Synthesis and Chemistry of Trifluoroacetyl Hypofluorite with Elemental Fluorine. A Novel Method for Synthesis of α-Fluorohydrins

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Sodium trifluoroacetate reacts with fluorine in the presence of traces of water or HF to give mainly trifluoroacetyl hypofluorite, CF_3COOF (1). This uncommon reagent was reacted in situ with a number of stilbenes and with diphenylacetylene. The oxygen-bound fluorine clearly acts as an electrophile, since Markownikoff addition of 1 to the double bond was observed. However, in cases where the Hammett constant σ_p^+ of the ring substituent is low, as in 4-chloro- (**15**) or 4-methyl- (**32**) stilbenes, some of the regioselectivity is lost. Usually only syn adducts were found except in cases where the 1-fluoro carbocation is stabilized, as in the case of *trans*-4-methoxystilbenes (**23**), or more than usual sterically hindered, as in *trans*-2-(carbomethoxy)stilbene (**20**). The stereoselectivity achieved in the reaction of 1 with stilbenes was compared with the stereoselectivity of fluoroxyperfluoroalkanes, R_fOF, with the same olefins. In the light of this comparison it seems to us that the oxygen-bound fluorine in 1 is more electrophilic in character than in R_fOF compounds. The reaction products of diphenylacetylene (**28**) with 1, which are in sharp contrast to the products of the parallel reaction of **28** with CF_3OF, support this observation. The strong electrophilic character of the oxygen-bound fluorine of 1 is also demonstrated by aromatic electrophilic fluorination taking place on the activated ring of 4-methoxystilbene (**23**). In almost all cases the 1-fluoro-2-hydroxy (or 2-trifluoroacetoxy) compounds adopt the more stable gauche conformation as is evident from their NMR (^1H and ^{19}F) spectra. In the case of steric disturbance, however, as in **21b** and **22b**, a deviation from the gauche conformation was observed and discussed. The 1-fluoro-2-trifluoroacetoxy compounds were readily hydrolyzed to the corresponding α-fluorohydrins, thus opening a new route for the synthesis of this important group.

The chemistry of acetyl hypohalites has not, so far, been well developed. Although the existence of acetyl hypochlorite in solution has been known for more than a century, relatively little work has been carried out with this reagent.[1] Trifluoroacetyl hypochlorite has only recently been synthesized by using chlorine monofluoride. However, apart from the fact that this material is thermally unstable and tends to explode, nothing is known of its chemistry.[2] It is true that trifluoroacetyl hypofluorite, CF_3COOF (1), was synthesized some years ago,[3] but the tedious synthetic method, together with the low overall yield, accounts for the fact that not even a single work has been published with this relatively simple molecule since then. We report herein a new and convenient synthesis of this reagent, using elemental fluorine, and describe some reactions of 1 with several olefins as well.

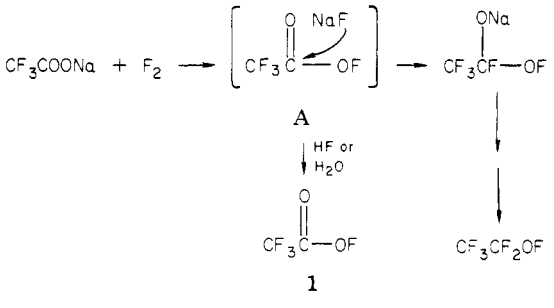
When a stream of fluorine diluted with nitrogen is passed through trichlorofluoromethane (Freon) at −75 °C, an oxidizing solution is obtained. After addition of *cis*-stilbene to this solution, the known[4] *erythro*-1,2-difluoro-1,2-diphenylethane is isolated (eq 1), clearly showing that

$$F_2(\text{soln}) + \textit{cis}\text{-PhCH=CHPh} \rightarrow \textit{erythro}\text{-PhCHFCHFPh} \quad (1)$$

fluorine dissolved in Freon is the agent responsible for the oxidizing ability of the solution. Nevertheless, this reaction is very limited in scope since the solubility of fluorine even at low temperature is extremely low. Other conventional solvents are even less suitable than Freon, either being unstable to this highly reactive halogen or dissolving even less fluorine.

When fluorine gas is passed through a suspension of sodium trifluoroacetate in Freon at −75 °C, a solution results whose oxidizing ability increases with the amount of fluorine passed. A few preliminary experiments with olefins showed that this time we are not dealing with a solution of fluorine but undoubtedly with a reagent or mixture of reagents formed by the reaction between elemental fluorine or sodium trifluoroacetate. Separate experiments showed that fluorine does not react, under the above conditions, with sodium fluoride or with trifluoroacetic acid.

Scheme I



When the above-mentioned oxidizing solution is prepared under anhydrous conditions and no HF is allowed to be present, it can be shown that the main oxidizing moieties are a mixture of mono- and bis(fluoroxy)perfluoroalkanes. Under mild conditions it is possible to direct the reaction to give fluoroxypentafluoroethane, CF_3CF_2OF, as the main oxidizing agent in the solution. We have reason to believe that the reaction between fluorine and sodium trifluoroacetate follows the path shown partially in Scheme I.[5]

The nucleophilic fluoride within the cage pair of molecule A is able to attack the carbonyl even under mild conditions, thus leading eventually to the fluoroxy compounds. It occurred to us that if the sodium fluoride in the cage A would become solvated, its nucleophilic power would be considerably reduced. Indeed, when damp CF_3COONa was used, or when traces of HF were present in the reaction mixture, it was found that the oxidizing ability of the resultant solution was largely due to the presence of CF_3COOF (1). When this hypofluorite was

(1) de la Mare, P. B. D.; Wilson, M. A.; Rosser, M. J. *J. Chem. Soc., Perkin Trans. 2* **1973**, 1480 and references therein.
(2) DesMarteau, D. D. 174th National Meeting of the American Chemical Society, Chicago, IL, Aug 1977; American Chemical Society: Washington, DC, 1977.
(3) Gard, G. L.; Cady, G. H. *Inorg. Chem.* **1965**, *4*, 594.
(4) Merritt, R. F. *J. Org. Chem.* **1966**, *31*, 3871.
(5) A detailed report of the synthesis and reactions of fluoroxypentafluoroethane will appear soon. See also: Rozen, S.; Lerman, O. *J. Am. Chem. Soc.* **1979**, *101*, 2782.

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Table I

compd	mp, °C[a,b]	% yield[c]	IR, ν, cm⁻¹ C=O	IR, ν, cm⁻¹ OR[d]	mass spectrum[e]
3a or 3b			1795	1170	312 (M^+), 203 ($PhCHOCOCF_3^+$), 109 ($PhCHF^+$)
6a	99	62		3450	198 ($M - 18^+$), 109 ($PhCHF^+$), 107 ($PhCHOH^+$)
6b	99	58		3450	as for 6a
9a			1795	1170	370 (M^+), 203 ($PhCHOCOCF_3^+$), 167 ($MeOOCC_6H_4CHF^+$)
9b		75[f]	1730	1170	as for 9a
10a	126[g]	80	1725	3600	274 (M^+), 167 ($MeOOCC_6H_4CHF^+$), 107 ($PhCHOH^+$)
10b	47[h]	25[i]	1725	3600	as for 10a[j]
13a	79		1800 1690	1160	354 (M^+), 203 ($PhCHOCOCF_3^+$), 151 ($CH_3COC_6H_4CHF^+$)
14a	121	28	1680	3600 3450	258 (M^+), 151 ($CH_3C_6H_4CHF^+$), 107 ($PhCHOH^+$)
16a + 17a[k]			1790	1150	
18a	116	32		3600	250 (M^+), 143 ($ClC_6H_4CHF^+$), 107 ($PhCHOH^+$)
19a	113	32		3420	250 (M^+), 141 ($ClC_6H_4CHOH^+$), 109 ($PhCHF^+$)
21a[l]		40	1790	1170	350 ($M - 20^+$), 203 ($PhCHOCOCF_3^+$), 167 ($MeOOCC_6H_4CHF^+$)
21b[l]		14	1710	1170	as for 21a
22a	57	40	1715	3430	256 ($M - 18^+$), 167 ($MeOCOC_6H_4CHF^+$), 107 ($PhCHOH^+$)
22b	oil	14	1710	3600 3420	as for 22a
24a + 24b[k]			1795	1160	
25a	86	57		3420	264 (M^+), 155 ($MeO(F)C_6H_3CHOH^+$), 109 ($PhCHF^+$)
25b	94	14		3420	as for 25a
36a + 38a[m]	67-70	48			230 (M^+), 123 ($MeC_6H_4CHF^+$), 121 ($MeC_6H_4CHOH^+$), 109 ($PhCHF^+$), 107 ($PhCHOH^+$)
36b	83	8		3600 3440	230 (M^+), 121 ($MeC_6H_4CHOH^+$), 109 ($PhCHF^+$)

[a] Unless otherwise stated all new fluorohydrins have the correct microanalysis. [b] Although many of the trifluoroacetoxy compounds were usually purified by chromatography, no special attempt was made to obtain analytical samples. [c] The yields of the fluorohydrins are based on the starting stilbenes. [d] R = H or $COCF_3$. [e] Besides the M^+, ($M - 18^+$) or ($M - 20^+$) peak only the strongest peaks are presented. [f] As indicated by GC. [g] Compound 10a crystallizes as the hydrate which is quite common with such alcohols. [h] Though we homogenized the fluorohydrin to one spot in TLC, we were not able to obtain a good microanalysis on this compound. [i] In contrast to the other materials, mild basic hydrolysis also affected the carbomethoxy group, so the yield of the hydrolysis product was low. [j] The benzilic ions *m/e* 167 and 107 for 10b appear as base peaks only by chemical ionization. [k] The data are for the mixture of the trifluoroacetates; only the corresponding fluorohydrins were separated. [l] The trifluoroacetoxy isomers were separated by high-pressure LC. [m] Inseparable mixture; the 36a/38a ratio is 3:1.

reacted in situ with a number of olefins, it was concluded that 1 constituted at least 80% of the active oxidizing agents present in the solution. This fact makes the hypofluorite solution an attractive synthetic reagent, and a possible use which immediately presents itself is the preparation of α-fluorohydrins (Scheme II).

Only one practical method is at present known for the synthesis of fluorohydrins, the opening of epoxide rings with HF, BF_3, or triethylammonium fluoride.[6] A recent publication describes the addition, in the electrophilic mode, of xenon difluoride in trifluoroacetic acid to certain olefins, thus producing 1-fluoro-2-(trifluoroacetoxy)-ethanes.[7] However, these latter products are accompanied by a considerable amount of the corresponding difluorides. A further disadvantage of this reaction is its lack of stereoselectivity, the threo and erythro isomers being obtained in nearly equal amounts.

Resembling the fluoroxy compounds of type R_fOF, the oxygen-bound fluorine in 1 behaves as an electrophile. *trans*-Stilbene (2), like all other olefins used in this work, reacted with 1 immediately (Scheme II). The cis addition product, *threo*-1-fluoro-2-(trifluoroacetoxy)-1,2-diphenylethane (3a) was obtained. Usually the trifluoroacetates were identified by NMR and mass spectroscopy and by the very characteristic IR absorption peak around 1800 cm^{-1}. However, they were not always isolated as such but were hydrolyzed under mild basic conditions to the corresponding fluorohydrins, usually in quantitative yield. Thus when 3a was treated with wet pyridine, *threo*-1-fluoro-2-hydroxy-1,2-diphenylethane (6a) was formed, whose properties matched those given in the literature.[6a] Complete stereoselectivity is also obtained in the addition of 1 to *cis*-stilbene (7). The syn product, *erythro*-1-fluoro-2-(trifluoroacetoxy)-1,2-diphenylethane (3b), was hydrolyzed, and the *erythro*-fluorohydrin 6b was obtained in good yield. Complete stereo- and regioselectivity are found also with *trans*- and *cis*-4-(carbomethoxy)stilbenes (8 and 11). Only the syn products were formed. Thus *threo*-1-fluoro-2-hydroxy-1-[4-(carbomethoxy)phenyl]-2-phenylethane (10a) was obtained from 8 after hydrolysis of the corresponding trifluoroacetoxy compound 9a. Similarly, *erythro*-fluorohydrin isomer 10b was formed when the *cis*-stilbene 11 was reacted with 1. Similar results were found when *trans*-4-acetylstilbene (12) served as a substrate. Spectroscopic data (see Experimental Section and Tables I and II) leave no doubts concerning the way the addition of 1 takes place. Again good stereo- and regioselectivity were found as exemplified by the syn adduct *threo*-1-fluoro-2-(trifluoroacetoxy)-1-(4-acetophenyl)-2-phenylethane (13a) which was isolated and then hydrolyzed to the corresponding fluorohydrin 14a (Scheme II).

The stereochemistry of the products was determined by their NMR spectra (^1H and ^{19}F). In the nonfluorinated vicinally substituted alkanes the vicinal H–H coupling constant is larger in the erythro than in the threo isomer.[8] However, when a pair of very electronegative atoms such as F,F or F,O are found vicinal to each other, the gauche

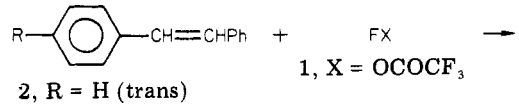
(6) (a) Aranda, G.; Jullien, J.; Martin, J. A. *Bull. Soc. Chim. Fr.* **1965**, 1890; **1966**, 3850. (b) Olah, G. A.; Meidar, D. *Isr. J. Chem.* **1978**, *17*, 148.
(7) Zuppan, M.; Pollack, A. *Tetrahedron* **1977**, *33*, 1017.
(8) de la Mare, P. B. D.; Wilson, M. A. *J. Chem. Soc., Perkin Trans. 2* **1973**, 653 and references therein.

Table II. ^{1}H NMR[a] and ^{19}F NMR Spectra of ArCH(F)CH(OR)Ar (R = H or $COCF_3$)

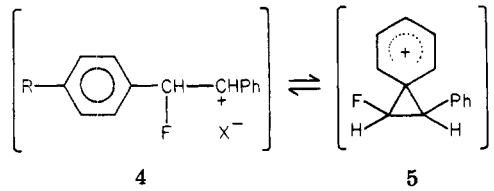
compd	^{1}H NMR, δ			^{19}F NMR, φ*		J_{HH}[c]	$J_{FH(gem)}$[d]	$J_{FH(vic)}$
	CHF	CHOR	Me	CHF[b]	$COCF_3$			
3a	5.65	6.16		181.2	75.5	7.8	47	13
6a	5.42	4.91		180.5		7.3	47	13
6b	5.48	4.94		183		5.5	47	12.5
9a	5.73	6.14	3.9			7.5	47	13.8
10a	5.49	4.91	3.89	183.6		7.3	47	13
10b	5.60	5.04	3.91	186.5		4.5	45	13
13a	5.74	6.15	2.54	183.9	75.5	7.3	47	13.8
14a	5.62	5.10	2.61	183.9		7.3	47	13.2
18a	5.39	4.86		181.5		7.3	47	13
19a	5.35	4.90		180.9		7.3	47	12.7
21a[e]	6.69	6.46	3.92	197.3	75.3	2.3	45	24
21b[e]	6.86	6.24	3.9	193.7	75.5	3.0	47	22.5
22a	6.51	4.99	3.73	180.8		3.8	47	20
22b	6.43	4.88	3.93	180.4		5.8	47	16
25a	5.35	4.85	3.83	180, 134.8[f]		7.3	48	12.3
25b	5.44	4.9	3.87	183.3, 135[f]		5.5	47	12
35a	5.64	6.13	2.31	180.7	76.4	7.6	47	13
36a	5.40	4.87	2.28	181		7.4	48	13
36b	5.48	4.94	2.34	183.6		5.5	45	12
37a	5.61	6.15	2.35	180	75.5	7.9	47	13
38a	5.38	4.90	2.28	180		7.3	48	13

[a] All NMR spectra were recorded for solutions in $CDCl_3$; the chemical shifts are reported in δ units with Me_4Si serving as internal standard; the aromatic protons resonate between 7.1 and 7.8 ppm as multiplets; the CHF and CHOR protons appear as double doublets, and the same is true for the fluorine atom in the ^{19}F NMR spectrum; the integration in all the spectra is in excellent agreement with the assigned structures. [b] The fluorine chemical shifts are reported in ppm upfield from $CFCl_3$ (internal standard). [c] All coupling constants are reported in Hz. [d] The J_{FH} geminal and vicinal constants can be evaluated from the ^{1}H as well as from the ^{19}F NMR spectrum. [e] The trifluoroacetoxy isomers were separated by high-pressure LC. [f] A characteristic chemical shift for an aromatic fluorine atom ortho to a methoxy group.

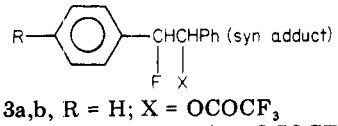
Scheme II



2, R = H (trans)
7, R = H (cis)
8, R = COOMe (trans)
11, R = COOMe (cis)
12, R = COMe (trans)



4 5



3a,b, R = H; X = $OCOCF_3$
9a,b, R = COOMe; X = $OCOCF_3$
13a, R = COMe; X = $OCOCF_3$
6a,b, R = H; X = OH
10a,b, R = COOMe; X = OH
14a, R = COMe; X = OH

a = threo; b = erythro

conformation is preferred, consequently causing a reversal of the coupling constants;[9] i.e., J_{HH}(threo) > J_{HH}(erythro). It is noteworthy that the fluorine in threo isomers always resonates at a lower field than that of the fluorine in the corresponding erythro isomer (see Table II in the Experimental Section).

The excellent stereoselectivity observed in the above-mentioned cases is in some constrast to the good but not complete cis addition of CF_3OF[10] and CF_3CF_2OF[5] to stilbenes. The formation of the syn products is explainable as the result of the intermediacy of the "tight ion pair" 4 (Scheme II) which rapidly collapses, mainly as a result of the substantial destablizing inductive effect of the vicinal fluorine on the resulting carbocation. It is assumed that 4 exists in equilibrium with the phenonium ion 5 which also inevitably leads to the syn addition product.[10] An additional factor which has to be considered is the mutual interaction between the electron lone pairs of the fluorine and the oxygen atoms which are responsible for the gauche conformation in the final product. It is possible that these forces, although not very strong,[9b] are operative in the transition state as well. So a "tight ion pair" is formed not only between the anion and the 1-fluoro carbocation but also between the anion and the fluorine atom as well. The loss, to some extent, of the stereoselectivity in reactions with fluoroxy compounds R_fOF (R_f = perfluoralkyl) is explained by the randomization effect caused by the leakage of 4 and/or 5 (X = OR_f) to the open carbocation $PhCHF-\overset{+}{C}HPh$.

The better stereoselectivity of the hypofluorite 1 when reacted with stilbenes, compared to the perfluoroxy reagents R_fOF, can be explained by comparing the hardness of the two bases R_fO^- and CF_3COO^-. Both anions are clearly hard based, and the difference between them must lie in the extent of the electronegativity of the groups connected to the negative oxygen. As will be seen, one can conclude, from the NMR spectra and from additional experimental facts, that the trifluoroacetoxy group posseses greater electronegativity than the perfluoroxy group. In the former case, then, the resulting anion will be a harder base. The conjugate acid $PhCHF-\overset{+}{C}HPh$ should be a hard

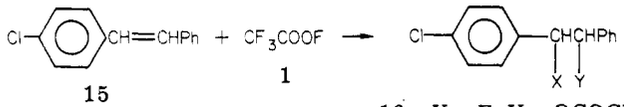
(9) (a) Phillips, L.; Wray, V. *J. Chem. Soc., Chem. Commun.* **1973**, 90. (b) Zefirov, N. S.; Samoshin, V. V.; Sabotin, O. A.; Baranenkov, V. I.; Wolfe, S. *Tetrahedron* **1978**, *34*, 2953.

(10) Barton, D. H. R.; Hesse, R. H.; Jackmann, G. P.; Ogunkoya, L.; Pechet, M. M. *J. Chem. Soc., Perkin Trans. 1* **1974**, 739.

one, principally due to the vicinal fluorine-containing electronegative group, outweighing the effect of the hydrogen one on the charged carbon. The reaction of this hard acid will be faster with the harder base, resulting, of course, in a greater stereoselectivity.[11] Apparently, cyclic concerted mechanisms are not operative here principally because the fluorine atom, which lacks low-lying unoccupied orbitals, cannot form a three-center bond. Other examples of a two-stage mechanism for the addition of fluoroxy compounds have been described.[12]

The reaction of the unsymmetrical stilbenes with **1** well demonstrates the electrophilic character of the oxygen-bound fluorine. The Hammett constants σ_p^+ for carbomethoxy and acetyl groups are notably high (+0.489 and >+0.502, respectively) and are responsible for the complete regiospecificity of the adducts in the Markownikoff mode. For identification of the products a mass spectral analysis proved to be of great help. The main fragmentation path either in 1-fluoro-2-trifluoroacetates or in α-fluorohydrins is a result of cleavage of the central C–C bond. The peaks of the two resultant benzylic ions are always the most dominant in all the spectra.

When *trans-p*-chlorostilbene (**15**) is considered, the inductive effect of the chlorine atom is opposed to its direct resonance interactions, resulting in a low σ_p^+ (+0.11). Indeed, when **15** was reacted with **1**, two *threo*-1-fluoro-2-trifluoroacetoxy esters **16a** and **17a** were formed in al-



15 1

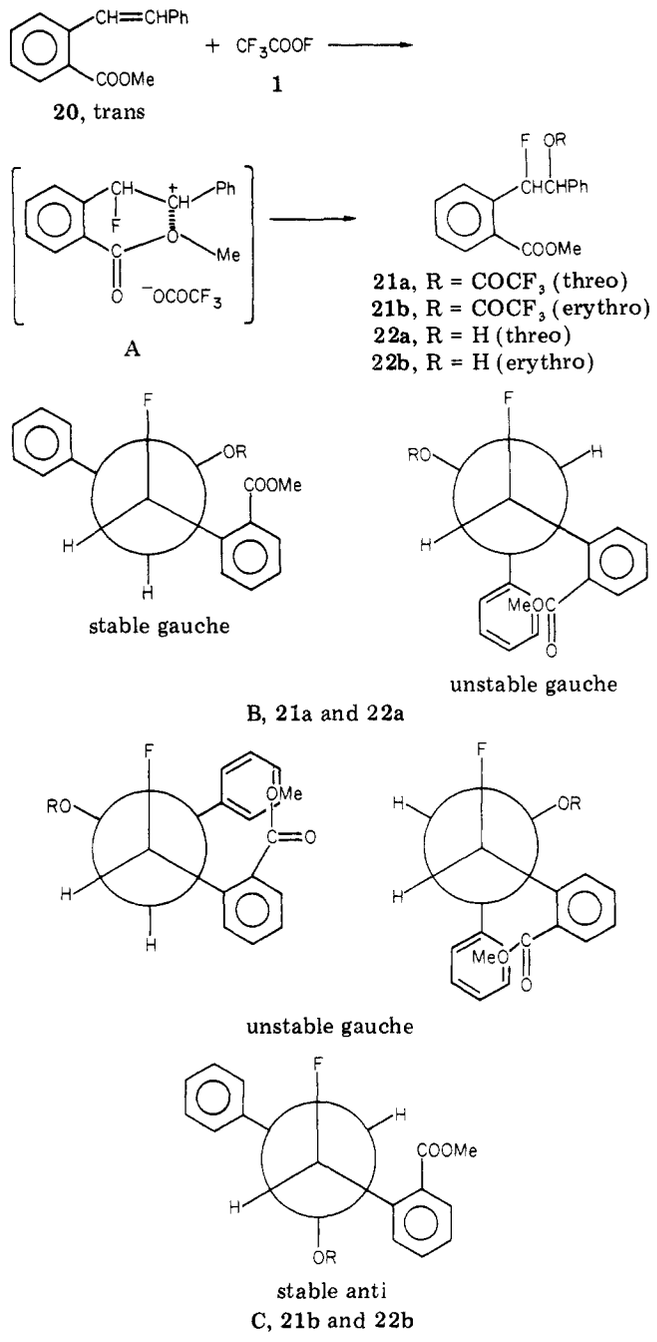
16a, X = F; Y = $OCOCF_3$
17a, X = $OCOCF_3$; Y = F
18a, X = F; Y = OH
19a, X = OH; Y = F

a = threo

most equal quantities. Although both esters had the same retention time on GC, their existence was clearly evident from the NMR spectrum which showed two almost identical sets of lines for the protons attached to the benzilic carbons. Even better indication for the mixture can be extracted from the mass spectrum which exhibits two base peaks of equal intensity, *m/e* 203 $(C_6H_5CHOCOCF_3)^+$ and 237 $(ClC_6H_4CHOCOCF_3)^+$, together with their benzilic counterions *m/e* 143 $(ClC_6H_4CHF)^+$ and 109 $(C_6H_5CHF)^+$. After hydrolysis we were able to separate the two resulting fluorohydrins by using high-pressure LC, thus obtaining *threo*-1-fluoro-2-hydroxy-1-(4-chlorophenyl)-2-phenylethane (**18a**) and *threo*-1-fluoro-2-hydroxy-1-phenyl-2-(4-chlorophenyl)ethane (**19a**). It is worth noting that also in this reaction a full threo stereospecifity is obtained for both isomers (see also Table II), indicating again an exclusive syn addition.

The reaction of *trans-o*-(carbomethoxy)stilbene (**20**) with **1** is interesting from several aspects. It was expected, and then confirmed, that this reaction would be regioselective in the Markownikoff sense.[13] However, in contrast to the reaction of the *p*-(carbomethoxy)stilbenes **8** or **11** with **1**, the complete stereoselectivity was lost. *threo*- and *erythro*-1-fluoro-2-(trifluoroacetoxy)-1-[2-(carbomethoxy)-phenyl]-2-phenylethanes (**21a** and **21b**, respectively) were

Scheme III

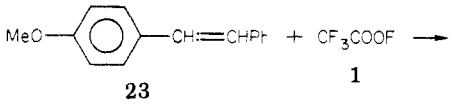


isolated in a ratio of 5:2. A Dreiding model of the intermediate 1-fluoro carbocation A (Scheme III) reveals that the ortho-methyl ester exerts a considerable steric hindrance upon the cationic center, not allowing an immediate consecutive attack from the trifluoroacetoxy anion. What is more, the oxygen atoms of the carbomethoxy group can be very close to the carbocation (1.1–1.3 Å), thus permitting an interaction between the positive charge and the oxygen. Such interaction can also be found in other reactions such as, for example, in acetoxyl migrations. Consequently, the somewhat prolonged lifetime of the unstable 1-fluoro carbocation is the reason for the achievement of some degree of randomization. The configuration of the adducts **21a** and **21b** (or, for that matter, of the corresponding fluorohydrins **22a** and **22b**) cannot be routinely determined from their spectral data. The major isomer, for which a threo configuration is assumed (syn addition), can adopt one stable gauche conformation in which the two aromatic rings are anti to each other. The second gauche confor-

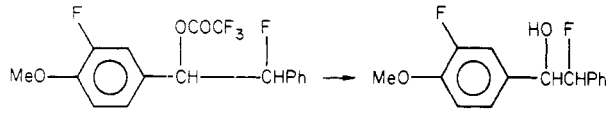
(11) Ho, Tse-Lok. *Chem. Rev.* **1975**, *75*, 1 and references therein.
(12) Hesse, R. H. *Isr. J. Chem.* **1978**, *17*, 60.
(13) We have isolated here a small chromatographic fraction, about 3–5% in yield, whose mass spectrum indicates an anti Markovnikov addition. Such a compound can be formed because of the existence of a certain degree of steric hindrance and because of the inductive field effect on the carbomethoxy group on the nearer olefinic carbon.

mation should be unfavorable since there is considerable steric repulsion between the carbomethoxy and the unsubstituted phenyl (B in Scheme III). This explains well the unusually low H–H and high F–H (vicinal) coupling constants of the fluorine and hydrogen atoms bonded to the central benzilic carbons (J_{HH} = 2.3 and 3.8 Hz and $J_{FH(vic)}$ = 24 and 20 Hz for **21a** and **22a**, respectively; see Table II). In contrast to all other stilbenes described here, the erythro isomers **21b** and **22b** are not likely to possess a gauche conformation. The stabilization energy gained by the "gauche effect" of compounds possessing vicinal fluorine–oxygen atoms is about 1 kcal/mol.[9b] The considerable steric disturbance for both gauche conformers caused by the carbomethoxy group outweighs this effect so that the anti conformer becomes the most stable one for **21b** or **22b** (C in Scheme III). The foregoing also explains the larger H–H (6 Hz) and the smaller F–H_{vic} (16 Hz) coupling constants for the fluorohydrin **22b**.

When the stilbene is substituted by an electron-donating group as in *trans*-4-methoxystilbene (**23**), complete regiospecifity is still preserved, and the electrophilic fluorine again attaches itself to the more electron-rich carbon atom.



23 1



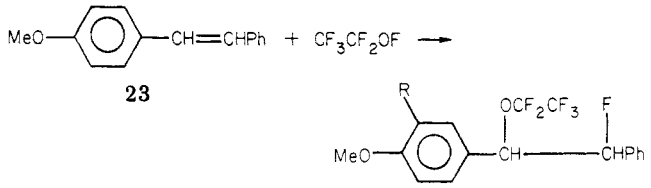
24a,b 25a,b

a = threo; b = erythro

As with the *trans*-*o*-(carbomethoxy)stilbene (**20**), the reaction of **1** with **23** was not strictly stereoselective, and after hydrolysis two isomers, **25a** and **25b**, were isolated in a ratio of 4:1, respectively. Clearly, the reason for the somewhat lower stereoselectivity in this case is due to the stabilizing influence of the methoxy group on the intermediate 1-fluoro carbonium ion $MeOC_6H_4\overset{+}{C}H$–CHFPh. A further interesting point is that fluorination has occurred on the activated ring. The fluorine chemical shift at ϕ* 135 leaves no doubt concerning the position of the fluorine substituent, ortho to the methoxy group.[14] Further evidence is given by the mass spectrum which shows unequivocally that the aromatic fluorine atom is situated in the anisole ring.

An interesting question arises as to which of the two now-known types of reagents, R_fOF and CF_3COOF, contains the more electrophilic oxygen-bound fluorine. It is difficult to obtain an answer from the rate of reactions of these reagents with olefins since such reactions occur virtually instantaneously with the addition of the substrate. As we have shown in Scheme I, we were able to synthesize fluoroxypentafluoroethane, CF_3CF_2OF, from fluorine and sodium trifluoroacetate. When this fluoroxy compound was reacted with **23**, two pairs of products, **26a,b** and **27a,b**, were obtained, the ratio of **a** to **b** being 2:1.[5]

The lower stereoselectivity in the reaction of **23** with CF_3CF_2OF compared with **1** has already been discussed. A more interesting point is that only 30% of the additional product underwent electrophilic aromatic fluorination, producing **27**, while the remaining 70% the anisole ring



23

26a,b, R = H
27a,b, R = F

a = threo; b = erythro

has not been attacked, resulting in **26**. Since aromatic substitution is usually slower than addition to a double bond, the question remains as to whether the perfluoroxy group in **26** does not deactivate the aromatic ring to such an extent as to prevent subsequent ring fluorination. When, however, the NMR shifts of the benzylic hydrogen, which is attached in one case to the perfluoro ether group and in the other to the trifluoroacetate, are compared, it is seen that the hydrogen in the first case absorbs at a higher field by 0.9 ppm than in the second case.[15] This fact supports the assumption that the trifluoroacetoxy group is more electronegative than the pentafluoroxy group, and clearly the retarding effect on electrophilic ring substitution in the case of the reaction of **23** with CF_3C-OOF should be stronger. Nevertheless, it was in the case of the reaction with **1** that complete ring fluorination did occur. One can thus conclude that the hypofluorite **1** is more polarizable, its oxygen-bound fluorine atom bears a formally stronger positive charge, and hence it is a stronger electrophile than the corresponding fluorine in compounds of type R_fOF.

Interesting additional support for the greater electronegativity of the trifluoroacetoxy group over that of the perfluoroalkoxy group, and consequently the greater electrophilic character of the oxygen-bound fluorine in **1** over that in CF_3OF, for example, is found in the comparison of the reactions of these two reagents with diphenylacetylene (**28**). In the case of CF_3OF, the main

$$\underset{\mathbf{28}}{PhC{\equiv}CPh} + CF_3OF \rightarrow \underset{\mathbf{29}}{PhCF_2CF(OCF_3)Ph}$$

reaction product found by Barton and Hesse[16] was the dibenzyl derivative **29**. This product results from the addition of elements of CF_3OF and of F_2 (the anion CF_3O^- readily breaks down to CF_2O and F^-).

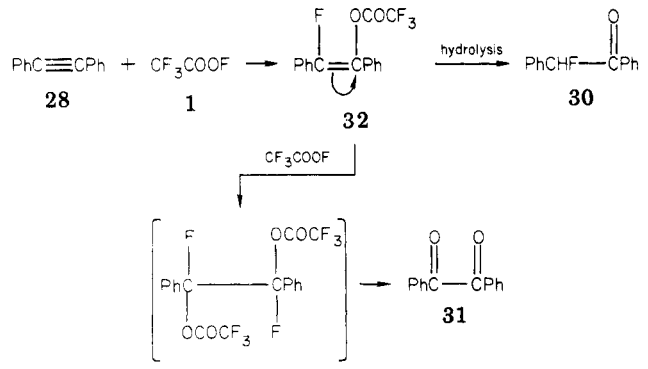
When **28** was reacted with the hypofluorite **1**, the result was entirely different. After the reaction was stopped, an oily mixture was obtained from which two products, identified as α-fluoro-α-phenylacetophenone (**30**; 30% yield) and benzil (**31**; 55% yield) were isolated by chromatographic separation. However, these were found not to be direct reaction products but to be the result of secondary reactions, mainly occurring during the workup and the chromatography of the crude reaction mixture. When the mixture was subjected to rapid TLC, it was possible to separate a small quantity of unstable material which, although it could not be obtained completely pure, showed the properties expected for α-fluoro-β-(trifluoroacetoxy)-stilbene (**32**). The IR spectrum contained strong absorption peaks at 1800 and 1170 cm^{-1}, showing the presence of the trifluoroacetoxy group. A relatively strong molecular peak (m/e 310) could be seen in the mass spectrum, the NMR showed only aromatic protons, and the position of

(14) The shifts of *o*-fluoroanisols are substantially different from those of the meta isomers or unsubstituted fluorophenyls. See also: "Progress in NMR Spectroscopy"; Emsley, J. W., Feeney, J., Sutcliffe, L. H., Eds.; Pergamon Press: Elmsford, NY, 1971; Vol 7.

(15) This phenomena is shown consistently in every pair of molecules examined by us, the members of the pairs differing only in the presence of a trifluoroacetyl or a pentafluoroethoxy group.

(16) Barton, D. H. R.; Danks, L. J.; Ganguly, A. K.; Hesse, R. H.; Tarzia, G.; Pechet, M. M. *J. Chem. Soc., Perkin Trans. 1* **1976**, 101.

Scheme IV



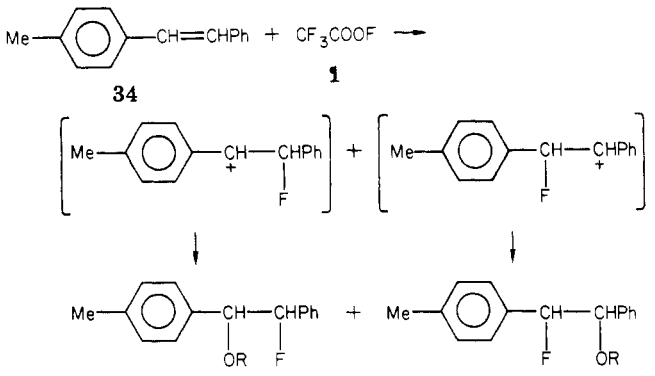
33 (not isolated)

the absorption maxima in the UV spectrum of this material (λ_{max} 228, 279, and 296 nm) are all in agreement with the suggested structure. It is not surprising that the reaction was somewhat slowed down at this stage, since the double bond in this stilbene is strongly deactivated. Compound **30** is obviously the hydrolysis product of **32**. Addition of a further molecule of CF_3COOF (**1**) to **32** produces the intermediate **33** which should readily break down to benzil (Scheme IV). It may be seen that during the addition of the second molecule of **1** to **32** the electrophilic fluorine attaches itself to the carbon substituted by the very electronegative trifluoroacetoxy group. This is in striking contrast to the reaction of **28** with CF_3OF in which **29** is the main product and no benzil was formed. It is also worth noting the finding of Merritt, concerning the addition of F_2O to acetylenes.[17] There, as in Barton and Hesse's work and in contrast to the behavior of CF_3COOF, all the reaction products contained the *gem*-difluorobenzyl ($PhCF_2$) group.

Up to this point, we have described the reactions of **1** mainly with three groups of stilbenes: (a) compounds possessing strong electron-withdrawing groups with large positive σ_p^+ values (**8**, **11**, and **12**; the resulting compounds have excellent regio- and stereospecificity); (b) compounds (**20** and **23**) which are able, although by different mechanisms, to stabilize the intermediate α-fluoro carbocation, so losing some of the stereoselectivity but showing excellent regioselectivity; (c) compound **15** that has a small positive σ_p^+ value, hence losing all regioselectivity but keeping excellent stereoselectivity.

trans-p-Methylstilbene (**34**) provides an opportunity to examine a stilbene with a substituent whose σ_p^+ value is in the medium range, and this should cause some loss of regioselectivity. In addition, its stabilizing effect on the intermediate α-fluoro carbocation should permit some degree of randomization, so both threo and erythro isomers should be formed.

Indeed, when **34** was reacted with **1**, the NMR spectrum clearly indicated the presence of at least three compounds. The crude mixture was then hydrolyzed, thus enabling the separation of two components in a ratio of 1:9. The major component, although appearing homogeneous on high-pressure LC, proved to be an inseparable mixture of **36a** and **38a** in a ratio of 3:1. The ratio can be determined by the mass spectrum of the mixture or by comparing the fluorine signals in the ^{19}F NMR spectrum (see Table II). It is worth pointing out the good qualitative relationship between the Hammett constants and the regioselectivity. With a σ_p^+ of −0.32 the reaction between **1** and **34** lost only 25% of its regioselectivity, while in the case of 4-chloro-



35a,b, R = $COCF_3$ 37a, R = $COCF_3$
36a,b, R = H 38a, R = H

a = threo; b = erythro

stilbene (**15**; $\sigma_p^+ = 0.11$) none was preserved. The minor component proved to be the erythro isomer **36b**, the configuration being established by its ^1H and ^{19}F NMR spectra (see Table II). This isomer originates from the partial stabilization of the α-fluoro carbocation, as in the case of **23**, although its smaller proportion in the reaction products reflects the difference between the methyl and the methoxy groups.

Experimental Section

Melting points were determined with a Buchi capillary apparatus. ^1H NMR spectra were measured with a Bruker WH-90 spectrometer at 90 MHz and with tetramethylsilane as internal standard. ^{19}F spectra were recorded with a Bruker HFX-10 at 84.67 MHz and were reported in parts per million upfield from $CFCl_3$ as internal standard. Mass spectra were measured with a Du Pont 21-491B spectrometer. Silica gel 60 (Merck; 70–230 mesh) was used for column chromatography. Analytical samples were usually obtained by high-pressure LC with silica gel (Merck, 10-μm packing).

Fluorination of Stilbenes (General Procedure). Caution: Fluorine, oxyfluoro compounds, and hypofluorites can be very poisonous compounds, so the reaction should be performed with appropriate care in order to avoid skin contact with or breathing of these reagents. In numerous experiments we have conducted in the last three years, however, neither explosions nor any accidents have occurred. About 3% fluorine (Matheson Gas Products) diluted with nitrogen was bubbled through a suspension of CF_3COONa in trichlorofluoromethane (Freon) at −75 °C for 4–6 h. No special care was taken to dry the salt, and no HF trap was used when the fluorine was passed through the reaction mixture. A good vibromixer was used to ensure efficient mixing. Samples of the solution were treated with an acidic solution of KI, and the liberated iodine was titrated with thiosulfate. When the desired concentration of the oxidizing reagents was achieved (usually 2–4 mmol), a cold solution of one of the stilbenes (1–3 mmol) in 30 mL of CH_2Cl_2 was added in one portion. After less than 1 min the reaction mixture was poured into dilute thiosulfate solution, and the organic layer was separated, washed several times, dried over $MgSO_4$, and evaporated. Some of the trifluoroacetoxy esters were purified by chromatography although no attempt was made to obtain analytical samples. In other cases, however, after the IR spectrum was taken, the crude product was dissolved in ethanol, a few drops of wet pyridine were added, and the reaction was stirred for 2–4 h at room temperature. The solvents were evaporated, and the crude fluorohydrin was subjected to high-pressure LC using CH_2Cl_2 as eluent and crystalized from petroleum ether. Since **1** accounts for at least 80% of the oxidizing mixture (on the basis of the yields of some α-fluoro-β-trifluoroacetoxy derivatives), we are referring to this oxidizing mixture as **1**.

In Tables I and II all physical and spectroscopic data are presented. Note, however, that usually only the fluorohydrins have been analytically purified, although the trifluoroacetoxy esters were often more than 90% pure. The yields of these esters are not given, but since the basic hydrolysis is usually almost

(17) Merritt, R. F.; Ruff, J. K. *J. Org. Chem.* **1965**, *30*, 328.

qualitative, their yields should be equal, or only slightly higher, than the yields of the respective fluorohydrins.

Reaction of Diphenylacetylene (28) with 1. Compound **28** (180 mg, 1 mmol) was added to Freon containing 2.5 mmol of **1**. The IR spectrum of the crude product mixture showed a wide carbonyl absorption at 1800 cm^{-1}. Fast TLC indicated that there is neither benzil (**31**) nor α-fluoro-α-phenylacetophenone (**30**) in the crude reaction mixture. After column chromatography or high-pressure LC, however, 80 mg of **28** was first recovered, followed by **30** (30% yield based on converted starting material): mp 49 °C;[16] ^1H NMR δ 6.50 (CHF, 1 H, d, J = 49 Hz), 7.25–8.0 (m, 10 aromatic protons); ^{19}F NMR ϕ* 176.3 (d, J = 49 Hz). The main fraction proved to be benzil (55% yield based on converted starting material) identical in all respects with an authentic sample.

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Registry No. **1**, 359-46-6; **2**, 103-30-0; **3a**, 72301-32-7; **3b**, 72301-33-8; **6a**, 3451-35-2; **6b**, 3527-61-5; **7**, 645-49-8; **8**, 1149-18-4; **9a**, 72318-09-3; **9b**, 72318-10-6; **10a**, 72301-34-9; **10b**, 72301-35-0; **11**, 46925-32-0; **12**, 20488-42-0; **13a**, 72301-36-1; **14a**, 72301-37-2; **15**, 1657-50-7; **16a**, 72301-38-3; **17a**, 72301-39-4; **18a**, 72301-40-7; **19a**, 72301-41-8; **20**, 38453-72-4; **21a**, 72301-42-9; **21b**, 72301-43-0; **22a**, 72301-44-1; **22b**, 72301-45-2; **23**, 1694-19-5; **24a**, 72301-46-3; **24b**, 72301-47-4; **25a**, 72301-48-5; **25b**, 72301-49-6; **28**, 501-65-5; **30**, 720-43-4; **31**, 134-81-6; **32**, 72301-50-9; **34**, 1860-17-9; **35a**, 72301-51-0; **36a**, 72301-52-1; **36b**, 72301-53-2; **37a**, 72301-54-3; **38a**, 72301-55-4.

Ozonolysis. The Added Aldehyde Effect[1]

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The effect of increasing amounts of *n*-butyraldehyde on ozonide yield and stereochemistry in the ozonolysis of *cis*- and *trans*-2,5-dimethyl-3-hexenes has been studied. A similar study was carried out on *trans*-2,2,5,5-tetramethyl-3-hexene. The results are interpreted by using a mechanistic scheme involving syn and anti carbonyl oxide isomers as well as some contribution from nonconcerted ozonide formation.

Recent years have seen an accumulation of an enormous amount of data on the ozonolysis reaction along with continued efforts to provide a comprehensive mechanistic scheme for the reaction.[2] Theoretical chemists have also found the problem to be an interesting one and have made suggestions which both challenge longstanding views and provide stimulation for new experimental approaches.[3-6]

For some time now we have been involved in an approach to the ozonolysis mechanism problem in which the effects of a number of reaction variables on typical reaction parameters (yield, stereochemistry, etc.) are systematically studied.

One of the reaction variables which has received some attention by us and other workers is that of solvent.[7-17] In a small number of instances such studies have included the special case in which aldehyde is added to the reaction medium[11,16,18-21] or is the actual solvent.[22] Such studies present particularly challenging problems in interpretation because in theory aldehydes are capable of influencing the reaction in at least two general ways, i.e., by exercising a medium (polar) effect on the process occurring and/or by participating at one or more points in the overall chemistry.

One of the remarkable effects of aldehyde as ozonolysis solvent is a suppression, partial or complete, of formation of ozonide.[22] Inasmuch as all of the current mechanistic proposals retain a step in which aldehyde and carbonyl oxide combine to give ozonide, this observation is troublesome and requires further consideration.

Story et al.[22] explain their results by postulating a reductive ozonolysis, that is, a reaction in which aldehyde is oxidized to acid and an ozonolysis intermediate (they suggest the Staudinger[23] molozonide) is reduced. Bailey et al.[20] have observed a similar effect of added aldehyde on ozonide yield but suggest that the aldehyde is oxidized by some other intermediate, possibly a 1,2,3-trioxolane or carbonyl oxide.

In a study designed to determine more specifically the point in the overall reaction scheme where the aldehyde is exerting an influence or actually intervening, we recently reported[16] that adding aldehyde to the solid 1,2,3-trioxolane formed in the ozonolysis of *trans*-di-*tert*-butylethylene (**1**) leads to decreased and ultimately zero ozonide yield. The latter is obtained when the solid 1,2,3-trioxolane is allowed to warm up in 100% aldehyde. These results

(1) Taken in part from the Ph.D. dissertation of Jang-Szu Su, UMSL.
(2) For a recent comprehensive summary of this topic see: Bailey, P. S. "Ozonation in Organic Chemistry"; Academic Press: New York, 1978.
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