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A NEW METHOD FOR THE ELECTROPHILIC FLUORINATION OF VINYL STANNANES.

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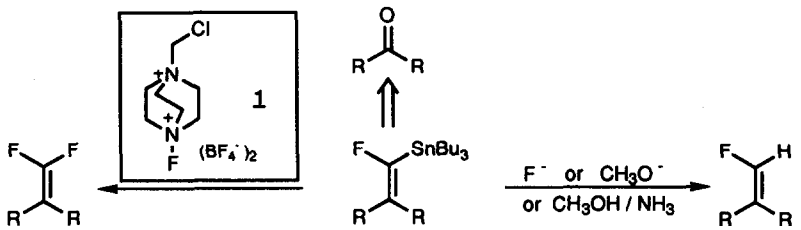
Abstract: A new method for the electrophilic fluorination of vinyl stannanes using commercially available 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis-(tetrafluoroborate) (1) has been developed.

The terminal fluoro olefin group has been used in the design of a number of mechanism-based enzyme inhibitors and other bioactive molecules.[1] The introduction of fluorine into bioactive organic targets is most commonly accomplished with DAST[2] or SF_4[3], however, the dangers of handling these corrosive reagents limits their general utility. Recent reports have documented the electrophilic fluorination of alkenyl and heteroaryl stannanes with F_2,[4] $CsSO_4F$,[5] and $XeF_2/AgPF_6$.[6] These reagents require either extreme caution in handling, are potentially explosive, or are very expensive. We sought a mild method for the preparation of vinyl fluorides that would employ a commercially available, inexpensive, and safe reagent which would be compatible with a wide range of functionality. Herein we report preliminary results on the electrophilic fluorination[7] of vinyl stannanes with 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(tetrafluoroborate) (1).[8]

Previously reported methodology[9] describes the two-step synthesis of (fluorovinyl)stannanes from ketones and their use in the synthesis of terminal fluoro olefins. As an extension of



this method, we report the first use of 1 for the electrophilic fluorination of (fluorovinyl)stannanes affording difluoro olefins.[10] The substrates employed were prepared by Horner-Wittig reaction of commercially available or suitably protected ketones with diethyl 1-fluoro-1-(phenylsulfonyl)methanephosphonate,[11] followed by conversion of the fluorovinyl sulfones to (fluorovinyl)stannanes with 2 equivalents of tributyltin hydride in refluxing benzene.[12]

The conversion of (fluorovinyl)stannanes to difluoro olefins is a facile process that proceeds in fair to good yields (Table, Entries 1-5). Typically, the reaction was run in CH_3CN (distilled from CaH_2) with 1 equivalent of reagent 1, and the mixture was heated at 80°C for 15-30 minutes. The progress of the reaction was monitored by GC and TLC. After completion, the mixture was filtered hot through a plug of silica gel with a few column volumes of eluent chosen for flash chromatography. The pre-filtration removes polar impurities as well as tin-containing by-products, and greatly facilitates purification by flash chromatography. A variety of functional groups is compatible with this conversion as seen with the examples in the table. However, silyl protected alcohols present in the substrate are partially removed under the reaction conditions, leading to diminished yields. In most cases, GC-MS analysis of reaction mixtures indicated varying amounts (3-25%) of monofluoro olefins present in the reaction mixture, which prompted us to examine the use of 1 for the synthesis of monofluoro olefins.

In the example chosen (Entry 6), the substrate was prepared by radical substitution of the vinyl sulfone[13] with tributyltin hydride, and the desired fluorodestannylation was accomplished in 71% yield, accompanied by 18% of protonolysis of the vinyl stannane.

In a typical procedure (Entry 6), reagent 1 [8] (354 mg, 1 mmol) was added to a solution of vinyl stannane 12 (1 mmol) in CH_3CN (5 ml) and the mixture was placed in an oil bath at 80°C and stirring was continued under Ar. After 30 minutes, the yellowish mixture was poured hot onto a plug of silica gel in a fritted glass funnel and eluted with 4 column volumes of cyclohexane. The product containing fractions were combined and evaporated affording 208 mg of crude product. GC analysis indicated 70% of desired product and 25% of protonolysis. Flash chromatography on silica gel (cyclohexane) afforded 33 mg (18%) of 1,1-diphenylethylene, followed by 141 mg (71%) of 13 as a colorless liquid.

In conclusion, a facile new method for the synthesis of fluoro olefins from vinyl stannanes is reported. We are currently studying the scope of the reaction and the application of this methodology to the stereospecific synthesis of complex fluoro olefins.[14]

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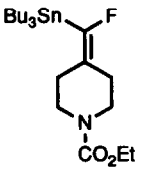
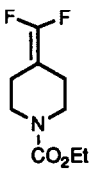
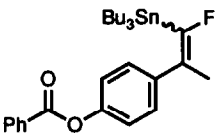
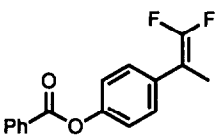
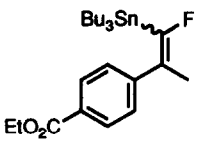
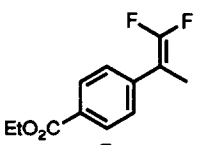
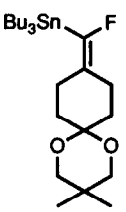
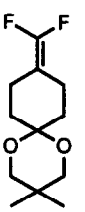
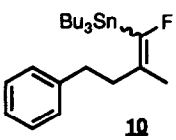
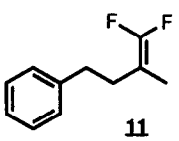
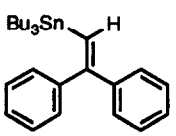
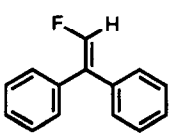
TABLE : ELECTROPHILIC FLUORINATION OF VINYL STANNANES WITH 1-CHLOROMETHYL-4-FLUORO-1,4-DIAZONIABICYCLO[2.2.2]OCTANE BIS(TETRAFLUOROBORATE) (1) IN CH_3CN AT 80 ^{O}C.

ENTRY	SUBSTRATE	PRODUCT (YIELD)	^{19}F NMR
1	 2	 3 (45%)	- 97.03 (s)
2	 4	 5 (74%)	-88.16 (dd, J = 34.5, 2.9) -88.71 (d, J = 37.3)
3	 6	 7 (58%)	- 90.52 (dd, J = 43.5, 3.2) -90.95 (d, J = 42.9)
4	 8	 9 (42%)	-98.48 (s)
5	 10	 11 (35%)	- 96.66 (d, J = 57.6) - 97.01 (d, J = 57.5)
6	 12	 13 (71%)	-128.56 (d, J = 84)

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14. All new compounds gave spectral data consistent with their assigned structure and satisfactory HRMS or elemental analysis.

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