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p-Fluorobenzoyl Chloride for Characterization of Active Hydrogen Functional Groups by Fluorine-19 Nuclear Magnetic Resonance Spectrometry

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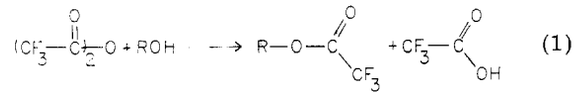
The base-catalyzed reactions of *p*-fluorobenzoyl chloride provide a convenient method for ^{19}F NMR analysis of alcohols, phenols, carboxylic acids, amines, and thiols. The ^{19}F chemical shift and yield data for *p*-fluorobenzoyl derivatives for nearly 100 compounds are presented. The yield data for these *p*-fluorobenzoyl derivatives suggest a simple, and in many cases, quantitative method for introducing a fluorine tagging group. The ^{19}F chemical shifts indicate a wide chemical shift range (~10 ppm) for a large number of compounds. Furthermore, most chemical classes (e.g., phenols, alcohols, etc.) have fairly well resolved chemical shift regions.

Although a number of ^{19}F NMR reagents have been developed by various laboratories for the characterization of functional groups, the presently available reagents have a variety of drawbacks which have limited widespread utilization. For example, trifluoroacetyl chloride and trifluoroacetic anhydride reagents have been utilized by a number of workers (*1–7*). These reagents readily react with a number of active hydrogen functional groups (e.g., phenols, alcohols, primary, and secondary amines, etc.) providing trifluoroacetate derivatives. The general reaction for the trifluoroacetic anhydride reagent is given below.



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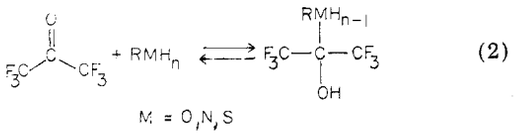
In these studies the trifluoroacetic anhydride reagent has been utilized to characterize hydroxyl groups in poly(propylene oxides) (*4*), steroids (*5*), monosterates (*6*), and polyols (*7*). However, the lability of the trifluoroacetate derivatives to hydrolysis in many cases hinders quantitative results with these derivatives.

Leader (*8*) has suggested the use of hexafluoroacetone for the characterization of various functional groups. The reagent reacts with active hydrogen groups as indicated in the scheme below



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The reagent has been shown to react with alcohols, amines, mercaptans, and other compounds with active hydrogens (*8–13*). For primary alcohols and nonhindered secondary alcohols the equilibrium indicated in eq 2 usually shifts far to the right. However, the equilibrium shifts to the left for even moderately hindered secondary alcohols and other active hydrogen functional groups (*13*). Furthermore, the ^{19}F chemical shifts for the hexafluoroacetone adducts are very susceptible to solvent, concentration, and temperature variations.

Another crucial area of concern is the sensitivity of the ^{19}F chemical shift parameter to subtle changes in molecular structure for a given derivative. Both the hexafluoroacetone adducts and trifluoroacetyl derivatives provide good ^{19}F chemical shift ranges; however, ^{19}F spectral overlap does occur in certain cases (e.g., phenol and primary amines). In contrast, derivatives of the 2,2,2-trifluorodiazoethane reagent (*14*) provide stable derivatives; however, the total ^{19}F chemical shift range for various trifluoroethyl derivatives is not as promising. Nevertheless, this reagent is useful for specific functional group characterization. For example, trifluoroethyl esters can be separately characterized in the presence of other active hydrogen compounds when paramagnetic reagents ($Eu(fod)_3$) are added which specifically complex with the carbonyl groups of these esters (*14*).

More recently, Zuber and co-workers (*15*) have introduced the use of pentafluoropropionic anhydride as an ^{19}F reagent for preparing pharmaceutical derivatives. However, stability of the derivatives to hydrolysis could be a problem with some of these pentafluoropropionate ester derivatives. Also, Yen and co-workers (*16*) have reported the use of trifluoromethanesulfonyl chloride to characterize active hydrogen functional groups. However, yield data or derivative stability was not reported in this work.

In view of the limitations for the reagents noted above we have explored the utility of *p*-fluorobenzoyl chloride as an analytical reagent to characterize active hydrogen functional groups. Manatt and co-workers (*17*) have previously used this reagent to derivatize amines which were subsequently coupled to cross-linked polystrene. In the presence of certain amine bases (e.g., DABCO, 1,4-diazabicyclo[2.2.2]octane) this reagent provides high yields of relatively stable ester or amide derivatives of alcohols, phenols, thiols, and primary and secondary amines, as indicated by the general reaction below.

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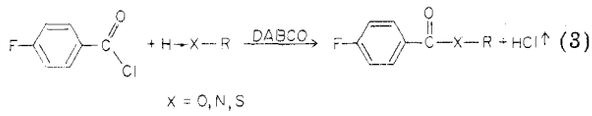


(3)

Superficially, it would appear that the ^{19}F NMR chemical shifts for the *p*-fluorobenzoate derivatives should be relatively insensitive to substrate changes because of the six to seven intervening bonds between the fluorine nuclide and the substrate group (–X–R). However, Taft (*18*) has previously demonstrated the facile ability of para-substituted fluorobenzenes to propagate substituent effects to the fluorine nuclide. It has been suggested that the very small perturbations in the fluorine electronic environment (and subsequent ^{19}F NMR chemical shifts) for para-substituted fluorobenzenes is one of the most sensitive probes currently available to investigate these subtle structural interactions (*18*). However, ^{19}F chemical shifts for these *p*-fluorobenzoate derivatives are susceptible to solvent variations which can be as large as 1 ppm or more. The ^{19}F chemical shifts reported in this paper utilized chloroform-*d* as the solvent, although the *p*-fluorobenzoyl derivatives can be prepared in a variety of solvents (e.g., chloroform-*d*, pyridine, tetrahydrofuran, etc.).

In this paper, we report the ^{19}F chemical shifts and yields for ~70 model alcohols, phenols, carboxylic acids, and primary and secondary amines. The addition of DABCO has been found to be a very effective basic catalyst which provides high yields for most derivatives under mild reaction conditions. In addition, the ^{19}F chemical shift range for the *p*-fluorobenzoyl derivatives are generally larger than the ranges found for other ^{19}F NMR tagging reagents (e.g., trifluoroacetates). A disadvantage of the *p*-fluorobenzoyl derivatives is the multiplet pattern due to J_{HF} coupling to ring protons. This can be removed by proton decoupling; however, variable nuclear Overhauser effects could cause quantitation errors unless these are suppressed by appropiate techniques.

EXPERIMENTAL SECTION

The ^{19}F nuclear magnetic resonance (NMR) spectra were obtained utilizing a JEOL FX-60QS NMR spectrometer operating at 56.20 MHz. Spectra were also obtained with a JEOL PS-100 NMR spectrometer operating at 94.1 MHz. Both NMR spectrometers were used with internal deuterium lock systems operating at 9.4 and 15.14 MHz, respectively. For all ^{19}F NMR spectra, 1,2-difluorotetrachloroethane (Peninsular Chemical Research or Aldrich Chemical Co.) was used as the ^{19}F chemical shift reference with chloroform-*d* as the solvent. Chemical shifts (δF) were measured in parts per million (ppm) with a negative value indicating shielding relative to the reference. The compound α,α,α-trifluoroacetophenone, (Aldrich Chemical Co.) was used as an integration standard for determination of the yield data. It should be noted that the yield data could be in error because of several factors including different ^{19}F relaxation times (T_1's). Yield data was obtained from spectra without ^1H decoupling in order to suppress errors due to variable nuclear Overhauser effects. We estimate a relative error in the yield data of ±5% in the present study; however, it could be much higher in certain cases (*1*, *14*).

In a typical preparation 0.1 mmol of the model compound, 0.1 mmol of 1,4-diazabicyclo[2.2.2]octane (DABCO), and 0.11 mmol of *p*-fluorobenzoyl chloride (20 μL) were added to a (0.5 mL) solution containing the solvent and references. All derivatives were prepared directly in 5-mm NMR tubes. The samples were allowed to react for a minimum of 1–2 h before the ^{19}F spectrum was obtained. For the case of hindered tertiary alcohols longer reaction times were usually employed (vida infra).

DISCUSSION AND RESULTS

p-Fluorobenzoyl Ester Derivatives of Alcohols. The ^{19}F chemical shift and yield data for various *p*-fluorobenozate derivatives of alcohols are presented in Table I. The total ^{19}F chemical shift range for the *p*-fluorobenzoate alcohol derivatives in Table I is ~2.1 ppm. This is somewhat larger than previously found for trifluoroacetate derivatives (*1*). The

Table I. ^{19}F Chemical Shift and Yield Data for *p*-Fluorobenzoate Derivatives of Alcohols

alcohols	δ_F[a]	yield[b]
methanol	−38.40	100
ethanol	−38.73	78
2-propanol	−39.07	60
1-propanol	−38.63	100
1-butanol	−38.86	100
2-butanol	−39.06	85
2-methyl-1-propanol	−38.73	100
2-methyl-2-propanol	−39.69	23
2-methyl-1-butanol	−38.80	100
neopentyl alcohol	−38.74	89
1-methylcyclohexanol	−39.33	8
1-ethylcyclopentanol	−39.45	4
2-octanol	−39.11	70
4-methyl-4-nonanol	−39.68	3
cyclohexanol	−38.88	100
benzyl alcohol	−38.12	79
p-methoxybenzyl alcohol	−38.39	100
phenethyl alcohol	−38.54	100
3-phenyl-1-propanol	−38.62	85
benzhydrol	−37.60	60
1-adamantanol	−39.68	56
cyclopropyl carbinol	−38.83	100
1-indanol	−38.57	92
2,3-butanediol	−38.27	97
ethylene glycol	−37.91	76
triphenylmethanol	−37.00	*c*

[a] Spectra were obtained 1–2 h after reaction. Chemical shifts were determined relative to 1,2-difluorotetrachloroethane. The solvent was chloroform-*d* in every case. [b] Percent yields were based on integration of α,α,α-trifluoroacetophenone and the corresponding integration of the *p*-fluorobenzoate derivative peak (see text for reaction times). [c] The yield was not determined.

^{19}F NMR chemical shift trend for the series ethanol, 2-propanol, and 2-methyl-2-propanol indicates a progressive increase in shielding which is also similar to the results for the trifluoroacetate derivatives (*1*, *2*). Namely, increasing shielding is observed for progressive alkyl substitution at the α carbon.

In contrast, an α-phenyl substituent deshields the ^{19}F nucleus (e.g., the *p*-fluorobenzoate ester of benzyl alcohol compared with methanol, −38.12 and −38.40 ppm, respectively). The addition of a second phenyl group at the α carbon deshields the ^{19}F nucleus to an even greater extent than one phenyl group (e.g., benzhydrol vs. benzyl derivative). However, electron donating and/or withdrawing substituents on the aromatic ring can significantly alter this trend. For example, it should be noted that *p*-methoxybenzyl alcohol (−38.39 ppm) exhibits a significant shielding increase relative to the benzyl alcohol derivative (−38.12 ppm) which is consistent with the electron donating ability of the methoxy group.

In comparing the shift due to phenyl substitution at the β position relative to the α position in the alkyl chain, phenethyl alcohol (−38.54 ppm) is more shielded than benzyl alcohol by −0.42 ppm. Increasing the chain length to three methylene groups as in 3-phenyl-1-propanol (−38.62 ppm) indicates even slightly higher shielding. However, in the 3-phenyl-1-propanol case the ^{19}F nucleus is less shielded than if a methyl group were in its place as in 1-butanol (−38.86 ppm). Thus, the effect of replacement of a phenyl group for a hydrogen at the γ, β, and α position is progressive shielding.

On the basis of the discussion above, the following additivity relationship adequately predicts the ^{19}F chemical shifts for the alcohols in Table I within ±0.12 ppm. The only derivatives not examined in this correlation were the ethylene glycol and 2,3-butanediol derivatives.

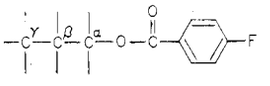
$$\delta_F = -38.40 \text{ ppm} + N_\alpha(\alpha) + N_\beta(\beta) + N_\gamma(\gamma) \quad (4)$$

Table II. ^{19}F Chemical Shift and Yield Data for *p*-Fluorobenzoyl Chloride Derivatives of Phenols

sample	δ_F [a]	yield [b]
phenol	−37.23	90
o-cresol	−37.20	100
m-cresol	−37.30	100
p-cresol	−37.37	100
m-phenylphenol	−36.90	100
p-phenylphenol	−36.99	99
4-*n*-propylphenol	−37.36	100
3-ethylphenol	−37.32	100
4-ethylphenol	−37.34	100
3-*tert*-butylphenol	−37.38	100
m-methoxyphenol	−37.13	100
p-methoxyphenol	−37.23	100
resorcinol	−36.78	55
catechol	−36.62	84
m-chlorophenol	−36.59	86
o-chlorophenol	−36.68	83
o-nitrophenol	−35.95	100
m-nitrophenol	−35.86	100
p-nitrophenol	−35.72	80
o-bromophenol	−36.64	80
m-bromophenol	−36.54	72
p-bromophenol	−36.73	61
1-naphthol	−36.83	100
2-naphthol	−37.06	88

[a] Spectra were obtained 1–2 h after reaction. Chemical shifts were determined relative to 1,2-difluorotetrachloroethane. The solvent was chloroform-*d* in every case. [b] Percent yields were based on integration of α,α,α-trifluoroacetophenone and the corresponding integration of the *p*-fluorobenzoate derivative peaks.

In this equation α, β, and γ are constants with values of −0.39, +0.03, and +0.04 ppm, respectively, for alkyl substitution. For phenyl substitution, α and β have values of +0.44 and +0.27 ppm, respectively.



(5)

Although the α effect crucially depends on the number of substituents attached to the α carbon (N_α), the β and γ effects appear to be less sensitive to the degree of substitution at these positions. In any case, it is quite remarkable that the fluorine nuclide is sensitive to subtle structural changes eight or nine bonds removed from these substrate variations.

The yields for the alcohols depend on the degree of alkyl substitution at the α carbon of the alcohol hydrocarbon framework. Thus, primary alcohol yields are nearly quantitative in every case. Secondary alcohols exhibit a modest decrease in yield of approximately 10%, while tertiary alcohols show little or no tendency to react with *p*-fluorobenzoyl chloride, after 1–2 h. However, if the reaction vessel is stored in a desiccator for 2 weeks and an excess of *p*-fluorobenzoyl chloride is present, a reaction yield of 5–50% can be obtained.

***p*-Fluorobenzoate Ester Derivatives of Phenols.** The ^{19}F chemical shift data for *p*-fluorobenzoate derivatives of phenols cover a range of ~2.4 ppm as indicated by the data in Table II. The magnitude of these shifts is approximately five times those found for similar trifluoroacetate derivatives (*1–4*). A typical ^{19}F spectrum for the *p*-fluorobenzoate derivative of *p*-bromophenol is indicated in Figure 1A. As illustrated in Figure 1B the residual *p*-fluorobenzoic acid can be easily removed by washing with an aqueous 5% solution of sodium bicarbonate. The derivatives containing an ortho substituent generally exhibit a decrease in shielding relative to an unsubstituted phenol (e.g., *o*-cresol, −37.20 ppm, and phenol, −37.23 ppm). The size of the ortho substituent can dramatically increase this deshielding effect. Similar deshielding results were found by Ho and Leader where bulky ortho groups generally exhibit a deshielding of the ^{19}F chemical shifts for ortho-substituted phenol adducts formed by hexafluoroacetone (*8–11*). This was also found for *p*-fluorobenzoate phenol derivatives (e.g., *o*-cresol, −37.20 ppm, compared with 2-*tert*-butyl-4-methylphenol, −35.01 ppm). In addition, a decrease in shielding is generally observed for larger fused aromatic ring phenols (e.g., 1- and 2-naphthol). These results probably reflect the critical dependence of the geometric orientation of the fluorine nuclide relative to the ring current of the phenolic ring derivative.

Table III. Substituent Effects for *p*-Fluorobenzoyl Derivatives of *o*-, *m*-, *p*-Phenols

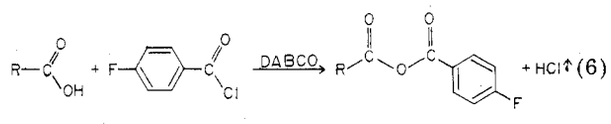
substituent	$\delta_{^{19}F}$ chemical shift relative to phenol, [a] ppm ortho-	meta-	para-
$-O-CH_3$		−0.10	0.00
$-CH_3$	+0.03	−0.07	−0.14
−Cl	+0.55	+0.64	
−Br	+0.59	+0.69	+0.47
−Ph		+0.33	+0.24
$-NO_2$	+1.58	+1.37	+1.57

[a] Positive values indicate deshielding relative to phenol.

One of the more interesting features of the ^{19}F chemical shift data for the *p*-fluorobenzoate phenol derivatives is the trend for ortho-, meta-, and para-substituted phenols compared with simple phenol derivative. These data are summarized in Table III. Not only are different ^{19}F chemical shifts observed for a given substituent at different ring positions (e.g., ortho, meta, and para) but, in addition, the ^{19}F chemical shielding or deshielding observed clearly reflects electron donation or withdrawal, respectively, for a given substituent. For example, the nitro substituent clearly exhibits substantial deshielding at all positions relative to phenol. It is also interesting to note that the para position is more sensitive to these electronic effects than the meta position as expected (*18*).

For the phenols in Table II, yields for the derivatives were generally greater than 80%. In addition, it should be noted that the yields exhibited by the phenols were critically dependent on the presence of the 1,4-diazabicyclo[2.2.2]octane. For example, in the absence of DABCO the yields were usually less than 10%.

***p*-Fluorobenzoyl Derivatives of Carboxylic Acids.** The reaction of carboxylic acids with *p*-fluorobenzoyl chloride gives an anhydride product as shown below.



(6)

Yields for the carboxylic anhydrides are poor when compared to the amine, alcohol, or phenol derivatives. This is probably due to the instability of the derivatives toward hydrolysis. The yields are generally around 50% and the ^{19}F chemical shift range for the *p*-fluorobenzoanhydrides is ~1.30 ppm (Table IV). This can be compared to a 0.80 ppm range reported for 2,2,2-trifluoroethyl ester derivatives of carboxylic acids (*14*).

Several trends are observed for the ^{19}F chemical shifts of the anhydride derivatives. The chemical shifts for phenyl substituents on the α carbon are progressively shielded as illustrated by the chemical shifts for diphenylacetic acid (−35.02 ppm) and triphenylacetic acid (−35.12 ppm). Conversely, larger condensed aromatic carboxylic anhydride derivatives (e.g., benzoic, 1- and 2-naphtholic, and anthracene-9-carboxylic) are progressively deshielded with increasing ring size. As was found for the phenol derivatives, para-substituted benzoic acids exhibit significant chemical shift variations.

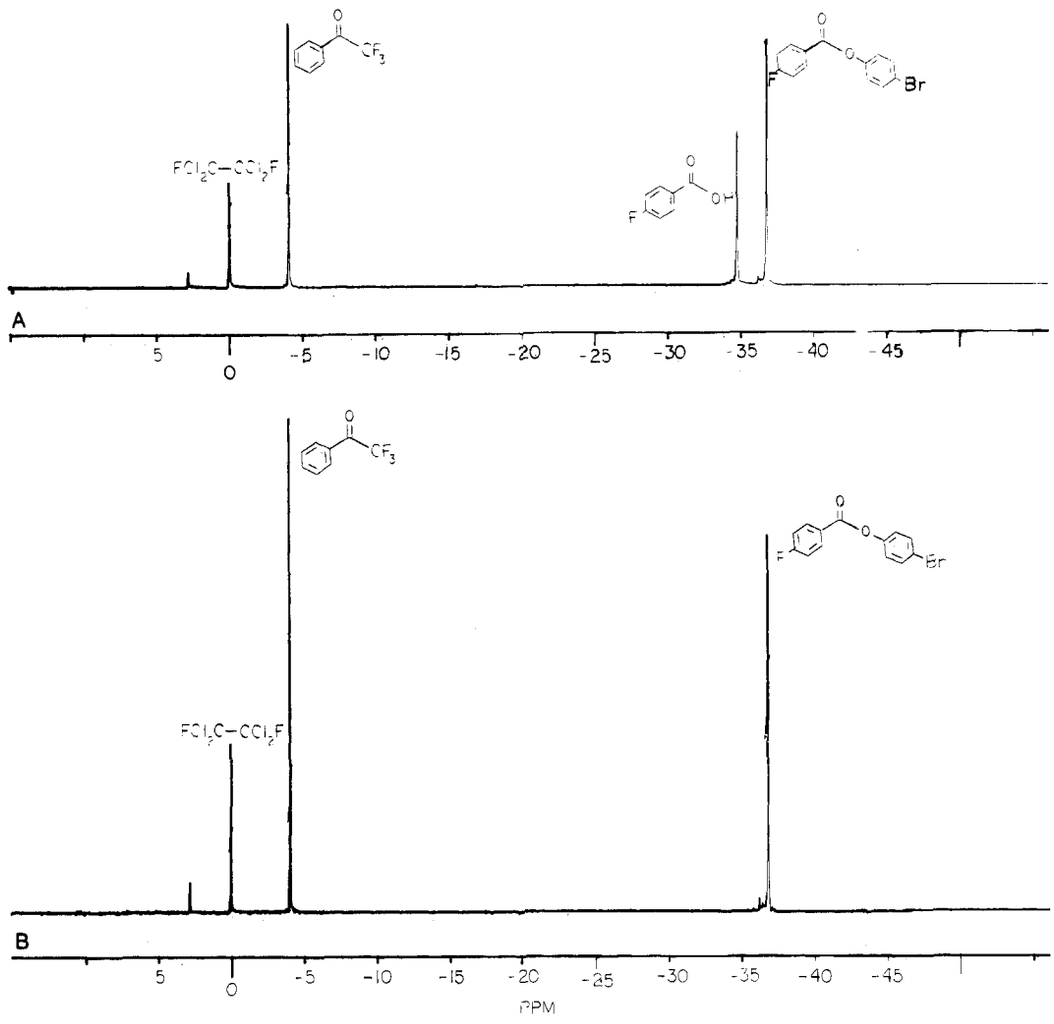


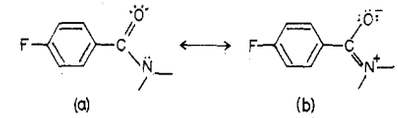
Figure 1. (A) ^{1}H decoupled ^{19}F NMR spectrum of the *p*-fluorobenzoate derivative for *p*-bromophenol (spectrum before treatment with 5% sodium bicarbonate). (B) ^{1}H decoupled ^{19}F NMR spectrum of the *p*-fluorobenzoate derivative for *p*-bromophenol (spectrum after treatment with 5% sodium bicarbonate).

Table IV. ^{19}F Chemical Shift and Yield Data for *p*-Fluorobenzoate Anhydride Derivatives of Carboxylic Acids[a]

sample	δ_F, ppm	yield[b]
benzoic acid	−35.05	100
p-nitrobenzoic acid	−33.87	34
m-bromobenzoic acid	−34.51	51
p-bromobenzoic acid	−34.63	49
o-chlorobenzoic acid	−34.82	52
m-chlorobenzoic acid	−34.49	50
p-chlorobenzoic acid	−34.65	65
diphenylacetic acid	−35.02	57
triphenylacetic acid	−35.12	50
(2-naphthoxy)acetic acid	−34.37	51
anthracene-9-carboxylic acid	−34.73	100
1-naphthoic acid	−35.18	60
2-naphthoic acid	−34.96	46
3-hydroxy-2-naphthoic acid	−34.85	20
hydroxyl group	−36.83	99

[a] Spectra were obtained 1-2 h after reaction. Chemical shifts were determined relative to 1,2-difluorotetrachloroethane. The solvent was chloroform-*d* in every case. [b] Percent yields were based on integration of α,α,α-trifluoroacetophenone and the corresponding integration of the *p*-fluorobenzoate derivative peaks.

***p*-Fluorobenzoyl Derivatives of Amines.** The ^{19}F chemical shift data for the amine derivatives are presented in Table V. Primary and secondary amines react in a normal manner in the presence of 1,4-diazabicyclo[2.2.2]octane to yield mono-*p*-fluorobenzamide derivatives with ^{19}F chemical shifts ranging from −40.38 to −41.92 ppm for simple primary alkyl amines and from −41.78 to −44.22 for secondary alkyl amines. However, secondary nitrogens in heterocyclic ring compounds exhibit a larger range of ^{19}F chemical shifts (e.g., −35.90 to −39.39 ppm). As suggested in previous work (*1*) the importance of the valence-bond form (b) may play an important role in explaining the deshielding of the ^{19}F chemical shift.



(7)

This is especially evident in the case of nitrogen heterocyclic compounds (e.g., imidazole and indole derivatives) where in valence-bond form (b) the derivative would exist with extended conjugation. In the derivative series imidazole, indole, and carbazole (chemical shifts of −35.90, −36.58, and −39.83 ppm, respectively) the importance of valence-bond form (b) is reduced because steric hinderance of the phenyl rings would not allow a coplanar arrangement of the *p*-fluorobenzene ring and the aromatic or pyrolidine ring. This effect was also noted in ^{19}F chemical shifts of secondary trifluoroacetamides (*1*).

***p*-Fluorobenzoyl Derivatives of Thiols.** Although only a few thiol ester derivatives were prepared in this study, it is apparent that some of the same trends noted for the alcohols are also observed with the thiol derivatives. For example, 1-hexanethiol, benzyl mercaptan, and thiophenol exhibit a progressive decrease in shielding, −37.93, −37.30, and −36.89

Table V. ^{19}F Chemical Shift and Yield Data for *p*-Fluorobenzoyl Derivatives of Amines[a]

sample	δ_F, ppm	yield[b]
n-butylamine	−41.50	95
isobutylamine	−41.43	88
sec-butylamine	−41.59	100
tert-butylamine	−41.92	100
phenethylamine	−41.19	100
aniline	−40.38	53
benzylamine	−40.00	100
diphenylamine	−41.78	82
2,2,6,6-tetramethylpiperidine	−41.81	76
n-ethyl-*n*-butylamine	−44.16	83
di-*n*-butylamine	−44.22	95
diethylamine	−43.75	76
homopiperazine	−42.86	87
iminodibenzyl	−42.54	86
diisopropylamine	−43.14	87
methylamine	−42.86	73
indoline	−41.87	100
benzanilide	−42.20	84
pyrrole	−39.39	68
carbazole	−39.83	*c*
imidazole	−35.90	68
2-methylimidazole	−36.12	100
2-ethyl-4-methylimidazole	−36.87	100
indole	−36.58	*c*
indole-2,3-dione	−36.14	51
indazole	−36.45	100
urea	−35.62	50

[a] Spectra were obtained 1–2 h after reaction. Chemical shifts were determined relative to 1,2-difluorotetrachloroethane. The solvent was chloroform-*d* in every case. [b] Percent yields were based on integration of α,α,α-trifluoroacetophenone and the corresponding integration of the *p*-fluorobenzoate derivative peaks. [c] The yields were not determined.

Table VI. The ^{19}F Chemical Shift and Yield Data for *p*-Fluorobenzoate Derivatives of Thiols[a]

sample	δ_F	yield[b]
1-hexanethiol	−37.93	18
2-propanethiol	−38.00	22
benzyl mercaptan	−37.30	54
thiolphenol	−36.89	92
p-thiocresol	−37.04	95
thiolactic acid	−36.23	27

[a] Spectra were obtained 1–2 h after reaction. Chemical shifts were determined relative to 1,2-difluorotetrachloroethane. The solvent was chloroform-*d* in every case. [b] Percent yields were based on integration of α,α,α-trifluoroacetophenone and the corresponding integration of the *p*-fluorobenzoate derivative peaks.

ppm, respectively (Table VI). This is analogous to the trend observed for a typical primary alcohol (1-butanol), benzyl alcohol, and phenol (Tables I and III). In addition, the thiol derivatives are slightly more deshielded (~0.4–1.0 ppm) than the alcohols and phenols. Nevertheless, substantial ^{19}F overlap occurs between the thiol and the phenol derivatives. In addition, certain benzyl alcohol (e.g., benzhydrol) derivatives also have ^{19}F chemical shifts in this region. Thus, the presence of thiols in a complex mixture containing phenols represents a serious ^{19}F spectral overlap problem in utilizing this reagent.

CONCLUSIONS

The results of the present study demonstrate the potential utility of ^{19}F NMR for characterizing various functional groups. That is, the ^{19}F chemical shift parameter for *p*-fluorobenzoyl derivatives is sufficiently sensitive to allow distinctions within a given series (e.g., alcohols) and is dependent upon the number and type of moiety present at the carbon atom containing the heteroatom. In summary, a larger range of ^{19}F chemical shifts is observed for the *p*-fluorobenzoyl derivatives when compared with the same trifluoroacetate (*1–4*) and trifluoroethyl (*14*) derivatives. It is also interesting to note that the ^{19}F chemical shift range for the *p*-fluorobenzoyl derivatives is as large as the entire ^{1}H NMR chemical shift range (~10 ppm). In conclusion, the *p*-fluorobenzoyl chloride reagent should be useful for the analysis of various complex mixtures (e.g., fuels and biological samples) where relatively stable derivatives are desired.

Registry No. DABCO, 280-57-9; *p*-fluorobenzoyl chloride, 403-43-0; methanol, 67-56-1; ethanol, 64-17-5; 2-propanol, 67-63-0; 1-propanol, 71-23-8; 1-butanol, 71-36-3; 2-butanol, 78-92-2; 2-methyl-1-propanol, 78-83-1; 2-methyl-2-propanol, 75-65-0; 2-methyl-1-butanol, 137-32-6; neopentyl alcohol, 75-84-3; 1-methylcyclohexanol, 590-67-0; 1-ethylcyclopentanol, 1462-96-0; 2-octanol, 123-96-6; 4-methyl-4-nonanol, 23418-38-4; cyclohexanol, 108-93-0; benzyl alcohol, 100-51-6; *p*-methoxybenzyl alcohol, 105-13-5; phenethyl alcohol, 60-12-8; 3-phenyl-1-propanol, 122-97-4; benzyhydrol, 91-01-0; 1-adamantol, 768-95-6; cyclopropyl carbinol, 2516-33-8; 1-indanol, 6351-10-6; 2,3-butanediol, 513-85-9; ethylene glycol, 107-21-1; triphenylmethanol, 76-84-6; phenol, 108-95-2; *o*-cresol, 95-48-7; *m*-cresol, 108-39-4; *p*-cresol, 106-44-5; *m*-phenylphenol, 580-51-8; *p*-phenylphenol, 92-69-3; 4-*n*-propylphenol, 645-56-7; 3-ethylphenol, 620-17-7; 4-ethylphenol, 123-07-9; 3-*tert*-butylphenol, 585-34-2; *m*-methoxyphenol, 150-19-6; *p*-methoxyphenol, 150-76-5; resorcinol, 108-46-3; catechol, 120-80-9; *m*-chlorophenol, 108-43-0; *o*-chlorophenol, 95-57-8; *o*-nitrophenol, 88-75-5; *m*-nitrophenol, 554-84-7; *p*-nitrophenol, 100-02-7; *o*-bromophenol, 95-56-7; *m*-bromophenol, 591-20-8; *p*-bromophenol, 106-41-2; 1-naphthol, 90-15-3; 2-naphthol, 135-19-3; benzoic acid, 65-85-0; *p*-nitrobenzoic acid, 62-23-7; *m*-bromobenzoic acid, 585-76-2; *p*-bromobenzoic acid, 586-76-5; *o*-chlorobenzoic acid, 118-91-2; *m*-chlorobenzoic acid, 535-80-8; *p*-chlorobenzoic acid, 74-11-3; diphenylacetic acid, 117-34-0; triphenylacetic acid, 595-91-5; (2-naphthoxy)acetic acid, 120-23-0; anthracene-9-carboxylic acid, 723-62-6; 1-naphthoic acid, 86-55-5; 2-naphthoic acid, 93-09-4; 3-hydroxy-2-naphthoic acid, 92-70-6; *n*-butylamine, 109-73-9; isobutylamine, 78-81-9; *sec*-butylamine, 13952-84-6; *tert*-butylamine, 75-64-9; phenethylamine, 64-04-0; aniline, 62-53-3; benzylamine, 100-46-9; diphenylamine, 122-39-4; 2,2,6,6-tetramethylpiperidine, 768-66-1; ethyl-*n*-butylamine, 13360-63-9; di-*n*-butylamine, 111-92-2; diethylamine, 109-89-7; homopiperazine, 505-66-8; iminodibenzyl, 494-19-9; diisopropylamine, 108-18-9; methylamine, 74-89-5; indoline, 496-15-1; benzanilide, 93-98-1; pyrrole, 109-97-7; carbazole, 86-74-8; imidazole, 288-32-4; 2-methylimidazole, 693-98-1; 2-ethyl-4-methylimidazole, 931-36-2; indole, 120-72-9; indole-2,3-dione, 91-56-5; indazole, 271-44-3; urea, 57-13-6; 1-hexanethiol, 111-31-9; 2-propanethiol, 75-33-2; benzyl mercaptan, 100-53-8; thiophenol, 108-98-5; *p*-thiocresol, 106-45-6; thiolacetic acid, 507-09-5; methyl *p*-fluorobenzoate, 403-33-8; ethyl *p*-fluorobenzoate, 451-46-7; 2-propyl *p*-fluorobenzoate, 2928-09-8; 1-propyl *p*-fluorobenzoate, 2928-10-1; 1-butyl *p*-fluorobenzoate, 3888-64-0; 2-butyl *p*-fluorobenzoate, 90172-12-6; 2-methyl-1-propyl *p*-fluorobenzoate, 29240-31-1; 2-methyl-2-propyl *p*-fluorobenzoate, 58656-98-7; 2-methyl-1-butyl *p*-fluorobenzoate, 90172-13-7; neopentyl *p*-fluorobenzoate, 69912-03-4; 1-methylcyclohexyl *p*-fluorobenzoate, 90172-14-8; 1-ethylcyclopentyl *p*-fluorobenzoate, 90194-68-6; 2-octyl *p*-fluorobenzoate, 90172-15-9; 4-methyl-4-nonyl *p*-fluorobenzoate, 90172-16-0; cyclohexyl *p*-fluorobenzoate, 90172-17-1; benzyl *p*-fluorobenzoate, 59986-44-6; *p*-methoxybenzyl *p*-fluorobenzoate, 90172-18-2; phenethyl *p*-fluorobenzoate, 90172-19-3; 3-phenyl-1-propyl *p*-fluorobenzoate, 90172-20-6; benzyhydryl *p*-fluorobenzoate, 53914-67-3; 1-adamantanyl *p*-fluorobenzoate, 90172-21-7; cyclopropylmethyl *p*-fluorobenzoate, 90172-22-8; 1-indanyl *p*-fluorobenzoate, 90172-23-9; 2,3-butandiyl di-*p*-fluorobenzoate, 90172-24-0; ethylene glycyl di-*p*-fluorobenzoate, 90172-25-1; triphenylmethyl *p*-fluorobenzoate, 70446-86-5; phenyl *p*-fluorobenzoate, 2714-90-1; *o*-cresyl *p*-fluorobenzoate, 90172-26-2; *m*-cresyl *p*-fluorobenzoate, 90172-27-3; *p*-cresyl *p*-fluorobenzoate, 32792-48-6; *m*-phenylphenyl *p*-fluorobenzoate, 90172-28-4; *p*-phenylphenyl *p*-fluorobenzoate, 90172-29-5; 4-*n*-propylphenyl *p*-fluorobenzoate, 80079-07-8; 3-ethylphenyl *p*-fluorobenzoate, 90172-30-8; 4-ethylphenyl *p*-

fluorobenzoate, 80079-06-7; 3-*tert*-butylphenyl *p*-fluorobenzoate, 90172-31-9; *m*-methoxyphenyl *p*-fluorobenzoate, 90172-32-0; *p*-methoxyphenyl *p*-fluorobenzoate, 80079-00-1; resorcinyl di-*p*-fluorobenzoate, 90172-33-1; 1,2-phenylene di-*p*-fluorobenzoate, 90172-34-2; *m*-chlorophenyl *p*-fluorobenzoate, 90172-35-3; *o*-chlorophenyl *p*-fluorobenzoate, 90172-36-4; *o*-nitrophenyl *p*-fluorobenzoate, 90172-37-5; *m*-nitrophenyl *p*-fluorobenzoate, 2710-17-0; *p*-nitrophenyl *p*-fluorobenzoate, 2710-18-1; *o*-bromophenyl *p*-fluorobenzoate, 90172-38-6; *m*-bromophenyl *p*-fluorobenzoate, 90172-39-7; *p*-bromophenyl *p*-fluorobenzoate, 656-21-3; 1-naphthyl *p*-fluorobenzoate, 90172-40-0; 2-naphthyl *p*-fluorobenzoate, 90172-41-1; benzoic acid anhydride with *p*-fluorobenzoic acid, 1800-04-0; *p*-nitrobenzoic acid anhydride with *p*-fluorobenzoic acid, 90172-42-2; *m*-bromobenzoic acid anhydride with *p*-fluorobenzoic acid, 90172-43-3; *p*-bromobenzoic acid anhydride with *p*-fluorobenzoic acid, 90172-44-4; *o*-chlorobenzoic acid anhydride with *p*-fluorobenzoic acid, 90172-45-5; *m*-chlorobenzoic acid anhydride with *p*-fluorobenzoic acid, 90172-46-6; *p*-chlorobenzoic acid anhydride with *p*-fluorobenzoic acid, 25569-91-9; diphenylacetic acid anhydride with *p*-fluorobenzoic acid, 90172-47-7; triphenylacetic acid anhydride with *p*-fluorobenzoic acid, 90172-48-8; (2-naphthoxy)acetic acid anhydride with *p*-fluorobenzoic acid, 90172-49-9; anthracene-9-carboxylic acid anhydride with *p*-fluorobenzoic acid, 90172-50-2; 1-naphthoic acid anhydride with *p*-fluorobenzoic acid, 90172-51-3; 2-naphthoic acid anhydride with *p*-fluorobenzoic acid, 90172-52-4; 3-hydroxy-2-naphthoic acid anhydride with *p*-fluorobenzoic acid, 90172-53-5; *N*-*n*-butyl-*p*-fluorobenzamide, 3851-81-8; *p*-fluoro-*N*-isobutylbenzamide, 88358-25-2; *p*-fluoro-*N*-*sec*-butylbenzamide, 90172-54-6; *p*-fluoro-*N*-*tert*-butylbenzamide, 49834-29-9; *p*-fluoro-*N*-phenethylbenzamide, 33799-96-1; *p*-fluoro-*N*-phenylbenzamide, 366-63-2; *N*-benzyl-*p*-fluorobenzamide, 725-38-2; *N*,*N*-diphenyl-*p*-fluorobenzamide, 79606-49-8; 1-(*p*-fluorophenylcarbonyl)-2,2,6,6-tetramethylpiperidine, 90172-55-7; *N*-*n*-butyl-*N*-ethyl-*p*-fluorobenzamide, 90172-56-8; *N*,*N*-di-*n*-butyl-*p*-fluorobenzamide, 90172-57-9; *N*,*N*-diethyl-*p*-fluorobenzamide, 10366-88-8; 1,4-bis(*p*-fluorophenylcarbonyl)hexahydro-1,4-diazepine, 90172-58-0; 9-(*p*-fluorophenylcarbonyl)-10,11-dihydro-5*H*-dibenz[*b*,*f*]azepine, 90172-59-1; *N*,*N*-diisopropyl-*p*-fluorobenzamide, 24167-56-4; *p*-fluoro-*N*-methylbenzamide, 701-49-5; 1-(*p*-fluorophenylcarbonyl)indoline, 90172-60-4; *p*-fluoro-*N*-phenyl-*N*-(phenylcarbonyl)benzamide, 90193-57-0; 1-(*p*-fluorophenylcarbonyl)-pyrrole, 90172-61-5; 9-(*p*-fluorophenylcarbonyl)carbazole, 90172-62-6; 1-(*p*-fluorophenylcarbonyl)imidazole, 90172-63-7; 1-(*p*-fluorophenylcarbonyl)-2-methylimidazole, 90172-64-8; 2-ethyl-1-(*p*-fluorophenylcarbonyl)-4-methylimidazole, 90172-65-9; 1-(*p*-fluorophenylcarbonyl)indole, 90172-66-0; 1-(*p*-fluorophenylcarbonyl)indole-2,3-dione, 90172-67-1; 1-(*p*-fluorophenylcarbonyl)indazole, 90172-68-2; *N*,*N*′-bis(*p*-fluorophenylcarbonyl)urea, 90172-69-3; 1-hexanethiol *p*-fluorobenzoate, 90172-70-6; 2-propanethiol *p*-fluorobenzoate, 90172-71-7; benzyl mercaptan *p*-fluorobenzoate, 90172-72-8; thiophenol *p*-fluorobenzoate, 90172-73-9; *p*-thiocresol *p*-fluorobenzoate, 90172-74-0; thiolacetic acid anhydride with *p*-fluorobenzoic acid, 90172-75-1.

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Depth Resolved Spectroscopic Analysis of Solid Samples Using Photoacoustic Spectroscopy

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The use of impulse response measurements for signal recovery in photoacoustic spectroscopy is described. The technique is compared with the use of sequential single frequency modulation methods and is shown to give improved results in depth profiling studies. An instrument capable of performing impulse response photoacoustic spectroscopy (IMPAS) is described and applied to a number of multilayer samples.

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There are many areas in which the ability to study the distribution of chromophores within solid or quasi-solid samples would be of considerable use; for example, the study of dyeing processes, the fabrication of multilayer materials, and the study of transport mechanisms in biological materials. A major claim for photoacoustic spectroscopy (PAS) has always been that it provides a nondestructive method of acquiring depth related spectroscopic information from solid samples. Despite this, very little has been reported in the literature on depth-profiling using PAS. It has been shown (*1–3*) that it is possible to discriminate between the waxy,

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