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VINYL FLUORIDES FROM VINYL STANNANES

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ABSTRACT: Fluorination of vinyl stannanes takes place in moderate yields with xenon difluoride in the presence of silver hexafluorophosphate. An electrophilic fluorination mechanism is assumed.

The replacement of hydrogen by fluorine in bioactive organic molecules frequently results in dramatic changes in properties.[1] Consequently, a number of selective methods for the introduction of fluorine have been developed.[2] As part of a larger project, we had a need for a mild method for the preparation of vinyl fluorides. The electrophilic fluorination of a vinyl stannane suggested itself for several reasons. Fluorination of aryl stannanes with F_2 or $CsSO_4F$ has been reported.[3a] Similar reactions of aryl silanes,[3b] as well as other aryl metals[3c,d] are also known. In general, however, the electrophilic fluorination of organometallic species has not been widely explored.[4a,b] Halogenation of vinyl stannanes to produce vinyliodides, bromides and chlorides is well-

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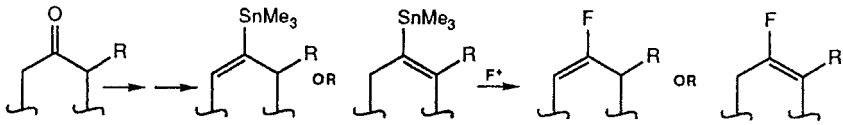
Scheme 1



precedented.[5,6,7] Since the regiospecific formation of vinyl stannanes from ketone enolates (via the enol triflates) is also known,[6] a versatile synthesis of vinyl fluorides from the electrophilic fluorination of the corresponding vinyl stannanes suggested itself (Scheme 1).

Vinyl fluorides have been prepared by treatment of vinyllithium compounds with N-*tert*-butyl-N-fluorobenzenesulfonamide[8] as the source of F^+. An early attempt to use commercially available N-fluoro-N-*n*-propyl-*p*-toluenesulfonamide[9] as the source of electrophilic fluorine in a reaction with vinyl stannanes was disappointing. Either no reaction took place, or at vigorous reflux in dichloromethane, β-elimination of HF from the reagent occurred.[9] N-fluoropyridinium triflate,[10] a versatile, commercially available electrophilic source of fluorine, was also examined. This reagent also failed to produce any of the desired vinyl fluoride under a variety of reaction conditions. More reactive N-fluoropyridinium salts[10] or N-fluorobenzenesulfonimide[11] were not examined. The direct fluorination of a vinyl stannane using F_2 has been reported[7] although in low yield (< 5%).

Another easily handled source of electrophilic fluorine is xenon difluoride (XeF_2). Treatment of vinyl stannanes with XeF_2 in dichloromethane led in low yield (10 - 20% for entry 1) to the desired vinyl fluoride accompanied by large amounts of alkene. The reaction was slow at ambient temperature and required 2 - 3 d for complete consumption of the vinyl stannane. At 90°C in dichloromethane (sealed tube) rapid

conversion of stannane to alkene took place. The formation of alkene was postulated to be a consequence of homolytic decomposition of XeF_2 with generation of HF.[12] Nevertheless, suppression of this side reaction could not be accomplished by addition of organic or inorganic bases. Activation of the vinyl stannane by treatment with LiF/12-C-4, CsF or CsF-Al_2O_3[13] followed by addition of XeF_2 led to no improvement of the yield of vinyl fluoride. Treatment with XeF_2-BF_3·Et_2O gave alkene predominantly.[14]

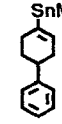
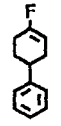
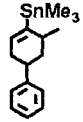
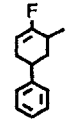
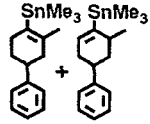
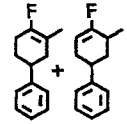
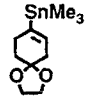
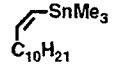
The remaining option was to activate the XeF_2 rather than the vinyl stannane. The naive proposal was to use XeF_2 in conjunction with silver hexafluorophosphate ($AgPF_6$). Abstraction of one of the fluorine atoms from xenon by the silver ion might produce XeF^+ which would be an extremely reactive electrophilic fluorinating agent.[15] In the event, treatment of vinylstannanes with equimolar amounts of XeF_2 and $AgPF_6$ in dichloromethane at 23°C led to complete consumption of the stannane within 6 h with the formation of the desired vinyl fluoride in 24 - 52% yields (Table). Use of 0.5 equivalent of $AgPF_6$ led to a much slower reaction (2 - 3 d) and lower yield (20 - 30%) of the vinyl fluoride. In all cases, except for entry 5, the stannanes were completely consumed to produce only vinyl fluorides and alkenes. In the case of entry 5, fluorination afforded a complex reaction mixture.

Low temperatures and longer reaction times ($\geq$ 6 h) led to larger amounts of the alkene, which may be formed as a consequence of the one-electron pathway for decomposition of XeF_2.[12] In two cases (entries 5 and 6), therefore, a comparison was made between the reaction at 23°C and 35°C. At higher temperature, the reaction was faster and yield slightly higher for entry 6. However, although the reaction was faster as well for entry 5, the yield of vinyl fluoride was lower and afforded side products.

Entries 3 and 4 of the table show that vinyl fluorides can be prepared regiospecifically. In general, this is not easily

Table

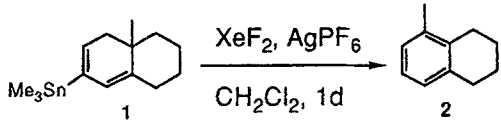
Fluorination of vinyl stannanes with XeF_2 and $AgPF_6$ in CH_2Cl_2 at 25°C.

Entry	Substrate	Product	Reaction time (h)	Yield[a] %
1			3	51
2			6	24
3			3	50[b]
4			3	52[c,d]
5			6 (2)[e]	35 (23)[e]
6			18 (3)[e]	35 (43)[e]

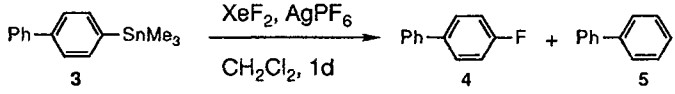
a) Isolated yields after column chromatography on silica gel; b) both starting material and product were 8:1 ratios of cis to trans isomers; c) see ref. 23; d) both starting material and product were 2:1 ratios of tetrasubstituted to trisubstituted alkene isomers; e) reaction temperature 35°C.

accomplished through the elimination of HF from a geminal difluoride.[16] The reaction also appeared to be stereospecific (entries 2 and 6). In the cyclododecyl case, ^{1}H-NMR chemical shifts support the assignment of E stereochemistry for the

Scheme 2



Scheme 3



enol triflate as the major stereoisomer (8.3 : 1). Also, the stannylation of the enol triflate using Wulff's condition[6] took place stereospecifically. The E stereochemistry for the vinyl stannane was determined by a positive nOe between the two well-resolved allylic methylene protons. The magnitude of the fluorine-vinyl proton coupling constant, $J_{(FC=CH)}$ = 23.4 Hz, is consistent with E stereochemistry for entry 2. Furthermore, Z-fluorocyclododecene has been prepared by elimination of HF from 1,1-difluorocyclododecane.[17] The reported value of $J_{(FC=CH)}$ for the Z isomer is 37.0 Hz.[17] For entry 6, $J_{(FC=CH)}$ = 43.5 Hz which is consistent with the assigned Z stereochemistry. The assignment of Z stereochemistry for the corresponding enol triflate[18] and vinyl stannane[19] were based on ^{1}H-NMR chemical shifts and coupling constants. The fluorination of a cross conjugated vinyl stannane **1** afforded **2**, the product of oxidative rearrangement, in approx. 43% yield as the major product, while the desired vinyl fluoride was not formed (Scheme 2).

The fluorination of aryl stannane **3** was also performed (Scheme 3). The aryl stannane was completely consumed to afford biphenyl **5** as the major product along with approx. 20%

of aryl fluoride **4**. Although the yield of aryl fluoride is typically higher when F_2 or $CsSO_4F$ are used as the F^+ source, this reaction deserves closer scrutiny.

Conclusion. A simple and convenient method for the regio - and stereospecific conversion of vinyl stannanes to vinyl fluorides has been developed. Both reagents, XeF_2 and $AgPF_6$, are solids at room temperature and are easy to handle. Yields are modest and may be subject to improvement as more is learned about the mechanism of these fluorinations. The mechanism has been assumed to be ionic, however, it should be emphasized that single-electron alternatives have not been ruled out.

Experimental. Reagent grade dichloromethane was distilled from phosphorus pentoxide. Xenon difluoride was purchased from PCR and used as received. ^{1}H-NMR and ^{13}C-NMR spectra were recorded on General Electric QE-300 and GE-500 (Oxford magnet) NMR spectrometers. Chemical shifts were measured in parts per million (ppm) relative to deuterated chloroform (7.26 ppm) as an internal standard. ^{19}F-NMR spectra were recorded on a Nicolet NT-300 instrument, and chemical shifts are reported upfield from fluorotrichloromethane (0.00 ppm) as an external standard. Multiplicities are designated as singlet (s), doublet (d), triplet (t), quartet (q) and multiplet (m). Broad signals are designated with br. High resolution mass spectra were recorded on a VG-70SE instrument. Column chromatography was performed on Brinkmann silica gel (0.040-0.063 mm). Infrared spectra were recorded on a Perkin-Elmer 1430 double beam instrument. Solid samples were recorded on NaCl plates as thin films deposited by evaporation from dichloromethane, and oils were recorded neat. Absorptions are reported in wave numbers (cm^{-1}) and their intensities are designated as strong (s), medium (m), or weak (w). Broad signals are designated with br.

General Reaction Procedure. The vinyl stannane (0.96 mmol) dissolved in 13 mL of dichloromethane was transferred

to a dry two-neck flask[20] under a static nitrogen atmosphere and equipped with a magnetic stirrer via cannula using positive nitrogen pressure. An equimolar amount of XeF_2[21] dissolved in 6 mL of dichloromethane[22] followed by an equimolar amount of $AgPF_6$[20,21] dissolved in 6 mL of dichloromethane were rapidly added in the same manner. The reaction was monitored for the disappearance of XeF_2 using KI-starch paper. The reaction mixture was partitioned between saturated sodium bicarbonate and dichloromethane and the organic phase was dried with anhydrous magnesium sulfate, and filtered through a short pad of silica and further eluted with dichloromethane. After solvent evaporation, the products were isolated and purified by silica gel column chromatography eluting with pentane.

1-fluoro-4-phenylcyclohexene (Entry 1);

^{1}H-NMR (300 MHz, $CDCl_3$): 1.85-2.05 (m, 2H), 2.22-2.30 (m, 3H), 2.35-2.45 (m, 1H), 2.75-2.85 (m, 1H), 5.24-5.31 (dm, J = 16.8 Hz, 1H), 7.19-7.23 (m, 1H), 7.22-7.25 (br d, J = 7.5 Hz, 2H), 7.29-7.35 (br t, J = 7.5 Hz, 2H).

^{13}C-NMR (125 MHz, $CDCl_3$): 25.7-25.9 (d, J = 24.4 Hz, 1 C), 29.5-29.6 (d, J = 9.5 Hz, 1C), 30.4-30.5 (d, J = 9.5 Hz, 1C), 39.6, 101.4-101.5 (d, J = 14.9 Hz, 1C), 126.2, 126.7, 128.4, 145.6, 158.6-160.6 (d, J = 255.0 Hz, 1C).

^{19}F-NMR (283 MHz, $CDCl_3$): -104.0 - -103.9 (br d, J = 11.3 Hz, 1F).

IR (neat): 3080 (m), 3060 (m), 3020 (m), 2920 (s), 2840 (m), 1705 (s), 1600 (m), 1490 (m), 1450 (m), 1440 (m), 1370 (s), 1285 (m), 1265 (m), 1210 (m), 1150 (m), 1130 (s), 1030 (m), 980 (m), 910 (m), 880 (w), 820 (m), 800 (w).

mp 66 - 68°C.

1-fluorocyclo-(E)-dodecene (Entry 2);

^{1}H-NMR (300 MHz, $CDCl_3$): 1.34-1.61 (m, 16H), 1.95-2.02 (br q, J = 6.9 Hz, 2H), 2.23-2.35 (dt, J = 23.4 Hz, 6.9 Hz, 2H), 4.89-5.02 (dt, J = 23.4, 8.1 Hz, 1H).

^{13}C-NMR (125 MHz, $CDCl_3$): 21.9-22.1 (d, J = 24.4 Hz, 1 C), 22.5-22.6 (d, J = 10.1 Hz, 1C), 23.5, 23.9, 24.2, 24.4, 24.4, 24.5, 24.6, 27.1, 106.6-106.8 (d, J = 21.5 Hz, 1C), 159.0-161.0 (d, J = 245.6 Hz, 1C).

^{19}F-NMR (283 MHz, $CDCl_3$): ⁻105.1 - ⁻104.9 (q, J = 23.5 Hz, 1F).

IR (neat): 2930 (s), 2860 (m), 1700 (m), 1470 (m), 1445 (br), 1370 (w), 1350 (w), 1230 (w), 1220 (w), 1180 (w), 1133 (w), 1110 (w), 1086 (w), 1070 (w), 1050 (w), 1030 (w), 927 (w), 910 (w), 860 (w), 815 (w).

HRMS calcd. for $C_{12}H_{21}F$ (M^+) 184.1627, found 184.1627.

1-fluoro-6-methyl-4-phenylcyclohexene (Entry 3);

^{1}H-NMR (300 MHz, $CDCl_3$): (Reported for the cis-isomer) 1.13-1.15 (d, J = 6.9 Hz, 3H), 1.56-1.68 (td, J = 12.6, ⁻11.1 Hz, 1H), 2.04-2.12 (m, 1H), 2.19-2.35 (m, 2H), 2.60-2.70 (m, 1H), 2.79-2.90 (tm, J = 12.9 Hz, 1H), 5.20-5.27 (dm, J = 17.4 Hz, 1H), 7.19-7.23 (m, 1H), 7.21-7.24 (br d, J = 7.2 Hz, 2H), 7.29-7.34 (br t, J = 7.5 Hz, 2H).

^{13}C-NMR (125 MHz, $CDCl_3$): (Reported for the cis-isomer) 17.2-17.3 (d, J = 2.9 Hz, 1C), 31.4-31.5 (d, J = 8.6 Hz, 1C), 32.0-32.2 (d, J = 23.0 Hz, 1C), 39.5-39.6 (d, J = 7.2 Hz, 1C), 40.2, 101.3-101.5 (d, J = 17.2 Hz, 1C), 126.3, 126.7, 128.5, 145.7, 161.8-163.9 (d, J = 257.1 Hz, 1C).

^{19}F-NMR (283 MHz, $CDCl_3$): (Reported for the cis-isomer) ⁻112.54 - ⁻112.48 (dm, J = 17.3 Hz, 1F). (Reported for the trans-isomer) ⁻108.48 - ⁻108.38 (m, 1F).

IR (neat): (Reported for the cis and trans isomers) 3060 (w), 3030 (m), 2980 (s), 2920 (s), 2880 (m), 2860 (m), 2840 (m), 1697 (s), 1605 (m), 1495 (s), 1455 (s), 1435 (m), 1380 (m), 1357 (m), 1335 (w), 1290 (w), 1280 (w), 1200 (w), 1172 (m), 1160 (s), 1150 (s), 1427 (m), 1112 (s), 1097 (s), 1070 (w), 1030 (m), 1012 (m), 982 (w), 917 (w), 885 (m), 841 (w), 821 (m), 770 (s), 742 (m), 708 (s).

HRMS calcd. for $C_{13}H_{15}F$ (M^+) 190.1158, found 190.1156.

1-fluoro-2-methyl-4-phenylcyclohexene (Entry 4);

^{1}H-NMR (300 MHz, $CDCl_3$): 1.66 (br s, 3H), 1.87-1.93 (br dd, J = 11.7, 5.7 Hz, 1H), 1.97-2.01 (m, 1H), 2.18-2.24 (m, 3H), 2.32-2.39 (m, 1H), 2.80-2.86 (m, 1H), 7.19-7.23 (m, 1H), 7.22-7.25 (br d, J = 7.5 Hz, 2H), 7.30-7.35 (br t, J = 7.8 Hz, 2H).

^{13}C-NMR (125 MHz, $CDCl_3$): 13.98-14.02 (d, J = 5.5 Hz, 1 C), 25.8-26.0 (d, J = 24.7 Hz, 1C), 29.1-30.1 (d, J = 9.6 Hz, 1C) 37.1-37.2 (d, J = 5.5 Hz, 1 C), 40.0, 108.6-108.7 (d, J = 12.3 Hz, 1C), 126.2, 126.8, 128.4, 149.3, 152.4-154.4 (d, J = 249.6 Hz, 1C).

^{19}F-NMR (283 MHz, $CDCl_3$): -111.0 (br s, 1F).

IR (neat): 3060 (m), 3022 (m), 2920 (s), 2780 (s), 1725 (m), 1700 (w), 1600 (w), 1495 (m), 1450 (m), 1380 (w), 1355 (m), 1230 (w), 1150 (s), 1110 (s).

HRMS calcd. for $C_{13}H_{15}F$ (M^+) 190.1158, found 190.1149.

1-fluoro-4-(ethylene ketal)-cyclohexene (Entry 5);

^{1}H-NMR (300 MHz, $CDCl_3$): 1.84-1.89 (br t, J = 6.3 Hz, 2H), 2.26-2.27 (br s, 2H), 2.37-2.39 (br s, 2H), 3.99 (s, 4H), 5.06-5.14 (dtm, J = 16.8, 3.9 Hz, 1H).

^{13}C-NMR (125 MHz, $CDCl_3$): 24.1-24.3 (d, J = 25.3 Hz, 1 C), 30.6-30.7 (d, J = 9.8 Hz, 1C), 32.8-32.9 (d, J = 8.4 Hz, 1C), 64.5, 64.5, 99.4-99.5 (d, J = 19.7 Hz, 1C), 107.2, 157.8-159.8 (d, J = 255.4 Hz, 1C).

^{19}F-NMR (283 MHz, $CDCl_3$): -121.32 - -121.26 (br d, J = 15.7 Hz, 1F).

IR (neat): 3400 (w), 2930 (s), 2880 (s), 2680 (w), 1707 (s), 1612 (w), 1511 (m), 1475 (m), 1450 (s), 1440 (s), 1380 (s), 1350 (s), 1330 (s), 1300 (m), 1260 (s), 1200 (s), 1150 (s), 1120 (s), 1060 (s), 1050 (s), 1040 (s), 1015 (s), 985 (s), 950 (s), 865 (s), 810 (s), 790 (m).

HRMS calcd. for $C_8H_{11}O_2F$ (M^+) 158.0743, found 158.0745.

1-fluoro-(Z)-dodecene (Entry 6);

^{1}H-NMR (300 MHz, $CDCl_3$): 0.85-0.90 (br t, J = 6.9 Hz, 3 H), 1.26 (br s, 16H), 2.02-2.13 (m, 2H), 4.61-4.82 (dtd, J = 43.5, 7.5, 4.5 Hz, 1H), 6.28-6.59 (ddt, J = 86.1, 4.8, 1.2 Hz, 1H).

^{13}C-NMR (125 MHz, $CDCl_3$): 14.1, 22.7, 29.1, 29.2, 29.3, 29.4, 29.6, 29.6, 31.9, 33.8, 111.1-111.2 (d, J = 5.6 Hz, 1C), 146.5-148.5 (d, J = 255.3 Hz, 1C).

^{19}F-NMR (283 MHz, $CDCl_3$): -130.24 - -129.78 (dd, J = 86.1, 43.5 Hz, 1F).

IR (neat): 2980 (m), 2920 (s), 2850 (s), 1670 (w), 1460 (w), 1260 (w), 1100 (m), 1020 (m), 800 (w).

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20) The flask was covered with aluminum foil to prevent decomposition of $AgPF_6$ by light.
21) The reagent was weighed in a glove box.
22) Sonication was used to dissolve the XeF_2.
23) We were unable to absolutely purify the vinyl stannane via silica gel column chromatography or distillation. The yield, therefore, was approximated based on the vinyl stannane present in the initial mixture (based on ^{1}H-NMR integration).

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