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Preliminary Note

Solvent effects in the fluorination of aromatic molecules with 'F-TEDA-BF_4'

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Abstract

The type of functionalization of an aromatic molecule achieved with 1-chloromethyl-4-fluoro-1,4-diazobicyclo-(2,2,2)octane bis-tetrafluoroborate, 'F-TEDA-BF_4', in trifluoroacetic acid depends on its structure: naphthalene and phenanthrene gave fluorinated products, anthracene gave the trifluoroacetate, while an addition process occurred with 9-methoxy-phenanthrene in methanol, and an addition–elimination process in trifluoroacetic acid.

Keywords: Solvent effects; Fluorination; Aromate molecules; F-TEDA-BF_4; Structural effects; Addition processes

The selective direct introduction of fluorine into aromatic molecules is still only a partly solved problem and, in addition to hydrogen substitution, replacement of other substituents, addition processes and the polymerization processes are also observed, especially if hydroxy or alkoxy substituents are present [1]. The course of an aromatic molecule's transformation depends on the reagent used (F_2, CF_3OF, CF_3COOF, XeF_2), on the structure of the organic molecule and on the very important rule of reaction conditions (solvent, temperature, concentration, the method of mixing the substrate and reagent, etc.) as has been already pointed out [2]. Recently, various types of *N*-fluoro compounds have been found to be appropriate fluorine sources for milder introduction into organic molecules [3]. A very important breakthrough was achieved by Banks and coworkers [4] with the preparation of 1-alkyl-4-fluoro-1,4-diazobicyclo-(2,2,2)octane salts which are handled very easily, especially the tetrafluoroborate salts, which are now commercially available as F-TEDA-BF_4 [5]. Functionalization of the benzene ring with this new reagent was achieved by the conversion of Grignard reagents [4]; however, methyl-substituted benzene derivatives (toluene, xylenes) required very long reaction times in acetonitrile [6].

Polyaromatic molecules are more reactive than benzene; however, we found that 24 h reaction of naphthalene with F-TEDA-BF_4 in acetonitrile under reflux gave only 30% of the fluorinated product. However, a 4 h reaction in trifluoroacetic acid at 70 °C gave 1- and 2-fluoronaphthalene (3:1 ratio) in 75% yield (Scheme 1). The similar reaction of phenanthrene gave 9-fluoro-phenanthrene (75%), while another type of functionalization was observed with anthracene and 9-trifluoroacetoxy anthracene was isolated in 60% yield[1].

In addition, we have studied the effect of solvent on the course of functionalization of 9-methoxy- and 9-hydroxy-phenanthrene with F-TEDA-BF_4 and found that the transformations are indeed strongly directed by the solvent used. In trifluoroacetic acid, the use of an equimolar amount of the reagent transforms 9-methoxy-phenanthrene, following an addition–elimination process, into 9-fluoro-10-methoxy-phenanthrene. In methanol, an addition reaction resulting in the formation of 9-fluoro-10,10-dimethoxy-9,10-dihydrophenanthrene occurred exclusively. In acetonitrile, demethylation was observed, forming 9-fluoro-10-hy-

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[1] In a typical experiment, 1 mmol of phenanthrene was suspended in 5 ml of trifluoroacetic acid, 1.1 mmol of F-TEDA-BF_4 was added and the reaction mixture heated at 70 °C for 4 h. After cooling, the solvent was evaporated in vacuo, the oil product poured into water, extracted with methylene chloride and purified by TLC when a 75% yield of 9-fluoro-phenanthrene was obtained.

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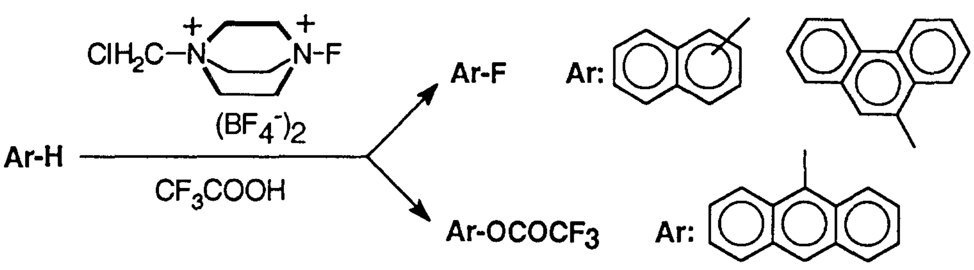
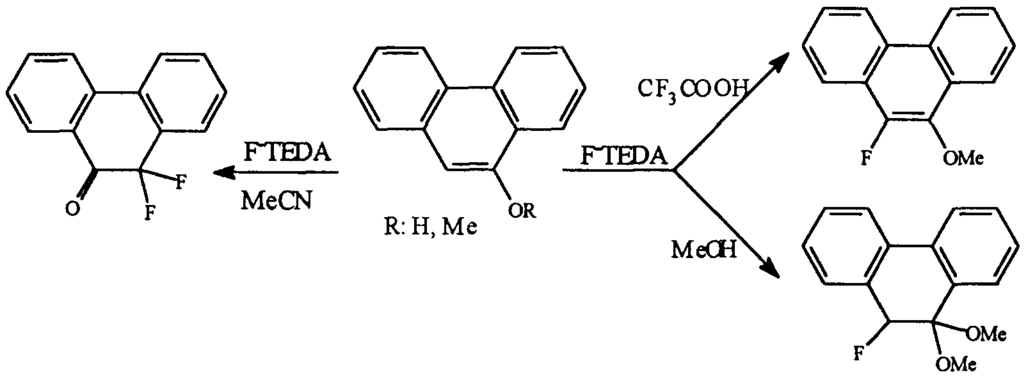


Scheme 1.



Scheme 2.

droxy-phenanthrene (Scheme 2), which reacted further to give 9,9-difluoro-10-oxo-9,10-dihydro-phenanthrene. In the case of 9-hydroxy-phenanthrene, functionalization not only depends on the solvent used, but also on the way the reagent is added to the reaction mixture. In all three solvents, immediate addition of an equimolar amount of the reagent resulted in a mixture of 9-fluoro-10-hydroxy-phenanthrene and 9,9-difluoro-10-oxo-9,10-dihydro-phenanthrene, the first being predominant. With slow addition over a 0.5 h period, exclusive formation of the 9,9-difluoro-10-oxo-9,10-dihydro derivative was found when using acetonitrile or trifluoroacetic acid as solvents, and the same derivative was predominant in the methanol-mediated reaction. Using a twofold molar excess of F-TEDA-BF_4 in acetonitrile, transformation of 9-hydroxy- and 9-methoxy-phenanthrene into 9,9-difluoro-10-oxo-9,10-dihydro-phenanthrene was achieved in more than 85% yield.

The present results confirmed that F-TEDA-BF_4 appears to be a very promising reagent for the mild and selective introduction of fluorine into aromatic molecules, and further studies on the use of this new reagent for the functionalization of aromatic and heteroaromatic molecules are in progress.

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