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On the Modes of Reaction of Xenon Difluoride with Organic Substrates: The Influence of Solvent and Vessel

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Xenon difluoride (XeF_2) is a stable, commercially available solid that is attracting increasing attention as an "electrophilic" fluorinating agent.[1] We wish to report that the choice of solvent and reaction vessel profoundly influences the mode of reaction of this reagent with organic substrates. Our own studies with XeF_2 have focused on reactions with trimethylsilyl derivatives:[2] this strategy avoids formation of hydrogen fluoride during reaction and has enabled us to demonstrate conditions for two discrete modes of reaction which we now describe.

Our work with divalent xenon is part of a comparative study of the chemistry of hypervalent derivatives of the Periodic Table triad Te, I, and Xe that is ultimately directed to the application of novel reactions to biological problems.[2−4] In this context XeF_2 provides access to fluoro derivatives of biological interest and to methods for the rapid introduction of the isotope ^{18}F ($t_{1/2}$ 110 min) into biological ligands for positron emission tomography (PET).[5] We are particularly interested in (i) how the nonbonding molecular orbitals of the hypervalent three-center, four-electron [3c-4e] bonds in these species (Te^{IV}, I^{III}, and Xe^{II}) influence their mode of reaction and (ii) the ability of these reagents to function first as electrophiles (e.g. An_2Te^+OH, PhI^+OAc, or Xe^+F) and subsequently as exceptionally good leaving groups (i.e. An_2Te, PhI, or Xe).[6] These considerations led us to predict and demonstrate the fluorodesilylation of aryltrimethylsilanes (**4** → **6**) (Scheme 1) using xenon difluoride.[2a]

We have previously shown that the XeF_2-mediated fluorodesilylation of aryltrimethylsilanes (**4** → **6**) occurs in CH_2Cl_2, $CHCl_3$, $CFCl_3$, or C_6F_6 solution and observed that no reaction takes place in CH_3CN solution.[2a] In another study we showed that trimethylsilyl benzoates **7** react with XeF_2 in CH_2Cl_2 or C_6F_6 to give rearranged aryl fluoroformates **8** whereas in CH_3CN the products are derived from aryl radicals **2**.[2b] These results prompted us to make further studies of the influence of solvent on XeF_2 reactions. It has previously been shown that XeF_2 is moderately stable in CH_2Cl_2 and $CHCl_3$ and more stable in CH_3CN.[7,8] We have confirmed that the ^{19}F NMR spectra of XeF_2 in CH_2Cl_2, $CHCl_3$, C_6F_6, CH_3CN, and CH_3CN/D_2O solution with fluorinated ethylene propylene (FEP) liners show that the solute is stable over hours and the characteristic "triplet", made up of a singlet (δ_F −179) plus a ^{129}Xe doublet (*J* 5642 Hz), confirms that it is un-ionized (i.e. F−Xe−F). In contrast, when we attempted the determination of the ^{19}F spectra in glass NMR tubes very rapid decomposition occurred and no signals due to un-ionized XeF_2 could be detected with the important exception of CH_3CN solution in which the un-ionized XeF_2 is quite stable and shows a clean ^{19}F spectrum.[8] Clearly, the glass surface catalyzes the rapid decomposition of XeF_2 and we presume that the weakly basic solvent CH_3CN effectively neutralizes the acidic surface of the glass.

All our previous studies[2] have been carried out in glass vessels. We therefore investigated the fluorodesilylation of *p*-tolyltrimethylsilane (**4**, R = Me) under identical conditions but in an FEP flask and found that no reaction took place. We repeated the reaction in a dry glass flask that had been prewashed with alkali (NaOH) and again no reaction was observed. It is clear that the acidic surface of the glass is necessary for the fluorodesilylation reaction (**4** → **6**), presumably to generate the electrophile FXe^+. When this cannot occur, i.e., in FEP, alkali washed glass, or CH_3CN solution, the XeF_2 remains un-ionized and does not react as an electrophile.

The reaction conditions upon which two distinct modes of reaction of XeF_2 with organic substrates critically depend can now be recognized. Under protic conditions ionization occurs and the reacting species is the electrophilic fluoroxenonium cation (FXe^+), which in the case of fluorodesilylation (**4** → **6**) leads to the observed product by a mechanism that we have discussed previously.[2,6] The ligand coupling of the xenon intermediate (**5** → **6**) probably occurs via homolytic cleavage of the carbon−xenon bond and subsequent in-cage coupling to fluorine in accord with the principles recently described by Frohn and Bardin.[9] Some escape of the aryl radical then satisfactorily accounts for the minor radical derived products that we observed.[2a] This contrasts with the observation of Bardin and co-workers,[10] who reported that in CH_3CN together with a trace of fluoride catalyst (CsF) the products are hydrocarbons (e.g. **1**) formed via the aryl radicals **2**. They rationalize the formation of these radicals in terms of a one-electron oxidation of an intermediate anion **3**.[10] This mechanism is entirely consistent with the presence of only un-ionized XeF_2 under their conditions. Similarly, we now recognize that reaction of trimethylsilyl benzoates **7** with ionized XeF_2 leads to the rearranged products **8** whereas un-ionized XeF_2 acts as a one-electron oxidizing agent giving radical-derived products (e.g. **1**).[2b]

On the basis of the mechanistic studies described above we anticipated that if reaction of XeF_2 with trimethylsilyl enol ethers[11a] occurs via a SET mechanism then MeCN/glass would provide convenient and optimal reaction conditions. To test this hypothesis 1-((trimethylsilyl)oxy)cyclohexene (**10**) was reacted with XeF_2 under these conditions and this did indeed result in a very clean and quantitative transformation to 2-fluorocyclohexanone (**9**). Subsequently we have studied a series of trimethylsilyl enol ethers and obtained similar results: details of the scope of this convenient α-fluorination procedure together with further evidence for a SET mechanism occurring via a radical cation (Scheme 2) will be published elsewhere.[11b] In contrast, use of C_6F_6 as solvent in a glass flask results in a much more complex reaction and the composition of the product mixture is dependent upon reaction time and workup conditions. In addition to compound **9**, probably formed via electrophilic addition of FXe^+ to the enol ether, cyclohexanone (**11**) and rearrangement products including ϵ-caprolactone (**12**) are formed (Scheme 1). Rearrangement to oxepane derivatives is characteristic of electron-deficient intermediates[2b,12] and probably occurs by a mechanism of the type shown in Scheme 3.

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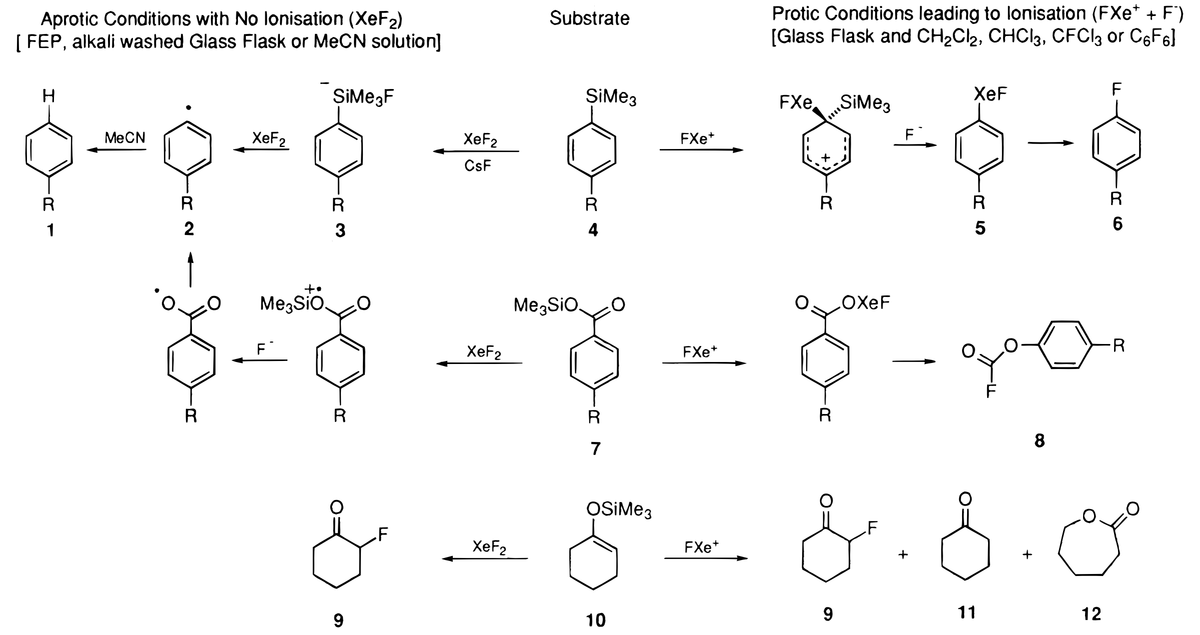
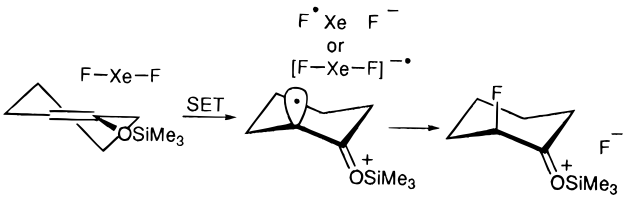
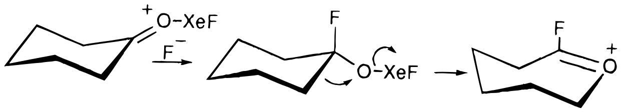
Scheme 1



Scheme 2



Scheme 3



The reaction of XeF_2 as either a one-electron oxidant (XeF_2) or an electrophile (FXe^+) has been discussed,[1,13–15] and it is well-known that HF catalyzes the latter mode of reaction. However, the influence of solvent and flask has not previously been recognized. Reutov and co-workers[16] have suggested that trace amounts of "active electrophilic fluorinated silicon derivatives" catalyze the fluorination of cyclophanes: Shellhamer and co-workers[17] have suggested that "adventitious HF" formation occurs as a result of traces of "moisture on the surface of solid XeF_2". We now believe that in both these cases acidic protons associated with the glass flasks catalyze the reactions. In a recent review Tius[1] makes the following introductory statement: "Most reactions with XeF_2 can be conducted in glass apparatus with no apparent diminution in yield." This view must now be modified: the choice of flask and solvent is critical but has received little attention. We have analyzed the primary literature for 54 discrete types of reaction reviewed by Tius.[1] For this reaction set the types of vessel used were as follows: FEP or similar flask (7), glass flask (12); both FEP and glass (3); metal containers (2); and nature of the flask not specified (30). The choice of solvent [CH_2Cl_2 (57%), $CHCl_3$ (2%), CH_3CN (5%), C_6F_6 (2%), other solvents or mixtures (34%)] was also variable and there was no systematic selection or correlation with the choice of vessel.

Finally, to exploit the catalytic effect of glass, we have investigated a series of ten XeF_2 reactions that have been described as requiring HF catalysis.[1,12] Our preliminary studies now show that when these reactions are carried out in dry CH_2Cl_2 solution in a glass flask the formation of the relevant products does occur without the need for addition of HF. This is a much more convenient procedure for performing electrophilic reactions of XeF_2 and should encourage wider usage of this reagent.

In summary, we have described the previously unrecognized influence of solvent and vessel on the mode and quality of reaction of XeF_2 and have demonstrated examples of how an understanding of this influence leads to improved synthetic procedures for both the one-electron oxidation (e.g. α-fluorination) and electrophilic addition (e.g. glass catalysis) modes.

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