Chemistry of Novel Compounds with Multifunctional Carbon Structure. Part 4.[1] Steric and Electronic Influences on the Diastereoisomeric Chemical Shift Differences in ^{19}F N.m.r. Spectra by Introduction of Fluorine, Phenyl, and Heteroatom Groups into Acetates

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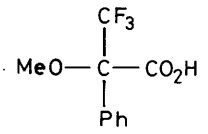
In order to develop reagents more efficient than MTPA for the determination of enantiomeric excess, several fluoroacetic esters (**2b**)—(**7b**) have been prepared which have various heteroatom-centred groups or bulky groups at the α position. These compounds have been converted into the corresponding s-butyl ester (**8a**)—(**13a**), α-phenylethyl ester (**8b**)—(**13b**), and α-phenylethylamide (**8c**)—(**13c**) diastereoisomers; the chemical shift differences between each pair of diastereoisomers (Δδ) have been obtained from the ^1H and ^{19}F n.m.r. spectra for each derivative. The influence on Δδ values of steric and possible electronic effects which arise upon introduction of a phenyl or a heteroatom group into the fluoroacetate structure are discussed.

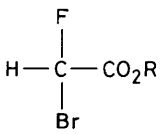
Following rapid progress in the fields of asymmetric synthesis and the total synthesis of complex chiral natural products, there has been an urgent need for precisely designed and widely applicable reagents for the determination of enantiomeric excess (e.e.). Although several methods have been reported,[2] derivatization of an enantiomeric mixture with α-methoxy-α-trifluoromethylphenylacetic acid (MTPA) (**1**) (Mosher's method)[3] is still one of the most popular and convenient means for this purpose. There are, however, many examples where the determination of e.e. by this method has failed because of the close similarity between the chemical and/or magnetic characteristics of the two MTPA diastereoisomers. With this in mind, we have attempted to probe the structural requirements necessary to make a reagent useful for e.e. determinations. We were also interested in the C–F bond reactivity of novel chiral fluoroacetates.[4]

Molecular Designing.—The major structural imperfections of MTPA (**1**) from the ^1H and ^{19}F n.m.r. viewpoint, seemed to lie in the presence of the fluorine atoms not on the chiral centre but on the carbon atom adjacent to it. Also the OMe and F signals are broad as a result of long-range coupling between the two nuclei.[3] As alternative reagents which might exceed the capability of MTPA, we focused on chiral molecules bearing both a single fluorine atom and an appropriate heteroatom-centred functionality or a bulky group directly attached to the α position (*i.e.* on the chiral centre) of the acetate structure, compounds (**2**)—(**7**). We thought that the steric effect of a bulky group and also the possible electronic effect[5] derived from the introduction of various heteroatoms onto the chiral carbon might necessarily affect the ^1H and ^{19}F n.m.r. chemical shifts of the two corresponding diastereoisomers.

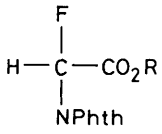
Synthetic Studies.†—We have recently reported the general synthesis[1,6,7] of novel fluoroacetic acid esters with various heteroatom-containing functional groups on the α position. However, the reactivity and the manipulation of these multifunctional esters or the corresponding acids have not been investigated in spite of their great potential interest from both synthetic and mechanistic viewpoints. In order to elucidate the



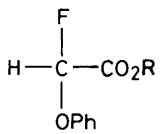
MTPA (**1**)



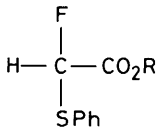
(**2**)



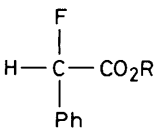
(**3**)



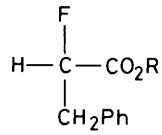
(**4**)



(**5**)

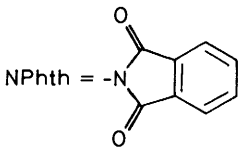


(**6**)

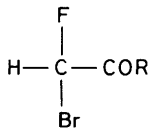


(**7**)

a; R = H
b; R = Et



† All compounds were prepared only for obtaining the Δδ values between the two diastereoisomers, therefore, they are all racemates.



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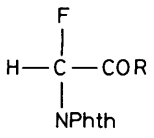

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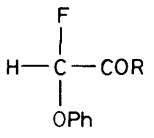

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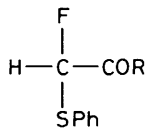

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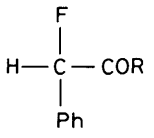

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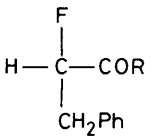

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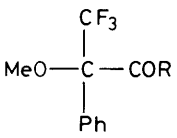


(14)

a; R = OCH(Me)Ph
b; R = OCH(Me)Ph
c; R = NHCH(Me)Ph
d; R = OBu^t
e; R = Cl

general chemical behaviour of these compounds, we attempted to convert the acids (**2a**)—(**5a**) or the corresponding ethyl esters (**2b**)—(**5b**) into the s-butyl ester (**8a**)—(**11a**), α-phenylethyl ester (**8b**)—(**11b**), and α-phenylethylamide (**8c**)—(**11c**) diastereoisomers, representative derivatives in Mosher's test.[3]

Ethyl bromofluoroacetate (**2b**) was converted into the s-butyl (**8a**) and α-phenylethyl (**8b**) esters by the transesterification method using titanium tetraisopropoxide as a catalyst.[4] The α-phenylethylamide derivative (**8c**) was obtained by condensation of bromofluoroacetic acid (**2a**) with α-phenylethylamine in the presence of dicyclohexylcarbodi-imide. Although both the s-butyl ester (**9a**) and the phenylethyl ester (**9b**) diastereoisomers were prepared successfully from (**3b**) by the above transesterification method, it proved difficult to obtain the α-phenylethylamide derivative (**9c**). Thus both saponificative[8] and non-saponificative[9] hydrolyses of (**3b**) appeared to give a mixture of defluorination and/or deimidation products (**15**)—(**19**) after solvolysis or during work-up. Condensation of (**3b**) with α-phenylethylamine afforded the amination product (**20**) because of the presence of the electron-withdrawing phthalimido group on the α position to fluorine. Direct conversion of the ester (**3b**) into the acid chloride (**9e**)[10] was also unsuccessful. Since the reaction of the bromo acid (**2a**) with potassium phthalimide was difficult, the t-butyl ester (**8d**) prepared from (**2a**) was first converted into the phthalimido derivative (**9d**). Acid treatment of (**9d**) produced the fluoro(phthalimido)acetic acid (**3a**). Finally, (**3a**) was condensed with α-phenylethylamine by a mixed anhydride method to afford the amide (**9c**).

Although fluoro(phenoxy)acetic acid (**4a**) was obtained easily by alkaline hydrolysis of the ethyl ester (**4b**), both the corresponding s-butyl (**10a**) and α-phenylethyl (**10b**) esters were prepared most conveniently from the ethyl ester (**4b**) rather than the acid (**4a**) by the above mentioned transesterification. The amide derivative (**10c**) was prepared by condensation of the ester (**4b**) with α-phenylethylamine without any solvent or catalyst. In contrast to the phenoxy derivative (**4b**), ester hydrolysis of the phenylthio derivative (**5b**) under various conditions[8,9] seemed to produce a mixture of defluorination and desulphenylation products (**15**), (**16**), (**21**), and (**22**) instead of the desired acid (**5a**). However, the three desired diastereoisomeric derivatives were obtained in a similar manner to (**10a**—**c**), *i.e.*, by direct transesterification with s-butyl and α-phenylethyl esters for (**11a**) and (**11b**) and by direct condensation with α-phenylethylamine for (**11c**), respectively.

The three kinds of diastereoisomers for compounds (**12**)—(**14**) were prepared from the corresponding acids or the esters (**6**), (**7**), and (**1**), respectively, by similar methods mentioned above.

Effects of the α-Substituents on Δδ Values.—^{1}H *N.m.r. study.* The ^{1}H chemical shift differences between the two diastereoisomeric isomers (Δδ) relating to these derivatives are summarized in Table 1. Heteroatom-substituted acetates (**8**)—(**11**) generally show larger Δδ values when compared with the corresponding carbon-substituted analogue (**13**). The effect of direct introduction of a phenyl group onto the chiral carbon, structures (**12**) and (**14**), is much more remarkable. However, severe limitations must be encountered, as Mosher has inferred,[3] in the e.e. determination method using ^{1}H n.m.r. because of the rather small Δδ values in general. The compounds (**8**)—(**11**) are superior to MTPA derivatives (**14**) in that the ^{1}H signals of the fluorine-bearing chiral carbons of (**8**)—(**11**) appear at much lower fields (δ 5.5—6.5 p.p.m.) than OMe protons of (**14**), where there is, generally, less disturbance because of overlap by the other miscellaneous protons which are present in the molecule.

^{19}F *N.m.r. study.* More remarkable results on the effects of the α-substituents on Δδ values were obtained from ^{19}F n.m.r. data shown in Table 2.

Effect of a bulky group and a fluorine atom on chiral centre. As has been mentioned in the ^{1}H n.m.r. discussion, it is apparent that a bulky group (Ph) directly attached to a chiral centre induces much greater magnetic influence on the ^{19}F n.m.r. chemical shifts between the two diastereoisomers, as evidenced by the data for compounds (**12**) and (**13**). The aryl group is attached not directly, but through a heteroatom, to the chiral centre for (**10**) and (**11**), and also (**9**) in a sense. However, the Δδ values of these compounds are comparable to, or better than, those of MTPA (**14**) which has a phenyl group on the chiral centre. This fact strongly suggests the necessity for a fluorine directly attached to the chiral centre. A further advantage of these α-fluoroacetate derivatives (**8**)—(**13**) is that their fluorine signals (*ca.* 10—15 Hz width) are sharper than that of MTPA (*ca.* 20—25 Hz) under our standardized measuring conditions.*

Effect of heteroatoms on chiral centre. Since the Δδ values are obtained for limited numbers of diastereoisomers and, further, there seems to be no real consistency between the Δδ values and the structural nature of R, it is difficult to predict the general tendency of the acetate structure–Δδ value relationship. However, if there were no electronic effect derived from the presence of the heteroatom on the chiral centre for compounds (**8**)—(**11**), the diastereoisomers of the sterically similar carbon analogue (**13**) should have given much larger Δδ values. Therefore, as we had expected, there must be some electronic effect of such heteroatoms which induces the α-fluorine chemical shift difference in the applied magnetic field.

As a result, the presence of both a bulky group and a single fluorine atom, and also a heteroatom group in some cases, on the chiral carbon atom is an important structural requirement in designing improved reagents for e.e. determination.

* Since our n.m.r. spectrometers and measuring conditions were different from those of Mosher, the Δδ values we obtained for MTPA diastereoisomers are not always consistent with his data.[3]

Table 1. ^{1}H Chemical shift difference Δδ (in Hz) of diastereoisomers (**8**)—(**14**) by 270 MHz ^{1}H n.m.r.[a]

		X						
		Br	NPhth[b]	OPh	SPh	Ph	CH_2Ph	
	proton	(**8**)	(**9**)	(**10**)	(**11**)	(**12**)	(**13**)	(**14**)
R = Et, —O—C(Me^3)—H^2 (**a**)	1	N.d.[c]	1.1	1.3	2.4	3.4	3.7	2.7
	2	N.d.[c]	6.4	N.d.	N.d.	5.7	N.d.	2.7
	3	1.7	16.4	6.1	13.8	30.4	N.d.	21.4
R = Ph, —O—C(Me^3)—H^2 (**b**)	1	8.3	3.7	0.7	2.1	5.6	7.1	23.0
	2	2.7	N.d.	N.d.	6.2	4.9	2.9	11.4
	3	N.d.	31.0	6.0	15.9	24.4	N.d.	15.9
R = Ph, —NH—C(Me^3)—H^2 (**c**)	1	7.9	13.4	1.2	9.3	9.8	N.d.	11.0
	2	7.2	0.5	N.d.	16.7	1.2	N.d.	3.1
	3	2.9	14.9	2.6	87.6	11.5	N.d.	10.8

[a] See Experimental section for details of conditions and method for determination of Δδ values. [b] Phthalimidyl group. [c] Not detectable.

Table 2. ^{19}F Chemical shift difference Δδ (in Hz) of diastereoisomers (**8**)—(**14**) by 254 MHz ^{19}F n.m.r.[a]

	X						
	Br	NPhth[b]	OPh	SPh	Ph	CH_2Ph	
	(**8**)	(**9**)	(**10**)	(**11**)	(**12**)	(**13**)	(**14**)
R = Et, —O—C(Me)—H (**a**)	52.1	N.d.[c]	35.1	19.9	103.0	25.0	N.d.
R = Ph, —O—C(Me)—H (**b**)	9.2	213.3	7.5	254.8	111.2	19.0	51.5
R = Ph, —NH—C(Me)—H (**c**)	29.4	147.9	17.0	32.2	303.4	5.5	45.9

[a] See Experimental section for details of conditions and method for determination of Δδ values. [b] Phthalimidyl group. [c] Not detectable.

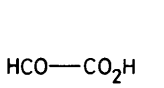
Compound (**12**) which has both a fluorine and a phenyl group on the chiral centre has advantages over the other compounds examined. In a preliminary experiment,* however, an unfortunate problem of racemization at the benzylic position seemed to arise when attempts were made to obtain the optically active form of (**12**). Further investigations, including preparation of optically active forms of (**8**)—(**11**) and elucidation of the possible heteroatom effect, are under way.

* Attempted preparation of optically active *R*(−)-(**12**) (R = OH)[11] by reaction of *S*(+)-mandelic acid with diethylaminosulphur trifluoride[12] or by reaction of *R*(−)-phenylglycine with sodium nitrite in hydrogen fluoride–pyridine[13] resulted in partial and in complete racemization, respectively.

Experimental

General.—I.r. spectra were recorded on a JASCO A-102 spectrophotometer. ^{1}H N.m.r. spectra were measured in $CDCl_3$ with $SiMe_4$ as internal standard and recorded on JEOL PMX-60 (60 MHz) and JEOL GX-270 (270 MHz) spectrometers. ^{19}F N.m.r. spectra were measured in $CDCl_3$ with $CFCl_3$ as internal standard and taken with a JEOL GX-270 (254 MHz) spectrometer. Upfield shifts are quoted as negative. E.i. mass spectra were taken with a JEOL JMS-D300 spectrometer. Column chromatography and preparative t.l.c. (p.l.c.) were performed using Kieselgel 60 (Merck, Art. 9385 and Art. 7748, respectively).

Materials.—Ethyl fluoro(phthalimido)acetate (**3b**), ethyl fluoro(phenoxy)acetate (**4b**), and ethyl fluoro(phenylthio)-



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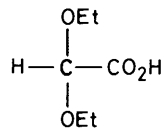

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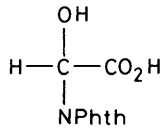

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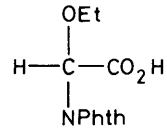

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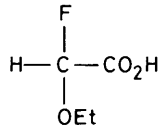

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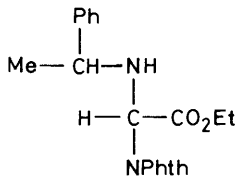

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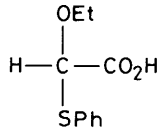

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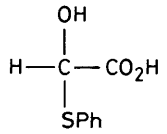

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acetate (**5b**) were prepared according to our method.[1,4] s-Butyl ester and α-phenylethyl ester diastereoisomers of compounds (**8a**)—(**11a**) and (**8b**)—(**11b**) were prepared according to the typical procedure described below.

To a solution of the ethyl ester (0.5 mmol) in s-butyl alcohol or α-phenylethyl alcohol (1 ml) was added dropwise titanium tetraisopropoxide (0.5 mmol) and the whole was heated at 100—120 °C for 1—3 h. Evaporation of the excess of alcohol under reduced pressure gave a residual oil which was purified by silica gel column chromatography or p.l.c. to afford a pair of diastereoisomeric esters.

N-α-Phenylethylacetamide derivatives (**8c**)—(**11c**) were prepared by direct condensation of the esters (**2b**)—(**5b**) with α-phenylethylamine without solvent or by the mixed anhydride method. The three diastereoisomer derivatives for the reference compounds (**12a—c**)—(**14a—c**) were also prepared in a similar manner as described above. Since all compounds were prepared for obtaining the Δδ values, the diastereoisomeric mixture was not separated. All spectral data were recorded as a diastereoisomeric mixture and the yields were obtained on a single experiment and not optimized. **CAUTION**. Some of these α-fluoroacetate derivatives prepared may be *highly toxic.*

s-Butyl bromofluoroacetate (**8a**). Colourless oil in 55% yield; $\nu_{max.}$(neat) 1 760 cm^{-1} (CO); δ_H 0.95 (3 H, t, *J* 7.4 Hz, CH_2Me), 1.297 and 1.303 (Δδ 1.7 Hz) (3 H, d, *J* 6.2 Hz, CH*Me*), 1.51—1.78 (2 H, m, CH_2), 5.01 (1 H, m, MeC*H*), and 6.65 (Δδ 0.0 Hz) (1 H, d, $J_{H,F}$ 50.7 Hz, FCH); δ_F −150.7 and −150.9 (Δδ *52.1 Hz*) (d, $J_{F,H}$ 51.5 Hz) [Found: *m/z* 182.9486. $C_4H_5BrFO_2$ (M^+ − Et) requires *m/z* 182.9457; *m/z* 184.9461. $C_4H_5Br^*FO_2$ (M^+ − Et) requires *m/z* 184.9437].

α-Phenylethyl bromofluoroacetate (**8b**). Colourless oil in 50% yield; $\nu_{max.}$(neat) 1 765 (CO) and 1 605 cm^{-1} (Ph); δ_H 1.63 (Δδ = 0.0 Hz) (3 H, d, *J* 6.60 Hz, Me), 6.01 and 6.02 (Δδ = 2.7 Hz) (1 H, q, *J* 6.6 Hz, CH), 6.55 and 6.58 (Δδ = 8.3 Hz) (1 H, d, $J_{H,F}$ 50.5 Hz, FCH), and 7.24—7.31 (5 H, m, Ph); δ_F −151.15 and −151.18 (Δδ 9.2 Hz) (d, $J_{F,H}$ 50.5 Hz) [Found: M^+, 259.9755. $C_{10}H_{10}BrFO_2$ requires *M*, 259.9847; Found: M^+, 261.9987. $C_{10}H_{10}Br^*FO_2$ requires *M*, 261.9829; *m/z* 181.0693. $C_{10}H_{10}FO_2$ (M^+ − Br) requires *m/z* 181.0665].

N-α-*Phenylethylbromofluoroacetamide* (**8c**). Colourless crystals in 73% yield; $\nu_{max.}$(KBr) 3 260 (NH) and 1 655 cm^{-1} (CO); δ_H 1.57 and 1.58 (Δδ = 2.9 Hz) (3 H, d, *J* 6.8 Hz, Me), 5.14 and 5.17 (Δδ 7.2 Hz) (1 H, q, *J* 7.2 Hz, MeC*H*), 6.58 and 6.61 (Δδ 7.9 Hz) (1 H, d, $J_{H,F}$ 51.2 Hz, FCH), 6.51 (1 H, br s, NH), and 7.35 (5 H, m, Ph); δ_F −148.2 and −148.4 (Δδ 29.4 Hz) (d, $J_{F,H}$ 51.5 Hz); [Found: M^+, 258.9961. $C_{10}H_{11}BrFNO$ requires *M*, 259.0008; Found: M^+, 260.9949. $C_{10}H_{11}Br^*FNO$ requires *M*, 260.9988; *m/z* 180.0833. $C_{10}H_{11}FNO$ (M^+ − Br) requires *m/z* 180.0824].

s-Butyl fluoro(phthalimido)acetate (**9a**). Colourless oil in 82% yield; $\nu_{max.}$(KBr) 1 790, 1 770, and 1 735 (CO), and 1 605 cm^{-1} (Ar); δ_H 0.88 and 0.96 (3 H, t, *J* 7.5 Hz, CH_2Me), 1.28 and 1.34 (Δδ 16.4 Hz) (3 H, d, *J* 6.4 Hz, CH*Me*), 5.06 and 5.08 (Δδ 6.4 Hz) (1 H, q, *J* 6.4 Hz, MeC*H*), 6.318 and 6.323 (Δδ 1.1 Hz) (1 H, $J_{H,F}$ 49.2 Hz, FCH), and 7.85—8.00 (4 H, m, Phth); δ_F −155.56 (Δδ = 0.0 Hz) (d, $J_{F,H}$ 50.0 Hz) [Found: M^+, 279.0918. $C_{14}H_{14}FNO_4$ requires *M*, 279.0907; *m/z* 206.0245. $C_{10}H_5FNO_3$(M^+ − OBu^s) requires *m/z* 206.0252].

α-Phenylethyl fluoro(phthalimido)acetate (**9b**). Colourless oil in 93% yield; $\nu_{max.}$(neat) 1 785 and 1 735 (CO) and 1 595 cm^{-1} (Ar); δ_H 1.59 and 1.71 (Δδ 31.0 Hz) (3 H, d, *J* 6.6 Hz, Me), 6.112 (Δδ 0.0 Hz) (1 H, q, *J* 6.6 Hz, MeC*H*), 6.32 and 6.33 (Δδ 3.7 Hz) (1 H, d, $J_{H,F}$ 49.1 Hz, FCH), 7.18—7.40 (5 H, m, Ph), and 7.73—7.97 (4 H, m, Phth); δ_F −155.025 and −155.864 (Δδ 213.3 Hz) (d, $J_{F,H}$ 49.7 Hz) {Found: M^+, 327.0882. $C_{18}H_{14}FNO_4$ requires *M*, 327.0907; *m/z* 178.0323. $C_9H_5FNO_2$ [M^+ − $CO_2CH(Me)Ph$] requires *m/z* 178.0305}.

t-Butyl bromofluoroacetate (**8d**).—A solution of bromofluoroacetic acid (1.07 g, 6.8 mmol) and a catalytic amount of toluene-*p*-sulphonic acid in dichloromethane (2 ml) and isobutene (10 ml) was heated at 50 °C in a sealed tube for 4 days. Evaporation of the solvent gave an oil which was dissolved in ether (20 ml). The ethereal layer was washed with a small amount of 10% Na_2CO_3 and dried ($MgSO_4$). Evaporation of the solvent gave a colourless oil (1.39 g, 96%); b.p. 51 °C/15 mmHg; $\nu_{max.}$(neat) 1 760 cm^{-1} (CO); δ_H 1.53 (9 H, s, Bu^t), and 6.45 (1 H, d, $J_{H,F}$ 51.0 Hz, CH); [*m/z* 196.9594. $C_5H_7BrFO_2$ (M^+ − Me) requires *m/z* 196.9612; *m/z* 198.9596. $C_5H_7Br^*FO_2$ (M^+ − Me) requires *m/z* 198.9595; *m/z* 110.9241. CHBrF (M^+ − $COOBu^t$) requires *m/z* 110.9246; *m/z* 112.9243. CHBr*F (M^+ − $COOBu^t$) requires *m/z* 112.9227].

t-Butyl Fluoro(phthalimido)acetate (**9d**).—A mixture of t-butyl bromofluoroacetate (**8d**) (0.99 g, 4.7 mmol) and potassium phthalimide (1.26 g, 6.8 mmol) in dimethylformamide (10 ml) was heated at 90 °C for 1 h. Solvent was removed under reduced pressure and the residual oil was dissolved in AcOEt (10 ml) and washed with small amount of 10% Na_2CO_3 and dried ($MgSO_4$). Evaporation of the solvent gave a yellow oil, which was chromatographed on silica gel with hexane–AcOEt (5:1) as eluant to give the *title compound* (**9d**) (0.73 g, 56%). Recrystallisation from CCl_4–hexane gave an analytical sample as colourless prisms, m.p. 127—128 °C (Found: C, 60.3; H, 4.95; N, 5.15. $C_{14}H_{14}FNO_4$ requires C, 60.21; H, 5.05; N, 5.02%); $\nu_{max.}$(KBr) 1 785 and 1 730 (CO) and 1 600 cm^{-1} (Ar); δ_H 1.58 (9 H, s, Bu^t), 6.29 (1 H, d, $J_{H,F}$ 50.0 Hz, CH), and 7.70—8.15 (4 H, m, Phth); *m/z* 206 (M^+ − OBu^t), 178 (M^+ − $COOBu^t$), and 57 (Bu^{t+}).

Fluoro(phthalimido)acetic Acid (**3a**).—A solution of the t-butyl ester (**9d**) (0.145 g, 0.52 mmol) and trifluoroacetic acid

(0.57 g) in chloroform (4 ml) was heated at reflux for 4 h. Evaporation of the solvent gave the *title compound* (**3a**) (0.118 g, 100%). Recrystallisation from CCl_4–AcOEt gave an analytical sample as colourless needles, m.p. 137—138 °C (Found: C, 53.55; H, 2.95; N, 6.15. $C_{10}H_6FNO_4$ requires C, 53.82; H, 2.71; N, 6.28%); $\nu_{max.}$(KBr) 3 500 (NH), 1 780 and 1 720 (CO), and 1 600 cm^{-1} (Ar); δ_H[$(CD_3)_2CO$] 5.15 (1 H, br s, OH), 6.45 (1 H, d, $J_{H,F}$ 48.8 Hz, FCH), and 7.84—8.02 (4 H, m, Phth); δ_F[$(CD_3)_2CO$] −156.02 (d, $J_{F,H}$ 49.7 Hz); *m/z* 224 (M^+ + 1), 223 (M^+), and 178 (M^+ − CO_2H).

N-α-*Phenylethylfluoro(phthalimido)acetamide* (**9c**). Colourless crystals in 66% yield; $\nu_{max.}$(KBr) 3 380 (NH), 1 795 and 1 750 (CONCO), and 1 680 cm^{-1} (CONH); δ_H 1.62 and 1.68 (Δδ 14.9 Hz) (3 H, d, *J* 7.1 Hz, Me), 5.260 and 5.262 (Δδ 0.5 Hz) (1 H, q, *J* 7.1 Hz, MeC*H*), 6.33 and 6.38 (Δδ 13.4 Hz) (1 H, d, $J_{H,F}$ 49.9 Hz, FCH), 6.87 (1 H, m, NH), 7.38—7.52 (5 H, m, Ph), and 7.78—7.96 (4 H, m, Phth); δ_F −154.588 and −155.170 (Δδ 147.9 Hz) (d, $J_{F,H}$ 49.9 Hz) [Found: M^+, 326.1020. $C_{18}H_{15}FN_2O_3$ requires *M*, 326.1066; *m/z* 105.0744. C_8H_7 (PhMeCH$^+$) requires *m/z* 105.0704].

s-Butyl fluoro(phenoxy)acetate (**10a**). Colourless oil in 76% yield; $\nu_{max.}$(neat) 1 760 (CO) and 1 590 cm^{-1} (Ph); δ_H 0.93 and 1.29 (3 H, m, CH_2*Me*), 1.28 and 1.31 (Δδ 6.1 Hz) (3 H, d, *J* 6.4 Hz, CH*Me*), 1.65 (2 H, m, CH_2), 5.02 (1 H, m, MeC*H*), 5.938 and 5.945 (Δδ 1.3 Hz) (1 H, d, $J_{H,F}$ 59.2 Hz, FCH), and 7.13—7.32 (5 H, m, Ph); δ_F −129.7 and −129.8 (Δδ 35.1 Hz) (d, $J_{F,H}$ 59.5 Hz) [Found: M^+, 226.0985. $C_{12}H_{15}FO_3$ requires *M*, 226.1004; *m/z* 125.0414. C_7H_6FO (M^+ − COOBu^s) requires *m/z* 125.0402].

α-*Phenylethyl fluoro(phenoxy)acetate* (**10b**). Colourless oil in 63% yield; $\nu_{max.}$(neat) 1 765 (CO) and 1 595 cm^{-1} (Ph); δ_H 1.59 and 1.63 (Δδ 6.0 Hz) (3 H, d, *J* 6.8 Hz, Me), 5.944 and 5.948 (Δδ 0.7 Hz) (1 H, d, $J_{H,F}$ 58.8 Hz, FCH), 6.03 (1 H, m, MeC*H*), and 7.07—7.44 (10 H, m, Ph); δ_F −129.759 and −129.789 (Δδ 7.5 Hz) (d, *J* 58.8 Hz) {Found: M^+, 274.0986. $C_{16}H_{15}FO_3$ requires *M*, 274.1004; *m/z* 105.0706. C_8H_9 [Ph(Me)CH$^+$] requires *m/z* 105.0704}.

N-α-*Phenylethylfluoro(phenoxy)acetamide* (**10c**). Colourless crystals in 66% yield; $\nu_{max.}$(KBr) 3 300 (NH), 1 660 (CO), and 1 590 cm^{-1} (Ph); δ_H 1.563 and 1.572 (Δδ 2.6 Hz) (3 H, d, *J* 6.9 Hz, Me), 5.19 (1 H, m, MeC*H*), 5.915 and 5.920 (Δδ 1.2 Hz) (1 H, d, $J_{H,F}$ 50.8 Hz, FCH), 6.80 (1 H, br s, NH), and 7.07—7.40 (10 H, m, Ph); δ_F −129.09 and −129.16 (Δδ 17.0 Hz) (d, $J_{F,H}$ 61.1 Hz) [Found: M^+, 273.1175. $C_{16}H_{16}FNO_2$ requires *M*, 273.1165; *m/z* 180.0839. $C_{10}H_{11}FNO$ (M^+ − OPh) requires *m/z* 180.0823].

s-Butyl fluoro(phenylthio)acetate (**11a**). Colourless oil in 96% yield; $\nu_{max.}$(neat) 1 755 cm^{-1} (CO); δ_H 0.83 and 0.88 (3 H, t, *J* 7.4 Hz, CH_2*Me*), 1.07 and 1.13 (Δδ 13.8 Hz) (3 H, d, *J* 6.2 Hz, CH*Me*), 1.40—1.62 (2 H, m, CH_2), 4.78 (1 H, m, MeC*H*), 5.96 and 5.97 (Δδ 2.4 Hz) (1 H, d, $J_{H,F}$ 52.8 Hz, FCH), and 7.28—7.61 (5 H, m, Ph); δ_F −158.13 and −158.21 (Δδ 19.9 Hz) (d, $J_{F,H}$ 53.5 Hz) [Found: M^+, 242.0792. $C_{12}H_{15}FO_2S$ requires *M*, 242.0776; *m/z* 141.0179. C_7H_6FS (M^+ − COOBu^s) requires *m/z* 141.0174].

α-*Phenylethyl fluoro(phenylthio)acetate* (**11b**). Colourless oil in 52% yield; $\nu_{max.}$(neat) 1 750 (CO) and 1 600 cm^{-1} (Ph); δ_H 1.43 and 1.49 (Δδ 15.9 Hz) (3 H, d, *J* 6.6 Hz, Me), 5.82 and 5.85 (Δδ 6.2 Hz) (1 H, d, *J* 6.2 Hz, MeC*H*), 6.050 and 6.057 (Δδ 2.1 Hz) (1 H, d, $J_{H,F}$ 51.6 Hz, FCH), and 7.25—7.40 (10 H, m, Ph); δ_F −158.3 and −159.3 (Δδ 254.8 Hz) (d, $J_{F,H}$ 51.8 Hz) [Found: M^+, 290.0815. $C_{16}H_{15}FO_2S$ requires *M*, 290.0777; *m/z* 141.0192. C_7H_6FS (PhSCHF$^+$) requires *m/z* 141.0175].

N-α-*Phenylethylfluoro(phenylthio)acetamide* (**11c**). Colourless crystals in 79% yield; $\nu_{max.}$(KBr) 3 380 (NH), 1 665 (CO), and 1 590 cm^{-1} (Ph); δ_H 1.13 and 1.45 (Δδ 87.6 Hz) (3 H, d, *J* 7.0 Hz, Me), 4.93 and 4.99 (Δδ 16.7 Hz) (1 H, q, *J* 7.0 Hz, MeC*H*), 6.06 and 6.09 (Δδ 9.3 Hz) (1 H, d, $J_{H,F}$ 52.2 Hz, FCH), 6.18 and 6.29 (1 H, br s, NH), and 7.18—7.64 (10 H, m, Ph); δ_F −156.18 and −156.30 (Δδ 32.2 Hz) (dd, $J_{F,H}$ 52.3, 3.7 Hz) [Found: M^+, 289.0979. $C_{16}H_{16}FNOS$ requires *M*, 289.0937; *m/z* 180.0815. $C_{10}H_{11}FNO$ (M^+ − SPh) requires *m/z* 180.0823].

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