Oxidizing Aromatic Amines to Nitroarenes with the HOF–MeCN System

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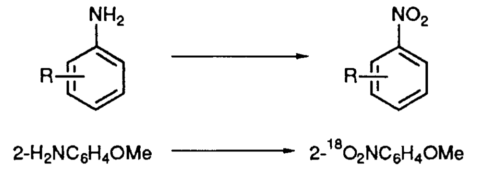
Fluorine reacts with wet acetonitrile to produce an oxidizing agent which oxidizes all types of aromatic amines to the corresponding nitroarenes, also offering a way to make ^{18}O containing nitro derivatives.

Recently we have shown that the HOF–MeCN system, obtained directly from F_2, is an excellent oxygen transfer agent. We have already used this system for alkene epoxidation[1] and for activation of chemically inert sites by inserting oxygen into the deactivated tertiary C–H bond.[2] We report here another general, fast and efficient oxygen transfer process which results in oxidation of various anilines to the corresponding nitro derivatives. Previously, such oxidations have been performed mainly with peracetic acid, sodium perborate and dimethyl dioxirane[3] (for rings with electron



Scheme 1 *Reagents*: $F_2 + H_2O + MeCN$ (→ HOF–MeCN)

R	Yield (%)	R	Yield (%)
4-Ac	95	$2\text{-}NH_2$	85 [$1,2\text{-}(O_2N)_2C_6H_4$]
$2\text{-}CO_2Me$	100	4-NHAc	80
$4\text{-}NO_2$	95	$4\text{-}CO_2H$	80
2-OMe	82	3-OH	71

donating substituent) or with peroxytrifluoroacetic acid and peroxydisulphuric acid[4] (for electron-deficient anilines).

When anilines with electron-withdrawing groups such as 4-aminoacetophenone, methyl anthranilate and 4-nitroaniline (Scheme 1), were treated with the HOF–MeCN oxidizing system an instantaneous reaction took place and the corresponding nitro derivatives were formed and isolated in practically quantitative yield.† Scheme 1 indicates that the ease and the efficiency of the reaction is preserved with electron-rich anilines as well. Thus 2-aminoanisole and 2-aminoaniline were oxidized in >80% yield. It is worth noting that if the oxidation of a single amino group in compounds such as 2-aminoaniline is required, the second NH_2 should be protected beforehand as demonstrated by 4-aminoacetanilide which was converted to 4-nitroacetanilide in good yield.

Unlike other oxidation methods the present reaction offers the opportunity to convert the amino group into a nitro one even in the presence of a free hydroxy group. Thus 4-aminobenzoic acid and 3-aminophenol were converted into the respective nitro derivatives without formation of the corresponding perbenzoic acid and quinone compounds. To the best of our knowledge this is the first time a direct oxidation of a hydroxy aniline has been performed.

Since the reaction is essentially an oxygen transfer process and since, unlike most other chemical oxidations, the oxygen atom originates directly from the water, the HOF–MeCN system presents a rare opportunity for easy and economical labelling of the nitro group with other than the ${}^{16}O$ isotope. Thus the reaction of 2-aminoanisole with the oxidative solution obtained from the action of F_2 on $H_2{}^{18}O$–MeCN resulted in the formation of 2-nitroanisole with both oxygens of the nitro group containing the ${}^{18}O$ isotope [*m/z* 157 (M^+), no peaks at 153 and 155].

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† In a typical experiment about 20% of F_2 in N_2 was passed through a well agitated solution of water (3.5 ml) in MeCN (70 ml) cooled to −15 °C. To the oxidizing agent (30 mmol) thus obtained the corresponding aniline (10 mmol), dissolved in $CHCl_3$ (10 ml), was added. After 2 min the mixture was poured into aqueous sodium hydrogen carbonate, extracted with chloroform and washed with water. Evaporation afforded the corresponding nitro derivatives which were in all cases identical with authentic samples.