Fluorination with Xenon Difluoride. Reaction with Phenyl-Substituted Olefins[1]

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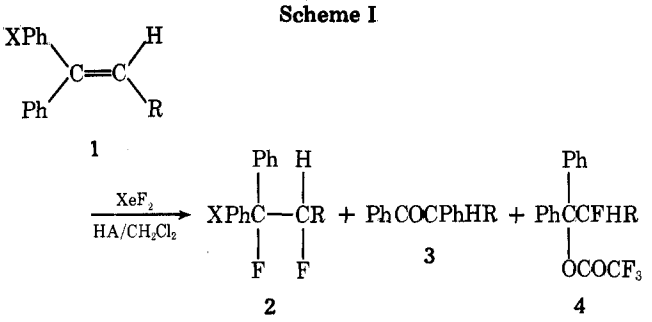
Xenon difluoride reacts with 1,1-diphenylethylenes in the presence of hydrogen fluoride or trifluoroacetic acid as catalyst to form the corresponding 1,2-difluoro-1,1-diphenylethanes in nearly quantitative yields. Reaction with 1,1-diphenyl-2-fluoroethene in the presence of trifluoroacetic acid results in 1,2,2-trifluoro-1,1-diphenylethane and 2,2-difluoro-1,1-diphenyl-1-trifluoroacetoxyethane. Reaction with styrenes gives vicinal difluorides in lower yield.

Filler and co-workers[2-6] have demonstrated the utility of xenon difluoride as a selective fluorinating agent of aromatic compounds in the liquid phase. Furthermore, Mackenzie and Fajer[7] have fluorinated aromatic compounds in the vapor phase, but only limited data are available on fluorine addition to olefins with this reagent.[8] In the course of our efforts to elucidate the reaction of xenon difluoride with olefins, we found it instructive to fluorinate some 1,1-diphenylethylenes and substituted styrenes. The fluorination of 1,1-diphenylethylene has been achieved with a variety of reagents such as lead tetraacetate–hydrogen fluoride,[9] aryliodoso difluorides,[10] and molecular fluorine at low temperatures.[11] The process with lead tetraacetate–hydrogen fluoride and aryliodoso difluorides led to rearranged products, e.g., phenyl migration to yield 1,1-difluoro-1,2-diphenylethane[9,10] and fluorination with molecular fluorine[11] gave both addition and substitution products.

The preparation of fluoroalkanes represents a different problem from that of the preparation of other haloalkanes and necessitates a specific method of fluorination.[12] Earlier workers[2-8] have used vacuum lines and autoclaves for fluorination of organic molecules with xenon difluoride. We now report the reaction of xenon difluoride using very simplified laboratory techniques, e.g., Kel-F vessels, weighing of xenon difluoride in Teflon epruvettes, room temperature, atmosphere pressure, etc. By fluorination of substituted 1,1-diphenylethylenes **1a–h** (Scheme I) 1,1-diphenyl-1,2-difluorides

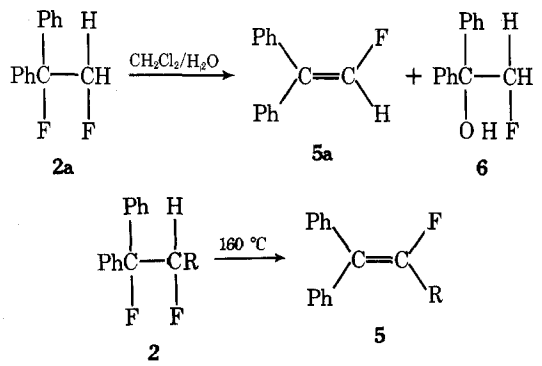
Scheme I



a, X = R = H
b, X = H; R = CH_3
c, X = H; R = F
d, X = *p*-OCH_3; R = H
e, X = *p*-CH_3; R = H
f, X = *m*-CH_3; R = H
g, X = *p*-Cl; R = H
h, X = *m*-Cl; R = H

2a–h were isolated using hydrogen fluoride as catalyst. In addition to vicinal difluorides (**2a–h**) small amounts of deoxybenzoin **3a** (5%) and **3b** (15%) were formed (Table I). The fluorination reaction when catalyzed by trifluoroacetic acid results in a high yield of **2a** and **2b** without formation of deoxybenzoin **3a** or **3b**, but reaction with 1,1-diphenyl-2-fluoroethylene in the presence of trifluoroacetic acid results in the formation of trifluoro product **2c** (60%) and the trifluoroacetate derivate **4c** (35%). The addition of trifluoroacetic anion was in accordance with Markownikoff type regioselectivity forming corresponding 1,1-diphenyl-1-trifluoroacetoxy-2,2-difluoroethane (**4c**). The structures of the products were determined by NMR and mass spectrometry and their NMR data are presented in Table II. Treatment of 1,2-difluoro-1,1-diphenylethane (**2a**) in methylene chloride solution with water for 30 min resulted in two products: 1,1-diphenyl-2-fluoroethene (**5a**, 70%) and 30% of 1,1-diphenyl-1-hydroxy-2-fluoroethane (**6**) (relative ratios determined by NMR) (Scheme II). The products were separated by prepar-

Scheme II

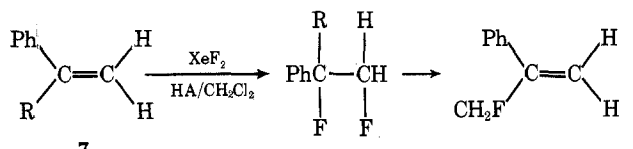


ative TLC. On the other hand, heating of the vicinal difluorides **2** to 160 °C resulted in formation of the eliminated products **5**.

The reactions of xenon difluoride with aryl substituted alkenes **1d–h** resulted in formation of vicinal difluorides for all, but the reaction with the *p*-methoxy derivate **1d** is quicker than that with the *m*-chloro derivate. From the NMR data of all the substituted derivates **2d–h** (Table II) we can see no significant effect of different substituents bonded to the phenyl ring on the chemical shift of fluorine or hydrogen atoms. Furthermore, we also have not observed any greater effect of substituents on coupling constants.

The reaction with styrene (**7a**) catalyzed by hydrogen fluoride resulted in formation of 1,2-difluoro-1-phenylethane (**8a**, Scheme III), which could be purified by preparative GLC. The

Scheme III



a, R = H
b, R = CH_3

product is very unstable and must be stored at −15 °C. The reaction with 2-phenylpropene (**7b**) gave very unstable 1,2-difluoro-2-phenylpropane (**8b**) which could be purified by

Table I. Fluorination of Substituted Diphenylethylenes with XeF_2 in CH_2Cl_2 at 20 °C. Yields of Products (%)

Olefin	HA	2	3	4
1a	HF	90	5	
	CF_3COOH	95		
1b	HF	80	15	
	CF_3COOH	95		
1c	HF	95		
	CF_3COOH	60		35

preparative GLC. However, the product decomposed (elimination of HF) in methylene chloride in 45 min, thus forming 2-phenyl-3-fluoropropene-1 (9).

Fluorine addition to phenyl-substituted olefins with xenon difluoride appears to be strongly catalyzed by hydrogen fluoride or trifluoroacetic acid, as indicated by observations that in the absence of these catalysts reactions are very slow. We found no evidence either for the formation of fluorine-substituted products which might arise via a substitution fluorination of the phenyl ring, or of an ethylenic hydrogen atom, or for the presence of hydrogen fluoride addition products, as observed in gas-phase fluorinations[8] with xenon difluoride. Extensive work is in progress on acid-catalyzed liquid-phase fluorinations of various alkenes in order to establish the mechanism of these reactions.

Experimental Section

Ir spectra were recorded by using a Perkin-Elmer 257 spectrometer, and ^1H and ^{19}F NMR spectra by a JEOL JNM-PS-100 from CCl_4 solution 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 a Varian Aerograph Model 1800 and TLC on Merck PSC-Fertigplatten silica gel F-254 (activated for 3 h at 120 °C before use).

Materials. Pure samples of olefins were prepared by known methods: 1,1-diphenylethylene,[13] 1,1-diphenylpropene,[14] phenyl-substituted 1,1-diphenylethylenes.[13] Other olefins were commercially available and purified before use. Hydrogen fluoride of Fluka Purum quality was used without further purification. Methylene chloride was purified[15] and stored over molecular sieves. Xenon difluoride was prepared by a photosynthetic method[16] and its purity was better than 99.5%.

1,2-Difluoro-1,1-diphenylethane (2a). To a solution of 1 mmol of 1a in methylene chloride (6 ml), 1 mmol of xenon difluoride was added at 25 °C and under stirring 1 ml of 1 M trifluoroacetic acid was introduced into the reaction mixture. After a few seconds the colorless solution turned dark blue and xenon gas was slowly evolved. After 30 min the gas evolution had ceased and the reaction appeared to be complete. The reaction mixture was diluted with methylene chloride (15 ml), washed with 10 ml of 5% $NaHCO_3$ and water, and dried over anhydrous sodium sulfate. The solvent was evaporated in vacuo. The crude product was purified with preparative TLC (SiO_2, *n*-hexane–methylene chloride, 9.5:0.5). The product **2a** (205 mg, 95%) with mp 38–40 °C (lit.[11] mp 40–42 °C) was isolated. NMR data are stated in Table II.

1,1-Diphenyl-2-fluoroethene (5a). To a solution of 1 mmol of **1a** in methylene chloride (6 ml), 1 mmol of xenon difluoride was added at 25 °C and under stirring anhydrous hydrogen fluoride (0.5–1 mmol) was introduced into the reaction mixture. After a few seconds the colorless solution turned dark blue and xenon gas was evolved. After 30 min the reaction mixture was diluted with methylene chloride, washed with 10 ml of aqueous $NaHCO_3$, and dried over anhydrous Na_2SO_4 and solvent was evaporated in vacuo. The crude, oily product was purified by preparative VPC (SE-30, Chromosorb A, AW, 15%, 210 °C). 1,1-Diphenyl-2-fluoroethene (**5a**, 170 mg, 86%) and 10 mg (5%) of deoxybenzoin were isolated. The spectroscopic data are in agreement with those in the literature.[11]

1,1-Diphenyl-1-hydroxy-2-fluoroethane (6). 1,2-Difluoro-1,1-diphenylethane (**2a**, 1 mmol) was dissolved in methylene chloride (5 ml) and treated for 30 min with 10 ml of water. After separation the methylene chloride layer was dried over anhydrous Na_2SO_4 and the solvent was evaporated in vacuo. The crude reaction mixture was analyzed by NMR spectroscopy and a 70:30 ratio of 1,1-diphenyl-2-fluoroethene (**5a**) and 1,1-diphenyl-1-hydroxy-2-fluoroethane (**6**), respectively, was found. GLC separation yielded 86% of 1,1-diphenyl-2-fluoroethene (**5a**). On the other hand, the separation of the crude reaction mixture by preparative TLC (SiO_2, *n*-hexane–methylene chloride 9.5:0.5) resulted in 26% of a colorless oily product (**6**) [mass spectrum calcd for $C_{14}H_{13}OF$ *m/e* 216.0955, found *m/e* 216.0940, *m/e* 216 (M^+, 3), 198 (100), 183 (50), 165 (24), 105 (22), 77 (14); NMR δ H 4.65 ppm (d), δ Ph 7.2 ppm (m), J_{FH} = 45 Hz] and 63% of 1,1-diphenyl-2-fluoroethene (**5a**).

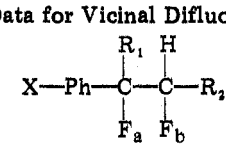
1,2-Difluoro-1,1-diphenylpropane (2b). The fluorination, workup procedure, and TLC purification were essentially the same as described for **2a**. **2b** was isolated in 95% yield as an unstable liquid product, which easily eliminated hydrogen fluoride: NMR data are stated in Table II; mass spectrum calcd for $C_{15}H_{14}F_2$ *m/e* 232.1072, found *m/e* 232.1059, *m/e* 232 (M^+, 8), 212 (6), 185 (100), 165 (22), 77 (13).

1,1-Diphenyl-2-fluoropropene (5b). The fluorination, workup procedure, and the VPC purification were essentially the same as described for **5a**. **5b** (82%) [oily product; mass spectrum calcd for $C_{15}H_{13}F$ *m/e* 212.1006, found *m/e* 212.0985, *m/e* 212 (M^+, 100%), 198 (15), 197 (16), 165 (15), 133 (11); NMR δ CH_3 1.95 ppm (d), δ Ph 7.2 ppm (m), $J_{CH_3,F}$ = 17.2 Hz] and 50% of methyldeoxybenzoin (**3b**) [mass spectrum calcd for $C_{15}H_{14}O$ *m/e* 210.1004, found *m/e* 210.1027, NMR δ CH_3 1.52 ppm (d), δ H 4.6 ppm (q), δ Ph 7.7 ppm (m), J_{H,CH_3} = 6.7 Hz] were isolated.

1,2,2-Trifluoro-1,1-diphenylethane (2c). The fluorination, workup procedure, and VPC purification were essentially the same as described for **5a** (Carbowax 20M, Varaport-30 70/80, 10%, 165 °C). **2c**: a colorless, stable liquid, yield 95%. Mass spectrum: calcd for $C_{14}H_{11}F_3$ *m/e* 236.0813, found *m/e* 236.0813. NMR data are stated in Table II.

2,2-Difluoro-1-trifluoroacetoxy-1,1-diphenylethane (4c). The fluorination and workup procedure were essentially the same as described for **2a**. VPC separation yielded 60% of 1,2,2-trifluoro-1,1-diphenylethane (**2c**) and 35% of liquid product 2,2-difluoro-1-tri-

Table II. NMR Data for Vicinal Difluorides (2a–h, 7a, 7b)



Compd	δ_{F_a}, ppm	δ_{F_b}, ppm	δ_H, ppm	δ_{R_1}, ppm	δ_{R_2}, ppm	$J_{F_aF_b}$, Hz	J_{F_bH}, Hz	J_{F_aH}, Hz	$J_{F_aR_1}$, Hz	J_{R_2H}, Hz
2a	−169.5	−245	4.85	7.2	4.85	18	47	22		
2b	−173.3	−194.3	5.3	7.2	1.33	17	45	18		6
2c	−172.5	−141.7	6.2	7.2	−141.7	11.7	54	5.5		54
2d	−167.5	−254	4.8	7.3	4.8	18	47	22		
2e	−169.5	−254	4.8	7.2	4.8	18	47	22.5		
2f	−170	−245	4.8	7.2	4.8	18	47	24		
2g	−169.5	−245	4.8	7.2	4.8	18	47	23		
2h	−169.5	−245	4.8	7.2	4.8	18	47	24		
7a	−208.5	−247.5	4.6	5.66	4.6	16	48 J_{R_1H} = 7 Hz	30 $J_{R_1R_2}$ = 4 Hz	50	$J_{F_aR_2}$ = 22 Hz $J_{F_bR_1}$ = 16 Hz
7b	−172.5	−246	4.5	1.68	4.5	13.5	48 $J_{R_1F_b}$ = 3 Hz	33	21	$J_{F_aR_2}$ = 18 Hz

fluoroacetoxy-1,1-diphenylethane (4c): mass spectrum calcd for $C_{16}H_{11}O_2F_5$ *m/e* 330.0701, found *m/e* 330.0670, *m/e* 330 (M^+, 46), 279 (100), 165 (33), 105 (42), 77 (21); NMR δ H 7.1 ppm (t), J_{FH} = 55.5 Hz.

Phenyl-Substituted Derivates of 1,2-Difluoroethanes (2d–h). The reaction time for **1d** was 10 min, while the reaction time for **1h** was 1 h. The fluorination, workup procedure, and TLC purification were the same as described for **2a**. The products were unstable, oily compounds. NMR data are listed in Table II. Mass spectra: **2d,** calcd for $C_{15}H_{14}F_2O$ *m/e* 248.1013, found *m/e* 248.1000, *m/e* 248 (M^+, 1), 228 (100), 215 (12), 198 (14), 183 (16), 165 (20), 77 (10); **2e,** calcd for $C_{15}H_{14}F_2$ *m/e* 232.1064, found *m/e* 232.1063, *m/e* 232 (M^+, 16), 199 (100), 184 (13), 183 (13), 119 (10), 84 (22); **2f,** calcd for $C_{15}H_{14}F_2$ *m/e* 232.1064, found *m/e* 232.1063, *m/e* 232 (M^+, 14), 199 (100), 184 (14), 183 (12), 119 (12); **2g,** calcd for $C_{14}H_{11}F_2Cl$ *m/e* 252.0517, found *m/e* 252.0518, *m/e* 254 ($M^+ + 2$, 6), 252 (M^+, 17), 221 (33), 219 (100), 183 (26), 92 (17); **2h,** calcd for $C_{14}H_{11}F_2Cl$ *m/e* 252.0517, found *m/e* 252.0518, *m/e* 254 ($M^+ + 2$, 7), 252 (M^+, 20), 221 (33), 219 (100), 183 (30), 92 (18).

1,2-Difluoro-1-phenylethane (8a). The fluorination, workup procedure, and VPC purification were essentially the same as for **5a** (SE-30, Chromosorb A, AW, 10%, 150 °C). Liquid unstable product (50%) was isolated. NMR data are stated in Table II. Mass spectrum: calcd for $C_8H_8F_2$ *m/e* 142.0603, found *m/e* 142.0592, *m/e* 142 (M^+, 33), 109 (100), 83 (7), 77 (8).

1,2-Difluoro-2-phenylpropane (8b), 2-Phenyl-3-fluoropropene-1 (9). The fluorination, workup procedure, and VPC purification were essentially the same as for **5a** (SE-30, Chromosorb A, AW, 10%, 150 °C). **8b** was isolated in 22% yield as a liquid, unstable product. NMR data are listed in Table II. Mass spectrum: calcd for $C_9H_{10}F_2$ *m/e* 156.0759, found *m/e* 156.0748, *m/e* 156 (M^+, 10), 136 (100), 103 (65), 87 (35), 77 (31). **9** was isolated in 38% yield as a liquid product: mass spectrum calcd for C_9H_9F *m/e* 136.0688, found *m/e* 136.0687, *m/e* 136 (M^+, 100), 103 (80), 78 (27), 77 (27); NMR δ F −237 ppm (td), J_{FH} = 51, 2 Hz.

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Registry No.—**1a,** 530-48-3; **1b,** 778-66-5; **1c,** 390-75-0; **1d,** 4333-75-9; **1e,** 948-55-0; **1f,** 4333-70-4; **1g,** 18218-20-7; **1h,** 29265-81-4; **2a,** 379-83-9; **2b,** 309-45-5; **2c,** 14090-30-3; **2d,** 59888-08-3; **2e,** 59888-09-4; **2f,** 59888-10-7; **2g,** 59888-11-8; **2h,** 59888-12-9; **3b,** 2042-85-5; **4c,** 52108-02-8; **5a,** 390-75-0; **5b,** 59888-13-0; **6,** 337-72-4; **7a,** 100-42-5; **7b,** 98-83-9; **8a,** 33315-79-6; **8b,** 59888-14-1; **9,** 14584-33-9; xenon difluoride, 13709-36-9.

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Mechanism of Bromination of 6-Azauracil in Aqueous Acid Solutions

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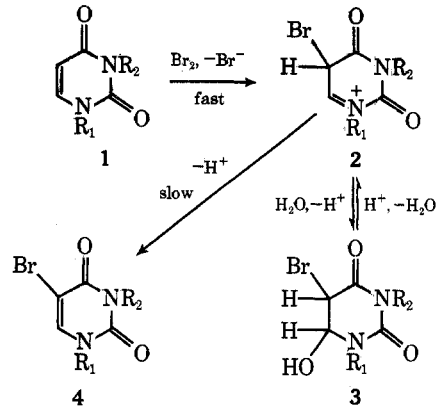
In dilute aqueous sulfuric acid solution the rates of bromination of 6-azauracil and 3-methyl-6-azauracil vary inversely with the hydronium ion concentration, whereas under the same conditions 1,3-dimethyl-6-azauracil is barely reactive. It is suggested that 6-azauracil and its 3-methyl derivative react with bromine via their anions resulting from deprotonation at N_1. It appears that a 6-aza nitrogen depresses the rate of bromine attack at the 5 position of a uracil by at least 10^{10}.

We have recently obtained evidence that the primary route for the monobromination of uracils (**1**, R_1, R_2 = H or Me) in aqueous acidic solutions involves two discrete steps[1] (Scheme I). Firstly, there is a rapid reaction of **1** and bromine

Scheme I



to give the cation **2** which is then captured by water to yield an observable intermediate[1] **3**. Secondly, there is a slow acid-catalyzed[1] dehydration **3** ⇄ **2** → **4**. Such a mechanism would appear to be less likely for the analogous brominations of 6-azauracils (**6** in Scheme II), since the cationic intermediate **5** should be much less stable than **2**.

In aqueous solution, the 6-azauracils (**6**, R_1, R_2 = H or Me) react smoothly with bromine to give the appropriate 5-bromo derivatives[2,3] (**7**). In contrast to the behavior of uracils, this reaction is quite slow, and may be conveniently followed by monitoring the decrease in uv absorbance at 400 nm due to bromine. In dilute aqueous acid, and in the presence of an excess of a substrate (**6**), the rate of disappearance of bromine obeys first-order kinetics. Table I lists the derived second-order rate constants[4] for the reaction of bromine with substrates **6** (R_1 = R_2 = H) and **6** (R_1 = H; R_2 = Me) at various acid concentrations. These clearly show an inverse dependence upon the hydronium ion concentration, and thus suggest a mechanism in which bromine attacks the anion **8** (Scheme II). Support for this interpretation is the observation