Fluorination with Xenon Difluoride. 23. Fluorination of Ortho Substituted Aromatic Molecules

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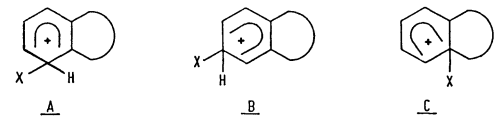
The fluorination of 9,10-dihydroanthracene and triptycene with xenon difluoride in the presence of hydrogen fluoride occurred at α and β position with β attack predominating over α attack, while the reaction with acenaphthene resulted in the formation of 2- and 4-fluorosubstituted products, regioselectivity being very little affected by the nature of the catalyst: hydrogen fluoride, boron trifluoride and pentafluorothiophenol. The fluorination of 1,2,3,4-tetrahydro-1,4-methanonaphthalene resulted in the formation of 6-fluoro-1,2,3,4-tetrahydro-1,4-methanonaphthalene, 6,7-difluoro-1,2,3,4-tetrahydro-1,4-methanonaphthalene and rearranged product 1-(2,2-difluoroethyl)indan.

It has been demonstrated that xenon difluoride is a mild fluorinating agent for the fluorination of alkenes, acetylenes, aromatic and heteroaromatic molecules, which has been recently reviewed.[1] It is known that the mechanism of the fluorination of organic molecules with xenon difluoride depends on the following factors: the structure of the molecules, the catalyst used, solvent polarity and temperature, and the formation of free radical intermediates, ion radical intermediates and fluorocarbonium ions has been suggested. It has been demonstrated that the following substrates are convenient catalyst: hydrogen fluoride, hydrogen fluoride–pyridine, trifluoroacetic acid, boron trifluoride etherate, boron trifluoride, pentafluorothiophenol, and bromine.

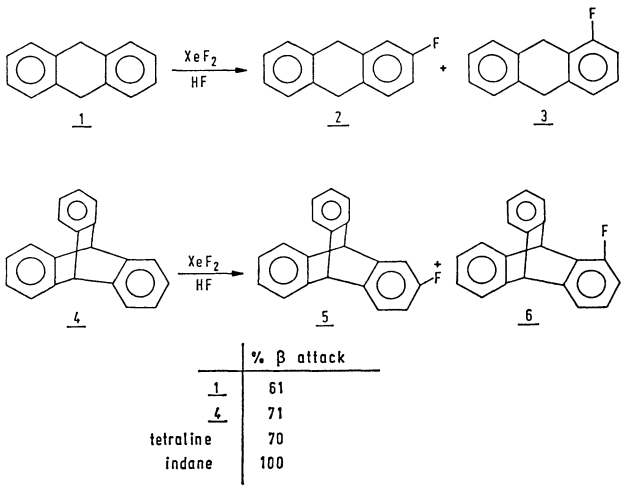
The electrophilic substitution reactions of ortho substituted aromatic molecules received considerable attention from different points of view.[2] There are three possible attacks of electrophilic agent which leads to α, β, or ipso substituted products. The regioselectivity of the substitution depends on the nature of the substituents on the ortho position. We have recently found[3] that the regioselectivity in fluorination of indan, tetralin, and *o*-xylene with XeF_2 has been explained by differences in the stabilization of carbonium ions A and B (Scheme 1) formed after α and β attack of electrophile. We now report results of further investigations on the effect of the structure of orthosubstituted aromatic molecules on regioselectivity in fluorination reactions with xenon difluoride.



Scheme 1.

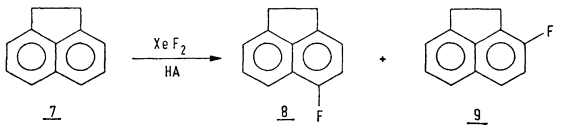
Results and Discussion

Under conditions usually used for the fluorination of organic molecules (1 mmol of organic substrate in 2—5 ml of dichloromethane, 1 mmol of xenon difluoride and hydrogen fluoride as catalyst), polymeric materials resulted in the case of 9,10-dihydroanthracene (**1**), triptycene (**4**), and acenaphthene (**7**). We have found that a much higher dilution (50 ml of solvent for 1 mmol of substrate) must be used. The reaction with 9,10-dihydroanthracene (**1**, Scheme **2**) was completed in 20 min and the reaction mixture was isolated by the usual work-up procedure. The crude reaction mixture shows in its ^{19}F NMR two signals: −126 ppm (dd, 39%) and −137.7 ppm (m, 61%). The products were separated by preparative TLC: 2-fluoro-9,10-dihydroanthracene (**2**), and 1-fluoro-9,10-dihydroanthracene (**3**) were isolated. The fluorination of triptycene (**4**) resulted also in the formation of two products: 2-fluorotriptycene (**5**) and 1-fluorotriptycene (**6**), separated by preparative TLC. It can be seen (Scheme 2) that the regioselectivity of the fluorine attack on triptycene is very similar to that in tetralin,[3] while in the case of 9,10-dihydroanthracene a lower regioselectivity was observed. In both cases, the yields of isolated products (**2**, **3**, **5**, and **6**) were considerably lower than those reported for the fluorination of indan or tetralin,[3] which can be ascribed to a significant amount of polymeric materials formed.



Scheme 2.

The fluorination of acenaphthene (**7**, Scheme 3) must be also carried out in a higher dilution than usual and this resulted in the formation of two products. The structures of the products 3-fluoroacenaphthene (**9**) and 5-fluoroacenaphthene (**8**) were established on the basis of the spectroscopic data, which are in agreement with those in the literature.[5] We have also studied the effect of catalyst (Scheme 3, relative yields) on the regioselec-

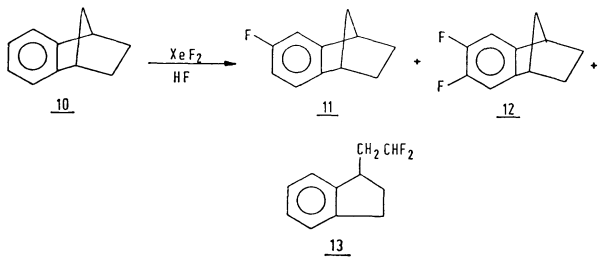


HA	% 8
HF	74
BF_3	74
C_6F_5SH	70

Scheme 3.

tivity of the substitution and found that it is very little influenced. However, it reflected on the yields of products formed. The reaction in the presence of hydrogen fluoride resulted in 50% formation of products **8** and **9**, while the reaction catalyzed by boron trifluoride resulted in only 20% formation of **8** and **9** and was accompanied by a higher amount of polymeric material. The reaction in 50 ml of dichloromethane and in the presence of pentafluorothiophenol was very slow, while the reaction in 10 ml of dichloromethane gave results comparable to those found by HF-catalyzed reaction in a higher dilution (50 ml of dichloromethane).

The fluorination of 1,2,3,4-tetrahydro-1,4-methanonaphthalene (**10**, Scheme 4) resulted in the formation of three products. ^{19}F NMR spectrum of the crude



Scheme 4.

reaction mixture shows three signals: −116 ppm (dt, 26%), −118 ppm (m, 63%), and −142.5 ppm (t, 11%). The products were isolated by preparative GLC, and on the basis of spectroscopic data we have established that the lowest signal in ^{19}F NMR corresponds to 1-(2,2-difluoroethyl)indan (**13**); the next signal to 6-fluoro-1,2,3,4-tetrahydro-1,4-methanonaphthalene (**11**), and the last signal to 6,7-difluoro-1,2,3,4-tetrahydro-1,4-methanonaphthalene (**12**).

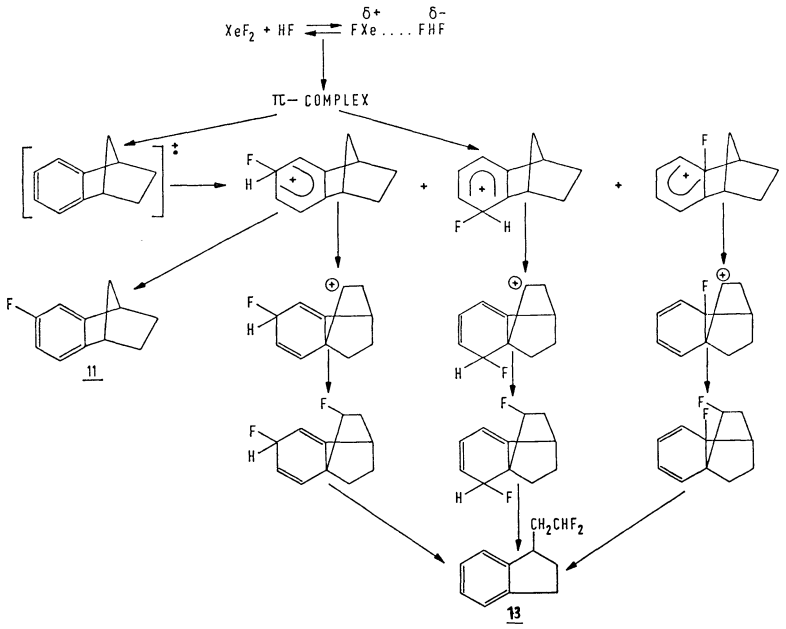
The mechanism of the fluorination with xenon difluoride is very similar to those already suggested.[3] However, on Scheme 5, three possible pathways which can explain the formation of rearranged 1-(2,2-difluoroethyl)indan (**13**) formed by the fluorination of **10**, are presented. The rearranged product could result from three different intermediates, formed after α, β, or ipso attack, followed by a two-step rearrangement.

Experimental

IR spectra were recorded by using a Perkin-Elmer 727 B spectrometer and ^1H and ^{19}F NMR spectra by JEOL-JNM-PS 100 from CCl_4 or $CDCl_3$ solutions with Me_4Si or CCl_3F as internal reference. Mass spectra and high resolution measurements were taken on a CEC 21-110 spectrometer. Gas liquid partition chromatography was carried out on Varian Aerograph Model 1800 and TLC on Merck PSC Fertigplatten Silica gel F 254 (activated for 3 h at 120 °C before use).

Materials. 9,10-Dihydroanthracene and acenaphthene are commercially available and were crystallized before use. Triptycene[6] and 1,2,3,4-tetrahydro-1,4-methanonaphthalene[7] were synthesized. Hydrogen fluoride and boron trifluoride of Fluka Purum quality were used without further purification. Dichloromethane was purified[8] and stored over molecular sieves. Xenon difluoride was prepared by a photosynthetic method[9] and its purity was higher than 99.5%.

1-Fluoro-9,10-dihydroanthracene (3) and 3-Fluoro-9,10-dihydroanthracene (2). To a solution of 1 mmol of **1** in dichloromethane (50 ml), 1 mmol of xenon difluoride was added at



Scheme 5.

25 °C and, under stirring, a catalytic amount of HF was introduced into the reaction mixture. After a few seconds, the colorless solution turned dark blue and xenon gas slowly evolved. After 20 min the gas evolution ceased and the reaction appeared to be complete. The reaction mixture was washed with 10 ml of 5% $NaHCO_3$ aq solution and water, and dried over anhydrous sodium sulfate. The solvent was evaporated *in vacuo*. The crude reaction mixture was separated by preparative TLC (cyclohexane: chloroform=9: 1). 2-Fluoro-9,10-dihydroanthracene (**2**): 42 mg (21%), mp 112—114 °C, NMR spectra: $\delta F = -137.7$ ppm, $\delta H = 3.2$ ppm (broad s, 4H), 7.0—8.1 ppm (m, 7H); mass spectrum: *m/e* 198 (M^+, 100%), 197 (23), 196 (18), 184 (24), 183 (17), 165 (28), 163 (17), 135 (33), 133 (28), 122 (89), 119 (22), 117 (22), 96 (10). Found: C, 84.64; H, 5.29%. Calcd for $C_{14}H_{11}F$: C, 84.82; H, 5.59%. 1-Fluoro-9,10-dihydroanthracene (**3**): 18 mg (9%), mp 76—78 °C, NMR spectra: $\delta F = -126$ ppm, $\delta H = 3.14$ ppm (broad s, 4H), 7.1—8.3 ppm (m, 7H); mass spectrum: *m/e* 198 (M^+, 100%), 197 (23), 184 (21), 183 (24), 135 (35), 133 (22), 123 (25), 122 (64), 109 (72), 96 (25). Found: C, 84.62; H, 5.28%. Calcd for $C_{14}H_{11}F$: C, 84.82; H, 5.59%.

*1-Fluorotriptycene (**6**) and 2-Fluorotriptycene (**5**).* The fluorination and work-up procedure were essentially the same as described for **2** and **3**. The products were separated by preparative TLC (petroleum ether: $CHCl_3$=19: 1). 1-Fluorotriptycene (**6**): 34 mg (12%), mp 243—245 °C, (lit,[10] mp 246—247 °C), NMR spectra: $\delta F = -120$ ppm (m), $\delta H =$ 5.4 ppm (d, $J = 1.5$ Hz, 1H), 5.75 ppm (broad s, 1H), 6.6—7.5 ppm (m, 11H); mass spectrum: *m/e* 272 (M^+, 100%), 271 (35), 196 (77), 195 (45), 180 (37), 179 (45), 135 (38), 123 (18), 122 (42), 120 (58), 102 (32), 77 (42), 76 (35). 2-Fluorotriptycene (**5**): 64 mg (23%), mp 228—230 °C (lit,[11] mp 232—234 °C), NMR spectra: $\delta F = -122.25$ ppm (m), $\delta H =$ 5.3 ppm (broad s, 2H), 6.6—7.6 ppm (m, 11H); mass spectrum: *m/e* 272 (M^+, 100%), 271 (42), 197 (25), 196 (87), 195 (43), 180 (16), 179 (33), 135 (29), 122 (21), 120 (79), 119 (26), 117 (26), 102 (39), 77 (17), 76 (46).

*3-Fluoroacenaphthene (**9**) and 5-Fluoroacenaphthene (**8**).* To a solution of 1 mmol of **7** in dichloromethane (50 ml in the case of HF, BF_3, and C_6F_5SH catalyzed reaction, and 10 ml in the second experiment catalyzed by C_6F_5SH), 1 mmol of xenon difluoride was added at 25 °C and, under stirring, a trace amount of catalyst (HF or BF_3, and 1 mmol in the case of C_6F_5SH) was introduced into the reaction mixture. After the work-up procedure, the crude reaction mixture was analyzed by ^{19}F NMR, and the relative yields of products **8** and **9** are presented in Scheme 3. We were unable to separate the two isomers, although many different stationary phases in GLC and various solvent systems in TLC were examined. Both isomers were purified by preparative GLC (FFAP-10%, Crom AW, $T = 120$ °C) and the following percentages of the mixture of **8** and **9** were isolated: 50% in the case of HF-catalyzed reaction, 20% in the case of BF_3, and 45% in the case of C_6F_5SH. The reaction mixture shows in its ^{19}F NMR spectrum two signals: $\delta F = 126.75$ ppm ($\delta F_{lit} = -123.58$ ppm for 3-fluoroacenaphthene (**9**)[5]) and -134.25 ppm ($F_{lit} = -131.44$ ppm for 5-fluoroacenaphthene (**8**)[5]).

*Fluorination of 1,2,3,4-Tetrahydro-1,4-methanonaphthalene (**10**).* The fluorination and work-up procedure were essentially the same as described for **2** or **3**. Products were separated by preparative GLC (FFAP-10%, Crom AW, $T = 130$ °C). 6-Fluoro-1,2,3,4-tetrahydro-1,4-methanonaphthalene (**11**): 52 mg (32%) of volatile liquid product, NMR spectra: $\delta F = -118$ ppm (m, $J = 10.5$ Hz and 6 Hz), $\delta H = 1.2$ ppm (m, 2H), 1.75 ppm (m, 4H), 3.3 ppm (broad s, 2H) and 6.8 ppm (m, 3H); mass spectrum, Calcd for $C_{11}H_{11}F$ *m/e* 162.0844, Found 162.0849, *m/e*: 162 (M^+, 47%), 150 (13), 147 (31), 146 (21), 135 (20), 134 (100), 133 (74), 121 (12), 119 (36), 117 (54), 116 (34), 115 (32), 84 (14), 63 (12), 57 (14). 6,7-Difluoro-1,2,3,4-tetrahydro-1,4-methanonaphthalene (**12**): 13 mg (7%) of volatile liquid product, NMR spectra: $\delta F = -142.5$ ppm (*t*, $J = 9$ Hz), $\delta H = 1.2$ ppm (m, 2H), 1.75 ppm (m, 4H), 3.3 ppm (broad s, 2H), 6.9 ppm (m, 2H); mass spectrum, Calcd for $C_{11}H_{10}F_2$ *m/e* 180.0767, Found: 180.0774, *m/e* 180 (M^+, 26%), 165 (16), 162 (42), 152 (75), 151 (30), 147 (18), 146 (14), 134 (63), 133 (32), 116 (100), 115 (44), 56 (30). 1-(2,2-Difluoroethyl)indan (**13**): 18 mg (10%) of volatile liquid product, NMR spectra: $\delta F = -116.25$ ppm (dt, $J = 60$ Hz and 15 Hz), $\delta H = 1.8$ (m, 2H), 2.31 ppm (tdd, $J = 15$ Hz, 6 Hz and 6 Hz, 2H), 2.85 ppm (t, $J = 6$ Hz, 2H), 3.27 ppm (m, 1H), 5.82 ppm (tt, $J = 60$ Hz and 6 Hz, 1H), 7.05 ppm (m, 4H); mass spectrum: Calcd for $C_{11}H_{12}F_2$ *m/e* 182.0907, Found 182.0896, *m/e*: 182 (M^+, 16%), 117 (100), 116 (16), 115 (36), 91 (16), 51 (15).

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