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A mild method for introducing iodine monofluoride into alkenes and iodination of aromatics using xenon difluoride ¹

Dale F. Shellhamer *, Brian C. Jones, Benjamin J. Pettus, Tobiah L. Pettus, Joy Merry Stringer, Victor L. Heasley

Department of Chemistry, Point Loma Nazarene College, San Diego, CA 92106, USA

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Abstract

Reaction of xenon diffuoride (XeF₂) and iodine (I₂) or *N*-iodosuccinimide (NIS) with alkenes gives iodofluoro products in good yields. Aromatics react with XeF₂ and I₂ or NIS to undergo electrophilic aromatic iodination. Iodine monofluoride (IF) generated from XeF₂ is less reactive than IF generated from I₂ and fluorine gas. This difference in reactivity suggests that the interhalogen IF is delivered to the alkene or aromatic from a complex with XeF₂. \bigcirc 1998 Elsevier Science S.A. All rights reserved.

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1. Introduction

The importance of monofluorinated molecules and their biological significance has been reviewed [1-3]. Halofluorination of alkenes is one of the useful synthetic methods to incorporate a fluorine atom into an organic molecule [4]. Methods to generate iodine monofluoride (IF) include reaction of *N*-iodosuccinimide (NIS) or iodine (I₂) with hydrogen fluoride pyridine in tetramethylene sulfone as solvent [5], triethylamine trihydrofluoride with NIS in methylene chloride or diethyl ether [6], ammonium hydrogen fluoride and aluminum fluoride with NIS under sonication [7], tetrabutylphosphonium dihydrogentrifluoride with NIS, iodine and silver fluoride [8], direct reaction of elemental fluorine with iodine at low temperature [9], potassium fluoride-poly (hydrogen fluoride) salts with NIS [10], or reaction of iodine trifluoride with iodine [11].

Chambers et al. [12], Rozen and Zamir [13], and Rozen et al. [14] generated IF and BrF from elemental fluorine. These interhalogens react with aromatics to give electrophilic aromatic iodination and bromination.

In an earlier study, we reported that xenon diffuoride (XeF_2) reacts with alkylhypochlorites and alkylhypobromites to generate chlorine monofluouride [15] and bromine

* Corresponding author.

monofluoride (unpublished results). In that paper, we proposed a complex between the alkylhypochlorite and XeF_2 to account for the minor products from reaction of *t*-butylhypochlorite, XeF_2 and cyclohexene [15]. We concluded that this method was not suitable for generation of iodine monofluoride since only *t*-butylhypoidite has been reported and it is sensitive to light and moisture [16,17]. In this paper, we report on the mild reaction of XeF_2 with I_2 or NIS to generate IF in situ.

2. Results and discussion

We treated iodine monochloride with several alkenes (Table 1) and aromatics (Table 2) to demonstrate the synthetic utility of this reaction. Reactions are easy to accomplish and give high yields. Products were identified by comparison of their GC–MS data from independents synthesis [5]. commercial samples, or from comparison with spectral data in the literature [8,10].

We suspect that a complex (1) is involved in the reaction of XeF₂ and I₂ or NIS which delivers the elements of fluorine and iodine to the alkene. Support for a complex include:

$$XeF_2 + \frac{1}{2}(NIS) \iff \left[XeF_2 \cdot \frac{1}{2}(NIS)\right] \longrightarrow (1 + Xe)$$
complex

(a) Products are not formed with polar solvents like acetonitrile. Apparently, the equilibrium does not favor the com-

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Table 1 Iodofluorination of alkenes Alkene + $XeF_2 + I_2(NIS) \rightarrow IF$ Products

Run	Alkene ^a	Iodine source "	Solvent ^b	Yield ^c	
1	cyclohexene		CH ₂ Cl ₂ (1.0 ml)	10	
2	cyclohexene	1.	CH ₂ Cl ₂ (0.5 ml)	75	
3	cyclohexene	\mathbf{l}_2	CH ₂ Cl ₂ (0.25 ml)	90	
4	cyclohexene	NIS	CH_2Cl_2	55	
5	cyclohexene	l ₂	$n-C_6H_{14}$	70	
6	l-hexene	I ₂	CH_2Cl_2	853	
7	l-hexene	I,	$n - C_6 H_{14}$	65 ^d	
8	3-hexene	12	CH_2Cl_2	85	
9	3-hexene	1,	$n-C_6H_{14}$	65	
10	styrene	12	CH_2Cl_2	50	
11	styrene	l ₂	$n-C_6H_{14}$	40	
12	3-hexyne	I ₂	CH_2Cl_2	50	
13	3-hexyne	I ₂	$n - C_6 H_{14}$	5	

^a Alkene and I₂ (NIS) 0.166 mmol. XeF₂ 0.083 mmol.

^b Solvent 0.25 ml unless noted.

 $^{\rm c}$ Yield by GC with chlorobenzene as internal standard corrected for flame response and XeF₂ as limiting reagent. Average of at least two runs.

^d Regioisomers 2-fluoro-1-iodohexane:1-fluoro-2-iodohexane ratio 87:13 by GC analysis.

plex in very polar solvents. Generally, as a result of low solubility, non polar solvents are not a good medium for XeF_2 reactions. However, in this case, yields are acceptable even in hexane as solvent (Table 1, Runs 5, 7, 9, 11).

(b) The yield of iodofluorination products increases as the concentration increases (Table 1, Runs 1, 2, 3). Apparently, dilute solutions do not favor the complex.

(c) Solid iodine must be added to a solution of the alkene and XeF_2 ; or solid XeF_2 must be added to a solution of I_2 and alkene. Products are not formed when both I_2 and XeF_2 are added in solution. This observation suggests the complex is formed when the iodine source in solution helps to dissolve the solid XeF_2 , or the solubilized XeF_2 helps to dissolve solid I_2 or NIS.

Table 2		
Iodination of aromatics Aromatic + Xel	$F_2 + I_2(NIS) \rightarrow Aromatic I$	odide

(d) Aromatics like benzene react with XeF₂ and I₂ or NIS to give iodobenzene (Table 2, Runs 1, 2, 3). Iodobenzene is less reactive and *p*-diiodobenzene is produced from iodobenzene and XeF₂ with I₂ but not NIS (Table 2, Runs 5, 6, 7). Reaction of anisole with XeF₂ and I₂ or NIS gives *p*-iodoanisole (Table 2, Runs 8, 9, 10). However, free (uncomplexed) IF generated from I₂ and fluorine gas reacts with benzene to give mostly diiodobenzenes (Table 2, Run 4), and with anisole to give only tars (Table 2, Run 11) [13,14] (see Scheme 1).

Iodine monofluoride generated from XeF_2 as the source of fluorine displays different characteristics in reactivity from IF generated from molecular fluorine and I_2 and is demonstrated in Scheme 1 for benzene and anisole. We suggest that this difference in reactivity is best explained by formation of a complex (1) with XeF₂ and I_2 or NIS.

3. Experimental details

Xenon difluoride was purchased from PCR. The remaining chemicals were obtained from the Aldrich Chemical Company. Solvents were dried over sieves and the alkenes were distilled prior to use. NMR data were obtained on a Varian Unity 300 (University of San Diego) in CDCl₃ and are relative to Me₄Si or CFCl₃. Mass spectral analyses were obtained at 70 eV on a Hewlett-Packard 5890 GC interfaced with an HP 5970B mass selective detector. Gas chromatography analysis was accomplished on an HP 5890 (FID detector) interfaced to a 3396 integrator. The GC and GC-MS analyses were done with a 25-m Hewlett-Packard ultraperformance column of internal diameter 0.20 mm with a methyl silicone stationary phase of 0.33 µm film thickness. Initial temperature of 50°C for 2 min, then ramp at 10°C/min to 200°C. All products were identified by comparison of their GC-MS data from independent synthesis [5], commercial

Run	Alkene ^a	lodine source ^a	Solvent ⁺	Yield [°]
l	benzene	I,	CH ₂ Cl ₂	iodobenzene (90)
2	benzene	L	$n - C_6 H_{14}$	iodobenzene (50)
3	benzene	NIS	CH_2Cl_2	iodobenzene (10)
4	benzene	$I_2 + F_2^{-d}$	CFCl ₃ /CHCL ₃	iodobenzene (30) ^{-d} , o -diodobenzene (30), p-diodobenzene (40)
5	iodobenzene	L.	CH ₃ Cl ₂	<i>p</i> -diodobenzene (60)
6	iodobenzene	L.	$n - C_6 H_{14}$	<i>p</i> -diodobenzene (30)
7	iodobenzene	NIS	CH ₂ Cl ₂	no reaction
8	anisole	$\mathbf{I}_{\mathcal{F}}$	CH ₂ Cl ₂	<i>p</i> -iodoanisole (40)
9	anisole	L	$n-C_6H_{14}$	<i>p</i> -iodoanisole (10)
10	anisole	NIS	CH_2CI_2	<i>p</i> -iodoanisole (95)
11	anisole	$I_2 + F_2$ °	CFCl,	tar () "

^a Aromatic 0.199 mmol; XeF₂ 0.083 mmol; I₂ or NIS 0.183 mmol.

^c Yield by GC with chlorobenzene as internal standard corrected for flame response and XeF₂ as limiting reagent. Average of at least two runs,

^d Ref. [13].

^e Reaction run at - 78°C. From Ref. [14].

^b Solvent 0.25 ml.



samples, or from comparison with spectral data in the literature [8,10]. The following procedure is representative for alkenes and aromatics. To a dry polyethylene bottle with a magnetic stirring bar was added 0.25 ml solvent, followed by 14.0 mg (0.083 mmol) XeF₂ and 0.199 mmol alkene or aromatic compound. The mixture was stirred at room temperature and then solid 0.183 mmol NIS (41.2 mg) or I₂ (46.4 mg) was added. After 1.5 h, 20 μ l of 1.0 M chlorobenzene in carbon tetrachloride was added as internal standard followed by 5% aqueous sodium bicarbonate. The organic layer was removed and the aqueous phase extracted two more times with methylene chloride. The combined organic layers were dried over anhydrous magnesium sulfate. Yields and product distributions were obtained by GC analysis with the peak areas corrected for flame response. Products were confirmed by comparison of GC–MS data with commercial products or products from independent synthesis [5,8,10].

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