Acylation of Electron-rich Aromatic Nucleus with Fluorinated Immonium Salts

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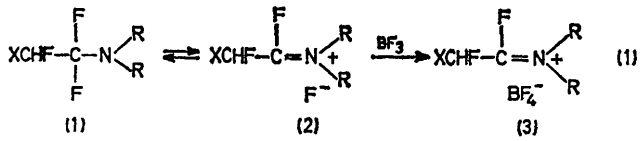
Summary Fluorinating acylation of electron-rich aromatic compounds with fluorinated immonium salts, obtained by action of boron trifluoride on α-fluorinated amines, is described.

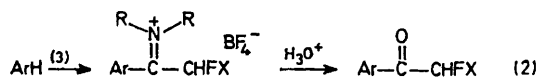
THE reactivity of fluoroamine reagents (**1**), used extensively for the replacement of hydroxy-groups by fluorine,[1] is explained by their equilibria with the ionic form (**2**) [equation (1)].[2]

We noticed that the action of a Lewis acid (*e.g.* BF_3), on α fluorinated amines (easily obtained by addition of secondary amines to fluorinated alkenes) produces salts (**3**) which have some analogy with the well known immonium salts, *e.g.* Vilsmeier reagents, Arnold reagents, or phosgene-immonium salts.[3] The structure of the salt (**3a**), obtained as a hygroscopic precipitate in Et_2O, was confirmed by n.m.r.



(1) (2) (3) (1)

R = Et; a, X = Cl
b; X = F
c; X = CF_3



(2)

spectroscopy in CD_2Cl_2: ^1H (Me_4Si ref.), δ 7·53 (q, CHFCl); $^2J_{HF}$ 45·4 Hz; $^3J_{HF}$ 10·6 Hz; ^{19}F ($CFCl_3$ ref.) φ 38 (q, N^+=C–F), and 150 p.p.m. (q, CHFCl); $^3J_{FF}$ 13·4 Hz.

The salts (**3**) are able to acylate electron-rich aromatic compounds, providing an easy way to introduce an α fluorinated carbonyl group into the molecule [see Table and equation (2)].

For example BF_3–Et_2O (0·03 mol) was added to a solution of (**1a**) (0·03 mol) in CH_2Cl_2 (50 ml). Indole (0·03 mol) was then added and the mixture was stirred at room temperature during 8 h. After usual work up, the acylated product was recrystallised from $CHCl_3$; m.p. 180 °C; δ (MeCN) 6·75 (CHFCl); φ 145 p.p.m., $^2J_{HF}$ 51 Hz.

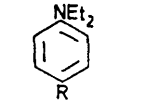
Nitrogen substrates react more easily than their oxygen analogues (for example we obtained α-chloro-α-fluoro-3-methyl-4-methoxyacetophenone from 2-methylanisole in 30% overall yield).

TABLE

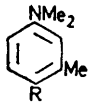
Aromatic compound	Reagent (3)	Acylation product	Yield[a] (%)
(4a)	(3b)	(4b)	45
	(3a)	(4c)	37
(5a)	(3a)	(5b)	40
(6a)	(3a)	(6b)	43
(7a)	(3a)	(7b)	78
	(3b)	(7c)	58
	(3c)	(7d)	35
(8a)	(3a)	(8b)	52
(9a)	(3a)	(9b)[b]	30
		(9c)[b]	35

[a] Overall yield from the difluoroamine. [b] The two isomers were separated by distillation and were identified by n.m.r. spectroscopy.

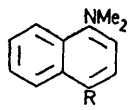
This fluorinating acylation is regioselective with substituted benzenes; only the *para*-isomer is isolated. Indole is acylated at the 3-position and thiophen at the 2-position.



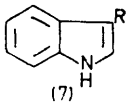
(4)
a; R = H
b; R = $COCHF_2$
c; R = COCHClF



(5)
a; R = H
b; R = COCHClF



(6)
a; R = H
b; R = COCHClF



(7)
a; R = H
b; R = COCHClF
c; R = $COCHF_2$
d; R = $COCHFCF_3$

(8)
a; R = H
b; R = COCHClF

(9)
a; R^1 = R^2 = H
b, R^1 = COCHClF, R^2 = H
c, R^1 = H, R^2 = COCHClF

However, in the *N*-methylpyrrole example, both possible isomers were isolated in a ratio of 1·1:1, in contrast to the higher selectivity towards the 2-position observed with the Vilsmeier reagent.[4] Furthermore an attempt to acylate *N*-methylpyrrole with *NN*-dimethylfluorochloroacetamide–$POCl_3$ failed.

(*Received, 19th May* 1975; *Com.* 565.)

[1] C. M. Sharts and W. A. Sheppard, 'Organic Reactions,' vol. 21, Wiley, New York, 1974, p. 158.
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[4] H. J. Anderson and H. Nagy, *Canad. J. Chem.*, 1972, **59**, 1961.

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