Journal of Fluorine Chemistry, 46 (1990) 297–305

Received March 11, 1989; accepted May 5, 1989

N-HALOGENO COMPOUNDS. PART 11. PERFLUORO-[N-FLUORO-N-(4-PYRIDYL)-METHANESULPHONAMIDE], A POWERFUL NEW ELECTROPHILIC FLUORINATING AGENT

RONALD ERIC BANKS* and ARDESHIR KHAZAEI

Chemistry Department, The University of Manchester Institute of Science and Technology, Manchester M60 1QD (U.K.)

SUMMARY

Perfluoro-[N-fluoro-N-(4-pyridyl)methanesulphonamide] (III), synthesised via direct fluorination of the sodio derivative of perfluoro-[N-(4-pyridyl)methanesulphonamide] (I), readily converts diethyl sodio(phenyl)malonate and anisole to diethyl fluoro(phenyl)malonate and ortho- plus para-fluoroanisole respectively at ambient temperature; at 60 °C it quickly converts benzene to fluorobenzene. The sodio-precursor (I) of the N-F compound (III) is easily made from pentafluoropyridine and trifluoromethanesulphonamide.

INTRODUCTION

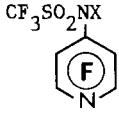
Considerable interest now attaches to electrophilic fluorinating agents of the N-F class. Progress was summarized recently in a paper dealing with the then-latest reagent, N-fluoroquinuclidinium fluoride [1]; subsequently, information has become available

*To whom enquiries should be addressed.

0022-1139/90/$3.50

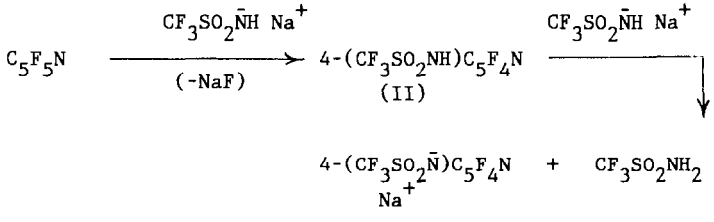
about N-fluoroquinuclidinium triflate* [2a], two camphor-derived enantioselective N-fluoro-sultams [3], and yet more [5] N-fluorosulphonamides of the Barnette type [4]. Both of the quinuclidinium reagents and three of the N-fluoro-N-alkyl-p-toluenesulphonamides (alkyl = methyl, propyl, neopentyl) are now available commercially [from Fluorochem (UK) and PCR (USA) or Kali-Chemie (FRG), respectively (the last company will provide other N-fluorosulphonamides on request)]. The new N-fluorosulphonamide described in this paper, namely perfluoro-[N-fluoro-N-(4-pyridyl)-methane-sulphonamide](III) was designed to be as powerful as the DesMarteau reagent, $(CF_3SO_2)_2NF$ [6], which is capable of converting benzene to fluorobenzene slowly at room temperature [6], but less tedious to prepare [7].

DISCUSSION



(I) X = Na
(II) X = H
(III) X = F

Treatment of pentafluoropyridine in THF at 80 °C with a two-molar equivalent of the sodium salt of trifluoromethanesulphonamide was found to yield the corresponding salt (I) of perfluoro-[N-(4-pyridyl)methane-sulphonamide] (II) in excellent yield:



*N-Fluoroquinuclidinium tetrafluoroborate is also known now [2b].

The new salt (I), an easily-handled white solid which is readily freed from the byproduct, trifluoromethanesulphonamide (removed by sublimation), yields the parent sulphonamide (II) when acidified (H_2SO_4aq).

Using the virtually all-glass Merritt-type vacuum fluorination apparatus described recently [1], the sodium salt of perfluoro-[N-(4-pyridyl)methanesulphonamide] (I) dissolved in cold (ca. -30 °C) acetonitrile was exposed to low-pressure neat fluorine (10-15 mmHg) until uptake of the halogen became imperceptible. Work-up of the product by standard procedures gave a semi-solid, shown by n.m.r. (^{19}F, ^{1}H) analysis, iodimetric estimation of 'positive' fluorine ($\geq N\text{-}F + 2I^- \rightarrow \geq N^- + F^- + I_2$) [8], and elemental analysis to be a ≥ 90% pure sample of the new N-fluoro-compound perfluoro-[N-fluoro-N-(4-pyridyl)methanesulphonamide] (III) (89% yield), the contaminant being the corresponding N-H compound (II). This mixture proved to be a very powerful "F^+ - transfer" agent, capable of effecting the conversions $PhCNa(CO_2Et)_2 \longrightarrow PhCF(CO_2Et)_2$ (93%, isolated material) and $C_6H_5OMe \longrightarrow$ o- and p-FC_6H_4OMe (3:1 ratio; 98% yield, determined by n.m.r.) with consummate ease at ambient temperature; electrophilic fluorination of benzene, though, not observed to occur at room temperature during several hours, proceeded readily at 60 °C, giving an 88% "n.m.r. yield" of fluorobenzene within 10 minutes.

Perfluoro-[N-fluoro-N-(4-pyridyl)methanesulphonamide] (III) thus appears to be about as powerful an electrophilic fluorinating agent as the DesMarteau reagent $(CF_3SO_2)_2NF$, which effects the halogenation $C_6H_6 \rightarrow C_6H_5F$ in 100% yield based on 50% completion of reaction during 18 hours at 22 °C (benzene was used in excess, as in our experiment) [6]. Additionally, not only does synthesis of this new reagent (III) from commercial methanesulphonyl chloride require six steps compared with nine in the case of $(CF_3SO_2)_2NF$ [6,7], but the fluorination procedure used here to construct the required N-F bond [(I) → (III)] is both more convenient and potentially less hazardous than that described so far for effecting the conversion $(CF_3SO_2)_2NH \rightarrow (CF_3SO_2)_2NF$ [6]. Note that the synthesis of $(CF_3SO_2)_2NF$ could be shortened to eight stages (from CH_3SO_2Cl) if treatment of the sodium salt $(CF_3SO_2)_2NNa$ [acidified in the reported procedure [7] to give the N-F compound's immediate precursor,

$(CF_3SO_2)_2NH$] with fluorine proved to proceed smoothly, as in the analogous reaction leading to the pyridyl compound (III).

Work is in progress here to develop a flow-fluorination procedure for the conversion (I) ⟶ (III), and to produce N-fluoro material (III) free from the corresponding N-H compound (II). Interestingly, fluorination of the sodium salt (I) in trichlorofluoromethane at -72 °C appears, from ^{19}F n.m.r. analysis of the crude product, to contain *inter alia* the O-fluorinated compound 4-$[CF_3S(O)(OF)=N]C_5F_4N$ as well as (mainly) the N-fluoro derivative (III).

EXPERIMENTAL

Spectroscopic Analyses

I.r., n.m.r. and mass spectra were recorded using a Perkin-Elmer spectrophotometer model 197, Perkin-Elmer R32 instrument [90 MHz (^1H); 84.6 MHz (^{19}F)], 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) and CF_3CO_2H or $CFCl_3$ (both ext.; ^{19}F), absorptions to high field of reference signals being assigned negative values.

Starting Materials

Commercial pentafluoropyridine (Aldrich) was used as received. Trifluoromethanesulphonamide [m.p. 118-119 °C (lit. [9] 119 °C) (Found: C, 7.8; H,1.1; N,9.0; S, 21.5%. Calc. for $CH_2F_3NO_2S$: C, 8.05; H, 1.3; N, 9.4; S, 21.5%)] was prepared on a 50-g scale from trifluoromethanesulphonyl fluoride and ammonia according to the literature [7], the yield being 75% [after purification by sublimation (twice)]. The trifluoromethanesulphonyl fluoride (b.p. -21.7 °C) was prepared from commercial methanesulphonyl chloride (Lancaster Synthesis) via halogen-exchange with potassium hydrogen difluoride [9] and subsequent electrochemical fluorination (Simons Process) of the methanesulphonyl fluoride thus obtained in a 50-litre cell of classical design [10]; the overall yield was 70%.

Fluorination Apparatus

Full details of the apparatus and technique used to effect the controlled liquid-phase fluorination of the sodium salt of perfluoro-[N-(4-pyridyl)methanesulphonamide] can be found in a recent publication [1].

Preparation of the Sodium Salt of Perfluoro-[N-(4-pyridyl-methanesulphonamide]

Initially, the sodium salt of trifluoromethanesulphonamide was prepared in 92% yield according to a published procedure [7] ($CF_3SO_2NH_2$ + MeONa in MeOH) except that toluene not benzene was used to wash the resulting solid. A mixture of this salt (8.65 g, 50.6 mmol), pentafluoropyridine (4.20 g, 24.8 mmol), and dry THF (50 cm^3), sealed in an evacuated Pyrex ampoule (150 cm^3) fitted with a PTFE-glass valve (Rotaflo), was shaken mechanically at 80 °C for 24 hours in an explosion-proof cabinet. The product was diluted with dry diethyl ether (50 cm^3) then filtered to remove sodium fluoride. Evaporation of the filtrate (Rotavapor) followed by sublimation of the solid residue at 30 °C in vacuo to remove trifluoromethanesulphonamide (3.80 g) (identified by ^1H and ^{19}F n.m.r. and i.r. analysis) provided the sodium salt of perfluoro-[N-(4-pyridyl)methanesulphonamide] (n.c.) (7.10 g, 22.2 mmol, 89.5%) (Found: C, 22.6; H, <0.1; F, 41.6; N, 8.6; S, 10.0. $C_6F_7N_2NaO_2S$ requires C, 22.5; H, 0.0; F, 41.6; N, 8.3; S, 10.0%), m.p. 285 °C, δ_F [ext. TFA; soln. in $(CD_3)_2CO$] -1.3 (t,3Hz; CF_3SO_2), -19.7 (complex, 2-, 6-F), -75.9 (complex, 3-,5-F) p.p.m. (rel.int. 3:2:2). Treatment of a sample (2.00 g, 6.25 mmol) of this salt with 10% aqueous sulphuric acid (30 cm^3), followed by continuous ether extraction (Et_2O) of the resultant solution, evaporation (Rotavapor) of the dried ($MgSO_4$) extract, and sublimation of the residue at 60 °C, in vacuo, provided perfluoro[N-(4-pyridyl)methanesulphonamide] (n.c.) (0.95 g, 3.19 mmole, 51%) (Found: C, 24.1; H, 0.3; F, 44.8; N,9.3; S, 10.3. $C_6HF_7N_2O_2S$ requires C, 24.2; H, 0.3; F, 44.6; N, 9.4; S, 10.0%), m.p. 69-70 °C, δ_F

(ext.TFA; soln. in $CDCl_3$) + 3.0 (t, 7.2Hz; CF_3SO_2), -7.9 (complex, 2-, 6-F), -67.1 (complex, 3-,5-F) p.p.m. (rel.int. 3:2:2), δ_H [soln. in $(CD_3)_2CO$] 7.45 (br.s; NH) p.p.m.

Preparation of Perfluoro-[N-fluoro-N-(4-pyridyl)methanesulphonamide]

A 200-cm^3 fluorination reactor [1] was charged with a solution of the sodium derivative of perfluoro-[N-(4-pyridyl)methanesulphonamide] (2.0 g, 6.25 mmol) in dry acetonitrile (200 cm^3; distilled off P_2O_5) containing 5A molecular sieve (0.1 g). The solution was cooled (-30 to -35 °C) and the contents degassed before fluorine was admitted to the evacuated reactor to a pressure of 10 mmHg. Consumption of the halogen began immediately, and more fluorine was admitted periodically from the calibrated stainless steel reservoir to maintain the pressure in the range 10-15 mmHg. After 6 hours, during which time the reaction mixture became noticeably yellow, uptake of fluorine appeared to cease. The non-volatile product, plus material obtained by washing out the reactor with dry acetonitrile, was filtered to remove sodium fluoride and spent molecular sieve, then evaporated *in vacuo* at ambient temperature. The semi-solid pale-yellow residue (1.5 g) was shown by i.r. and n.m.r. spectroscopy to be perfluoro-[N-fluoro-N-(4-pyridyl)-methanesulphonamide] (III) (n.c.) contaminated with perfluoro-[N-(4-pyridylmethanesulphonamide] (II); the ratio of N-F (III) to N-H (II) compound was 10:1 by ^{19}F n.m.r. analysis, and 9.8 : 1.0 by standard [8] iodimetric estimation of the fluorine attached to nitrogen in a sample (0.320 g) of the mixture. Evaporation of the recovered acetonitrile at ambient temperature and *ca*. 10 mmHg pressure provided more of the N-fluoro-compound (III) [0.44 g; total yield of (III) after allowing for the presence of (II; 0.56 mmol) = 5.52 mmol, (89%)] still contaminated with approximately 9 mole-% of its N-H analogue (II) according to ^{19}F n.m.r. spectroscopy, and possessing the following elemental analysis : Found: C, 23.0; H, 0,2; F, 47.7; N, 8.8; S, 9.8%.Calc. for $C_6F_8N_2O_2S$: C, 22.7; H, 0.0; F, 48.1; N, 8.8; S, 10.1%. The ^{19}F n.m.r. spectrum of the mixture dissolved in $CDCl_3$ showed absorptions for the N-F compound (III) at -24.5 (m; NF) and -73.5 (m; CF_3SO_2) (both measured relative to ext. $CFCl_3$), and -6.3 (complex; 2-,6-F) and -61.2 (complex; 3-,5-F) (both relative to ext. CF_3CO_2H) p.p.m. (rel.int. 1:3:2:2).

Fluorination with Perfluoro-[N-fluoro-N-(4-pyridyl)-methanesulphonamide] (III)

(a) Diethyl phenylmalonate

A solution of diethyl sodio(phenyl)malonate in anhydrous tetrahydrofuran [prepared in conventional fashion by adding a 60% dispersion of NaH (0.64 mmol) in oil to $PhCH(CO_2Et)_2$ (0.15 g, 0.635 mmol) dissolved in THF (10 cm^3)] was added dropwise to a cold (-10 °C) THF solution (15 cm^3) of a 9:1 molar mixture (from the experiment described immediately above) of perfluoro-[N-fluoro-N-(4-pyridyl)-methanesulphonamide] (III) and its N-H precursor (II) containing 0.20 g (0.63 mmol) of the N-F compound (III). The reaction mixture was allowed to warm to room temperature, then worked-up as described for the product from the fluorination of diethyl sodio(phenyl)malonate with N-fluoroquinuclidinium fluoride [1], to provide diethyl fluoro(phenyl)malonate (0.15 g, 0.59 mmol, 93%) as a colourless oil [Found: C, 61.5; H, 6.2; M (mass spec.) 254. Calc. for $C_{13}H_{15}FO_4$: C, 61.4; H, 5.9; M, 254] with correct spectroscopic properties (i.r.; ^1H and ^{19}F n.m.r.).

(b) Benzene

An excess of benzene (0.262 g, 3.36 mmol) and hexafluorobenzene (as an internal ^{19}F n.m.r. standard) were added by microsyringe to perfluoro-[N-fluoro-N-(4-pyridyl)methanesulphonamide] (III) [0.040 g, 0.126 mmol; 0.014 mmol of the N-H analogue (II) was present too] dissolved in $CDCl_3$ and contained in a 5 mm (o.d.) n.m.r. tube. The mixture was frozen (-196 °C) and de-gassed (3 freeze-pump-thaw cycles) before the tube was sealed in vacuo, allowed to warm to room temperature, and the contents (a homogeneous, colourless solution) subjected to n.m.r. analysis (probe temp. 35 °C). No reaction appeared to have occurred, so the n.m.r. tube was warmed to 60 °C (water bath), kept at that temperature for 10 minutes (the contents became yellow), allowed to cool to room temperature then returned to the n.m.r. spectrometer. The ^{19}F n.m.r. spectrum obtained revealed

that complete conversion of the N-F compound (III) to perfluoro-[N-(4-pyridyl)methanesulphonamide] (II) had occurred, with the associative formation of fluorobenzene in 88% yield.

(c) Anisole

Experiment (b) above was repeated, using anisole (methoxybenzene; 0.060 g, 0.555 mmol), hexafluorobenzene (0.01 g, 0.054 mmol), and a 9:1 molar mixture (0.024 g) of perfluoro-[N-fluoro-N-(4-pyridyl)methanesulphonamide] (III) (0.076 mmol) and its N-H counterpart (II) in deuteriochloroform. N.m.r. analysis of the reaction mixture (after the sealed tube had warmed to room temperature and been shaken manually for 10 minutes) revealed that the N-fluoro-compound had been consumed completely, causing the formation of a 3:1 mixture of o- and p-fluoroanisole in 98% yield.

ACKNOWLEDGEMENTS

We are deeply grateful to the University of Ahwaz, Iran, for the award of a scholarship (to A.K.) and to Dr A.C. Alty for some practical advice.

REFERENCES

1 R.E. Banks, R.A. Du Boisson, W.D. Morton and E. Tsiliopoulos, J.Chem.Soc., Perkin Trans I, (1988) 2805.

2 (a) R.E. Banks and I. Sharif, J.Fluorine Chem., 41 (1988) 297;
(b) R.E. Banks and I. Sharif, unpublished work.

3 E. Differding and R.W. Lang, Tetrahedron Lett., 29 (1988) 6087.

4 W.E. Barnette, J.Am.Chem.Soc., 106 (1984) 452; U.S. Pat. 4 479 901/1984 (to Du Pont).

5 B. Wilkes, D. Naumann, W. Rudolph, and R.Sander, Ger.Offen. DE 3 623 184 A1/1988 (to Kali-Chemie AG).

6 D.D. DesMarteau, U.S.Pat. 4 697 011/1987; S.Singh, D.D. DesMarteau, S.S. Zuberi, M. Witz, and H.-N. Huang, J.Am.Chem.Soc., 109 (1987) 7194.

7 J. Foropoulos and D. D. DesMarteau, Inorg.Chem., 23 (1984) 3720.

8 R.E. Banks and E.D. Burling, J.Chem.Soc., (1965) 6077.

9 T. Gramstad and R.N. Haszeldine, J.Chem.Soc., (1956) 173.

10 J.H.Simons, U.S. Pat. 2 519 983/1950 (to 3M).