

**HETARYLATION OF C-NUCLEOPHILES: A NEW COURSE
FOR THE REACTION OF N-FLUOROPYRIDINIUM SALTS WITH
CARBANIONS.**

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Summary: The N-fluoropyridinium tetrafluoroborate reactions with carbanions were found either to follow the cine -(tele)-AEa-substitution or go through possible formation of a carbenic (cationic) intermediate; as a result 2- or 4-pyridyl derivatives are formed.

Chemistry of N-fluoropyridinium salts (FP), unique organic compounds, containing the fluorine atom at the positively charged sp^2 -hybridized nitrogen atom dates back to Meinert's discovery of the unstable N-fluoropyridinium fluoride [1]. Interest in these structures have been provoked by preparation of N-fluoropyridinium salts stabilized by nucleofugic anions [2] and by their activity as electrophilic fluorinating agents [3,4].

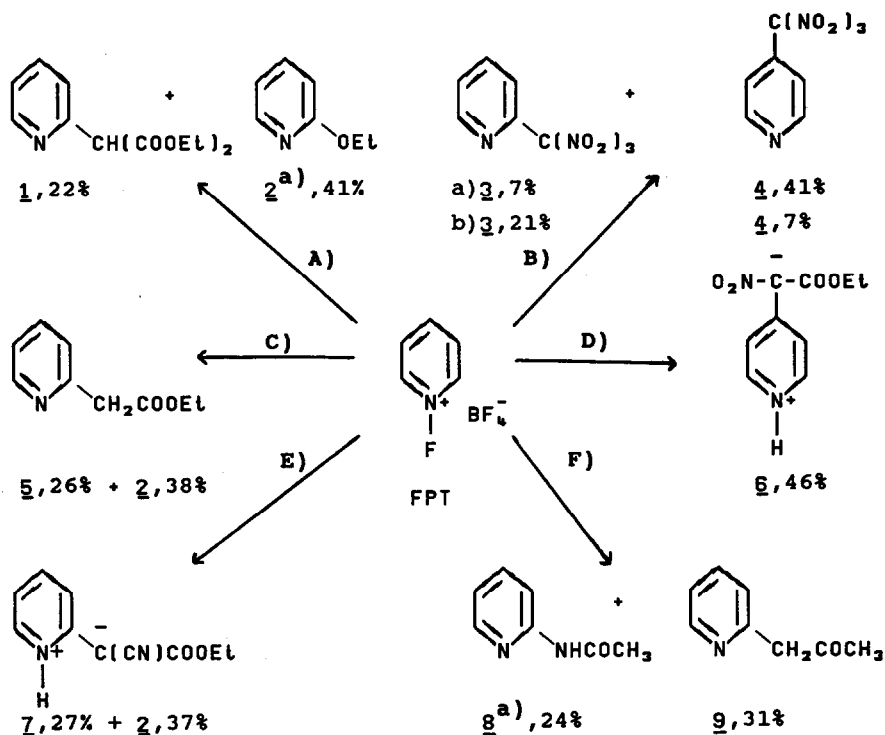
Later it has been found that FP when treated with triethylamine or pyridine, can be converted into the respective 2-fluoropyridines [5]. 2-Alkoxy- and 2-acetoxypyridines have been obtained in yields from moderate to excellent by the action of alkoxide- and acetate-ions on FP [6,7,8].

As to C-nucleophiles, there is some evidence for their preferential fluorination when they react with FP [3,4]. However our previous data [9] indicated that the main product of the reaction of FP with trinitromethane salts in acetonitrile was the product of pyridylation of the C-nucleophile - 2-trinitromethylpyridine, rather than fluorotrinitromethane.

Here we report that in fact the predominant course of the reactions of

the most accessible FP salt, N-fluoropyridinium tetrafluoroborate (FPT), with a number of representative C-nucleophiles is pyridylation (Scheme 1). The GLC-MS analysis of the reaction mixtures indicated the absence (less than 5 mole %) both of the products of fluorination and of pyridine which could have been formed if fluorination of C-nucleophiles took place. The regioselectivity of the process, namely the formation of 2- or 4- isomers may be influenced both by the reaction conditions and the nature of carbanion.

Scheme 1*



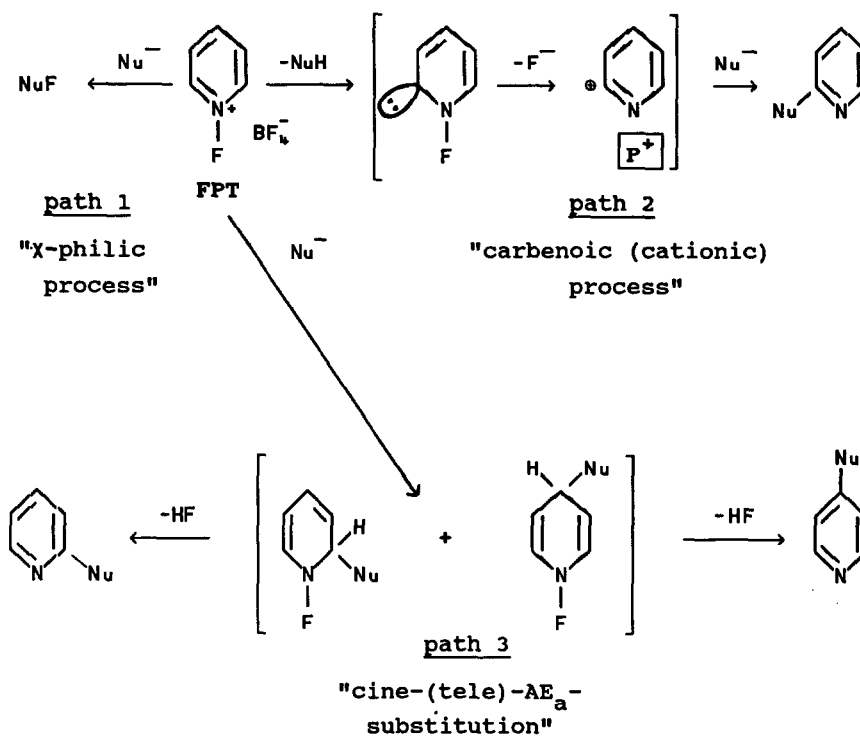
a) products of solvolysis

- A) $\text{Na}^+ \text{CH}(\text{COOEt})_2$; EtOH B) $\text{K}^+ \text{C}(\text{NO}_2)_3$; a) H_2O , b) CH_3CN
 C) $\text{Na}^+ \text{CH}(\text{COCH}_3)\text{COOEt}$; EtOH D) $\text{Na}^+ \text{CH}(\text{NO}_2)\text{COOEt}$; H_2O
 F) $\text{K}^+ \text{CH}(\text{COCH}_3)_2$; CH_3CN E) $\text{Na}^+ \text{CH}(\text{CN})\text{COOEt}$; EtOH

* All yields refer to the isolated products, purified by column chromatography. Besides the products shown reaction mixture contain small amounts of minor products, such as 2-fluoropyridine, etc.

The structure of products **1-9** allowed us to assume that the interaction of FPT with carbanions either follows the cine-(tele)- AE_a -substitution [9,11] (Scheme 2, path 3) or goes through possible formation of a carbenic (cationic) intermediate P^+ [6,11] (Scheme 2, path 2) as a result of abstraction of acidic α -proton from the FPT molecule by the C-nucleophile. It seems reasonable to suggest that the interaction of FPT with weakly-basic carbanions proceeds preferentially as the cine-(tele)- AE_a -substitution-like process. This assumption is supported by the high yields of the 2- and 4-pyridylation products (even in such a nucleophilic solvent as water); and by the dependence of the regioselectivity of the reaction on the nature of the solvent. When the reaction of FPT with strongly-basic carbanions occurs one can suppose the intermediate formation of the highly reactive 2-pyridylium cation P^+ (Scheme 2) [6,8,11], which could lead to the formation of products such as **2** and **3** (Scheme 1).

Scheme 2



Preferential attack of carbanions at the pyridinium ring rather than at the fluorine atom (X-philic attack [12], Scheme 2, path 1), typical for the reactions with other nucleophiles (e.g. various π -donors [3,4]) , can be explained in terms of theory of the charge-controlled reactions [13].

Thus, FPT may be considered as an example of a typical ambident electrophile [14]. The observed hetarylation ability of FPT offers a promising opportunity for the synthesis of various polyfunctional pyridine derivatives.

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References and Notes

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10) Typical procedure:

1,84g (0,01mole) of N-fluoropyridinium tetrafluoroborate (FPT) was added to a stirred solution of appropriate carbanion in abs. EtOH at -70°C or in abs. CH_3CN at -40°C . The mixture was kept at this temperature until the FPT has been consumed completely (KI / starch indicator); then the reaction mixture was filtered and concentrated. Products 1-9 were isolated by column chromatography (eluent hexane-ether, 2:1). All products were characterized by NMR-, IR-spectroscopy, mass-spectrometry and analytical data.

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