Selective and Efficient Direct Fluorination of Polycyclic Aromatic Hydrocarbons Using 1-Fluoro-4-hydroxy-1,4-diazoniabicyclo[2.2.2]octane Bis(tetrafluoroborate)

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A new N-F fluorinating reagent 1-fluoro-4-hydroxy-1,4-diazoniabicyclo[2.2.2]octane bis(tetrafluoroborate) (*Accufluor™ NFTh)* was effectively used for selective fluorination of polycyclic aromatics. Naphthalene was site-selectively fluorinated to 1-fluoronaphthalene, phenanthrene to 9-fluorophenanthrene, and pyrene to 1-fluoropyrene. In a series of substituted naphthalenes the regioselectivity and effectiveness of fluorination depended on the position and the nature of the substituents.

The well established role of a fluorine atom on the biological activity of organic molecules[1] aroused a certain interest in the wider scientific community and intense research in this field of organic chemistry[2] in recent decades. The development of a variety of new reagents and methods for fluorination of organic molecules resulted from these efforts, but a considerable breakthrough was achieved after introduction of reagents incorporating a reactive N-F bond, [3] recently culminating in the promotion of 1-fluoro-4-alkyl-1,4-diazoniabicyclo[2.2.2]octane salts[4] as versatile fluorinating reagents.[5]

Fluorine-substituted polycyclic aromatic hydrocarbons (FPAH) are of interest in experimental carcinogenesis as useful synthons.[6] Some attempts have been made to achieve direct one-step fluorofunctionalization of PAH with varying success as concerns selectivity and efficiency using XeF_2 ,[7] $CsSO_4F$ [8] and F-TEDA-BF_4 .[5] We now report that a new member of the series of 1,4-diazoniabicyclo[2.2.2]octane salts, 1-fluoro-4-hydroxy-1,4-diazoniabicyclo[2.2.2]octane bis (tetrafluoroborate)[9] (**1**, *Accufluor™ NFTh),* is an effective reagent for direct site-selective introduction of a fluorine atom into PAH under mild reaction conditions.

Fluorination of naphthalene with NFTh in acetonitrile solution was found to be very regioselective and resulted in formation of 1-fluoronaphthalene in high yield (**4a**, Scheme).

The nature of the substituent and its position considerably influenced the course and the efficiency of the fluorination of substituted naphthalene derivatives with NFTh. 1-Fluoronaphthalene was converted to a mixture of 1,4-difluoro- (**4b**) and 1,2-difluoronaphthalene (**3b**) in 5.5 : 1 relative ratio and moderate yield, while the fluorination of 1-methylnaphthalene (**2c**) resulted in a 3 : 1 mixture of para (**4c**) and ortho (**3c**) fluorinated products, also accompanied with the 2,4-difluoro substituted derivative (**Table 1**). The fluorination of 1-naphthole (**2d**) and 1-methoxynaphthalene (**2e**) resulted in the formation of equimolar amounts of both ortho and para isomers, and the ortho fluorination was found to be predominant again in the case of treatment of 1-*i*-propoxylnaphthalene (**2f**). Regiospecific formation of 1-fluoro-2-substituted naphthalenes in over 85% yield was observed when a series of naphthalene derivatives substituted with an electron donating substituent bonded to position 2 was fluorinated with NFTh in acetonitrile. In the case of 2-hydroxy or 2-methoxy derivatives, the primarily

Table 1. Fluorination of Naphthalene (**2a**) and its 1-Substituted Derivatives (**2b-f**) with Accufluor™ NFTh [a]

X	r. time [min]	rel. distrib.[b] of fluorinated prods. [%] **3**	**4**	**other**	yield [c] [%]
H	30	<2	90	8[d]	82
F	180	15	85	/	65
Me	180	22	68	10[e]	65
OH	10	45	42	13[f]	80
OMe	15	48	48	4[f]	85
OiPr	10	68	30	2[f]	85

[a]Standard reaction conditions: 1 mmol of substrate **2**, 15 mL of MeCN, 1.05 mmol of reagent **1**, stirring at 80°C; [b]Determined from ^{19}F NMR spectra of crude reaction mixture; [c]Determined from ^{19}F NMR spectra of crude reaction mixture with $C_{10}F_8$ as internal standard and calcd. on starting material; [d]1,4-Difluoronaphthalene; [e]2,4-Difluoro-1-methylnaphthalene; [f]2,2-Difluoro-1(*2H*)-naphthalenone.

Scheme.

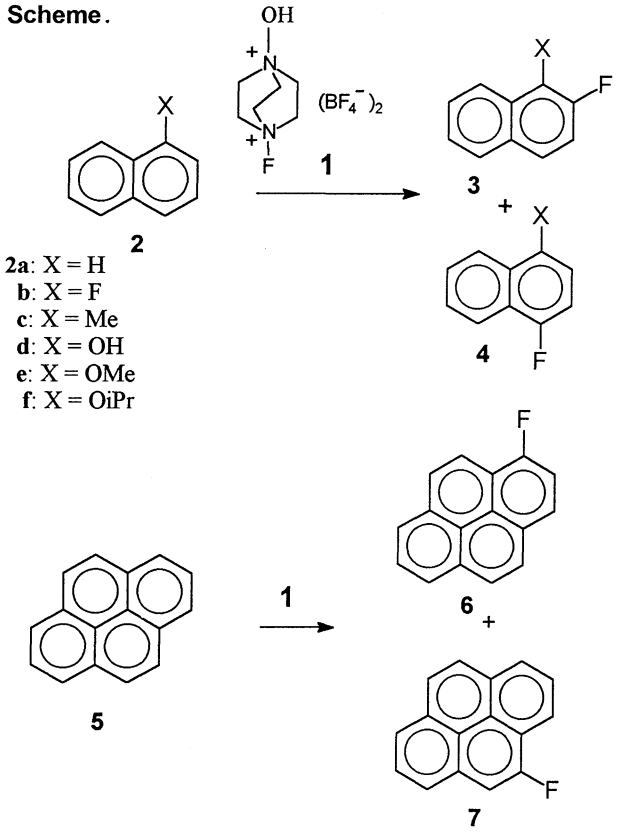

Table 2. The effect of reaction conditions on the fluorination [a] of pyrene with Accufluor™ NFTh

			relative distr.of prods.[b]			
entry	temp [°C]	time [min]	**6**	**7**	**di-F**	yield[%][c]
1	80	5	63	22	15	80
2	60	30	64	16	20	75
3	22	60	85	11	4	75
4	10	150	90	10	<1	75
5	5	300	93	7	<1	75

[a] Standard reaction conditions: 1 mmol of substrate, 20 mL of MeCN, 1.05 mmol of reagent **1**, stirring; [b]Determined from ^{19}F NMR spectra of crude reaction mixture; [c]Overall yield of fluorinated products determined from ^{19}F NMR spectra of crude reaction mixture with $C_{10}F_8$ as internal standard and calcd. on starting material.

formed products were further fluorinated to 1,1-difluoro-2(*1H*)-naphthalenone. A mixture of both products in 7 : 3 relative ratio was isolated when 1-hydroxy or 1-methoxynaphthalene were treated with an equimolar amount of NFTh, while the use of a 2.2 fold excess of the reagent resulted in almost quantitative formation of 1,1-difluoro-2(*1H*)-naphthalenone.[10]

Phenanthrene was selectively transformed into 9-fluorophenanthrene in 85% yield after 5 min reaction with NFTh in anhydrous MeCN solution under reflux, while pyrene (**5**) under the same reaction conditions gave a mixture of 1- (**6**) and 4-fluoropyrene (**7**), also accompanied by 1,4-difluoropyrene. The regioselectivity and the degree of overfluorination could be regulated by reaction conditions. By lowering the reaction temperature and prolonging the reaction time almost regioselective formation of 1-fluoropyrene could be achieved (Table 2) in reasonable yield.

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References and Notes

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