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Polymers as Reagents and Catalysts. XI. Stereospecific Iodofluorination of Alkenes in the Presence of Polymer Supported Hydrogen Fluoride[1)]

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Synopsis. *N*-Iodosuccinimide reacted with phenyl substituted alkenes in the presence of insoluble polymer supported hydrogen fluoride, which was prepared by reaction of hydrogen fluoride with crosslinked poly(styrene-co-4-vinylpyridine) containing 40—45 mol% of 4-vinylpyridine, thus forming vicinal iodofluorides in high yields. Reactions proceeded with Markovnikov type regioselectivity, and in the case of (*Z*)- and (*E*)-stilbene, (*Z*)- and (*E*)-1-phenylpropene and indene anti stereospecificity was also observed. Iodofluorinations of phenyl substituted acetylenes occurred regio and stereospecifically, forming (*Z*)-1-fluoro-2-iodo-1-phenylalkenes, with lower yields than those observed in the case of alkenes.

Polymeric resins can be chemically transformed so that they can act as reagents or catalyst, and besides offering simpler experimental techniques, the chemical reactivity can also be changed when the reagent is attached to a polymer backbone.[2)] Our continued interest in methods for mild introduction of fluorine into organic molecules stimulated us to search further for new reagents. It is now known that appropriate synthesis of a polymer supported reagent is one of the most important factors influencing its effectiveness. We have already demonstrated that polymer-supported (difluoroiodo) arene could be prepared by reaction of xenon difluoride[3,4)] with polymer supported iodobenzene, while Patrick and coworkers[5)] have shown that a similar reagent cannot be prepared by reaction of HgO–HF with polymer supported (dichloroiodo)arene. Banks and coworkers[6)] have also very nicely demonstrated how important is the appropriate synthesis of a polymer supported reagent which should be able to convert alcohols into fluorides.

Hydrogen fluoride has been often used for the preparation of fluorine containing molecules, its great disadvantage being its toxicity to living beings and the fact that usually pressure equipment and low temperatures must be used in order to prevent decomposition of some organic molecules. Some of the experimental difficulties can be avoided by use of a mixture of hydrogen fluoride and pyridine which was extensively employed by Olah and coworkers.[7)]

We have found that crosslinked poly(styrene-co-4-vinylpyridine), containing 40—45 mol% of 4-vinylpyridine, reacted with hydrogen fluoride thus forming an easily handled reagent.[8)] We have recently showed that polymer-supported hydrogen fluoride could be used for chloro- and bromofluorination of alkenes at room temperatures, and that reaction proceed with Markovnikov type regioselectivity.[9)]

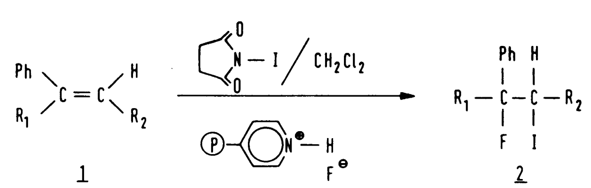
Results and Discussion

Vicinal iodo fluoro compounds are very unstable compounds and could be prepared with varying degrees of success from a mixture of *N*-iodosuccinimide and hydrogen fluoride. On the other hand, we found that the reactivity of difluoro iodosubstituted compounds strongly depends on the nature of the substituent. Reactions of (difluoroiodo)arenes with olefins usually resulted in rearranged geminal difluorides,[10)] while reactions of (difluoroiodo)methane with various alkenes gave vicinal iodofluorides at room temperature. Reactions follow Markovnikov type regioselectivity and are in most cases stereospecifically anti.[11—15)] Vicinal iodo fluoro compounds are usually accompanied by vicinal difluoro compounds, which are formed by further reaction with fluoride anion or by rearrangement of products. However, this reaction pathway is diminished when (difluoroiodo)methane is used as reagent, but its greatest disadvantage is the high price of xenon difluoride which is used for its room-temperature preparation.

We first studied the reactions of *N*-iodosuccinimide in dichloro methane in the presence of insoluble polymer supported hydrogen fluoride with 1,1-diphenylethene, and found that after 2.5 hours it was quantitatively converted to 1-fluoro-1,1-diphenyl-2-iodoethane. Further, we studied the effect of the structure of the olefin on iodofluorination, and for this reason all the reactions were run for only one hour. Crude reaction mixtures were analyzed by ^{1}H and ^{19}F NMR spectra using octafluoronaphthalene as internal reference.

The effect of the structure of the olefin on iodofluorination is presented in Scheme 1. It is evident that 1,1-diphenylethene is the most reactive olefin, while the introduction of an electron withdrawing group in to the phenyl ring, i.e. 1-(4-chlorophenyl)-1-phenylethene or the introduction of a halogen atom on the double bond, e.g. 2-fluoro-1,1-diphenylethene, diminished the reactivity. All the reactions follow the Markovnikov type regioselectivity and vicinal iodo fluoro compounds were not accompanied by difluorides or rearranged products.

Further, we studied the stereochemistry of iodofluorination of various phenyl substituted alkenes. In all cases, i.e. (*E*)- or (*Z*)-1-phenylpropene, (*E*)- or (*Z*)-stilbene, and indene the formation of only one product was observed. The structures of the products were determined on the basis of their spectroscopic data and their comparison to those of independently synthesized compounds. Iodofluorination of all five olefins followed Markovnikov type regioselectivity and proceeded stereospecifically anti. In order to get information about the effect of the structure of the olefin on the course of the reaction, all the reactions were performed at room temperature for one hour and the

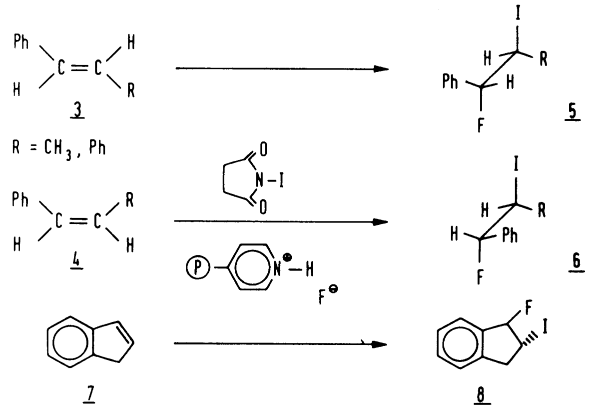


THE EFFECT OF SUBSTITUENTS ON CONVERSION OF ALKENES TO IODO FLUORO COMPOUNDS a)

1		2(%)	1		2(%)
R_1	R_2		R_1	R_2	
H	H	67	p-ClC_6H_4	H	18
CH_3	H	70	C_6H_5	F	12
H	CH_3	61	C_6H_5	CH_3	62
C_6H_5	H	71			

a) 1h reaction at 20°C

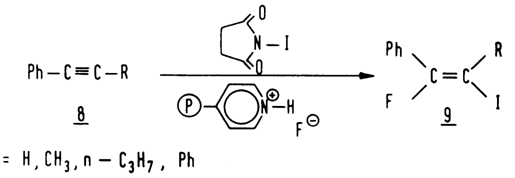
Scheme 1.



Scheme 2.

amounts of vicinal iodo fluoro compounds determined in the crude reaction mixtures were as follows: 61% from (*E*)-1-phenylpropene, 45% from (*Z*)-1-phenylpropene, 40% from (*E*)-stilbene, 38% from (*Z*)-stilbene, and 56% from indene.

Further, we studied iodofluorination of acetylenes and found that reactions occurred regiospecifically, thus forming (*Z*)-1-fluoro-2-iodo-1-phenylethenes. The substituent R influenced the conversion of acetylene. After a 1.5 h reaction the following amounts of iodo fluoro compounds were determined: 16% from phenylacetylene, 25% 1-phenylpropyne, 31% from 1-phenyl-1-pentyne, while reaction with 1,2-diphenylacetylene failed. Prolongation of the reaction time to 2.5 hours resulted in enhanced reaction and the following amounts were observed: 18, 30, 28, and 5% (data correspond to the same order of substrates as above). However, further prolongation of reaction time did not enlarge the yields of iodofluorides, and after 7 hours even smaller amounts of products than those observed after 2.5 hour reactions were found, which could be explained by decomposition of the products. The structures of the products were determined on the basis of their spectroscopic data and comparison to



Scheme 3.

those of the independently synthesized ones.[16] It is known that the solvent plays an important role in the transformation of organic molecules with polymer-supported reagents, and for this reason we tried to increase the amount of iodo fluoro compounds from acetylenes by varying the solvent. However it was found that reactions did not occur in tetrahydrofuran and acetonitrile.

The polymer resins could be easily recovered after reaction, and reused several times.

Experimental

IR spectra were recorded using a Perkin Elmer 727 B instrument and ^1H and ^{19}F NMR spectra with a Jeol JNM PS-100 spectrometer with Me_4Si or CCl_3F as internal reference. For determination of the amounts of products formed, octafluoronaphthalene was used as internal standard. Mass spectra and high resolution measurements were taken with a CEC-21-110 spectrometer. GLC was carried out on a Varian Aerograph 1800 instrument and TLC on Merck silica gel F-254. Crosslinked poly(styrene-co-4-vinylpyridine) and polymer supported hydrogen fluoride were prepared according to previously published procedures,[8,17] while *N*-iodosuccinimide of Fluka Purum Quality was used without further purification.

Addition and Isolation Procedures. 0.15 g of polymer supported hydrogen fluoride was mixed with 2 ml of dichloro methane and 1 mmol of *N*-iodosuccinimide was added at 0 °C and stirred until complete dissolution of *N*-iodosuccinimide occured. Further, 0.5 mmol of olefin or acetylene was added and the reaction mixture was stirred for various times (1—7 h), depending on the reactivity of the alkene or acetylene. Polymer beads were filtered off and washed with 5 ml of dichloro methane, the filtrate was washed with water (10 ml, twice), dried over anhydrous sodium sulfate, and the solvent evaporated in vacuo. The crude reaction mixtures were analyzed by ^{19}F NMR spectroscopy (amounts of products were determined by the use of octafluoronaphthalene in ^{19}F NMR as internal standard). Pure products were isolated as described previously[12–16] and their structures determined by comparison of spectroscopic data to the literature ones. The yields of pure products formed after reactions of olefins and acetylenes were: 1-Fluoro-2-iodo-1-phenylethane (reaction time: 1h, yield of pure product 56%) 2-fluoro-1-iodo-2-phenylpropane (r.t.: 1h, 58%), 1,1-diphenyl-1-fluoro-2-iodoethane (r.t.: 1h, 61%), 1-fluoro-2-iodo-1-phenyl-1-(4′-chlorophenyl)ethane (r.t.: 1h, 16%), 1,2-difluoro-1,1-diphenyl-2-iodoethane (r.t.: 1h, 11%), 1,1-diphenyl-1-fluoro-2-iodopropane (r.t.: 1h, 54%), *erythro*-1-fluoro-2-iodo-1-phenylpropane (r.t.: 1h, 55%), *threo*-1-fluoro-2-iodo-1-phenylpropane (r.t.: 1h, 38%), *erythro*-1,2-diphenyl-1-fluoro-2-iodoethane (r.t.: 1h, 34%), *threo*-1,2-diphenyl-1-fluoro-2-iodoethane (r.t.: 1h, 33%), *trans*-1-fluoro-2-iodoindane (r.t.: 1h, 49%), (*Z*)-1-fluoro-2-iodo-1-phenylethylene (r.t.: 2.5h, 15%), (*Z*)-1-fluoro-2-iodo-1-phenylpropene (r.t.: 2.5h, 26%), (*Z*)-1-fluoro-2-iodo-1-phenyl-1-pentene (r.t.: 2.5h, 24%), (*Z*)-1,2-diphenyl-1-fluoro-2-iodoethylene (r.t.: 2.5h, 4%).

Regenerations of Resins. Beads were washed with methanol, dichloro methane, and chloroform, and dried in air. 5 g of polymer beads were suspended in 5 ml of chloroform and under stirring hydrogen fluoride (1.5 g) was introduced for 0.5 h at 0 °C. The beads were filtered off, washed with chloroform and dried to constant weight at room temperature. Polymer beads can be reused at least ten time for fluorination.

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