

POLYMER-SUPPORTED ARYLIODINE(III) DIFLUORIDE*

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Synthesis of polymeric aryl iodine(III) difluoride is described. Reaction with phenyl-substituted olefins results in formation of rearranged geminal difluorides. Reaction with norbornene results in formation of 2-*exo*-7-*syn*-difluoronorbornane.

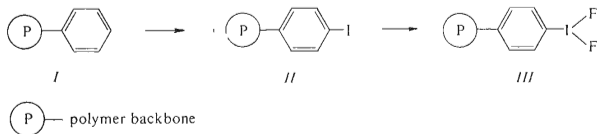
Chemical reactions on solid supports have provided chemistry with several important reagents. Applications for organic, inorganic and biochemical reactions have emerged since the introduction of solid-phase peptide synthesis by Merrifield.² The advantage of polymer-supported organic reagents lies in the simplicity of preparative procedures (for review see^{3,4}). The addition of chlorine to olefinic double bonds using phenyl iodine(III) dichlorides has been studied by several groups of workers⁵⁻⁸. The corresponding aryl iodine(III) difluorides received much more limited attention as fluorinating agents, possibly because of the difficulties involved in their preparation and storage⁹⁻¹³. We have recently found¹⁴ that methyl iodine(III) difluoride reacts with phenyl-substituted olefins in the presence of hydrogen fluoride as catalyst to form corresponding 1-fluoro-2-iodo-1-phenylalkanes and not the rearranged geminal difluorides observed in similar fluorination reactions with aryl iodine(III) difluorides. We report the preparation of polymer-supported aryl iodine(III) difluoride (*III*) and its reactions with phenyl-substituted olefins and norbornene.

Aryl iodine(III) difluorides have already been used for fluorination of 1,1-diphenylethene¹³ and styrene¹², but the resulting iodobenzene had to be separated from the geminal difluorides. With polymer-supported aryl iodine(III) difluoride (*III*), the separation procedures are reduced to filtration of the polymer iodobenzene. "Pop-corn" polystyrene¹⁵ was used as starting material in the preparation of the polymeric aryl iodine(III) difluoride (*III*) as outlined in Scheme 1.

Iodination of polystyrene (*I*) with iodine and iodine(V) acid yields, after 160 h of stirring at 110°C, polymeric aryl iodine *II*. By means of elemental analysis we have determined that approximately one third of the phenyl rings were iodinated.

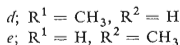
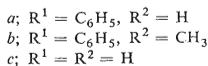
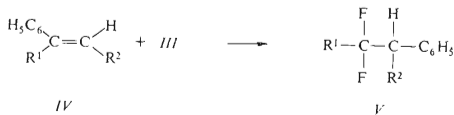
* Part I in the series Polymer-Supported Reagents in Organic Synthesis. Preliminary communication see¹.

The reaction with xenon difluoride in the presence of hydrogen fluoride in dichloromethane at 25°C gave polymeric difluoride *III*. The quantity of active fluorine on the polymer resins was estimated by iodometry. In order to establish the conversion of the iodinated polymer *II* to the fluorinated reagent *III*, we have varied the amount



SCHEME 1

of added xenon difluoride. From experimental data presented in Table I it can be seen that losses of active fluorine are greater when larger amounts of xenon difluoride are added (fluorination of phenyl rings). For this reason, we have used in subsequent studies the polymeric reagent prepared by using 2.4 mmol of xenon difluoride per gram of the polymer support *II*. In order to standardize the conditions necessary for the study of the reaction mechanism of the reagent *III* with an olefin, the fluorination of 1,1-diphenylethylene (*IVa*) in dichloromethane at room temperature was investigated. A 2 h reaction in the presence of HF catalyst resulted in the formation of rearranged 1,1-difluoro-1,2-diphenylethane (*Va*) (Scheme 2), which was identified



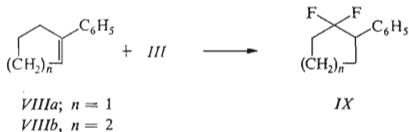
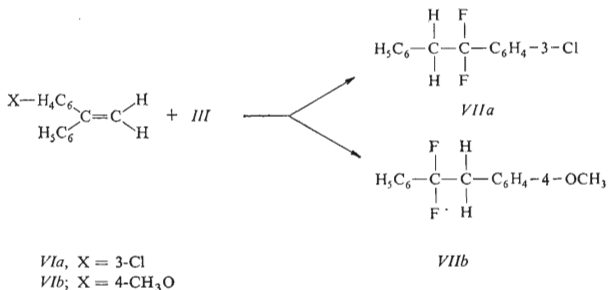
SCHEME 2

TABLE I
Fluorine Content in the Polymer-Supported *III*

mmol of XeF_2 per g of <i>II</i>	0.96	1.58	2.24	2.61	3.04
mmol of F_2 bond on <i>III</i>	0.66	1.13	1.54	1.75	2.19

by its $^1\text{H-NMR}$ and mass spectra. The reaction was extended to several other olefins: 1,1-diphenyl-1-propene (*IVb*), styrene (*IVc*), 2-phenyl-1-propene (*IVd*) and *trans*-1-phenyl-1-propene (*IVe*). Under the conditions mentioned above, all the reactions resulted in the formation of rearranged geminal difluorides *V*. Carpenter¹² showed that hydrogen fluoride, or other strong acid such as trifluoroacetic acid, is necessary as catalyst in fluorination reactions of aryl iodine(III) difluorides with olefins *IVa* and *IVc*, and proposed an ionic mechanism with a phenonium ion intermediate.

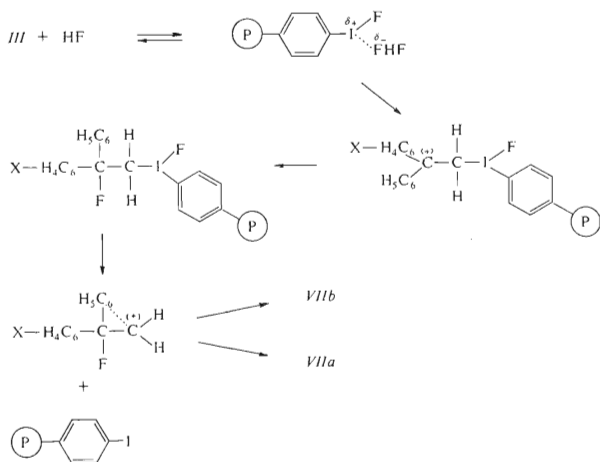
We obtained more evidence which supports the phenonium ion intermediate by fluorination of 1-phenyl-1-(4-methoxyphenyl)ethylene (*VIb*), when 1,1-difluoro-1-phenyl-2-(4-methoxyphenyl)ethane (*VIIb*) was formed. Furthermore, the fluorination of 1-phenyl-1-(3-chlorophenyl)ethylene (*VIa*) resulted in 1,1-difluoro-1-(3-chlorophenyl)-2-phenylethane (*VIIa*) (Scheme 3). The structure of the products were established on the basis of their $^1\text{H-NMR}$ data, δF 100 p.p.m. (t), for *VIIa* and δF 105.5 p.p.m. (t), for *VIIb*, which correspond to geminal difluorides. In the mass spectrum, the fragments of the product *VIIb* were methoxytropylium ion m/e 121 and difluorobenzylum ion m/e 127, which indicates *p*-methoxyphenyl-group migration, while on the other hand, from product *VIIa* the fragments were tropylium ion m/e 91 and difluorochlorobenzylum ion m/e 161, which indicates phenyl-group migration. The fluorination of the cyclic phenyl-substituted olefins 1-phenylcyclo-



SCHEME 3

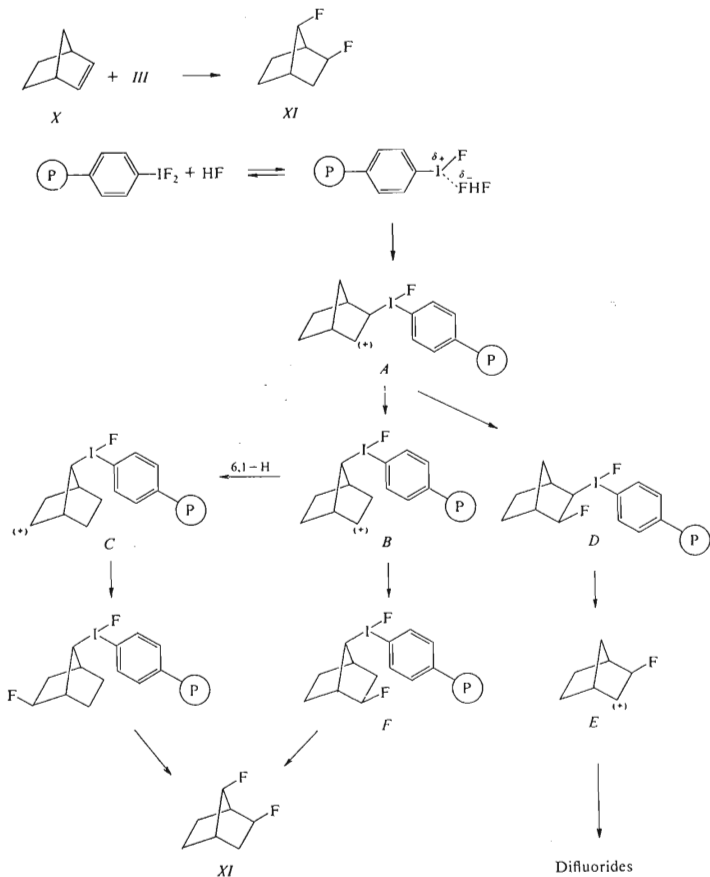
pentene (*VIIIa*), and 1-phenylcyclohexene (*VIIIb*) also resulted in formation of geminal difluorides *IX* (Scheme 3), which could be identified by their $^1\text{H-NMR}$ and mass spectra.

In the light of these results we propose a mechanism, similar to that already suggested by Carpenter^{1,2}, which is presented in Scheme 4. It might be expected that in the presence of hydrogen fluoride, polymer aryliodine(III) difluoride (*III*) behaves as an electrophile (reactions were completely quenched when no HF was added), adding on a olefin, thus forming a carbonium ion which is then attacked by a fluorine anion. In the next step, dissociation of the carboniodine bond results in the formation of a carbonium ion, accompanied by phenyl-group migration (or *p*-methoxyphenyl-group migration).



SCHEME 4

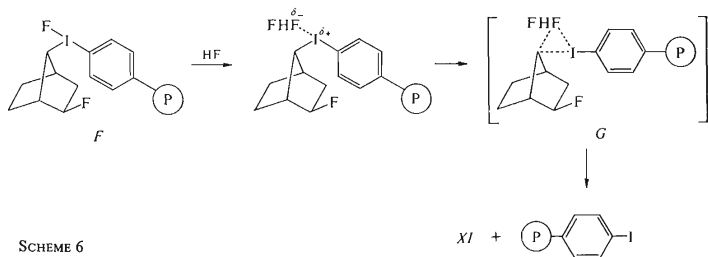
The reactions of the bicyclic olefin norbornene (*X*) have been used as a mechanistic probe to elucidate the mechanism and stereochemistry of various reactions¹⁶⁻²¹. It is possible from the identification of the products to differentiate the possible mechanistic pathways leading to those products; (i) a concerted *cis*-molecular addition, (ii) a free radical reaction, or (iii) a reaction path proceeding *via* cationic intermediates. Reaction of polymer aryliodine(III) difluoride (*III*) with norbornene results in only one product which was purified by preparative GLC. Comparison of the retention time and comparison of ^{19}F and $^1\text{H-NMR}$ and mass spectra with



SCHEME 5

Difluorides 2,3-di-*exo*, 2-*exo*-3-*endo*-, 2,5-di-*exo*-, 2-*exo*-5-*endo*-, 2-*exo*-7-*syn*- and 2-*exo*-7-*anti*-norbornane, *cf.*²².

identical compounds isolated by fluorination of norbornene with xenon difluoride²², enabled us to establish the structure of the product as 2-*exo*-7-*syn*-difluoronorbornane (XI)²² (Scheme 5). The formation of only one product XI could be explained by the reaction of norbornene with the polarized molecule of polymer aryliodine(III) difluoride, thus primarily forming the carbonium ion A. (Scheme 5), which undergoes the Wagner-Meerwein rearrangement, in turn forming ion B. The next step in the hydride shift 6,1 in which the carbonium ion C is formed which can then be attacked by the nucleophile. The S_N2 substitution of aryliodine function by fluoride anion can produce 2-*exo*-7-*syn*-difluoronorbornane (XI). However, another explanation of the formation of only one product is the reaction of the carbonium ion B with the nucleophile, thus forming F, which, *via* intramolecular substitution, results in product XI. Suggested pathways for this intramolecular substitution are presented in Scheme 6.



The adduct, *F*, polarized by hydrogen fluoride, results in difluoride XI *via* the transition state *G*. The primarily formed carbonium ion *A* could be attacked by the fluorine anion, thus forming the species *D*, but dissociation of the carbon-iodine bond must result in the formation of fluorocarbenium ion *E*, which would rearrange by Wagner-Meerwein and hydride shift, thus resulting in six difluorides. The fluorocarbenium ion *E*, formed in the reaction of xenon difluoride with norbornene, undergoes this rearrangement thus forming, after fluorine anion attack six difluorides²². In the light of the data mentioned above, we could eliminate this reaction pathway.

The conditions employed for the preparation of geminal phenylsubstituted difluorides were mild, and the purity of the products was high, as shown by GLC or TLC and NMR spectra. After purification, the polymer iodobenzene could be reused several times for preparation of the polymer aryliodine(III) difluorides (III). Application of the new polymer-supported reagent with various other organic compounds is in progress.

EXPERIMENTAL

IR spectra were recorded by using a Perkin-Elmer 257 spectrometer, ^1H - and ^{19}F -NMR spectra (δ scale in p.p.m.) by a Jeol JNM-PS-100 from CCl_4 solution with tetramethylsilane or CCl_3F as internal reference. Mass spectra and high resolution measurements were taken on a CEC-21-110 spectrometer. Gas-liquid partition chromatography was carried out on a Varian Aerograph Model 1800 and TLC on Merck PSC-fertigplatten SILICA GEL F-254 preparative runs on silica gel in the system methanol-chloroform 1 : 9, if not stated otherwise.

Materials

Pure samples of olefins were prepared by known methods: 1,1-diphenylethylene²³, 1-phenyl-1-(3-chlorophenyl)ethylene²³, 1-phenyl-1-(4-methoxyphenyl)ethylene²³, 1,1-diphenylpropene²⁴, *trans*-1-phenylpropene²⁵, 1-phenylcyclopentene²⁶, 1-phenyl-cyclohexene²⁶. Other olefins were obtained from commercial sources and distilled or purified by VPC to conform with published physical and spectral data. Hydrogen fluoride of Fluka purum quality was used. Xenon difluoride was prepared by the photosynthetic method²⁷ and its purity was better than 99.5%.

Iodination of "pop-corn" Polystyrene

A mixture of 100 ml of 50% sulphuric acid, 400 ml of nitrobenzene, 60 g of iodine, 20 g of iodine(V) acid, 150 ml of tetrachloromethane and 60 g of polystyrene (*I*) were heated under stirring to 110°C for 160 h, cooled down, the product *II* was separated by filtration, washed five times with 100 ml of ethanol and extracted in a Soxhlet apparatus with dichloromethane. The yield was 67 g. Elemental analysis: found 66.1% C, 5.2% H; one third of the phenyl rings were iodinated.

Polymer-Supported Aryliodine(III) Difluoride (*III*)

10 ml of dichloromethane, 1 g of iodinated polystyrene *II* and various amounts (from 150 mg to 500 mg) of xenon difluoride were placed in a 25 ml polyethylene reaction flask. The reaction was started by catalytic amounts of hydrogen fluoride. After the mixture had been stirred at room temperature for 2 h, the solvent was evaporated *in vacuo*. The amount of active fluorine bonded to iodine atoms of the polymer support was established by titration. A solution of 50 ml of potassium iodide (0.6 g of potassium iodide in 100 ml of a 1 : 4 methanol-water solution) and 1 ml of diluted hydrogen chloride (1 : 1) was added to 1 g of fluorinated polymeric support *III*. The mixture was stirred at room temperature in a dark, inert atmosphere for 12 h. Liberated iodine was titrated with sodium thiosulphate (0.025N).

In order to establish the conversion of the iodinated polymer *II* to fluorinated reagent *III*, we varied the amount of the added xenon difluoride. The results of these studies are presented in Table I. Losses of active fluorine are greater, when larger amounts of xenon difluoride are added. In subsequent we have used polymeric reagent prepared by using 2.4 mmol of XeF_2 per g of the polymer *II*.

Fluorination with the Polymer Aryliodine(III) Difluoride *III*

In a 25 ml polyethylene flask, equipped with magnetic stirrer, 10 ml of dichloromethane, 0.5 g of the iodinated polymer *II* and 200 mg of xenon difluoride were added. The reaction was started at room temperature by catalytic amounts of hydrogen fluoride. After 2 h of stirring, 1 mmol of olefin was added and the stirring continued for another 2 h. Afterwards, 0.1 ml of the mixture hydrogen fluoride- $\text{N}(\text{C}_2\text{H}_5)_3$ (30% of $\text{N}(\text{C}_2\text{H}_5)_3$) was introduced and stirred for 10 min. The

mixture was diluted with 10 ml of dichloromethane and neutralized with a saturated water solution of sodium hydrogen carbonate. The iodinated polystyrene was filtered off and the dichloromethane layer was separated, washed with water (50 ml, twice) and dried over anhydrous sodium sulphate. The solvent was evaporated *in vacuo* and the product was purified by preparative TLC or GLC.

1,1-Difluoro-1,2-diphenylethane (Va): 96% of a solid product, purified by preparative TLC yield 79%, m.p. 65°C, (the literature⁹ m.p. 66°C). The spectroscopic data are in agreement with the literature¹².

1,1-Difluoro-1,2-diphenylpropane (Vb): 95% of an oily product, purified by preparative TLC, yield 74% yellow oil¹². NMR data: δF -109.8, -112.0 (ABX), δH 3.7 (m), δCH_3 1.5 (d), δ arom. 7.5 (m). $J_{FF} = 285$ Hz, $J_{FH} = 16.5$ Hz, $J_{HCH_3} = 7.5$ Hz. Mass spectra: calculated for $C_{15}H_{12}F_2$ m/e 232.1063, found m/e 232.1055.

1,1-Difluoro-2-phenylethane (Vc): 86% of a liquid, purified by preparative GLC (SE-30/Crom A (AW) 45/60-10%, $T = 150^\circ C$, yield 75% of yellow liquid), the spectroscopic data are in agreement with the literature¹².

2,2-Difluoro-1-phenylpropane (Vd): 97% of an oil, purified by preparative TLC, yield 85% of yellow liquid. NMR data: δF -90.75 (m), δ -CH₂ -3.1 (t), δCH_3 1.5 (t), δ arom. 7.2 (m), $J_{FCH_3} = 18$ Hz, $J_{FH} = 15$ Hz. Mass spectrum: calculated for $C_9H_{10}F_2$ m/e 156.0740, found m/e 156.0756, m/e : 156 (20%), 92 (15), 91 (100), 65 (30).

1,1-Difluoro-2-phenylpropane (Ve): 90% of an oil, purified by preparative TLC, yield 82% of a liquid, NMR data: δF -130.9, -135.7 (ABMX), δ -CF₂H -5.8, $\delta CHCH_3$ (C₆H₅) 3.1, δCH_3 1.3, $J_{FF} = 290$ Hz, $J_{FH} = 58$ Hz, $J_{FH} = 15$ Hz, $J_{HCH_3} = 7.5$ Hz. Mass spectrum: calculated for $C_9H_{10}F_2$ m/e 156.0740, found m/e 156.0758.

1,1-Difluoro-1-(3-chlorophenyl)-2-phenylethane (VIIa): 80% of an oil, purified by preparative TLC, 70% of an oil. NMR data: δF -100 (t), δH 3.25 (t), δ arom. 7.2 (m), $J_{FH} = 15$ Hz. Mass spectrum: calculated for $C_{14}H_{11}ClF_2$ m/e 252.0517, found m/e 252.0510, m/e : 254 (M⁺ + 2, 4%), 252 (M⁺, 12%), 215 (40), 179 (40), 178 (46), 163 (10), 161 (30), 91 (100), 89 (18), 77 (20), 76 (20), 75 (16), 51 (25).

1,1-Difluoro-1-phenyl-2-(4-methoxyphenyl)ethane (VIIb): 95% of an oil, purification by preparative TLC 1 : 9, yield 83% of an yellow oil. NMR data: δF -105.0 (t) p.p.m., δH 3.3 (t), δOCH_3 3.7 (s) p.p.m., δ arom. 7.2 (m), $J_{FH} = 16.5$ Hz. Mass spectrum: calculated for $C_{15}H_{14}F_2O$ m/e 248.1008, found m/e 248.1008, m/e : 248 (100), 209 (46), 197 (40), 165 (46), 139 (40), 127 (46), 121 (60), 77 (40).

1-Phenyl-2,2-difluorocyclopentane (IXa): 91% of greasy product, purified by preparative TLC (silicagel, cyclohexane-chloroform 4 : 1), yield 80% of an yellow oil. NMR data: δF -101.3 (m), δ arom. 7.3 (m), δH 2 (m). Mass spectra: calculated for $C_{11}H_{12}F_2$ m/e 182.0902, found m/e 182.0911, m/e : 182 (M⁺, 3%), 155 (14), 154 (100), 153 (33), 152 (21), 117 (47), 115 (50), 77 (10), 76 (17).

1-Phenyl-2,2-difluorocyclohexane (IXb): 85% of greasy product, purified by preparative TLC, 73% of an yellow oil), NMR data: δF -103.5 (m), δ arom. 7.5 (m), δH 1.7 (m). Mass spectra: calculated for $C_{12}H_{14}F_2$ m/e 196.0125, found m/e 196.1060, m/e : 196 (M⁺, 35%), 176 (9), 173 (9), 158 (14), 154 (55), 153 (21), 152 (13), 130 (22), 129 (17), 128 (30), 127 (100), 117 (37), 104 (30), 91 (33), 77 (38), 69 (48), 68 (55), 58 (34).

2-Exo-7-syn-Difluoronorbornane (XI): 69% of crystalline product, purified by preparative GLC (Chromosorb Regular 100, 10% DDP, $T = 120^\circ C$), yield 56% of volatile waxy crystals, m.p.

(sealed capillary) 116–119°C (lit.²¹ 95–97°C), NMR data: δ_{F-2} – 179.5 (dm), δ_{F-7} – 223.5 (dm) δ_{H-2} 5.1 (dd), δ_{H-7} = 5.21 (d), $J_{F-2,H-2}$ = 60 Hz, J_{F-2} = 40 Hz, $J_{F-7,H-7}$ = 63 Hz, $J_{F-7,H}$ = 12.6 Hz. Mass spectra: calculated for $C_7H_{10}F_2$ m/e 132.0750, found m/e 132.0752. For $C_7H_{10}F_2$ (132:1) calculated: 63.60% C, 7.63% H; found: 63.32% C, 7.40% H.

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