Reaction of Xenon Difluoride with Indene in Aqueous 1,2-Dimethoxyethane and Tetrahydrofuran[1]

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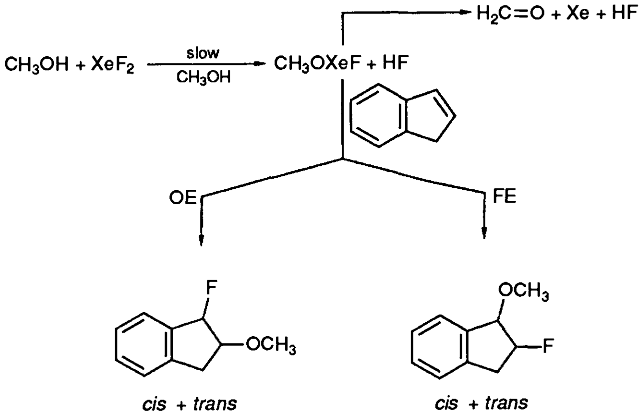
Xenon difluoride (XeF_2) reacts with indene in 1,2-dimethoxyethane–water (90:10) to give *cis*- and *trans*-2-fluoro-1-hydroxyindans. Our data indicate that neither xenon oxide (XeO) nor hydroxyxenon fluoride (HOXeF) is an intermediate in this reaction even though XeO is a suspected intermediate from aqueous hydrolysis of XeF_2.

Recently we reported on the reaction of XeF_2 with alkenes in alcohol solvents.[2] Our data suggest that XeF_2 reacts with alcohols to form alkoxyxenon fluoride intermediates. These intermediates can react with alkenes as apparent fluorine electrophiles (FE) or as positive oxygen electrophiles (OE). The preferred pathway (FE *vs.* OE) depends on the catalyst and the alcohol utilized for the reaction.[2] This sequence is summarized in Scheme 1 for reaction of XeF_2 with indene in methanol as solvent.



Scheme 1

By analogy with alcohols, we hypothesized that XeF_2 might react with water to form an intermediate, hydroxyxenon fluoride (HOXeF). In fact, HOXeF may be the intermediate or the precursor to xenon oxide (XeO), which has been proposed as the intermediate for aqueous hydrolysis of XeF_2.[3,4] An intermediate such as HOXeF might react with alkenes, as does hypofluorous acid (HOF) which adds to give fluorohydrins *via* a positive oxygen electrophile pathway [eqn. (1)].[5a] Hypofluorous acid also reacts with aromatics to give phenols rather than fluoroaromatics [eqn. (2)].[5b]

In aprotic solvents, xenon difluoride can be induced to react with alkenes by an ionic[6] or radical[7] pathway. Electrophilic aromatic substitution with XeF_2 proceeds *via* radical cation intermediates.[6a]

Our goal in this study was to investigate the reaction of XeF_2 with indene in water and to determine the mechanism of product formation.

Results

XeF_2 reacts with indene in 1,2-dimethoxyethane–water (DME–H_2O, 90:10) or tetrahydrofuran–water (90:10) to give the fluorohydrins **1** and **2** [eqn. (3)], the fluorohydrin-derived ketones **3** and **5**, and several monofluoroindenes.† Product distributions are reported in Table 1. The isolated fluorohydrins **1** and **2** were found to oxidize to **3** with XeF_2 in DME–H_2O under the reaction conditions employed [eqn.(4)]. Apparently 1-hydroxyindan-2-one (**5**) was formed by hydrolysis of 2-fluoroindanone (**3**) under the reaction conditions since GLC analyses during the reaction showed that the concentrations of **1** and **2** decreased while that of **5** increased during the reaction sequence. The product ratios are given in Table 1.

Table 1 Product distributions (% by GLC) for XeF_2 + indene in DME–H_2O (90:10)

	Product			
Reaction time/min	**1**	**2**	**3**	**5**
15	32	—	—	68
30	30	6	5	59
45	20	5	3	72
60	15	—	—	85

Independent synthesis of the 1-fluoro-2-hydroxyindans **6** and **7** was accomplished with pyridine–hydrogen fluoride[8] and indene oxide [eqn. (5)].‡ GLC-MS analysis of the indene + XeF_2 reaction at various intervals during the reaction show that neither the 1-fluoro-2-hydroxyindans (**6** and **7**) nor the *trans*- or *cis*- 1,2-dihydroxyindans§ (**8** and **9**) were formed during the reactions. Control experiments show that the fluorohydrins **6** and **7** do not rearrange to **1** and **2** during the reaction of XeF_2 with indene in DME–H_2O.

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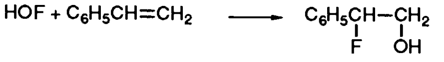
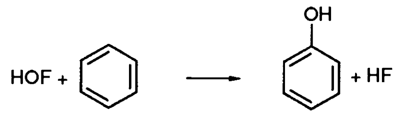
† There are five monofluoroindenes detected by gas chromatography-mass spectrometry (GLC-MS) in the reaction mixture. These products make up *ca.* 15% of the overall product mixture and they have the following retention times (min) and relative ratios (in parentheses): 15.8 (5.8); 16.4 (2.3); 16.5 (1.1); 16.6 (2.4) and 16.7 (1.0). Each compound has a parent ion at *m*/*z* 134. These minor components are isomers from aromatic substitution and from substitution on the five-membered ring of indene. No further attempt was made to isolate or identify these minor components.

‡ Indene oxide was prepared from indene and peracetic acid. M. Korach, D. R. Nielsen and W. H. Rideout, *J. Am. Chem. Soc.*, 1960, **82**, 4328.

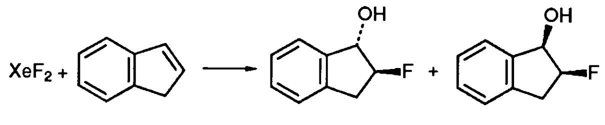
§ Compounds **8** and **9** were prepared according to the method of W. E. Rosen, L. Dorfman and M. P. Linfield, *J. Org. Chem.*, 1964, **29**, 1723.



$$HOF + C_6H_5CH{=}CH_2 \longrightarrow C_6H_5\underset{F}{C}H{-}\underset{OH}{C}H_2 \quad (1)$$

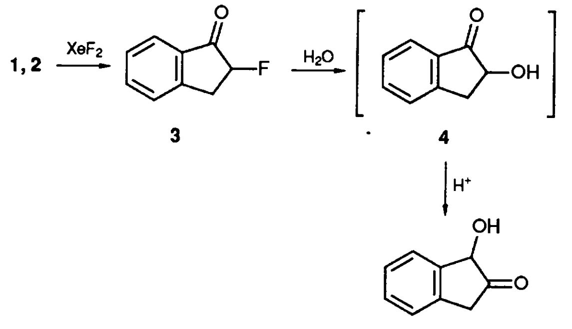


(2)



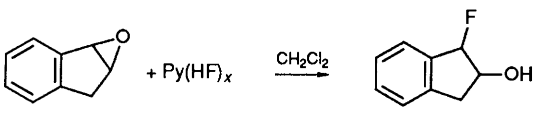
(3)

trans - **1** *cis* - **2**



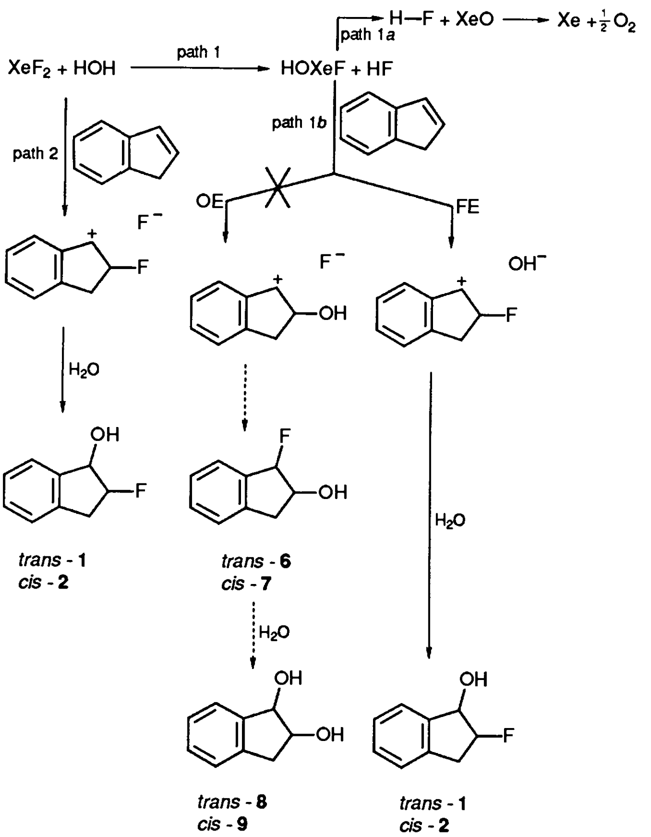
(4)

3 **4** **5**



(5)

trans - **6**
cis - **7**



Scheme 2

Discussion

Our previous experience with XeF_2 in alcohol solvents,[2] and the chemistry of HOF,[5] suggests that HOXeF should react with indene by an OE pathway (Scheme 2, path 1*b*). Control experiments showed that OE products (**6**–**9**) were not produced in the reaction of XeF_2 with indene in DME–H_2O. Thus the observed products **1** and **2** must be formed either by an FE pathway (path 1*b*) or by direct reaction of XeF_2 with indene (path 2).

The disappearance of XeF_2 was followed by titration with thiosulphate. We found that, in the absence of indene, only *ca.* 10% of the XeF_2 had reacted after 3 h in DME–H_2O. Addition of 1 equiv. of indene to this reaction mixture after 3 h caused the XeF_2 to react completely in *ca.* 2 h. Therefore, reaction of XeF_2 with water in DME–H_2O (90:10) is too slow (path 1, Scheme 2) to compete with the direct reaction of XeF_2 with indene (path 2).* This is in contrast to the reaction of XeF_2 with alcohols which is faster than direct reaction with alkenes such as indene.[2] Our evidence is contrary to the hypothesis that HOXeF is an intermediate in the aqueous hydroxyfluorinations of indene described here.

The reactions of XeF_2 with water in DME–H_2O, in the absence of alkene, was followed by xenon-129, fluorine-19, and oxygen-17 (^{17}O enriched water) NMR spectroscopy. Neither HOXeF nor XeO was stable enough to be detected by these methods.

Experimental

General Procedures and Instrumentation.—Xenon difluoride was purchased from PCR, Inc. The remaining chemicals and solvents were obtained from the Aldrich Chemical Company. Indene was distilled prior to use. ^1H NMR spectra were obtained on a Varian T60A (Point Loma Nazarene College) or a JEOL FX-90Q (Air Force Astronautics Laboratory). ^{19}F NMR data were obtained on the JEOL FX-90Q. Spectra are referenced relative to Me_4Si or $CFCl_3$. All J values are given in Hz. GLC-MS data were obtained on a Hewlett-Packard 5970B Mass Selective Detector (70 eV) interfaced to an HP5890 gas chromatograph. The column was a 25 m ultraperformance column of internal diameter 0.20 mm, with a methyl silicone stationary phase of 0.33 μm film thickness, which was operated under the following conditions: initial temperature 45 °C for 3.0 min; ramp rate 5 °C min^{-1} to 180 °C. Product ratios were obtained on an HP5890 gas chromatograph (flame ionization detector) with a similar methyl silicone capillary column and conditions. IR spectra were recorded on a Nicolet 710 Fourier Transform spectrometer.

Reaction of Indene with XeF_2 *in DME–Water.*—To indene (35 mg, 0.30 mmol) in DME–water (90:10; 0.45 cm^3) was added XeF_2 (25 mg, 0.15 mmol). The reaction was quenched with aqueous sodium hydrogen carbonate (5%), extracted with methylene dichloride, and dried ($MgSO_4$). Analysis by GLC gave products [retention time/min: **1** (20.7), **2** (21.7), **3** (22.5), and **5** (23.2)] with the distributions listed in Table 1 (yields 50–60%). Products **1**–**3** were isolated by column chromatography (silica gel) with hexane and diethyl ether–hexane as eluents. The following data were obtained:

1: ^1H NMR, 90 MHz ($CDCl_3$) δ 1.90–2.40 (m, 2 H), 3.12 (dd, J 31.7 and 3.1, 1 H), 5.21 (dm, J 50–55, 1 H) and 7.18–7.60 (m, 4 H); ^{19}F NMR ($CDCl_3$) δ −202; GLC-MS m/z (relative intensity) 152 (M^+, 100), 151 (51), 134 (16), 133 (17), 132 (49), 131 (50), 104 (99) and 103 (81).

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* The rate of hydrolysis of XeF_2 increases as the ratio of water to DME increases. Indene, however, is not soluble in aqueous DME of >20% water.

2: ^{1}H NMR, 90 MHz ($CDCl_3$) δ 1.80–2.20 (m, 2 H), 3.11 (dd, *J* 21.4 and 5.3, 1 H), 5.40 (dm, *J* 50–55, 1 H) and 7.20–7.60 (m, 4 H); ^{19}F NMR ($CDCl_3$) δ −186; GLC-MS *m*/*z* (relative intensity) 152 (M^+, 100), 151 (53), 134 (18), 133 (30), 132 (49), 131 (51), 104 (99) and 103 (80).

3: ^{1}H NMR, 90 MHz ($CDCl_3$) δ 2.90–3.90 (m, 2 H), 4.61 (dm, 1 H) and 7.10–7.60 (m, 4 H); ^{19}F NMR ($CDCl_3$) δ −194 (ddd, *J* 51, 22 and 9); GLC-MS *m*/*z* (relative intensity) 150 (M^+ 100), 131 (6), 130 (6), 122 (83), 121 (31), 104 (18), 102 (27), 101 (35), 76 (42) and 50 (32); IR (neat, KBr) ν/cm^{-1} 1730 and 1610 (lit.,[9] 1730 and 1610).

Independent Synthesis of 2-*Hydroxyindan*-1-*one* (**4**).—2-Hydroxyindan-1-one was prepared from 2-diazoindan-1-one as described in the literature.[10] Spectral data not found in the literature for **4** is as follows: ^{1}H NMR, 60 MHz (CCl_4) δ 2.97 (dd, *J* 16.0 and 5.2, 1 H), 3.20 (s, 1 H), 3.53 (dd, *J* 16.0 and 7.6, 1 H), 4.43 (dd, *J* 7.6 and 5.2, 1 H) and 7.20–7.90 (m, 4 H); *m*/*z* (relative intensity) 148 (M^+, 94), 147 (30), 120 (23), 119 (61), 91 (100), 89 (25), 65 (37), 63 (29), 39 (29) and 29 (13).

Oxidation of trans-1,2-*Dihydroxyindane* (**8**) *with* XeF_2.—*trans*-1,2-Dihydroxyindane† (**8**) was prepared from indene oxide* with pyridine–hydrogen fluoride.[8] To **8** (22.0 mg, 0.148 mmol) in DME–H_2O (90:10; 0.45 cm^3) was added XeF_2 (30.0 mg, 0.179 mmol). After 1 h at room temperature, aqueous sodium hydrogen carbonate (5%) was added. The mixture was extracted with methylene dichloride and dried ($MgSO_4$). GLC-MS analysis of the mixture gave **5** (retention time 23.3 min) and **4** (retention time 24.7 min). Compound **4** gave the same GLC-MS data as listed above. We were unable to isolate the less stable 1-hydroxyindan-2-one isomer. Its structure is based on the following GLC-MS data. Mass spectrum *m*/*z* (relative intensity) 148 (M^+, 5), 120 (82), 119 (61), 91 (100), 89 (17), 65 (43), 63 (22), 39 (30) and 29 (16).

Independent Synthesis of trans- *and* cis-1-*Fluoro*-2-*hydroxyindans* **6** *and* **7**.—To indene oxide (6.73 g, 0.0510 mol),* dry pyridine (61 cm^3), and dry chloroform (70 cm^3) in a polyethylene bottle, with stirring at 0 °C, was added dropwise pyridine–hydrogen fluoride (70 cm^3).[8] The mixture was stirred at room temperature for 16 h and then poured into water, extracted with $CHCl_3$, and dried ($MgSO_4$). The product mixture was distilled (75–80 °C/0.5 Torr) but polymerized when kept neat. The distilled products **6** and **7** were stable for several days in solution. The ^{1}H and ^{19}F NMR spectra were identical to those reported in the literature.[11] GLC-MS retention times of **6** and **7** are 20.6 and 22.2 min, respectively.

6: *m*/*z* (relative intensity) 152 (M^+ 45), 134 (5), 133 (12), 132 (17), 123 (57), 109 (43), 104 (100), 78 (31), 77 (35) and 51 (31).

7: 152 (M^+ 66), 134 (6), 133 (16), 132 (18), 123 (70), 109 (54), 104 (100), 78 (31), 77 (37) and 51 (33).

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*·† See footnotes page 401.