Thermically-Initiated Fluorinations at Saturated Carbon Atoms with Xenon Difluoride

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Synopsis. The heating of several hydrocarbons with xenon difluoride at 95—120 °C in stainless steel reactors equipped with teflon jackets resulted in mono-, di-, and trisubstituted products.

It has been demonstrated that xenon difluoride reacts with several types of organic molecules but the main interest was directed towards the fluorination of alkenes, aromatic, and heteroaromatic molecules.[1–3] In most cases fluorinations have been carried out in a liquid phase and the presence of an appropriate catalyst has also been pointed out. On the other hand much less attention has been paid to reactions carried out at higher temperatures or in the vapor phase. Fourteen years ago Mackenzie and Fajer[4] reported that xenon difluoride also reacted with several aromatic molecules at temperatures between 100—200 °C but substitution reactions were also accompanied by the additional process, their extension depending on the structure of the substrate, molar ratio of xenon difluoride to the starting compound and temperature.

In our continuous interest in the fluorination of organic compounds with xenon difluoride we found it instructive to investigate reactions with several saturated hydrocarbons.

Results and Discussion

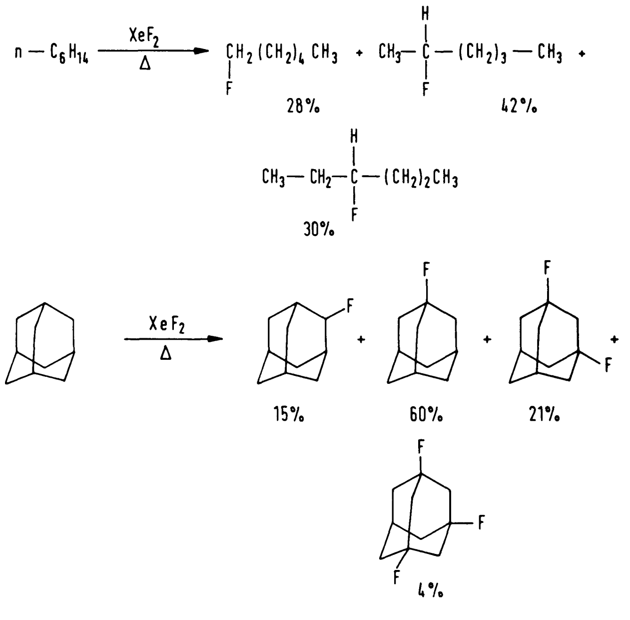
Direct substitution of hydrogen at a saturated carbon atom by fluorine represents a different problem from that of the introduction of chlorine or bromine[5] and several special techniques have been developed.[6] Adcock and coworkers[7] made an important contribution to direct fluorine introduction using a low temperature reaction of fluorine with an aerosol suspension of hydrocarbons. Barton and coworkers[8] recently found that functionalization of saturated carbon atoms is also possible with fluorine or CF_3OF but only one report on direct hydrogen atom substitution with xenon difluoride appeared and experimental details were so sparse that we were unable to repeat the direct fluorination of adamantane in CS_2 which should result in the formation of 1-fluoroadamantane.[9] Patrick and coworkers[10] have recently demonstrated that functionalization of a saturated carbon atom is also possible by xenon difluoride and they found that carboxylic acids are transformed to fluoro-substituted products by decarboxylation.

Mixtures of 2 mmols of several hydrocarbons, e.g. hexane or adamantane, with 2 mmols of xenon difluoride were heated in 20 ml sealed glass tubes up to 70 °C no reaction occurred. Further increases in temperature to 80—90 °C resulted in a violent reaction accompanied by flame and a complete decomposition of xenon difluoride, and the crude reaction mixture containing a small amount of unreacted substrate, hydrogen fluoride and tar was obtained. We then replaced the glass ampoules with 35 ml reflon jackets inserted in stainless steel containers and found that the heating of 2 mmols of cyclohexane and 2 mmols of xenon difluoride at 105 °C resulted in the complete decomposition of xenon difluoride. Again only tar was obtained. However, when the 35 ml teflon reactor was filled with 15 mmols of cyclohexane and 3 mmols of xenon difluoride and the mixture was heated for 2.5 h at 105 °C, the reaction mixture containing fluorocyclohexane with 18% yield (calculation based on xenon difluoride) was obtained. Reproducible fluorination of cyclohexane with xenon difluoride under the above-mentioned conditions could be observed only when the teflon jacket was thoroughly cleaned and dried.

The 2.5 h reaction of 15 mmols of hexane and 3 mmols of xenon difluoride at 105 °C resulted in the formation of three monofluoro-substituted products with a total yield of 15—20% (calculation based on xenon difluoride). Product distributions were determined by ^{19}F NMR and a good reproducibility of product distribution was observed (data stated in the Scheme are the average of three experiments and differ by only ±2%). It is evident from the product distribution that secondary carbon atoms are more reactive than primary to fluorine substitution by xenon difluoride.

Free radical reactions with adamantane have been studied in detail with the relative reactivity of C_1 and C_2 carbon strongly depending on the reagent, i.e. reaction with R_2N^+H proceeds 99% at C_1, reaction with $^\cdot CCl_3$ proceeds 86% at C_1 while chlorination in CCl_4 yields nearly equivalent amounts of 1- and 2-chloroadamantane.[11] The 70 min reaction of 2 mmols of adamantane and 2 mmols of xenon difluoride in a teflon reactor at 105 °C gave a crude reaction mixture containing four fluoro-substituted products. Total yield of fluoro-substituted products, calculation based on xenon difluoride, was 18—20%. The yield of fluoro-substituted products was nearly doubled when instead of 2 mmols only 1 mmol of adamantane was used in the presence of 2 mmols of xenon difluoride while product distribution was only slightly influenced. Crude reaction mixtures were analyzed by ^{19}F NMR spectroscopy and product distribution resulting in the experiment using 2 mmols of adamantane is presented in the Scheme.

SCHEME



Pure samples of products were isolated by preparative GLC and structures were determined on the basis of spectroscopic data and their comparison with the literature. From the product distribution it is evident that the difference in reactivity between the secondary and tertiary carbon atoms in adamantane is much larger than that observed in hexane between the primary and secondary carbon atoms.

Experimental

IR spectra were recorded using a Perkin Elmer 727-B spectrometer and ^{1}H and ^{19}F NMR spectra by a Jeol JNM-PS-100 with Me_4Si or CCl_3F as the internal reference. Mass spectra and high resolution measurements were taken on a CEC-21-110 spectrometer. Gas liquid partition chromatography was carried out on a Varian 2700 Model.

Fluorination of Cyclohexane and Hexane. 15 mmols of hexane or cyclohexane and 3 mmols of xenon difluoride were placed in a teflon jacket (35 ml) which was inserted into a stainless steel container. The reaction mixture was heated for 150 min at 105±2 °C, cooled, after which 20 ml of ether was added to the reaction mixture, washed with aqueous $NaHCO_3$, water (twice), dried over Na_2SO_4, and the solvent partly evaporated under vacuum. Crude reaction mixtures were analyzed by ^{19}F NMR (octafluoronaphthalene was added as the internal standard). Fluorination of hexane resulted in the formation of three products with a total yield of 20% of fluoro-substituted products (calculation based on xenon difluoride). The crude reaction mixture contained the following three products: 1-Fluorohexane,[12] 2-fluorohexane,[13] and 3-fluorohexane[14] with relative yields of 28±2, 42±2, and 30±2%, respectively. The fluorination of cyclohexane gave only one product with a yield of 18% (calculation based on xenon difluoride) while pure fluorocyclohexane was isolated by preparative GLC (OV 17 10%, Chromosorb A 45/60, 60 °C), with 12% yield. Spectroscopic data are in agreement with those in the literature.[15]

Fluorination of Adamantane. 2 mmols of adamantane and 2 mmols of xenon difluoride were placed in a teflon jacket (35 ml) which was inserted into a stainless steel container. The reaction mixture was heated for 70 min at 105±2 °C, cooled and then 20 ml of ether were added to the reaction mixture, washed with aqueous $NaHCO_3$, water (twice), dried over Na_2SO_4, and the solvent evaporated under vacuum. The crude reaction mixture was analyzed by ^{19}F NMR, indicating the presence of four products: 1-fluoroadamantane, 2-fluoroadamantane, 1,3-difluoroadamantane, and 1,3,5-trifluoroadamantane with the following relative yields (determined by ^{19}F NMR): 60±2, 15±2, 21±3, and 4±0.5%, respectively. Separation of the combined crude reaction mixtures, obtained in three experiments, by GLC (OV-17 10%, Chromosorb A 45/60, 110 °C) gave pure 1-fluoroadamantane, 1,3-difluoroadamantane, and the mixture of 2-fluoroadamantane and 1,3,5-trifluoroadamantane, which were further separated by GLC (DNP 10% 3 m, Chromosorb W HP 80/100, 150 °C).

1-Fluoroadamantane: 35 mg (7.6%) of crystalline product, mp (sealed tube) 210—212° (mp$_{\mathrm{lit}}$ 210—212 °C),[16] NMR δF: −129.3 (broad s), δH: 1.6 (m, 6H), 1.9 (m, 6H), 2.2 (broad s, 3H). Mass spectrum: Calcd. for $C_{10}H_{15}F$ *m/z* 154.1158, found *m/z* 154.1155, *m/z* (rel intensity) 155 (M^++1, 11%), 154 (M^+, 87), 111 (20), 98 (39), 97 (100), 96 (34), 94 (21), 93 (31), 91 (10), 79 (19), 77 (14), 67 (12), 53 (10), 43 (26), 41 (24), 39 (27).

2-Fluoroadamantane: 8 mg (1.7%) of crystalline product, mp (sealed tube) 254—255 °C (mp$_{\mathrm{lit}}$ 254—255 °C),[17] NMR δF=−175 (dm, $^2J_{FH}$=51 Hz), δH=1.7 (m, 10H), 2.1 (m, 4H), 4.7 (dm, $^2J_{FH}$=51 Hz, 1H). Mass spectrum: Calcd for $C_{10}H_{15}F$ *m/z* 154.1158, found *m/z* 154.1160, *m/z* (rel intensity) 155 (M^++1, 12%), 154 (M^+, 100), 114 (41), 111 (12), 98 (14), 97 (27), 96 (13), 95 (15), 93 (34), 92 (26), 91 (19), 81 (13), 80 (21), 79 (51), 78 (15), 77 (17), 67 (17), 56 (12), 55 (10), 53 (12), 41 (25).

1,3-Difluoroadamantane: 13 mg (2.5%) of crystalline product, mp 239—240° (mp$_{\mathrm{lit}}$ 240—241 °C),[16] NMR δF=−137 (broad s), δH=1.5 (broad s, 2H), 1.8 (m, 8H), 2.1 (t, $^3J_{FH}$=5.5 Hz, 2H), 2.5 (broad s, 2H). Mass spectrum: Calcd for $C_{10}H_{14}F_2$ *m/z* 172.1063, found *m/z* 172.1065, *m/z* (rel intensity) 173 (M^++1, 8%), 172 (M^+, 66), 116 (25), 115 (89), 114 (31), 111 (32), 110 (10), 109 (10), 97 (52), 96 (17), 93 (15), 91 (10), 77 (13), 59 (14), 58 (44), 56 (19), 51 (10), 43 (100), 42 (13), 41 (22).

1,3,5-Trifluoroadamantane: 2.2 mg (0.5%) of crystalline product, mp (sealed tube) 243—245 °C (mp$_{\mathrm{lit}}$ 244—245 °C),[16] NMR δF=−142 (broad s), δH=1.8 (m, 6H), 2.1 (m, 6H), 2.5 (m, 1H). Mass spectrum: Calcd. for $C_{10}H_{13}F_3$ *m/z* 190.0969, found *m/z* 190.0966, *m/z* (rel intensity) 191 (M^++1, 10%), 190 (M^+, 91), 134 (22), 133 (81), 132 (28), 129 (28), 115 (100), 114 (14), 111 (26), 110 (10), 109 (16), 102 (10), 97 (18), 77 (13), 65 (10), 59 (26), 57 (14), 56 (67), 51 (17), 41 (18).

References

1) R. Filler, *Isr. J. Chem.*, **17**, 71 (1978).

2) M. Zupan, "Xenon Halide Halogenations" in "The Chemistry of Functional Groups, Supplement D," ed by S. Patai and Z. Rappoport, Wiley, New York (1983), p. 657.

3) M. Zupan, *Vestn. Slov. Kem. Druš.*, **31**, (Suppl.), 151 (1984).

4) D. R. MacKenzie, J. Fajer, *J. Am. Chem. Soc.*, **92**, 4994 (1970).

5) "The Chemistry of the Carbon-Halogen Bond," ed by S. Patai, Wiley, New York (1973), Vols. 1 and 2; de la Mare, P.B.D. "Electrophilic Halogenation," Cambridge University Press, Cambridge (1976).

6) W. A. Sheppard and C. M. Sharts, "Organic Fluorine Chemistry," W. A. Benjamin, New York (1969); R. D. Chambers, "Fluorine in Organic Chemistry," Wiley, New York (1973).

7) J. L. Adcock, K. Horita, and E. B. Renk, *J. Am. Chem. Soc.*, **103**, 6937 (1981).

8) D. H. R. Barton, R. H. Hesse, R. E. Markwell, and M. M. Pechet, *J. Am. Chem. Soc.*, **98**, 3034 (1976); D. Alker, D. H. R. Barton, R. H. Hesse, J. Lister-James, R. E. Markwell, M. M. Pechet, S. Rozen, T. Takeshita, and H. T. Toh, *Nouv. J. Chim.*, **4**, 239 (1980).

9) A. T. Podkhalyuzin and M. P. Nazarova, *Zh. Org. Khim.*, **11**, 1568 (1975).

10) T. B. Patrick, K. K. Johri, and D. H. White, *J. Org. Chem.*, **48**, 4158 (1983).

11) C. V. Smith and W. E. Billups, *J. Am. Chem. Soc.*, **96**, 4307 (1974).

12) G. Filipovich and G. V. D. Tiers, *J. Phys. Chem.*, **63**, 761 (1959).

13) R. A. Bartsch and J. F. Bunnett, *J. Am. Chem. Soc.*, **90**, 408 (1968).

14) J. K. Borchardt, J. C. Swanson, and W. H. Saunders Jr., *J. Am. Chem. Soc.*, **96**, 3918 (1974).

15) F. A. Bovey, W. W. Anderson, F. P. Hood, and R. L. Kornegay, *J. Chem. Phys.*, **40**, 3099 (1964).

16) K. S. Bhandari and R. E. Pincock, *Synthesis*, **9**, 655 (1974).

17) G. A. Olah, J. T. Welch, D. Y. Vankar, M. Nojima, I. Kerekes, and J. A. Olah, *J. Org. Chem.*, **44**, 3872 (1979).