=0$) and for 1-octene ($\delta=h=\xi=0$). In the latter case a β-value close to 0 is expected. The β-values for 1-butyl trifluoroacetate and 1-butyl methyl sulphide ($\delta=\alpha=h=\xi=0$ for both) as well as for n-pentanoic acid ($\delta=h=\xi=0$) are the first determined for these functionalities.

The β-values of n-pentanonitril and 1-nitrobutane ($\delta=h=0$) were determined assuming that ξ for these compunds is equal to zero ($\xi=0$ for C=O and N=O bases[9]). The β-value obtained for pentanonitril (0.50) deviates from that reported for acetonitril (0.31).[9]

It is not possible to calculate β-values for the remaining substrates since other solvatochromic parameters for these compounds are unknown.

A similar calculation based on the trifluoroacetic acid CF_3 carbon shift and the C−F coupling constants provided the coefficients and β-values presented in Tables 4 and 5. β-Values determined from C=O shift displacements and changes in one bond C−F coupling constants agree quite well. The former values are more certain since C=O shift displacements fall in a 8 times broader range than the C−F coupling constant changes. β-Values determined from CF_3 carbon shift displacements and changes in two bond C−F coupling constants display larger variations from those determined from C=O shift displacements. This may be due to uncertainties of β-values calculated on basis of the narrow range CF_3-shift displacements and two bond C−F coupling constant changes.

Table 5. Calculated basicity parameter (β-) values for 1-butyl derivatives.

X in Bu^n−X	Trifluoroacetic acid parameter used for calculation[a]			
	$\delta_{C=O}$	δ_{CF_3}	$^1J_{CF}$	$^2J_{CF}$
$CH=CH_2$	0.60	0.01	0.21	0.05
$OCOCF_3$	0.19	0.09	0.19	0.09
COOH	0.91	0.83	0.91	0.78
NO_2	0.50	0.25	0.58	0.65
SMe	0.31	0.17	0.30	0.22
CHO	0.43	0.34	0.49	0.41
COMe	0.52	0.42	0.55	0.49
SO_2Me	0.51	0.32	0.53	0.65
CN	0.62	0.46	0.57	0.52

[a] The β-values calculated on basis of $\delta_{C=O}$ are the most accurate, see text.

Table 6. ^{13}C NMR chemical shifts[a] and $^{13}C-^{19}F$ couplings (Hz) of previously unassigned 1-butyl derivatives (1 M solution in tetrachloromethane).

Compound	Carbon atom 1	2	3	4	Me or CF_3	C=O,C=S or C=N	$^1J_{CF}$	$^2J_{CF}$
1-Butylthiotrifluoroacetate	31.48	29.37	22.52	14.10	116.27	184.47	291.7	40.3
1-Butyltrifluoroacetate	68.02	30.91	19.51	14.16	115.25	157.65	285.8	42.3
1-Butyldithioacetate	37.31	30.29	23.01	14.53	39.68	231.59		
1-Butylisothiocyanate	45.53	33.12	20.64	14.24				
1-Butylthionoacetate	72.55	30.99	20.00	14.59	34.80	218.88		
1-Nitrobutane	75.75	30.00	20.31	14.08				
1-Butyl methylsulfone	54.94	25.18	22.45	14.48	41.08			
1-Butylcyanide	28.22	22.54	17.42	14.06				

[a] Position of signals were measured relative to a dioxane standard [1](67.40 ppm) and are given in ppm relative to tetramethylsilane.

EXPERIMENTAL

1-Butyl thiotrifluoroacetate and 1-butyl trifluoroacetate were prepared from 1-butanethiol or 1-butanol and trifluoroacetic acid (50 % excess, 7 d 20 °C, neutralisation with saturated aqueous $NaHCO_3$, extraction with CH_2Cl_2, and distillation). 1-Butyl dithioacetate was prepared as described for the isobutyl analogue.[14] 1-Butyl thionoacetate[15] and 1-butyl thioacetate[16] were obtained according to literature methods. The remaining compounds are commercially available and were distilled before use.

^{13}C NMR spectra of the 1-butyl derivatives were recorded as described in Ref. 1 with 10 s repetition time. The ^{13}C NMR signals of trifluoroacetic acid were obtained accumulating 1000 scans with 60 s repetition time. The ^{13}C NMR spectra of 1-butyl thiotrifluoroacetate, -trifluoroacetate, -dithioacetate, -isothiocyanate, -thionoacetate, -methylsulfone, and cyanide as well as that of 1-nitrobutane have not been reported previously. The signals were assigned (Table 6) from proton coupled spectra through the multiplicity of the one bond C–H coupling constants and, when informative, also two bond C–H coupling constants.

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