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CHEMISTRY OF ORGANO HALOGENIC MOLECULES, LXXV. POLYMER-SUPPORTED HYDROGEN FLUORIDE

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SUMMARY

Polymer-supported hydrogen fluoride prepared by reaction of hydrogen fluoride with crosslinked poly(styrene-co-4-vinylpyridine) containing 40-45 mol % of 4-vinylpyridine did not react with trans-stilbene, 1,2-diphenylacetylene, and cyclohexanol under various conditions, whereas 1-phenyl-1-hydroxy-4-tert-butylcyclohexane was converted to 1-phenyl-4-tert-butylcyclohexene. Bromofluorination of various phenyl-substituted olefins with N-bromosuccinimide in the presence of polymer supported hydrogen fluoride in methylene chloride proceeds with Markovnikov type regioselectivity. Fluorination and halofluorination of norbornene with xenon difluoride or N-bromosuccinimide or N-chlorosuccinimide in the presence of polymer-supported hydrogen fluoride resulted in up to five products, with a large increase in halonortricyclane formation, compared to reactions in the presence of hydrogen fluoride-pyridine. Polymer-supported hydrogen fluoride, in comparison to hydrogen fluoride-pyridine, enhanced the endo attack of the electrophile on norbornadiene by fluorination or halofluorination.

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INTRODUCTION

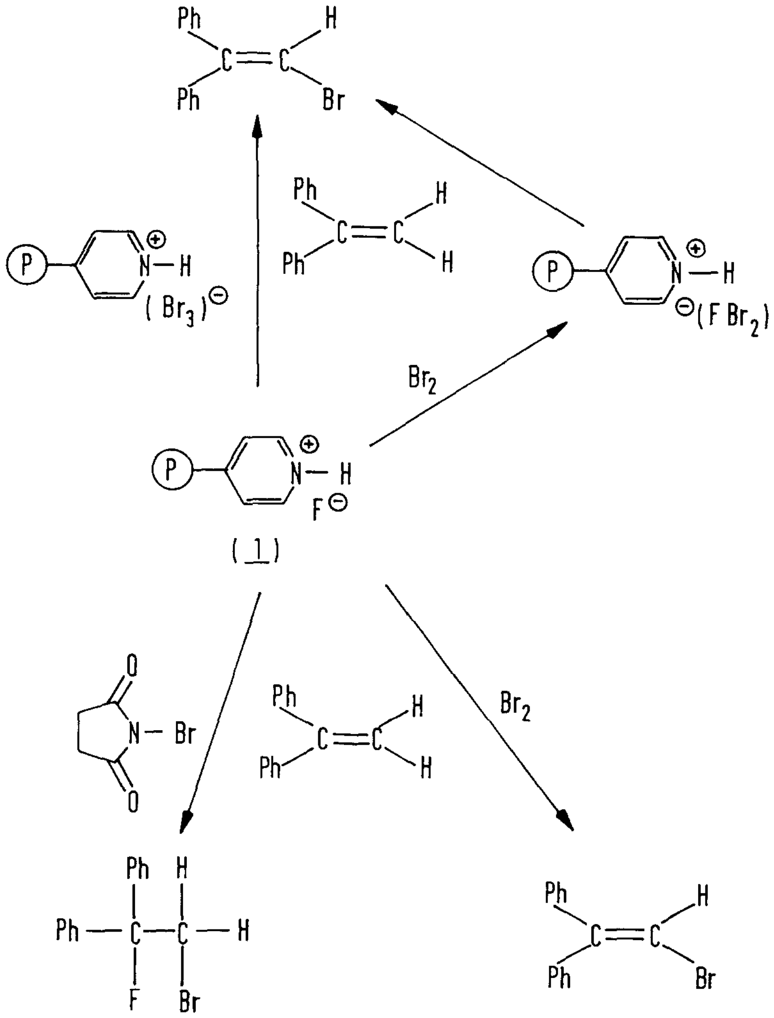
Our continued interest in fluorination of organic molecules under mild conditions and the well-known advantages of polymer-supported reagents (1) stimulated us to search further for new polymer supported reagents for introduction of fluorine. We have already demonstrated that reaction of xenon difluoride with iodinated polystyrene gave polymer-supported aryliodo(III)difluoride which reacted with various olefins, and the remaining polymer-supported iodobenzene, could be very easily removed from the reaction mixture (2). On the other hand, Patrick and coworkers (3) have shown that polymer-supported aryliodo(III)difluoride cannot be prepared by reaction of HgO-HF with polymer-supported aryliodo(III)dichloride. The importance of an appropriate synthesis of polymer-supported fluorinating reagents has also been demonstrated by Banks and coworkers (4) by the preparation of a polymer-supported fluoroalkylamine reagent for the transformation of alcohols into fluorides. Collona (5) and Cainelli with coworkers (6) have shown that anion exchange resins containing a quaternary ammonium group in fluoride form could be used for substitution of a halogen or tosyl group by fluorine. Polymer-supported resins have also been used for the preparation of labelled compounds (7), containing ^{18}F.

RESULTS AND DISCUSSION

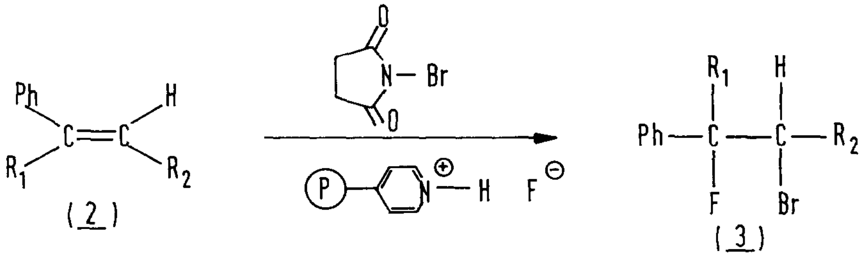
In the past hydrogen fluoride has been used for the preparation of fluorine-containing organic molecules, but difficulties arise involving its handling, the need for pressure equipment, low temperatures, and the ease of polymerisation of some organic molecules. Olah and coworkers (8) have demonstrated that some of the experimental difficulties can be avoided by the use of a mixture of hydrogen fluoride and pyridine. Recently, 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 (9).

Olah and coworkers have shown that an HF-pyridine mixture converts alcohols to fluorides, and alkenes and alkynes to fluoro or difluoro substituted alkanes (8). We first studied the reactions of polymer-supported hydrogen fluoride with *trans* stilbene and 1,2-diphenylacetylene and found that no reaction occurred. As it is known that the reactivity of polymer supported reagents is very dependent on the solvent used, we have carried out reactions in methylene chloride, methanol, ether, and tetrahydrofuran, for various times (2 - 22 hours) and at various temperatures (20° or reflux), and in no case was transformation of the starting material observed. Polymer-supported hydrogen fluoride also failed to react with cyclohexanol, while reaction with 1-phenyl-1-hydroxy-4-tert-butylcyclohexane resulted in the formation of 1-phenyl-4-tert-butylcyclohexene in 98% yield (87% after purification (16)).

Further, we studied the possibility of using polymer-supported hydrogen fluoride for halofluorination of alkenes. Polymer-supported hydrogen fluoride (1) reacted with bromine in methylene chloride, but further reaction of the resulting polymer resins with 1,1-diphenylethene led to the formation of 1,1-diphenyl-2-bromoethene only, which was also the only product in the reaction where bromine was added to a mixture of polymer-supported HF and 1,1-diphenylethene. In the reaction of polymer-supported HF and the poly(styrene-*co*-4-vinylpyridine)complex with hydrogen bromide and bromine (10) with 1,1-diphenylethene, no vicinal bromofluoride resulted (Scheme 1), and its formation was only observed when the alkene was added to a reaction mixture of polymer-supported HF and N-bromosuccinimide (NBS).



Scheme 1

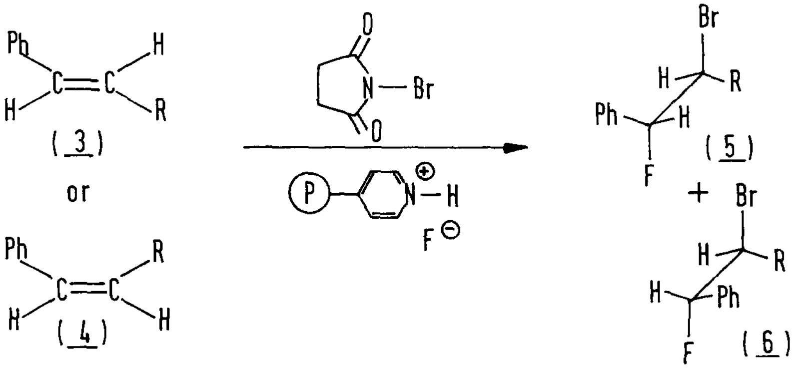


THE EFFECT OF SUBSTITUENTS ON CONVERSION OF ALKENES TO BROMOFLUORIDES[a]

(2)	3 (%)	(2)	3 (%)
R_1 = Ph , R_2 = H	92	R_1 = Ph , R_2 = Br	11
R_1 = Ph , R_2 = CH_3	75	R_1 = R_2 = H	44
R_1 = Ph , R_2 = F	30	R_1 = CH_3 , R_2 = H	48
R_1 = Ph , R_2 = Cl	17	R_1 = H , R_2 = Br	17[b]

a) 1h reaction at 20° C

b) 3h reaction at 20°C



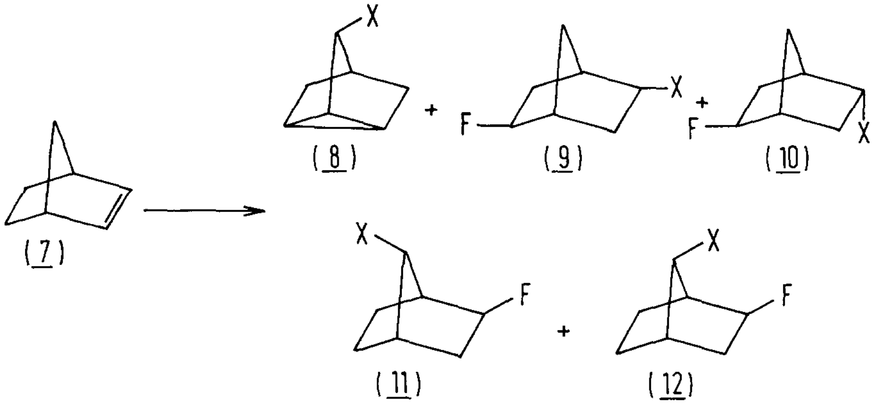
ALKENE		RELATIVE YIELDS (%)	
	R	5	6
3	CH_3	100	—
	Ph	100	—
4	CH_3	25	75
	Ph	70	30

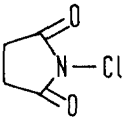
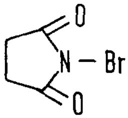
Scheme 2

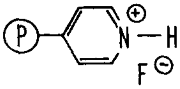
The mixture of NBS and polymer-supported HF in methylene chloride converted various phenyl-substituted olefins (2) to vicinal bromofluorides (3, Scheme 2), their structure being established by spectroscopic data and comparison with previously synthesized compounds (11). The effect of substituents on the bromofluorination of alkenes is presented in Scheme 2; prolongation of reaction time enhanced the conversion of alkenes up to 90%. The isolation of products from the reaction mixture comparising only filtration of resins and washing the filtrate with water is much easier as compared to reactions with an HF-pyridine mixture, where the reaction mixture must be poured ont ice and the products extracted.

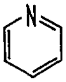
The stereochemistry of bromofluorination of phenyl-substituted olefins is very similar to that already observed by reaction with an HF-pyridine mixture (11) and the results are presented in Scheme 2.

We have further studied fluorination and halofluorination of norbornene (7) with xenon difluoride or N-chlorosuccinimide (NCS) or N-bromosuccinimide in the presence of polymer-supported hydrogen fluoride. Product distributions, determined by glc, are presented in Scheme 3, and a large increase of halonortricyclane formation is observed, as compared to reaction in the presence of HF-pyridine (12). A similar increase in fluoronortricyclane formation has already been observed in the reaction of xenon difluoride with norbornene, in the presence of pentafluorothiophenol (13).



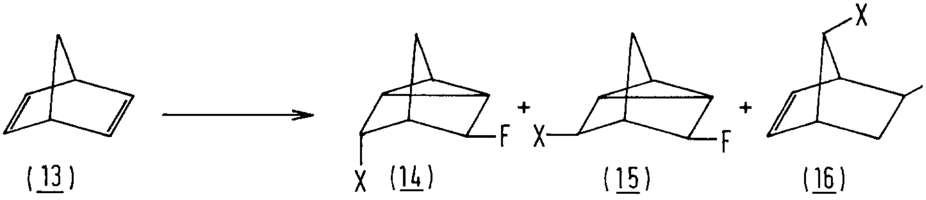
		X	PRODUCT DISTRIBUTION (8)	(9)	(10)	(11)	(12)
XeF_2 +	a	F	71	4	6	11	8
	b	F	14	10	19	35	22
 +	a	Cl	76	trace		3	21
	b	Cl	26	2	3	31	38
 +	a	Br	81	trace		5	14
	b	Br	20	3	5	37	35

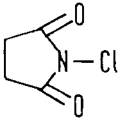
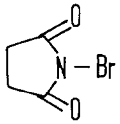
a) 

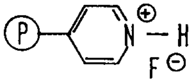
b) HF / 

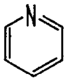
Scheme 3

Halofluorination of norbornadiene in the presence of hydrogen fluoride-pyridine resulted in *endo* and *exo* attack of the electrophile, their ratio depending on the halogen (14). The effect of polymer-supported hydrogen fluoride on the *endo* and *exo* attack of the halogen atom on norbornadiene, using xenon difluoride, N-bromosuccinimide or N-chlorosuccinimide is presented in Scheme 4.



REAGENT		X	PRODUCT DISTRIBUTION		
			(14)	(15)	(16)
XeF_2 +	a	F	45	44	11
	b	F	27	68	5
 +	a	Cl	36	29	35
	b	Cl	36	59	5
 +	a	Br	49	30	21
	b	Br	35	65	–

a) 

b) HF/ 

Scheme 4

In all three cases the amount of rearranged product (16) is increased, while in the fluorination and bromofluorination in the presence of polymer-supported HF increased amounts of 3-endo-halo-5-exo-fluoronortricyclane (14) were observed, proving increased endo attack of the electrophile, compared to reaction in the presence of HF-pyridine.

The polymer resins could be easily recovered after the reactions and reused several times.

EXPERIMENTAL

Ir spectra were recorded using a Perkin Elmer 727 B instrument and ^{1}H and ^{19}F nmr spectra with a Jeol JNM-PS-100 spectrometer with Me_4Si or CCl_3F as internal reference. Mass spectra and high resolution measurements were obtained with a CEC-21-110 spectrometer. Glc partition chromatography was carried out on a Varian Aerograph Model 3700, and a CDS 111 integrator. Crosslinked poly(styrene-co-4-vinylpyridine) and polymer-supported hydrogen fluoride were prepared according to previously published procedures (9), xenon difluoride was prepared by a photosynthetic method (15) and its purity was better than 99.5%, while N-chlorosuccinimide NCS and N-bromosuccinimide NBS of Fluka Purum Quality were used without further purification.

Addition and Isolation Procedures

A) Bromo and Chlorofluorination

0.3 g of polymer-supported hydrogen fluoride was mixed with 2 ml of methylene chloride and 1.2 mmol of NBS or NCS were added at 0°C, and stirred for 0.5 hour, and for 1 hour at room temperature, then 1 mmol of alkene was added and the reaction mixture stirred for various times (1-22 hours, depending on the reactivity of the alkene; 1,1-diphenylethene, norbornene, and norbornadiene were quantitafively converted to products after 2 hours). Polymer beads were filtered off and washed with 5 ml of methylene chloride, the filtrate was washed with water (10 ml, twice), dried over Na_2SO_4 and the solvent evaporated in vacuo. Crude reaction mixtures were analyzed by glc and ^{19}F nmr spectroscopy (conversions were determined by use of octafluoronaphthalene in ^{19}F nmr as internal reference). Pure products were isolated as described prevously (11, 12, 13, 14) and their structures determined by comparison of the spectroscopic data with published data. The yields of pure products were grater than 75%.

B) Fluorination

To a mixture of 1 mmol of alkene and 0.3 g of polymer supported HF in 2 ml of methylene chloride at 0°C, 1 mmol of XeF_2 was added and the reaction mixture was stirred for 1 hour at room temperature. Polymer beads were filtered off, washed with 5 ml of methylene chloride, the filtrate was washed with water (10 ml, twice), dried over Na_2SO_4, and the solvent evaporated in vacuo.

Regeneration of Resins

Beads were washed with methanol, methylene chloride, and chloroform, and dried in air. 5 g of polymer beads were suspended in 50 ml of chloroform and under stirring hydrogen fluoride (1.5 g) was introduced for 0.5 hour 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 10 times for fluorination.

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