Elemental fluorine. Part 14.[1] Electrophilic fluorination and nitrogen functionalisation of hydrocarbons

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Selective fluorination of a range of hydrocarbons was achieved by reaction with either elemental fluorine or Selectfluor™, an electrophilic fluorinating reagent of the N–F class. An electrophilic mechanism is envisaged. On prolonged reaction, the strongly acidic reaction medium that is formed upon substitution of hydrogen by fluorine when Selectfluor™ is used as the fluorinating reagent, promotes loss of fluoride from the initial fluorinated product. Trapping of the subsequent carbocation by the acetonitrile solvent in a Ritter type process gives overall nitrogen functionalisation of hydrocarbons. Amidation of hydrocarbons could also be achieved in a one-stage process by reaction of the hydrocarbon with fluorine and a Lewis acid, such as boron trifluoride–diethyl ether, in acetonitrile.

Introduction

The search for efficient methodology for the selective conversion of saturated hydrocarbons to functionalised derivatives has been the focus of substantial effort from many research groups worldwide over the last 20 years.[2–4]

Effective processes for the selective transformation of hydrocarbons to functionalised derivatives are urgently required. Many approaches have been investigated[2–4] but low yields, long reaction times, lack of selectivity and high expense, limit the use of many of these approaches. In general, the functionalised alkane products are typically more reactive than the alkane starting materials and reactions must be carried out to very low conversion in order to minimize by-product formation.

Halogenation of alkanes offers direct methodology for the functionalisation of hydrocarbons since derived haloalkanes can, of course, be used as substrates for the synthesis of a wide range of functional systems. In particular, chlorination of hydrocarbons and other saturated systems has been extensively studied and the effects of solvent, temperature, stereochemistry, rearrangement and relative reactivities of various C–H bonds in saturated systems towards chlorine for a wide range of substrates are well documented.[5] Both thermal and photochemical chlorination processes are established and are usually operated at high temperature (>300 °C) in the vapour phase but, due to the harsh reaction environment, free radical chlorination of hydrocarbons exhibit low selectivity and, in general, give all possible monochlorinated products upon reaction with alkanes.

In contrast, the replacement of C–H by a C–F bond in saturated systems upon reaction with fluorine has received little attention and a systematic survey of reactions between fluorine and a variety of hydrocarbons has not been reported. Tedder[6] studied gas phase reactions between, for example, fluorine and *n*-butane and noted only minor differences in the reactivities of each carbon site. More recently Barton[7] and Rozen,[8] demonstrated that tertiary C–H bonds may be selectively transformed to C–F bonds. However, in all of the reactions reported by these workers only replacement of tertiary C–H bonds was reported and reactions were carried out in a solvent mixture consisting of chloroform and $CFCl_3$ (a solvent now unavailable under the terms of the Montreal Protocol) at low temperatures, unsuitable for scale-up procedures. Nevertheless, these pioneering studies suggest that direct fluorination could be a viable method for the selective functionalisation of hydrocarbons, provided that more appropriate reaction media and temperature could be used. Furthermore, the fact that many selectively fluorinated molecules can possess significantly different chemical, biological and physical properties compared to the corresponding non-fluorinated derivatives, features that find many useful applications in the life-science industries,[9] provides a further stimulus for the development of efficient and selective direct fluorination methodology.

The transformation of a carbon–hydrogen bond to a carbon–fluorine bond using fluorine is a very exothermic process[10] (ΔH = −430.5 kJ mol^{-1}) and there is much discussion in the literature[11] concerning whether the mechanism of such substitution reactions follow either a free radical or electrophilic pathway. Since fluorine is less than 1% dissociated at room temperature,[10] the concentration of fluorine atoms may not be sufficient to initiate a radical chain process. An alternative initiation step (ΔH = 16.3 kJ mol^{-1}, Fig. 1), originally suggested by Miller,[12]

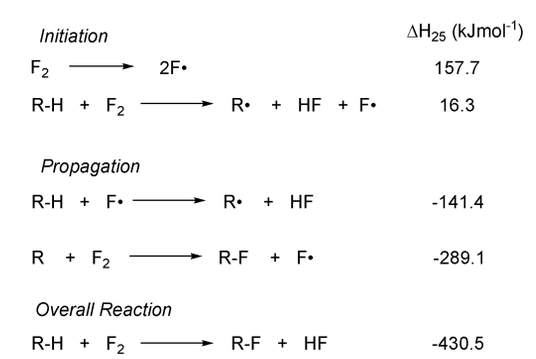

Fig. 1 Thermodynamic data for the fluorination of methane.

probably occurs but conclusive evidence for this pathway has not been established.

Barton and Rozen suggested[7,8] that the replacement of hydrogen by fluorine in saturated systems proceeds by an electrophilic mechanism involving 3 centre, 2 electron bond

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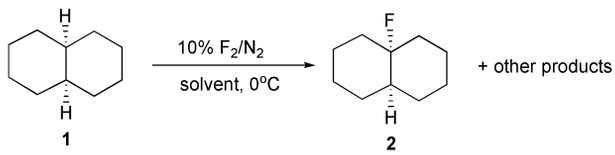
Table 1 Survey of solvents for fluorination of hydrocarbons.

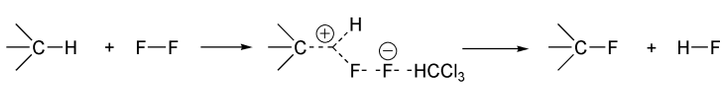


1 2

Concentration of substrate **1** in solvent = 0.3 M

Solvent	F_2–substrate	*cis*-9-Fluorodecalin, **2**		
		Yield %[a]	Conv. (%)	Tar[c] (%)
CH_3CN	1 : 1	<10	13[b]	0
CH_3CN	5 : 1	57	64	0
CH_3CN	16 : 1	10	99[b]	13
CH_3CN–$CFCl_2CF_2Cl$ (1 : 4)		56	63	0
CH_3CN–$CFCl_2CF_2Cl$ (1 : 9)		52	92	0
CH_3CN–$CFCl_2CF_2Cl$ (1 : 19)		27	40	0
CH_3CN–CH_2Cl_2 (1 : 19)		0	2	0
CH_3CN–*p*-dinitrobenzene (50 : 1)		60	83	
CH_3CN–*p*-dinitrobenzene (13 : 1)		66	85	
CH_3CH_2CN		50	78	0
HCOOH	1 : 1	0	2[b]	trace
H_2SO_4		0	25[b]	25
CF_3COOH		<1	69[b]	33
$CFCl_2CF_2Cl$–CF_3SO_3H (1 : 1)		<1	100[b]	28
$CFCl_2CF_2Cl$–CF_3SO_3H(19 : 1)		<1	80[b]	28
BF_3–CH_2Cl_2 (1 : 20)		0	91[b]	9
BF_3–CH_2Cl_2 (1 : 5)		0	92[b]	8
CF_3CH_2OH		0	61[b]	0
$CFCl_2CF_2Cl$		8	85[b]	28
CH_2Cl_2	1 : 5	<1	4[b]	
CH_2Cl_2	1 : 10	<1	11	
CH_3NO_2		33	97	24

[a] After work-up. [b] Conversion was estimated using GC-MS. [c] % tar by weight.



Scheme 1

carbocationic intermediates (Scheme 1), analogous to aliphatic electrophilic nitration processes (S_E1 process) described by Olah.[13] Furthermore, the direct fluorination of *trans*-decalin† proceeded with retention of stereochemistry which, it was suggested, could only be attributed to an electrophilic process. However, it must be noted that various free radical reactions, including chlorination of decalin at the tertiary position, can also occur with retention of stereochemistry.[14]

In an attempt to address the problem of the mechanism of direct fluorination (radical or electrophilic?), we reasoned that a comparison of fluorination reactions between alkanes and both fluorine and established electrophilic fluorinating reagents would provide an indication as to the nature of the process. A range of electrophilic fluorinating agents[15] are now commercially available, *e.g.* Selectfluor™ (Air Products) and a series of radical clock experiments by Differding[16] and Wong[17] established that quinuclidine fluorinating agents such as Selectfluor™ are electrophilic in character. If similar product profiles could be obtained in reactions between hydrocarbons and both fluorine and Selectfluor™, we could reasonably suggest that the mechanism of both processes are electrophilic in nature. However, until our recent communication,[18] fluorination of alkanes by N–F reagents had not been reported.

In this paper, we describe our studies directed towards the fluorination of various hydrocarbons and compare the results of direct fluorination reactions using elemental fluorine with those carried out using an established electrophilic fluorinating agent, Selectfluor™, with a view to probing the mechanism of direct fluorination processes. Furthermore, we aimed to establish viable reaction conditions (solvent and temperature, *etc.*) and extend the range of hydrocarbons that could be fluorinated to those that do not possess tertiary sites.

Results and discussion

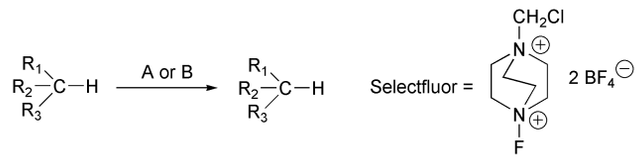
In earlier parts of this series, we established that selective direct fluorination of aromatics[19,20] and a variety of dicarbonyl derivatives[21] is significantly affected by the nature of the reaction medium and can be accomplished by using either an acidic or a high relative permittivity reaction medium, such as formic acid and acetonitrile respectively, which promote selective electrophilic fluorination processes.

In order to establish a suitable solvent that could be used as a reaction medium for selective direct fluorination of hydrocarbons at convenient temperatures, we carried out a series of reactions between fluorine and *cis*-decalin **1** in a range of solvents at 0 °C (Table 1). In each case the conversion of the starting material, the yield of *cis*-9-fluorodecalin **2** and tar formation were recorded for comparison. *cis*-Decalin **1** was chosen as the model substrate for comparison with Rozen's results (see above).

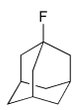
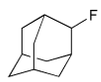
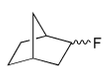
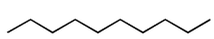
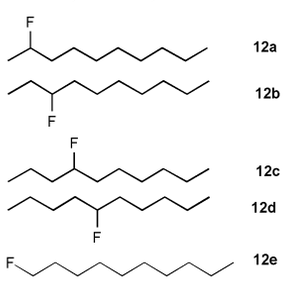
Several points from the data collected in Table 1 are worth noting; (1) acid reaction media, used effectively in electrophilic fluorination reactions of aromatic[19] and 1,3-dicarbonyl substrates,[21] gave low yields of 9-*cis*-fluorodecalin and substantial amounts of tarry material; (2) low yields of fluorodecalin were obtained in chlorinated solvents; (3) nitromethane, a solvent with high relative permittivity allows the preparation of

† The IUPAC name for decalin is decahydronaphthalene.

Table 2 Fluorination of hydrocarbons



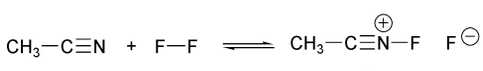
A, 10% F_2 in N_2 (*v*/*v*), CH_3CN, 0°C; B, Selectfluor, CH_3CN, reflux 16 h.

Substrate	Conditions A or B Conversion (%)	Product		
 **4**		 **5**	 **6**	Others
	A (70)	65%	23%	14%
	B (100)	43%	8%	5%
 **7**		 **8**	others	
	A (53)	63%	4%	
	B (100)	21%		
 **9**		 **10**		
	A (60)	41%, **10a** *exo*, **10b** *endo* 5.3 : 1		
 **11**		 **12a** **12b** **12c** **12d** **12e**		
	A (61)	**12**, 63%, 2.4 :1.3 : 1 :1.1 : 0.4[a]		
	B (84)	**12**, 58%, 2.4 :1.3 :1 :1.1[a]		

[a] Not individually assigned (see text).

reasonable yields of 9-fluorodecalin but tar formation limits the effective use of this solvent; (4) the most suitable solvents for direct fluorinations, of those surveyed, are the nitriles and, for subsequent direct fluorination reactions, our reaction medium of choice was, therefore, acetonitrile; (5) addition of *p*-dinitrobenzene, a radical inhibitor, to the acetonitrile reaction medium made no significant difference to the outcome of the fluorination, indicating that an electrophilic, rather than a radical, process is more likely.

The effectiveness of nitriles as reaction media does not, therefore, depend solely on relative permittivity because nitromethane is not a suitable medium. It is tempting to think that interaction between acetonitrile and fluorine is occurring and an electrophilic N–F reagent **3** is generated *in situ* (Scheme 2)



3

Scheme 2

but, while complexes involving interaction of acetonitrile and fluorine have been observed at low temperatures by Legon,[22] we could not observe the presence of an N–F type complex by ^{19}F NMR under the present reaction conditions. Moreover, when we attempted the process in two separate steps, that is, first passing fluorine through acetonitrile, followed by addition of decalin, then no product was observed.

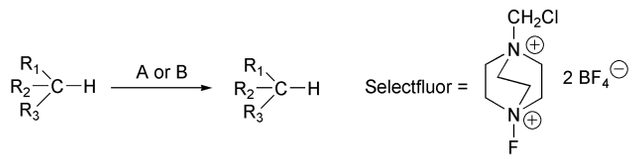
Direct fluorinations of several hydrocarbons were carried out (Conditions A, Table 2) and the products of these reactions compared with those obtained by fluorination of the same hydrocarbon substrates using Selectfluor™ (Conditions B, Table 2). Direct fluorinations were carried out at 0 °C, but reflux temperature of the acetonitrile was required in order that fluorinations with Selectfluor™ proceeded at a reasonable rate.

Fluorination of adamantane **4** by fluorine and Selectfluor™ both gave mixtures consisting of 1- and 2-fluoroadamantane, **5** and **6**, and small quantities of other products. In each case, the major monofluorinated product **5** could be isolated by column chromatography. Fluorination of cyclohexane **7** gave fluorocyclohexane **8** and trace amounts of other products. The low isolated yield of fluorocyclohexane **8** obtained upon fluorination by Selectfluor™ is due to handling losses of the highly volatile product during reaction (reflux at ~80 °C) and/or work-up. Direct fluorination of norbornane‡ **9** gave a mixture of *endo* and *exo*-2-fluoronorbornane, **10a** and **10b**, in a ratio of 5.3 : 1.

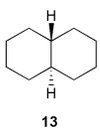
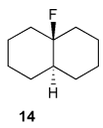
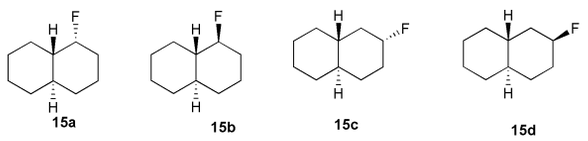
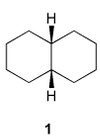
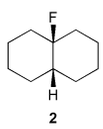
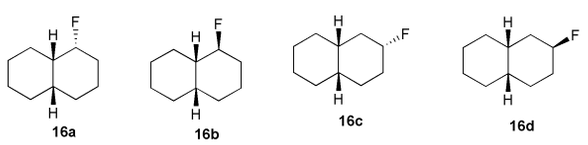
Direct fluorination of *n*-decane **11** gave a mixture of all five monofluorinated products **12** in the ratio 2.4 : 1.3 : 1 : 1.1 : 0.4 which gave ^{19}F NMR signals at −173.4, −181.4, −181.7,

‡ The IUPAC name for norbornane is bicyclo[2.2.1]heptane

Table 3 Fluorination of *cis*- and *trans*-decalin



A, 10% F_2 in N_2 (*v/v*), CH_3CN, 0°C; B, Selectfluor, CH_3CN, reflux 16 h.

Substrate	Conditions A or B	Product	Yield (%)	Conversion (%)
 **13**	A	 **14**	54	68
	B	 **15a** **15b** **15c** **15d**	**15**, 30 **15a** :**15b** :**15c** :**15d** 1 :1.14 :1.36 :2.24	75
 **1**	A	 **2**	57	64
	B	 **16a** **16b** **16c** **16d**	**16**, 25 1.6 : 1.3 : 1 : 1.4[a]	81

[a] Not individually assigned (see text).

−182.7 and −217.6 ppm respectively and many unidentified products in trace quantities. The triplet observed at −217.6 ppm is readily identified as product **12e** arising from conversion of CH_3 sites to CH_2F. The four other monofluorinated derivatives **12a**–**d** bearing fluorine atoms at secondary carbon sites were isolated as an isomeric mixture by preparative scale GC but it is very difficult to assign with certainty which ^{19}F resonance corresponds to each isomer. However, the high frequency ^{19}F NMR resonance (−173.4 ppm) can be assigned to the 2-fluorodecane **12a** by comparison with literature data of a similar system (2-fluorooctane[23] δ_F −170.8 ppm).

Fluorination of *n*-decane **11** by Selectfluor™ gave a similar product distribution; fluoro-decanes **12** were obtained in low yield in a ratio of 2.4 : 1.3 : 1.0 : 1.1, also showing a slight preference for fluorination at the 2-position to give **12a**.

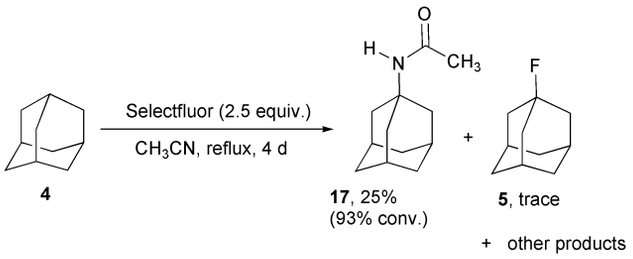
In contrast to the reactions described above, fluorination of *cis*- and *trans*-decalin, **1** and **13**, led to differing products which depended upon the fluorinating agent used (Table 3). Reaction of fluorine with *cis*- and *trans*-decalin gave *cis*- and *trans*-9-fluorodecalin, **2** and **14**, respectively arising from substitution of the tertiary hydrogen atoms with retention of configuration, consistent with Rozen's observations.[8] However, reaction of *trans*-decalin **13** with Selectfluor™ gave products **15a**–**d** arising from fluorination at the CH_2 sites only and no fluorination of tertiary sites was observed, as determined by ^{19}F NMR. The four monofluorinated products **15a**–**d** were obtained in the ratio 1 : 1.14 : 1.36 : 2.24 and each isomer gave a doublet ($^2J_{HF}$ ~49 Hz) in the ^{19}F NMR spectrum at −196.6 (**15a**), −177.3 (**15b**), −167.9 (**15c**) and −183.1 (**15d**) ppm respectively consistent with the presence of a CHF group. The structures of isomers **15a**–**d** were established by analysis of the ^1H NMR resonances centred at 4.54 (**15a**), 4.08 (**15b**), 4.47 (**15c**) and 4.87 (**15d**) ppm after a consideration of the relevant coupling constants (typical values $^2J_{HF}$ 50 Hz, $^3J_{Haxial–Haxial}$ 10 Hz, $^3J_{Haxial–Hequatorial}$ 5 Hz).

By a similar procedure, fluorination of *cis*-decalin **1** by Selectfluor™ gave a mixture of four monofluoroisomers **16a**–**d** in which the fluorine atom is attached to the secondary sites and no evidence of fluorination at the tertiary position was detected by ^{19}F NMR. In this case, the resonances observed in the ^1H NMR spectrum that are assigned to the CHF hydrogen atoms are too broad to be of diagnostic use (see above) but the isomers **16a**–**d** could be tentatively identified by a comparison of the chemical shift values observed in the ^{19}F NMR spectrum at −166.0 (**16c**), −173.4 (**16b**), −179 1 (**16d**) and −183.9 (**16a**) in the ratio 1 : 1.3 : 1.4 : 1.6 with those obtained for the *trans*-decalin isomers described above.

From the fluorination reactions described above, we can see that for fluorination of cyclohexane **7**, adamantane **4** and decane **11** the product profiles obtained when using either fluorine or Selectfluor™ are very similar and so an electrophilic process for direct fluorination can be considered more likely. However, fluorination of the decalin substrates **1** and **13** gave totally different products depending on whether fluorine or Selectfluor™ was used. The preferential fluorination of the secondary sites of decalin by Selectfluor™ is probably due to the increased steric demand of this fluorinating agent, which is too bulky to access the electronically preferred tertiary site.

As shown above, reactions between Selectfluor™ and hydrocarbons gave reasonable yields of the desired fluorinated products. However, an attempt to increase the yield of fluoroadamantane by heating adamantane **4** with Selectfluor™ over a prolonged period actually led to the isolation of *N*-acetylated adamantane **17** as the major product and only a small quantity of the expected fluoroadamantane **5** was observed (Scheme 3).

In order to establish the course of this reaction, the reaction was repeated and samples were taken at regular intervals and analysed by GC/MS. This analysis showed that the yield of fluoroadamantane **5** reaches a maximum value after approximately five hours and then decreases as the reaction time progresses. Concomitantly, the yield of acetamide **17** is negligible until after three hours and then steadily increases as reaction time increases. Therefore, we can reasonably suggest



Scheme 3

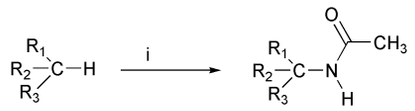
that *N*-acetamide **17** derives from the fluoroadamantane **5**. An indication as to the mechanism of this process was provided by measuring the acidity of the reaction mixture which became increasingly acidic, reaching pH < 1, over the course of the reaction due to the formation of the highly acidic quinuclidine derivative **18** (Scheme 4). Ionisation of fluoroadamantane **5** to the corresponding tertiary carbocation **19** occurs when the concentration of **18** is sufficiently high (after five hours) and the cation **19** then reacts with the nucleophilic acetonitrile in a Ritter type process. Aqueous work-up finally yields the acetamide (Scheme 4). In contrast to these results, Lawrence and co-workers suggested a radical mechanism to account for the formation of fused bicyclic systems upon reaction of menthol and Selectfluor™ in various nitriles, by a related transformation.[24]

This experiment demonstrated that amidation could be achieved in one-pot by the reaction of the alkane with a fluorinating agent, a strong acid and acetonitrile. We then sought to accomplish the same transformation but using fluorine as the fluorinating agent, a Lewis acid and acetonitrile. Indeed, we found that *N*-functionalisation could be achieved in good isolated yield by passing fluorine through a mixture consisting of the hydrocarbon substrate, boron trifluoride–diethyl ether and acetonitrile (Table 4) and a representative mechanism for this process is outlined in Scheme 5.

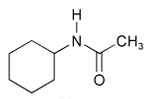
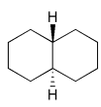
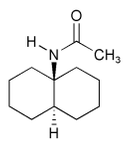
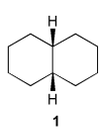
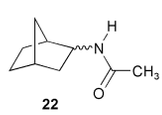
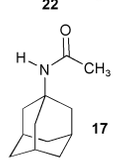
Amidation of *cis*- and *trans*-decalin led to the formation of the *trans*-amide **21** in both cases, consistent with the intermediacy of a carbocation species (Scheme 6).

In summary, both tertiary and secondary sites of hydrocarbons may be selectively fluorinated by both fluorine and Selectfluor™. Since the product profiles of both processes are similar we can reasonably suggest that the mechanism of both fluorination processes are electrophilic in nature, confirming the suggestion of Barton and Rozen. Fluorination of alkanes by Selectfluor™ is, however, complicated by the formation of amide derivatives after prolonged reaction due to the highly acidic nature of the reaction medium. The formation of amides promoted by either Selectfluor™ or fluorine–Lewis acid does provide effective methodology for the efficient *N*-functionalisation of hydrocarbons.

Table 4

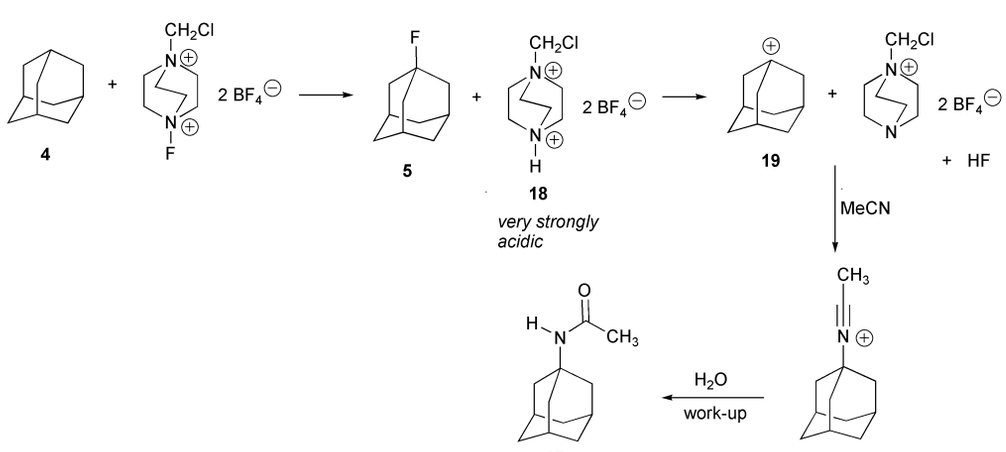


i, 10% F_2 in N_2 (*v/v*), $BF_3.Et_2O$, CH_3CN, 0°C

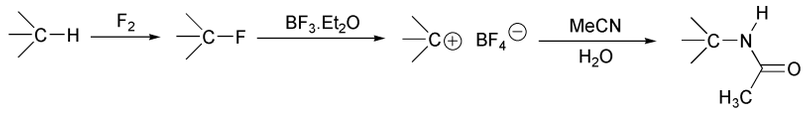
Substrate	Product	Yield (%)	Conversion (%)
 7	 20	51	53
 13	 21	45	49
 1	**21**	49	67
 9	 22	45	60
 4	 17	54	74

Experimental

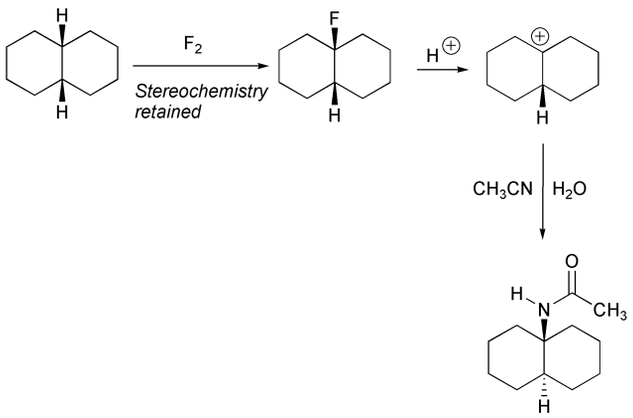
All starting materials were obtained commercially (Aldrich) and all solvents were dried using literature procedures. NMR spectra were recorded in deuteriochloroform, unless otherwise stated, on a Varian VXR 400S NMR spectrometer with tetramethylsilane and trichlorofluoromethane as internal standards. Spectral assignments were made with the aid of data collected by ^1H–^1H COSY and ^1H–^{13}C HETCOR experiments and coupling constants are given in Hz. In ^{19}F NMR spectra, upfield shifts are quoted as negative. Mass spectra were recorded on either a VG 7070E spectrometer or a Fissons VG Trio 1000 spectrometer coupled with a Hewlett Packard 5890 series II gas chromatograph. Accurate mass measurements were performed by the EPSRC National Mass Spectrometry service, Swansea,



Scheme 4



Scheme 5



Scheme 6

UK. Elemental analyses were obtained on either a Perkin-Elmer 240 or a Carlo Erba Elemental Analyser. Melting points were recorded at atmospheric pressure and are uncorrected. Column chromatography was carried out on silica gel (Merck No. 1–09385, 230–400 mesh) and TLC analysis was performed on silica gel TLC plates using dichloromethane as eluant.

Reactions with elemental fluorine

General procedure. Elemental fluorine, as a 10% (v/v) mixture with nitrogen, was passed at a rate of *ca.* 50 ml min^{-1} through a stirred, cooled (0 °C) mixture which consisted of the substrate and acetonitrile. After addition of the fluorine, the reaction mixture was poured into water (100 ml), neutralised ($NaHCO_3$) and extracted with dichloromethane (3 × 40 ml). The combined, dried ($MgSO_4$), organic extracts were evaporated to give a crude product. The composition of a weighed crude reaction mixture was determined by GCMS analysis and the conversion of start material was calculated from GC peak intensities. The amount of fluorinated product in the crude product was determined by adding a known amount of fluorobenzene to a weighed amount of the crude product mixture. Comparison of the relative intensities of the appropriate ^{19}F NMR resonances gave the yield of fluorinated derivative, based upon the conversion obtained above. Analytical samples of fluorinated products were obtained by either preparative scale GC or column chromatography. Yields of fluorinated products are quoted as yields based on the conversion of starting material.

1-Fluoroadamantane 5. Adamantane **4** (4.00 g, 29 mmol), fluorine (205 mmol) and acetonitrile (140 ml) gave a pale brown crude product which contained 1-fluoroadamantane **5** (51%), 2-fluoroadamantane **6** (18%); *m*/*z* (EI^+) 154 (M^+, 75%), 111 (19) and, unidentified products (11%). Purification of the mixture by column chromatography on silica gel using 6 : 1 cyclohexane–DCM as the eluent gave 1-fluoroadamantane **5** (2.06 g, 65%, 70% conv.) as a white solid; mp 256–258 °C (lit.,[25] 257–259 °C); R_f 0.52 (Found: C, 77.8; H, 9.9. $C_{10}H_{15}F$ requires: C, 77.9; H, 9.8%); δ_F −128.8 (s); δ_H 1.62 (2 H, m, CH_2), 1.88 (2 H, m, CH_2CF), 2.23 (1 H, s, CH); δ_C 31.5 (d, $^3J_{CF}$ 9.6, CH), 36.1 (d, $^4J_{CF}$ 1.9, CH_2), 43.0 (d, $^2J_{CF}$ 17.1, CH_2CF), 92.8 (d, $^1J_{CF}$ 183.2, CF); *m*/*z* (EI^+) 154 (M^+, 75%), 97 (100).

Fluorocyclohexane 8. Cyclohexane **7** (10.92 g, 130 mmol), fluorine (65 mmol) and acetonitrile (140 ml) gave a yellow crude product mixture (11.08 g) which contained fluorocyclohexane **8** (4.43 g, 63%, 53% conv.), difluorocyclohexane (1%); *m*/*z* (EI^+) 120 (M^+, 12%), 99 (10), 85 (55) and unidentified products (3%). Purification of the crude product by preparative scale GC gave an analytical sample of fluorocyclohexane **8** as a colourless liquid; bp 101–103 °C (lit.,[26] 62 °C/180 mmHg) (Found: M^+, 102.0845. $C_6H_{11}F$ requires: M^+, 102.0845); δ_F −171.47 (br s); δ_H 1.30–1.75 (10 H, m, CH_2), 4.57 (1 H, dm, $^2J_{HF}$ 48.8, CHF); δ_C 22.8 (d, $^3J_{CF}$ 7.7, C-3), 25.2 (d, $^4J_{CF}$ 1.5, C-4), 32.3 (d, $^2J_{CF}$ 18.7, C-2), 91.5 (d, $^1J_{CF}$ 169.8, CHF); *m*/*z* (EI^+) 102 (M^+, 8%), 82 (40, M^+ − HF), 67 (100).

2-Fluoronorbornane 10a,b. Norbornane **9** (4.93 g, 51 mmol), fluorine (195 mmol) and acetonitrile (140 ml) gave a reaction mixture that was poured into iced water (150 ml), neutralised ($NaHCO_3$) and filtered to remove the solid brown crude product (7.02 g) which contained *exo*- and *endo*-2-fluoronorbornane **10a**,**b** (1.43 g, 41%, 60% conv.) in the ratio **10a** : **10b**, 5.3 : 1.0 and, unidentified products (16%). Purification of the crude product by preparative scale GC gave a sample of *exo*- and *endo*-2-fluoronorbornane **10a**,**b** as an isomeric mixture and as a white solid; mp 54–60 °C (sealed tube); *exo*-2-fluoronorbornane **10a**: δ_H 0.91–2.49 (10 H, m, CH_2 and CH), 4.58 (1 H, dm, $^2J_{HF}$ 56.4, CHF); δ_F −160.48 (m); δ_C 22.3 (d, $^3J_{CF}$ 10.3, C-6), 27.9 (s, C-5), 34.7 (d, $^3J_{CF}$ 1.2, C-7), 34.8 (s, C-4), 39.9 (d, $^2J_{CF}$ 19.3, C-3), 42.0 (d, $^2J_{CF}$ 19.4, C-1), 96.2 (d, $^1J_{CF}$ 181.6, C-2); *endo*-2-fluoronorbornane **10b**: δ_H 0.91–2.49 (10 H, m, CH_2 and CH), 5.02 (1 H, dm, $^2J_{HF}$ 57.9, CHF); δ_F −189.85 (ddd, $^2J_{HF}$ 57.9, $^3J_{HF}$ 29.3, $^3J_{HF}$ 16.2); δ_C 19.9 (d, $^3J_{CF}$ 10.3, C-6), 29.1 (s, C-5), 36.5 (d, $^3J_{CF}$ 2.3, C-4), 36.9 (d, $^3J_{CF}$ 4.9 C-7), 37.2 (d, $^2J_{CF}$ 22.1, C-3), 41.2 (d, $^2J_{CF}$ 17.5, C-1), 94.7 (d, $^1J_{CF}$ 184.0, C-2); *m*/*z* (EI^+) 114 (M^+, 11%), 99 (20).

Fluorodecane 12. *n*-Decane **11** (11.08 g, 78 mmol), fluorine (78 mmol) and acetonitrile (140 ml) gave a brown crude product mixture (12.07 g) which contained 2-, 3-, 4- and 5-fluorodecane (4.80 g, 63%, 61% conv.) in the ratio of 1.0 : 1.1 : 1.3 : 2.4 (unassigned, see text), a trace amount of 1-fluorodecane; δ_F −217.56 (m) and, unidentified products (26%). Purification of the crude product by preparative scale GC gave an analytically pure sample of 2-, 3-, 4- and 5-fluorodecane as an isomeric mixture and as a colourless liquid (Found: C, 74.7; H, 13.4. $C_{10}H_{21}F$ requires: C, 74.95; H, 13.2%); δ_F −172.46 (m, J_{HF} 19.2), −180.38 (m, J_{HF} 17.3), −180.71 (m, J_{HF} 17.2), −181.62 (m, J_{HF} 18.8); δ_H 0.85–0.98 (4.5 H, m, CH_2 and/or CH_3), 1.24–1.70 (14.8 H, m, CH_2 and/or CH_3), 4.30–4.74 (1.0 H, m, CHF); *m*/*z* (EI^+) 140 (M^+ − HF, 1%), 111 (9), 97 (22).

***trans*-9-Fluorodecalin 14.** *trans*-Decalin **13** (3.00 g, 22 mmol), fluorine (110 mmol) and acetonitrile (140 ml) gave a yellow crude product (5.00 g) which contained *trans*-9-fluorodecalin **14** (1.26 g, 54%, 68% conv.) and trace amounts of difluorodecalin. Purification of the crude product by preparative scale GC gave an analytically pure sample of *trans*-9-fluorodecalin **14** as a colourless liquid; bp 197–198 °C (Found: C, 76.8; H, 11.0. $C_{10}H_{17}F$ requires: C, 76.9; H, 10.9%); δ_F −177.11 (m); δ_H 1.15–1.80 (m); δ_C 21.6 (d, $^3J_{CF}$ 1.5, C-2), 25.8 (s, C-3), 28.7 (d, $^3J_{CF}$ 1.1, C-4), 37.1 (d, $^2J_{CF}$ 23.4, C-1), 43.1 (d, $^2J_{CF}$ 21.5, C-10), 94.5 (d, $^1J_{CF}$ 172.7, C-9); *m*/*z* (EI^+) 156 (M^+, 15%), 136 (100, M − HF).

***cis*-9-Fluorodecalin 2.** *cis*-Decalin **1** (3.00 g, 22 mmol), fluorine (110 mmol) and acetonitrile (140 ml) gave a yellow crude product (7.44 g) which contained *cis*-9-fluorodecalin **2** (1.25 g, 57%, 64% conv.), spectral data below; difluorodecalin (5%),

m/*z* (EI$^+$) 174 (M$^+$, 66%), 154 (44, M$^+$ − HF); an unsaturated component (2%), *m*/*z* (EI$^+$) 136 (M$^+$, 100%); and, unidentified products (8%). Purification of the crude product by preparative scale GC gave an analytically pure sample of *cis*-9-fluorodecalin **2** as a colourless liquid; bp 202–203 °C (Found: C, 76.65; H, 11.1. $C_{10}H_{17}F$ requires: C, 76.9; H, 10.9%); δ_F −140.57 (m); δ_H 1.20–1.85 (m); δ_C 20.0–38.1 (broad overlapping signals, CH_2), 40.8 (d, $^2J_{CF}$ 19.5, C-10), 96.9 (d, $^1J_{CF}$ 169.8, C-9); *m*/*z* (EI$^+$) 156 (M$^+$, 15%), 136 (94, M − HF), 113 (100).

Reactions with Selectfluor™

General procedure. A solution consisting of Selectfluor™, substrate and acetonitrile (130 ml) was stirred and heated (65 °C). After 24 h the reaction mixture was poured into water, neutralised ($NaHCO_3$) and extracted with dichloromethane (3 × 50 ml). The combined, dried ($MgSO_4$) organic extracts were evaporated to give a crude product which was analysed by GCMS and ^{19}F NMR as described above. Purification of the crude product by preparative scale GC gave an analytically pure sample of the monofluorinated products.

1-Fluoroadamantane 5. Adamantane **4** (1.0 g, 7 mmol), Selectfluor™ (4.7 g, 13 mmol) and acetonitrile (100 ml) gave a pale brown crude product mixture (1.5 g) which contained 1-fluoroadamantane **5** and 2-fluoroadamantane **6** in the ratio of 5.5 : 1 respectively, adamantanol (4 area%); *m*/*z* (EI$^+$) 152 (M$^+$, 20%), 95 (100), *N*-(adamantyl)acetamide (1 area%); *m*/*z* (EI$^+$) 193 (M$^+$, 43%), 136 (53) and unidentified products. Purification of the mixture by column chromatography on silica gel using 6 : 1 cyclohexane–DCM as the eluent gave 1-fluoroadamantane **5** (0.5 g, 68%, 73% conv.) as a white solid; physical and spectral data as above.

Fluorocyclohexane 8. Selectfluor™ (13.91 g, 39 mmol), cyclohexane **7** (3.00 g, 36 mmol) and acetonitrile (130 ml) gave a colourless product (8.00 g) which contained fluorocyclohexane **8** (0.77 g, 21%, 100% conv.). Purification by preparative scale GC gave an analytically pure sample of fluorocyclohexane **8** as a colourless oil; physical and spectral data as above.

***n*-Fluorodecane 12.** Selectfluor™ (21.42 g, 61 mmol), *n*-decane **11** (7.81 g, 55 mmol) and acetonitrile (210 ml), after 18 h, gave an orange liquid (10.77 g) which contained fluorodecane **12** (4.28 g, 58%, 84% conv.) and small amounts of other unidentified products. Purification by preparative scale GC gave an isomeric mixture of 2-, 3-, 4- and 5-fluorodecane in the ratio of 2.39 : 1.27 : 1.09 : 1.00 (unassigned, see text) and, as a colourless liquid (Found: M$^+$ − HF, 140.1565. $C_{10}H_{21}F$ requires M$^+$ − HF, 140.1565); δ_F −172.46 (m, J_{HF} 19.2), −180.38 (m, J_{HF} 17.3), −180.71 (m, J_{HF} 17.2), −181.62 (m, J_{HF} 18.8); δ_H 0.85–0.98 (5 H, m, CH_2 and/or CH_3), 1.24–1.70 (15 H, m, CH_2 and/or CH_3), 4.30–4.74 (1.00 H, m, CHF); *m*/*z* (EI$^+$) 140 (M$^+$ − HF, 1%), 111 (9), 97 (22).

***trans*-Fluorodecalin 15.** Selectfluor™ (24.85 g, 70 mmol), *trans*-decalin **13** (5.38 g, 70 mmol) and acetonitrile (250 ml) after 4.5 h gave a brown liquid (4.37 g) which contained *trans*-fluorodecalin **15** (2.21 g, 25%, 81% conv.) and trace amounts of other products. Purification of the crude product by preparative scale GC gave an analytically pure sample of *trans*-fluorodecalin **15** as an isomeric mixture of 2-fluoro$_{(eq)}$-*trans*-decalin **15c**, 1-fluoro$_{(eq)}$-*trans*-decalin **15b**, 2-fluoro$_{(ax)}$-*trans*-decalin **15d** and 1-fluoro$_{(ax)}$-*trans*-decalin **15a** in the ratio of 1.36 : 1.14 : 2.24 : 1.00 respectively and, as a colourless oil (Found: C, 77.0; H, 11.1. $C_{10}H_{17}F$ requires C, 76.9; H, 11.0%); **15a**: δ_F −196.61 (mq, $^2J_{HF}$ 49.6); δ_H 0.60–2.10 (16 H, m, CH_2 and CH), 4.54 (1 H, ddt, $^2J_{HF}$ 49.2, $^3J_{HF}$ 3.2, $^3J_{HF}$ 2.0, CHF); **15b**: δ_F −177.34 (d, $^2J_{HF}$ 49.3); δ_H 0.60–2.10 (16 H, m, CH_2 and CH), 4.08 (1 H, dddd, $^2J_{HF}$ 49.8, $^3J_{HF}$ 10.8, $^3J_{HF}$ 9.9, $^3J_{HF}$ 4.8, CHF); **15c**: δ_F −167.97 (dd, $^2J_{HF}$ 49.4, $^3J_{HF}$ 4.5); δ_H 0.60–2.10 (16 H, m, CH_2 and CH), 4.47 (1 H, dtt, $^2J_{HF}$ 49.2, $^3J_{HF}$ 10.8, $^3J_{HF}$ 4.8, CHF); **15d**: δ_F −183.07 (tq, $^2J_{HF}$ 47.8, $^3J_{HF}$ 10.2); δ_H 0.60–2.10 (16 H, m, CH_2 and CH), 4.87 (1 H, d sept, $^2J_{HF}$ 48.4, $^3J_{HF}$ 2.0, CHF); *m*/*z* (EI$^+$) 156 (M$^+$, 82%), 136 (76, M$^+$ − HF).

***cis*-Fluorodecalin.** Selectfluor™ (13.85 g, 39 mmol), *cis*-decalin **1** (3.00 g, 22 mmol) and acetonitrile (120 ml), after 1.5 h, gave a yellow liquid (3.20 g) which contained *cis*-fluorodecalin **16** (0.77 g, 30%, 75% conv.) and trace amounts of other products. Purification of the crude product by preparative scale GC gave an analytically pure sample of *cis*-fluorodecalin as an isomeric mixture of 1-fluoro$_{(ax)}$-*cis*-decalin **16a**, 1-fluoro$_{(eq)}$-*cis*-decalin **16b**, 2-fluoro$_{(eq)}$-*cis*-decalin **16c** and 2-fluoro$_{(ax)}$-*cis*-decalin **16d** in the ratio of 1.6 : 1.4 : 1.3 : 1.0 (unassigned, see text) and, as a colourless oil; (Found: C, 77.0; H, 11.1. $C_{10}H_{17}F$ requires C, 76.9; H, 11.0%); δ_F (−57 °C) −166.55 (d, $^2J_{HF}$ 47.8), −173.43 (d, $^2J_{HF}$ 49.3), −179.08 (d, $^2J_{HF}$ 49.6), −183.92 (q, $^2J_{HF}$ 37.9); δ_H (−57 °C) 1.07–2.06 (16 H, m, CH and CH_2), 4.45–4.84 (1 H, m, CHF); *m*/*z* (EI$^+$) 156 (M$^+$, 22%), 136 (86, M$^+$ − HF).

Nitrogen functionalisation reactions

Method 1.

***N*-(1-Adamantyl)acetamide 17.** Fluorine (208 mmol) as a 10% (v/v) mixture with nitrogen was passed through a stirred, cooled (0 °C) mixture consisting of adamantane **4** (7.07 g, 52 mmol) and acetonitrile (140 ml). After addition of the fluorine, boron trifluoride–diethyl ether (29.54 g, 208 mmol) was added and, after 5 min at rt, the reaction mixture was poured into water, neutralised ($NaHCO_3$) and extracted using dichloromethane. The combined dried ($MgSO_4$) organic extracts were evaporated to give a brown crude product mixture which, upon recrystallisation from acetonitrile, gave *N-(1-adamantyl)acetamide* **17** (5.25 g, 74%, 70% conv.) as a white solid; mp 150–151 °C (Found: C, 74.55; H, 9.9; N, 7.3. $C_{12}H_{19}NO$ requires C, 74.55; H, 9.9; N, 7.3%); δ_H 1.66 (6 H, br s, CH_2), 1.89 (3 H, s, CH_3), 1.97 (6 H, s, CH_2CN), 2.05 (3 H, m, CH), 5.20 (1 H, br s, NH); δ_C 24.7 (s, CH_3), 29.4 (s, CH), 36.3 (s, CH_2), 41.6 (s, CH_2CN), 51.8 (s, CN), 169.3 (s, CO); *m*/*z* (EI$^+$) 193 (M$^+$, 100%), 178 (24, M$^+$ − CH_3), 150 (18, M$^+$ − $COCH_3$).

Method 2 – General procedure. Fluorine as a 10% (v/v) mixture with nitrogen was passed through a stirred, cooled (0 °C) mixture consisting of the hydrocarbon, boron trifluoride–diethyl ether and acetonitrile. After addition of the fluorine, the reaction mixture was poured into water, neutralised ($NaHCO_3$) and extracted using dichloromethane. The combined dried ($MgSO_4$) organic extracts were evaporated to give a crude product which was purified as stated below.

***N*-(Cyclohexyl)acetamide 20.** Cyclohexane **7** (9.8 g, 117 mmol), fluorine (59 mmol), boron trifluoride–diethyl ether (16.6 g, 117 mmol), and acetonitrile (120 ml) gave a crude product mixture which was distilled to give cyclohexane (4.6 g, 55 mmol); bp 67 °C. The brown solid which remained gave, after recrystallisation, *N-(cyclohexyl)acetamide* **20** (4.5 g, 51%, 53% conv.) as a white solid; mp 104–105 °C (from acetonitrile) (lit.[27] mp 104 °C); (Found: M$^+$, 141.1153. $C_8H_{15}NO$ requires: M$^+$, 141.1153); δ_H1.06–2.0 (10 H, m, CH_2), 1.94 (3 H, s, CH_3), 3.74 (1 H, m, H-1), 5.43 (1 H, br s, NH); δ_C 23.6 (s, CH_3), 24.8 (s, C-4), 25.5 (s, C-3), 33.2 (s, C-2), 48.1 (s, C-1), 169.0 (s, C=O); *m*/*z* (EI$^+$) 141 (M$^+$, 8%), 98 (4, M$^+$ − $COCH_3$), 70 (6), 60 (58), 43 (100).

***N*-(*trans*-9-Decalyl)acetamide 21.** *cis*-Decalin **1** (2.2 g, 16 mmol), fluorine (65 mmol), boron trifluoride–diethyl ether (2.3 g, 16 mmol), and acetonitrile (120 ml) gave a crude product

mixture which was distilled to give decalin (0.7 g, 5 mmol); bp 55 °C/10 mmHg. The brown solid which remained gave, after recrystallisation, *N-(trans-9-decalyl)acetamide* **21** (0.8 g, 49%, 67% conv.) as a white solid; mp 183–184 °C (from acetonitrile) (Found: C, 73.6; H, 10.9; N, 7.3. $C_{12}H_{21}NO$ requires: C, 73.8; H, 10.9; N, 7.2%); δ_H 0.85–1.68 (18 H, m, CH and CH_2), 1.94 (3 H, s, CH_3), 2.57 (2 H, m, CH_2), 4.89 (1 H, br s, NH); δ_C 21.6 (s, CH_2), 24.6 (s, CH_3), 26.1 (s, CH_2), 28.6 (s, CH_2), 34.4 (s, CH_2), 45.2 (s, CH), 55.9 (s, CNH), 169.2 (s, CO); *m/z* (EI^+) 195 (M^+, 1%), 152 (18), 136 (100), 121 (141).

***N*-(*trans*-9-Decalyl)acetamide 21.** *trans*-Decalin **13** (3.0 g, 22 mmol), fluorine (44 mmol), boron trifluoride–diethyl ether (3.1 g, 22 mmol) and acetonitrile (120 ml) gave, after heating (82 °C), a crude product mixture which was distilled to give decalin (1.5 g, 11 mmol); bp 50 °C/8 mmHg. The brown solid which remained gave, after recrystallisation, *N*-(*trans*-9-decalyl)-acetamide **21** (1.0 g, 45%, 49% conv.) as a white solid; spectral and physical data as above.

***N*-(*exo*-2-Norbornyl)acetamide 22.** Norbornane **9** (2.4 g, 25 mmol), fluorine (59 mmol), boron trifluoride–diethyl ether (3.6 g, 25 mmol) and acetonitrile (120 ml) gave a reaction mixture which was poured into water, neutralised ($NaHCO_3$) and filtered to remove norbornane (1.0 g, 10 mmol). The liquid which remained was worked up as above and gave, after recrystallisation, *N-(exo-2-norbornyl)acetamide* **22** (1.0 g, 45%, 60% conv.) as a white solid; 141–142 °C (from acetonitrile) (Found: C, 70.2; H, 10.2; N, 9.3. $C_9H_{15}NO$ requires: C, 70.6; H, 9.8; N, 9.1%); δ_H 1.08–1.55 (8 H, m, CH_2), 1.80 (1 H, m, H-3), 1.94 (3 H, s, CH_3), 2.19 (1 H, m, H-2), 2.27 (1 H, m, H-4), 3.71 (1 H, m), 5.35 (1 H, br s, NH); δ_C 23.8 (s, CH_3), 26.4 (s, C-6), 27.1 (s, C-5), 35.6 (s, C-7), 35.7 (s, C-4), 40.5 (s, C-3), 42.3 (s, C-1), 52.8 (s, C-2), 169.4 (s, CO); *m/z* (EI^+) 153 (M^+, 75%), 138 (21, $M^+ - CH_3$), 124 (23), 94 (100).

***N*-(1-Adamantyl)acetamide 17.** Fluorine (28 mmol), adamantane **4** (1.50 g, 11 mmol), boron trifluoride–diethyl ether (24.57 g, 173 mmol) and acetonitrile (140 ml) gave a dark yellow solid (1.52 g) which contained *N-(1-adamantyl)acetamide* **17** (26%); spectral and physical data as above, and a small number of unidentified products.

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