Synthesis of 1-Fluoro-2-Phenylvinyl Piperidino Ketones

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A new palladium-catalysed synthesis of 1-fluoro-2-phenylvinyl piperidino ketones is described.

(2*E*)-, (2*E*,4*E*)-Unsaturated amides constitute an important class of compounds occurring widely in a number of natural products which show biological activities;[1] *e.g.* the local anaesthetic activity of *N*-dialkylaminoalkyl cinnamamides **1** has been reported[2] and 1,3-benzodioxol-5-ylvinyl piperidine ketone **2** has anticonvulsant activity. As unusual behaviour is

$XC_6H_4CH{=}C(R)HCONH[CH_2]_2NEt_2$

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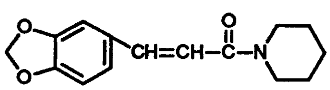

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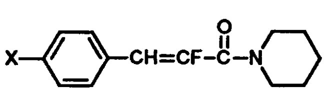
often ascribed to materials as the result of the introduction of fluorine atoms, and fluorine-containing compounds are useful or show potential in medicinal chemistry,[3] it was of interest to prepare and evaluate pharmacologically a series of *N*-alkyl(2-aryl-1-fluorovinyl)carboxamides. However, there is no report of the synthesis of 2-aryl-1-fluorovinylcarboxamides **3** in the literature.



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Results and Discussion

Recently we reported a palladium-catalysed reaction of bromoacetic ester with aldehydes in the presence of tributylphosphines leading to the conversion of aldehydes into α,β-unsaturated esters with high stereoselectivity in 52–85% yields.[4] This methodology has been successfully applied to the synthesis of fluorinated analogues, α-fluoro-α,β-unsaturated *N*-alkylamides **3**. A mixture of benzaldehyde, fluoroiodomethyl piperidino ketone, tributylarsine and a catalytic amount of palladium(0) (10 mol%) was stirred at 110 °C for 24 h; 1-fluoro-2-phenylvinyl piperidino ketone **6d** was obtained in 56% yield; there was no improvement in yield with increased reaction time or temperature. Tributylphosphines could also be used in this reaction, but the yield was lower (40%). In order to improve the yield of the desired α-fluoro-α,β-unsaturated amides, the more reactive triethylarsine was used instead of tributylarsine; thus the yield of the ketone **6d** could be raised to 64% with high *Z* stereoselectivity (Z/E = 95/5), but a 9% yield of 2-phenylvinyl piperidino ketone **7d** was also obtained with high *E* selectivity (E/Z = 100/0) (the total yield was 73%, and two products could be easily separated by chromatography).

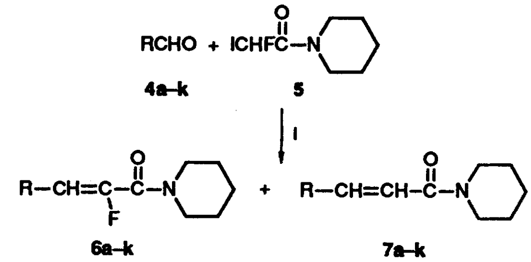
We then attempted the reaction of a series of aldehydes **4** with fluoroiodomethyl piperidino ketone **5** and triethylarsine under palladium catalysis (Scheme 1), the metal always being added in the form $Pd(PPh_3)_4$. The results are collected in Table 1.

Using this method, the α-fluoro-α,β-unsaturated amides could be obtained in 45–68% yields, and the α,β-unsaturated amides were obtained in 4–19% yields; the total yields were 51–88%. On the basis of literature data[5] referring to $RCH{=}CFCO_2Et$, the chemical shift of the fluorine of the *Z*-isomer is upfield and that of the *E*-isomer is downfield.

Table 1 Synthesis of α-fluoro-α,β-unsaturated amides **6**[a]

Compound[b]	R	Yield[c] (%) 6	Yield[c] (%) 7	$Z:E$[d] 6	$Z:E$[d] 7
a	$4\text{-}ClC_6H_4$	64	16	93:7	0:100
b	$4\text{-}NO_2C_6H_4$	68	19	86:14	0:100
c	$4\text{-}FC_6H_4$	56	9	95:5	0:100
d	C_6H_5	64	9	95:5	0:100
e	1,3-Benzodioxol-5-yl	47	4	93:7	0:100
f	(*E*)-PhCH=CH	50	4	62:38	37:63
g	2-Furyl	45	7	86:14	0:100
h	$c\text{-}C_6H_{11}$[e]	50	16	71:29	0:100
i	2-Naphthyl	50	6	93:7	0:100
j	$2,4\text{-}Cl_2C_6H_3$	54	14	85:15	0:100
k	$2\text{-}BrC_6H_4$	51	9	89:11	0:100

[a] $ICHFCON[CH_2]_4CH_2$ (2 mmol), Et_3As (2 mmol), RCHO (1 mmol) and $Pd(PPh_3)_4$ (0.1 mmol), *T* 110 °C, *t* = 24 h. [b] All products are new and were characterized by ^1H NMR, ^{19}F NMR, IR, MS and elemental analysis. [c] Isolated. [d] Ratios of *E*- and *Z*-isomers estimated on the basis of ^{19}F NMR spectra. [e] $Pd(PPh_3)_4$ (0.2 mmol).

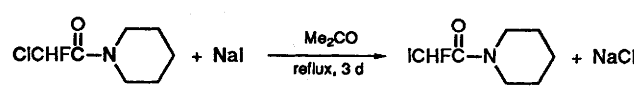


Scheme 1 *Reagents and conditions:* i, Et_3As, $Pd(PPh_3)_4$ (10 mol%), 110 °C, 24 h

This olefination method could be used with aliphatic aldehydes, both saturated and α,β-unsaturated, as well as aromatic aldehydes with different ring substituents. When an α,β-unsaturated aldehyde was used, the attack was also at the carbonyl carbon giving a 4-alkyl-1-fluorobuta-1,3-dienyl piperidino ketone.

Unfortunately, when $ICHFCONH_2$ was used, the desired product 2-fluoro-3-phenylpropenamide was obtained, but the yield was low (30%).

Fluoroiodomethyl piperidino ketone was prepared by a Finkelstein reaction[6] of fluorochloromethyl piperidino ketone[7] (Scheme 2).



Scheme 2

Therefore, this one-pot reaction provides an efficient and practical method for the convenient synthesis of the title compounds which have not been reported previously. It is noteworthy that in the absence of $Pd(PPh_3)_4$, no reaction occurred; the Pd catalyst is required in the reaction, but the mechanism is not clear and is being investigated.

Experimental

M.p.s and b.p.s are uncorrected. IR spectra were obtained as KBr disks (solid products) and as films (liquid products) on a Shimadazu IR-440 spectrometer. ^{1}H NMR spectra were determined at 200 MHz using a XL-200 spectrometer, and chemical shifts are reported downfield from internal Me_4Si; ^{19}F NMR spectra were recorded at 84.26 MHz using a FX-90 spectrometer, and chemical shifts are reported upfield from external CF_3CO_2H. *J*-Values are given in Hz. Mass spectra were recorded on a Finnigan-4021 mass spectrometer and HRMS spectra were recorded on a Finnigan MAT 8430 mass spectrometer. Fluorochloromethyl piperidino ketone,[7] $Pd(PPh_3)_4$[8] and triethylarsine[9] were prepared by literature methods; the aldehydes were commercially available research grade chemicals, and were redistilled or recrystallised prior to use.

General Procedure for Preparation of 1-*Fluorovinyl Piperidino Ketones*.—Reactions were carried out in an oven-dried Schlenk bottle equipped with a nitrogen inlet and magnetic stirrer and flushed with nitrogen. Triethylarsine (2.0 mmol) was injected into a mixture of aldehyde **4** (1.0 mmol), fluoroiodomethyl piperidino ketone **5** (2.0 mmol) and $Pd(PPh_3)_4$ (0.1 mmol) under nitrogen. The mixture was stirred and heated at 110 °C for several hours after which chromatography on silica gel eluting with light petroleum (b.p. 60–90 °C)–ethyl acetate (8:2) gave the pure product **6**.

2-(p-*Chlorophenyl*)-1-*fluorovinyl piperidino ketone* **6a**. Yield 64%; *Z*/*E* = 93/7; m.p. 71–72.5 °C (*Z*); 6a*Z*: $\delta_F(CDCl_3)$ 34.92 (1 F, d, *J* 37.6); $\delta_H(CDCl_3)$ 1.63 (6 H, m), 3.58 (4 H, m), 6.45 (1 H, d, *J* 37.6), 7.32 (2 H, d, *J* 8) and 7.50 (2 H, d, *J* 8); 6a*E*: $\delta_F(CDCl_3)$ 29.70 (1 F, d, *J* 22.0); $\delta_H(CDCl_3)$ 1.34 (2 H, m), 1.58 (4 H, m), 3.69 (2 H, m), 3.35 (2 H, m), 6.42 (1 H, d, *J* 22.0) and 7.21–7.32 (4 H, m); ν_{max}/cm^{-1} 2940, 1630, 1500, 1450, 1280 and 825; *m*/*z* 267 (M^+, 100), 269 (33), 268 (23), 248 (12), 247 (24.5), 218 (20), 183 (41), 156 (30.5), 155 (17), 135 (11), 120 (69) and 84 (67) (Found: C, 62.8; H, 5.5; N, 5.0. $C_{14}H_{15}ClFNO$ requires C, 62.80; H, 5.61; N, 5.23%).

2-(p-*Chlorophenyl*)*vinyl piperidino ketone* **7a**. Yield 16%; *E*/*Z* = 100/0; $\delta_H(CCl_4)$ 1.55 (6 H, m), 3.5 (4 H, m), 6.78 (1 H, d, *J* 16) and 7.15–7.65 (5 H, m).

1-*Fluoro*-2-(p-*nitrophenyl*)*vinyl piperidino ketone* **6b**. Yield 68%; *Z*/*E* = 86/14; m.p. 129–130 °C (*Z*); 6b*Z*: $\delta_F(CDCl_3)$ 30.06 (1 F, d, *J* 37.4); $\delta_H(CDCl_3)$ 1.65 (6 H, m), 3.60 (4 H, m), 6.48 (1 H, d, *J* 37.4), 7.66 (2 H, d, *J* 9) and 8.21 (2 H, d, *J* 9); 6b*E*: $\delta_F(CDCl_3)$ 23.92 (1 F, d, *J* 21.6); $\delta_H(CDCl_3)$ 1.41 (2 H, m), 1.61 (4 H, m), 3.40 (2 H, m), 3.63 (2 H, m), 6.45 (1 H, d, *J* 21.6), 7.51 (2 H, d, *J* 8.4) and 8.20 (2 H, d, *J* 8.4); ν_{max}/cm^{-1} 2950, 1630, 1600, 1510, 1450, 1340, 1260, 1102, 860 and 750; *m*/*z* 278 (M^+, 94), 279 (13), 259 (8), 258 (6), 194 (11), 156 (12), 136 (7), 84 (34) and 58 (100) (Found: C, 60.3; H, 5.2; N, 9.8. $C_{14}H_{15}FN_2O_3$ requires C, 60.4; H, 5.4; N, 10.07%).

2-(p-*Nitrophenyl*)*vinyl piperidino ketone* **7b**. Yield 19%; *E*/*Z* = 100/0; $\delta_H(CDCl_3)$ 1.63 (6 H, m), 3.63 (4 H, m), 7.06 (1 H, d, *J* 16), 7.53–7.93 (3 H, m) and 8.16–8.43 (2 H, m).

1-*Fluoro*-2-(p-*fluorophenyl*)*vinyl piperidino ketone* **6c**. Yield 56%; *Z*/*E* = 95/5; m.p. 53.5–54.5 °C (*Z*); 6c*Z*: $\delta_F(CDCl_3)$ 34.54 (1 F, s) and 36.89 (1 F, d, *J* 38.0); $\delta_H(CDCl_3)$ 1.68 (6 H, m), 3.60 (4 H, m), 6.49 (1 H, d, *J* 38.0), 7.08 (2 H, t, *J* 8.8) and 7.58 (2 H, m); 6c*E*: $\delta_F(CDCl_3)$ 31.09 (1 F, d, *J* 22.0) and 36.16 (1 F, s); $\delta_H(CDCl_3)$ 1.31 (2 H, m), 1.57 (4 H, m), 3.35 (2 H, m), 3.59 (2 H, m), 6.42 (1 H, d, *J* 22.0), 7.00 (2 H, t, *J* 8) and 7.28 (2 H, t, *J* 8); ν_{max}/cm^{-1} 2940, 1635, 1515, 1450, 1230, 1165, 840 and 510; *m*/*z* 251 (M^+, 100), 252 (12), 232 (10), 231 (25), 202 (34), 167 (95), 156 (28), 138 (63) and 119 (38) (Found: C, 66.6; H, 5.8; N, 5.4. $C_{14}H_{15}F_2NO$ requires C, 66.93; H, 5.98; N, 5.58%).

2-(p-*Fluorophenyl*)*vinyl piperidino ketone* **7c**. Yield 9%; *E*/*Z* = 100/0; $\delta_H(CCl_4)$ 1.1–1.5 (6 H, m), 3.43 (4 H, m), 6.65 (1 H, d, *J* 16) and 7.06–7.56 (5 H, m).

1-*Fluoro*-2-*phenylvinyl piperidino ketone* **6d**. Yield 64%; *Z*/*E* = 95/5; b.p. 140 °C, 0.45 mmHg; $\delta_F(CCl_4)$ 36.1 (d, *J* 38, *Z*) and 30.0 (d, *J* 22, *E*); $\delta_H(CDCl_3)$ 1.26 (*E*) and 1.66 (*Z*) (6 H, m), 3.32 (*E*) and 3.57 (*Z*) (4 H, m), 6.41 (*E*) and 6.48 (*Z*) [1 H, d, *J* 22 (*E*), 38 (*Z*)] and 7.26–7.59 (5 H, m); ν_{max}/cm^{-1} 3050, 2950, 1640, 1450, 1280, 1100, 760 and 670; *m*/*z* 233 (M^+, 100) 234 (17), 214 (9), 213 (15), 184 (12), 156 (11), 149 (23), 121 (10), 101 (19.8) and 84 (13.3) (Found: C, 71.9; H, 7.2; N, 6.0. $C_{14}H_{16}FNO$ requires C, 72.10; H, 6.87; N, 6.01%).

2-*Phenylvinyl piperidino ketone* **7d**. Yield 9%; *E*/*Z* = 100/0; $\delta_H(CCl_4)$ 1.6 (6 H, m), 3.5 (4 H, m), 6.7 (1 H, d, *J* 16) and 7.3 (6 H, m).

2-(1,3-*Benzodioxol*-5-*yl*)-1-*fluorovinyl piperidino ketone* **6e**. Yield 47%; *Z*/*E* = 93/7; m.p. 92–93 °C (*Z*); 6e*Z*: $\delta_F(CDCl_3)$ 38.07 (1 F, d, *J* 38.4); $\delta_H(CDCl_3)$ 1.66 (6 H, m), 3.57 (4 H, m), 5.98 (2 H, s), 6.44 (1 H, d, *J* 38.4), 6.80 (1 H, d, *J* 8), 7.00 (1 H, d, *J* 8) and 7.26 (1 H, s); 6e*E*: $\delta_F(CDCl_3)$ 33.04 (1 F, d, *J* 21.6); $\delta_H(CDCl_3)$ 1.30–1.43 (2 H, m), 1.57–1.70 (4 H, m), 3.38 (2 H, m), 3.62 (2 H, m), 5.96 (2 H, s), 6.37 (1 H, d, *J* 21.6), 6.76–6.81 (2 H, m) and 7.26 (1 H, s); ν_{max}/cm^{-1} 2920, 1670, 1620, 1500, 1490, 1450, 1250, 1040, 930, 910, 820, 630 and 510; *m*/*z* 277 (M^+, 100), 278 (15), 257 (39), 228 (19), 194 (10), 165 (10), 166 (25), 135 (22), 107 (44), 84 (55) and 69 (39) (Found: C, 64.7; H, 5.7; N, 4.8. $C_{15}H_{16}FNO_3$ requires C, 64.98; H, 5.78; N, 5.05%).

2-(1,3-*Benzodioxol*-5-*yl*)*vinyl piperidino ketone* **7e**. Yield 4%; *E*/*Z* = 100/0; $\delta_H(CCl_4)$ 1.47 (6 H, m), 3.44 (4 H, m), 5.89 (2 H, s), 6 34 (1 H, d, *J* 16), 6.67–7.10 (3 H, m) and 7.40 (1 H, d, *J* 16).

1-*Fluoro*-4-*phenylbuta*-1,3-*dienyl piperidino ketone* **6f**. Yield 50%; *Z*/*E* = 62/38; m.p. 79–81 °C (*Z*,*E*); 6f*Z*,*E*: $\delta_F(CDCl_3)$ 38.87 (1 F, d, *J* 34.0); $\delta_H(CDCl_3)$ 1.65 (6 H, m), 3.60 (4 H, m), 6.48 (1 H, dd, *J* 10, 34.0); 6.76 (1 H, d, *J* 16), 7.08 (1 H, dd, *J* 10, 16) and 7.27–7.50 (5 H, m); 6f*E*,*E*: $\delta_F(CDCl_3)$ 33.9 (1 F, d, *J* 20.0); $\delta_H(CDCl_3)$ 1.26 (2 H, m), 1.66 (4 H, m), 3.49 (2 H, m), 3.66 (2 H, m), 6.32 (1 H, dd, *J* 20.0, 11.4), 6.65 (1 H, d, *J* 15.7), 7.04 (1 H, dd, *J* 15.7, 11.4) and 7.26–7.46 (5 H, m); ν_{max}/cm^{-1} 2900, 1660, 1635, 1455, 1285, 760 and 695; *m*/*z* 259 (M^+, 100), 260 (18), 239 (19), 210 (10), 175 (16), 168 (9), 155 (16), 147 (24), 127 (27), 91 (7) and 84 (41) (Found: C, 73.7; H, 7.0; N, 5.15. $C_{16}H_{18}FNO$ requires C, 74.13; H, 6.95; N, 5.41%).

4-*Phenylbuta*-1,3-*dienyl piperidino ketone* **7f**. Yield 4%; *E*/*Z* = 63/37; $\delta_H(CDCl_3)$ 1.70 (6 H, m), 3.66 (4 H, m), 6.54 (*Z*) and 6.76 (*E*) [1 H, d, *J* 14.8 (*E*), 10.8 (*Z*)], 6.93–6.96 (1 H, m) and 7.2–7.6 (7 H, m).

1-*Fluoro*-2-(2-*furyl*)*vinyl piperidino ketone* **6g**. Yield 45%; *Z*/*E* = 86/14; m.p. 41.5–44.5 °C; $\delta_F(CDCl_3)$ 33.96 (d, *J* 20.4, *E*) and 34.32 (d, *J* 37.2, *Z*); $\delta_H(CDCl_3)$ 1.28 (*E*) and 1.67 (*Z*) (6 H, m), 3.42–3.49 (*E*) and 3.60 (*Z*) (4 H, m), 6.33 (*E*) and 6.64 (*Z*) [1 H, d, *J* 20.4 (*E*), 37.2 (*Z*)], 6.40–6.74 (2 H, m) and 7.30–7.50 (1 H, m); ν_{max}/cm^{-1} 2950, 1640, 1450, 1280, 1020 and 670; *m*/*z* 223 (M^+, 100), 224 (25), 203 (21), 139 (60.5), 112 (52) and 84 (43) (Found: M^+, 223.0994. $C_{12}H_{14}FNO_2$ requires *M*, 223.1009).

2-(2-*Furyl*)*vinyl piperidino ketone* **7g**. Yield 7%; *E*/*Z* = 100/0; $\delta_H(CDCl_3)$ 1.62 (6 H, m), 3.62 (4 H, m), 6.42–6.53 (2 H, m), 6.82 (1 H, d, *J* 16) and 7.36–7.48 (2 H, m).

2-*Cyclohexyl*-1-*fluorovinyl piperidino ketone* **6h**. Yield 50%; *Z*/*E* = 71/29; m.p. 30–32 °C (*Z*); 6h*Z*: $\delta_F(CDCl_3)$ 41.82 (1 F, d, *J* 36.8); $\delta_H(CDCl_3)$ 1.26–1.76 (16 H, m), 2.46–2.64 (1 H, m), 3.52 (4 H, m) and 5.47 (1 H, dd, *J* 8.4, 36.8); 6h*E*: $\delta_F(CDCl_3)$ 37.41 (1 F, d, *J* 22.6); $\delta_H(CDCl_3)$ 1.00–1.70 (16 H, m), 2.10–2.30 (1 H, m), 3.40 (2 H, m), 3.54 (2 H, m) and 5.26 (1 H, dd, *J*

22.6, 10.8); ν_{max}/cm^{-1} 2900, 1640, 1450, 1280, 1030 and 660; *m/z* 239 (M^+, 61.5), 240 (20), 156 (84), 136 (46), 112 (14), 84 (100), 73 (17) and 55 (51) (Found: C, 70.4; H, 9.7; N, 5.5. $C_{14}H_{22}FNO$ requires C, 70.29; H, 9.21; N, 5.86%).

2-*Cyclohexylvinyl piperidino ketone* **7h**. Yield 16%; E/Z = 100/0; $\delta_H(CCl_4)$ 1.28–1.93 (17 H, m), 3.53 (4 H, m), 6.16 (1 H, d, *J* 16) and 6.78 (1 H, dd, *J* 7, 16).

1-*Fluoro*-2-(2-*naphthyl*)*vinyl piperidino ketone* **6i**. Yield 50%; Z/E = 93/7; m.p. 86–88 °C (*Z*); 6i*Z*: $\delta_F(CDCl_3)$ 35.50 (1 F, d, *J* 38.4); $\delta_H(CDCl_3)$ 1.70 (6 H, m), 3.64 (4 H, m), 6.68 (1 H, d, *J* 38.4), 7.48–7.54 (2 H, m), 7.72–7.76 (1 H, m), 7.83–7.87 (3 H, m) and 8.05 (1 H, s); 6i*E*: $\delta_F(CDCl_3)$ 30.51 (1 F, d, *J* 22.0); $\delta_H(CDCl_3)$ 1.25 (2 H, m), 1.52–1.55 (4 H, m), 3.33–3.38 (2 H, m), 3.62–3.68 (2 H, m), 6.55 (1 H, d, *J* 22.0), 7.39–7.51 (3 H, m) and 7.77–7.81 (4 H, m); ν_{max}/cm^{-1} 3050, 2920, 1670, 1635, 1610, 1505, 1470, 1455, 1440, 1275, 1100, 915, 830, 740 and 480; *m/z* 283 (M^+, 100), 284 (27), 264 (17), 263 (69), 199 (65), 171 (54), 151 (25), 128 (11) and 84 (59) (Found: C, 76.1; H, 6.1; N, 4.8. $C_{18}H_{18}FNO$ requires C, 76.33; H, 6.36; N, 4.95%).

2-(2-*Naphthyl*)*vinyl piperidino ketone* **7i**. Yield 6%; E/Z = 100/0; $\delta_H(CDCl_3)$ 1.64 (6 H, m), 3.62 (4 H, m), 6.98 (1 H, d, *J* 15.8) and 7.40–7.88 (8 H, m).

2-(2,4-*Dichlorophenyl*)-1-*fluorovinyl piperidino ketone* **6j**. Yield 54%; Z/E = 85/15; $\delta_F(CDCl_3)$ 28.05 (d, *J* 20.0, *E*), 33.81 (d, *J* 37.2, *Z*); $\delta_H(CDCl_3)$ 1.26 (*E*) and 1.66 (*Z*) (6 H, m), 3.32 (*E*) and 3.60 (*Z*) (4 H, m), 6.63 (*E*) and 6.80 (*Z*) [1 H, d, *J* 20.0 (*E*), 37.2 (*Z*)], 7.19–7.31 (1 H, m), 7.38–7.43 (1 H, m) and 7.78 (1 H, d, *J* 8.4); ν_{max}/cm^{-1} 2900, 1640, 1470, 1440, 1275, 1100 and 670; *m/z* 301 (M^+, 39), 303 (24), 282 (6), 284 (3), 268 (51), 266 (100), 219 (18), 217 (26), 156 (35), 154 (42) and 84 (15) (Found: M^+, 301.0435. $C_{14}H_{14}FNO$ requires *M*, 301.0437).

2-(2,4-*Dichlorophenyl*)*vinyl piperidino ketone* **7j**. Yield 14%; E/Z = 100/0; $\delta_H(CDCl_3)$ 1.62 (6 H, m), 3.60 (4 H, m), 6.83 (1 H, d, *J* 15.8), 7.14–7.54 (3 H, m) and 7.85 (1 H, d, *J* 15.8).

2-(2-*Bromophenyl*)-1-*fluorovinyl piperidino ketone* **6k**. Yield 51%; Z/E = 89/11; m.p. 52–55 °C; $\delta_F(CDCl_3)$ 23.92 (d, *J* 20.0, *E*) and 30.06 (d, *J* 37.0, *Z*); $\delta_H(CDCl_3)$ 1.46 (*E*) and 1.68 (*Z*) (6 H, m), 3.26 (*E*) and 3.60 (*Z*) (4 H, m), 6.65 (*E*) and 6.80 (*Z*) [1 H, d, *J* 20.0 (*E*), 37.0 (*Z*)], 7.14–7.22 (1 H, m), 7.31–7.38 (1 H, m), 7.62 (1 H, d, *J* 8) and 7.83 (1 H, d, *J* 8); ν_{max}/cm^{-1} 2920, 1630, 1450, 1100, 1020, 730 and 680; *m/z* 311 (M^+, 36), 313 (34), 294 (2), 292 (3), 232 (100), 148 (55), 149 (23), 120 (49) and 84 (19) (Found: C, 53.85; H, 4.7; N, 4.2. $C_{14}H_{15}BrFNO$ requires C, 53.85; H, 4.81; N, 4.49%).

2-(2-*Bromophenyl*)*vinyl piperidino ketone* **7k**. Yield 9%; E/Z = 100/0; $\delta_H(CDCl_3)$ 1.64 (6 H, m), 3.60 (4 H, m), 6.80 (1 H, d, *J* 15.5), 7.12–7.60 (4 H, m) and 7.88 (1 H, d, *J* 15.5).

Fluoroiodomethyl Piperidino Ketone **5**.—A solution of NaI (22.7 g, 15 mol) in absolute acetone (60 cm^3) was added to a stirred solution of fluorochloromethyl piperidino ketone (9.1 g, 0.05 mol) in acetone (10 cm^3). After the addition, the mixture was heated under reflux for *ca.* 3 days until the reaction was complete (^{19}F NMR). After cooling and removal of the solvent, distilled water (50 cm^3) was added to the deep red residue, and the oily material was extracted with ethyl acetate (3 × 150 cm^3) and the extract dried and concentrated. The residue was isolated by column chromatography on silica gel with light petroleum (b.p. 60–90 °C)–ethyl acetate (8:2) as eluent to give the pure ketone **5**, (8.9 g, 65%), m.p. 60–62 °C; $\delta_F(CDCl_3)$ 78.8 (1 F, d, *J* 52); $\delta_H(CDCl_3)$ 1.61 (6 H, m), 3.46 (4 H, m) and 7.19 (1 H, d, *J* 52); ν_{max}/cm^{-1} 2900, 2800, 1650, 1450, 1250, 1050, 1000 and 506; *m/z* 271(M^+, 5), 272 (M^+ + 1, 25), 144 (M^+ − I, 100), 112 (99), 84 (38), 69 (90), 55 (29) and 42 (59).

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