N-Halogeno Compounds. Part 9.[1] *N*-Fluoroquinuclidinium Fluoride—a New Electrophilic Fluorinating Agent[2]

Ronald Eric Banks,* Richard Arthur Du Boisson, William David Morton, and Efthimios Tsiliopoulos
Chemistry Department, The University of Manchester Institute of Science and Technology, Manchester M60 1QD

N-Fluoroquinuclidinium fluoride, prepared in high yield by treatment of a cold, dilute solution of quinuclidine in trichlorofluoromethane with fluorine at low pressure in a specially designed, virtually all-glass vacuum system, acts as a site-selective electrophilic fluorinating agent towards carbanionic substrates [$PhCNa(CO_2Et)_2 \longrightarrow PhCF(CO_2Et)_2$; $Me_2CLiNO_2 \longrightarrow Me_2CFNO_2$; $RMgX \longrightarrow RF$ (R = Ph, X = Br; R = c-C_6H_{11}, X = Cl); $CH_2CH_2OCH_2CH_2N{-}CH{=}CH(CH_2)_3CH_2 \longrightarrow CH_2(CH_2)_3COCHF$; $PhSiCl_3/F^-$ (*in situ*) $\longrightarrow$ PhF].

Easily handled reagents capable of delivering positive fluorine continue to be sought as interest mounts in the selective positioning of C–F bonds in organic molecules with biological associations.[3] Our renewed efforts in this area were prompted by the appearance recently of publications dealing with the new electrophilic fluorinating agents of the N–F class *N*-fluoropyridin-2(1*H*)-one (**1**)[4] and *N*-fluoro-*N*-alkylsulphonamides (**2**),[5] in which attention was drawn to supply problems associated with the prototypical compound of this group, perfluoro-*N*-fluoropiperidine (**3**).[6] Not mentioned was the problem that transfer of 'F^+' from (**3**) to a carbanionic substrate liberates the imidoyl fluoride perfluoro-1-azacyclohex-1-ene (**6**), which then competes with its progenitor for the substrate.[7] Clearly, loss in this manner of perhaps hard-won starting material heightens the unattractiveness of the low-yield synthesis of perfluoro-*N*-fluoropiperidine (**3**) by the Simons Process [electrochemical fluorination of pyridine (*ca.* 8% yield)[8] or 2-fluoropyridine (*ca.* 13%)[9] in anhydrous hydrogen fluoride]. Drawbacks to the use of reagents (**1**) and (**2**) will be mentioned later.

Whilst considering how to overcome problems which detract from the use of perfluoro-*N*-fluoropiperidine (**3**) and the analogous electrophilic fluorinating agents (**4**) and (**5**),[7] we discovered *N*-fluoroquinuclidinium fluoride (**7**; NFQNF) and, moreover, learned of the synthesis of its piperidinium analogues (**8**)—(**10**).[10] Except for the *N*-methyl compound (**8**), which decomposes rapidly at room temperature,[10] these *N*-fluoroammonium compounds were judged to deserve attention because (*a*) they had been synthesized *via* high-yield fluorination steps [(**7**), 77%;[11] (**9**) and (**10**), 85%[10]] and (*b*) simple transfer of 'F^+' from each to a carbanionic substrate would release a neutral entity (tertiary amine) that ought to cause minimal complications. Wishing to avoid handling perchloryl fluoride,† the reagent used to convert the appropriate penta-alkylpiperidines into the *N*-fluoropiperidinium chlorates (**8**)—(**10**),[10] we elected to confine our attention to NFQNF (**7**); this salt was doubly attractive since many years ago we had failed to isolate or tame its aromatic analogue *N*-fluoropyridinium fluoride (**11**).[12]

(**1**)

(**2**) R = Me, Bu^t, Bu^tCH_2, 2-norbornyl, cyclohexyl

(**3**) X = CF_2, Y = F
(**4**) X = O, Y = F
(**5**) X = CF_2, Y = CF_3

(**6**)

(**7**)

(**8**) R = Me
(**9**) R = Et
(**10**) R = Bu

(**11**) W = X = Y = H, Z = F
(**12**) W = X = Y = H, Z = OSO_2CF_3
(**13**) W = X = Me, Y = H, Z = OSO_2CF_3
(**14**) W = X = H, Y = Cl, Z = OSO_2CF_3
(**15**) W = Y = H, X = CO_2Me, Z = OSO_2CF_3

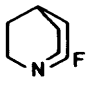
Synthesis of N-*Fluoroquinuclidinium Fluoride* (**7**).—The liquid-phase fluorination technique adopted was based on the excellent method described briefly in the mid-60's by Merritt and Johnson[13] for the controlled addition of elemental fluorine across C=C bonds *via* a polar mechanism.[13,14] Thus, using a closed, evacuated apparatus constructed mainly from borosilicate glass with accessories resistant to elemental fluorine at ambient temperature,[11] neat fluorine at <20 mmHg was bled into efficiently stirred highly dilute solutions (*ca.* 1% w/v) of quinuclidine in trichlorofluoromethane cooled to temperatures in the range −35 to −84 °C. For small-scale work, we consider this technique to be often vastly superior‡ to the flow method normally advocated,[15] in which fluorine heavily diluted with

† See the hazard warnings given by C. M. Sharts and W. A. Sheppard, *Org. React.*, 1974, **21**, 225—236; note particularly the quotation concerning the fluorination of amines from the paper by D. M. Gardner, R. Helitzer, and D. H. Rosenblatt, *J. Org. Chem.*, 1967, **32**, 1115.

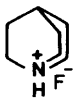
‡ This is particularly true when fluorine is used directly from an electrolytic generator rather than from a commercial cylinder equipped with sophisticated valves and flowmeters.

nitrogen is used at ambient pressure: there is little wastage of fluorine, the progress of reactions can easily be monitored *via* simple pressure readings, substrates can be exposed to accurately known amounts of fluorine, and anhydrous conditions are more easily maintained. When substitution of hydrogen by fluorine is sought, the hydrogen fluoride liberated must be scavenged by adding sodium or potassium fluoride or a molecular sieve (4 or 5A) to the solution of the substrate to avoid excessive etching of the glass reactor; the vessel shown in the plate has seen two year's extensive use with a number of substrates,[11] *e.g.* adamantane derivatives, in addition to quinuclidines, and is still perfectly serviceable.

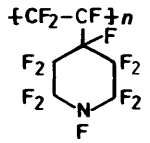
That quinuclidine reacts with fluorine by addition to give *N*-fluoroquinuclidinium fluoride was discovered through attempting to replace the tertiary hydrogen[16] to give 4-fluoroquinuclidine.[11] Thus, the finely divided white solid which began to precipitate when a cold (−72 °C), dilute (*ca.* 1%, w/v), anhydrous solution of the tertiary amine in trichlorofluoromethane was exposed to fluorine at *ca.* 15 mmHg proved to be a *ca.* 9:1 mixture of NFQNF (**7**) and quinuclidine hydrofluoride



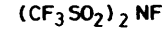
(**16**)



(**17**)



(**18**)



(**19**)

(**17**). Treatment of this mixture with hot anhydrous acetone removed the hydrofluoride (**17**), allowing the NFQNF to be isolated in 86% yield as an extremely hygroscopic white solid, m.p. 126—128 °C. Since steps had been taken to eliminate hydrogen fluoride from the fluorine (generated on site, electrolytically) and to exclude moisture from the apparatus, solvent, and substrate, the formation of so much quinuclidine hydrofluoride signalled that some C–F for C–H substitution had occurred; this situation was also consistent with the observation that when fluorine consumption ceased, the molar ratio F_2:$C_7H_{13}N$ was 1.3:1. Examination by ^{19}F n.m.r. spectroscopy of the crude residue removed from the trichlorofluoromethane solvent indeed revealed the presence of 2-fluoroquinuclidine (**16**).* Raising the reaction temperature to −35 °C scarcely affected the yield of NFQNF [83% (isolated material)] or of quinuclidine hydrofluoride (13%).

Use of a conventional flow system in which a fluorine–nitrogen blend (5—10%, v/v, F_2 in N_2) was bubbled through a highly dilute (1% w/v) solution of quinuclidine in cold (−72 °C) trichlorofluoromethane gave a complex mixture of products containing (according to ^{19}F n.m.r. analysis) several fluorides as salts (F^-) and very little *N*-fluoro material ($^+$N–F). These two types of fluorine nuclei are easily differentiated by n.m.r. chemical-shift difference; *e.g.* NFQNF in deuterium oxide gives a ^{19}F spectrum comprising two singlets of equal intensity at δ(CF_3CO_2H) −51.2 and +135.1 p.p.m. [*cf.* δ_{NF} for *N*-fluoropyridinium triflate (**12**)[17] in CD_3CN and neat *N*-fluoropiperidine[18] is +125.3 and +55.8 p.p.m. respectively].†

Properties of N-*Fluoroquinuclidinium Fluoride* (**7**).—Freshly isolated NFQNF appears to be stable indefinitely when stored at ambient temperature under dry air in a poly(ethylene) bottle. Unfortunately, from the viewpoint of using it to fluorinate carbanions, however, it is noticeably hygroscopic, and when exposed in the form of a thin layer to air it undergoes a 10% increase in weight during 40 min and becomes sticky and slightly yellow. NFQNF is readily soluble in water, methanol, ethanol, trifluoroacetic acid, and ethyl acetate and reasonably so in acetonitrile, but appears to be insoluble in alkanes, arenes, chloromethanes, acetone, diethyl ether, THF, DMF, or DMSO. It melts quietly at 126—128 °C and is less flammable than quinuclidine in air, igniting only on direct contact with a flame or after prolonged heating on a metal plate. It does not explode when struck with a hammer.

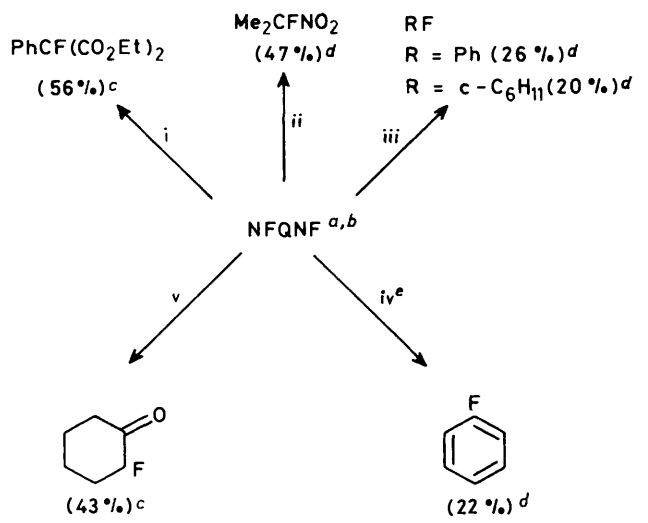
Disappointingly, neither acceptable nor reproducible wt.% composition values (C, H, and N) for NFQNF could be obtained by standard combustion procedures, a situation we ascribe to the hygroscopic nature of the compound. (The best of several sets of analytical date corresponded closely to a monohydrate; no information about water content could be gleaned using the Karl-Fischer method because the reagent attacked the NFQNF.) However, the structure was secured through the application of a full-range of spectroscopic techniques. When compared with that of quinuclidine, the ^1H n.m.r. spectrum showed the expected similarities; and the ^{13}C parameters were fully consistent with *N*-fluoroquinuclidinium ion. The ^{19}F n.m.r. spectrum (see above) clearly supported the presence of the $\overset{+}{N}$–F moiety and revealed that the counterion was fluoride. I.r. analysis supported the presence of an N–F bond (sharp absorption at 925 cm^{-1}),‡ and chemical confirmation was provided by the rapid liberation of iodine from potassium iodide in aqueous acetone according to the equation NFQNF + $2I^- \longrightarrow$ QN + $2F^-$ + I_2. Also fully consistent with the presence of an $\overset{+}{N}F$ group was the ability of NFQNF to effect the fluorinations shown in the Scheme. None of the products are new: the reactions were chosen simply to demonstrate the potential of NFQNF as an electrophilic fluorinating agent and to establish a comparison with other N–F reagents. Thus, in terms of efficiency, it is superior where the conversion $PhCNa(CO_2Et)_2 \longrightarrow PhCF(CO_2Et)_2$ is concerned to *N*-fluoropyridin-2(1*H*)-one (**1**) [39% yield of the C–F compound even when a 2 molar proportion of (**1**) was used[4a]] but not to a Barnette reagent [(**2**; R = neopentyl) gave an 81% yield[5]]; and the same is true for the fluorination of the Grignard reagents [*e.g.* (**1**) ⟶ 15% PhF;[4b] (**2**) (R = Bu^t) ⟶ 50% PhF[5]]. NFQNF and Purrington's reagent (**1**)[4b] appear equally efficient in the case of the synthesis of 2-fluorocyclohexanone *via* the morpholino enamine, but an *N*-fluorosulphonamide reagent (**2**; R = Bu^t) clearly is the more efficient when it comes to the conversion $Me_2CNO_2 \longrightarrow Me_2CFNO_2$ (*ca.* 85%).[5]

* The possibility that the 2-fluoroquinuclidine (**16**) arose *via* the reaction NFQNF + quinuclidine ⟶ (**16**) + (**17**) was eliminated by adding quinuclidine (1 mol equiv.) to a stirred slurry of NFQNF in $CFCl_3$ at room temperature (the quinuclidine dissolved) and (after 5 h) showing by n.m.r. spectroscopy (^1H and ^{19}F) that no change had occurred.

† Vigalok *et al.*[10] quote a δ($CFCl_3$) value of +155.1 p.p.m. for *N*-butyl-*N*-fluoro-2,2,6,6-tetramethylpiperidinium chlorate (**10**) dissolved in D_2O, the datum having been determined with CF_3CO_2H as external standard and then recalculated relative to $CFCl_3$. We suspect that an error has crept in somewhere.

The ^{19}F n.m.r. absorption assigned to the $\overset{+}{N}F$ group in the triflate (**12**) is reported to lie 48.75 p.p.m. downfield from an internal $CFCl_3$ reference signal. We have computed the shift with respect to CF_3CO_2H by adding 76.55 p.p.m.

‡ The spectrum, run on a KBr–NFQNF disc prepared without taking precautions to exclude atmospheric moisture, showed broad absorptions characteristic of water [noticeably O–H (str.) at 3 440 cm^{-1}].



Scheme. [a] Molar ratios (NFQNF:substrate) close to 1:1 were employed. [b] Yields were not optimized. [c] Isolated material. [d] Yield estimated by g.l.c. and ^{19}F n.m.r. analyses (using internal standards). [e] Presumably triggered by fluoride attack on silicon. *Reagents* i, $PhC(CO_2Et)_2Na^+$ in THF, −10 to 20 °C; ii, $Me_2\bar{C}NO_2Li^+$ in MeOH, 0 °C; iii, RMgX in Et_2O (R = Ph, X = Ph, X = Br; R = c-C_6H_{11}, X = Cl); iv, $PhSiCl_3$ in THF, −50 to 20 °C; v, $CH_2CH_2OCH_2CH_2N$–$CH{=}CH(CH_2)_3CH_2$ in CH_2Cl_2 at −196 to 20 °C, then aqueous 1M HCl

Owing to its solubility characteristics (see above), all the reactions of NFQNF except that involving the lithium salt of 2-nitropropane were carried out under heterogeneous conditions, unlike those with reagents (**1**) and (**2**); this is a distinct disadvantage when working with NFQNF, and, coupled with the reagent's unwelcome hygroscopicity where carbanionic substrates are concerned, detracts from its adoption. On the other hand, Barnette's reagents (**2**) seemingly cannot be prepared (from $ArSO_2NHR + F_2$–N_2) with the same efficiency as NFQNF [yields range from 71 (R = *endo*-2-norbornyl) to 11% (R = cyclohexyl), with the most popular ones (R = *exo*-2-norbornyl or Bu^t) standing at 47 and 14% respectively];[5] and *N*-fluoropyridin-2(1*H*)-one (isolable in 63% yield before final purification by sublimation; route: 2-$Me_3SiOC_5H_4N + F_2$–N_2) must be stored 'in the freezer as it darkens and decomposes slowly'.[4a]

Newer Reagents.—Since the above study of NFQNF was completed, three other types of electrophilic fluorinating agent of the N–F class have been reported: polymeric analogues of the Banks reagent, perfluoro-*N*-fluoropiperidine (**3**) [*e.g.* (**18**) (idealized structure)];[19] *N*-fluorobis(trifluoromethanesulphon)-imide (**19**) and its congeners;[20] * and *N*-fluoropyridinium salts containing $CF_3SO_3^-$, $C_4F_9SO_3^-$, BF_4^-, PF_6^-, SbF_6^- or ClO_4^- counterions.[22,23] The triflates (**12**), (**13**), and (**14**) of the last group are already available commercially† and seem destined to become widely used to effect specific electrophilic fluorination. Historically, their development stems from work carried out by Simons[24] during World War II on the direct liquid-phase fluorination of pyridine, and it is interesting to compare their stabilities with that of presumptive *N*-fluoropyridinium fluoride (**11**), which decomposes violently at *ca.* 0 °C.[25] Of all the N–F reagents mentioned here [including NFNQF (**7**)], only the pyridinium triflate (**15**)[22] and the perfluorinated sulphonimide (**19**)[20] appear to have been found capable of effecting the fluorination of an unactivated arene (benzene).

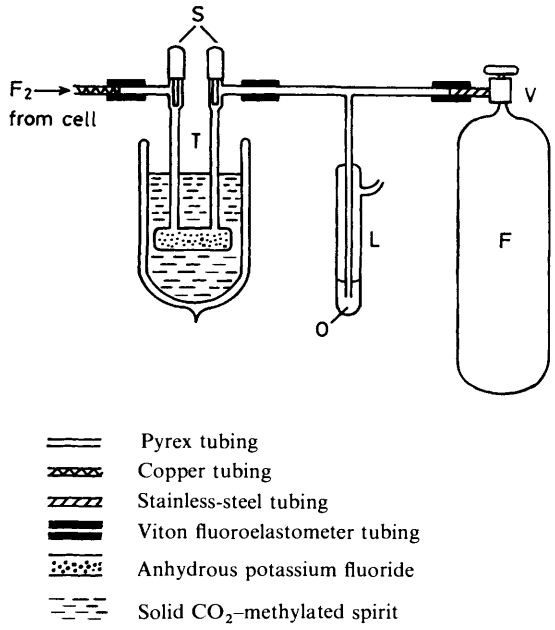


Figure 1.

Experimental

Spectroscopic Analyses.—I.r., n.m.r., and mass spectra were recorded using a Perkin-Elmer spectrophotometer model 197, Perkin-Elmer R32 [90 MHz (^1H); 84.6 MHz (^{19}F)] or R34 [220 MHz (^1H)], Bruker WP80 [80 MHz (^1H); 75.3 MHz (^{19}F); 20.1 MHz (^{13}C)], and Varian XL300 [300 MHz (^1H); 75 MHz (^{13}C)] instruments, and an A.E.I. MS902 (70 eV ionisation beam energy) spectrometer, respectively. N.m.r. chemical shifts were measured relative to Me_4Si [int., ^1H; ext. (D_2O lock), ^{13}C] or CF_3CO_2H (ext., ^{19}F), positive values being assigned to absorptions appearing downfield from reference signals.

Starting Materials.—Trichlorofluoromethane (B. D. H.) was distilled under an atmosphere of nitrogen and stored over molecular sieve (4A), in the dark, at −4 °C before use. Quinuclidine (Aldrich) was manipulated under nitrogen in an efficient dry box; its solutions in trichlorofluoromethane were thus prepared under anhydrous conditions and transferred to the fluorination reactor using syringe techniques. Fluorine was prepared using a 60 A generator [ICI medium-temperature (80—85 °C) cell; electrolyte, molten KF·2HF; maximum output *ca.* 40 g F_2 per hour]; it was freed from hydrogen fluoride by passage through a substantial bed of sodium fluoride pellets then (see Figure 1) a cold (−72 °C) Pyrex trap (T) fitted with Rotaflo stopcocks (S) and containing powdered potassium fluoride before being bled into an evacuated pre-passivated (with F_2) stainless-steel cylinder (F) of known volume equipped with a needle valve (V) (it was found convenient to use cylinders of *ca.* 2.2 and 5.0 l capacity as fluorine reservoirs). A Pyrex lute L containing a chlorofluorocarbon oil (O) was placed between the cold trap and the cylinder to enable the filling process to be monitored and to show when the cylinder was full to a pressure just above atmospheric. Before using the fluorine generator to fill cylinders, it was purged thoroughly with dry oxygen-free nitrogen then operated at low amperage (2–4 A) overnight. The

* Studies on perfluorinated *N*-aryl and *N*-heteroaryl compounds, $Ar_FNFSO_2R_F$, will be reported in due course.[21]

† Onoda-Fluorinate FP Series (**12**) = FP-T500; (**13**) = FP-T300; (**14**) = FP-T700, Onoda Cement Co. Ltd., Tokyo 135, Japan.

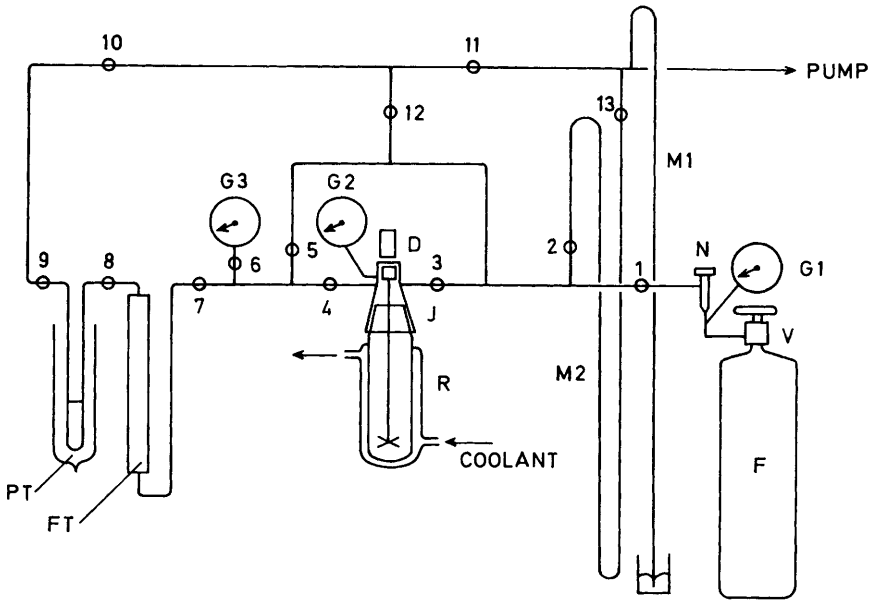


Figure 2.

current was then increased to 10 A and the purity of the fluorine estimated by standard procedures (determination of iodine released from aqueous potassium iodide by a known volume of F_2); only material of $\geqslant 98\%$ purity was used to load cylinders.

Fluorination Apparatus.—This comprised three components: (1) a Pyrex (mainly) vacuum system designed to allow neat fluorine at subatmospheric pressures to be dispensed at ambient temperature; (2) a specially designed stirred Pyrex reactor; and (3) temperature control equipment. The complete set-up is depicted in Figure 2. Once disconnected from the vacuum (oil) pump, the complete apparatus was portable because it was clamped on a conventional metal frame and tray base that fitted snugly into a standard fume cupboard.

The vacuum system was constructed from borosilicate glass (Pyrex), 13 greaseless PTFE-Pyrex stopcocks (Rotaflo) and a single Fischer-Porter PTFE-glass needle valve (N). Flexible connections to the fluorine reservoir F, the Pyrex reactor R, the residual fluorine trap FT (packed with potassium iodide crystals), and the pump trap PT (cooled to -196 °C with liquid nitrogen) were made from short lengths of Viton fluoroelastomer tubing [poly(hexafluoropropene-co-vinylidene fluoride); Isoversinic, 6 mm bore, 3 mm wall thickness (supplied by Jencons Ltd, UK] whose inner surfaces had been fully passivated with fluorine *in situ*. Brass vacuum gauges G1–3 (supplied by Gallenkamp Ltd., Manchester) of the Bourdon type with integral B14 male cones were sited in Pyrex sockets lubricated with chlorofluorocarbon grease [Voltalef (supplied by Fluoro-Chem Ltd.)]. Gauge G1 enabled the amounts of fluorine taken from the storage cylinder F to be determined; G2 was used to follow the rate of uptake of fluorine; G3 was used occasionally to check for leaks in the fluorine scrubbing section. The mercury in the standard manometer M1 was protected from attack by adventitious fluorine with a shallow layer of chlorocarbon oil; the same oil (Kel-F No. 10) was the sole manometric fluid present in M2 (not used in the present study), which was included to allow very low pressures of fluorine to be measured accurately.

Two types of Pyrex reactor R (*ca.* 200 cm^3) were used in the present work: a jacketed variety (Figures 2 and 3) cooled with refrigerated methanol, and an unjacketed counterpart which could be cooled to even lower temperatures by immersion in standard cooling baths. Each reactor was fabricated from a pair of B55 ground-glass joints (J). Reactor bodies were constructed with four anti-vortex baffles (creases) down the upper two-thirds of their lengths. Lids carried stopcock-controlled (Rotaflo) entrance and exit ports for fluorine and three ground-glass sockets to accommodate a stirrer mechanism (size B19), a thermocouple pocket (size B7; this terminated just above the stirrer blades), and a Bourdon-type vacuum gauge G2 (size B14), respectively. The last socket was used initially to purge the reactor with dry nitrogen and introduce solutions of compounds to be fluorinated. All ground-glass joints were lubricated with Voltalef grease.

The Pyrex stirrer (Figure 3), which was driven magnetically (D) at *ca.* 700 r.p.m. after the fashion of the rotor in a spinning-band distillation unit, possessed four vanes and was hollow throughout; a small hole positioned in the shaft wall opposite the fluorine inlet port enabled the halogen to be sucked down the shaft and ejected from the hollow vanes into the reaction medium, thus ensuring rapid mixing.

When using the jacketed reactor, reaction temperatures were controlled by passing refrigerated methanol through the jacket. The cooling unit comprised a centrifugal pump which drew dry methanol from a Pyrex reservoir (500 cm^3, containing activated 3A molecular sieve) and circulated it through the reactor's jacket *via* a coiled copper tube (1.5 m × 6 mm o.d.) immersed in a cooling bath (5-l Dewar vessel; methylated spirit–CO_2). The temperature of the methanol at the jacket's exit pipe was monitored with a thermocouple connected to a standard thermostat device which controlled the power supply to the centrifugal pump.

Fluorination of Quinuclidine.—A dry solution of quinuclidine (2.23 g, 20.1 mmol) in trichlorofluoromethane (20 cm^3) was transferred by syringe from a drybox to the jacketed reactor described above; after introducing more solvent ($CFCl_3$, 175 cm^3), the reactor was closed and the stirred charge cooled to -72 °C and degassed by repeated (× 3) evacuation of the vessel to constant pressure (*ca.* 3 mmHg). During this procedure, only stopcocks 4, 5, 11, and 12 were open, all other sections of the apparatus through to the closed stainless-steel needle valve V of

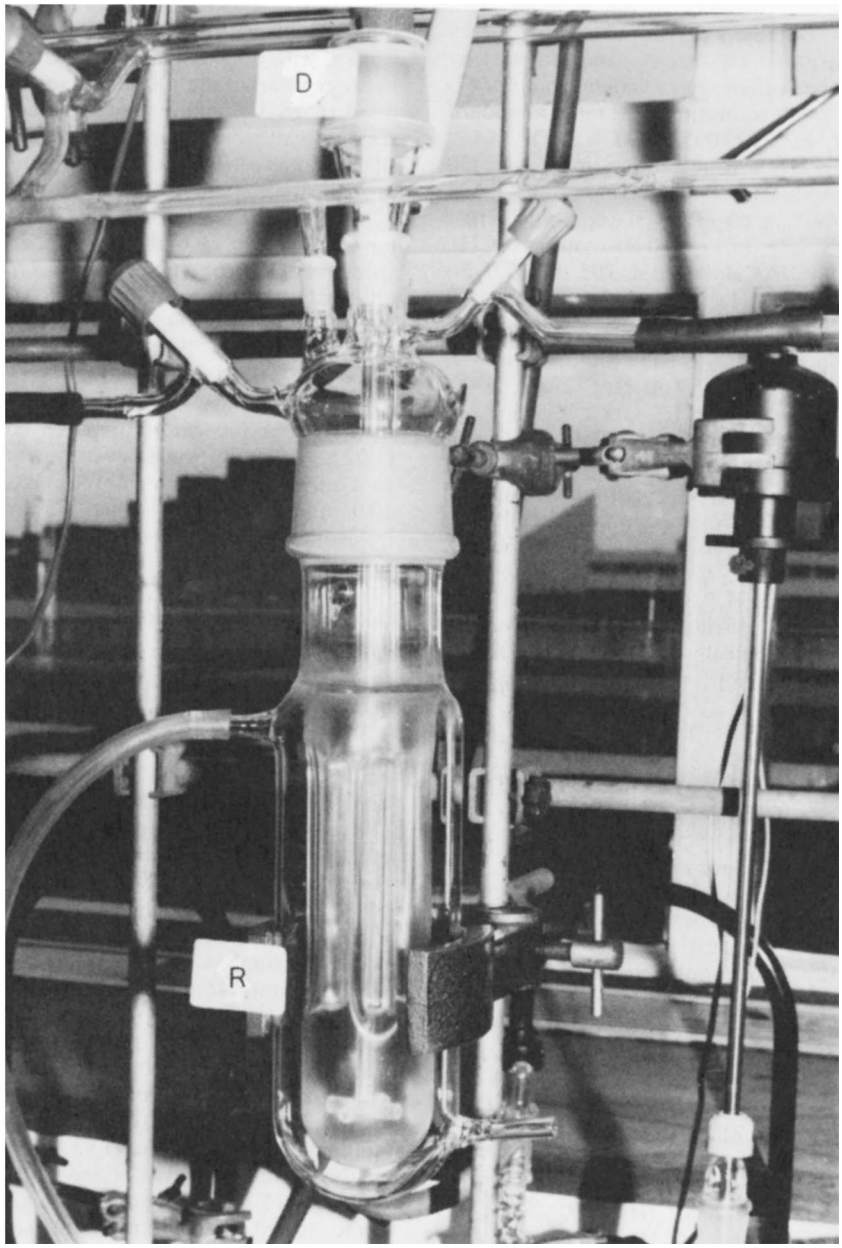


Figure 3.

the fluorine reservoir F having been evacuated previously and sealed off. Stopcocks 4, 5, and 12 were then closed and needle valve V was opened slowly. After noting the pressure of fluorine on gauge G1, valve N and stopcocks 1 and 3 were opened slightly (in that order) to create a pressure of not more than 20 mmHg in the reaction vessel R (indicated by gauge G2). Uptake of fluorine commenced immediately and stopcocks 1 and 3 were adjusted periodically to maintain the fluorine pressure in the range 10—20 mmHg. After 5.5 h, during which time a white precipitate appeared in the reaction vessel, consumption of fluorine became imperceptible, so valve N was closed and the pressure remaining in the cylinder F noted on gauge G1; this enabled the amount of fluorine removed from the reservoir to be calculated. Stopcocks 4, 7, 8, 9, 10 and 11 were then opened and, with the pump trap now cooled in liquid nitrogen, the residual fluorine in the reactor and line heading to it was pumped slowly out *via* the tube packed with potassium iodide. Subsequent determination of the iodide liberated (volumetrically, using standard sodium thiosulphate) enabled the amount of fluorine (1.0 g, 26 mmol) consumed in the reaction with the quinuclidine to be calculated.

Reactor R was isolated from the vacuum system by closing stopcocks 3 and 4 and then allowed to warm to room temperature before the precipitate which had accumulated was recovered by standard techniques (filtration of the reactor's contents under an atmosphere of dry nitrogen; then thorough removel of residual solid from the reactor with the minimum volume of fresh trichlorofluoromethane, followed by filtration of the washings), washed quickly with trichlorofluoromethane (*ca.* 35 cm^3), and dried *in vacuo* over sodium hydroxide (pellets). The crude product (2.92 g) thus recovered was shown by n.m.r. spectroscopy (^1H, ^{19}F, and ^{13}C) to be a mixture of *N*-fluoroquinuclidinium fluoride (**7**) and quinuclidinium fluoride (**17**) [88:12 by integration of the FN^+ and F^- signals in the ^{19}F spectrum; 90:10 by titration ($Na_2S_2O_3$) of the iodine liberated from aqueous acetonic potassium iodide by a sample (0.7112 g)

of the mixture]. The mixture was heated under reflux with AnalaR acetone and the insoluble material was recovered by filtration, freed from acetone *in vacuo*, and shown by spectroscopic methods to be N-*fluoroquinuclidinium fluoride* (**7**) (2.56 g, 17.2 mmol, 86%) {high resolution m.s.: most abundant fluorine-containing peak, *m/z* 129.0952 [$(M - HF)^+$, 64%; $C_7H_{12}FN$ requires 129.0999]; low resolution m.s.: *m/z* 130 [$C_7H_{13}FN^+$ $(M - F)^+$, 4.5%], 129 [$(M - HF)^+$, 32.6%], 114 (15%), 111 ($C_7H_{13}N^+$, 69.7%), 60 (39.6%), and 42 ($C_3H_6^+$, 100%); δ_H (300 MHz; 10% soln. in D_2O) 1.95 (complex, CH), 2.05 (unresolved br mult., CH_2CH_2N), and 3.95 ('q', CH_2N) p.p.m. (rel. int. 1:6:6); δ_F (84.6 MHz; 20% soln. in D_2O) −51.2 (s, F^-) and 135.1 (br s, $\overset{+}{N}F$) p.p.m. (rel. int. 1:1); δ_C (20.1 MHz; 20% soln. in $CDCl_3$; $^{13}C\{^1H\}$, ORD multiplicities in parentheses) 19.48 [d (d), CH, $^4J_{C,F}$ 4.60 Hz], 27.89 [d (t), CH_2CH_2NF, $^3J_{C,F}$ 3.35 Hz], 61.39 [d (t), CH_2CH_2NF, $^2J_{C,F}$ 9.24 Hz] p.p.m.}, an extremely hygroscopic white solid, m.p. 126—128 °C, which gave unacceptable microanalytical figures (Found: C, 48.3; H, 8.1; N, 7.7. $C_7H_{13}F_2N$ requires C, 56.4; H, 8.7; N, 9.4%. Sets of values for three other samples taken from a single batch prepared later in 89% yield were: C, 47.0, 46.0, 51.0; H, 8.3, 8.1, 9.0; N, 7.8, 7.6, 8.3% respectively; note that $C_7H_{13}F_2N{\cdot}H_2O$ requires C, 50.3; H, 9.0; N, 8.4%). Evaporation, *in vacuo*, of the acetonic filtrate provided a further hygroscopic white solid shown spectroscopically to be *quinuclidinium fluoride* (**17**) (0.3 g, 2.3 mmol, 11%) {*m/z* (top mass peak) 132 [$(M + 1)^+$, 2.5%], 131 [$C_7H_{14}FN^+(M^+)$, 0.6%], 130 ($C_7H_{13}FN^+$, 2.0%), 129 ($C_7H_{12}FN^+$, 16.3%), 128 ($C_7H_{11}FN^+$, 8.3%), 111 ($C_7H_{13}N^+$, 4.1%), 60 (39.6%), and 42 ($C_3H_6^+$, 100%); δ_H (220 MHz; 10% soln. in D_2O) 1.94 (s, CH), 2.03 (br s, CH_2CH_2N), and 3.95 (br s, CH_2N) (rel. int. 1:6:6); δ_F (84.6 MHz; 20% soln. in D_2O) −51.2 (s) p.p.m.}.

Evaporation of the trichlorofluoromethane solution (and washings) recovered from the reactor left a yellowish brown solid (0.065 g) which attacked glass slowly at room temperature (etching occurred) and was deduced from its spectroscopic properties to be essentially 2-fluoroquinuclidine (**16**) {δ_H (220 MHz; 20% soln. in $CDCl_3$) complex absorption systems at 1.10—1.70, 1.72—2.20, and 2.61—3.30, ddd at 5.15 (CHF; $^2J_{H,F}$ 48 Hz, $^3J_{H,F}$ 8 and 6 Hz) (rel. int. *ca.* 13:1); δ_F (84.6 MHz; same soln.) −71 (br complex) p.p.m. (impurity bands at −1.3, −57.0, −84.8 p.p.m.); δ_C (75 MHz; same soln.; $^{13}C\{^1H\}$, ORD multiplicities in parentheses) 21.72 [d, (d), CH, $^3J_{C,F}$ 2.1 Hz], 24.59 [s, (t), CH_2CH_2N], 25.85 [s, (t), CH_2CH_2N], 33.69 [d (t), CH_2CHFN, $^2J_{C,F}$ 27.1 Hz], 39.29 [s (t), CH_2N], 44.64 [s (t), CH_2N, $^3J_{C,F}$ 9.4 Hz], and 98.96 [d (dd), CHFN, $^1J_{C,F}$ 193.4 Hz] p.p.m.; *m/z* 148 (top mass peak; $C_7H_{12}F_2^+$, 4.5%), 147 ($C_7H_{11}F_2N^+$, 29.2%), 130 ($C_7H_{13}FN^+$, 11.7%), 129 [$C_7H_{12}FN^+$ (M^+), 65.6%], 128 ($C_7H_{11}FN^+$, 15.7%), 114 ($C_6H_9FN^+$, 20.2%), 101 ($C_5H_8FN^+$, 23.0%), 60 (96.9%), and 42 ($C_3H_6^+$, 100%)} possibly contaminated with its hydrofluoride.

The fluorination was repeated several times at −72 °C and also at other temperatures. Yields of *N*-fluoroquinuclidinium fluoride (**7**) never fell below 80%, and the best results were as follows (temp. (°C), quinuclidine (mmol), fluorine (mmol), yield of (**7**) (%), yield of the hydrofluoride (**17**) (%) respectively): −84 (ethyl acetate/liq. N_2; unjacketed reactor), 19.6, 24, 81, 10; −72, 19.7, 26, 89, 8; −65, 20.3, 27, 86, 10; −50, 19.9, 24, 83, 12; −35, 19.8, 25, 83, 13.

Fluorination of Organic Substrates with N-*Fluoroquinuclidinium Fluoride* (**7**).—(a) *Diethyl phenylmalonate.* A solution of diethyl sodio(phenyl)malonate in anhydrous tetrahydrofuran [prepared in conventional fashion by adding a 60% dispersion of NaH (15.9 mmol) in oil to $PhCH(CO_2Et)_2$ (3.16 g, 13.4 mmol) in THF (10 cm^3)] was added under dry nitrogen to a stirred slurry of *N*-fluoroquinuclidinium fluoride (2.00 g, 13.4 mmol) in tetrahydrofuran (15 cm^3) at −10 °C. The reaction mixture was allowed to warm to room temperature and then diluted with diethyl ether (100 cm^3). The mixture was then washed with 0.5M oxalic acid (30 cm^3), 10% aqueous potassium hydrogen carbonate (30 cm^3), and saturated brine (30 cm^3), dried ($MgSO_4$), and evaporated under reduced pressure. The residue was worked up chromatographically [flash method; silica eluted with dichloromethane–hexane, 1:2 (v/v)] to provide diethyl fluoro(phenyl)malonate (1.77 g, 6.97 mmol, 52%) [Found: C, 62.0; H, 5.8; F, 7.6%; *M* (mass spec.), 254. Calc. for $C_{13}H_{15}FO_4$: C, 61.4; H, 5.9; F, 7.5%; *M*, 254] with correct spectroscopic properties [i.r., n.m.r. (^1H, ^{19}F, ^{13}C), mass]; δ_C (20.1 MHz; 80% soln. in $CDCl_3$) 13.07 (s, CH_3), 62.18 (s, CH_2), 93.61 (d, CF, $^1J_{C,F}$ 199.59 Hz), 125.10 (d, 2-, 6-C, $^3J_{C,F}$ 8.44 Hz), 127.69 (s, 3-, 5-C), 128.80 (s, 4-C), 132.95 (d, C-1, $^2J_{C,F}$ 21.90 Hz), and 164.89 (d, CO_2, $^2J_{C,F}$ 25.92 Hz).

(b) *Phenylmagnesium bromide.* This Grignard reagent in diethyl ether (50 cm^3) [prepared conventionally from PhBr (1.57 g, 10.0 mmol)] was added slowly (30 min), under nitrogen, to a stirred slurry of *N*-fluoroquinuclidinium fluoride (1.49 g, 10.0 mmol) in diethyl ether (15 cm^3). A reaction occurred immediately. Work-up of the product by standard techniques provided quinuclidine (1.05 g, 9.46 mmol) and fluorobenzene (0.25 g, 2.60 mmol 26%) (Found: C, 75.3; H, 4.7; F, 20.0%; *M* (mass spec.), 96. Calc. for C_6H_5F: C, 75.0; H, 5.2; F, 19.8%; *M*, 96), both with correct spectroscopic properties (i.r., n.m.r.). Bromobenzene (1.0 mmol) was also shown to be present in the crude product by g.l.c. techniques (calibrated column).

(c) *Cyclohexylmagnesium chloride.* Experiment (b) was repeated using a Grignard reagent prepared by treating chlorocyclohexane (1.12 g, 9.45 mmol) with magnesium in diethyl ether (50 cm^3). The reaction product was added to water (100 cm^3) and the organic material was extracted with diethyl ether (4 × 70 cm^3). Distillation of the extract gave *ca.* 96% pure (by g.l.c.) fluorocyclohexane (0.19 g, 1.86 mmol, 20%), b.p. 60—63 °C at 20 cmHg, identified by comparison of its i.r. and n.m.r. (^1H and ^{19}F) spectra with those of an authentic sample prepared from cyclohexene and anhydrous hydrogen fluoride. The distillation residue (0.17 g, 1.43 mmol, 15%) was shown by g.l.c. and ^1H n.m.r. spectroscopy to be chlorocyclohexane, indicating incomplete formation of the initial Grignard reagent; the yield of fluorocyclohexane based on chlorocyclohexane consumed was therefore 23%.

(d) *2-Nitropropan-2-yl-lithium.* A solution of *N*-fluoroquinuclidinium fluoride (1.93 g, 12.9 mmol) in anhydrous methanol (20 cm^3) was added dropwise to a stirred, ice-cold solution of 2-nitropropan-2-yl-lithium (1.27 g, 13.4 mmol) in the same solvent (20 cm^3), using nitrogen-atmosphere techniques. After 30 min, the mixture was allowed to warm from 0 °C to room temperature when it was diluted with diethyl ether (100 cm^3), washed with 30-cm^3 portions of 0.5M aqueous oxalic acid, 10% aqueous potassium hydrogen carbonate, and saturated brine, dried ($MgSO_4$), and evaporated under reduced pressure. The residue (1.08 g) was shown by g.l.c. and n.m.r. analysis (^1H and ^{19}F) to comprise methanol, 2-fluoro-2-nitropropane (0.48 g, 4.49 mmol, 35%), and 2-nitropropane (0.52 g, 5.84 mmol).

(e) *1-Morpholinocyclohexene.* A mixture of *N*-fluoroquinuclidinium fluoride (2.00 g, 13.4 mmol), 1-morpholinocyclohexene (Aldrich; 2.23 g, 13.35 mmol), and dry dichloromethane (25 cm^3) was stirred magnetically under anaerobic conditions (200 cm^3 Rotaflo tube) for 48 h. The product was shaken with 1M hydrochloric acid (100 cm^3) and the organic material was recovered with dichloromethane (4 × 50 cm^3); the combined extracts were dried ($MgSO_4$) and evaporated (Rotavapor) and the pale-yellow oily residue was chromatographed [flash; silica eluted with 45:65 (v/v) dichloromethane–light petroleum (b.p. 40—60 °C)] to yield 2-fluorocyclohexanone (0.95 g, 8.20 mmol, 61%) [Found: C, 61.9; H, 7.8; F, 16.8%; *M* (mass spec.), 116. Calc. for C_6H_9FO: C, 62.1; H, 7.75;

F, 16.4%; *M*, 116], with correct spectroscopic properties (i.r., n.m.r.).

(f) *Trichloro(phenyl)silane.* A slurry of *N*-fluoroquinuclidinium fluoride (1.46 g, 9.79 mmol) in dry tetrahydrofuran (5 cm^3) was added slowly to a stirred solution of the silane (2.03 g, 9.60 mmol) in the same medium (5 cm^3) held under dry nitrogen at −50 °C. The mixture was allowed to warm to room temperature and then heated under reflux (2 h) before being filtered to allow the liquid portion to be analysed by g.l.c. and n.m.r. techniques. The yield of fluorobenzene was 22%.

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