The Chemistry of Methyl Hypofluorite: Its Reactions with Various Unsaturated Centers

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Methyl hypofluorite was until recently grouped as a hypothetical member of those smallest organic molecules which had not been synthesized. Passing F_2 through a solution of methanol in MeCN or PrCN resulted in its successful preparation. MeOF is an unique reagent, since it generates the novel electrophilic methoxylium moiety in contrast to the much more common methoxide group. This hypofluorite was reacted with several types of olefins including benzylic, cyclic, bicyclic, straight chain, and steroidal ones. In most cases the regioselectivity is very good, reflecting the unique polarization of the reagent: $MeO^{\delta+}F^{\delta-}$. The stereoselectivity tends to be less emphasized, but usually *anti* addition is dominant.

Until recently methyl hypofluorite–MeOF, along with hypothetical molecules such as MeHe and MeOHe, was a member of an exclusive family containing the smallest organic molecules which had never yet been synthesized.[1] It was a "common understanding" that CH_3OF would be unstable, since the hydrogen and the fluorine atoms would be too close to prevent a spontaneous HF elimination. Three years ago, however, we conducted some experiments which indicated that MeOF is a real molecule,[2] and a year later it was isolated and fully characterized.[3] We have also shown that MeOF is a very unique reagent in the sense that apart from $[MeOXe]^+BF_4^-$ [1e] it is the only source for the electrophilic methoxylium species "MeO^+",[4] attaching itself to the electron-rich sites of various enol derivatives[5] as well as of activated aromatic rings.[6] Because of its characteristically fast reactions a research program was also promoted in the field of the radioactive ^{11}C isotope (half-life time of 20 min) which is very important in positron emitting tomography (PET).[7] We report here on our efforts to investigate and further develop the chemistry of this new and unusual reagent, especially its reactions with various types of olefins.

MeOF is easily made by bubbling F_2 through a cold mixture of methanol–acetonitrile (−45 °C) or methanol–propionitrile (−78 °C). As with the other two members of this family, HOF[8] and *t*-BuOF,[9] acetonitrile plays an important role in stabilizing the methyl hypofluorite and widens considerably its synthetic potential. Although this hypofluorite can be isolated in pure form,[3] for all practical purposes it is used as formed in solution without any special purification. When working with small volumes (2–3 mL), concentrations of up to 2 M could be obtained in the MeOH/PrCN system, but with larger and more practical volumes of about 100–200 mL of MeOH/MeCN, the maximum concentration was found to be about ca. 0.3 M. These limits are dictated by the concentration of the fluorine gas and the time it takes to pass it through the reaction mixture. We found that higher fluorine concentrations are responsible for faster decomposition, since MeOF is decomposed in the vapor phase by F_2. On the other hand, too low a fluorine concentration results in longer reaction times, limiting again the methyl hypofluorite concentration, since its half-life time is about 1–1.5 h at the conditions present in the reaction mixture.

Similar to HOF, but unlike many other hypofluorites, including CF_3OF,[10] CF_3CF_2OF,[11] and CH_3COOF,[12] MeOF does not possess an electrophilic fluorine, and in most cases we find the "MeO" pole of the molecule to act as the electrophile. Thus, when compounds with terminal benzylic double bonds were reacted with MeOF a regioselective reaction took place. As preliminarily reported,[3] styrene (**1**) produced the adduct 1-fluoro-1-phenyl-2-methoxyethane (**3**), while in the present investigation 2-vinylnaphthalene (**2**) gave 1-fluoro-1-(2-naphthyl)-2-methoxyethane (**4**). Similar regioselectivity was observed with nonterminal olefins, and *trans* β-methylstyrene (**5**)

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(1) Addition of the elements CH_3O and F across double bonds in a two-step reaction has been described, especially when electrophilic fluorinating reagents reacted with olefins in the presence of MeOH which captured the intermediate fluorocarbocation to produce fluoro methoxy adducts. The methoxy moiety, however, always occupied the electron-poor pole of the starting double bond. See, for example: (a) Barton, D. H. R.; Hesse, R. H.; Jackman, G. P.; Pechet, M. M. *J. Chem. Soc., Perkin Trans. 1* **1977,** 2604. (b) Djuric, S. W.; Garland, R. B.; Nystead, L. N.; Pappo, R.; Plume, G.; Swenton, L. *J. Org. Chem.* **1987,** *52,* 978. (c) Stavber, S.; Zupan, M. *J. Org. Chem.* **1987,** *52,* 919. (d) Shellhamer, D. F.; Curtis, C. M.; Hollingsworth, D. R.; Ragains, M. L.; Richardson, R. E.; Heasley, V. L.; Heasley, G. E. *Tetrahedron Lett.* **1982,** *23,* 2157–2160. (e) Shellhamer, D. F.; Curtis, C. M.; Dunham, R. H.; Hollingsworth, D. R.; Ragains, M. L.; Richardson, R. E.; Heasley, V. L.; Shackelford, S. A.; Heasley, G. E. *J. Org. Chem.* **1985,** *50,* 2751–2758. In their first paper, Shellhamer *et al.* actually claimed the formation of CH_3OF, but this claim was withdrawn in their second paper.

(2) Rozen, S.; Hebel, D.; Kol, M. 199th ACS National Meeting; Boston, MA, 1990; FLUO17 (see also *Chem. Eng. News* **1990,** May 7, 62.

(3) Kol, M.; Rozen, S.; Appelman, E. *J. Am. Chem. Soc.* **1991,** *113,* 2648.

(4) It should be clear that, as with other electrophilic species such as "F^+", "MeO^+" indicates only that in the transition state the molecule is polarized in such a way that the methoxylium pole acts as an electrophile. This feature is enhanced by the counter pole being a good leaving group. For more detailed discussion on the subject see: Lerman, O.; Tor, Y.; Hebel, D.; Rozen, S. *J. Org. Chem.* **1984,** *49,* 806.

(5) Rozen, S.; Mishani, E.; Kol, M. *J. Am. Chem. Soc.* **1992,** *114,* 7643.

(6) Kol, M.; Rozen, S. *J. Org. Chem.* **1993,** *58,* 1593.

(7) McCarthy, T. J.; Bonasera, T. A.; Welch, M. J.; Rozen, S. *J. Chem. Soc., Chem. Commun.* **1993,** 561.

(8) Rozen, S.; Brand, M.; Kol, M. *J. Am. Chem. Soc.* **1989,** *111,* 8325. Appelman, E. H.; Dunkelberg, O.; Kol, M. *J. Fluorine Chem.* **1992,** *56,* 199.

(9) Appelman, E. H.; French, D.; Mishani, E.; Rozen, S. *J. Am. Chem. Soc.* **1993,** *115,* 1379.

(10) Hesse, R. H. *Isr. J. Chem.* **1978,** *17,* 60.

(11) Rozen, S.; Lerman, O. *J. Org. Chem.* **1980,** *45,* 4122.

(12) Lerman, O.; Tor, Y.; Hebel, D; Rozen, S. *J. Org. Chem.* **1984,** *49,* 806.

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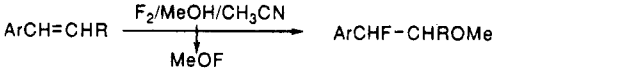
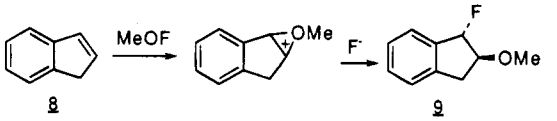
was converted into 1-fluoro-1-phenyl-2-methoxypropane as a mixture of two diastereoisomers **6** and **7** in a ratio of 1.5:1. Examination of the J_{HH} and J_{HF} coupling constants leads to the conclusion that the major component **6** is the erythro derivative resulting from anti addition, while **7** is the corresponding threo isomer. The anti addition was found to be even more dominant with the more rigid indene (**8**), which formed *trans* 1-fluoro-2-methoxyindan (**9**).[1e,13] This is in sharp contrast to the almost exclusive *syn* addition found in reactions where the oxygen-bound fluorine serves as an electrophile.[14] Such an addition mode points to a cyclic oxonium bridge intermediate resembling the more common cyclic halonium formed by all electrophilic halogens, except fluorine, in their reactions with double bonds. Similar oxygen bridges are also formed when the HOF·CH_3CN complex reacts with olefins to give epoxides.[15]



1	Ar = Ph;	R = H	3
2	Ar = 2-naphthyl;	R = H	4
5 (*trans*)	Ar = Ph;	R = Me	6 (*erythro*) + 7 (*threo*)



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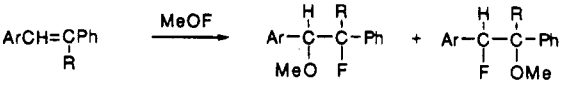
In order to exclude the possibility of a two-step reaction in which the methanol from the solvent is involved in the process of forming the fluoromethoxy derivatives, we conducted a few experiments where the gaseous MeOF was carried with a stream of nitrogen from the reactor it was formed in, via a cold empty trap designed to capture traces of MeOH, to a second reactor where the substrate was dissolved in pure CH_3CN. The results were essentially identical with the ones where the substrates were added directly to the original reactor, offering an additional proof that the reactive species is indeed the MeOF molecule. Adding radical inhibitors such as *m*-dinitrobenzene, or employing radical initiation procedures such as irradiation with a sun lamp at −40 °C, did not alter the reaction course. Irradiation at room temperature, however, did result in fast radical decomposition of both the reagent and the substrate. These experiments clearly point toward the ionic character of the reactions between MeOF and olefins.

Other benzylic olefins with less polarized double bonds reacted with MeOF with reduced regioselectivity. *trans* α-Methylstilbene (**10**) gave a mixture of 1-fluoro-1-methyl-2-methoxy-1,2-diphenylethane (**11**) and its regioisomer (**12**) in a ratio of 4:1, while with almost symmetrical olefins such as 4-methylstilbene (**13**) the two corresponding adducts **14** and **15** were obtained as a 1:1 mixture in 75% yield. It should be noted that **13** was reacted previously with CF_3COOF and gave similar mixtures of the corresponding adducts.[16]

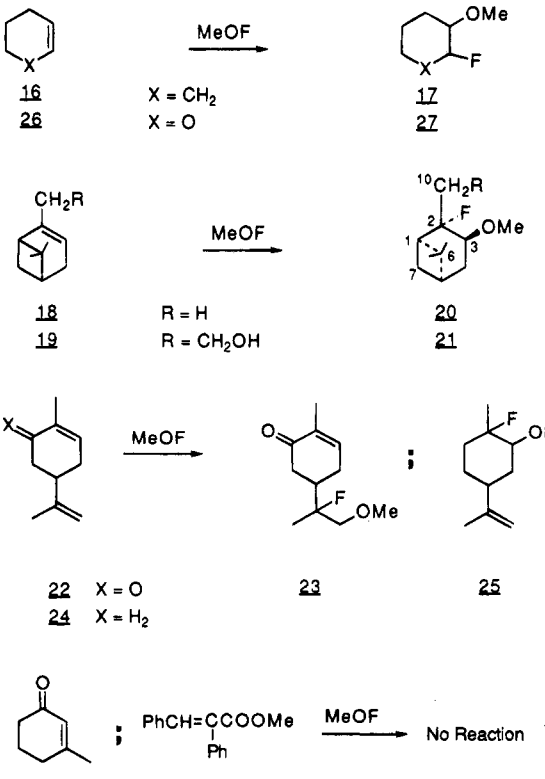
Nonbenzylic olefins also reacted well with MeOF. Cyclohexene (**16**) formed the expected 1-fluoro-2-methoxycyclohexane (**17**)[12] in about 50% yield. The sensitive bicyclic olefins α-pinene (**18**) and nopol (**19**) were also



10 (*trans*)	Ar = Ph; R = Me	11	12
13 (*trans*)	Ar = *p*-$CH_3C_6H_4$; R = H	14	15

reacted producing, via anti addition, the corresponding adducts **20** and **21**. The stereo- and the regioselectivity of the products are based mainly on ^1H NMR (a COSY experiment for **20** indicates that the hydrogen geminal to the methoxy group is equatorial), ^{19}F NMR (reveals axial fluorine), and ^{13}C NMR (using the DEPT program). The latter shows that C-1, C-3, and methyl C-10 in **20** are in β positions to the fluorine atom ($^2J_{CF}$ = 21, 14 and 29 Hz, respectively) while the γ C-7 is in the trans configuration to it ($^3J_{CF}$ = 11 Hz).[17] The fact that the strained bicyclic skeleton was not converted to the corresponding 4-isopropylcyclohexane derivative is indicative of the mildness of the reagent. The same can be said of the fact that the free hydroxyl group of **19** did not interfere and was not oxidized by MeOF.

Carvone (**22**) represents another interesting case, where two different olefinic bonds are found in the same molecule. Only the more electron-rich exocyclic double bond reacted forming the adduct **23**. Limonene (**24**), which lacks the deactivating carbonyl, behaves similarly, and this time when an excess of **24** was reacted with MeOF the more electron-rich endocyclic trisubstituted double bond was the one which reacted to form the adduct **25** in higher than 40% yield. Electron-poor double bonds such as the one present in 3-methylcyclohexenone or methyl α-phenylcinnamate were completely resistant to MeOF and only the starting materials were isolated, emphasizing the ionic character of this reaction. At the other end of the scale, the electron-rich olefin 3,4-dihydro-2*H*-pyran (**26**) reacted rapidly to produce 2-fluoro-3-methoxytetrahydropyran (**27**) in 85% yield.



16 X = CH_2 17
26 X = O 27

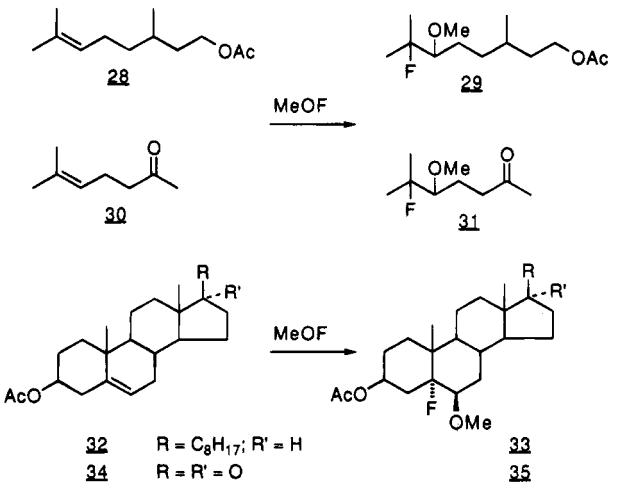
18 R = H 20
19 R = CH_2OH 21

22 X = O 23 25
24 X = H_2

Aliphatic olefins also react with MeOF quite satisfactorily. While citronellol acetate (**28**) was converted to 3,7-

(13) Hebel, D.; Rozen, S. *J. Org. Chem.* **1987**, *52*, 2588.
(14) Rozen, S.; Lerman, O.; Kol, M.; Hebel, D. *J. Org. Chem.* **1985**, *50*, 4753.
(15) Rozen, S.; Kol, M. *J. Org. Chem.* **1990**, *55*, 5155.
(16) Rozen, S.; Lerman, O. *J. Org. Chem.* **1980**, *45*, 672.

dimethyl-7-fluoro-6-methoxyoctyl acetate (**29**) in only 30% yield, a shorter aliphatic chain 2-methylhept-2-en-6-one (**30**) yielded the expected adduct (**31**) in 90%. We noticed that such differences in yields between shorter and longer chains are quite characteristic with reagents possessing a relatively weak X—F bond. In addition to the main reaction course, such reagents tend also to decompose homolytically resulting in nonspecific radical reactions. In fact, the same effect was observed with steroids. Cholesterol acetate (**32**) reacted with MeOF to produce 5α-fluoro-6β-methoxycholestanol acetate (**33**) in only 25% yield, while 17-oxoandrostan-5-en-3β-ol acetate (**34**) gave the 5α-fluoro-6β-methoxy adduct (**35**) in 45% yield. These trans-diaxial adducts are typical to F—X reagents when X is a relatively bulky group. Similar additions across the 5,6 double bonds were observed, for example, with IF.[18]



In conclusion, it has been shown that MeOF is a clearly defined reagent which can add to various types of double bonds with a unique regioselectivity. This originates in the fact that this reagent generates the novel methoxylium moiety which acts as an electrophile in its reactions with olefins.

Experimental Section

^{1}H NMR spectra were recorded with Bruker AC-200 and AM-360 WB spectrometers, with $CDCl_3$ as solvent and Me_4Si as internal standard. The proton broad band decoupled ^{13}C NMR spectra were recorded at 90.5 MHz. Here too, $CDCl_3$ served as a solvent and TMS as internal standard. The ^{19}F NMR spectra were measured at 338.8 MHz and are reported in parts per million upfield from $CFCl_3$, which also served as internal standard. Mass spectra were measured with a DuPont 21-491B instrument and GC/MS with a Varian-3400 equipped with Finnigan Mat ITD-800 detector. IR spectra were recorded as neat films, in $CHCl_3$ solution, or in KBr pellets on a Nicolet 205 FTIR spectrophotometer.

General Procedure for Working with Fluorine. Fluorine is a strong oxidant and a very corrosive material. An appropriate vacuum line made from copper or monel in a well-ventilated area should be constructed for working with this element. Additional experimental information of how we handle it appears in some other publications.[19] For the occasional user, however, various premixed mixtures of F_2 in inert gases are commercially available, simplifying the whole process. The reactions themselves can be carried out in glass vessels. If elementary precautions are taken, work with fluorine is relatively simple, and we have had no bad experiences working with this element.

Preparation of MeOF and Its Reactions with Olefins. A mixture of 15% F_2 in N_2 was bubbled for 1 h at a rate of 110 mL/min into a cold (−40 °C) solution of 5 mL of MeOH in 115 mL of CH_3CN placed in a Teflon vessel. The amount of the MeOF thus obtained could be easily determined by reacting aliquots of the reaction mixture with aqueous KI and titrating the liberated iodine. After the desired concentration of MeOF was achieved, usually around 0.1−0.3 M, a cold (−40 °C) solution of the olefin in $CHCl_3$ was added and the mixture allowed to warm to room temperature. The reactions were usually carried out on scales of 3−20 mmol using a 1.5−4-fold excess of MeOF. It should be noted that although pure liquid MeOF can explode,[3] it is perfectly safe when diluted with solvents. If needed, a stream of nitrogen could be employed for transferring the gaseous MeOF to a secondary reactor containing only cold (−40 or −78 °C, respectively) aceto- or propionitrile. By employing this procedure about 25% of the MeOF decomposes, but the oxidizing solution in the secondary reactor is HF and MeOH free. The reactions were usually monitored by GC, TLC, or NMR and in most cases were complete within 5−25 min after reaching room temperature. The term "usual workup" refers to terminating the reaction by pouring it into 500 mL of $NaHCO_3$ solution, extraction with $CHCl_3$, washing it with water until neutral, drying the organic layer over $MgSO_4$, and finally evaporating the solvent. The crude reaction mixture was usually subjected to vacuum flash chromatography using silica gel 60-H (Merck) with mixtures of EtOAc in petroleum ether serving as eluent.

Reaction of Styrene (1) with MeOF. To a cold (−40 °C) MeOH/MeCN solution containing 7 mmol of MeOF was added 570 mg of **1** in 10 mL of CH_2Cl_2. After the usual workup the adduct **3** was obtained in 75% yield as an oil.[3] ^{1}H NMR: 7.32 (5 H, s), 5.58 (1 H, ddd, J_1 = 49 Hz, J_2 = 8 Hz, J_3 = 4 Hz), 3.65 (2 H, m), 3.39 (3 H, s). ^{19}F NMR: −183.76 (ddd, J_1 = 49 Hz, J_2 = 30 Hz, J_3 = 19 Hz). MS, *m/e*: 154 (M^+), 134 [(M − HF)$^+$]. Anal. Calcd for $C_9H_{11}FO$: C, 70.11; H, 7.19. Found: C, 69.83; H, 7.17. Similar results were obtained when gaseous MeOF was transferred with the stream of nitrogen into a reactor which contained a CH_2Cl_2 solution of **1**

Reaction of Vinylnaphthalene (2) with MeOF. To a cold (−75 °C) MeOH/PrCN solution containing 12 mmol of MeOF was added 530 mg of **2** in 10 mL of $CHCl_3$. After the usual workup the adduct **4** was obtained in 45% yield as an oil. ^{1}H NMR: 7.6 (7 H, m), 5.75 (1 H, ddd, J_1 = 49 Hz, J_2 = 8 Hz, J_3 = 4 Hz), 3.80 (2 H, m), 3.46 (3 H, s). ^{19}F NMR: −183.61 (ddd, J_1 = 49 Hz, J_2 = 30 Hz, J_3 = 19 Hz). ^{13}C NMR: 128−123 (ar *C*), 93.4 (*C*F, $^1J_{CF}$ = 176 Hz), 76.1 (CH_2O, $^2J_{CF}$ = 24 Hz), 59.4 (OCH_3). MS, *m/e*: 204 (M^+); 184 [(M − HF)$^+$].

Reaction of *trans*-β-Methylstyrene (5) with MeOF. To a cold (−45 °C) MeOH/MeCN solution containing 16 mmol of MeOF was added 520 mg of **5** in 5 mL of CH_2Cl_2. After the usual workup a diastereoisomeric mixture of **6** and **7** in a ratio of 1.5:1 was obtained in 70% yield as an oil. MS, *m/e*: 168 (M^+); 121 [(M − MeOH − Me)$^+$]; 59 [(CH_3CHOCH_3)$^+$]. Anal. Calcd for $C_{10}H_{13}FO$: C, 71.43; H, 7.74. Found: C, 70.73; H, 7.33. For **6**. ^{1}H NMR: 7.33 (5 H, s), 5.41 (1 H, dd, J_1 = 47 Hz, J_2 = 4 Hz), 3.55 (1 H, m), 3.36 (3 H, s), 1.15 (3 H, dd, J_1 = 6.3 Hz, J_2 = 1.5 Hz). ^{19}F NMR: −131.12 (dd, J_1 = 47 Hz, J_2 = 17 Hz). ^{13}C NMR: 128−125 (ar *C*), 94.9 (*C*F, $^1J_{CF}$ = 177 Hz), 79.3 (CH_2O, $^2J_{CF}$ = 24 Hz), 57.0 (OCH_3), 13.6 (CH_3). For **7**. ^{1}H NMR: 7.33 (5 H, s), 5.26 (1 H, dd, J_1 = 47 Hz, J_2 = 6.5 Hz), 3.55 (1 H, m), 3.44 (3 H, s), 0.95 (3 H, d, J = 6.4 Hz). ^{19}F NMR: −121.1 (dd, J_1 = 47 Hz, J_2 = 14 Hz). ^{13}C NMR: 128−125 (ar *C*), 96.9 (*C*F, $^1J_{CF}$ = 176 Hz), 79.1 (CH_2O, $^2J_{CF}$ = 24 Hz), 57.6 (OCH_3), 15.1 (CH_3).

Reaction of Indene (8) with MeOF. To a cold (−40 °C) MeOH/MeCN solution containing 12 mmol of MeOF was added 284 mg of **8** in 10 mL of CH_2Cl_2. After the usual workup the adduct **9** was obtained in 90% yield as an oil.[12] ^{1}H NMR: 7.45−7.20 (4 H, m), 5.93 (1 H, dd, J_1 = 56 Hz, J_2 = 4 Hz), 4.25 (1 H, m), 3.53 (3 H, s), 3.36 (1 H, dd, J_1 = 16 Hz, J_2 = 7 Hz), 2.82 (1 H, dd, J_1 = 16 Hz, J_2 = 5 Hz). ^{19}F NMR: −174.30 (dd, J_1 = 56 Hz, J_2 = 18 Hz). ^{13}C NMR: 130−127 (ar *C*), 100.0

(17) (a) Coxon, J. M.; Hydes, G. J.; Steel, P. J. *J. Chem. Soc., Perkin Trans 2* **1984,** 1351. (b) Rozen, S.; Ben-Shoshan, G. *Org. Magn. Reson.* **1985,** *23,* 116.

(18) Rozen, S.; Brand, M. *J. Org. Chem.* **1985,** *50,* 3342 and references cited therein.

(19) See, for example: Hebel, D.; Rozen, S. *J. Org. Chem.* **1991,** *56,* 6298.

(CF, $^1J_{CF}$ = 179 Hz), 86.95 (CHO, $^2J_{CF}$ = 21 Hz), 57.7 (OCH_3), 35.79 (CH_2). MS, *m/e*: 166 (M^+), 146 [(M − HF)$^+$], 135 [(M − OMe)$^+$]. Anal. Calcd for $C_{10}H_{11}FO$: C, 72.27; H, 6.67. Found: C, 72.38; H, 6.54.

Reaction of *trans*-α-Methylstilbene (10) with MeOF. To a cold (−40 °C) MeOH/MeCN solution containing 9 mmol of MeOF was added 425 mg of **10** in 7 mL of $CHCl_3$. After the usual workup and chromatographic purification the main adduct **11** was obtained in 70% yield as an oil. ^{1}H NMR: 7.16 (10 H, m), 4.38 (1 H, d, J = 14 Hz), 3.24 (3 H, s), 1.69 (3 H, d, J = 23 Hz). ^{19}F NMR: −153.71 (dq, J_1 = 22 Hz, J_2 = 14 Hz). ^{13}C NMR: 128−125 (ar *C*), 98.2 (*C*F, $^1J_{CF}$ = 176 Hz), 68.9 (*C*HO, $^2J_{CF}$ = 26 Hz), 57.6 (OCH_3), 22.9 (CH_3, $^2J_{CF}$ = 23 Hz),). MS, *m/e*: 224 [(M − HF)$^+$], 121 (PhCHOMe$^+$). Anal. Calcd for $C_{16}H_{17}FO$: C, 78.69; H, 6.97. Found: C, 78.43; H, 6.68.

Reaction of *trans*-4-Methylstilbene (13) with MeOF. To a cold (−70 °C) MeOH/PrCN solution containing 7 mmol of MeOF was added 352 mg of **13** in 5 mL of $CHCl_3$. After the usual workup an inseparable mixture of the two regioisomers **14** and **15** (each as a mixture of diastereoisomers) was obtained in 80% yield as an oil. ^{19}F NMR (for **14** erythro and threo isomers respectively[20]): −184.21 (dd, J_1 = 46 Hz, J_2 = 14 Hz), −180.38 (dd, J_1 = 47 Hz, J_2 = 12 Hz), (for **15** erythro and threo isomers respectively): −182.80 (dd, J_1 = 46 Hz, J_2 = 14 Hz), −179.17 (dd, J_1 = 47 Hz, J_2 = 12 Hz). MS (for the mixture), *m/e*: 224 [(M − HF)$^+$], 209 [(M − HF − CH_3)$^+$]. Anal. (for the mixture) Calcd for $C_{16}H_{17}FO{\cdot}0.5H_2O$: C, 75.89; H, 7.11. Found: C, 75.43; H, 6.69.

Reaction of Cyclohexene (16) with MeOF. To a cold (−45 °C) MeOH/MeCN solution containing 16 mmol of MeOF was added 1.01 g of **16** in 5 mL of CH_2Cl_2. After the usual workup and microdistillation at 70 °C/16 mmHg, a diastereoisomeric mixture of **17** was obtained in 50% yield as an oil.[12] MS, *m/e*: 132 (M^+); 100 [(M − MeOH)$^+$]. ^{1}H NMR (for the trans isomer): 4.36 (1 H, dm, J = 50 Hz each wing $W_{h/2}$ = 30 Hz), 3.41 (3 H, s), (for the cis isomer): 4.73 (1 H, dm, J = 50 Hz each wing $W_{h/2}$ = 10 Hz), 3.46 (3 H, s).

Reaction of α-Pinene (18) with MeOF. To a cold (−40 °C) MeOH/MeCN solution containing 16 mmol of MeOF was added 1.22 g of **18** in 6 mL of CH_2Cl_2. After the usual workup the adduct 2-fluoro-3-methoxy-2,6,6-trimethylbicyclo[3.1.1]-heptane (**20**) was obtained in 40% yield as an oil. ^{1}H NMR (COZY): 3.62 (1 H, C*H*OMe, ddd, J_1 = 13 Hz, J_2 = 9 Hz, J_3 = 5 Hz), 3.45 (3 H, OCH_3, s), 2.36 (1 H, C_1-H, m, $W_{h/2}$ = 28 Hz), 2.16 (1 H, C_5-H, m, $W_{h/2}$ = 25 Hz), 2.05 (1 H, C_4-H, m, $W_{h/2}$ = 12 Hz), 1.95 (1 H, C_4-H, m, $W_{h/2}$ = 17 Hz), 1.75 (1 H, C_7-H, ddd, J_1 = 12 Hz, J_2 = 5.9 Hz, J_3 = 2.3 Hz), 1.47 (1 H, C_7-H, d narrow m, J = 12 Hz), 1.24 (3 H, s), 0.87 (3 H, s). ^{19}F NMR: −147.61 (m, $W_{h/2}$ = 60 Hz). ^{13}C NMR (DEPT): 96.6 (*C*F, $^1J_{CF}$ = 181 Hz), 77.9 (*C*HO, $^2J_{CF}$ = 14 Hz), 58.3 (OCH_3), 52.9 (*C-1*, $^2J_{CF}$ = 21 Hz), 40.16 (*C-5*), 38.1 (*C-6*), 28.0 (*C-10*, $^2J_{CF}$ = 29 Hz), 27.1 (*C-7*, $^3J_{CF}$ = 11 Hz), 27.4, 23.6 (*C-8*, *C-9*). MS, *m/e*: 171 [(M − Me)$^+$], 166 [(M − HF)$^+$], 151 [(M − HF − Me)$^+$]. Anal. Calcd for $C_{11}H_{19}FO$: C, 70.97; H, 10.22. Found: C, 70.67; H, 10.37.

Reaction of Nopol (19) with MeOF. To a cold (−40 °C) MeOH/MeCN solution containing 12 mmol of MeOF was added 1.67 g of **19** in 10 mL of CH_2Cl_2. After the usual workup the adduct **21** was obtained in 40% yield as an oil. ^{1}H NMR: 3.84 (3 H, C*H*OMe + CH_2OH, m), 3.45 (3 H, OCH_3, s), 2.44 (1 H, t, J = 11 Hz), 2.23 (2 H, m), 2.05−1.83 (4 H, m), 1.52 (1 H, d, J = 11 Hz), 1.30 (3 H, s), 0.93 (3 H, s). ^{19}F NMR: −156.7 (m). MS, *m/e*: 196 [(M − HF)$^+$], 181 [(M − HF − Me)$^+$]. Anal. Calcd for $C_{12}H_{21}FO_2$: C, 66.67; H, 9.72. Found: C, 66.56; H, 10.01.

Reaction of Carvone (22) with MeOF. To a cold (−40 °C) MeOH/MeCN solution containing 11 mmol of MeOF was added 410 mg of **22** in 1 mL of $CHCl_3$. After the usual workup the adduct **23** was obtained in 44% yield as an oil. IR: 1670 cm^{-1}. ^{1}H NMR: 6.75 (1 H, m), 3.45 (2 H, m), 3.39 (3 H, s), 2.41 (5 H, m), 1.78 (3 H, bs), 1.33 (3 H, d, J = 22 Hz). ^{19}F NMR: −158.7 (m). MS, *m/e*: 180 [(M − HF)$^+$]. Anal. Calcd for $C_{11}H_{17}FO_2$: C, 66.00; H, 8.50. Found: C, 65.88; H, 8.41.

Reaction of Limonene (24) with MeOF. To a cold (−40 °C) MeOH/MeCN solution containing 10 mmol of MeOF was added 3 g of **24** (22 mmol) in 5 mL of CH_2Cl_2. After the usual workup the adduct **25** was obtained as a diastereoisomeric mixture in 42% yield (based on CH_3OF) as an oil. ^{1}H NMR: 4.72 (2 H, bs), 3.36 (3 H, s), 3.27 (1 H, m), 2.18−1.42 (7 H, m), 1.73 (3 H, bs), 1.36 (3 H, d, J = 23 Hz). ^{19}F NMR: −153.35 (m, $W_{h/2}$ = 100 Hz). ^{13}C NMR: 149.8 (*C*=CH_2), 108.7 (C=*C*H_2), 94.1 (*C*F, $^1J_{CF}$ = 166 Hz), 80.6 (*C*HO, $^2J_{CF}$ = 34 Hz), 57.1 (OCH_3). MS, *m/e*: 166 [(M − HF)$^+$], 154 [(M − HF − CH_3-OH)$^+$].

Reaction of 3,4-Dihydro-2*H*-pyran (26) with MeOF. To a cold (−40 °C) MeOH/MeCN solution containing 12 mmol of MeOF was added 504 mg of **26** in 5 mL of CH_2Cl_2. After the usual workup the adduct **27** was obtained as a diastereoisomeric mixture in 85% yield as an oil. ^{1}H NMR: 5.45 (1 H, dd, J_1 = 51 Hz, J_2 = 2 Hz), 4.55 (1 H, m), 3.80 (2 H, m), 3.39 (3 H, s), 2.0−1.6 (4 H, m). ^{19}F NMR: −161.5 (m). MS (high resolution), *m/e*: calcd for $C_6H_{11}FO_2$ 134.0743 (M^+), found 134.0746.

Reaction of Citronellol Acetate (28) with MeOF. To a cold (−40 °C) MeOH/MeCN solution containing 14 mmol of MeOF was added 1.1 g of **28** in 5 mL of $CHCl_3$. After the usual workup the adduct **29** was obtained as a diastereoisomeric mixture in 30% yield as an oil. IR: 1740 cm^{-1}. ^{1}H NMR: 4.11 (2 H, t, J = 7 Hz), 3.50 (3 H, s), 3.05 (1 H, m), 2.04 (3 H, s), 1.5 (7 H, m), 1.38 (3 H, d, J = 8 Hz), 1.27 (3 H, d, J = 8 Hz). ^{19}F NMR: −140.9 (m). MS *m/e*: 228 [(M − HF)$^+$]. Anal. Calcd for $C_{13}H_{25}FO_3{\cdot}0.5H_2O$: C, 60.70; H, 10.12. Found: C, 61.12; H, 10.15.

Reaction of 2-Methylhept-2-en-6-one (30) with MeOF. To a cold (−40 °C) MeOH/MeCN solution containing 12 mmol of MeOF was added 504 mg of **30** in 5 mL of $CHCl_3$. After the usual workup the adduct **31** was obtained in 90% yield as an oil. ^{1}H NMR: 3.46 (3 H, s), 3.12 (1 H, ddd, J_1 = 12 Hz, J_2 = 10 Hz, J_3 = 3 Hz),), 2.6 (2 H, m), 2.15 (3 H, s), 2.0−1.6 (2 H, m), 1.33 (3 H, d, J = 22 Hz), 1.31 (3 H, d, J = 22 Hz). ^{19}F NMR: −141.0 (m). ^{13}C NMR: 208.1 (*C*O), 98.0 (*C*F, $^1J_{CF}$ = 168 Hz), 85.1 (*C*HO, $^2J_{CF}$ = 21 Hz), 60.21 (OCH_3), 39.67, 29.46, 24.4, 23.5 (CH_3, $^2J_{CF}$ = 23 Hz), 21.88 (CH_3, $^2J_{CF}$ = 24 Hz). MS *m/e*: 156 [(M − HF)$^+$]. Anal. Calcd for $C_9H_{17}FO_2$: C, 61.32; H, 9.73, F, 10.79. Found: C, 60.67; H, 9.45; F, 10.64.

Reaction of Cholesterol Acetate (32) with MeOF. To a cold (−40 °C) MeOH/MeCN solution containing 9 mmol of MeOF was added 903 mg of **32** in 10 mL of $CHCl_3$. After the usual workup the adduct **33** was obtained in 25% yield, mp = 98 °C (from MeOH). IR: 1740 cm^{-1}. ^{1}H NMR: 5.05 (1 H, m) 3.28 (3 H, s), 3.15 (1 H, m, eq C*H*OMe, $W_{h/2}$ = 13 Hz), 2.02 (3 H, s), 0.97 (3 H, Me-19, s), 0.65 (3 H, Me-18, s). ^{19}F NMR: −160.5 (d, $^3J_{HF}$ = 43 Hz). ^{13}C NMR: 170.4(*C*O), 98.7 (*C*F, $^1J_{CF}$ = 165 Hz), 82.4 (*C*HO, $^2J_{CF}$ = 33 Hz), 57.8 (OCH_3). MS *m/e*: 478 (M^+), 446 [(M − CH_3OH)$^+$]. Anal. Calcd for $C_{30}H_{51}FO_3$: C, 75.31; H, 10.67. Found: C, 75.07; H, 10.64.

Reaction of 17-Oxoandrostan-5-en-3β-ol Acetate (34) with MeOF. To a cold (−40 °C) MeOH/MeCN solution containing 8 mmol of MeOF was added 712 mg of **34** in 10 mL of $CHCl_3$. After the usual workup the adduct **35** was obtained in 45% yield, mp = 173 °C (from petroleum ether). IR: 1730, 1740 cm^{-1}. ^{1}H NMR: 5.12 (1 H, m) 3.33 (3 H, s), 3.23 (1 H, m, eq C*H*OMe, $W_{h/2}$ = 13 Hz), 1.09 (3 H, Me-19, s), 0.88 (3 H, Me-18, s). ^{19}F NMR: −160.5 (dm, $^3J_{HaxFax}$ = 40 Hz). ^{13}C NMR: 170.3(*C*O), 98.5 (*C*F, $^1J_{CF}$ = 167 Hz), 82.0 (*C*HO, $^2J_{CF}$ = 33 Hz), 58.0 (OCH_3). MS *m/e*: 380 (M^+), 288 [(M − CH_3OH − AcOH)$^+$]. Anal. Calcd for $C_{22}H_{33}FO_4$: C, 69.47; H, 8.68. Found: C, 69.17; H, 8.62.

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(20) The assignment is based mainly on the fact that the fluorine atom of erythro isomers of compounds with partial structure CFCX (X = various OR) usually resonates at higher fields than the threo isomers; see ref 15.