Alkylations with Methyl and Ethyl Fluorosulphonates

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FLUOROSULPHONIC ACID is one of the strongest acids known.[1] Well-established prejudice would then suggest that alkyl fluorosulphonates should prove excellent alkylating agents, and we find this to be so. Methyl and ethyl fluorosulphonates are comparable in reactivity to alkyl perchlorates[2] and trifluoromethanesulphonates,[3] trialkyloxonium salts,[4] and alkyl halide–Lewis acid and alkyl halide–silver salt combinations,[5] but offer advantages over most of these reagents since they are easily prepared and may be handled as safely as dimethyl sulphate.

Reaction $EtX + Et_3N \rightarrow Et_4N^+X^-$ *in* MeCN

X	log *k* −21·3°	0°	25°	*E* (kcal./mole) (± 0·5)	log *A* (± 0·5)
OSO_2F	−1·48	−0·76		10·7	7·8
OSO_2OEt[a]		−4·83	−3·91	13·7	6·1
p-$OSO_2C_6H_4Me$		−5·93	−4·92	14·9	6·0
OSO_2Me		−6·44	−5·48	14·3	5·0
I		−4·55	−3·71	12·5	5·5
Br		−5·34	−4·52	12·2	4·5

[a] $k \times \frac{1}{2}$, statistical correction.

Some time ago a kinetic study[6] of the Menshutkin reaction $EtX + Et_3N \rightarrow Et_4N^+X^-$ showed (Table) that ethyl fluorosulphonate was more reactive than the best conventional reagent by a factor of 10^4. The reactions were followed by titration of residual base with sulphuric acid, and, although accuracy was not high, the results confirm the expected bimolecular mechanism and show that the rates for $EtOSO_2Y$ correlate with σ^* for Y with ρ^* + 4·5. More recently a simple preparation of methyl and ethyl fluorosulphonates has been devised;[7] the esters pass over first (>80% yield) when a mixture of fluorosulphonic acid (1 mol.) and the dialkyl sulphate (1·2 mol) is distilled in glass. Methyl fluorosulphonate (b.p. 92—94°, m.p. ~ − 95°) shows a quite sharp proton resonance at τ 5·88 (J_{HF} ~ 0·4 Hz.). The ^{19}F resonance is at −31·2 p.p.m. relative to $CFCl_3$. The methyl protons of ethyl fluorosulphonate show a coupling to the fluorine of J_{HF} 0·9 Hz. Formation of FSO_3^- is detectable by the appearance of a new ^{19}F signal at −39·2 p.p.m. relative to $CFCl_3$. Reactions of methyl fluorosulphonate are thus conveniently followed by ^1H and ^{19}F n.m.r. using an excess of ester or SO_2 as solvent, and our preliminary observations using these techniques are summarized below (reaction with $MeOSO_2F$ except where stated).

Amines: 2,6-Lutidine is quaternised exothermically, as is *NN*-diethylaniline by $EtOSO_2F$, but *NN*-dimethyl-1-naphthylamine requires 0·5 hr. at 25° for complete reaction. *Amides*: *NN*-Dimethylformamide reacts instantly at 25° giving 95% $HC(OMe)NMe_2^+$ and 5% $HCONMe_3^+$ [broad peak at τ 1·94 (1H), singlet (9H) at τ 6·36]. Reaction at nitrogen was not detected with *NN*-dimethylacetamide but occurs to the extent of *ca.* 5% with tetramethylurea. *Nitriles*: Reaction with MeCN is complete in 4—5 hr. at 25°. The nitrilium salt is sparingly soluble in $MeOSO_2F$ and was redissolved in $HOSO_2F$ or SO_2 for n.m.r. observation. Olah and Kiovsky[8] report ^{14}N–^1H couplings in nitrilium salts and our observations agree with theirs except that we find the coupling $[CH_3C{\equiv}N\text{-}CH_2\mathit{CH}_3]^+$ to be 3·2 Hz. (and not 1·5 Hz.) and thus larger than $[CH_3C{\equiv}\mathit{NCH}_2CH_3]^+$, paralleling the situation[9] in EtNC and Et_4N^+. *Dimethyl sulphoxide* reacts exothermically, alkylation occurring on oxygen.[10] *Ethers*: Dimethyl ether yields crystalline trimethyloxonium fluorosulphonate within minutes at 25°, and tetrahydrofuran affords the crystalline methyltetrahydrofuranium salt[11] [multiplet (4H) at τ 5·28, singlet (3H) at 5·66, multiplet (4H) at 7·71]. Reaction with diethyl ether is quite slow and leads only to methyl–ethyl exchange. Over 1—2 days peaks due to MeOEt, Me_2O, and $EtOSO_2F$ appear, but no FSO_3^- is formed. In SO_2 solution, however, the diethylmethyloxonium ion is formed [quartet 4H at τ 5·42, singlet (3H) at τ 5·88, triplet (6H) at τ 8·50]. In $MeOSO_2F$, the nucleophilicity of FSO_3^- is enough to prevent salt formation. *Esters*: Methyl acetate is unchanged, while ethyl acetate undergoes methyl–ethyl exchange, though more slowly than diethyl ether and the ethoxymethoxymethylcarbonium ion has not yet been observed by the use of SO_2 as solvent.

Alkylation of less nucleophilic centres might be achieved with $MeOSO_2F–SbF_5$ mixtures, and we are currently exploring this possibility. It is worth noting that no examples of $MeOSO_2F$ acting as a sulphonyl halide or fluorinating agent have yet emerged but these possibilities must always be borne in mind.

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