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# FLUORINATION WITH XENON DIFLUORIDE. REACTIONS OF PHENYL-SUBSTITUTED OLEFINS IN THE PRESENCE OF TRIFLUOROACETIC ACID

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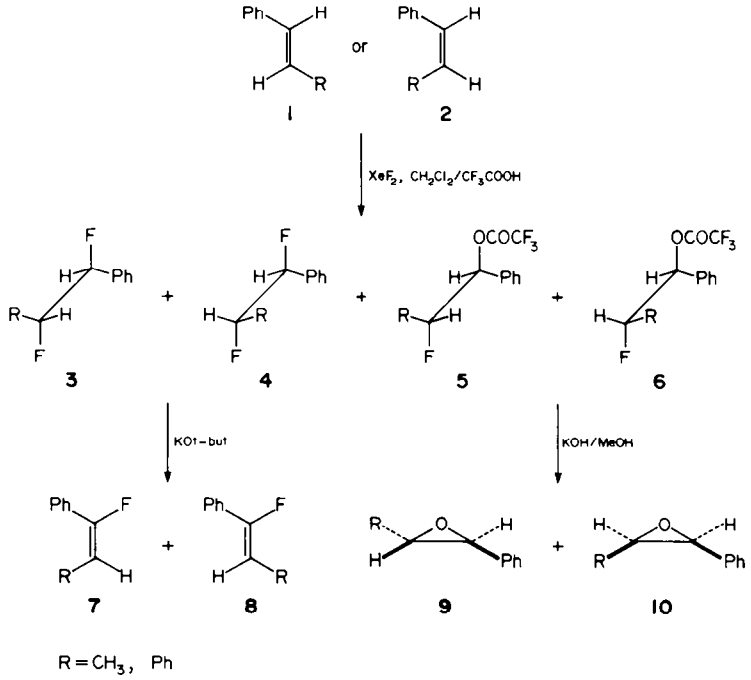
**Abstract**—Trifluoroacetic acid-catalyzed liquid-phase fluorination with xenon difluoride of phenyl-substituted olefins, e.g. cis- and trans-1-phenylpropene and cis- and trans-stilbene, results in the formation of vicinal difluorides and fluoro-trifluoroacetates. The reaction is non-stereospecific. d,l-Erythro and d,l-threo fluoro-trifluoroacetates are formed in a highly regiospecific Markovnikov manner in 50% yield. The formation of $\beta$-fluorocarbonium ions is suggested.

Recently we observed that xenon difluoride fluorinates readily phenyl-substituted olefins,[1,2] acetylenes,[3] and phenanthrene[4] in the presence of hydrogen fluoride as catalyst to give the corresponding 1,2 - difluoro or 1,1,2,2 - tetrafluorophenyl - ethanes or fluorinated phenanthrenes in high yields and under mild conditions. In the course of our efforts to elucidate the stereochemistry and the reaction mechanism of fluorine addition with xenon difluoride, we fluorinated some trans and cis isomers of phenyl-substituted olefins **1** and **2** respectively. We chose these olefins because the stereochemistry of their halogenation is well known[5] and so there was a possibility of drawing conclusions from the stereochemical results about the reaction pathway. We have studied the effect of the catalyst, trifluoroacetic acid, on the stereochemistry of the fluorine addition and the product distribution.

## RESULTS AND DISCUSSION

In the $CF_3COOH$ catalyzed reactions of isomeric olefins **1, 2** with xenon difluoride in methylene chloride at room temperature, a mixture of four products was formed: d,l-erythro **3** and d,l-threo **4** difluorides, d,l-erythro **5** and d,l-threo **6** fluoro-trifluoroacetates (Scheme 1). The products were separated by preparative GLC or TLC and their mass, $^{19}F$ and $^1H$ NMR spectra were recorded. The structures of the difluorides were assigned from the products formed by treatment by base and under conditions suitable for trans elimination. The products (cis-fluoro **7**, and trans-fluoro **8** alkenes) were identified on the basis of differences in their NMR spectra: $J_{FH}$ trans $> J_{FH}$ cis. The structures of trifluoroacetates **5**, **6** were assigned from the products formed when they were treated with methanolic potassium hydroxide under




Scheme 1.

conditions suitable for anti-elimination, thus giving the corresponding olefin oxides **9**, **10**. They were easily identified by spectroscopic methods. The product distribution in $CF_3COOH$ catalyzed addition with xenon difluoride to each of the four olefins is presented in Table 1. The results for all of the olefins show that the addition of fluorine is clearly a non-stereospecific process. The d,l-erythro **5** and d,l-threo **6** fluoro-trifluoroacetates are formed in a highly regiospecific manner in about 50% yield. The processes are also non-stereospecific, but the stereochemistry of the fluoro-trifluoroacetate formation parellels that of difluorides. The non-stereospecific addition could be caused by an open or partly bridged cation (the product intermediate), by radical processes or finally, by isomerization of the olefins or products under the reaction conditions. We found that the lack of stereospecifity cannot be ascribed to the prior isomerization of the olefins (in the cis-series we observed isomerization of the order of 30% for stilbene), or to secondary isomerization of the products, since all have been shown to be stable under the reaction conditions. The absence of a free-radical inhibition effect (molecular oxygen) on the product distribution ruled out free-radical processes.

It is clear that the stereochemical results must be explained within the framework of an electrophilic mechanism. The formation of fluoro-trifluoroacetates in a highly regiospecific manner also supports this view. The effect of the concentration of trifluoroacetic acid on the product distribution is presented in Table 2. It is interesting that with a smaller amount of trifluoroacetic acid (0.4 mmol) fluoro-trifluoroacetates are formed in high yield. In the presence of 1.03 mmol of trifluoroacetic acid, 52% and 50% of trifluoroacetates **3** and **4** are formed from trans- and cis-stilbene, respectively. On the other hand, at higher concentrations of trifluoroacetic acid only a small increase in the formation of trifluoroacetates was observed.

Table 1. Product distribution in fluorination of olefins (**1** and **2**) with $XeF_2$ in $CH_2Cl_2$ at 25°C in the presence of $CF_3COOH$

| Olefin | R | Relative yields(%)[a,b] 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|
| trans(**1**) | $CH_3$ | 34 | 19 | 29 | 18 |
| | Ph | 30 | 18 | 35 | 17 |
| cis(**2**) | $CH_3$ | 34 | 19 | 31 | 16 |
| | Ph | 26 | 24 | 26 | 24 |

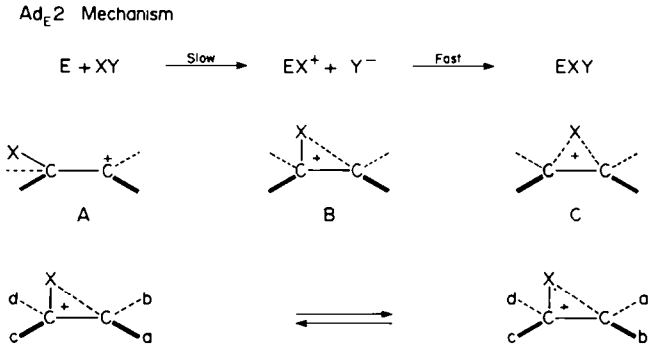
[a] determined by $^{19}F$ NMR spectroscopy.
[b] ratio olefin/$CF_3COOH$ = 1.03.

Table 2. The effect of $CF_3COOH$ concentration on product distribution in fluorination of trans and cis stilbene

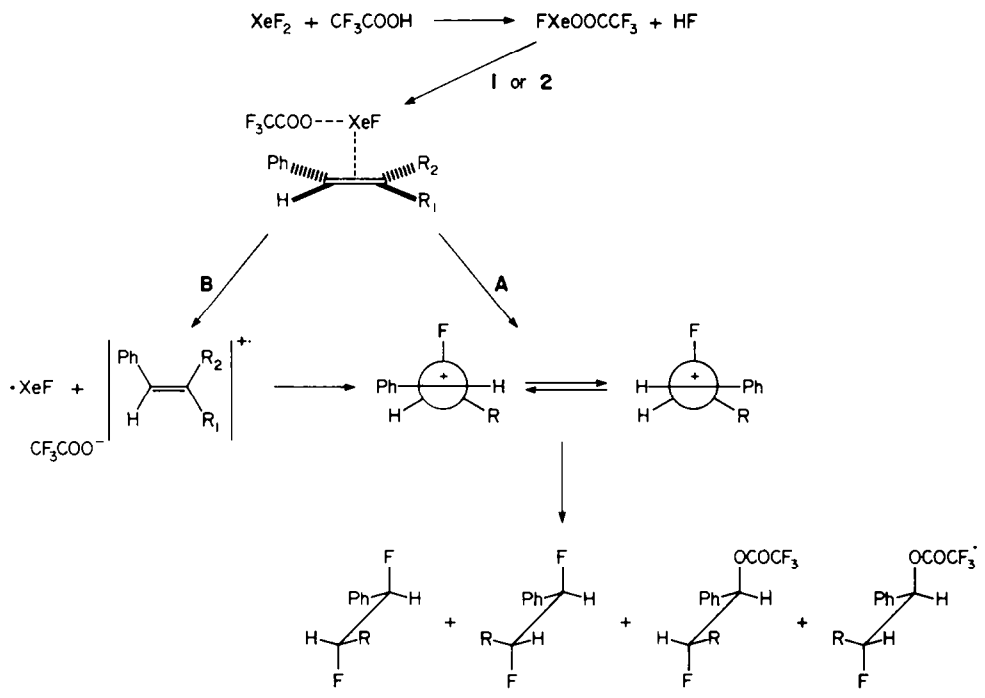
| mmol $CF_3COOH$ / mmol olefin | Relative yields(%) 3 | 4 | 5 | 6 |
|---|---|---|---|---|
| Trans stilbene | | | | |
| 0.40 | 38 | 23 | 26 | 13 |
| 0.80 | 35 | 20 | 30 | 15 |
| 1.03 | 30 | 18 | 35 | 17 |
| 2.05 | 27 | 17 | 39 | 17 |
| 3.08 | 25 | 17 | 41 | 17 |
| Cis stilbene | | | | |
| 0.40 | 30 | 30 | 21 | 19 |
| 0.80 | 29 | 26 | 23 | 22 |
| 1.03 | 26 | 24 | 26 | 24 |
| 2.05 | 25 | 23 | 27 | 25 |
| 3.08 | 25 | 23 | 27 | 25 |

The mechanism of the electrophilic addition of halogens has been intensively investigated from both kinetic and stereochemical points of view.[5,6] The most important mechanism for an electrophilic addition in the liquid phase is stepwise addition via a carbonium ion intermediate ($AdE_2$). It is now known that the nature of the intermediates (Scheme 2) depends on the halogen X, the structure of the substrate and on the reaction medium, ranging from a strongly bridged ion of type *C* to a weakly bridged species of type *B* of an open chain ion like *A*. If the cation has an open (*A*) or partly bridged (*B*) structure, a mixture of syn and anti adducts is generally expected.

Turning to the results obtained with cis- and trans-olefins, we see that the ratios of d,l-erythro **3** and d,l-threo **4** difluorides as well as d,l-erythro **5** and d,l-threo **6** fluorotrifluoroacetates (Table 1) are nearly independent of the starting olefin. In the trans-series, anti addition of fluorine (**3**/**4** = 1.67–1.79) and also of fluoro-trifluoroacetate predominates (**5**/**6** = 1.6–2.06). On the basis of results obtained in the $CF_3COOH$ catalyzed reaction with xenon difluoride, the following mechanism could be suggested. Xenon difluoride reacts with trifluoroacetic acid,[7] giving xenon-fluoro-trifluoroacetate, a reagent of electrophilic character. In the next step a $\pi$-complex is probably formed between this electrophilic species and olefin **1** or **2**, which could be transformed by a heterolytic Xe–F bond cleavage (Scheme 3, path **A**) into an open $\beta$-fluorocarbonium ion intermediate. The




Scheme 2.



Scheme 3.

intermediate from the trans-olefin collapses with a fluorine anion or trifluoroacetate anion preferentially to an anti-adduct; on the other hand, the cis-olefin intermediate can freely rotate about the newly formed single bond, thus assuming a sterically more favorable conformation, identical to that of the trans-olefin intermediate.

It is therefore clear why the product ratios are independent of the starting olefin. The proposed mechanism is also supported by the well known fact, that fluorine is a very poor neighbouring group for preventing any bridging phenomena in the above mentioned $\beta$-fluorocarbonium ion intermediate. Furthermore, another possibility (path **B**) is the formation of an ion radical, as has already been observed in the fluorination of benzene and its derivates[8] in hydrogen fluoride catalyzed fluorination, transforming in the next step by XeF or $XeF_2$ into an open carbonium ion. The lower oxidation potentials of olefins (in comparison to those of phenyl homologues) make the suggested path **B** quite reasonable.[9]

## EXPERIMENTAL

IR spectra were recorded using a Perkin-Elmer 257 spectrometer, $^1H$ and $^{19}F$ NMR spectra by a Jeol JNM-PS-100 from $CCl_4$ solution with TMS or $CCl_3F$ as internal references. Mass spectra and high resolution measurements were taken on a CEC-21-110 spectrometer. GLC was carried out on a Varian Aerograph, model 1800, and TLC on Merck PSC-Fertig-Platten silicagel F-254 (activated for 3 h at 120°C before use).

### *Materials*

Olefins were prepared by known methods: cis - 1 - phenylpropene,[10] trans - 1 - phenylpropene.[11] Other olefins were commercially available and purified before use. Trifluoroacetic acid was distilled before use. Methylene chloride was purified and stored over molecular sieves.[12] Xenon difluoride was prepared by the photosynthetic method[13] and its purity was better than 99.5%.

### *Addition and isolation procedures*

To a solution of 1 mmol of olefin in methylene chloride (6 ml) in a Kel-F-vessel, 1 mmol of xenon difluoride was added at 25° and under stirring trifluoroacetic acid (0.4–3.08 mmols) was introduced into the reaction mixture. After a few seconds the colourless solution turned dark blue and xenon gas was slowly evolved. After ten minutes gas evolution ceased and the reaction appeared to be complete. The reaction mixture was diluted with methylene chloride (15 ml), washed with 10 ml of $NaHCO_3$, water and dried over anhydrous sodium sulphate. The crude reaction mixtures were analyzed by $^{19}F$ NMR spectroscopy (each experiment was repeated three times; the maximum error of determination of composition was in the range of 2.5%) and then separated by preparative GLC or TLC.

### *D,l-erythro*(**3**) *and d,l - threo - 1,2 - difluoro - 1 - phenylpropane*(**4**) *and d,l-erythro*(**5**) *and d,l - threo - 1 - trifluoroacetoxy - 2 - fluoro - phenylpropane*(**6**)

The products were separated by preparative GLC (DDP Chromosorb Regular 80/100, T = 170°C). 25% of d,l-erythro(**3**), 13% of d,l-threo(**4**), 22% of d,l-erythro(**5**) and 13% of d,l-threo(**6**) were isolated as colourless, liquid compounds, decomposing on heating. The NMR data of products **3** and **4** are in agreement with those in the literature.[14] The structures of the products were also established by elimination of hydrogen fluoride under basic conditions, thus converting them to cis - 1 - fluoro - 1 - phenyl - propene **7** (NMR data: $J_{PH}$ 22Hz, $J_{HCH_3}$ 7.2 Hz) and trans - 1 - fluoro - 1 - phenylpropene **8** ($J_{FH}$ 36 Hz and $J_{HCH_3}$ 6.75 Hz). NMR data for d,l - erythro - 2 - fluoro - 1 - trifluoroacetoxy - 1 - phenyl - propane **5**: $\delta F - 202.5$ ppm, $\delta H_1$ 5.69 ppm, $\delta H_2$ 4.6 ppm, $\delta CH_3$ 1.2 ppm, $\delta CF_3$-84 ppm, $J_{FH_2} = 51$ Hz, $J_{FH_1} = 16.5$ Hz, $J_{FCH_3} = 24$ Hz, $J_{H_1H_2} = 3.9$ Hz, $J_{H_2CH_3} = 6$ Hz. and for d,l - threo - 2 - fluoro - 1 - trifluoroacetoxy - 1 - phenylpropane **6**: $\delta F - 199.5$ ppm, $\delta CF_3 - 84$ ppm, $\delta H_1$ 5.6 ppm, $\delta H_2$ 4.6 ppm, $\delta CH_3$ 1.11 ppm, $J_{FH_2} = 51$ Hz, $J_{FH_1} = 13.5$ Hz, $J_{FCH_3} = 24$ Hz, $J_{H_1H_2} = 7.5$ Hz, $J_{H_2CH_3} = 6$ Hz. Mass spectrum; calcd for $C_{11}H_{10}O_2F_4$ *m/e* 250.0635, found 250.0609, *m/e* (relative int.) 250 ($M^+$, 17%), 203(100), 91(60), 77(40), 69(50).

The structures of the trifluoroacetates were established by elimination under basic condition, thus converting them to trans-olefin oxide **9** (NMR data: $J_{HCH_3}$ 5 Hz, $J_{HH}$ 2 Hz, $\delta CH_3$ 1.3 ppm) and cis-olefin oxide **10** (NMR data: $J_{HCH_3}$ 5.2 Hz, $J_{HH}$ 2.4 Hz, $\delta CH_3$ 1.0 ppm). The NMR data are in agreement with those in the literature.[15]

*Meso*(**3**) *and d,l - 1,2 - difluoro - 1,2 - diphenylethane* (**4**) *and d,l-erythro* (**5**) *and d,l - threo - 1 - fluoro - 2 - trifluoroacetoxy - 1,2 diphenylethane* (**6**)

Difluorides were separated from trifluoroacetates by preparative GLC (Carbowax 20 M, Varaport 30 80/100, T = 200°C). The structures of the difluorides (difluorides **3** and **4** were not separated) were determined by elimination under basic conditions. 1 mmol of the reaction mixture of difluorides (meso: d,l-products = 2.5) was dissolved in 3 ml t-butanol and 1.5 mmols K t-butoxide were added. The reaction mixture was stirred at room temperature 20 h and for 5 h at 50°C, then cooled, mixed with water and extracted with $CH_2Cl_2$. The extract was washed with dilute acid and water, dried ($Na_2SO_4$), filtered and evaporated, and the residue was analyzed by GLC and NMR spectroscopy. The product was a 2.2:1 mixture of cis- and trans-fluorostilbene. Two compounds were separated by preparative GLC (Carbowax 20 M, Varaport 30 70/80, T = 180°C).

The spectroscopic data of fluorostilbenes are in agreement with the literature ones.[14] 1 mmol of the mixture of fluoro-trifluoroacetoxy products (**5**/**6** = 1.5) was suspended in 3 ml of methanolic solution of KOH (100 mg), heated for 1 h at 60°C and cooled, 10 ml of water were added and the solution was extracted with methylene chloride. The extract was washed with water, dried ($Na_2SO_4$), diluted and evaporated and the residue was analyzed by NMR. The product was a 1.45:1 mixture of trans **9** and cis-phenyloxides **10** respectively. The NMR spectra of products **9** and **10** are in agreement with those recorded on the products obtained in the reaction of trans- and cis-stilbene in chloroform with m-chloro-perbenzoic acid. NMR data: $\delta H$ = 3.7 ppm for product **9** and $\delta H$ = 4.17 ppm for product **10** are in agreement with the literature.[14] NMR data for d,l - erythro - 1 - fluoro - 2 - trifluoroacetoxy - 1,2 - diphenylethane **5**: $\delta F - 206$ ppm, $\delta CF_3 - 83.83$ ppm, $J_{FH} = 15$ Hz, $J_{FH} = 46.5$ Hz, and for d,l - threo - 1 - fluoro - 2 - trifluoroacetoxy - 1,2 - diphenylethane **6**: $\delta F - 200.09$ ptm, $\delta CF_3 - 83.80$ ppm, $J_{FH} = 48$, 13.5 Hz. Mass spectrum; calcd for $C_{16}H_{12}O_2F_4$ *m/e* 312.0791, found 312.0802, *m/e* (relat. inten.): 312 ($M^+$, 16%), 203(62), 109(100), 95(9), 83(6).

To test the stability of the products **2**, **3**, **4**, **5** in the reaction mixture, a sample (0.2 g) of known composition was dissolved in 2 ml of methylene chloride, 20 mg of xenon difluoride and a catalytic amount of hydrogen fluoride was added and the mixture was stirred at 25°C for 30 min. After work-up, the NMR spectra showed no significant differences in product distribution.

*Fluorination in the presence of oxygen*

1 mmol of trans-olefin **1** was dissolved in 6 ml of $CH_2Cl_2$, 1 mmol of xenon difluoride was added at 25°C, under stirring oxygen was introduced into the reaction mixture and 1 mmol of trifluoroacetic acid was then added. After 20 min. the reaction mixture was diluted with $CH_2Cl_2$, washed with 10ml of 5% $NaHCO_3$, water, dried ($Na_2SO_4$), filtered and evaporated and the residue was analyzed by NMR. The product distribution was 32% of **3**, 20% of **4**, 29% of **5** and 19% of **6** in the case of trans-phenylpropene, and 30% of **3**, 20% of **4**, 35% of **5** and 15% of **6** in the case of trans-stilbene. The free radical inhibitor had no effect on the product distribution (see Table 1).

*Isomerization of the olefins under the reaction conditions*

(a) 1 mmol of olefin **1** or **2**, dissolved in methylene chloride, was stirred for 1 h at room temperature in the presence of trifluoroacetic acid. After work-up, the reaction mixture was analyzed by GLC. No significant isomerization (less than 1%) of the olefin was observed except for the case of cis-stilbene, which isomerized in the range of 7%.

(b) In experiments made under the same reaction conditons as those for fluorination, in which a smaller amount (0.4, 0.5, or 0.6 mmols) of xenon difluoride and 1 mmol of olefin were used, the unreacted olefins were analyzed by GLC after the work-up. No significant isomerization of trans olefins was observed, while the isomerization of cis - 1 - phenylpropene took place in the range of 5–7% and cis-stilbene in the order of 30%.

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